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FOSTERING DIFFUSION OF SCIENTIFIC CONTENTS OF NATIONAL SOCIETY CARDIOVASCULAR JOURNALS: THE NEW ESC SEARCH ENGINE

Fernando Alfonso[1,2], Lino Gonçalves[3], Fausto Pinto[1] (Editor-in-Chief, Revista Portuguesa de Cardiologia), Adam Timmis[1] (Editor-in-Chief, Heart), Hugo Ector[1] (Editor-in-Chief, Acta Cardiologica), Giuseppe Ambrosio[1], Panos Vardas[1] (Editor-in-Chief, Hellenic Journal of Cardiology) On behalf of the Editors' Network European Society of Cardiology Task Force.

European Society of Cardiology (ESC) National Society Cardiovascular Journals (NSCJs) are high-quality biomedical journals focused on cardiovascular diseases. The Editors´ Network of the ESC devises editorial initiatives aimed at improving the scientific quality and diffusion of NSCJ. In this article we will discuss on the importance of the Internet, electronic editions and open access strategies on scientific publishing. Finally, we will propose a new editorial initiative based on a novel electronic tool on the ESC web-page that may further help to increase the dissemination of contents and visibility of NSCJs.

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This is a joint simultaneous publication initiative involving all interested National Society Cardiovascular Journals of the European Society of Cardiology

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СОДЕЙСТВИЕ РАСПРОСТРАНЕНИЮ НАУЧНОГО СОДЕРЖАНИЯ КАРДИОВАСКУЛЯРНЫХ ЖУРНАЛОВ НАЦИОНАЛЬНЫХ ОБЩЕСТВ: НОВЫЙ ESC ПОИСКОВИК

Fernando Alfonso[1,2], Lino Gonçalves[3], Fausto Pinto[1] (Главный Редактор, Portuguesa de Cardiologia), Adam Timmis[1] (Главный Редактор, Heart), Hugo Ector[1] (Главный Редактор, Acta Cardiologica), Giuseppe Ambrosio[1], Panos Vardas[1] (Главный Редактор, Hellenic Journal of Cardiology) По поручению группы Клуба редакторов Европейского Общества Кардиологов.

Кардиоваскулярные журналы национальных обществ (NSCJs), входящих в Европейское Общество Кардиологов (ESC) являются биомедицинскими журналами по кардиоваскулярной тематике, ориентированными на высокое качество. Клуб редакторов ESC разрабатывает инициативы редакций, направленные на улучшение научного качества и распространение NSCJ. В этой статье мы поговорим о важности Интернета, электронных изданий и стратегии открытого доступа к научным публикациям. Наконец, мы предлагаем новые инициативы редакций, основанные на новейшем электронном инструменте на web-странице ESC, который может способствовать увеличению распространения содержания и доступность NSCJs.

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The National Society Cardiovascular Journals (NSCJs) of the European Society of Cardiology (ESC) are high-quality biomedical journals devoted to publishing original research and educative material on cardiovascular diseases [1–3]. These journals officially belong to the corresponding ESC National Cardiac Societies. Many of them have achieved major international recognition, are included in most important bibliometric databases, and have made major scientific impact [1–5]. Some NSCJs offer full-text English content and are freely available in electronic editions. However, NSCJs are largely heterogeneous and some of them are only published in local languages with a limited visibility [1–3].

The main goal of biomedical journals is to publish high-quality scientific information. To achieve this goal, journals should compete for the best research carried out in their field, the "prestige" of the journal being the main driver to attract original contributions [1–3]. In turn, a journal's prestige is based on credibility, diffusion and scientific impact [6]. To ensure that the scientific process is fully respected, journals rely in the "peer review" system. This process not only allows the editors to select the best possible material for publication, but also assures the readers that the quality of the information follows the highest scientific standards. In fact, the process significantly improves the final quality of manuscripts eventually published. Once an article is definitely accepted for publication, the journal should guarantee its expedited publication and widespread diffusion among the scientific community [1–3].

The Editors' Network of the ESC provides a unique platform for devising editorial initiatives aimed to improve the scientific quality, and facilitate diffusion of the contents of NSCJs [1–5]. Herein we will discuss the importance of the internet and electronic editions in scientific publishing.

We will also review the growing relevance of open access (OA) strategies. Last but not least, we will propose a new initiative based on a novel electronic tool that may further help to increase the diffusion, dissemination and overall visibility of NSCJs. This tool, located on the ESC website, should foster collaboration among the different NSCJs and also broaden exposure from diverse scientific sites and ESC official journals. Hopefully, this will help to further expand the scientific impact of European cardiovascular research.

Electronic editions and the internet: a paradigm shift in scientific publishing

Sharing the results of late breaking research through peer-reviewed journals remains the mainstay of the scientific process and progress in science [1–3]. The success of research requires articles to be read, spread, discussed and cited by interested investigators. Therefore, in the fast moving and globalised world of science, journals should ensure maximal accessibility and diffusion of their articles.1–3 Indeed, most publications have already moved into a new 'online era' where the emphasis is placed on the internet and electronic editions [1–3]. Just a few years ago, scholars did all their reading in paper journal issues obtained as personal copies circulating within their organisations, or by retrieving issues from library archives [7]. Today the predominant reading mode is to download a digital copy and either read it directly on the screen or as a printout [7]. Currently, readers and investigators readily retrieve articles with just a click on their home or office computers [7].

Interestingly, the internet not only affects research but also clinical practice. Nowadays, physicians are often approached and challenged by patients who have downloaded medical information from the internet. Often they face either unnecessarily worried patients or patients with unrealistic expectations. Although some patients are confused, others are overinformed and demand in-depth explanations regarding their diagnosis, management and prognosis. Patient-oriented information should be provided by scientific societies to address these demands. Therefore, even everyday clinical practice should accommodate the socio-cultural change induced by the internet.

Access to medical information has been revolutionised by electronic editions. Likewise, bibliometric databases are also evolving. Medline, the ISI Web of Science and, more recently, Scopus offer comprehensive online information on medical literature [8–11]. In addition, Google Scholar is increasingly used by many investigators [8–11]. Scopus and, especially, Google Scholar obtain data from larger data sources including widely diverse scientific items (not only ISI publications) and therefore offer a slightly different perspective on the field. Interestingly, Google Scholar is free, and various studies suggest that it provides accurate search and data analyses that differ little from those obtained from classical bibliometric sources [8–11].

Traditionally, the most commonly used source of bibliometric data is the Thomson ISI Web of Knowledge, in particular the Science Citation Index and the Journal Citation Reports, which provide the yearly journal Impact Factors. Recently, other indicators such as SCImago scientific journal rank (SJR) and the Eigenfactor have emerged as alternative indices of a journal's quality [8–11]. These consider not only the number but also the "quality" or relevance of the citations received by a given paper. Quantitative publication metrics (research output) and citation analyses (scientific influence) are key determinants of the scientific success of individual investigators and institutions because the "publish or perish" dictum still prevails in most academic settings [8–11]. In this scenario, electronic editions and accessibility on the internet certainly play a critical role. Nowadays, once a paper is electronically published on a journal website, the information can propagate rapidly in the community, and extremely high downloads could be the result of mechanisms such as the "Matthew effect" (richer get richer) [12]. Indeed, the relationship between the number of citations acquired by an article and the number of downloads has been explored [13]. Hit counts on a journal website for an article during the week after its online publication predict the number of citations of that article in subsequent years [14]. Of note, Uniform Resource Locators (URLs) are being increasingly used in scientific publications [15] Citation of URLs provides the possibility of calculating an objective electronic Impact Factor (eIF) to measure their impact on scientific research [15]. However, the stability of URLs remains a matter of concern, and this should be guaranteed by the responsible organisation because URLs are vulnerable to technical problems and may become inaccessible in a time-dependent manner [15].

Notably, the internet offers a new window into science and provides new insights on access and use of research [16]. Currently, web-usage data can be analysed in depth to outline a "map of knowledge". According to Butler [16], when readers click from one page to another while looking through online scientific journals, they generate a chain of connections between links they think belong together. These "click- stream events" may be analysed to map such connections and to provide a snapshot of interconnections between disciplines. Usage maps reveal how often users looking at an article in journal A moved on to an article in journal B during a browser session. By aggregating all these complex relationships using network-visualisation algorithms, maps can be generated based on the "distances" between journals and disciplines [16]. The structure of these maps is quite similar to those created using citation data: a network of clusters in different fields within which journals have strong connections with one another but fewer links to other clusters. Interestingly, journals in the humanities and social sciences figure much more prominently in these maps than in citation-based maps [16]. Another key difference between citation- and usage-based maps is that the former only reflect citations by researchers who publish, and ignore the impact of papers on the medical community who read

and apply the literature in medical practice but who rarely publish. Citation data may undervalue papers written in practitioner-based fields that are widely read but not cited proportionally [16]. Moreover, usage maps are more up-to-date than citation ones because of the inherent delay in publication, therefore providing a different time slice of the scientific process. Accordingly, both usage and citation data each provide complementary information on the impact of papers and journals on the scientific community [16].

Electronic editions provide unique publishing possibilities and open up new venues in scientific communication [1–3]. For instance, they offer a flexible layout and structure for articles, new formats and the possibility of including additional documentation attached to the paper as media enhancements (videos, etc). Important sections such as methods and additional data can be now presented as supplementary material without additional cost. Electronic managing systems facilitate both the processes of peer review and publishing [1–3]. Open peer review and even post-publication readers» comments can be uploaded on the journal website, facilitating interactivity and a more transparent and dynamic scientific process. Finally, statistics on electronic papers (downloads and citation metrics) are offered for the interest of readers and researchers [17].

Publicly available data are advocated as a means to further promote transparency in research and more open science [18–20]. Online editions allow the publication of longer papers free from the economic burden of print charges. Posting the complete anonymised "raw dataset" has been advocated in this regard [18–20]. The raw data can be used to confirm original results by independent analyses and also to explore related or new hypotheses, particularly when combined with other publicly available datasets. From an ethical perspective, it appears unacceptable that, while patients are willing to share data about themselves with investigators and sponsors, the latter may be unwilling to share the trial data with others. Data sharing among genomic investigators has already been successful. However, this strategy may cause concerns such as inappropriate analyses, "data dredging" and drawing inappropriate conclusions [18–20]. The International Committee of Medical Journal Editors has developed guidelines for the preparation of raw clinical data for publication [18]. Interestingly, this practice has been associated with a 69% increase in citations, independently of journal Impact Factor, date of publication and author country of origin [20]. The correlation between publicly available data and increased literature impact may further motivate investigators to share their detailed research data.

On the other hand, Web 2.0 has also been increasingly used in the medical field [21–25]. RSS feeds, podcasts, personal publishing platforms (blogs), social networks (such as Twitter and Facebook) and social media are proposed as innovative tools for educating and updating clinicians. They allow physicians to distribute, share and comment on medical information [21–25]. However, the scientific community is less than eager to regard them as equivalent to the traditional models of information dissemination in peer-reviewed medical journals. In this regard, some have proposed that platforms of post-publication peer review may provide the required safeguard in this new setting [22]. In addition, intuitive browsing of journal content on smart- phones and the iPad is being provided by a growing number of publications (including the European Heart Journal) [24, 25] to enhance diffusion of contents [21]. Furthermore, some Web 2.0 technologies facilitate collaborative data collection for clinical trials [23] Google Docs, for instance, is freely available and allows multiple users to enter patient data into electronic case report forms of multicentre trials through mobile devices [23].

Finally, we should keep in mind that English represents the "lingua franca" of science. This is important, and efforts should be made within the ESC to prevent tower-of-Babel phenomena in the digital era [1–3]. However, this may create major problems and unique challenges for non-English-speaking investigators and countries.26 In fact, some NSCJs only publish in their mother tongue and are therefore not readily accessible to the international scientific community. Some NSCJs have decided to publish their articles in both their native language and English, to address healthcare professionals and international scholars, respectively. Difficult concepts are easier to remember in the mother tongue. Interestingly, Public Library of Science journals encourage non-English-speaking authors to provide a version of their article in their original language as supporting material [27]. Science should not be considered an "ivory tower" separated from the rest of society, but rather imbedded in it to facilitate its cultural assimilation [27].

Some editorial perspectives on "open access" initiatives

The internet and electronic editions set the basis for OA initiatives [28, 29]. The two main characteristics of OA publications are: (1) all published contents are freely accessible through the internet; (2) readers are given copyright permission as long as authors and publishers receive adequate attribution [28]. In turn, this model requires two major changes from the traditional subscription-based model. First, OA shifts the financing of publication from readers (subscription fees from individuals or universities) to authors and investigators (through the corresponding funding organisation or academic institutions) by means of article-processing fees [28]. Second, the copyright is no longer used to prevent, but rather to stimulate, republication. Subscription-based journals usually require authors to transfer the copyright to the journal so that they are empowered to restrict access to paying customers and threaten competing publications with infringement lawsuits. Major subscription-based journals are partly financed by individuals and medical societies but mainly by bundled e-license agreements between publishers and universities

or librarians [28, 29]. Individual electronic articles can also be accessed on a pay-per-view basis. Readers are charged one way or the other in the traditional way, whereas authors and investigators are charged in the OA model [28, 29]. Some commercial publishers charge authors a publication fee to substitute for subscription revenue while significantly limiting reuse. These initiatives, however, should not be considered real OA. Some traditional publishers have recently instituted "hybrid" initiatives where authors are allowed (after paying a fee) to make individual articles OA [28, 29].

In the early 90s, pioneer OA journals were founded by individual investigators based on voluntary work and were usually hosted in individual or university servers [29]. Thereafter, many established journals made their articles OA when they implemented their digital editions in parallel with print editions. This was especially the case for official journals of medical societies and in non-English-speaking countries in an attempt to increase their readership and impact [30] In the last decade, new, formal, OA journals have flourished using article-processing charges to finance publications [29]. Interestingly, some major publishers (BioMed Central, Public Library of Science) have specialised in OA [29]. OA has two major pathways: "gold" OA (via direct publishing) and «green» OA (traditional publication in subscription-based journals with parallel open posting of the final manuscript on the web). Green OA is delivered by repositories, whereas gold OA is delivered by journals [31]. Licences range from any kind of reuse provided that proper attribution is made (CC-BY) to those that limit commercial use (CC-BY-NC) [31].

The health of the free-access author-pay model can be demonstrated by data showing the steady growth of papers published in OA journals (20% per year) and also in the number of OA journals (15% per year), either as new journals or traditional journals switching to this model [32]. Currently, 30% of all peer-review journals in the world are OA [31].

OA benefits science by accelerating dissemination and uptake of research findings. A major advantage of OA is that readers can use any web-based research tool to access and review the literature [28]. These articles are quickly recognised and their results are readily picked up and discussed by peers [33]. As already mentioned, there are two main modalities of OA: OA journals and self-archiving. Interestingly, some studies suggest that articles immediately published as OA on the journal site (gold route) have higher impact than self-archived or otherwise openly accessible OA articles (green route) [33].

Overall OA initiatives increase diffusion of content, citations and eventually the Impact Factor of the corresponding journals [33–35]. Early studies analysed the effect of "online status" on the Impact Factor of biomedical journals [36]. They found that providing online access with «full text on the net» increases the visibility of a journal [36]. In addition, the presence of journals on Medline as "full text on the net" also boosts their Impact Factor [37]. This bias is explained by the tendency to peruse what is more readily available [37]. OA initiatives also appear to increase the Impact Factor [33–35]. However, some argue that this effect may confound between open and electronic access. Nevertheless, recent reports suggest that, in most developed countries, journal articles receive an increase in citations when they come online freely, but experience an additional jump when they first come online through commercial sources [35]. This effect appears to be reversed in poor countries, where free-access articles are much more likely to be cited [35]. All together, these findings suggest that free internet access widens the circle of those who read and make use of scientific research. In addition, this "OA impact advantage" does not appear to be a "quality bias" from authors self- selecting what to make OA, because some studies suggest that this advance persists after adjustment for many other potential confounders related to the editorial and research quality [38].

Interestingly, a randomised trial on OA publishing analysed the effects of free access on article downloads and citations [39]. Articles placed in the OA condition received significantly more downloads and reached a broader audience within the first year. However, in this particular study, OA articles were cited no more frequently, nor earlier, than subscription-access articles within 3 years. It was suggested that the process of "social stratification", accounting for a concentration of scientific authors at a small number of elite research universities with excellent access to the scientific literature, might help to explain this apparent paradox [39]. Moreover, this controlled study suggests that the real beneficiaries of OA publishing may not be the research community but rather communities of medical practice that consume, but rarely contribute to, the corpus of literature [39].

As discussed, embargoes are currently imposed by publishers for economic reasons. This may be a significant barrier to access in biomedical sciences. As previously emphasised, it has been suggested that users favour electronic access and often eschew articles that are not available electronically [40]. In a shy attempt to tackle these problems, many journals now offer free access to all articles 6 months after publication and welcome the publication of articles as OA after a fee is paid by the authors.

However, research funding bodies are becoming increasingly sensible to this ethical issue. Many would argue that it is unethical to use the research grants from government (people's money) and not allow the scientific community to have free access to the results of the study. To address such issues, the Berlin Declaration suggested the establishment of OA repositories. All investigators who have received public grants should submit the full text of the paper published from their study to PubMed Central and also ensure self- archiving at the corresponding university or research institution. Obviously, OA journals provide an attractive solution to the problem of restricted access to results of publicly funded research [41].

Most countries and founding bodies are currently taking further actions to ensure OA for publicly funded

research [41–43]. Researchers are compelled to make their work publicly available in repositories (green road) within 12 months of publication. Other bodies even suggest that authors should make their work free by the publisher upfront (gold road). Clearly, research budgets should be reallocated with this aim, although the logistics required and the implications of this change remain a matter of ongoing debate. In July 2012, a new OA policy was announced by the European Union that recommended OA policies for all member states [31, 41–43]. Hopefully, this will represent a paradigm shift in scientific publishing and will herald a new era of academic discovery.

The ESC search engine

In the last decade, the amount of documents and educational material available on ESC websites has increased exponentially. This situation has led to increasing difficulty for users to find the information they need. It has become obvious that a more comprehensive search solution is necessary. For this reason, the ESC decided to provide a better search experience for ESC site visitors [44]. The ESC search engine uses semantic analysis to provide the best results from the keywords typed in [45]. This search engine project has four goals: (1) to provide a single entry point to multiple data sources (in fact, from a single entry point, the user will be able to explore an ESC-rich database of slides, scientific reports, guidelines, abstracts, clinical cases, news and articles from ESC journals); (2) to propose a tool that can treat requests expressed in natural language in a very user-friendly way; (3) to locate content that would be difficult to find or access otherwise, therefore saving precious time; (4) to allow visitors to find content by topic or person in an intuitive way.

In 2008, the ESC Board, chaired by Roberto Ferrari, decided to support the development of a semantic search engine that would be able to search for information on the ESC Central website and also on the websites of all six Associations (EHRA, EACVI [formerly EAE], EAPCI, HFA, EACPR, ACCA). This idea was based on the previously reported need to provide the user with a quick and easy way of obtaining information from hundreds of thousands of documents available on all these websites. Moreover, this engine is also looking into the ESC journals' family where it is possible to obtain results from more than 30 000 papers! Not surprisingly, this tool is a major success, already being the second most visited page of the ESC website, with 49 853 page views, in October and November of 2012 [46]. With the help of this search engine, it is now extremely easy to obtain information by just typing in the keywords on the top right hand side of the screen inside the http://www.escardio.org landing page (Fig. 1). The result is a list of documents addressing that specific topic, and the user can select the ones required (Fig. 2).

This results page contains a lot of information and functionalities. Within the document preview, you can see how the document looks (Fig. 2). The relevance score assigned

Figure 1. European Society of Cardiology (ESC) website landing page. The search engine box is located at the top right hand side of the screen (arrow).

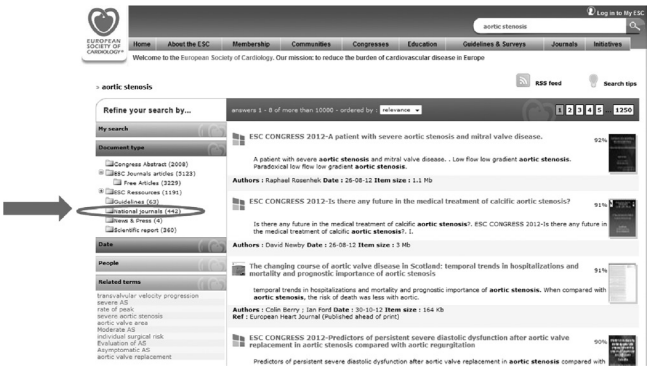

Figure 2. Results page with relevant information about the documents found. On the left, there is a toolbar with a filtering system to refine the search.

to this document is also displayed by the search engine. The type of document is also presented (guideline, abstract, slide presentation, scientific report, news, clinical case or a web document). The document origin can also be easily identified at a glance from a small institutional logo that can also be found on the results page, just below the icon showing the type of document. It is also important to know the document's availability. A padlock symbol is displayed when a document is behind a login so that you can still see that the resource exists, meaning that its access is for members only. This tool also allows the search to be refined by using filters located on the toolbar on the left. With this toolbar, the user can filter the type of document looked for (eg, only slides). It is also possible to filter only results from a given time period. During a congress, when a lot of content is published daily, the users can filter for what's new since the previous day, or only the results where a person is cited. Related terms are pro- posed by the engine from the keywords entered in the request to propose other related topics that could be of interest. If the same term is searched on a regular basis, the user may be interested in using the RSS feed functionality. Any search result page can be shown as an RSS feed which can be subscribed to, providing regular updates on what's new in the field.

Time to involve the national cardiac societies' journals!

This project is already in its adulthood and the time has now come to enter into a second phase of development and also involve the NSCJs. The ESC Board under Michel Komajda's presidency decided to support the development of this project. The ESC Editors' Network also gave an enthusiastic response and decided to contact those NSCJs that are already published in an electronic format and in English. Some of them already have a significant Impact Factor. The goal of this second phase of the project is to increase the visibility of the NSCJs and, as a consequence, to increase their readership and their level of reference in other international journals. Moreover, the excellent research that is performed at national level in many countries in Europe will become more visible worldwide.

This new tool is already available and, after typing in the keywords, the user gets two results: one from the ESC documents, and a second from the NSCJs. It will be possible for the user to see both in parallel and easily move from one result to the other with a simple click. The first NSCJs have been added to the search results and can now easily be identified and selected. The first five journals are: Revista Española de Cardiología, Heart and Blood Vessels (journal of the Cardiology Society of Serbia), Hellenic Journal of Cardiology, Egyptian Heart Journal and Romanian Journal of Cardiology. The Revista Portuguesa de Cardiologia is soon to be added. An arrangement has been made with the Brazilian Society of Cardiology, and its website is now including our search engine. This is an interesting way to raise awareness about this very useful tool and allow Brazilian cardiologists to have better access to our scientific resources. There is no doubt that providing this tool will strengthen even further the bonds between the ESC Central and the National Cardiac Societies, and European cardiovascular science will become more visible and readily accessible from any place in the world.

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OUTCOMES AND EFFECTIVENESS OF PERCUTANEOUS INTERVENTION IN PATIENTS WITH TAKAYASU'S ARTERITIS

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Aim. Takayasu's arteritis (TA) is a chronic inflammatory disease that affects predominantly the aorta. Percutaneous intervention (PI) may be use the TA. In this manuscript, we studied the outcomes (in-hospital and 6 months later) and effectiveness of PI in patients with TA.

Material and methods. The study was performed on 24 consecutive patients (39.3±11.8 (20–61) years; 4 men and 20 women) with TA who were treated with PI, surgical or medical therapy. Nine patients (7 females, 2 male) underwent PI. PI was performed after the erythrocyte sedimentation rate had been normalized in patients with TA.

Results. Although 9 patients received PI with stent for subclavian, carotid, renal and coronary artery, 1 patient received PI with only balloon for brachial artery. One percutaneous transluminal angioplasty and 10 stentings were performed. There was not any complication during interventional procedure. The patients were followed for 6 months. After 6 month, the arteries treated were patent and showed no proliferative lesions in Doppler ultrasound at 8 patients. At a woman patient, left subclavian artery restenosis was determined in Doppler ultrasound and confirmed by angiography. During angiography the stenotic lesion has been successfully treated with balloon angioplasty.

Conclusions. Takayasu's patients with active systemic disease must receive immunosuppressive therapy before PI. PI was performed after the active period such as during normal erythrocyte sedimentation rate. In these circumstances, PI in patient with TA may be safely and much less traumatic. Also, recurrence of stenosis in patient with TA has been treated successfully by reintervention without significant complications.

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Key words: Takayasu arteritis, percutaneous intervention, surgery, inflammation.

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PI — percutaneous intervention, TA — Takayasu's Arteritis.

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РЕЗУЛЬТАТЫ И ЭФФЕКТИВНОСТЬ ЧРЕСКОЖНОГО ВМЕШАТЕЛЬСТВА У БОЛЬНЫХ С СИНДРОМОМ ТАКАЯСУ

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Цель. Синдром Такаясу (СТ) — это хроническое воспалительное заболевание, поражающее преимущественно аорту. Чрескожные вмешательства (ЧВ) возможно использовать при ТП. В этой работе, мы изучили результаты (в стационаре и 6 месяцев позднее) и эффективность ЧВ у пациентов с СТ.

Материал и методы. Исследование проводили на 24 пациентах (39.3±11.8 (20–61) лет; 4 мужчин и 20 женщин) с СТ, которым было проведено ЧВ, хирургическое или медикаментозное лечение. Девять пациентов (7 женщин, 2 мужчин) прошли ЧВ. ЧВ было проведено пациентам с СТ после нормализации СОЭ.

Результаты. Хотя у 9 пациентов ЧВ проведено путем стентирования подключичной, сонной, почечной и коронарной артерии, 1 пациент получал ЧВ только через баллонную ангиопластику на плечевой артерии. Всего было выполнено одна чрескожная транслюминальная ангиопластика и 10 стентирований. Не было отмечено ни одного осложнения во время интервенционной процедуры. Пациенты наблюдались в течение 6 месяцев после пребывания в стационаре. После 6 месяцев леченные артерии были сохранны и не проявляли никаких пролиферативных поражений при допплеровском исследовании у 8 пациентов. У одной пациентки ультразвуковой допплерографией был определен рестеноз левой подключичной артерии, что было подтверждено ангиографией. Во время проведения ангиографии стенозирующее поражение было успешно вылечено с помощью баллонной ангиопластики.

Заключение. Пациенты с СТ и активным системным заболеванием должны получать иммуносупрессивную терапию перед ЧВ. ЧВ было проведено после активного периода, при нормальной СОЭ. При этих условиях ЧВ у пациентов с СТ может быть безопасно и гораздо менее травматично. Кроме того, рецидивы у пациентов с СТ возможно успешно лечить с помощью повторных вмешательств без существенных осложнений.

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Ключевые слова: артериит Такаясу, чрескожное вмешательство, хирургии, воспаление.

Introduction

Takayasu's arteritis (TA) is a chronic inflammatory disease that affects the large vessels, predominantly the aorta and its main branches and the pulmonary arteries, and it leads to vessel wall thickening, fibrosis, stenosis, and thrombus formation. The symptoms of this disease reflect the patient's high blood pressure and end organ ischemia including coronary, cerebral, and extremity ischemia. The mortality rate of TA is between 0 and 30% at five years, and the cause of death can be with congestive heart failure, coronary artery disease, cerebrovascular disease and renal failure [1, 2]. Therefore, an appropriate medical and invasive therapy is required for patients suffering from progressive disease. Some studies have revealed excellent results of percutaneous intervention for treating patients with TA [3, 4]. In this manuscript, we studied the outcomes (in hospi-

tal and six month later) and effectiveness of percutaneous intervention in patients with TA.

Material and methods

Patient population. From April 2005 to January 2010, a study was performed on 24 consecutive patients [39.3±11.8 (20–61) years; 4 men and 20 women] with TA who were treated with percutaneous intervention, surgical or medical therapy. Although lesions greater than 40% were included in this study, lesions greater than 70% reduction in vessel cross-sectional area of the vessel were treated by percutaneous intervention. Nine patients (7 females, 2 male) underwent percutaneous intervention. The patients had admitted to hospital complaining of headache, weakness and upper extremity claudication, also two patient had Class II angina pectoris. TA was diagnosed according to the American College of Rheumatology Criteria for the Classification of TA [5]. Patients with active systemic disease, as manifested by symptoms such as fever, musculoskeletal pains, or increased erythrocyte sedimentation rate received immunosuppressive therapy including steroids and/or methotrexate, azathioprin and cyclophosphamide before percutaneous intervention. The doses of immunosuppressive drugs were adjusted according to each patient's erythrocyte sedimentation rate and clinical status. Percutaneous interventions were performed after the erythrocyte sedimentation rate had been normalized (<15 mm/h) in these patients.

Interventional Procedure. Informed and written consent was obtained from all patients before the procedure. All patients were administered loading doses of acetylsalicylic acid 300 mg and clopidogrel 600 mg before percutaneous intervention. On admission anticoagulation was performed with unfractionated heparin 5000 IU iv bolus followed by 24000 IU over 24 hours. During percutaneous intervention 5000–7500 IU iv bolus is given followed by 1000 IU an hour later, then additional heparin to achieve an activated clotting time of 250–350 seconds. After the procedure, acetylsalicylic acid (100mg/once daily) was prescribed indefinitely. Clopidogrel was prescribed continuously for 1 year. All procedures were performed with the patients under local anaesthesia with sedatives. The electrocardiogram, arterial oxygen saturation, and blood pressure parameters were closely monitored. Using standard catheterization techniques, a 6F to 8F guiding catheter was introduced into the proximal portion of the stenotic artery. Patients with a significant stenosis (those with an estimated greater than 70% reduction in vessel cross-sectional area) of the vessel were treated by angioplasty or stenting. Following angioplasty or stenting, selective angiography was

Table 1

Affected vessels, treatment options and procedure site

Age, Sex	Hypertension	Affected vessels	Treatment	Procedure site
50, F	+	LSCA	Medical	-
32, M	+	LSCA, LRA, RRA, LVA	Stent	LRA
20, F	-	LSCA	Medical	-
38, F	-	RSCA	Medical	-
49, F	+	CABGX3 (LAD, D1, RCA), LSCA, RVA	Stent	LSCA, RCA
55, F	+	Op LSCA, LCCA, LRA	Stent	LSCA
39, F	-	Op LSCA, RCCA	Stent	LSCA
61, F	-	Op LSCA, RCCA, RVA	Medical	-
43, F	-	LSCA, RCCA, LCCA, RAA	Stent	LSCA
32, M	-	CABGX2 (LAD, RCA), RRA, RCCA	Medical	-
49, F	-	RAA, RBA, LBA	Medical	-
32, M	+	RSCA, RRA, LVA	Stent	RSCA, RRA
26, F	-	Op LSCA, LCCA	Stent	LCCA
51, F	-	LSCA, RSCA	Stent	RSCA
38, F	-	RSCA	Op	RSCA
41, F	-	RSCA, RCCA	Op	RCCA
20, F	-	RBA, LBA, LSCA	PTA	LBA
35, F	-	RSCA, RAA	Medical	-
30, F	-	RCCA, LCCA	Medical	-
47, F	-	RCCA, LCCA, RSCA, RVA	Medical	-
42, F	-	LCCA, LSCA, LVA	Medical	-
61, F	-	RSCA	Medical	-
30, F	-	LCCA, LSCA	Medical	-
24, M	-	LCCA, RCCA, LSCA, RSCA	Medical	-

Abbreviations: LSCA — left subclavian artery, LRA — left renal artery, RRA — right renal artery, LVA — left vertebral artery, RSCA — right subclavian artery, CABG — coronary artery bypass grafting, PTA — percutaneous transluminal angioplasty, LAD — left anterior descending artery, D1 — diagonal artery 1, Cx — circumflex artery, RCA — right coronary artery, RVA — right vertebral artery, Op — operation, CA — celiac artery, RCCA — right common carotid artery, LCCA — left common carotid artery, RAA — right axiller artery, RBA — right brachial artery, LBA — left brachial artery.

performed to determine the degree of dilation and whether dissection had occurred and to evaluate the intracranial circulation for signs of distal embolization.

Definitions and Follow-up. An intervention was considered technically successful if the residual stenosis was <30%. Six month later success of the percutaneous intervention was documented by Doppler ultrasound. In this technique, restenosis was defined by the presence of symptom recurrence and >50% restenosis.

Statistical analysis. Statistics were obtained using the ready-to-use programme of SPSS version 8.0. All the values such as age, period of the disease, erythrocyte sedimentation rate and stent size were expressed as mean ± standard deviation.

Results

The affected vessels, treatment options and percutaneous intervention site are summarized in Table 1. The mean period of the disease was 5.4±4.1 (1–13) years. The pre-treatment erythrocyte sedimentation rate was 54.91±25.10 mm/h. Percutaneous intervention was performed after the erythrocyte sedimentation rate had been normalized (9.80±2.10 mm/h) in these patients. While five patients had hypertension, none of the patients had diabetes mellitus and hyperlipidemia. Two patients treated before coronary artery bypass surgery and had a left internal mammarian artery (LIMA) bypass graft. While 2 patient undergone surgical revascularization, 12 patients received medical treatment. Although 9 patients received percutaneous intervention with stent, 1 patient received percutaneous intervention with only balloon. One percutaneous transluminal angioplasty (4X30 mm) and 10 stentings were performed [Mean size: 7.70±1.82 (3.0–9.0) mm X 31.00±14.17 (12.0–58.0) mm]. Percutaneous coronary intervention (right coronary artery stenting) and left subclavian artery stenting were performed 1 patient. 3.0X12 mm bare metal stent was used for proximal lesion of right coronary artery. Left renal artery stenting was performed 1 patient, subclavian artery (3 left, 1 right) stenting was performed 4 patients, and left common carotid artery stenting was performed 1 patient. Stent for right renal artery and right subclavian artery were performed 1 patients. Percutaneous transluminal angioplasty for left brachial artery was performed 1 patient. There were not any complication during interventional procedure. The patients were followed for 6 months. After 6 month, the arteries including subvlavian, brachial, carotid and renal treated were patent and showed no proliferative lesions in Doppler ultrasound at 8 patients. Also, transthoracic echocardiography and treadmill test (for 1 patient) were normal 6 months after the procedure. At a woman patient, left subclavian artery restenosis was determined in Doppler ultrasound and confirmed by angiography. During angiography the stenotic lesion has been successfully treated with balloon angioplasty.

Discussion

TA can be defined as a chronic inflammatory arteritis that attacks the aorta and its main branches [1, 2]. Management strategies for TA include medical treatment with steroids or immunosuppressive agents such as methotrexate, azathioprin and cycloposphamide and revascularization procedures such as surgical revascularization and/or percutaneous intervention [6–10]. During the active phase of the disease, the activity can be measured by the symptoms, an increase in the erythrocyte sedimentation rate, C reactive protein, interleukin-6, computerized tomography, magnetic resonance imaging, and fluorodeoxyglucose positron emission imaging [11–13], corticosteroids have been shown to improve systemic inflammatory symptoms within a few days or week. Immunosuppressive drugs such as methotrexate, azathioprin or cyclophosphamide have been used when steroids could not induce remission. In the chronic stage of this disease, the aim of treatment is revascularization of the affected organ, either by surgery or percutaneous intervention [8–10, 14]. Surgical treatment has been used to bypass the stenosed segment. This procedure may be complex and difficult, because it requires an intrathoracic approach, and is often complicated by graft occlusion and anastomotic site aneurysm. The stenotic lesions such as subclavian, carotid, brachial and renal in TA have been successfully treated with percutaneous intervention that has proved safe and with a good cost-benefit ratio, thus being an alternative for surgical revascularization [9, 10, 14]. Stent may achieve larger arterial lumen diameters, and may also eradicate or remarkably decrease gradients across stenotic lesions. Although recurrence of stenosis in patient with TA has been observed in 44.4% during angioplasty, 17.6% has been observed during angioplasty with stenting [15]. Also, the stents may not yield long-term arterial lumen patency in patients with TA as compared to atherosclerotic lesions [16]. However, recurrence of stenosis in patient with TA has been treated successfully by reintervention without significant complications, as in our woman patient [15]. Compared to atherosclerotic lesions, the lesions in patients with TA are very rigid due to their extensively diffuse, fibrotic, eccentric and calcified nature [17, 18]. To successful stenting in patients with TA, the rigid vessels can be dilated carefully with adequately high pressure. Since higher balloon inflation pressure causes chest pain, intimae dissection, bradycardia, and hypotension, close monitoring is required during procedure [19].

In this study, we were successfully performed percutaneous intervention in the subclavian, brachial, renal, carotid and coronary arteries. Narrowing of the brachiocephalic arteries is a common manifestation of peripheral vascular disease such as TA [20]. Of all the brachiocephalic artery origins, the left subclavian artery is usually the most severely affected. Percutaneous intervention such as angioplasty and/or stenting is still the most common method for percutaneous revascularization of subclavian and bra-

chial artery stenosis, especially short lesions. Fritz Angle et al [20] showed that percutaneous angioplasty/stenting of subclavian artery stenosis can be done with a very high technical success rate, as in our study. In this study, two patients treated before coronary artery bypass surgery and had a LIMA bypass graft. One of these patients had significant stenosis of the proximal left subclavian artery and right coronary artery and treated with stent. Use of the LIMA is associated with the best long-term patency of coronary artery bypass surgeries. However, significant stenosis of the proximal left subclavian artery can compromise flow to the LIMA. In patients with LIMA-coronary artery bypass, the development of left subclavian artery stenosis may cause angina, as in our patient, or myocardial infarction. Treatment options include percutaneous interventions or surgical revascularization. Surgery involves a carotid-to-distal subclavian bypass graft, or a subclavian-carotid transposition. The morbidity and mortality rates related to these surgical options are raised markedly by the presence of severe coronary artery disease. For this reason, we used percutaneous intervention in this patient.

Carotid artery stenting is a good technique that represents a therapeutic alternative to carotid endarterectomy for patients with significant carotid stenosis, as in our patient. Procedures in the carotid arteries were performed with a distal embolic protection device, as in our patient, with the purpose of reducing the risk of stroke during stent implantation. Compared to endarterectomy stenting is much less invasive and traumatic procedure. Also, it is technically simpler and faster than surgical endarterectomy. Finally, this procedure can be done with remarkably complications rates [21, 22].

Renal artery stenosis is the most common cause of secondary hypertension. Many of the stenosis progress to total occlusion and with the majority of the patients suffering loss of renal function manifested by increasing serum blood urea nitrogen and creatinine. Treatment of renal artery stenosis via percutaneous intervention may improve amelioration of blood pressure and/or renal functions [23, 24]. In this study, we observed both a better control of the blood pressure and preservation of the renal function.

Conclusion

In conclusion, Takayasu's patients with active systemic disease must receive immunosuppressive therapy such as corticosteroids, methotrexate, azathioprin and cyclopospha-mide before percutaneous intervention. Percutaneous interventions were performed after the active period such as during normal erythrocyte sedimentation rate. In these circumstances, percutaneous intervention in patient with TA may be safely and much less traumatic. Also, recurrence of stenosis in patient with TA have been treated successfully by reintervention without significant complications,

Study Limitations

These conclusions may not extend to the great population, therefore; the results of this study will need confirmation in larger studies.

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FACTOR INFLUENCING LENGTH OF STAY OF PATIENTS UNDERGOING BYPASS SURGERY AT SHAHEED MADANEE CARDIAC TEACHING HOSPITAL –TABRIZ — IRAN

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Aim. This study aimed to study the effect of patients' and physician's characteristics as a predictor of length of stay (LOS) in patients undergoing coronary bypass surgery.
Material and methods. This was a retrospective study conducted at Tabriz Shaheed Madanee Cardiac Teaching Hospital in Iran in 2010. The 349 patients who did undergo a bypass surgery during 2008–2010 were studied. Patients and physicians characteristic were collected from patients medical records using a researcher developed checklist. Independent Samples Test of ANOVA was conducted to compare LOS between categorical variables. Data was analyzed using the SPSS17 statistical package.
Results. The mean age of the patients was 59.7 years. Overall average LOS was 15.58 (10.02) days. The findings of this study indicate that older patients stayed in the hospital for a significantly longer period than did younger patients. Patients' stay at the hospital was statistically significant and longer than assessed expected length of stay estimated by physicians (P< 0.05). Patient admitted to the hospital through emergency department and patients with no hospitalization history stayed longer in the hospital (P≤0.01).).Early discharged patients and death cases also had a longer LOS (P ≤ 0.01).Patient whose attending physicians were working in private sector, in addition to Shaheed Madanee Hospital and had higher level of education stayed longer than those whose physicians worked only at Shaheed Madanee Hospital (P≤ 0.01).
Conclusion. Institutional characteristics –physicians practice both in private sector and public teaching hospital, physicians' level of education, discharge process guidelines, and admission protocols were most important factor in predicting LOS. The patient's hospitalization history whether patient was hospitalized before or not, was also a predictor.

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Key words: coronary arteries bypass surgery, Length of stay, Teaching Hospital.

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ФАКТОР, ВЛИЯЮЩИЙ НА ПРОДОЛЖИТЕЛЬНОСТЬ ПРЕБЫВАНИЯ ПАЦИЕНТОВ, ПЕРЕНЕСШИХ ОПЕРАЦИИ ШУНТИРОВАНИЯ В КАРДИОЛОГИЧЕСКОЙ КЛИНИЧЕСКОЙ БОЛЬНИЦЕ SHAHEED MADANEE – ТЕБРИЗ — ИРАН

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Цель. Это исследование было проведено с целью изучения влияния на характеристики пациентов и врачей такого предиктора, как продолжительность пребывания (ПП) пациентов, перенесших коронарное шунтирование.
Материал и методы. Это был ретроспективный анализ, проведенный в Кардиологической клинической Больнице Shaheed Madanee города Тебриза в Иране в 2010 году. Было исследовано 349 пациентов, которые прошли шунтирование в течение 2008–2010 гг. Характеристики пациентов и врачей были извлечены из медицинских записей пациентов с помощью специального контрольного списка, разработанного исследователями. Тест независимых выборок ANOVA проводился для сравнения ПП между категориальными переменными. Данные были проанализированы с использованием статистического пакета SPSS17.
Результаты. Средний возраст пациентов составил 59,7 года. Средняя ПП была 15.58 (10.02) дней. Результаты этого исследования показывают, что пожилые пациенты оставались в больнице в течение гораздо более длительного периода, чем у молодые пациенты. Пребывание пациентов в больнице было статистически значимо и дольше, чем ожидаемой ПП по оценкам врачей (P<0,05). Пациенты, поступившие в больницу через отделение неотложной помощи, и пациенты без истории госпитализации задерживались в больнице дольше (P=<0.01). Ранее выписанные пациенты, а также случаи смерти, также имели длительную ПП (P=<0.01). Пациент, чьи лечащие врачи работали в частном секторе, помимо больницы Shaheed Madanee, и имели более высокий уровень образования, оставались дольше, чем те пациенты, чьи врачи работали только в больнице Shaheed Madanee (P=<0.01).
Заключение. Институциональные характеристики — практика врачей и в частном секторе и в государственной клинической больнице, высокий уровень образования врачей, выполнение требований рекомендаций, и прием протоколов были важными факторами в прогнозировании ПП. История госпитализации пациента, был ли пациент госпитализирован до или после, также является предиктором.

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Ключевые слова: коронарное шунтирование, срок пребывания в больнице.

Introduction

Coronary artery bypass surgery is a safe and accepted technique to treat coronary artery diseases [1], with its own costs implications [2]. The annual cost of it is more than 10 billion US dollars for 500,000 coronary bypass surgeries in the United States [3]. Because of the large number of surgeries performed, even modest reductions in bypass unit cost by rationalizing the length of stay could significantly reduce expenditures at both the hospital and national levels [3].

However it has been shown that length of stay is associated with resource use [4], additionally it is a sensitive and specific marker of inefficiency in using scarce resources of hospitals in inappropriate length of stay [4].

However, there does not appear to be much evidence in the literature to support the assumptions that there is a golden

standard of length of stay for patients undergoing coronary bypass surgery, but finding of studies indicates that longer preoperative hospital stay can be a risk factor for deep wound infection [4, 5], in addition longer preoperative hospital stay was associated with a increased risk of surgical site infections [5]. In recent years, there has been data published from several studies suggesting that the predictors of length of stay as a patient outcome can range from clinical mix [1, 6, 7], to patient, [6, 8–10] and care providers characteristics [6, 8]. Therefore the risk of prolonged length of stay on patient's outcome may be no different than clinical predictors of patient outcome in regards to service quality. However it seems possible to decrease coronary bypass surgery patients' length of stay with lower resource utilization and costs without adversely affecting patient's outcomes. It is not something out of sight, and it can be achieved with minor interventions in clinical and administrative procedures, processes, providers behaviour, and the guidelines, for instance, some studies show that the development of fast-track anaesthetic techniques for cardiac surgery has helped to decrease intensive care unit (ICU) and hospital length of stay (LOS) without adversely affecting mortality and morbidity [4, 11].Therefore this study aimed to study the effect of patients' and physician's characteristics as a predictor in length of stay of patients undergoing coronary artery bypass surgery at Shaheed Madanee Cardiac Teaching Hospital in Tabriz.

Material and methods

We used a retrospective-observational study at Tabriz Shaheed Madanee Cardiac Teaching Hospital to study 349 hospitalized patients who did undergo a bypass surgery in 2010. About 349 hospitalized patients who did undergo a bypass surgery were studied. Study data were collected using a researcher developed checklist from patient medical records during 2008–2010.

Trained personnel collected data using a standardized checklist on 349 patient's undergone coronary bypass surgery during 2008–2010. Patients in this study had a coronary bypass grafting surgery (CABG) as their principal procedure defined by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code, according to their medical records. During years 2008–2010 we randomly selected 15 medical records every month out of those records showing that patient has undergone a bypass surgery

Study checklist included demographic information such as: patient's sex, occupation, patients insurance, marital status, type of admission, history of hospitalization, discharge status, physician specialties, physicians practice in private in addition to practice at Shaheed Madanee Hospital sector, and length of stay at the hospital. Furthermore, in regards to determining the assessment of physicians on expected length of stay of patients undergoing coronary bypass surgery data was collected from physicians who had enough experience in diagnosing and performing coronary bypass surgery. The pessimistic, optimistic and most likely length of stay for patients undergoing coronary bypass surgery at this hospital were collected though conducting interviews with physicians and then expected length of stay was calculated using the PERT (Program Evaluation and Review Technique) Weighted Average formula:

*Expected time = (Pessimistic value + 4*most likely value + Optimistic value) /6*

Frequencies and percentages were used to describe demographic information of patients. Independent Samples Test, ANOVA was conducted to compare LOS between categorical variables after testing the normality of their distribution and confirmation by a Kolomogrov-Smirnov test. One-Sample T Test was used to describe the differences between physicians' estimated and actual LOS derived from patients' records. Furthermore data was analyzed using the SPSS17 statistical package. The P values ≤ 0.05 were considered as statistically significant.

Results

Data were collected on all 349 patients undergone coronary bypass surgery. Overall average LOS derived from patients' records was 15.58 (±10.02) days. The mean age of the patients studied was 59.7 (9.8) years. Further analysis of the data indicates that older patients stayed in the hospital for a significantly longer period than did younger patients (P≤0.001). Table 1 summarizes the findings of the patients' characteristics according to gender, occupation, type of insurance (Insurance plan), mode of admission, history of hospitalization (previous hospitalization due to cardiac problems), discharge status, physicians' educational level, and their practice in private sector.

Study findings indicate females' LOS statistically was longer than male (p=0.014). There was no significant association between length of stay and patients' marital status and place of residence -rural or urban- (P>0.05). Significant association was observed between length of stay and type of admission and, hospitalization history, and physicians practice in private sector (P≤0.001), also, data related to practice in private sector for two physicians were not available. With the exception discharge status which was a little longer for partial recovery (P=0.049). Table 1 also reports the length of stay according to physicians status; patients whose physician was a specialist did stay one and half day longer than those whose physician was a sub-specialist, this difference wasn't statistically significant (P=0.061) (Table 1).

Table 2 indicates detailed pessimistic, optimistic and most likely length of stay according to physician's point of view. To calculate the expected length (time) of stay physicians were asked to estimate pessimistic, optimistic and most likely length of stay for patients undergoing coronary bypass surgery. Then the Expected length (time) of stay was determined using PERT Weighted Average formula.

The physicians estimated LOS was 10.72 days and actual LOS derived from patients' medical records was 15.58 days. The difference between estimated and actual LOS using One-Sample T Test was statistically significant (P≤0.05) (Table 2).

Table 1

Length of Stay according to Patient and Physician characteristics

Characteristics	No (%)	Mean of Length of Stay (SD)	Min_Max	p
Sex				
Male	246 (70)	14.77 (8.94)	3–60	0.014
Female	103 (30)	17.53 (10.79)	2–71	
Occupation				
Unemployed	109 (31.1)	17.56 (10.82)	2–71	0.052
Employee	33 (14.6)	13 (5.77)	6–31	
Technical worker	30 (5.9)	13.93 (6.22)	3–29	
Non-Technical worker	15 (8.6)	15.47 (9.07)	4–40	
Retired	51 (4.3)	17.56 (10.82)	4–46	
Farmer	34 (9.7)	15.68 (6.41)	3–33	
Other	77 (22)	14.10 (8.56)	3–60	
Patient Insurance type				
Health services	170 (48.7)	16.16 (9.48)	2–60	0.672
Social security	120 (34.4)	14.42 (8.81)	3–71	
Military insurance	40 (11.5)	16.55 (8.53)	4–54	
Private insurance	8 (2.3)	14.50 (3.85)	9–20	
Uninsured	11 (3.1)	14 (7.55)	5–27	
Patient Marital status				
Married	347 (99.5)	15.6 (9.86)	2–71	0.401
Single	2 (0.5)	13.5 (2.27)	6–21	
Type of admission				
Elective	261 (74.7)	14.11 (6.45)	2–60	<0.001
Emergency	88 (25.3)	19.94 (10.54)	2–71	
History of hospitalization (previous hospitalization due to cardiac problems)				
Yes	231 (66.2)	13.7 (9.09)	3–46	<0.001
No	118 (33.8)	19 (7.49)	2–71	
Discharge status				
Complete recovery	278 (79.7)	14.86 (7.59)	2–60	0.049
Partial recovery	42 (12)	15.57 (6.90)	4–36	
Death	29 (8.3)	22.30 (17.95)	4–71	
Physician's educational status				
Specialist	215 (61.6)	15.83 (7.24)	3–60	0.061
Sub-Specialists	134 (38.4)	14.35 (6.25)	2–46	
Physician's work in private sector				
Yes	106 (35)	13.45 (7.2)	3–60	<0.001
No	197 (65)	15.97 (8.35)	2–71	

Table 2

Physicians estimated LOS related to real LOS

Conditions	LOS (day)	p
Optimistic	5.64	
Pessimistic	20.34	
Most likely	9.59	
Te. (Expected Time)	10.72	< 0.05
Real LOS according medical record	15.58	

Discussion

Previous researchers have found that there is considerable variation in the resource use and LOS associated with bypass surgery. Our study examines the length of stay for a single regional specialist heart hospital in Tabriz. We found substantial associations between patients' and physician's characteristics and length of stay in this study. LOS was higher for patients, who were unemployed, retired, female, and had no hospitalization history due to cardiac problems, emergency admission patients, and death cases. These findings are generally consistent with prior studies that used medical records identify the predictors of length of stay [1, 2, 12]. Despite previous research findings failure to explain patients and physicians non clinical characteristics [7, 13] as predictors of variation of length of stay [1], our findings identify some association between institutional characteristics and length of stay as additional risk factors for prolonged length of stay which are consistent with previous findings [11, 14]. Length of stay differs due to many factors some of which may be modifiable such as discharge status and physicians practice in private and public sector at the same time [13, 14]. Therefore variation in pattern of staffing of physicians may affect the length of

stay [11, 14]. Research findings indicate that some hospitals adopted protocols to shorten the length of stay, which are being considered to be effective. These studies also revealed that hospital discharge policy, hospital size and managerial factor have a major role in LOS [11, 13, 14]. Furthermore several recent studies suggest using critical pathways, care maps, and a fast-track protocol is effective to increase the efficiency by reducing LOS [11, 14].

Our study provides such information that could be used to predict and distinguish patients who as a result longer period of stay in the hospital. Furthermore, we could determine that savings will be extended if we use integrated hospital and home care services. That is to say, since Shaheed Madanee Hospital is the only hospital serving a vast geographical area (more than three provinces in North West of the country) and most of the residents have difficulty in accessing the post-operative services, the providers and patients tend to prolong the hospital stay. Thereby offering post-operative services through home care can considerably reduce the LOS.

Further research is needed to address these issues, particularly in light of the trend toward shorter hospitalizations and resource utilization without sacrificing the quality of care [15].

On the other hand, due to non-linear pattern of hospital costs and revenue, most of the costs of hospitalization and profitable services for are incurred at the beginning of hospital stay, so, by reducing LOS hospital marginal profit's increase [16]. Along with this factor according to present study findings technical expectancy of LOS based on physician's estimation was significantly shorter than real LOS derived from medical records. In this regard, findings in the literature also indicate that other factors such as quality of care and hospitals volume can influence this issue [17].

Although we tried to limit the constraints of our study but there are still a number of limitations. First, our findings do not take into account the patients' residency and economic characteristics, although, these factors play an enormous role in LOS. In our study context due to lack of access to post-operative services in some setting some patient and provider prefer to longer LOS. Second, to be as an observational and retrospective study, the results were subject to documentation biases and missing data Third, We also had no access to and did not follow up transfer patients, thereby have no idea of their LOS. Fourth, we did not mention the other factor such as patient's co-morbidities and surgery condition that may influence LOS, due to incomplete medical records.

In summary, this research suggests that provider's characteristics — physician's practice both in private sector and public teaching hospital, discharge process guidelines, and admission protocols- were substantial predictors of length of stay. Patient non clinical characteristics such as gender, occupation, type of insurance and marital status did not play an important role in hospital stay except hospitalization history — those with no hospitalization history stayed for longer period. Furthermore the data from this study may be useful to administrators and physicians who are involved in the management of health programmers and hospital budget, to encourage shorter length of stay to reduce costs. Further research is needed to assess its impact on patient outcomes.

Conclusion

The factors that were significantly associated with length of stay were largely due to institutional characteristics — physicians practice both in private sector and public teaching hospital, physicians' level of education (specialist, subspecialist), discharge process guidelines, and admission protocols. The patient's hospitalization history was also a predictor (those with no hospitalization history stayed longer). The shorter length of stay seemed to be possible by administrative interventions to normalize the potential institutional predictors.

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TRANSCATHETER AORTIC VALVE IMPLANTATION IN PATIENTS WITH LEFT ATRIAL APPENDIX THROMBUS

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Aim. The transcatheter aortic valve implantation (TAVI) which developed in the recent years has become an alternative for surgery. However, in spite of new developments the process based vascular and neurological complications still remain to be a problem with elderly patients who also tend to have many co-morbid conditions. With this study we aimed to evaluate the TAVI efficacy and reliability on patients with scarcely relative contraindication and with intracardiac thrombus who are mostly left out of the study.

Methods and Results. There has been a successful TAVI process conducted in our clinic for antiplatelet and anticoagulation for 6 cases in which thrombus was seen in left atrial appendix (LAA) via transesophageal echocardiography (TEE) and which are not suitable for surgical valve replacement due to atrial fibrillation (AF) and severe AS comorbid reasons. Edwards SAPIEN XT valve was implanted to all patients transfemorally with general anaesthesia. The process was facilitated successfully and no major/minor stroke was observed in post-process early period, and 9 month controls, in average.

Conclusion. Other than AS, also AF, whose frequency increases with age, is an important risk factor for neurological complications. In patients who has AF and AS the source of the cardioembolic focus is mainly LAA. The post-TAVI antiplatelet and anticoagulation treatment is not clear for these patients. We tried to show that TAVI process is reliable in terms of the risk of stroke, in careful processing and suitable anticoagulation treatment for the patients with AF, AS and LAA in this first case study in literature, as far as we know.

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ТРАНСКАТЕТЕРНАЯ ИМПЛАНТАЦИЯ АОРТАЛЬНОГО КЛАПАНА У ПАЦИЕНТОВ С ТРОМБОЗОМ УШКА ЛЕВОГО ПРЕДСЕРДИЯ

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Цель. Транскатетерная имплантация аортального клапана (ТИАК), которая развивалась в последние годы, стала альтернативой для хирургии. Однако, несмотря на новые разработки, сосудистые и неврологические осложнения, лежащие в основе процесса, по-прежнему остаются проблемами у пожилых пациентов, которые, как правило, имеют много сопутствующих заболеваний. В данном исследовании мы стремились оценить эффективность и надежность ТИАК у пациентов с опасными противопоказаниями и с внутрисердечными тромбами, которые в большинстве случаев не включаются в исследования.

Методы и Результаты. Имелись успешные ТИАК, проведенные в нашей клинике для антитромбоцитарного и антикоагулянтного лечения 6 случаев, в которых тромб был замечен в ушке левого предсердия (LAA) с помощью чреспищеводной эхокардиографии, и которые являются не пригодными для выполнения хирургической операции по замене клапана вследствие фибрилляции предсердий (ФП) и тяжелого стеноза аорты (СА). Клапан Edwards SAPIEN XT был имплантирован всем пациентам трансфеморально под общей анестезией. Процесс был успешно проведен и не было отмечено большого/малого инсульта в раннем пост-операционном периоде, а также во время 9-месячного контроля, в среднем.

Заключение. СА, как и ФП, чья частота увеличивается с возрастом, являются важным фактором риска развития неврологических осложнений. У пациентов, которые уже имеют ФП и СА, кардиоэмболический акцент делается, в основном на LAA. Антитромбоцитарное и антикоагулянтное лечение после ТИАК для этих пациентов — не ясно, Мы постарались показать, что операция ТИАК является надежной с точки зрения риска инсульта, при тщательном уходе и подходящей антикоагулянтной терапии для пациентов с ФП, СА и тромбом в LAA, что в литературе впервые описано, насколько нам удалось установить.

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Ключевые слова: транскатетерная имплантация аортального клапана, мерцательная аритмия, левого предсердия приложение, тромб, инсульт.

Introduction

The frequency of aortic stenosis (AS) gradually increases along with the increase in the life span. AS is seen in abut 2–4% of the age >65 years population in Europe and North America [1]. Surgical aortic valve replacement (SAVR) is done by low operative mortality on the absence of severe comorbid conditions. Recovery of symptoms and increase in life spans are seen in patients who have AVR. Accordingly, 30% of the patients cannot have SAVR due to left ventricular dysfunction, older ages and comorbid conditions [2]. First transcatheter aortic valve implantation (TAVI) application on humans in 2002, developed in a fast manner to become a significant treatment option for surgery in inoperable patients or those who has high risk. According to the only randomized clinical study on this issue, PARTNER study, it has been shown that TAVI is superior to treatment in inoperable patients and could be a significant alternative in SAVR in patients carrying high risk [3, 4]. As well as it is a less invasive process when compared to surgery, major vascular complications and stroke is seen more often in TAVI process when compared to a surgical group. TAVI relative stroke risk increases when there are risk factors such as intensified calcification in valve, atheroma burden on aortic arch, elderly age, carotid artery stenosis, atrial fibrillation (AF) and intracardiac thrombus [5]. Therefore pres-

ence of thrombus within the intracardiac or left ventricular is indicated as exclusion criteria in choosing the patients for TAVI in the recent published studies [6, 7]. However, there is no data regarding the presence of thrombus in left atrial appendix (LAA).

Thus, in this study we aimed to show the reliability of TAVI process in terms of the risks of stroke along with appropriate anticoagulation and careful interference on patients with in AF, severe AS and thrombus LAA. In our knowledge this publication is the first study in the literature.

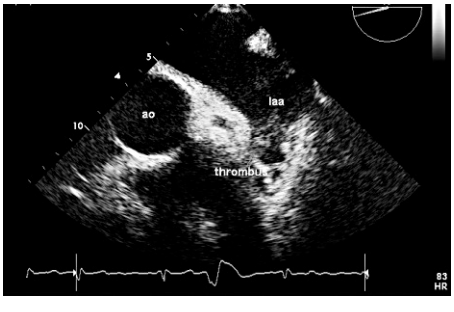
Material and methods

In our clinic TAVI process was applied to high risk carrier 70 patients with severe calcific AD and comorbid causes for surgical valve replacement between the dates July 2011 and December 2012. TEE was applied to 66 patients, not to the other 4 (one having oesophagus stenosis, the other having oesophagus varicose and the last two was undergone local anaesthesia) before the process. Thrombus presence was found via multi slice computerized tomography (MSCT) and TEE presence LAA in 6 of the patients (Fig. 1 and 2A-B). Fourth of the patients were female as 2 of them were male and the age average was 76 years. Basal characteristics of the patients and data regarding the TAVI process are given on Table 1. In echocardiography the average valve area was determined to be 0,7 cm^2, and the average mean gradient to be 50,6 mmHg. One of the patients had coronary artery disease which required revascularization and asymptomatic carotid artery disease in right internal carotid artery which caused 80% stenosis. A bare metal stent was implanted to the severe stenosis in the patient's circumflex artery before TAVI. Another patient had a mitral valve replacement 10 years ago and wasn't receiving an enough anticoagulation treatment. All of the patients were carrying high risk in terms of surgical means and they were accepted to be inoperable by the evaluations done by the cardiovascular surgeons. All patients were informed and their approval was taken before the process. An ethical approval was granted from the ethical committee of our hospital. TEE and MSCT were done to all of the patients before the process and it was evaluated for their compliance and additional pathology in valve morphology, aortic annulus, coronary ostium-annulus distance, calcification degree, and peripheral arteries. All six of the patients, thrombus was identified in LAA via TEE, MSCT. TAVI process was planned for all patients via transfemoral ways. Warfarin treatment was stopped for the patients who were previously using warfarin due to AF or mitral valve replacement, and enoxaparin 1 mg/kg treatment was started as two doses a day for the bridge treatment before the process. Along with this acetylsalicylic acid (ASA) and clopidogrel treatment was started for all of the patients. TAVI was applied when the international normalize ratio (INR) value was determined to be <1,5. For the appropriate access route was specified both doing MSCT and peripheral angiography before TAVI. TAVI was done transfemorally by using 14F Prostar XL (Prostar™ XL14Fr; Abbott Vascular, Abbott Park, IL, USA) vascular closing device for all 6 cases and under general anaesthetics along with TEE. During the process it was heparinised together to obtain the activated clotting time of the patients to be 250–300 seconds. Edwards SAPIEN XT (Edwards Lifesciences, Irvine, CA, USA) valve was implanted in an appropriate position to be 23 mm in four patients, 26 mm in one and 29 mm in the other patient.

Figure 1. Image of thrombus in left atrial appendix (showed with an arrow) via multi slice computerise tomography.

Results

The process was finished successfully for all of the patients. No post-TAVI vascular complication was observed. As no bleeding was observed in none of the patients, one patient was treated with a unit of erythrocyte suspension and the other was treated with two units, after the process. The patients were evaluated by the neurology



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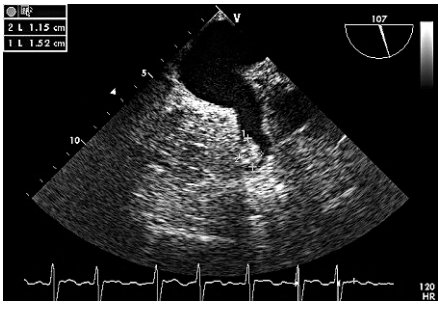

B

Figures 2A and B. Images of thrombus in left atrial appendix via transoesophageal electrocardiography.

Table 1

Basal characteristics of the patients

Characteristics	1st Case	2nd Case	3rd Case	4th Case	5th Case	6th Case
Age	81	70	73	80	81	70
Gender	Female	Female	Male	Female	Female	Male
STS score	12,8	10,3	13,5	12,3	12,9	13,7
Logistic EURO score	31,87	39,7	56,23	26,38	29,49	30,06
NYHA	3	4	3	3	3	4
CVD	No	Yes	No	No	No	No
AVA cm^2	0,5	0,8	0,7	0,7	0,8	0,7
Aortic Valve mean gradient (mmHg)	72	41	52	51	47	41
LVEF%	65	45	35	65	65	25

Abbreviations: STS — Society of Thoracic Surgeons, NYHA — New York Heart Association, CVD — cerebrovascular disease, AVA — aortic valve area, LVEF — left Ventricular Ejection Fraction.

department after the process. The patient follow-ups showed no major/minor stroke development. The aortic valve average mean gradients were measured to be 9 mmHg after the process. None of them showed any moderate or severe paravalvular aortic regurgitation. Warfarin treatment was started after the process and INR was tracked to be 2.0–2.5 for 1 month under warfarin+clopidogrel dual treatment. After a month clopidogrel treatment was stopped and warfarin treatment was continued. No major or minor stroke was observed or no moderate or severe paravalvular aortic deficiency was developed according to the patient follow-ups of approximately 9 months (6 patient follow-ups, respectively 16, 15, 8, 8, 7, 2 months). All of the patients showed significant improvements in their functional capacities and no major undesired event was developed during the follow-ups.

Discussion

In our publication which is the first study in the literature, we presented the successfully applied TAVI process without developing any stroke on the patients with thrombus in LAA and AF. Rhythm of all 6 patients to which TAVI was applied was AF and thrombus presence in LAA was seen in the TEE and MSCT conducted. No major/minor stroke was observed for neither of the patients as a result of the appropriate coagulation and successful process. No major adverse event (death, stroke, myocardial infarction, haemorrhage) during the 9 month follow-ups of the patients.

AS is a degenerative disease whose frequency increases gradually in the elderly and which decreases the survival rate in a fast manner as it becomes symptomatic. A certain treatment is the valve replacement. Although, the rates of the patients which cannot be operated to get a surgical valve replacement is 30–40% due to an elderly age and frequency of comorbid conditions [2]. It was first said in European Society of Cardiology (ESC) latest valve guidelines that TAVI process, which was first started to be applied on humans in 2002 and took place in the real world due to its fast development, can be an alternative to SAVR on patients carrying high risk [7]. However, in spite of these developments some patient groups cannot be benefitted enough from this treatment. The latest ESC valve guidelines included the ones having thrombus within the left ventricular in the absolute contraindications group. Intra cardiac thrombi were listed in the contraindication group within the latest American College of Cardiology (ACC) TAVI consensus. However, it does not mention the ones having left atrium or LAA thrombi. Although, overall proneness is to refrain to conduct this on these patients [3, 6, 7]. While determining the major stroke rates of 3.8% on day 30 and 5.1% on year 1 in cohort A from the PARTNER study, which is the only randomized controlled study, the cohort B showed major stroke rates to be 5% on day 30 and 8.4% on year 1. Along with this, within the studies done with diffusion-weighted magnetic resonance imaging the rates of silent ischemia was found to be 68–84% (DW-MRI) while the clinical importance of silent ischemia was not stated to be clear. It is known that the half of the stroke were related to the procedure and the other half develops within the 12 months after the procedure, and the post-process high risk period for stroke is the first 24 hours [3,9,10]. Emboli might be observed in every stage of the TAVI process such as left heart catheterisation, catheter manipulations, thrombus formation around the catheter or the sheath, calcified aortic valve tear up during balloon valvuloplasty, valve position and implantation and the extended time period after the process [11]. Age, hypertension, diabetes, calcified ascending aorta, female gender, story of stroke, AF and the degree of the atheroma plates in the aortic arch are included in the risk factors for emboli [6,12]. New AF related to TAVI which causes an increase in post procedural stroke risk for 3.9 times was determined to be 7.5% in the transfemoral arm, 11.5% in the transapical arm of cohort A, and 0.7% in cohort B of PARTNER [3,12].

AS and AF are both conditions that are highly probable to be found together and that increases in frequency as the age gets older. AF is responsible for most of the neurological complications seen in elderly ages and the cardioembolic focus is mainly on the thrombus in LAA. The effect and

reliability of anticoagulation towards the prevention of thromboembolism in AF is known for many years. In spite of this there is no standardized anticoagulation protocol for the TAVI applied patients having AF yet. In order to achieve a successful process in TAVI the TAVI related stroke risk should be minimised. In order to obtain this it should start with a pre-TAVI patient evaluation. Along with this, since the potential TAVI patients hold for many risk factors for cerebrovascular events, the risk classification and transfemoral/transapical approach should be specified by using all the techniques in imaging [11]. We have done risk evaluations for the patients by applying TEE, MSCT and peripheral angiography in terms of both appropriate access route determination and emboli. Appropriate antiplatelet and anticoagulation to be done before and after the process are the building blocks of the treatment. In our cases clopidogrel and warfarin was given for one month for the INR to be 2.0–2.5, and only warfarin treatment was applied after a month. Additionally new emboli protecting devices are being developed (e.g., Embrella [Edwards Lifesciences, Inc., Irvine, CA, USA], Claret [Claret Medical, Inc. Santa Rosa, CA, USA], SMT Embolic Deflection Device) in order to prevent process related emboli and the human studies regarding these are promising [12].

As far as we know no TAVI case is found for patients with AF and thrombus in LAA in the literature. There is only one statement for 2 cases of having AF along with either AS and no thrombus in LAA. As there were warfarin contraindication in these cases TAVI and LAA shut down process was applied in one to be within the same session and in the other one to be in different sessions [13,14]. Since there was no warfarin contraindication in our cases, after the process was successfully finished the follow-ups continued under the treatment of warfarin.

Conclusion

TAVI is a developing treatment method which shows a promise to be an alternative to surgery in the treatment of patients with symptomatic severe AS. Along with the technology, and the upcoming developments in valve systems, procedural techniques and periprocedural treatments it can be applied more safely. Along with the operators to become more familiar with TAVI and the new upcoming studies the groups that will benefit from this treatment can be better identified. With this study we have shown that TAVI can be safely applied without observing any early or late stage stroke on patients with atrial fibrillation, advanced age and thrombus in LAA, which are significant risk factors for stroke. However, the reliability of TAVI would be stated more clearly for these patients with randomized controlled studies which more patients attend to and holding for a longer follow up time period.

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IMPORTANCE OF ROENTGEN TUBE ANGLES IN CINEFLUOROSCOPIC INVESTIGATION OF MECHANICAL PROSTHESES

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Aim. We planned a cinefluoroscopy (CF) study to mark the ideal opening and closing tube angles for mitral and aortic positioned mechanical valves. Our hypothesis was that if we find an intensity zone where the valves were optimally seen, then starting the CF examination from that tube position would shorten the examination duration

Material and methods. Between January 2010 and August 2011, 192 consecutive patients (mean age 51,86±12,80 years; 101 women and 91 male) with mitral (n=135; monoleaflet: 37; bileaflet: 98) and aortic (n=87; monoleaflet:19; bileaflet: 68) and tricuspid (n=3; all bileaflet) prostheses were enrolled into the study. Cinefluoroscopy was performed with Philips Radiologic System. For each type and location of mechanical prostheses optimal opening-closing angles obtained and marked on x-y axis graphic. Furthermore, we investigated whether there is an intensity zone quadrant.

Results. Among patients with prosthetic bileaflet mitral valve in supine position optimal images were obtained: 34 (58,6%) patients were in RAO-Cranial, 12 (20,7%) were in left anterior oblique (LAO) cranial, 7 (12,1%) were in RAO caudal and 5 (8,6%) were in LAO caudal angles. Among patients with prosthetic bileaflet aortic valves in supine position shown: 27 (50%) patients were in LAO-cranial, 10 (18,5%) were in RAO- cranial, 9 (16,7%) were in LAO-caudal and 8 (14,8%) patients were in RAO-caudal angles.

Conclusion. According to our results it seems logical to start mitral position CF assessment by RAO-Cranial angles quadrant and for aortic position by LAO-Cranial angles quadrant to decrease time and lower radiation exposure.

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Key words: cinefluoroscopy, mechanical heart valve dysfunction, radiation consumption.

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CF — Cinefluoroscopy, LAO — Left anterior oblique, RAO — Right anterior oblique, SPSS — Statistical Package for Social Sciences, TEE — Transesophageal echocardiography, TTE — Transthoracic echocardiography.

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ВАЖНОСТЬ УГЛОВ РЕНТГЕНОВСКОЙ ТРУБКИ В КИНОФЛЮОРОГРАФИЧЕСКОМ ИССЛЕДОВАНИИ МЕХАНИЧЕСКИХ ПРОТЕЗОВ

Uğur Coşkun, Barış Ökçün, Murat Başkurt, Kadriye Kılıçkesmez, Cem Bostan, Ahmet Yıldız, Alev Arat, Tevfik Gürmen, Mehmet Serdar Küçükoğlu

Цель. Мы планировали кинофлюорографическое исследование (КФ), чтобы отметить идеальное открытие и закрытие углов трубки для митрального и аортального механических клапанов. Наша гипотеза, что если мы найдем зону интенсивности, где клапаны были бы оптимально видны, то, начало КФ с этого положения трубки позволило бы сократить продолжительность исследования.

Материал и методы. В период с января 2010 года по август 2011 г. 192 пациентов (средний возраст-51,86±12,80 лет; 101 женщин и 91 мужчина) с митральным (n=135; одностворчатый: 37; двухстворчатый: 98), аортальным (n=87; одностворчатый:19; двухстворчатый: 68) и трикуспидальным (n=3; все двухстворчатый) протезами были включены в исследование. КФ была выполнена с помощью Philips Radiologic System. Для каждого типа и местоположения механических протезов оптимальные углы открытия-закрытия были получены и отмечены на x-y оси графика. Кроме того, мы исследовали, имеется ли квадрант интенсивности зоны.

Результаты. Среди больных с протезированным двухстворчатым митральным клапаном в положении лежа на спине были получены оптимальные изображения: 34 (58,6%) больных были в правом переднем косом положении (RAO) краниальной проекции, 12 (20,7%) были в левом переднем косом положении (LAO) краниальной проекции, 7 (12,1%) были в RAO каудальной проекции и 5 (8,6%) были в LAO каудальной проекции. Среди больных с протезированным двухстворчатым аортальным клапаном в положении лежа на спине показано: 27 (50%) больных были в LAO краниальной проекции, 10 (18,5%) были в RAO краниальной проекции, 9 (16,7%) были в LAO каудальной проекции и 8 (14,8%) больных были в RAO каудальной проекции углов.

Заключение. Согласно нашим результатам, кажется логичным начинать оценку митральной позиции КФ с определения квадранта углов RAO краниальной проекции и аортальной — с LAO краниальной проекции, что позволит сократить время и снизить облучение.

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Ключевые слова: кинофлюорографическое исследование, механические клапаны сердца, дисфункция, излучение.

Introduction

Prosthetic cardiac valves have been used commonly for four decades. Although mechanical cardiac valve related complications are rare; thrombus formation and pannus ingrowths are serious and fatal problems leading to valve obstruction [1–3]. Transthoracic (TTE) and transesophageal echocardiography (TEE) are the standard techniques for the evaluation of prosthetic valve function [4–8]. Quantitative evaluation of leaflet (s) motion is very important. Leaflet (s) opening and closing angle measurements provide important information to recognize prosthetic dysfunction. For this purpose, cinefluoroscopy (CF) is considered the "gold standard" technique [9, 10]. Although CF investigation is practical and beneficial, sometimes it requires long examination durations causing prolonged radiation exposure both for the patient and the cardiologist.

During CF investigation of a particular mechanical heart valve optimal view of mechanical valve's opening

and closing functions are not known. If this was known the radiation duration could be shortened. We could not find any study dealing with this problem. Therefore, we planned a CF study to mark the ideal opening and closing tube angles for mitral and aortic positioned mechanical valves. Our hypothesis was that if we find an intensity zone where the valves were optimally seen, then starting the CF examination from that tube position would shorten the examination duration.

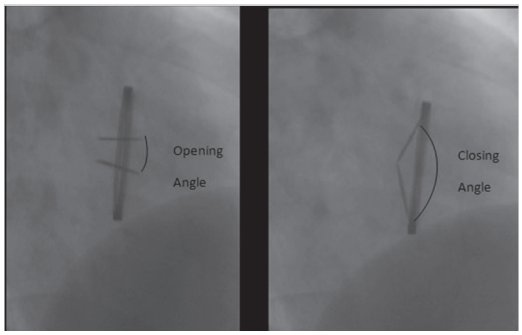

Figure 1. Optimal cinefluoroscopic opening and closing.

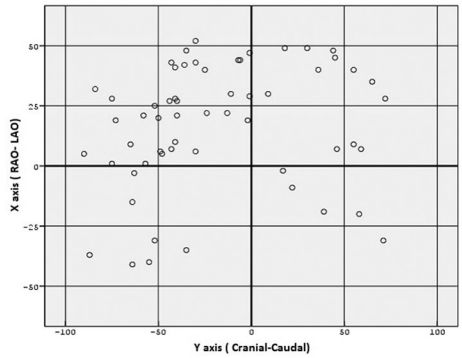

Figure 2. Patients with prosthetic bileaflet mitral valve in supine position.
Abbreviations: LAO — Left anterior oblique position tube angles, RAO — Right anterior oblique position.

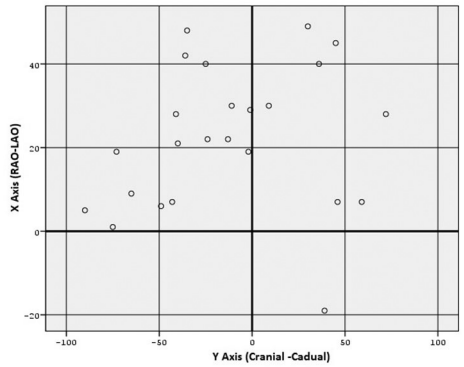

Figure 3. Patients with prosthetic monoleaflet mitral valve in supine position.
Abbreviations: LAO — Left anterior oblique position tube angles, RAO — Right anterior oblique position.

Material and methods

Between January 2010 and August 2011, 192 consecutive patients (mean age 51,86±12,80 years; 101 women and 91 male) with mitral (n=135; monoleaflet:37; bileaflet:98), aortic (n=87; monoleaflet:19; bileaflet:68) and tricuspid (n=3; all bileaflet) prostheses were enrolled into the study. The local ethics committee approved the study protocol, and written informed consent was obtained from all the patients. Patients with normal functioning mechanical valves were selected from our echocardiography laboratory. CF was performed with Philips Radiologic System on the day of the TTE examination. Every prosthetic valve was viewed in multiple projections including cranio-caudal angulations. The evaluation was considered appropriate when the prosthetic valve ring and tilting disk projection parallel to x-ray beam was obtained. In optimal cine-fluoroscopic image the valve leaflet (s) should display thin and linear appearance. This view allows the proper visualization of prosthetic leaflet motion so that opening and closing angles can be calculated (Fig. 1). To achieve optimal CF image, we started the examination first from the supine position and continued respectively with right lateral decubitus, left lateral decubitus, prone positions, and the modified versions of these positions (in lateral decubitus positions; semi-elevation of upper body, in prone position; semi-elevation of upper body, like the baby birth position, in supine position; semi-elevation of upper body and prostrate in prayer position are the examples of modified positions), in order to search for the optimal image. When optimal image was achieved x-ray tube angles were written down and 3 to 10 cardiac cine- cycles were recorded. Optimal CF angle was marked on x-y axis graphic for each valve separately. Patient's radiation doses were below the diagnostic coronary angiography.

Statistical analysis. Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) for Windows version 12 (Chicago, Illinois, USA). Continuous variables were expressed as mean ± SD, while categorical variables were displayed in numbers and percentages. Scatter dot graphics were used to determine the x-ray tube angles.

Results

Between January 2010 to August 2011, 192 patients with prosthetic cardiac valves were evaluated by fluoroscopy. 91 (47,3%) were male and 101 (52,6%) were female. 101 (44,4%) patients had prosthetic mitral valve, 58 (25,5%) had prosthetic valve in the aortic position, Thirty three patients had double prosthetic valves. Thirty (13,2%) patients had prosthetic valves both in mitral and aortic positions, and 3 (1,6%) patients had prosthetic valves both in mitral and tricuspid positions. 56 (24,7%) patients had monoleaflet prosthetic cardiac valves and 171 (75,3%) had bileaflet valves. Baseline characteristics of study population are presented in Table 1.

Fluoroscopic evaluation was performed respectively from supine, right lateral decubitus, left lateral decubitus and prone positions. Among patients with prosthetic bileaflet mitral valve, ideal x-ray tube angles were found from supine position in 58 (65,9%) patients, right lateral decubitus in 17 (19,3%), left lateral decubitus in 8 (9,1%), and in prone position in 5 (5,7%) patients. As shown in Table 2 and Figure 2, most of the patients in supine position were shown in right anterior oblique (RAO) –cranial angles: 34 (58,6%) patients were in RAO-Cranial angles, 12 (20,7%) were in left anterior oblique (LAO) cranial angles. Total of 7 (12,1%) patients were shown in RAO caudal angles and 5 (8,6%) were in LAO caudal angles. Monoleaflet prosthetic mitral valves were mostly shown from supine position RAO-Cranial: 18 (54,5%), 12 (36,4%) were shown from LAO –cranial and only 3 (9,1%) cases were shown from LAO caudal angles (Fig. 3).

Prosthetic aortic valves were also best shown from supine position in most of the cases. Of 68 patients with bileaflet prosthetic aortic valves, 54 (79,4%) were shown from supine position, 9 (13,2%) patients from right lateral decubitus position and 5 (7,4%) patients from prone position. In supine position 27 (50%) patients were shown from LAO-cranial, 10 (18,5%) patients were in RAO cranial, 9 (16,7%) patients were in LAO caudal angles and 8 (14,8%) patients were in RAO caudal angles (Tab. 3, Fig. 4). From 19 monoleaflet prosthetic aortic valve; 14 (73,7%) were shown from supine position, 3 (15,8%) from prone position and 2 (10,5%) patients from right lateral decubitus position.

Discussion

Although echocardiography is currently used routinely for the assessment of heart valve prostheses function, it has certain limitations that may be complemented with information provided by CF [11]. TTE, is usually unable to identify the type of heart valve prosthesis implanted, and frequently cannot detect opening and closing angles of the prosthetic leaflets because of metallic reverberations [11]. Therefore, CF assessment of mechanical heart valve prostheses is a complementary method to echocardiography [11]. CF, especially, should always be a part of diagnostic work-up if there is suspicion of prosthetic heart valve thrombosis and/or pannus formation causing mechanical valve dysfunction [3, 5, 9, 10].

However, achieving ideal opening and closing angles in some of the patients is very difficult and the CF examination may take longer and the radiation exposure may be excessive for both the patient and the physician. Gianculli et al. reported failure in obtaining ideal CF image in 26,7% of the prosthesis for mitral position and 6,9% for aortic position [11]. In our study, we did obtain optimal images, showing opening and closing angles in all of our patients. During CF, we started the examination first from the supine position and continued respectively with right lateral decubitus, left lateral decubitus, prone positions, and the modified versions

Table 1

Baseline characteristics of study population

Age	51,86±12,80
Sex (Female%)	52,6% (101)
Prosthetic aortic valve monoleaflet	8,4% (19)
Prosthetic aortic valve bileaflet	30,2% (68)
Prosthetic mitral valve monoleaflet	16,4% (37)
Prosthetic mitral valve bileaflet	43,5% (98)
Prosthetic tricuspid valve bileaflet	1,3% (3)

Table 2

Patients with prosthetic bileaflet mitral valve in supine position

RAO-Cranial Angles	34 (58,6%)
LAO-Cranial Angles	12 (20,7%)
RAO-Caudal Angles	7 (12,1%)
LAO Caudal Angles	5 (8,6%)

Abbreviations: LAO — Left anterior oblique position tube angles, RAO — Right anterior oblique position.

Table 3

Patients with prosthetic bileaflet aortic valve in supine position

RAO-Cranial Angles	10 (18,5%)
LAO-Cranial Angles	27 (50%)
RAO-Caudal Angles	(14,8%)
LAO Caudal Angles	9 (16,7%)

Abbreviations: LAO — Left anterior oblique position tube angles, RAO — Right anterior oblique position.

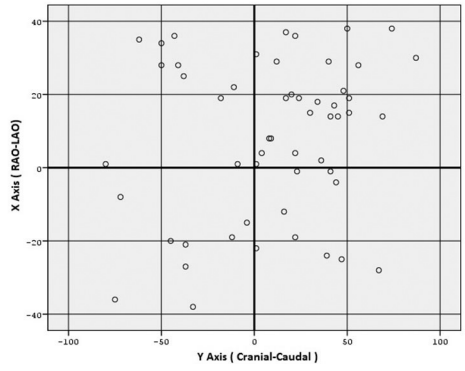

Figure 4. Patients with prosthetic bileaflet aortic valve in supine position.
Abbreviations: LAO — Left anterior oblique position tube angles, RAO — Right anterior oblique position.

of these positions (in lateral decubitus positions; semi-elevation of upper body, in prone position; semi-elevation of upper body, like the baby birth position, in supine position; semi-elevation of upper body and prostrate in prayer position are the examples of modified positions), in order to search for the optimal image. These multiple positions and

the modifications may explain our full achievement of the optimal image, unlike Gianculli et al.

Furthermore, we searched the literature to find a study investigating roentgen tube angle scatter chart in cranio-caudal and right-left oblique axis for mitral and aortic position mechanical prostheses, but we couldn't found any. Therefore, we planned this CF study to mark the ideal opening and closing tube angles for mitral and aortic position mechanical prosthesis to the right-left anterior oblique (X axis) and cranio-caudal (Y axis) planes. In the X-Y axis graphic, we divided the graphic to four quadrants: RAO-Cranial, RAO-Caudal, LAO-Cranial and LAO-Caudal quadrants. Our hypothesis was if we find an intensity zone quadrant with our marked points in X-Y axis plane graphic which will be give us a logical starting point to CF investigation we would achieve less CF time and radiation exposure.

Our study showed that for mechanical prosthesis on mitral position optimal images were mostly at supine position [58 prostheses (65,9%)] and RAO-Cranial angles quadrant [31 prostheses (53,4%)]. Left and right lateral decubitus and, prone patient positions did not have enough number to achieve intensity zone in X-Y axis graphic. In aortic mechanical prostheses optimal CF images were obtained mostly in supine patient position [54 patients (79,4%)], and the intensity zone was found mostly (25 patients (46%)) in LAO-Cranial angles quadrant.

Conclusion

Our results show that it is logical to start CF assessment of mechanical prosthesis by supine RAO-Cranial angles quadrant in mitral position and by supine LAO-Cranial angles quadrant in aortic position to obtain less time consumption and lower radiation exposure. If we can't record ideal image in supine position as we described before we should search in left lateral decubitus and right lateral decubitus positions. If all these positions fail to record ideal leaflet opening and closing angles we can try prone position on roentgen table as a final resort. We recommend an initial CF examination after mechanical valve replacement and save the images to compare with a future CF examination if needed. These recordings will decrease time and radiation consumption in a future CF examination. Furthermore, if the patient has problem in lying down on roentgen table we can set the initial roentgen tube angles from our first CF recordings and take ideal image in very brief time.

Our study may hopefully give way to further large-scaled studies, investigating CF examination specific to the location and type of the mechanical valve, in order to obtain an optimal imaging with shorter radiation exposure durations both for the patient and the physician.

Study Limitations

Most of our patients had bileaflet mechanical valves. Number of patients with monoleaflet valves was not enough to achieve an intensity zone on the RAO-LAO and cranial-caudal quadrants of the CF graphics. A study with larger number of patients with monoleaflet valves can be planned to establish rules for these types of valves.

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"CONTRAST" STUDY: COMPARİSİON OF NEPHROPROTECTİVE THREE PROTOCOLS: ACETYLCYSTEİNE-SODİUM BİCARBONATE-THEOPHYLLİNE, TO PREVENT CONTRAST-İNDUCED NEPHROPATHY

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Aim. The purpose of this study was to compare three prophylactic regimens, sodium-bicarbonate based hydration, sodium-bicarbonate + N-acetylcysteine (NAC), and sodium-bicarbonate + NAC + theophylline, for the prevention of contrast induced nephropathy.

Material and methods. We prospectively randomized 151 patients with baseline eGFR values between 30–59 ml/min/1.73m² who were also undergoing coronary angiography with three prophylactic treatments: intravenous hydration with sodium-bicarbonate (3 ml/kg/h for 1 hours before and 1 ml/kg/h for 6 hours after contrast exposure, group 1; n=50), hydration + NAC (600 mg p.o. twice daily the preceding day and the day of angiography, group 2; n=50), and hydration + NAC + theophylline (600 mg p.o. NAC and 200 mg theophylline p.o. twice daily for the preceding day and the day of angiography, group 3; n=51). The incidence of contrast induced nephropathy (0,5 mg/dl increase in serum creatinine from the baseline value 48 hours after intravascular injection of contrast) from the three groups was compared.

Results. Of the 151 patients, 4 patients (7.8%) in group 3 experienced CIN (p=0.01). CIN did not develop in group 1 and 2.

Conclusion. Among patients with eGFR values between 30–59 ml/min/1.73m undergoing coronary angiography, use of sodium-bicarbonate based hydration alone and sodium-bicarbonate with NAC was associated with a reduction in the rate of contrast induced nephropathy. Sodium-bicarbonate with theophylline therapy was found to have no effect for the prevention of contrast-induced nephropathy.

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"КОНТРАСТ" ИССЛЕДОВАНИЕ: СРАВНЕНИЕ НЕФРОПРОТЕКТИВНОСТИ ТРЕХ ПРОТОКОЛОВ: АЦЕТИЛЦИСТЕИН — НАТРИЯ БИКАРБОНАТ — ТЕОФИЛЛИН, ДЛЯ ПРЕДОТВРАЩЕНИЯ КОНТРАСТ-ИНДУЦИРОВАННОЙ НЕФРОПАТИИ

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Цель. Целью данного исследования стало сравнение трех профилактических режимов терапии: гидратации на основе натрия бикарбоната, натрия бикарбоната + N-ацетилцистеин (NAC), натрия бикарбоната + NAC + теофиллин, для профилактики контраст-индуцированной нефропатии.

Материал и методы. Мы рандомизировали 151 больного с исходной скоростью клубочковой фильтрации (СКФ) со значениями между 30–59 мл/мин/1.73м^2, которые проходили коронарную ангиографию, с тремя профилактическими схемами лечения: внутривенная гидратация натрия бикарбонатом (3 мл/кг/час в течение 1 часа до и через 1 мл/кг/ч в течение 6 часов после контрастного воздействия, 1 группа; n=50), гидратация + NAC (600 мг перорально, два раза в день, предшествующий день и день ангиографии, 2 группа; n=50), и гидратация + NAC + теофиллин (600 мг перорально NAC и 200 мг теофиллина перорально дважды в день в течение предыдущего дня и в день ангиографии, 3-я группа; n=51). Появление контраст-индуцированной нефропатии (0,5 мг/дл увеличение сывороточного креатинина от базового уровня через 48 часов после внутрисосудистого введения контраста) сравнивали в трех группах.

Результаты. Из 151 пациентов, у 4 больных (на 7,8%) в группе 3 была отмечена контраст-индуцированная нефропатия (p=0.01). Контраст-индуцированная нефропатия не развивалась в группах 1 и 2.

Заключение. Среди пациентов со значениями СКФ между 30–59 мл/мин/1.73м^2 при прохождении коронарной ангиографии, использование гидратации только натрия бикарбонатом и натрия бикарбонатом с NAC было связано со снижением частоты контраст-индуцированной нефропатии. Терапия натрия бикарбонатом с теофиллином не оказалась действенной в профилактике контраст-индуцированной нефропатии.

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Ключевые слова: контраст нефропатия, ангиография.

Introduction

Cardiovascular diseases are increasingly becoming the major cause of morbidity and mortality worldwide [1, 2]. Coronary angiography (CAG) is the gold standard method for the diagnosis of coronary artery disease (CAD) [3–5]. CAG-related complications are rare (less than 1–2%) and contrast-induced nephropathy (CIN) is an important one that increases in-hospital and long-term morbidity and mortality as a result of acute and chronic renal failure [4].

CIN was first defined in 1960 and is the third leading cause of hospital-acquired acute renal failure [6–8]. While the incidence of CIN is below 2% in patients with normo-functioning kidneys and 5% in mild renal failure, it can rise to up to 50% in patients with diabetes together with severe renal failure [6, 8, 9]. CIN is defined as at least 0.5mg/dl or 25% increase in serum creatinin (SCre) levels 48 hours after contrast media exposure [6, 8, 9]. In- hospital mortality is 35.7%, and 1-year mortality is 55% in patients requiring dialysis [6–9].

Although hydration with 0.9% NaCl came forward previously, recent studies revealed lower CIN incidence with hydration with sodium bicarbonate [6]. Since oxida-

tive stress plays an important role in CIN pathogenesis, free oxygen radical scavenger sodium bicarbonate seems more promising than saline in the prevention of CIN.

NAC is a potent antioxidant agent which has vasodilator effects on renal tissue. There are more than 70 clinical trials in literature about NAC's role in CIN prevention [10]. NAC was reported to reduce the relative risk of CIN by 32–56% in some meta-analysis [10–12].

Theophylline is a competitive adenosine antagonist [11,13]. Adenosine, caused by the destruction of ATP due to contrast agents, vasoconstrict afferent arteriole of the kidney, and the degradation of adenosine forms precursors of free oxygen radicals [14,15]. A meta-analysis of 7 randomized controlled studies showed significant results in favour of prophylactic theophylline administration against CIN [12].

Our aim in this study was to compare 3 previously unexplored approaches (hydration with sodium bicarbonate, hydration with sodium bicarbonate + oral NAC, and hydration with sodium bicarbonate + oral NAC + oral theophylline) for CIN prevention in patients with moderate degrees of chronic renal disease (estimated Glomerular Filtration Rate (eGFR) 30–60 mL/min/1.73m^2).

Material and methods

Patients. We enrolled 151 consecutive patients with eGFR 30 to 60 ml/min/1.73m^2 who were referred to Istanbul University Cardiology Institute for elective CAG. Istanbul university Cerrahpaşa Medical Faculty ethical committee approved our study, and written informed consent was obtained from all patients.

The GFR was estimated using the formula of modification of diet in renal disease (MDRD) Formula:

MDRD formula (mL/dk/1.73m^2): 186 x serum creatinine (µmol/L) x age (For women multiple by 0.742)

Calculations were made automatically from an on-line site, http://nkdep.nih.gov/professionals/gfr_calculators/orig_con.htm site.

Patients with acute coronary syndrome, contrast medium exposure within 10 days, eGFR <30 and >60 ml/min/1.73m^2, cardiogenic shock, New York Heart Association class 3–4, pregnancy, age <21 years, known allergy to NAC, theophylline or contrast agents, contraindications to theophylline, >4 Lown arrhythmia classification, hemodynamic instability or patients taking drugs that may interact with theophylline were excluded from the study.

All of the nephrotoxic drugs were discontinued at least 24 hours before contrast media exposure.

Study protocol. All patients were hydrated with an initial intravenous bolus of 3 ml/kg/h of alkaline saline solution with NaHCO3 for 1 hour before the procedure, followed by infusion of 1 ml/kg/h of the same solution during and for 6 hours after the procedure. The NaHCO3 solution was prepared by adding 154 mL of 1000mEq/L NaHCO3 to 846 mL of 5% dextrose in water.

Patients were randomized by using a randomization method in a 1:1:1 ratio to receive one of the following regimens:

- Group 1: Intravenous hydration with sodium bicarbonate (n=50)
- Group 2: Intravenous hydration with sodium bicarbonate plus NAC (600 mg p.o. twice daily the day before and the day of CAG) (n=50)
- Group 3: Intravenous hydration with sodium bicarbonate bicarbonate plus NAC (600 mg p.o. twice daily the day before and the day of CAG) plus theophylline (200 mg p.o. twice daily the day before and the day of CAG (n=51)

We used a computer-generated randomization scheme for group assignment.

CAG. CAG was performed using the femoral approach with Standard Judkins method. A nonionic, low-osmolar contrast agent, iopromid (Ultravist 300 mL iv flacon, Bayer®) was used in all patients. For all patients, the amount of contrast given during the procedure was recorded by nursing staff. Urine output was monitored for 12 hours after the procedure. The SCre and blood urea nitrogen (BUN) levels were measured 48 hours after contrast media exposure.

Follow-up and Endpoints. The primary endpoint of the study was the incidence of CIN, and the secondary end point was the need for dialysis. Follow-up data were obtained from the hospital's database. An absolute 0.5 mg/dL increase in SCr levels 48 hours after administration of radiocontrast medium was considered as CIN. Patients who developed CIN by 48 hours were closely followed, and BUN and SCre levels were repeated at the 5th and 10th day. If there was no evidence of significant decline in levels of BUN and SCre, a nephrology consultation was requested.

Statistical analysis. All of the statistical analysis was performed by Istanbul University Cerrahpaşa Medical Faculty Biostatistical department. Demographic features were analysed by arithmetic averages and standard deviations were measured (mean ±SD). Categorical variables were evaluated with the chi-square test. P-value lower than 0.05 was considered statistically significant. The association between two quantitative variables was assessed by correlation test and pearson-Brovais correlation coefficient (r value) was used. Negative "r" value referred inverse relation and positive "r" value referred relation in the same direction. While absolute "r" values less than 0.250 were considered an indicator of ignorable weak commitment, absolute "r" values ≥0.5 sought to mention casualty links. Oneway Anova test was used for analysis of more than two variables. Effects of related variables were evaluated by lineer regression test. SPSS for Windows 15.0 statistical package program was used.

Results

151 patients participated in our study and were divided into 3 groups. Patients' demographic features are given in Table 1.

There were no differences among groups regarding age, sex, hypertension, diabetes, peripheral arterial dis-

Table 1

Demographic and clinical features of groups

Characteristic	Hydration group N:50	Hydration+NAC N:50	Hydration+NAC+theophylline N:51	p value
Age	68.3 (±10.2)	67.2 (±9.4)	65.3 (±10.3)	NS
Chronic heart failure	12 (%24)	19 (%38)	9 (%7.6)	P<0.05
Diabetes mellitus	15 (%30)	17 (%34)	24 (%47.1)	NS
Hypertension	32 (%64)	30 (%60)	31 (%60.7)	NS
Peripheral arterial disease	2 (%4)	1 (%2)	2 (%4)	NS
History of MI	22 (%44)	27 (%54)	7 (%13.3)	P<0.05
Male gender	34 (%32)	36 (%72)	35 (%68.6)	NS
SAP	22 (%44)	15 (%30)	16 (%31.4)	NS
USAP	17 (%34)	23 (%46)	22 (%43.1)	NS
Heart failure	5 (%10)	8 (%16)	5 (%9.8)	NS
Initial eGFR (mL/dk/1.73m)	53.1±7.9	50.2±8.5	49.8±6.6	NS
Initial BUN level (mg/dL)	27.8±7.4	25±9.6	28.1±11.7	NS
Initial creatinine level (mg/dL)	1.33±0.1	1.36±0.2	1.39±0.2	NS

P<0.05: statistically significant, NS: statistically non-significant.

Abbreviations: BUN — blood urea nitrogen, eGFR — estimated glomerular filtration rate, calculated by MDRD formula, NAC — N-acetylcysteine, SAP — Stable angina pectoris, USAP — Unstable angina pectoris.

ease and history of myocardial infarction, however the incidence of patients with heart failure and history of myocardial infarction was significantly less in the third group than other groups (p<0.05). The reasons for hospital admission are shown in Table 1. There were no differences between groups according to CAG indications. Renal function tests (SCre and BUN levels) were performed before the procedure, and they were similar among groups (Table 1). Renal function tests after contrast exposure, contrast volumes and incidence of CIN are given in table 2. The mean contrast volume used and urine output measured for 12 hours after contrast exposure were not different between groups.

CIN only developed in the NAC + theophylline group (p=0.01) (Table 2). SCre levels returned to baseline levels in all of the patients who experienced CIN, and none of them required dialysis. 2-year follow-up of these patients by hospital data revealed no death, no major adverse cardiac events or need for dialysis.

The BUN levels measured at the 48th hour were not significantly different between the 3 groups. However, when were compared each treatment group, the SCre levels measured at the 48th hour were significantly higher in group 3 than group 1, and in group 3 than group 2 (p=0.038 and p=0.006, respectively) (Table 2).

No side effects due to sodium bicarbonate, NAC nor theophylline administration were detected during the study.

We also noted all of the medications that patients were chronically receiving. All medications, except clopidogrel, were similar between groups. Clopidogrel usage was significantly higher in the NAC + theophylline group (p=0.013). Other biochemical parameters (haemoglobin, haematocrit, sodium, potassium, uric acid, and proteinurea) measured before CAG were not different among groups.

Table 2

Renal functions after the procedure and Incidence of contrast-induced nephropathy

	Group 1* (n=50)	Group 2** (n=50)	Group 3*** (n=51)	p value
Contrast volume (mL)	105.5±56.3	101.9±46.3	97.9±50.5	NS
Diuresis (12 hour)	1420±105	1390±120	1404±110	NS
48. hour BUN (mg/dL)	28.3±11.4	25±10.2	29.5±10	NS
48. hour creatinine (mg/dL)	1.32±0.2	1.31±0.2	1.43±0.3	P<0.05
Contrast-induced nephropathy	0 (%0)	0 (%0)	4 (%7.8)	P=0.01

*only hydration with NaHCO3, ** hydration with NaHCO3 + NAC therapy, *** hydration with NaHCO3 + NAC + teofilin therapy.

P<0.05: statistically significant, NS: statistically non-significant.

Abbreviation: BUN — blood urea nitrogen.

Discussion

We compared 3 strategies for protection from CIN in patients with moderate degree renal failure (eGFR 30–60mL/min/1.73m^2) undergoing elective CAG and found that CIN only occurred in hydration + NAC + theophylline group. CIN did not develop in the hydration group or in the NAC plus hydration group.

Currently, many strategies have been studied to prevent CIN development, but unfortunately no medication or strategy has been proven to totally prevent CIN development (6,9,10,16). Medications promising and displaying positive results are NAC, theophylline, statins, ascorbic acid and sodium bicarbonate [6, 9, 10,16].

Imbalance between increased vasoconstriction associated with adenosine, endoteline and free oxygen radicals and decreased vasodilatation associated with nitric oxide and prostaglandins and direct toxic effect of contrast media on renal tubular cells are the most common mechanisms of CIN [6, 7, 9]. SCre begins to rise 24 hours after

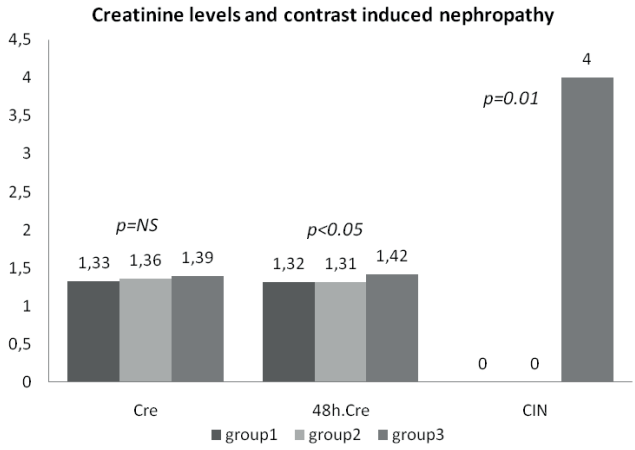

Figure 1. Creatinine levels and contrast induced nethropathy

contrast media administration, peaks on the 5th day, and most of the time returns back to normal levels within 10 days [6, 8, 9]. Incidence of patients requiring dialysis after contrast medium exposure is rare (1–4%) (2).

Our findings reveal absolute benefit of hydration with sodium bicarbonate and positive contribution with NAC for CIN protection. The importance of hydration in preventing CIN is accepted by physicians today, but which hydration protocol is better still remains unclear. Hydration with sodium bicarbonate has some advantages over hydration with 0.9% NaCl. First of all, sodium bicarbonate is a reactive free radical scavenger with antioxidant properties. It reduces free radical formation by alkalinizing renal medulla and urine and protects kidney from oxidant injury. Another advantage of sodium bicarbonate over saline is that sodium bicarbonate might be used in urgent situations because it is effective when given only 1 hour before contrast exposure [17–20].

We observed no increase, in fact a slight decrease, in SCre levels at the 48th hour in NAC + hydration group (initial cre=1.36 48th hour cre=1.31, p>0.05). This finding may indicate additional benefit of NAC compared to hydration alone (Fig. 1).

Recently published studies demonstrate that NAC might be more effective in patients who receive smaller amounts of contrast media (75–117 mL), high-osmolar contrast media, NAC therapy the day before the procedure, over 12 hours of hydration, and also in patients who are over 65 years, have diabetes and in whom SCre levels are not very high [10–12]. Some of these factors overlap with our study design so that we may have achieved positive results with NAC.

On the other hand, other published studies have shown that NAC therapy reduces SCre levels independent from eGFR values, even in patients with initial normal SCre levels by increasing renal tubular creatinine excretion. Therefore, some researchers state that creatinine levels are already reduced in patients on NAC therapy and NAC has no effect on CIN prevention [12, 21].

The prophylactic administration of theophylline does not appear to prevent CIN according to our findings. The renoprotective effect of theophylline is more obvious in patients with severe renal failure, however we excluded these patients [12,13]. Another probable explanation may be the decreased level of adenosine-related vasoconstriction due to adequate renoprotective effect obtained from sodium bicarbonate and NAC may be another explanation why we could not observe the benefits of theophylline. In fact, there are contradictory findings about theophylline in the literature. In an animal model, theophylline has not been employed to improve microcirculatuar blood flow, intra-renal hypoxia nor contrast-associated free radical formation after 30 minutes of iv contrast infusion [22]. Also most of the favourable results with theophylline in the literature are obtained from placebo-controlled studies and focused on to investigate the efficacy of saline in the hydration arm [12, 13, 23, 24]. Demir et al study which was designed in patients without renal failure nor diabetes; theophylline was not only found to have adverse effect on CIN but was also associated with side-effects. The investigators showed increases in serum creatinin levels by adding theophylline 200 mg/day to saline hydration and concluded that the adenosine receptor gene polymorphism or the different distribution of adenosine receptors in normal kidneys compared to injured ones may be the reason of this phenomenon [23]. Abizaid et al reported that aminophylline plus saline hydration does not reduce the incidence of CIN when compared with saline hydration alone [25]. Malhis et al searched for the theophylline's ability to reduce the incidence of CIN and stated that iv administration of theophylline in addition to sodium bicarbonate hydration prevents CIN in moderate and high risk patients. However the volume of contrast used in the procedures was higher in the group of patients who developed CIN than who did not developed CIN (196.4±116.8 ml vs 138.2±74.3 ml p=0.006) [26].

Only 4 patients of the 151 patients (2.6%) experienced CIN in our study. We should note in this report that 2.6% is an acceptable CIN incidence for the patients in moderate-risk group for CIN at the present time. In a similarly-designed study by Baskurt et al; the investigators studied the role of theophylline, NAC and saline hydration that was given before CAG for the prevention of CIN in patients with moderate degree renal failure. While a total of 12 patients of the 217 patients (5.5%) experienced CIN in saline hydration only and NAC + saline hydration group, none of the patients in theophylline + NAC + hydration group experienced CIN (p=0.033) [12]. We observed less CIN due to the development of CAG techniques and the use of less contrast media (119.9 ml vs 101.7 ml). Another possible explanation of this result may be the decreased level of adenosine-related vasoconstriction due to effective renoprotection obtained from sodium bicarbonate and NAC, so the benefit of theophylline could not be shown.

The number of patients on clopidogrel therapy was statistically higher in the NAC + theophylline group. Clopidogrel interacts with many drugs. A possible interaction between clopidogrel and theophylline may be the reason of CIN development in this group. However, we couldn't find any reported interaction between clopidogrel and theophylline in literature [27].

Conclusion

Hydration with sodium bicarbonate is an absolutely effective and safe approach for CIN prevention after elective CAG in patients with moderate degree of renal failure. NAC plus sodium bicarbonate combination therapy may provide further benefits. Theophylline therapy doesn't seem to provide additional benefit in preventing CIN in this group of patients. These findings should be confirmed in larger randomized trials.

Study limitations

The main limitations of our study were its single-centred basis and relatively small patient population size. Another issue is that it was not blinded. Furthermore, we did not include patients with mild or severe chronic renal failure, and our findings need to be clarified in these populations. We measured SCre levels only at the 48th hour, therefore we may have missed later increases in SCre levels and underestimated CIN incidence. We also did not study the effects of sodium bicarbonate on the urine or arterial pH, but these are influenced by other factors as well. It is also conceivable that we could have measured Cystatin-C levels as well. Cystatin-C is a sensitive marker of GFR, not affected by tubular transport, indicating renal functions better than creatinine.

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EFFECT OF SEVOFLURANE EXPOSURE ON ADRIAMYCIN-INDUCED INJURIES TO MYOCYTES

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The study is to investigate the potential protective effect of sevoflurane on adriamycin induced myocyte injury. We prepared primary myocyte culture from neonatal rats and subjected the cells to adriamycin treatment. We found that adriamycin treatment induced cell apoptosis, decreased cell vitality, which could be reversed with sevoflurane exposure after the drug treatment, potentially through the regulation of Bcl-2 anti-apoptotic pathway. The study suggested the potential roles of sevoflurane in clinical management of patients after adriamycin chemotherapy.

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Key words: anesthetics, sevoflurane, myocyte, chemotherapy, adriamycin.

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ЭФФЕКТ ВОЗДЕЙСТВИЯ СЕВОФЛЮРАНА НА АДРИАМИЦИН-ИНДУЦИРОВАННЫЕ ПОВРЕЖДЕНИЯ МИОЦИТОВ

Li-hua Fan[1], Xin Han[1], Qing-quan Lian[2], Jun Li[2], Hou-xing Lei[1], Nling Zhang[1], Xiang-dong Xu[1], Xiang-hong Lu[1]

Целью исследования является изучение потенциального защитного эффекта севофлюрана на адриамицин- индуцированные повреждения миоцитов. Мы подготовили первичную культуру миоцитов новорожденных крыс и подвергли клетки воздействию адриамицина. Мы обнаружили, что воздействие адриамицина индуцирует апоптоз клеток, снижает жизнеспособность клеток, что может быть обратимо воздействием севофлюрана после медикаментозного лечения, возможно, через регулирование Bcl-2 антиапоптозных путей. В исследовании предлагается потенциальная роль севофлюрана в области клинического ведения пациентов после химиотерапии адриамицином.

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Ключевые слова: анестетики, севофлюран, миоцит, химиотерапия, адриамицин.

Introduction

The previous exposure to chemotherapy drugs can increase the cell death after anesthesia and surgical procedures [1]. For instance, the adriamycin (Doxorubicin) that is widely used to leukemia and lymph tumors can induce injury to the heart even after the end of drug administration [2–4]. Therefore the searching of safety anesthesia agent is important in clinical management of patients following adriamycin chemotherapy.

Sevoflurane is one of the commonly used anesthetics, and has been found to inhibit the cellular injury caused by ischemia-reperfusion in the rat heart [5, 6]. The potential mechanism involves the upregulation of Bcl-2, for example. In present study we investigated if sevoflurane can also be protective for adriamycin induced cellular injury with cultured myocytes from neonatal rats. This would provide guidelines for clinical safety in management of patients underwent chemotherapy with adriamycin.

Materials and methods

Animal and cell culture. SPF level SD rats with pregnancy 16–18 days were purchased from Lasike animal company (SCXK-Hu-2007–0005), and maintained in the SPF animal facility of key lab of anesthesia, Wenzhou Medical College, the second affiliated hospital until delivery.

For primary myocyte culture [7], 10 SD rats at P0 were sacrificed and the heart was harvested. The tissue was dissected in 4 degree DMEM (Gibco, US) and rinsed in 4 degree D-hank solution (Suolaibao, Beijing, China). Then the cells were dissociated with 6 mL 0.125% trypsin (Gibco, US) for 3 minutes at 37 degree before the supernatant was collected. The digestion was stopped with 10% fetal bovine serum (FBS) -DMEM medium. The processes were repeated for 3–4 times and finally all supernatant was filtered to remove all remained tissues. The dissociated myocytes were seeded at 1X105 / mL in 25 mL bottle in 5% CO2 incubator (Thermo, US) for 48 hours. Then the cells were treated with 0.1% trypsin and reseeded at 5 X 104 /mL in 96 well plate (200 μL/well) or 6 well plate (2 mL/well with 24 mm X 24 mm cover slip inside) with 10% FBS-DMEM medium for 24 hours before experiment.

Treatments. The cells were randomly assigned into four groups (n=15 each): Control (C) group: no treatment; Adriamycin (D) group: 1 μM/L adriamycin (Meilun, Dalian, China) in presence for 24 hours; Sevoflurane (S) group: no treatment before Sevoflurane exposure; Adriamycin+ Sevoflurane group (DS) group: 1 μM/L adriamycin in presence for 24 hours before Sevoflurane exposure.

For Sevoflurane exposure, 95% air-5% CO2 mixture was passed through Vapor 2000 sevoflurane flowmeter (Draeger, Germany) at 2 L/min, and the concentration of sevoflurane was monitored by Vamos monitor for anesthetics (Draeger, Germany) to be stable at 2.4%. The cells were treated for 2 hours before additional 2 hours incubation.

Cell vitality. For Trypan Blue staining, 2 μL of 4% Trypan Blue solution was mixed with 18 μL cell suspension for 1 minute. Then the cells were counted within 3 minutes on the counting slide.

For MTT method, the cultured cells in 96 well plate were treated with 20 μL 5 mg/mL MTT solution and 200 μL DMEM for 4 hours. Then 150 μL DMSO was added for 10 minutes with shaking. Finally the plate was read with Multiskan MK3 at 490 nm for optic density (repeated for 3 times each).

Immunochemistry. The cells were fixed with 4% PFA at room temperature for 30 minutes before wash with PBS and 0.5% triton treatments. Then the primary antibody (mouse-α-SA, 1:200; mouse-Bax, 1:100; mouse-Bcl-2, 1:100) was incubated together with the cell overnight at 4 degree before PBS wash. Finally the secondary antibody was added for 2 hours at room temperature before visualization and image acquisition.

ELISA for cTnI and NT-proBNP measurement. The concentrations of cTnI and NT-proBNP were measured as described in the kit. Briefly, the sample was mixed with antibody, HRP-Streptavidin for incubation for 1 hour before visualized with solution A and B for 10 minutes in the dark. Finally the reaction was stopped with stop solution. The optical density was read at 450 nm and was calculated for sample concentration based on the standard curve from the standard samples.

Western blot for NF-κB. The total proteins were extracted and 30 μg protein sample was put on SDS-PAGE electrophoresis before PVDF-membrane transfer. Then the membrane was blocked with 5% milk powder solution for 2 hours then incubated with primary antibody at 1:1000 for 2 hours at 37 degree before secondary antibody incubation for 1 h at 37 degree. Finally the ECL kit was used for visualization and the band was scanned with TYTOOPH system for analyses. The β-actin band was used as internal control.

Flow cytometry for cell apoptosis examination (AnnexinV/PI double staining). The cells after treatment were treated with AnnexinV antibody-FITC and propidium iodide (PI) to analyze the pure apoptotic cell population.

Statistics. The data were analyzed with SPSS 17.0 software (Chicago, US). The data in normality distribution was represented with mean ± SD and intergroup comparisons were performed with One-way ANOVA. $P<0.05$ was considered as statistically significant.

Results

Cell vitality; the cTnI and NT-proBNP concentration

We found that the average survival rate of primary myocyte culture was 95%. With MTT method, the MTT values in D and DS group decreased in compared to the C group, suggesting for the toxicity of adriamycin treatment. The sevoflurane did not decrease the cell vitality since the S group showed no changes.

In addition, in compared to C group, we found that the cTnI and NT-proBNP concentration increased in D group but not the S and DS group. Interestingly, DS group showed lower cTnI and NT-proBNP concentration in compared to D group.

The cell apoptosis rate and protein expression levels

We found that in C group the cell apoptosis rate was low, which increased significantly in D group. The adriamycin treatment induced cell apoptosis was reduced by sevoflurane exposure (DS group).

Interestingly, these changes in cell apoptosis accompanied series changes of protein expression. The increase in Bax/Bcl-2 ratio in D group was eliminated by sevoflurane exposure (DS group). In addition, this accompanied with the increase in NF-κB protein expression.

Discussion

The present study set up a model of primary myocyte culture from neonatal rat with improvement from previous studies (95% survival rate and 83% purity). We found that as previously described [7], low concentration adriamycin treatment could trigger cell apoptosis after 24 hours incubation. In addition, we showed that the sevoflurane exposure, which is a common anesthetic in clinical management, could reduce the toxicity of adriamycin treatment. This validated the use of sevoflurane during anesthesia of patients underwent adriamycin chemotherapy.

Table 1

The cell vitality; the cTnI and NT-proBNP concentration in the medium (n=5)

Group	MTT value	cTnI (ng/ml)	NT-proBNP (ng/L)
C	0.62±0.28	7.9±2.7	164±20
D	0.39±0.14a	11.4±1.6a	228±12a
S	0.62±0.34	7.2±1.3	168±33
DS	0.41±0.16 ab	7.8±0.5b	180±34b

[a]P<0.05 in compared to C group; [b]P<0.05 in compared to D group.

Table 2

The cell apoptosis rate and protein expression levels (n=5)

Group	Cell apoptosis (%)	NF-κB	Bax	Bcl-2	Bax/Bcl-2
C	1.9±0.8	0.75±0.04	2.3±0.7	1.6±0.4	1.3±0.4
D	37.8±4.5a	1.21±0.13 a	2.8±1.2a	1.3±0.3a	2.2±0.4a
S	1.6±0.4 b	0.74±0.05 b	2.4±0.8 b	1.6±0.6	1.5±0.3
DS	10.4±1.1 ab	0.91±0.06 ab	2.5±0.7b	1.7±0.7b	1.7±0.3 ab

[a]P<0.05 in compared to C group; [b]P<0.05 in compared to D group.

cTnl is a sensitive and specific biomarker for heart injury in the early phase [8, 9]. NT-proBNP is an important biomarker for heart failure [10] and is ready to be detected in the culture medium. The present study utilized ELISA method to detect the changes of the two molecules and showed that sevoflurane exposure could actually prevent the further damage after adriamycin treatment.

We further explored the potential molecular signaling pathways involved in the protective effects of sevoflurane exposure. As expected, the Bcl-2 pathway is upregulated following adriamycin treatment, which was prevented by sevoflurane exposure, suggesting the potential target of sevoflurane [11]. In addition, the NF-κB protein expression is associated with the changes described.

In conclusion, we believe that sevoflurane might be a safe anesthetic for patients underwent adriamycin chemotherapy.

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DIAGNOSIS OF ARRHYTHMIA DISEASES USING HEART SOUNDS AND ECG SIGNALS

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This paper presents a novel method for the detection of Arrhythmia diseases using both heart sounds and ECG signals. This automated classification and analysis system is aimed to assist the cardiologist to make the diagnosis faster and more efficient. Most of the heart valve disorders are reflected to heart sounds and can be detected through Phono Cardio Gram (PCG) signal analysis. Heart sounds carry information about the mechanical activity of the cardiovascular system. The heart sound segmentation process segments the Phono Cardio Gram (PCG) signal into four parts: S1 (first heart sound),systole, S2 (second heart sound) and diastole. It can be considered as one of the most important phases in the auto-analysis of PCG signals. Systolic and Diastolic time periods of heart sound signals are used to detect the abnormality of heart functions. The Systolic and diastolic time periods are matched with the ECG signals. The interval between two consecutive R peak values in ECG signal is considered as one cardiac cycle. A single cardiac cycle consists of S1, Systole, S2 and Diastole. Both Echocardiogram and Electrocardiogram signals are analyzed for the accurate diagnosing of cardiac vascular diseases.

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Keywords: Heart Sound, PCG signal, HRV features, Arhythmia disease, Systole, Diastole.

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ДИАГНОСТИКА АРИТМИИ ПОМОЩЬЮ ЗВУКОВ СЕРДЦА И ЭКГ-СИГНАЛОВ

Kalaivani V.

Эта статья представляет новый метод выявления аритмии с использованием как звуков сердца, так и ЭКГ-сигналов. Эта автоматизированная классификация и анализ системы созданы для помощи кардиологам, чтобы установить диагноз быстрее и эффективнее. Большинство нарушений сердечных клапанов проявляется звуками, которые могут быть обнаружены с помощью анализа сигналов фонокардиограммы (PCG). Звуки сердца несут в себе информацию о механической деятельности сердечно-сосудистой системы. Процесс сегментации звуков сердца разделяет сигнал PCG на четыре части: S1 (первый звук сердца), систола, S2 (второй звук сердца) и диастола. Это можно рассматривать как один из важнейших этапов в авто-анализе PCG сигналов. Систолические и диастолические временные периоды звуковых сигналов сердца используются для обнаружения нарушения функции сердца. Они соответствуют ЭКГ-сигналам. Интервал между двумя последовательными пиковыми значениями R на ЭКГ сигнале рассматривается в качестве одного сердечного цикла. Один сердечный цикл состоит из S1, систолы, S2 и диастолы. Как на эхокардиограмме, так и на электрокардиограмме, сигналы анализируются для точной диагностики сердечно-сосудистых заболеваний.

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Ключевые слова: звук сердца, PCG сигнал, особенности вариабельности сердечного ритма, аритмия, систола, диастола.

Introduction

In recent times, phonocardiogram has been playing an important role in the diagnosing of cardio vascular diseases. With the decrease in cost and increase in computation power of personal computers, a sophisticated and cost-effective PC-based classification and analysis system can be developed to assist the cardiologist to make the diagnosis faster and more efficient. This system should be able to extract the features, process, classify, identify and analyze the heart sounds and ECG signals efficiently and reliably. More importantly, it can detect early signs of Arrhythmia diseases such as, Sinus Node Arrhythmias, Atrial Arrhythmias, Junctional Arrhythmias, Ventricular arrhythmias, Atrioventricular Blocks, Bundle Branch blocks and provide objective diagnosis based on some criteria defined by the cardiologist himself. The proposed system will not only extend cardiologist's capability and productivity during examination but also provide an automatic tool in the mass screening of heart diseases classification. So, the proposed system is suitable for people residing at rural areas and the remote places away from the city. Our proposed system plays an important role to save the life of patient by immediate analysis of Heart sounds and ECG signals in rural areas through Public Health Care Centers by Enhancing Modern Health Care Scenario.

Related Work

Shivnarayan Patidar et al (2013) proposed a method for the segmentation of cardiac sound signals using tunable-Q wavelet transform (TQWT). The murmurs from cardiac sound signals were removed by suitably constraining TQWT based decomposition and reconstruction. The envelope based on cardiac sound characteristic waveform (CSCW) was extracted after the removal of low energy components from the reconstructed cardiac sound signals. Ali Moukadem et al (2012) developed a module for the segmentation of heart sounds which was divided into three main blocks: localization of heart sounds, boundaries detection of the localized heart sounds and classification block to distinguish S1 and S2. The heart sounds localization method was based on the S-transform and Shannon energy, and was evaluated against the white additive Gaussian noise. The above works pave a foot path for the preliminary work of this paper.

Deboleena Sadhukhan et al (2012) proposed an algorithm for automatic detection of the R-peaks from a single lead digital ECG data. In order to localize the QRS regions, the squared double difference signal of the ECG data is used. Sabarimalai Manikandana M et al (2012) proposed a new R-peak detector, which is based on the new preprocessing technique and an automated peak-finding logic. The proposed peak-finding logic is based on the Hilbert-transform (HT) and moving average (MA) filter. The proposed preprocessor with a Shannon energy envelope (SEE) estimator is better able to detect R-peaks in case of wider and small QRS complexes, negative QRS polarities, and sudden changes in QRS amplitudes. The above methods are useful for the extraction of features of ECG signal.

Articles in the literatures focus on ECG signal processing algorithms for the Classification (i.e. the identification) of the diseases. Most research has been undertaken in identification of the cardiac diseases using ECG signals and in different physiological conditions. Progress has been made in the identification of the cardiac diseases and the analysis of features extracted from ECG signals.

Processing of Heart Sounds

Cardiac auscultation is one of the diagnostic technique and cost effective way to diagnose the condition of the heart valves. Heart sound has two major components called first heart sound S1 and second heart sound S2. The period between S1 and S2 is called systole and period between S2 and next S1 is called diastole. If there is a problem with one of the heart valves, erroneous sounds can be heard in either systole or diastole phase. In severe cases, the other sounds can completely dominate and distort S1 and S2. These sounds are called murmur and they are the indicators of valvular cardiac disorder. Moreover, the availability of new diagnosis tools such as echocardiogram resulted in decline in the auscultation method. But, cardiac auscultation still plays a key role in small clinics and rural medical facilities.

A phonocardiograph is used to record the heart sounds. Also, ECG signal is recorded simultaneously along with the heart sound using standard ECG equipment. In this paper, heart sound signal and ECG signal are both can be used for the detection of arrhythmia disease.

Heart sound is preprocessed for the classification. The raw heart sound is filtered by a band pass filter with pass band of 20-850 Hz to remove noise and for further analysis. Down sampling is done to match its sampling frequency to that of ECG signal so that each sample of two signals match up, this is for convenience during segmentation. Heart sound signal is then denoised using wavelet denoising technique.

Segmentation of heart sound detects and identifies each part of cardiac cycle, which are S1, Systole, S2 and Diastole. It is planned to measure amplitude and duration of first heart sound S1 and second heart sound S2. The first heart sound S1 results when blood is pumped from the heart to the rest of the body, during the latter half of cardiac cycle and it is comprised of sounds resulting from rise and release of pressure within the left ventricle along with the increase in ascending aortic pressure. After blood leaves the ventricles, the simultaneous closing of the semilunar valves, which connect the ventricles with the aorta and pulmonary arteries, causes the second heart sound.

Relation between Heart Sound and ECG signal

The Figure 1 shows ECG signal and Heart Sound. The ECG signal is compared with the Heart sound signal. The ECG signal represents the electrical pulses that cause the heart to beat. ECG signal with heart sound is shown in the following figure.

The spike in the ECG signal is called the QRS complex. It corresponds to the contractions of the ventricles (the lower chambers of the heart) which are the beginning of systole. The S1 sound starts at the peak of the QRS complex, (ie) the R positions on the ECG signal. The S2 sound occurs after the T wave but before the next QRS complex. The period between S1 and S2 is called Systole and the period between S2 and next S1 is called Diastole. Therefore, a single cardiac period consists of S1, Systole, S2 and Diastole. One cardiac period corresponds to the period between two consecutive R waves (RR interval).

In this paper, S1, Systole, S2 and Diastole are extracted from the Heart sound signal (PCG).Also, RR interval is extracted from ECG signal. These two are compared to detect the abnormality of the patient. Determination of RR interval plays a major role for the identification of arrhythmia diseases such as bradycardia and tachycardia. For the identification of other types of arrhythmia diseases, other parameters of ECG signal such as P wave, QRS complex, ST interval and T wave can be used (Fig.2-5).

Cardiac disease analyzing system

The raw ECG signal contains some low and high frequency noises. The baseline wander noise is low frequency noise and it mainly affects the edge function of ECG signal. The baseline wander noise can be removed by using the median filter. This baseline drift can be eliminated without changing or disturbing the characteristics of the ECG waveform. The muscle noise is high frequency noise and it affects the structure of the wave form. It can be removed using the daubechies wavelet transform. The wavelet transforms de-noising process consists of three steps which are given as: **Decompose:** In this step, wavelet function is selected and level of process defined. The ECG signal de-noising wavelet function, mother wavelet is used. **Threshold:** In this step, threshold is selected and applied to each coefficient level. **Reconstruction:** The reconstruction step subtracts the original signal from the threshold applied coefficient signal.

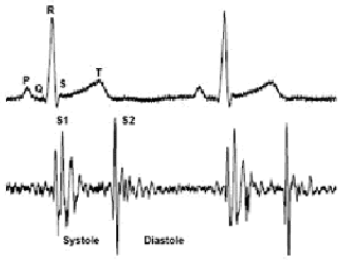

Figure 1. Relation between ECG and Heart Sound.

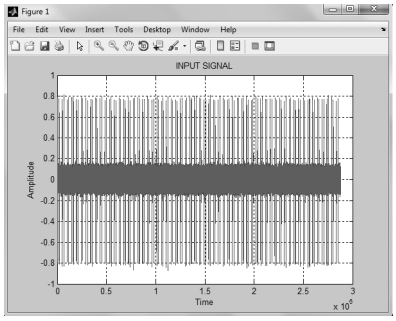

Figure 2. The input PCG signal.

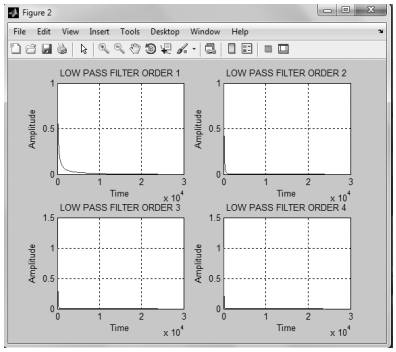

Figure 3. The levels of Low pass Filter to remove the noises in the PCG signal.

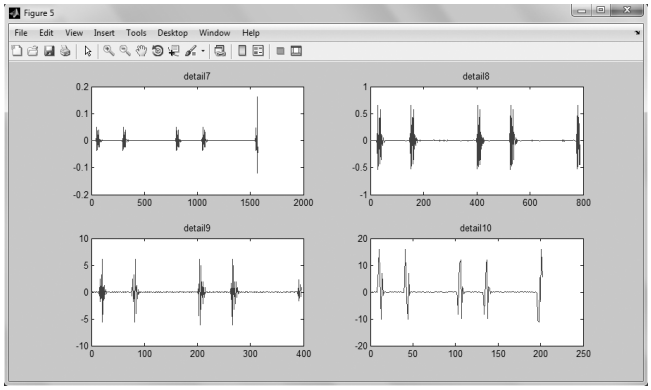

Figure 4. The levels of wavelet decompisition(Approximation and detail signals).

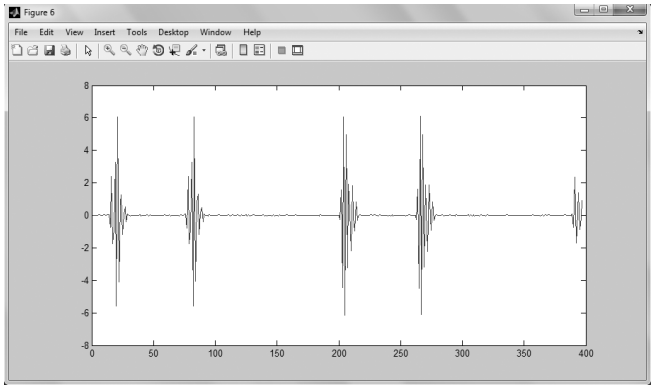

Figure 5. The segmented PCG signal to detect S1, Systole, S2 and Diastole.

Feature Extraction

The real time QRS detection algorithm extracts R-wave amplitude and R-wave time duration from the given signal. This algorithm contains four stages. The initial stage is derivative function which calculates the QRS-complex slope value using some five-point derivatives. The next stage is squaring function and it removes the negative data points using square the derivative values. The first two stages are used to calculate R-peak amplitude. Third stage is moving-window integration. It can calculate the R-peak slope value by using some sample rates. Final stage is fiducially marked which calculates the R-peak value and QRS complex time duration (width). The interval between two consecutive R waves is called RR interval. The RR-interval is based on the time duration of P, Q, R and ST-segment. The RR-interval is calculated using discrete wavelet transform. Based on R-peak value, the wavelet transform can extract the following features like: P, QRS-Complex and ST- segment. These features are used to calculate RR-interval value. This calculated RR interval is matched with the Systolic and diastolic intervals which is found using Heart Sound.

R-Peak Amplitude

Here third level of DB4 filter based de-noised ECG signal is used because it gives better R-peak value. Normally, derivative function is mainly used to calculate the height, width and amplitude values. In this process, five-point derivative function is used for the finding the QRS slope information. The QRS slope value gives the non-linear R-peak amplitude value. After differentiation, the ECG signal is squared in point by point. This makes all data points as positive and does nonlinear amplification of output to the derivative emphasizing the higher frequencies that is predominantly the ECG frequencies.

R-peak Time Duration

The R-peak time duration is calculated from the moving window integration. It is mainly based on the sample values. Generally, the window width is approximately as same as the widest possible QRS complex. The window is too wide and the integration waveform is merging to the QRS and T complexes together. The window is narrow means QRS complexes produce several R-peaks in the integration waveform. The QRS complex corresponds to the rising edge of the integration wave-

Table 1

Amplitude and duration of waves, intervals and segments of ECG signal

Sl. no	Features	Amplitude (mV)	Duration (ms)
1	P-wave	0.1-0.2	60-80
2	PR-segment	-	50-120
3	PR-interval	-	120-200
4	QRS-complex	1	80-120
5	ST-segment	-	100-120
6	T-wave	0.1-0.3	120-160
7	ST-interval	-	320
8	RR-interval	-	(0.4-1.2)s

Table 2

Range of HRV Features for normal and Arrhythmia disease

Attributes	NORMAL Values (msec)	ARRHYTHMIA Values (msec)
SDNN	24.4-97.9	152.9-375.9
SDANN	14.2-72.8	117-276.3
NNx	0-91	159-381
pNNx	0-27.2	75-87.2
RMSSD	11.5-51.6	197.7-520
meanHR	67.3-109.6	57.1-105
LF/HF	1.469-8.753	0.269-1.322
VLF	77.2-3523.05	1131.47-233610.4
LF	224.12-2276.93	1412.57-195993.7
HF	25.6-739.28	2260.32-148245
TP	326.93-6539.26	6042.08-577849.5

form. The time duration of the rising edge is equal to the width of the QRS complex. A fiducially mark for the temporal location of QRS complex is determined from the rising edges. According to the desired waveform, R-Peak is marked such as the maximal slope or the peak of the R wave (Table 1).

Heart rate variability analysis

The RR intervals are fed into the HRV feature analysis to obtain the Time domain and Frequency domain features. Heart Rate Variability is a non-invasive measure, which reflects the variation over time of the interval between consecutive heartbeats. It is the distance between two successive QRS complexes. It is measured as the distance between RR waves, like

$$RR = RR_{i+1} - RR_i \qquad 0 < i \le N$$

Where N is the total number of RR intervals. The above Equation is the measure of distance between RR intervals.

The RR intervals for regular heartbeats are between 600 ms and 1000 ms. The RR intervals for irregular heartbeats are usually shorter (RR_i<300 ms) or longer (RR_i>2000 ms) than the healthy people. The Heart Rate Variability Features are analyzed through Time domain analysis and Frequency domain analysis.

Extraction of Time Domain Features

Time Domain analysis consists of statistical calculations. The time domain features are Standard deviation of all NN intervals (SDNN), Average of all NN intervals (AVNN), Root of mean of sum of Squares of difference of adjacent NN intervals (RMSSD) and number of pairs of successive NNs that differ by more than x ms (NNx), percentage of NNx (pNNx).

AVNN

AVNN is the average of all NN intervals in the dataset. The average of RR intervals can be calculated as,

$$AVNN = \frac{1}{N}\sum_{i}^{N} = {}_{1}RR_i$$

Where N is the total number of RR intervals and RR_i is the i^{th} RR interval. The above Equation is the measure of average of all NN intervals.

Consider the following sample RR intervals. R_1=0.214, R_2=0.814, R_3=0.811, R_4=0.789, R_5=0.792.

$$AVNN = \frac{1}{N}\sum_{i}^{N} = {}_{1}RR_i$$

$$AVNN = \frac{1}{N}\,[RR_1 | RR_2 | RR_3 | RR_4 | RR_5],\ N=5$$

$$AVNN = \frac{1}{5}\,[0.214+0.814+0.811+0.789+0.792]$$

AVNN=0.684 s = 684 msec

SDNN

SDNN means standard deviation of all RR intervals. In statistics, standard deviation is a simple measure of the variability or dispersion of a data set. If the standard deviation is low then it indicates that the data points tend to be very close to the same value (the mean), where as if the standard deviation is high then it indicates that the data are spread out over a large range of values. The standard deviation is the root-mean-square (RMS) deviation of its values from the mean.

$$\text{SDNN} = \sqrt{\frac{1}{N}\sum_{i}^{N} = {}_{1}(RR_i - \overline{RR})^2}$$

Where RR_i is the RR interval. $\overline{RR}$ $\overline{RR}$ is the mean value of the RR_i. The above Equation is the measure of standard deviation of all NN intervals.

$$\overline{RR} = \frac{RR_1+RR_2+\cdots RR_N}{N}$$

Where N is the total number of RR intervals. The above Equation is the measure of mean of all NN intervals. For the above sample RR interval samples, the SDNN is calculated as follows:

$\overline{RR}$ $\overline{RR}$ = 0.684

Table 3

HRV Features for Arrhythmia ECG Signal

SDNN	SDANN	NNx	pNNx	RMSSD	meanHR	VLF	LF	HF	Total	LFHF	Class
33.5	25.4	8	1.7	19.3	96.8	246.99	565.4	128.24	940.64	4.409	0
40.2	27.3	5	1.1	17.9	92.9	519.08	584.01	148.85	1251.93	3.924	0
45.5	32.9	12	2.6	22.1	93.8	718.68	675.43	160.43	1554.54	4.21	0
39.9	27.1	13	2.8	28.8	93.3	198.81	363.81	68.65	631.27	5.299	0
78.8	41.7	39	9.1	32.1	87.3	435.79	1139.72	300.16	1875.67	3.797	0
94.2	69.2	41	10.4	39.2	80.3	2182.17	1990.8	353.95	4526.92	5.624	0
57.5	38.9	41	11	33.8	75	882.13	692.25	471.39	2045.78	1.469	0
97.9	72.8	91	27.2	51.6	68	3523.05	2276.93	739.28	6539.26	3.08	0
82.6	56	13	3.4	38.5	78.7	1999.12	586.97	113.43	2699.53	5.175	0
50.5	40.4	24	5.7	26.5	85.4	908	882.42	219.24	2009.66	4.025	0
80.3	47.3	21	4.5	24.9	94.1	1112.5	1016.78	158.16	2287.44	6.429	0
49.6	24.8	4	1	17.2	94.7	481.87	430.92	88.89	1001.68	4.848	0
56.9	39.5	41	13.4	35.6	67.3	853.86	1068.41	493.12	2415.4	2.167	0
24.4	14.2	0	0	11.5	109.6	77.2	224.12	25.6	326.93	8.753	0
240.5	143.3	159	84.6	274.3	82.6	83072.14	20244.68	17377.94	120694.8	1.165	1
375.9	276.3	273	80.5	520	105	233610.4	195993.7	148245.4	577849.5	1.322	1
152.9	117	259	77.3	197.7	69.1	1131.47	4377.8	8121.9	13631.16	0.539	1
361.4	259.5	195	75	452.1	57.1	19476.2	16136.16	59990.66	95603.02	0.269	1
258.2	208.8	248	84.1	355	62.6	20738.12	14248.97	42308.05	77295.15	0.337	1
153.6	118.3	381	87.2	211.5	90.8	2369.2	1412.57	2260.32	6042.08	0.625	1

$$SDNN = \sqrt{\frac{1}{5}[(0.214-0.684)^2 + (0.814-0.684)^2 + (0.811-0.684)^2 + (0.789-0.684)^2 + (0.792-0.684)^2}$$

SDNN=0.23515 s = 235.15 msec

RMSSD

RMSSD is the square root of the mean of sum of differences of successive RR intervals. It is described as,

$$\text{RMSSD} = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}(RR_{i+1} - RR_i)^2}$$

Where N is the total number of RR intervals. The above Equation is the measure of root mean of sum of squares of difference of adjacent NN intervals.

The RMSSD can be calculated as follows,

$$RMSSD = \sqrt{\frac{1}{4}[(0.814-0.214)^2 + (0.811-0.814)^2}$$

RMSSD= 0.30016 s= 300.16 m sec

NNx

NNx is the count of adjacent RR intervals that are differed by more than x ms.

$$NNx = \sum_{i=1}^{N}\{|RR_{i+1} - RR_i| > x\ ms\}$$

Where N is the total number of RR intervals. The above Equation is the measure of count of adjacent RR intervals having difference greater than x ms.

The adjacent intervals having difference of 50msec is calculated as,

|0.814-0.214| = 600 msec > 50 msec , Hence count=1

|0.811-0.814|= 3 msec

|0.789-0.811|= 22 msec

|0.792-0.789|= 3 msec

Hence NN_{50}=1

pNNx

pNNx is the percentage of differences between adjacent NN intervals that are > x ms. pNNx is calculated by dividing the NNx by the total number of RR intervals.

$$pNNx = \frac{NNx}{N} \cdot 100\ (\%)$$

Where N is the total number of RR intervals. The above Equation is the measure of percentage of NNx.

$$pNN_{50} = \frac{NN_{50}}{N} \cdot 100 = \frac{1}{5} \cdot 100$$

pNN50=20%

HRV Features for normal and Arrhythmia disease are demonstrated in Table 2-3.

Extraction of Frequency Domain Features

Frequency domain features are calculated by Fast Fourier transform. The feature Very Low Frequency (VLF) is calculated over 0 to 0.04 and Low Frequency (LF) between 0.04 and 0.15, High Frequency between 0.15 and 0.4 and the total power between 0 and 0.4. Then the ratio of Low frequency and high frequency (LF/HF) is calculated.

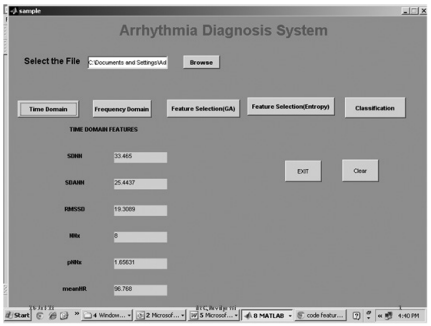

Figure 6. The Arrhythmia diagnosis system for the analysis of Heart sound and ECG signal.

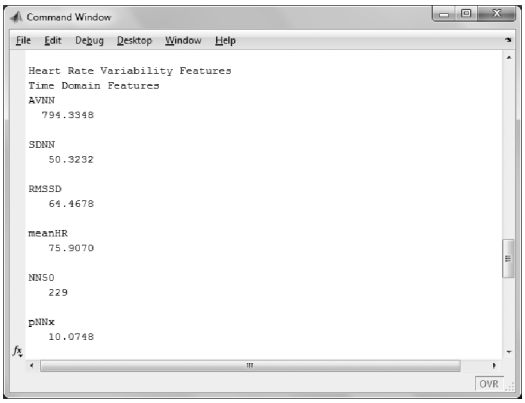

Figure 7. The experimental results of Time domain features.

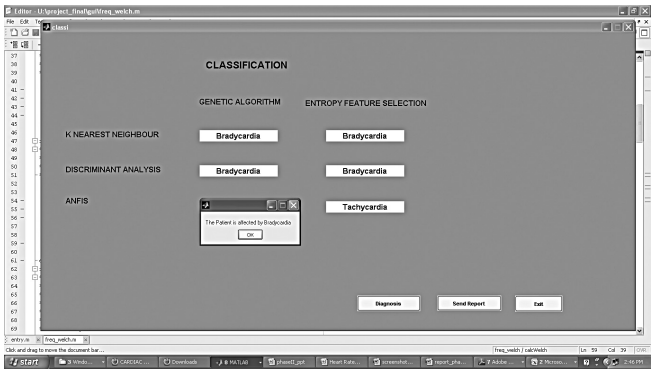

Figure 8. The classification results of arrhythmia diseases.

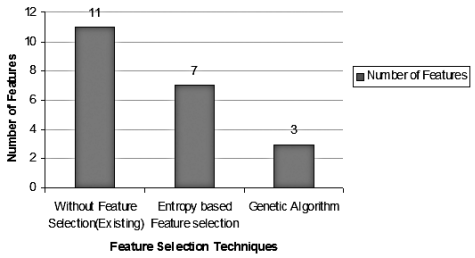

Figure 9. The comparison of feature selection methods.

The Fast Fourier transform is determined using the following equation.

$$F(u) = \frac{1}{N} \sum_{x=0}^{N-1} f(x) e^{-j2\pi ux/N}$$

Where N is the total number of RR intervals. The above Equation is the measure of fast fourier transform.

The power spectrum can be calculated as,

$$P(u) = R^2(u) + I^2(u)$$

$R^2(u)$ is the real part and $I^2(u)$ is the imaginary part of the digital signal. The above Equation is the measure of the power spectrum.

Feature Selection

Genetic algorithm is used for selecting the best fittest features which is used for the classification of Arrhythmia disease. The initial population is the difference of range of Heart Rate Variability features. Parents are selected according to their fitness. The better the individual are, the more chances to be selected they have. Roulette wheel selection is used for the selection of best fit individuals. Crossover selects individuals from parent population and creates a new offspring. After performing Cross over, mutation is carried out. For Example consider the binary representation of two chromosomes. The second part of parent1 is assigned to the second part of parent2 and vice versa.

Parent 1: 11 | 11111	**Child 1:** 11 **00000**
Parent 2: 00 | 00000	**Child 2:** 00 **11111**

Mutation

In mutation the offspring generated by crossover is randomly changed. The mutations used are Bit Flip mutation, Shift Mutation and Reordering of Chromosomes.

Bit Flip Mutation flips the bits from '1' to '0' and vice versa.

Parent 1: 1 0 0 1 **0** 1 0 **Child 1:** 1 0 0 1 **1** 1 0

Shift mutation moves a randomly chosen element to a random number of places to the left or right hand side.

Parent 1: 1 0 0 1 0 1 0 Child 1: 1 0 1 0 1 0 0 (Left shifting of third bit)

Reordering of Chromosomes reorders the randomly selected bits.

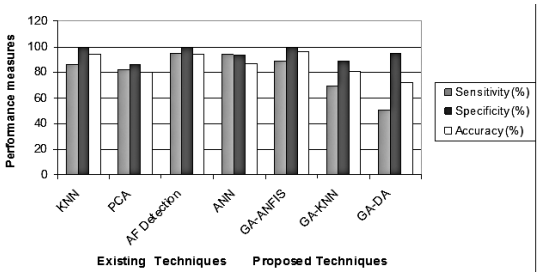

Figure 10. The performance measures of proposed method

Parent 1: 1 0 **0** 1 0 **1** 0 **Child 1:** 1 0 **1** 1 0 **0** 0

Termination Condition

–The termination conditions for the genetic algorithm are:

– Fixed number of iterations reached.

– Required Number of features obtained.

Classification using Neuro Fuzzy Classifier

Decision making of classification is performed in two stages: selection of coefficients computing by DWT and the ANFIS classifiers. ECG beats of arrhythmia diseases are obtained from the PhysioBank databases, which will be classified by ANFIS classifiers. It is aimed to classify the arrhythmia diseases such as Sinus Node Arrhythmias, Atrial Arrhythmias: Premature Atrial Contractions (PAC), Atrial Tachycardia, Atrial Flutter, Atrial Fibrillation, Junctional Arrhythmias: Premature Junctional Contractions (PJC), Ventricular arrhythmias: Premature Ventricular Contractions (PVC), Ventricular Tachycardia (VT), Ventricular Fibrillation, Atrioventricular Blocks, Bundle Branch blocks using Artificial Neuro Fuzzy Classifier(ANFIS). ANFIS is used as a Neuro Fuzzy classifier for the ECG analysis, the accuracy rates for the combined neural network model presented for the classification of the ECG beats is expected to be higher than stand alone classifier model. The Neuro Fuzzy network is also more tolerant to the noise and less sensitive to the morphological changes of the ECG characteristic and ANFIS also plays an important role in dealing with uncertainty when making decisions in medical application. ANFIS method is compared with K Nearest Neighbourhood classifier and Discriminant Analysis (Fig 6-9).

ECG Database

In the proposed work, it is planned to use the MIT/BIH arrhythmia database (www.physionet.org/physiobank/database/mitdb/). From the database, some of the records are taken for the preliminary work. For example, the arrhythmia database contains 70 records, each containing ECG signals for 1 min duration selected from 70 individuals. The signals were taken from, 58 men aged 27 to 63 years, and 12 women aged 22 to 44 years. These records are used for the identification of arrhythmia diseases for study purposes.

Conformance Testing

Testing is done using the measures of performance metrics (Fig. 10).

Performance Metrics

- Classification Accuracy(Acc)
- Sensitivity(Se)
- Specificity(Spe)
- Detection of Error Rate
- Classification Accuracy(Acc) -

$$Acc(\%) = \frac{TP+TN}{TP+TN+FP+FN} \times 100$$

Sensitivity(Se) -

$$Se(\%) = \frac{TP}{TP+FN} \times 100$$

Specificity(Spe) -

$$Spe(\%) = \frac{TP}{TP+FP} \times 100$$

Detection of Error Rate -

$$DetectionErrorRate(\%) = \frac{FP+FN}{TotalNumberof\ Records}$$

Where: TP – True Positive, TN- True Negative, FP-False Positive, FN-False Negative.

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PACE-ECG IN PREVIOUS MYOCARDIAL INFARCTION: AN UNFINISHED STORY

Cuneyt Kocas, Okay Abaci, Baris Okcun, Alev Arat Ozkan, Yusuf Atayev, Tevfik Gurmen, Cengiz Celiker, Murat Ersanli

Aim. The diagnosis of previous myocardial infarction (MI) is difficult in patients with pacemaker and usually further tests must be done to confirm the diagnosis. To overcome this difficulty five major ECG criteria have been proposed by authors: 1. Notching 0.04 second in the ascending limb of the S wave of leads V3,4 or 5 (Cabrera's sign), 2. Notching of the upstroke of the R wave in leads I, aVL or V6 (Chapman's sign), 3. Q wave >0.03 second in leads I, aVL or V6, 4. Notching of the first 0.04 second of the QRS complex in leads II, III, aVF, 5. Q wave >0.03 second in leads II, III, aVF. The aim of this study is to find the predictive value of the five major proposed criteria for MI in pacing ECG of patients with previous MI.

Material and methods. Twenty- three pacemaker patients with known MI (anterior 15, inferior 8) and 24 healthy pacemaker control patients; 17 female, 30 males, aged between 17-92 years with mean age of 59,5 ± 20 years, total 47 patients were studied. Documentation and localization of MI was based on history and confirmed by angiography and or scintigraphy.

Results. Sensitivity was lower in all parameters for prediction of any MI whereas specificity was higher and ODA was moderate. Cabrera's and Chapman's sign had moderate sensitivity (60%-60%) whereas high specificity (90%-90%) and ODA (81%-81%) for anterior MI. Sensitivity of Q wave in I, aVL or V6 was lower (47%) for anterior MI but specificity and ODA was higher 84% and 92% respectively.

Conclusion. In conclusion Cabrera's and Chapman's sign have a moderate sensitivity and higher specificity for recognising previous anterior MI in pacing patients.

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Key words: pacemaker, electrocardiography, previous MI, Cabrera, Chapman.

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О ПЕЙС-ЭКГ ПЕРЕНЕСЕННОМ ИНФАРКТЕ МИОКАРДА: НЕЗАКОНЧЕННАЯ ИСТОРИЯ

Cuneyt Kocas, Okay Abaci, Baris Okcun, Alev Arat Ozkan, Yusuf Atayev, Tevfik Gurmen, Cengiz Celiker, Murat Ersanli

Цель. Диагностика перенесенного инфаркта миокарда (ИМ) является трудной у пациентов с кардиостимулятором и, как правило, дальнейшие исследования должны быть проведены, чтобы подтвердить диагноз. Чтобы преодолеть эту трудность, авторами предложены пять основных ЭКГ-параметров: 1. Зубец 0.04 второй восходящей ветви волны S в отведениях V 3, 4 или 5 (признак Cabrera), 2. Зубец восходящей R-волны в отведениях I, aVL или V6 (признак Chapman), 3. Волна зубца Q >0.03 секунды в отведениях I, aVL или V6, 4. Зубец в первые 0.04 секунды комплекса QRS в отведениях II, III, aVF, 5. Волна зубца Q >0.03 секунды в отведениях II, III, aVF. Целью данного исследования является поиск прогностической ценности из пяти основных предложенных критериев для ИМ при пейс-ЭКГ у пациентов с перенесенным ИМ.

Материал и методы. Двадцать три пациента с кардиостимуляторами с известным ИМ в анамнезе (передне-стеночный 15, заднее-стеночный 8) и 24 здоровых пациента с кардиостимуляторами контрольной группы; 17 женщин, 30 мужчин в возрасте от 17–92 лет, средний возраст 59,5 лет, всего 47 больных были изучены. Документация и локализация ИМ были основаны на истории болезни и подтверждены ангиографией или сцинтиграфией.

Результаты. Чувствительность была ниже во всех параметрах для прогнозирования ИМ любой локализации, принимая во внимание, что специфичность была выше и общая диагностическая точность (ОДТ) была умеренной. Признаки Cabrera и Chapman имели умеренную чувствительность (60%-60%), при высокой специфичности (90%-90%) и ОДТ (81%-81%) на переднем ИМ. Чувствительность зубца Q отведениях I, aVL или V6 была ниже (47%) для переднего ИМ, но специфичность и ОДТ были выше 84% и 92%, соответственно.

Заключение. Признаки Cabrera и Chapman обладают умеренной чувствительностью и высокой специфичностью для определения перенесенного передне-стеночного ИМ у пациентов с кардиостимуляторами.

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Ключевые слова: кардиостимулятор, электрокардиография, перенесенный инфаркт миокарда, Cabrera, Chapman.

Introduction

Ventricular pacing changes ventricular depolarization and repolarisation process causing left bundle branch block (LBBB). Thus the diagnosis of previous myocardial infarction (MI) is difficult in patients with pacemaker and usually further tests must be done to confirm the diagnosis. To overcome this difficulty five major ECG criteria have been proposed by authors: 1. Notching 0.04 second in the ascending limb of the S wave of leads V3,4 or 5 (Cabrera's sign), [1] 2. Notching of the upstroke of the R wave in leads I, aVL or V6 (Chapman's sign) [2], 3. Q wave >0.03 second in leads I, aVL or V6 [3], 4. Notching of the first 0.04 second of the QRS complex in leads II, III, aVF [4], 5. Q wave > 0.03 second in leads II, III, aVF [5]. Limited number of studies evaluated these criteria and revealed low sensitivity but high specificity for the diagnosis of previous MI but these studies are performed in a small number of patients and methods for confirming previous MI are different [6, 7]. The aim of this study is to find the predictive value of the five major proposed criteria for MI in pacing ECG of patients with previous MI.

Material and methods

624 patients with implanted permanent pacemaker in our clinic were evaluated retrospectively. Twenty- three pacemaker patients with known MI (anterior 15, inferior 8) and 24 healthy pacemaker control patients; 17 female, 30 males, aged between 17–92 years with mean age of 59,5±20 years, total 47 patients were studied. Documentation and localization of MI was based on history and con-

Table 1

Sensitivity (%),Specificity (%) and Overall Diagnostic Accuracy (%) of five ECG criteria for all myocardial infarctions

ECG	Anterior Myocardial Infarction			Inferior	Myocardial Infarction	
Sign	Sensitivity	Specificity	ODA	Sensitivity	Specificity	ODA
Cabrera's	60 %	90 %	81 %	25 %	74 %	66 %
Chapman's	60 %	90 %	81 %	25 %	74 %	66 %
Q I,aVL,V6	47 %	84 %	72 %	25 %	74 %	66 %
N II,III, aVF	27 %	90 %	70 %	37 %	90 %	81 %
Q II,III, aVF	27%	81 %	64 %	50 %	85 %	79 %

Abbreviation: ODA - overall diagnostic accuracy.

firmed by angiography and or scintigraphy. Control group was constituted of patients without history of MI and with normal myocardial scintigraphy.

Pace lead was in right ventricular apical position in all patients. Pace mode was DDD-R in 16 (69.5%) of 23 patients in MI group and 17 (70.8%) of 24 patients in control group and VVI-R in 7 (31.5%) in MI group and 7 (29.2%) in control group. Complete ventricular capture was confirmed in all patients.

A surface 12-lead ECG was recorded in all patients and patients with full ventricular capture were included study. Two different experts, who were blinded to group status of the patients, manually analyzed all ECGs. Differences in interpretation were resolved by consensus. According to the literature five major ECG criteria were assessed in our study.

1. Notching 0.04 second in the ascending limb of the S wave of leads V3,4 or 5 (Cabrera's sign),

2. Notching of the upstroke of the R wave in leads I, aVL or V6 (Chapman's sign),

3. Q wave >0.03 second in leads I, aVL or V6,

4. Notching of the first 0.04 second of the QRS complex in leads II, III, aVF,

5. Q wave >0.03 second in leads II, III, aVF.

First three criteria were used to determine previous anterior MI whereas number 4, and 5 were used to find out old inferior MI.

Specificity, sensitivity and overall diagnostic accuracy of these criteria to find out previous MI were calculated as follows:

Sensitivity = True positive / (true positive+false negative)

Specificity = True negative / (true negative+false positive)

Overall diagnostic accuracy = (true positive+ true negative) / total study population

Results

Of the 23 patients with MI, a positive Cabrera's sign was found in 11 (47.8%) patients (9/15 with anterior MI, 2/8 with inferior MI), Positive Chapman's sign was seen in 6 (26.0%) patients (4/15 anterior MI, 2/8 inferior MI), Q wawe in I, aVL or V6 was found in 9 (39.1%) patients (7/15 anterior MI, 2/8 inferior MI), Notching of QRS complex in leads II, III, aVF in 7 (30.0%) patients (4/15 anterior MI, 3/8 inferior MI), Q wave in leads II, III, aVF in 8 (34.7%) patients (4/15 anterior MI, 4/8 inferior MI).

Table 2

Sensitivity (%), Specificity (%) and Overall Diagnostic Accuracy (%) of five ECG criteria for anterior and inferior myocardial infarctions

ECG Sign	Sensitivity	Specificity	ODA
Cabrera's	48%	96%	72%
Chapman's	48%	96%	72%
Q I, aVL, V6	39%	88%	64%
N II, III, aVF	30%	100%	66%
Q II, III, aVF	35%	91%	64%

Abbreviation: ODA — overall diagnostic accuracy.

Of the 24 control patients; there was a positive Cabrera's sign in 2 (8.3%) patients, a positive Chapman's sign in 2 (8.3%) patients, Q wave in I, aVL or V6 in 3 (12.5%), notching of the QRS complex in leads II, III, aVF in 1 (4.1%) patient and Q wave in leads II, III, aVF in 2 (8.3%) patients.

The sensitivity, specificity and overall diagnostic accuracy of all parameters for detecting previous MI are given in Table 1 and 2. Sensitivity was lower in all parameters for prediction of any MI whereas specificity was higher and ODA was moderate. Cabrera's and Chapman's sign had moderate sensitivity (60%-60%) whereas high specificity (90%-90%) and ODA (81%-81%) for anterior MI. Sensitivity of Q wave in I, aVL or V6 was lower (47%) for anterior MI but specificity and ODA was higher 84% and 92% respectively.

For previous inferior MI both notching in II, III, aVF and Q wave >0.03 second in II, III, aVF had lower sensitivity (37%-50%), but specificity (90% — 85%) and ODA (81%-79%) were higher.

Discussion

This study was aimed to find the predictive value of the five major proposed criteria for MI in pacing ECG of patients with previous MI. The diagnosis of previous MI in the presence of LBBB, fascicular block, Wolf-Parkinson-White syndrome or right ventricular pacing is challenging and despite several criteria have been proposed, the real diagnostic value of these criteria remains controversial [8–11]. From these criteria five of them have been studied commonly but results of these studies are controversial and most of them are rather old [6–11]. Kochiadakis et al [6] evaluated five criteria for determining previous

MI in paced patients and reported that Cabrera's and Chapman's signs and their combination was useful for recognising previous MI whereas determining the location of the infarct was impossible with any of these criteria. There are many limitations of this study; first temporary pacing used to produce a pacing ECG in patients with previous MI so these findings cannot be generalized to real life permanent pacemaker patients, secondly authors excluded patients with multiple previous necrosis and patients with atrial fibrillation and patients with ejection fraction less than 40%. Recently Theraulaz et al [7] investigated these criteria in permanent pacemaker patients with previous MI. They reported that the sensitivity of Cabrera's sign was moderate for detecting previous MI but poor for all other ECG criteria ranging from 9.1% to 40.9%. In their study specificity was relatively high for all ECG criteria ranging from 81.6% to 100%. None of the five criteria was useful to assess the site of previous MI. In means of specificity and sensitivity for determining all MI, our findings were similar but in our study sensitivity, specificity and ODA of Cabrera's and Chapman's sign in previous anterior MI was higher compared to their study. Usefulness of Cabrera's and Chapman's sign for determining the location of MI was also confirmed by Barold et al [8] and Kindwall et al [9].

The ECG criteria for the presence of previous inferior MI (notching of the QRS and qR in II, III, aVF) was lower sensitivity but a higher specificity in our study and these findings are consistent with previous studies [7–8].

The present study has important findings; first the specificity of all signs has higher than their sensitivity for anterior, inferior and all of MI. Second; Cabrera's and Chapman's signs have higher sensitivity, specificity and ODA for anterior MI and ODA for all MI. Third; Notching in II, III, aVF and Q wave >0.03 second in II, III, aVF have lower sensitivity but high specificity and ODA for inferior MI.

Limitations of study

First of all, this study is a single centre study with a small number of patients that may lead to patient selection bias, secondly our study group was consisted of right ventricular apical pacing patients so these results cannot be applicable to patients with different lead position in right ventricle of biventricular pacing, third; intraobserver variability may be seen in interpretation and analysis of the various ECG criteria.

Conclusion

In conclusion Cabrera's and Chapman's sign have a moderate sensitivity and higher specificity for recognising previous anterior MI in pacing patients. Although sensitivity was lower for other criteria for determining MI specificity were higher and their presence on a pace ECG should alert physician for previous MI.

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EFFICACY ASSESSMENT OF CRYO STORAGE OF DONOR HEARTS BY IMAGEJ BASED IMAGE ANALYSIS

Bao-quan Lin, Sheng-sheng Yang, Zhi-yong Zeng, Cong-wen Zhuang

Aim. Donor organ injury during cold preservation before transplantation negatively impacts graft survival. The current study was to examine available evidences for the efficacy of different cold storage solutions that are used to preserve donor hearts in vitro prior to orthotopic transplantation.

Material and methods. A systematic search of full-length articles published from 1980 to August 2012 was performed in PubMed and Google Scholar. Detailed searches were also made for availability of any sourceware for histopathology images of endomyocardial biopsies of stored hearts.

Results. Not even a single controlled trial has been published relating to this topic. However, we assessed all available literature pertaining to this topic, and performed original, simple yet innovative analyses using ImageJ, a Java based image analyses program, to show the tremendous power to objectively examine the efficacy of the storage solution. Our analysis suggest that ImageJ may be conveniently used to obtain evidences (or lack of it) of ischemic injury of donor hearts during cold storage.

Conclusions. Even the UNOS database does not provide histopathological evidences of cardiac biopsies of orthotopically transplanted hearts. We, however, make the case of the need for image analyses and making availability of images to allow establishing evidence of the usefulness of these storage solutions. We recommend obtaining endomyocardial biopsy prior to orthotopic transplantation and create a registry of H&E stained slides. This is the only step that will direct us towards evidence based care of such highly critical patients who need the equally challenging surgical intervention of cardiac transplantation.

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Key words: orthotopic cardiac transplantation, University of Wisconsin solution, Celsior, Somah, cardiac storage solution.

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ОЦЕНКА ЭФФЕКТИВНОСТИ КРИО ХРАНЕНИЯ ДОНОРСКОГО СЕРДЦА С ПОМОЩЬЮ IMAGEJ НА ОСНОВЕ АНАЛИЗА ИЗОБРАЖЕНИЙ

Bao-quan Lin, Sheng-sheng Yang, Zhi-yong Zeng, Cong-wen Zhuang

Цель. Повреждение донорского органа во время холодного хранения до трансплантации негативно сказывается на приживаемости. В данном исследовании изучаются имеющиеся доказательства эффективности различных растворов для холодного хранения, которые используются для сохранения донорских сердец in vitro до ортотопической трансплантации.

Материал и методы. Систематический поиск полноценных статей, опубликованных с 1980 по август 2012, был выполнен в PubMed и Google Scholar. Детальный поиск также был сделан в любых доступных хранилищах гистопатологических образцов эндомиокардиальных биоптатов сердец.

Результаты. Ни одно контролируемое исследование еще не было опубликовано по этой теме. Тем не менее, мы оценили всю доступную литературу, относящиеся к этой теме, и выполнили оригинальный, простой, но инновационный анализ с использованием ImageJ, Java на основе программы анализа изображения, чтобы показать огромное значение объективной оценки эффективности растворов для хранения. Наш анализ показывает, что ImageJ может быть удобно использован для получения доказательств (или отсутствия таковых) ишемического повреждения донорского сердца во время холодного хранения.

Заключение. Даже UNOS база не дает возможность обеспечить гистопатологическими свидетельствами кардиологические биоптаты ортотопически трансплантируемых сердец. Мы, однако, показываем необходимость проведения анализа изображения, чтобы позволить установить доказательства полезности этих растворов для хранения. Мы рекомендуем получение результатов эндомиокардиальный биопсии до ортотопической трансплантации и создание реестра H&E изображений. Это единственный шаг, который направит нас к обоснованной заботе об этих пациентах, находящихся в критическом состоянии, которые нуждаются в столь сложных хирургических вмешательствах по трансплантации сердца.

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Ключевые слова: ортотопическая трансплантации сердца, University of Wisconsin solution, Celsior, Somah, кардиологический раствор для хранения.

Introduction

Donor organ injury during cold preservation before transplantation negatively impacts graft survival [1]. Most cardiac preservation solutions provide safe cold ischemic storage times for 4 to 5 hours. University of Wisconsin and Celsior are considered gold standards [2, 3]. However, only recently, debates have sprung up regarding the availability of evidences of the efficacy of these solutions in prevention of ischemic injuries of donor hearts [4]. Few newer products like Somah have tried to approach this highly relevant area using rational pharmacological basis for storage. For example, Somah has tried to implement the availability of nitric oxide donor, which is extremely critical in the cardiac neurovascular bed [5].

Initially, we assessed the freely available transplantation database, the UNOS registry, to understand whether any controlled trial have been performed to assess the relative efficacies of the storage solutions [6]. We searched literature, primarily from PubMed, over the last 20 years and to our surprise, we found only very few (less than 5) studies that have addressed this highly critical area [7–10]. In addition, we found that the UNOS registry has only patients listed between 2004 and current. Furthermore, all the analyses have been entirely based on patient survival and some objective clinical data (ejection fraction, etc) of the efficacy

of the storage solutions. However, due to unavoidable multivariate interferences, such analyses can never provide insights into the efficacy of the storage solutions.

In the current study, we aimed to obtain image analyses of all available cardiac biopsy materials that have either been published or available from a public database. To our great surprise, we found very few figures that have actually represented the endomyocardial status of the transplanted graft. Clearly, we could not access even a single image of an in vitro stored donor human heart prior to transplantation. However, we, for the first time ever, utilize the freely available image analyses software from the National Institutes of Health (NIH, Bethesda, MD), ImageJ to demonstrate that all aspects of pathophysiology of ischemic donor heart damage after cold storage may be reliably examined by histomorphometry [11]. This is a simple to perform, but will provide us with enormously powered information to objectively assess the efficacy of the storage solutions, and the benefits of any supplements. There are several studies which have reliable demonstrated the power of image analysis in obtaining highly relevant pathophysiological information. We clearly make the case that pending wide spread use of our suggested methodology, we will continue to fall short of providing evidence based care to one of the highest level of critical patients that await or undergo cardiac transplantation.

Material and methods

Study identification. Detailed systematic PubMed/Medline and Google Scholar searches were performed using the following (single or combination) MeSH headings and subheadings and keywords: heart storage solution, University of Wisconsin solution, Celsior, Somah, ATP, nitric oxide, endomyocardial biopsy, comparative, UNOS, ischemia, cardiac ischemic, ischemic reperfusion injury, histopathology, morphometry, image analyses, apoptosis, cardiac injury, troponin, membrane, ploidy, necrosis, ischemic staging. Literature from 1980 till present (August 2012) was reviewed; less than 5 studies were found that have performed controlled trials of comparative assessments of storage solutions, namely University of Wisconsin and Celsior. However, the end point assessments in these studies were patient survival, and clearly, these studies did not provide any information regarding the histopathological status of the donor hearts at various stages including harvesting, short time storage and post-transplantation. Thereafter, we made endeavors to assess whether images of cardiac biopsies are available after storage of the donor hearts for variable periods of time. Here again, we met with very limited success.

Thereafter, we made the original analyses of the efficiency of imaging tools like ImageJ, a java based free program available from the NIH and obtained an image of a cardiac biopsy that was stored in University of Wisconsin solution, and used it to analyze whether different pathophysiological markers of ischemic heart injury may be examined using the image analyses tools available in ImageJ.

Selection criteria. As case series are probably the most widely reported surgical literature, it was decided not to restrict the selection to a specific study design. Between-groups comparisons in a (randomized) controlled design were not available even for a single study. As a consequence, studies were included if there was within-group pre-post treatment comparisons. No bias was introduced in study selection or methodological screening and all existing reports were analyzed.

Data extraction. ImageJ.Details of ImageJ are easily available from their website, including the different plugins. Those are not discussed here for avoiding repetition and sake of brevity.

Markers of cardiac ischemic injury after storage in different cold storage solutions. Specifically, the feasibility of ImageJ in assessing the following markers of cardiac injury were made: (A) FOR CARDIAC MUSCLES: (i) integrity of membrane (ii) volume of muscle mass (iii) distance between muscle bundles in cross section to assess edema (iv) nuclear swelling as a marker of cardiac apoptosis (B) FOR BLOOD VESSELS AND ENDOTHELIUM: (i) endothelial swelling (ii) endothelial nuclear integrity (iii) blood vessel diameter (iv) evidence of any intravascular or extravascular inflammatory cellular infiltrate.

Results

Here in Figure 1, we show that a simple hand tool in ImageJ may be used to outline a muscle mass that has been obtained in cross section. Further, all parameters may be obtained in one reading, for example, the diameter of the muscle obtained in cross section, the perimeter, area, Feret diameter and the standard deviations of all the measurements. These parameters may be very quickly obtained, and typical analyses for a single area may take less than 10 seconds. For a 512x512 frame, the whole analyses may be completed in less than 5 minutes, but providing very useful information on overall morphological architecture of the obtained myocardial biopsy tissue. Note that this mensuration can be used to derive several pertinent information regarding the state of the donor heart tissue and the stage of ischemic injury and/or its prevention by the storage solution. For example, the measurement of distance between the muscle masses will clearly define whether there has been any level of edema, a hallmark of early ischemic injuries. Furthermore, the measurement of the muscle mass is an easy indicator of the state of the muscle health and whether it has been affected to any extent by ischemic injury. We stress the tremendous importance of obtaining these baseline values to enable evidence-based care of this highly critical therapeutic area of cardiac transplantation.

In Figure 2, we demonstrate the power of the morphometric analyses by simple tools. Note the outlined blood vessel in yellow on the far left of the image. Such

diameter measurements of the blood vessels within a myocardial biopsy is a time frozen assessment of the state of endothelium-derived hyperpolarizing factor, and as such, shows the power of image analysis in obtaining the relevant pharmacological efficacy of storage solutions. In absence of nitric oxide, blood vessels may be tonically contracted, providing a poor outlook for the cardiac graft. Surprisingly, we failed to obtain any relevant images that have compared UW, Celsior or any other storage solution, with or without supplementation of nitric oxide donors. We urge that such simple measurements will help us clearly define the efficacy of storage solutions.

In Figure 3, we show the power of "threshold analyses". Morphometrically, the nuclei can be considered as particles. Such an image as shown here is easily obtained digitally, which thereafter can allow us to obtain numerous useful parameters: (i) optical density of the nuclei of muscle cells or endothelial cells; this important parameter is an imaging insight into the metabolic health of whether a nucleus is open faced or condensed and degenerating (ii) clustering of the nuclei; for example, degenerating nuclei of the endothelia will show clustering (iii) simple count of the particles will give an estimate of nuclear densities, for example a useful ratio between muscle and endothelial cells nuclei. An increase in such ratio may be observed if there is an infiltration of inflammatory cells, a hallmark of ischemic injury of transplanted heart. Furthermore, note the clarity of the images; in absence of availability of staining like CD68, it is still possible to speculate with reasonable confidence if there is a macrophage infiltration, because nuclei of such cells will be clearly visible in an intravascular location during the thresholding process in ImageJ.

In Figure 4, we show that stereological analyses may be obtained very quickly with ImageJ. We can easily overlay obtained biopsy images with grids, and thereafter measure useful parameters like nuclear density, nucleo-cytoplasmic ratios, and volume estimations by useful statistical tools like the Cavalieri. Needless to stress here is the fact that we should have open-access kind of sites where the valuable images be uploaded to be allowed for this kind of detailed, but easily performed image analyses to provide us with relevant information for scientifically understanding the importance of the different storage solutions for donor hearts.

In Figure 5, we show that the edges may be outlined in order to examine the integrity of the membranes of cardiac muscles and blood vessels. For example, edge analyses will allow understanding whether there has been any breach of membrane integrity, and such morphological information may be correlated with any available analyses of troponin assays. Places where highly sensitive troponin assays are unavailable may use such simple measurement tools to make accurate diagnosis of cardiac injury after transplantation.

In Figure 6, we show that optical density of a selected area may be easily obtained pixel by pixel. Such analyses

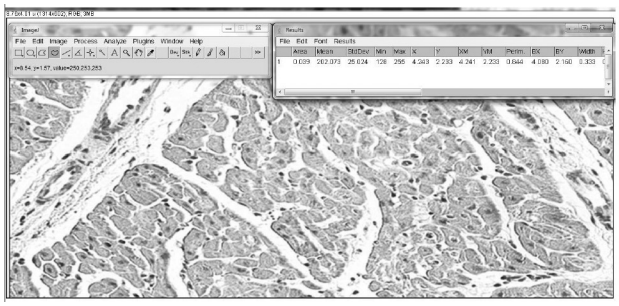

Figure 1. ImageJ used to outline muscle cell boundaries and morphometry obtained. This kind of analyses will provide insights into normal muscle mass and whether any regression or necrosis has occurred.

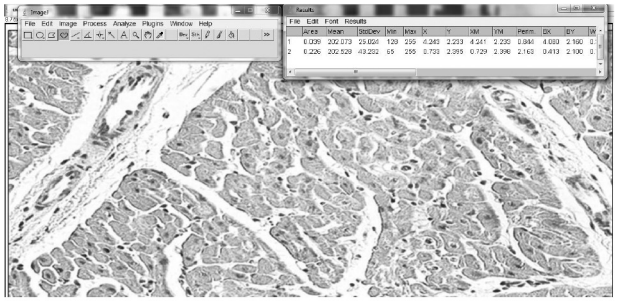

Figure 2. ImageJ can measure diameter of intra-cardiac blood vessels in endomyocardial biopsy obtained after cold storage. This can provide useful insights into the efficacy of storage solutions with supplements like nitroglycerin, nicorandil or Somah.

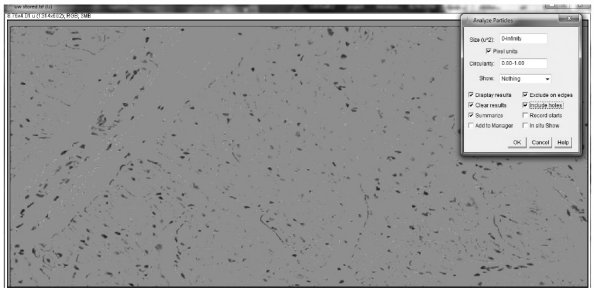

Figure 3. Particle count may be done to assess nuclear cluttering, which may provide further insights into any inflammatory infiltrate.

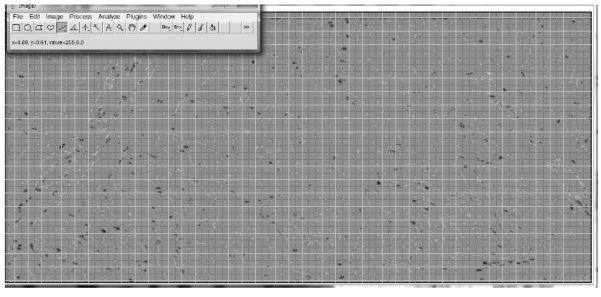

Figure 4. Detailed stereological analyses may be performed with ImageJ.

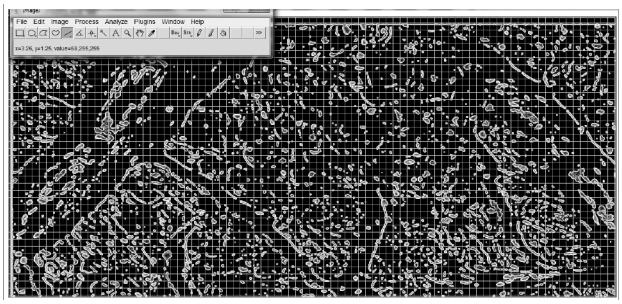

Figure 5. Edge analyses may be performed with ImageJ to examine cell membrane integrity.

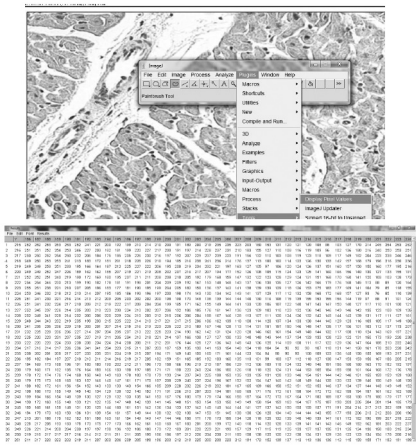

Figure 6. Pixel analysis may be done with ImageJ to obtain insights into nuclear ploidy.

will immediately provide the ploidy status of the endothelial or muscle nuclei.

Discussion

Here, we demonstrate for the first time ever, the usefulness of simple freely available image analysis tool like the ImageJ in obtaining highly useful information that can be implemented to objectively assess the efficacy of the different storage solutions for storage of donor organ prior to orthotopic cardiac transplantation. Pioneering work has been done for making cardiac transplantation a reality for patients suffering from New York Stage IV cardiac failure, as well as a number of different other indications. One important aspect is the storage of the heart after harvesting the donor organ. This is dependent fundamentally on the nature of the cryostorage solution. University of Wisconsin solution and Celsior are commonly used, and a few others like Somah have been introduced that have tried to incorporate rationale use of chemicals for cardiac storage. However, when we scanned the databases, especially the UNOS transplantation database (www.UNOS.org), we surprisingly could not access any useful myocardial biopsy information. We scanned manuscripts published over the last 20 years and again, there were lack of objective assessments of histopathology materials.

No doubt that Kaplan-Meier curve analyses are important aspects in understanding the outcomes of different kind of storage solutions on patient survival. But in the absence of detailed histopathological examinations of any kind of biopsy samples that we can procure, the lacunae in objectivity in the use of these storage solutions is apparent. In the current manuscript, we have demonstrated the immense power of ImageJ in obtaining all useful information pertaining to ischemic injury after in vitro storage of donor heart with different cryostorants. We have shown that both cardiac muscles and endothelial viability may be examined in details for evidences of ischemic or reperfusion injury.

Conclusion

In summary, we recommend obtaining endomyocardial biopsy prior to orthotopic transplantation and create a registry of H&E stained slides. This is the only step that will direct us towards evidence based care of such highly critical patients who need the equally challenging surgical intervention of cardiac transplantation.

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CLINICAL OPINION: BRUGADA SYNDROME AND SICK SYNUS SYNDROME — CASE WHICH WE MEET IN OUR PRACTICE

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In our work we describe the case of a patient with a Brugada syndrome. It is a rare syndrome which carries a potential risk of sudden cardiac death which occurs usually at an early age. Unfortunately it is most frequently the first clinical manifestation of this genetic disease. Sometimes, as in our patient it could co-exist with other cardiovascular abnormalities which give us an opportunity to establish the right diagnosis and apply adequate preventive measures. It is of paramount importance to explore the possibility of the existence of this syndrome in the patient's family members. The first diagnostic procedure is an ECG which is an inexpensive and readily available diagnostic tool.

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Key words: Brugada syndrome, implantable-cardioverter defibrillator, ECG, prevention, sudden cardiac death.

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bmp — beats per minute, DDDR — dual chambers paces, dual chambers sensed, dual response to this, and rate modifiable pacemaker, ICD — implantable-cardioverter defibrillator, ECG- electrocardiogram, SCN5A gene — sodium channel, voltage-gated, type V, alpha subunit gene.

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КЛИНИЧЕСКОЕ МНЕНИЕ: СИНДРОМ БРУГАДА И БОЛЬНЫЕ С СИНДРОМОМ SYNUS — СЛУЧАЙ, КОТОРЫЙ МЫ ВСТРЕТИЛИ В НАШЕЙ ПРАКТИКЕ

Tomislav Kostic[1], Zoran Perisic[1,2], Boris Djindjic[1,2], Goran Koracevic[1,2], Milan Zivkovic[1], Aleksandar Stojkovic[1], Dragana Stanojevic[1], Vladimir Mitov[3]

Рассматривается случай пациента с синдром Бругада. Это редкий синдром, который несет потенциальный риск внезапной сердечной смерти, обычно в раннем возрасте. К сожалению, часто смерть — первое клиническое проявление данного генетического заболевания. Иногда у в наших пациентов синдром Бругада может сосуществовать с другими сердечно-сосудистыеми нарушениями, которые дают нам возможность установить правильный диагноз и применить соответствующие превентивные меры. Крайне важно изучить возможность наличия этого синдрома у членов семьи пациента. Первая процедура диагностики — ЭКГ, которая является недорогим и легкодоступным средством диагностики.

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Ключевые слова: синдром Бругада, имплантируемый кардиовертер дефибриллятор, электрокардиограф, профилактика внезапной сердечной смерти.

Patient D.A. was admitted to the Cardiology Clinic due to sudden onset of weakness and slow heart rate, accompanied by dizziness. He was sent from a private clinic where 24-hour Holter monitoring was done and sinus pauses were recorded. Patient was under the continuous ECG monitoring in the coronary care unit. Complete laboratory analysis showed no deviation from the normal values. ECG recorded right bundle branch block with ST segment elevation of 2 mm in leads V1-V3 (Fig. 1). Biomarkers: D-dimer and troponin I was within normal limits. The next day, an echocardiography was done which showed normal structure of the atria and ventricles, without regional motion abnormalities, adequate valvular apparatus and ejection fraction was 65%. The patient was on monitor for 48 h and after that period it was decided to repeat Holter monitoring (24 h). The results showed that average cardiac frequency was 45 bpm, minimal 30 bpm, maximal 90 bpm, a few pauses in cardiac rhythm were detected, the largest 4.5 seconds. The patient was in sinus rhythm during whole monitoring period (Fig. 2). It was decided that the best option was to insert adaptive frequency biventricular DDDR pacemaker. The next day, in a local anaesthesia preparation of vein cephalica was made; electrodes were placed at the top of the right ventricle, appendage of the right atrium. The patient received antibiotics 4 days after the procedure and was discharged in good general condition. After 2 weeks the stitches were removed, and patient was advised to do genetic mapping of SCN5A gene. He denies previous illnesses and operations, his father died of a myocardial infarction at 47 years of age, mother and sister did not have any significant illnesses.

After two months of pacemaker implantation patient underwent complete cardiac examination. The repeated echocardiography, except the visible electrodes in the right heart chambers, showed that all parameters were within normal range. Repeated Holter monitoring (24h) showed that the patient was in sinus rhythm, maximal heart rate was 105 bpm, minimal 55 bpm, with no significant pauses. There was no ventricular premature beats, or malignant arrhythmias. The patient had no symptoms. At the same time patient's mother and sister, underwent through a complete cardiac examination, as well. ECG recording of both mother and sister showed right bundle branch block with no significant changes at the ST segment (Fig. 3).

In 1992, Brugada syndrome was introduced as a new clinical entity linking typical but variable, ST segment changes in the right precordial leads to an increased vulnerability for lethal ventricular arrhythmias. In the affected patients, no structural heart disease could be identified despite through invasive and non-invasive investigation. Brugada syndrome is genetically transmissible disease manifesting as an autosomal dominant and age-dependent trait. Up till now, more than 80 causative gene mutations have been identified, mostly located on the SCN5A gene, encoding the pore-forming a subunit of the cardiac sodium channel. Large number of phenotypic variations within families and the overlap with other channelopathies illustrate the complex genetic heterogeneity underlying this syndrome [1]. The diagnosis of Brugada syndrome is based on clinical and electrocardiographic features. Patients present with syncope or (aborted) sudden cardiac death due to malignant ventricular arrhythmias. No apparent structural heart disease can be found. Three different ECG patterns all featuring ST segment elevations in the right precordial leads have been recognized. Type I is the only pattern that is diagnostic for Brugada syndrome. It consist of a coved type ST segment elevation greater than 2 mm, followed by a descending negative T wave in at least one right precordial lead: V1-V3. Type II and III are saddleback-shaped patterns, with a high initial augmentation followed by an ST elevation greater than 2 mm for type II and less than 2mm for type III. Both patterns are suggestive of but not diagnostic for Brugada syndrome [2].

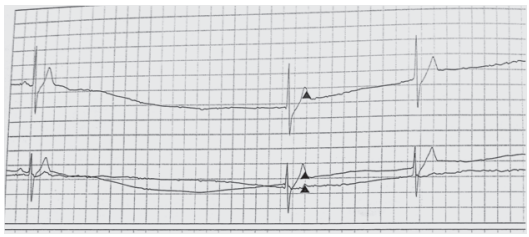

Figure 1. ECG recording from the initial 24-Holter Monitoring (24h) at the admission of our patient

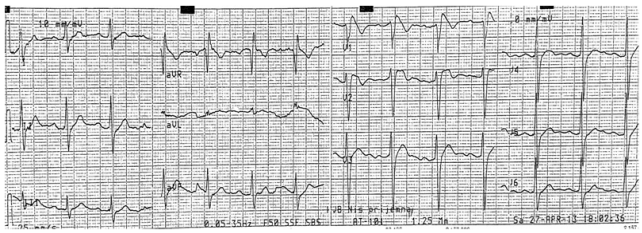

Figure 2. The patient's ECG recording.

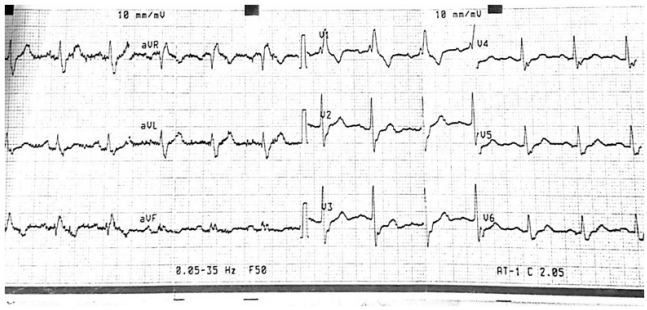

Figure 3. An ECG recording of the patient's sister.

Multiple case reports of ECG patterns that mimic those of Brugada syndrome have been published. Possible causes of ST segment elevation in the right precordial leads are: anti-arrhythmic drugs (class IC and IA, calcium channel blockers as verapamil), acute ischemia in right ventricle outflow tract (RVOT), hyperthermia and hypothermia, elevated insulin level, etc.

Furthermore, recent studies illustrate the dynamic character of these ECG patterns. Whenever a large number of baselines ECG were available during follow up, the diagnostic pattern could be documented in only approximately 25% of the tracings.

Because the presence of the spontaneous coved type I ECG pattern is thought to be a useful predictor of future arrhythmic events in asymptomatic patients, these findings are of great clinical importance [3]. The class IC antiarrhythmic drug test provided a tool to unmask these concealed forms. Intravenous administration of ajmaline, flecainide or procainamide was able to elicit the diagnostic coved-type Brugada syndrome ECG pattern [4]. On the basis of the results of comparative studies and clinical experience, ajmaline, in a dose of 1mg/kg, is considered to be the preferred drug. Recently, the full stomach drug test was proposed as an alternative tool in diagnosing Brugada syndrome.

The episodes of syncope and sudden death are caused by fast polymorphic ventricular tachycardia or ventricular fibrillation. These arrhythmias appear with no warning. The first patient with Brugada syndrome was seen in 1986. The native populations of Asia knew about the problem for many decades. In the Philippines the problem was known as "bangungut", in Japan as "pokuri" (unexpected sudden death during sleep).

Currently more than 70 SCN5A mutations have been linked to Brugada syndrome, all creating an impaired sodium influx. The loss of function SCN5A mutations also have been described as being responsible for Lev-Lenegr disease, or progressive conduction defect. This phenotypic overlap is illustrated by the frequent occurrence of conduction abnormalities in patients with Brugada syndrome. Also SCN5A previously was shown to be the cause of LQT3 syndrome a form of Romano-Ward long QT syndrome. The differences in the clinical findings between LQT3 and Brugada are due to the different biophysical features dictated by the position of the mutations within the gene [5].

In the past decade, risk stratification in Brugada syndrome has become the subject of intense interest owing to

the fact that early recognition of patients at increased future risk of sudden death can save many lives. The principal goal of risk stratification is the prediction of future arrhythmic events at any time during life. This is particularly difficult in adult patients who have never had any symptoms and in whom the diagnosis is incidental [6].

Asymptomatic persons may be recognized when the atypical ECG pattern is detected during routine examination. This ECG pattern cannot be distinguished from that in symptomatic patients. In other patients, the characteristic ECG pattern is recorded during screening after the sudden death of a family member with the disease. On the other hand, another group of symptomatic patients have been diagnosed as suffering syncope episodes of unknown cause or vasovagal origin or who have a diagnosis of idiopathic ventricular fibrillation. Subsequently, some of these patients are correctly diagnosed at follow up when ECG pattern changes spontaneously from normal to the typical pattern of the syndrome. This is also the case for those persons in whom the disease is unmasked by the administration of an antiarrhythmic drug given for other arrhythmias- for instance, atrial fibrillation [7].

An ICD pacemaker implantation is a treatment option for the patients with Brugada syndrome and ventricular tachycardia or fibrillation. Extensive research is ongoing to find alternative pharmacological options for these patients, especially for patients in whom an ICD implantation is contraindicated for various reasons. Quinidine and dimethyl lithospermate B (an extract of Danshen) have been suggested as drugs that reduce the tendency for ventricular arrhythmias. Larger patient groups and longer follow up period are necessary to evaluate these products [7–9].

In everyday clinical practice, we encounter patients with Brugada syndrome, and conduction abnormalities requiring permanent pacemaker implantation. Brugada syndrome in our patient was diagnosed due to specific ECG recording and genetic analysis of the SCN5A gene. Implantable cardioverter defibrillator was not the treatment option in our patient because he had no malignant arrhythmias as well as ventricular premature beats during the long follow-up period. Upgrade option of adding an ICD to in two-chamber pacemaker is advisable in adequate indication, and our patient is scheduled for regular check-ups every three months for complete cardiac examination.

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HYBRID URGENT PERCUTANEOUS INTERVENTION IN THE PATIENT WITH FEMORAL ARTERY INJURY AND SHOCK

Ozcem Barcin, Conkbayir Cenk, Akpinar Suha

An obese patient with comorbities was admitted to the emergency department with shock, widespread hematoma due to a previous above-knee amputation, and had emergency conventional peripheral angiography in a hybrid operating room after an initial diagnosis of femoral artery fistulisation.
Due to the graft infection, the femoropopliteal graft was removed a month previous. However, bleeding occurred in the native common femoral artery, which had been previously removed and repaired. According to this symptom, coil embolization and gelfoam process were performed as life-saving procedures.

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Key words: femoral artery injury, coil embolization, percutaneous transcatheter embolization.

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СРОЧНОЕ СМЕШАННОЕ ЧРЕСКОЖНОЕ ВМЕШАТЕЛЬСТВО ЧЕРЕЗ БЕДРЕННУЮ АРТЕРИЮ ПАЦИЕНТА С ТРАВМОЙ И ШОКОМ

Ozcem Barcin, Conkbayir Cenk, Akpinar Suha

Пациент с ожирением и сопутствующими заболеваниями был госпитализирован в отделение неотложной помощи с шоком, обширной гематомой, из-за предыдущей ампутации выше колена; ему проведена экстренная периферическая ангиография в условиях смешанной экстренной операционной после первичного диагноза фистулы бедренной артерии.
Из-за инфекции феморопоплитеальный графт был удален месяцем ранее. Однако, произошло кровотечение из общей бедренной артерии, которое было ранее остановлено. В соответствии с этим, эмболизация и применение гельфоума были выполнены в качестве жизнесохраняющей процедуры.

Российский кардиологический журнал 2014, 1 (105), Англ.: 52-53

Ключевые слова: травма бедренной артерии, эмболы, чрескожная транскатетерная эмболизация.

Introduction

Surgical interventions and vascular repair are performed widely worldwide in arterial injuries. Today, interventional intravascular procedures may be applied alone or in combination with surgery in hybrid operating rooms both for reducing operative risks, mortality and morbidity in patients who have comorbid risk factors.

In this paper, we wanted to discuss urgent percutaneous intervention in a patient for whom surgery was a high risk.

Case report

A seventy year old male patient was admitted to the emergency department with shock (blood pressure 60/40 mmhg). Upon physical examination, it was noted that he had an amputation above the knee in the left lower extremity, severe tension, hematome in stump site, and even leakage in suture line. His body temperature was 37.8°, and WBC and CRP were elevated. It was learned that he had undergone revascularization many times for the same limb, and his last intervention was a femoropopliteal bypass operation with graft. This patient had a couple of bypass interventions which were occluded and infected. Because of infection, the graft was removed, and the patient had an above the knee amputation. The patient had dehiscence of sutures in the femoral artery, leading to a large hematoma and shock.

The infected graft was removed after revascularization was done one month previous. Common femoral artery, proximal part of the graft was repaired, and an above-knee amputation was performed in the same session. Severe scar tissue was detected in his left inguinal region due to multiple operations. Ultrasonography revealed a widespread subcutaneous hematoma. The patient, who had many comorbidities, was immediately taken to the hybrid operating room. 5F sheath was inserted from the contralateral limb under local anaesthesia, turned to left common iliac artery from aortic bifurcation, and selective right femoral angiography was performed. On vascular imaging, contrast medium passage was observed to come out from above the potential native vessel (common femoral artery) of the femoropopliteal graft, which was reported to have been removed in the previous operation (Fig. 1). We immediately applied embolization with two 4 mm/40 mm and one 5 mm/50 mm of Boston scientific brand fiber coil. We saw that extravasation decreased but continued, so we performed balloon dilatation to the proximal part of the coil site, and that enabled the stop of flow and, thereby, embolization of the leakage site with gelfoam (Fig. 2). We detected that the complication was a partial stenosis in this artery due to the gelfoam going to the superficial femoral artery. Fistulisation was successfully stopped.

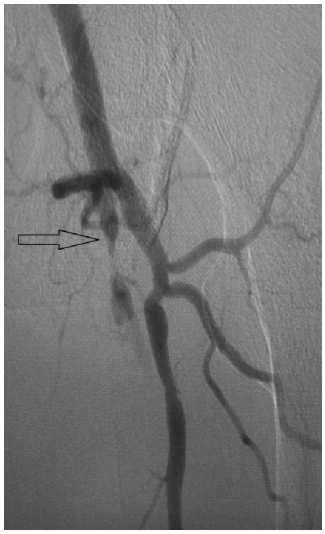

Figure 1. Contrast passage is seen in common femoral artery.

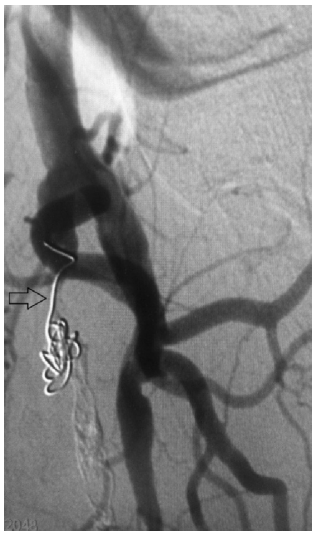

Figure 2. Passage is seen to be eliminated following coil and gelfoam application to the fistula in common femoral artery.

Boston Scientific brand of stent, 4.5 mm in diameter, was implanted to this stenosis, and the procedure was terminated successfully (Fig. 3).

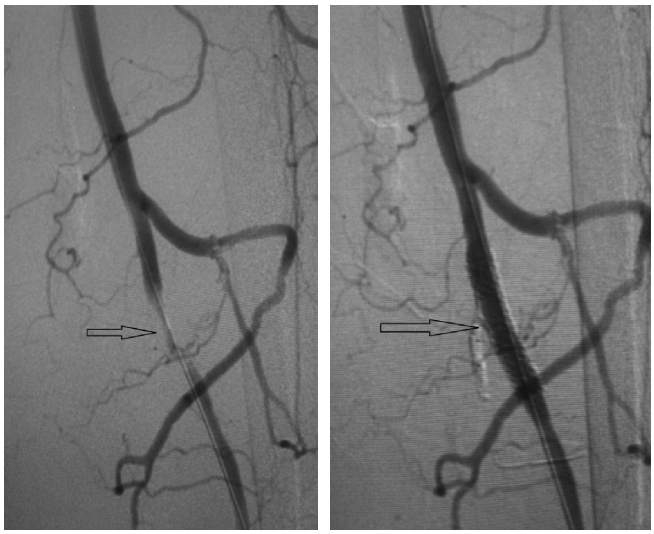

Figure 3. Stenosis in superficial artery developed due to gelfoam is seen on the left. Elimination of this stenosis with a 4.5 mm stent is seen on the right.

Discussion

Percutaneous transcatheter embolization is quite safe and has good results in certain lower extremity arterial injuries, particularly in patients with many comorbidities. The general approach in arterial injuries leading to extreme ischemia is urgent exploration and vascular repair. However, general anaesthesia, blood loss, infection, wound aperture and lymphorrhea are the risks of surgery. Exploration is quite difficult morbidly obese patients and in a surgical field which has scarring due to previous operations [1]. Percutaneous transcatheter arterial embolization is a good option for reducing surgical risks or when used in combination with surgery. PTE applications require experience and may be applied by interventional radiologists or vascular surgeons with a multidisciplinary approach [2]. In their study of 10 cases, Aksoy et al. used coil and gelfoam to stop haemorrhage in percutaneous approaches to lower extremity vascular injuries. They obtained successful results in all patients; they reported quite low rates of duration of hospital stay and complications [3]. Further developments in guidewires will enable safer PTE with less risk [4, 5].

On the other hand, if there is infection in the site of percutaneous embolization, intravenous antibiotics should be given before the procedure. Our patient recovered well from infection without fever, and CRP and WBC decreased. If the patient is in shock, PTE can be performed safely as in our case if there is infection, also.

In conclusion, although PTE requires a multidisciplinary approach, it can be performed safely in experienced hands to reduce surgical risks, particularly, in patients with multiple comorbidities.

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RIGHT-SIDED AORTIC ARCH WITH KOMMERELL'S DIVERTICULUM — SUDDEN ONSET IN INFANT

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Russ J Cardiol 2014, 1 (105), Engl.: 54-55

Key words: right-sided aortic arch, Kommerell's diverticulum.

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ПРАВОСТОРОННЯЯ ДУГА АОРТЫ С ДИВЕРТИКУЛОМ KOMMERELL — ВНЕЗАПНОЕ НАЧАЛО У РЕБЕНКА

Daniela Iacob[1], Butnariu Angela[1], Samasca Gabriel[2], Manole Simona[3]

Российский кардиологический журнал 2014, 1 (105), Англ.: 54-55

Ключевые слова: правосторонняя дуга аорты, дивертикул Kommerell.

Introduction

A right-sided aortic arch is an uncommon congenital defect of the aorta, being rare in the setting of a normal heart. Right-sided aortic arch may associate an aberrant left subclavian artery with a Kommerell's aneurysm producing compression of mediastinal structures [1, 2]. We report an infant with right-sided aortic arch, left descending thoracic aorta and a Kommerell's diverticulum, presenting for choking spells and acute respiratory failure.

Case report

A 10 months girl was admitted for sudden onset of choking spells and acute respiratory failure. Chest radiograph showed widening of upper mediastinum. Bronchoscopy revealed extrinsic compression of the trachea and of the right and left main stem bronchus. Echocardiography showed a right-sided aortic arch and normal heart anatomy. Computerized thoracic axial tomography and angiography revealed a right-sided aortic arch and a left descending thoracic aorta with an 8.6 mm Kommerell aneurysm involving the distal arch near the origin of the left subclavian artery (Fig. 1, Fig. 2). Serum levels of BNP and NT-proBNP were normal. It was decided to follow-up the case for the rate of growth of Kommerell's diverticulum over time.

Discussion

The right-sided aortic arch is rare, being found in 0.05–0.1% of imagistic series [1]. There are three types of aortic arch diverticulum. Type II aortic arch diverticulum associates an aberrant left subclavian artery arising as the last branch of the right-sided aortic arch or from an aortic diverticulum, named Kommerell's diverticulum [3]. Type II right-sided arch is the variant present in our patient.

In the right-sided aortic arch symptoms during infancy can be related to compression of mediastinal structures or to congenital heart abnormalities [4]. Adults present symptoms related to dissection or aneurismal dilatation compressing the surrounding structures and producing cough, choking spells, dyspnoea, stridor, wheezing [1]. Our infant presented an unusual sudden onset, with choking spells and acute respiratory failure, needing immediate bronchoscopy and computerized thoracic tomography.

The treatment of Kommerell's aneurysms varies from endoaneurysmorraphy for small aneurysms to interposition of graft for large Kommerell's aneurysms or for Kommerell's aneurysms associated with an aneurysm of the descending thoracic aorta [1, 4]. For small Kommerell's aneurysms it may be appropriate to observe the lesions and decide for intervention based on the rate of growth over time. This was the decision taken in our patient.

Conclusions

Right-sided aortic arch, left descending thoracic aorta and Kommerell's diverticulum are rare. Our infant patient presented an unusual sudden onset, with choking spells and acute respiratory failure. Computerized thoracic tomography with angiography offered essential diagnostic data, compulsory in treatment planning.

Acknowledgements

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Figure 1. Computerized thoracic tomography with angiography: 3D volume rendering technique reconstruction. Normal situated left heart, right aortic arch, Kommerell's diverticulum (arrow).

Figure 2. Computerized thoracic tomography with angiography, 3D volume rendering technique reconstruction of thoracic aorta: right aortic arch with incomplete left vascular ring (star), from which emerge left common carotid artery and left subclavian artery; Kommerell's diverticulum (arrow).

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RIGHT CORONARY ARTERY ORIGINATING FROM THE LEFT CORONARY SINUS: A RARE CORONARY ARTERY ANOMALY

Cenk Conkbayir

Anomalous origin of the right coronary artery (RCA) from the left coronary sinus is a rare congenital anomaly. Here, we report a case of a 54-year-old symptomatic woman who was admitted with a history of unstable angina pectoris, hypertension, coronary arteriosclerosis, diabetes mellitus, hypercholesterolemia and previous coronary bypass operation (CABG). Coronary angiography was performed and a right coronary artery was discovered, which was seen to arise from the left coronary sinus.

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Key words: right coronary anomaly, congenital.

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ПРАВАЯ КОРОНАРНАЯ АРТЕРИЯ, ПРОИСХОДЯЩАЯ ИЗ ЛЕВОГО КОРОНАРНОГО СИНУСА: РЕДКАЯ АНОМАЛИЯ КОРОНАРНОЙ АРТЕРИИ

Cenk Conkbayir

Аномальное отхождение правой коронарной артерии (RCA) из левого коронарного синуса — редкая врожденная аномалия. Здесь, мы сообщаем о случае 54-летней женщины, которая была госпитализирована с нестабильной стенокардией, гипертонией, коронарным атеросклерозом, сахарным диабетом, гиперхолестеринемией и предыдущими операциями аортокоронарного шунтирования (АКШ) в анамнезе. При коронарной ангиографии правой коронарной артерии был обнаружено, что она восходит из левого коронарного синуса.

Российский кардиологический журнал 2014, 1 (105), Англ.: 56-57

Ключевые слова: правая коронарнаяй аномалия, врожденный.

Introduction

The incidence of coronary artery anomalies has been reported to be between 0.2% to 1.3% in angiographic series and 0.3% in autopsy series [1]. Most anomalies are not of clinical significance. However, some anomalies are related to angina, dyspnoea, syncope, acute myocardial infarction and sudden death [2]. In spite of the fact that in the past, an anomalous origin of the RCA from the left sinus of Valsalva was considered a benign finding, it is now evident that this anomaly can be associated with atypical chest pain, myocardial ischemia, and sudden death [3].

Here, we present a 54-year-old woman with an anomalous right coronary artery which arose from the left coronary sinus. In addition, this woman had a previous history of having undergone a coronary artery bypass grafting operation due to multi-vessel disease 7 years ago.

Case report

A 54-year-old woman with a prior history of hypertension and hypercholesterolemia, myocardial infarction and CABG operation presented to our hospital. On admission, her blood pressure was 130/80 mmHG, with a regular pulse rate of 73/bpm. ECG showed normal sinus rhythm and negative T waves on V4–6. We performed coronary angiography due to the presence of unstable angina pectoris. Angiography demonstrated a normal left main coronary artery (LMCA), severe stenosis in the mid portion of the Left anterior descending artery (LAD), mild stenosis in proximal segment of the circumflex artery (CX), and the LIMA_LAD graft to be totally occluded, and a right coronary artery was discovered, which was observed to arise from the left coronary sinus, coursing to the right side of the heart (Fig. A, B, C).

Discussion

The incidence of coronary artery anomalies has been reported between 0.6% to 1.3% in angiographic series and 0.3% in autopsy series [4]. The inter-arterial course of the LCA, between the aortic root and the pulmonary artery trunk, correlates with a higher incidence of angina, syncope and sudden death [5]. The anomalous origin of LCA from the right sinus of Valsalva is not always associated with symptoms of angina pectoris. Other anatomical variants including a retro-aortic course of the anomalous LCA, a right ventricle-free wall course and a septal course, along the floor of the right ventricle, are considered benign [6]. In our case, a right coronary artery was discovered that was seen to have arisen from the left coronary sinus. The ideal imaging tool for the diagnosis and delineation of coronary artery anomalies is coronary angiography. Other imaging modalities include computed tomography, magnetic resonance imaging and transesophageal echocardiography. In our case, at first, we could not identify the right coronary artery and hence, we performed aortography. We realized that the right coronary artery was originating from the left coronary sinus. Then, we performed selective angiography and demonstrated the origin of the RCA from the upper portion of the left coronary sinus. Anomalous coro-

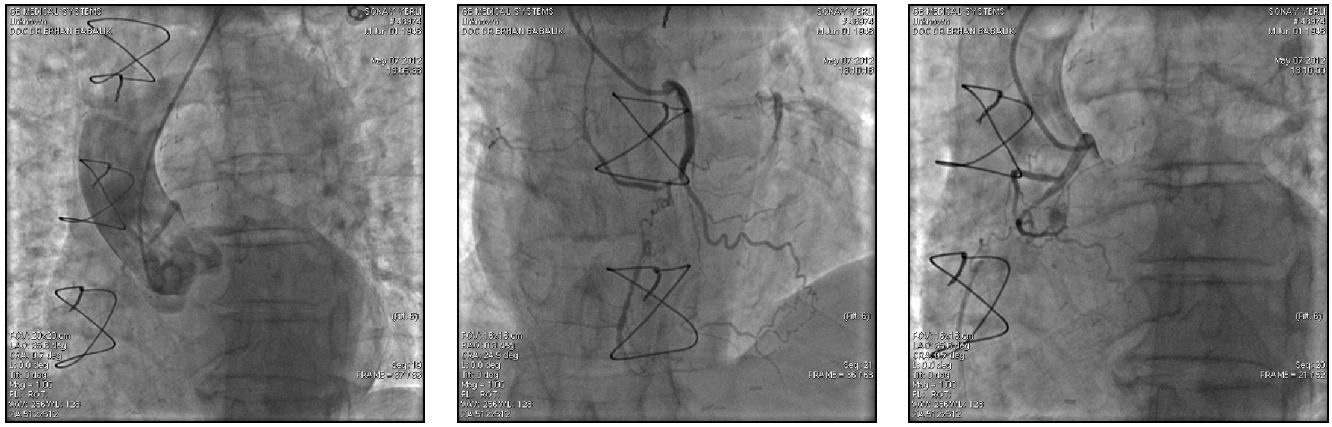

Figure 1

nary arteries do not appear to be associated with an increased risk of development of coronary atherosclerosis, but some patients with anomalous coronary arteries have symptoms of angina pectoris due to atherosclerosis [7]. Recently another case reported with anomalous origin of right coronary artery from the left coronary sinus which resulted with sudden death and successful surgical reimplantation [8]. Aortography and selective coronary angiography should both be well evaluated in patients with anomalies of the coronary artery.

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WHAT IS NEW ABOUT INTERCORONARY ARTERIAL CONTINUITY?

Cem Bostan, Ugur Coskun, Alev Arat Ozkan, Tevfik Gurmen

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Key words: Intercoronary arterial continuity, coronary circulation.

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ICC - Intercoronary arterial continuity, LAD - left anterior descending artery, LV - left ventricular, RCA - distal right coronary artery, PDA - posterior descending artery.

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ЧТО НОВОГО ВО ВНУТРИСОСУДИСТОЙ АРТЕРИАЛЬНОЙ ПРЕЕМСТВЕННОСТИ?

Cem Bostan, Ugur Coskun, Alev Arat Ozkan, Tevfik Gurmen

Российский кардиологический журнал 2014, 1 (105), Англ.: 58-59

Ключевые слова: внутрисосудистая артериальная преемственность, коронарное кровообращение.

Intercoronary arterial continuity (ICC) or "coronary arcade" are thought to arise from embryonic plexuses. These connections are distinct from collaterals being larger in diameter (≥1 mm), extramural and straight. Furthermore, the structure of them is typical of an epicardial artery with a well-defined muscular layer whereas collateral vessels resemble arterioles. [1] The incidence of ICC was found to be 0.002%. [2]

We report of a unique case with a novel connection between diagonal branch of left anterior descending artery (LAD) and distal right coronary artery (RCA). Left ventricular function is preserved despite totally occluded LAD and RCA.

A 56 years old male with no history of ischemic cardiopathy, presented with palpitation. He was smoker and his father had sudden death at 54 years of age. Physical examination was normal. Electrocardiography was within normal limits except for frequent unifocal ventricular extra systoles. Echocardiography revealed normal left ventricular (LV) functions with ejection fraction of 60%. After a positive treadmill exercise test indicating high risk, he was referred to coronary angiography. Ha had 3-vessel disease with LAD occlusion distal to the diagonal branch, with late antegrade visualization of distal LAD, RCA occlusion at proximal segment and 80% stenotic lesions in proximal parts of both well-developed obtuse marginals (Fig.1 A, B, C). Left coronary injection showed a communication of 1.9 mm diameter between diagonal branch of LAD and the posterior branch of RCA. (Fig.2 A, B). He was referred to surgery.

This case presents a novel connection between coronaries which definitely played a protective role in preserving LV function despite two totally occluded major arteries. ICC has been reported as the anatomical cause of bidirectional flow. Its presence was demonstrated in patients with and without coronary narrowing. Two types were described: 1) most common was between the anterior and posterior arteries in the distal portion of the posterior interventricular groove, and 2) between distal RCA and circumflex arteries in the posterior atrioventricular groove. [1 This is the first case between diagonal branch of left anterior descending artery and the right coronary artery out of grooves.

The functional significance of these connections is unclear and some authors speculated that they would represent a potential "self-cure" for obstructive disease. [1, 2] However Donaldson et al reported a case with >95% narrowing of the RCA in which LAD- posterior descending artery (PDA) continuity didn't prevent extensive transmu-

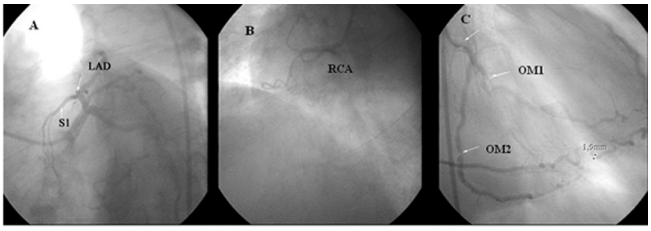

Figure 1. LAD was occluded distal to the diagonal branch (A); RCA was occluded proximally (B); both well developed obtuse marginal branches of circumflex artery had critical lesions (C).

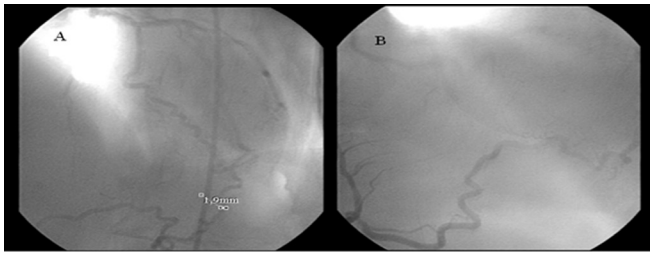

Figure 2. Inter coronary continuity: diagonal side (1.9 mm in diameter) (A); and right posterior descending side (B).

ral infarction in the distribution of the PDA, so that the theoretical protective role of "the potential self-cure" was questioned [2]. There are also some reports declaring that these connections can induce ischemia by steal phenomenon. [3, 4] The present case clearly demonstrates protective role of the existing continuity supplying RCA area.

In conclusion, ICC, a rare variant of coronary circulation, can be found between different parts of coronary circulation not only in the grooves of the heart but also in the epicardial surface as in the presented case. The potential protective role of this connections and factors influencing protective potency deserves further evaluation.

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THE LIST OF MATERIALS PUBLISHED IN THE RUSSIAN JOURNAL OF CARDIOLOGY, 2013, 4 (102) – 6 (104).

TO THE 50th ANNIVERSARY OF THE RUSSIAN SOCIETY OF CARDIOLOGY

FROM PREVENTIVE CARDIOLOGY TO NON-COMMUNICABLE DISEASE PREVENTION IN RUSSIA

Boytsov S. A., Oganov R. G.

Abstract
The increase in cardiovascular morbidity and mortality in the second half of the 20th century was mainly determined by the lifestyle and lifestyle-associated risk factors (RF). Russian epidemiologic and preventive studies, performed by the USSR Research Cardiology Centre (USSR Academy of Medical Sciences) and the State Research Centre for Preventive Medicine (Russian Ministry of Health), assessed the RF prevalence across different country regions, evaluated the RF input in the development of cardiovascular disease (CVD), and provided the evidence base for the strategies and policies on prevention of CVD and other non-communicable diseases. The decrease in Russian CVD mortality has been facilitated by the implementation of the National Project "Health", the Federal Target Programme "Social disease prevention and control", and a range of other legislative measures. Future studies should be focused on the epidemiology of CVD and other noncommunicable diseases across climatic and geographical regions; the role of influenza and acute respiratory diseases in CVD incidence; genetic RF; cardiovascular risk markers, including metabolomic and lipidomic markers; meta-genetic studies; vascular ageing; and vaccination for CVD prevention.

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Key words: prevention of cardiovascular disease and other non-communicable diseases, risk factors, preventive strategies, cardiovascular disease epidemiology.
State Research Centre for Preventive Medicine, Moscow, Russia.

CHALLENGES OF THE IMPLEMENTATION OF A NEW CARDIAC REHABILITATION SYSTEM IN RUSSIA

Aronov D. M., Bubnova M. G.

Abstract
The paper analyses the modern state of the cardiac rehabilitation system in Russia. The state system of the stage-based rehabilitation of patients with acute myocardial infarction (AMI) or patients who underwent coronary artery bypass graft (CABG) surgery was implemented in the 1980s, but collapsed due to the dramatic social changes of the past two decades. In 2013, based on the law "Healthcare of the Russian Federation citizens' which was approved by the Federation Council in 2011, the Ministry of Health launched the programme of the complex, stage-based rehabilitation of neurologic, cardiac, oncologic, and traumatlogical (central nervous system traumas) patients. The paper focuses on the cardiac rehabilitation of patients with acute coronary syndrome (ACS) and AMI, as well as individuals after CABG and intracoronary invasive interventions. The first stage is a cardiac hospital (including an intensive care unit), the second stage is an in-patient clinic of the rehabilitation centre, and the third stage is an out-patient clinic of the rehabilitation centre. The authors stress the importance of the problem which is still unresolved in Russia: the need for physical training programme as the crucial, obligatory component of cardiac rehabilitation. The data on medical and social value of cardiac rehabilitation are presented, which include significant reductions in lethality, hospital admissions, and disability, as well as a marked improvement in clinical course of the disease and quality of life. It is suggested that effective implementation of cardiac rehabilitation in the clinical settings is a method of reducing the excessive burden of mortality in Russia.

Russ J Cardiol 2013, 4 (102): 14-22
Key words: cardiac rehabilitation, rehabilitation stages, rehabilitation multidisciplinarity, physical training programme, school for ACS/AMI patients, pharmacist.
State Research Centre for Preventive Medicine, Moscow, Russia.

INFORMATION TECHNOLOGIES IN CARDIOLOGY: POTENTIAL FOR FURTHER DEVELOPMENT

Drapkina O. M.

Abstract
Medical education is based on a continuous, life-long desire of doctors to obtain reliable professional information. Distant learning in medicine, the so-called "educational system of the 21st century", stems from both the need for rapid sharing and accumulation of information and the doctors' need for continuous selfeducation. Modern distant learning incorporates two key elements: the medium of the information exchange (such as mail, TV, radio, and Internet) and the methods dependent of the information communication type. As a part of the Russian Cardiology Society's activities, the section "Information Technologies in Cardiology" facilitates generation, accumulation, and dissemination of medical information, using computer-based technologies and communications, such as Internet technologies which provide doctors with an access to professional medical knowledge in the field of cardiology.

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Key words: Internet, Russian Cardiology Society, continuous medical education, internal medicine specialist, internist.ru.
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STRENGTHS AND LIMITATIONS OF MODERN ECHOCARDIOGRAPHY IN CARDIOVASCULAR DISEASE DIAGNOSTICS

Vasyuk Yu.A., Shkolnik E. L.

Abstract
Recently, echocardiography has been playing an increasing role in the diagnostics of cardiovascular disease. Qualitative assessment of heart chamber sizes, myocardial mass, systolic and diastolic function is one of the most important tasks of echocardiography. Some of these parameters could be used as predictors of adverse prognosis. This paper presents the relevant recommendations by the European Association of Cardiovascular Imaging (EACVI) and the American Society of Echocardiography (ASE), which focus on the echocardiography standardisation, indications, and interpretation of the findings in patients with various cardiovascular diseases. The specific features of echocardiography indications and performance in Russia are also discussed.

Russ J Cardiol 2013, 4 (102): 28-32
Key words: echocardiography, indications, recommendations, standartisation.
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CARDIOVASCULAR DISEASE AND RENAL FUNCTION

Kobalava Zh. D., Villevalde S. V., Moiseev V. S.

Abstract
Cardiorenal interactions are one of the important and widely discussed problems of modern medicine. The paper discusses the evolution of the medical views on cardiorenal syndromes and chronic kidney disease. Russian and international data on prevalence, prognostic value, pathophysiologic mechanisms, prevention, and treatment of these conditions are presented. The authors discuss unresolved issues and potential directions of future research in the field of cardiorenal medicine.

Russ J Cardiol 2013, 4 (102): 33-37
Key words: cardiorenal syndrome, chronic kidney disease, nephroprotective strategies.
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DIAGNOSTICS OF INHERITED CONNECTIVE TISSUE DISORDERS: ACHIEVEMENTS AND FUTURE DIRECTIONS

Zemtsovskyi E. V.[1,2], Malev E. G.[1], Reeva S. V.[1,2], Luneva E. B.[1], Parfenova N. N.[1,2], Lobanov M. Yu.[2], Belyaeva E. L.[2], Vyutrikh E. V.[2], Timofeev E. V.[1,2], Belousova T. I.[2], Bergmane O. A.[2], Zaripov B. I.[1,2], Korshunova A. L.[1,2], Pankova I. A.[1]

Abstract
The paper reviews general factors underlying the variety of clinical manifestations of inherited connective tissue disorders (ICTD). The authors make an attempt to harmonise the existing ICTD terminology with the standard international classification. It is proposed to use the Russian term "dysplasia" as a synonym of ICTD and to divide all ICTD into inherited syndromes (IS) and dysplastic phenotypes. An example of fibrillinopathies is used to consider the clinical polymorphism and genetic heterogeneity of IS. The clinical significance of Marfanoid habitus as a phenotype is also discussed.

Russ J Cardiol 2013, 4 (102): 38-44
Key words: inherited connective tissue disorders, inherited dysplastic syndromes and phenotypes, mitral valve prolapse, Marfanoid habitus.
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FEATURES OF ANGINA DEVELOPMENT ACROSS AGE GROUPS: DATA FROM THE WORLD HEALTH SURVEY (WHS) AND THE WHO STUDY ON GLOBAL AGEING AND ADULT HEALTH (SAGE)

Maksimova T. M., Belov V. B., Lushkina N. P.

Abstract
Aim. Using the data from longitudinal studies, to identify the determinants of coronary heart disease (CHD) development.
Material and methods. Using the data from the two studies (2003 and 2007), a sample of people aged 50 years and older (135 men and 336 women), who were examined both in 2003 and 2007, was selected. All participants were divided into three groups: Group I – with CHD (angina) in 2003 and 2007; Group II – with CHD (angina) in 2007 only; and Group III – with no symptoms or signs of CHD (angina) in 2003 and 2007. The main health parameters, lifestyle characteristics, and health service use were assessed and analysed.
Results. Mean age of people free from CHD (angina) in 2003 was significantly lower than in those with CHD ($p<0,05$). In men and women from Group I, mean height values decreased by 2007, and in Group I men, there was also a statistically significant reduction in body weight ($p<0,05$). The highest percentage of individuals with normal body weight (body mass index 18,5–24,9) was observed

in people without CHD (angina) by 2007 (60% men and 42,1% women). In Group II, this percentage was 21,4% in men and 33,2% in women (approximately 33% and 22,6%, respectively, among people with long duration of the disease). CHD developed even in people with normal or low body weight. Joint pathology, diabetes mellitus, and dental health problems were associated with the development of CHD. In Group I, there was an increase in the prevalence of sleep disturbances (31,3%). No differences in the prevalence of risk factors were observed for Groups II and III. While hospital admissions due to CHD were less frequent than in other countries, the proportion of people seeking medical help was quite large.
Conclusion. In people aged 50+, age-related changes determine the development of CHD, regardless of the presence of risk factors. There is a need for more longterm prospective studies on the disease development, preventive measures, early diagnostics and adequate therapy across different contexts.

Russ J Cardiol 2013, 4 (102): 45-51
Key words: coronary heart disease, angina, risk factors, longitudinal study.
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AUTONOMIC NERVOUS SYSTEM IN ARTERIAL HYPERTENSION AND HEART FAILURE: CURRENT UNDERSTANDING OF ITS PATHOPHYSIOLOGIC ROLE AND INNOVATIVE TREATMENT APPROACHES

Konradi A. O.

Abstract
This review presents the modern understanding of the role of autonomic nervous system dysfunction in the development of arterial hypertension and heart failure. It also discusses the innovative treatment approaches which target various components of autonomic nervous system in order to treat cardiovascular disease.

Russ J Cardiol 2013, 4 (102): 52-63
Key words: autonomic nervous system, arterial hypertension, heart failure, baroreflex.
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ARTERIAL HYPERTENSION MANAGEMENT IN PREGNANCY

Stryuk R. I.

Abstract
Arterial hypertension (AH) in pregnancy is a heterogeneous pathology. It includes chronic AH (secondary AH and essential AH) which has been observed before pregnancy; gestational AH which develops approximately after 20 weeks of pregnancy and disappearing within 42 days after childbirth; pre-eclampsia (gestosis) which is a combination of AH and proteinuria; and unclassified AH which is diagnosed when blood pressure (BP) is first measured after 20 weeks of pregnancy, and elevated BP, with or without systemic signs and symptoms, is detected. AH in pregnancy increases the risk of complications both for the mother and the child, which points to the need for its active diagnostics and monitoring of the status of target organs and feto-placental complex. Pharmacotherapy of AH in pregnancy is based on the balance of its effectiveness and safety. Therefore, the first-choice medications are methyldopa, dihydropyridine calcium antagonists (nifedipine SR), and cardio-selective beta-blockers. AH in pregnancy is a risk factor of cardiovascular disease across life course stages in women.

Russ J Cardiol 2013, 4 (102): 64-69
Key words: arterial hypertension, pregnancy, diagnostics, pharmacotherapy, prognosis.
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ORIGINAL ARTICLES

HEART RATE VARIABILITY AND HEMOSTATIC PARAMETERS IN PATIENTS WITH CORONARY HEART DISEASE AND CHRONIC HEART FAILURE

Buy M. Z., Lebedeva A. Yu., Gordeev I. G., Volov N. A., Taratukhin E. O.

Abstract
Aim. To assess the association between the changes in heart rate variability (HRV) and hemostatic parameters in patients with coronary heart disease (CHD) and chronic heart failure (CHF) as its complication.
Material and methods. In total, 65 patients were examined at the O. M. Filatov City Clinical Hospital No. 15. The main group included 51 patients with CHD and CHF (35 men, 16 women; mean age 62±6 years). The control group included 14 CHD-free patients with arterial hypertension (7 men, 7 women; mean age 56±7 years). The examination included standard methods, plus the assessment of HRV and a wide range of coagulogram parameters.
Results. CHD patients with CHF demonstrated the hyperactivation of sympathetic nervous system, which was manifested in increased LF/HF (up to 2,5 U), together with the suppression of parasympathetic activity (SDNNi decrease up to 39,1 ms; $p<0,05$). Circadian sympathetic-parasympathetic interactions were persistently disturbed, with increased sympathetic effects on cardiac rhythm and inadequately increased parasympathetic activity during nighttime (LF/HF circadian index 1,0±0,5; $p<0,001$). The main group demonstrated a significant increase in protrombin index (83,4±22,7% vs. 68,5±11,23%; $p<0,05$), increased ADP-

induced (0,5 μM) platelet aggregation (1,42±0,45 U vs. 0,98±0,42 U), and increased thrombin time (18,6±6,4 vs. 12,9±2,9; p<0,01).
In CHD and CHF patients who had higher levels of sympathetic activation (LF/HF >2,0 U), protrombin time was reduced by 10,9%, while hematocrit was increased by 10,2%. In patients with elevated spontaneous platelet aggregation, increased sympathetic tone during nighttime was manifested in the reduction of mean cardiac interval duration (893,1±111,5 ms vs. 982,7±66,7 ms; p<0,05). The increase in nighttime sympathetic activation (nighttime LF/HF >2,0) was associated with a significant reduction (–20%) in ADP-induced platelet aggregation.
Conclusion. Chronic pathological sympathetic hyperactivation in patients with CHD and CHF affects hemocoagulation parameters. Increased spontaneous platelet aggregation, reduced protrombin time, and elevated hematocrit, together with catecholamine-induced vasospasm, might increase the risk of thrombotic complications.

Russ J Cardiol 2013, 5 (103): 6–11
Key words: coronary heart disease, chronic heart failure, sympathetic nervous system, hemostasis.
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PULSE WAVE VELOCITY AS A CARDIOVASCULAR RISK MARKER IN PATIENTS WITH STABLE CORONARY HEART DISEASE

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Abstract
Aim. To assess pulse wave velocity (PWV) as a potential marker of adverse prognosis, compared to conventional factors of cardiovascular risk.
Material and methods. The study included 184 patients with myocardial infarction (MI). The MI diagnosis was confirmed by the presence of pathologic Q-wave on electrocardiogram and/or diagnostic elevation of cardiac biomarkers. Carotidfemoral PWV, reflecting the status of elastic arteries, was assessed using a standard method, with the automatic computerised system Colson (France). The follow-up period (from the start of the study to either the end-point development or the study end) varied from 1 to 60 months. The Kaplan-Meier method was used for the assessment of cumulative survival.
Results. In patients with coronary artery disease (CHD), the five-year survival was 0,89 among those with PWV <10 m/s (8,3±0,13 m/s); 0,84 among those with PWV 10–12 m/s (11,1±0,32 m/s); and 0,44 among those with PWV ≥12 m/s (13,3±0,21 m/s). This difference was statistically significant. Moreover, among patients under 60 years, survival was 90,7%, while in their peers aged 60 years and older, it was only 78%. Among 184 participants, 54 had reduced left ventricular ejection fraction (LVEF) values (<40%). The five-year survival in those with LVEF>40% and <40% as 89,2% and 68,9%, respectively (the difference was statistically significant). In patients with type 2 diabetes mellitus, the survival was 69,6%, which was 19% lower than in patients with preserved systolic function.
Conclusion. In CHD patients, increased PWV has a prognostic value similar to that for conventional cardiovascular risk factors and, therefore, can be regarded as an additional novel predictor of adverse prognosis.

Russ J Cardiol 2013, 5 (103): 12–17
Key words: pulse wave velocity, arterial stiffness, cumulative survival, risk factors.
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PREDICTING THE LONG-TERM RISK OF REPEAT CORONARY EVENTS IN PATIENTS WITH UNSTABLE ANGINA

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Abstract
Aim. To stratify the patients with unstable angina (UA) by the levels of long-term (12 month) risk of repeat coronary events.
Material and methods. The study included 180 UA patients, who were divided into two groups: with or without adverse outcomes (death, myocardial infarction, recurrent UA, urgent myocardial revascularisation, life-threatening cardiac arrhythmias and blockades) during the follow-up period. The levels of biomarkers of UA pathogenesis were also measured.
Results. Independent risk predictors included mean platelet volume (MPV), fibrinogen, and left ventricular ejection fraction (LVEF). The risk of adverse UA outcomes in patients with MPV levels ≥9,1 fl (sensitivity 44%, specificity 79%), fibrinogen levels >4,4 g/l (sensitivity 62%, specificity 62%), and LVEF levels ≤54% (sensitivity 83%, specificity 97%) is increased 10 times. The proposed screening scale for risk stratification is highly effective (sensitivity 62,5%, specificity 89,05, AUC=0,799) in the identification of UA patients at a high risk of repeat coronary events.
Conclusion. The dynamic assessment of such biomarkers as MPV, fibrinogen, and LVEF is important for early, effective pharmacological and invasive treatment, as well as for effective secondary prevention of repeat coronary events.

Russ J Cardiol 2013, 5 (103): 18–22
Key words: prognosis, unstable angina, repeat coronary events.
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SQUATTING STRESS ECHOCARDIOGRAPHY POTENTIAL IN CORONARY HEART DISEASE DIAGNOSTICS

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Abstract
While stress echocardiography (EchoCG) is widely used in clinical practice for diagnosing silent myocardial ischemia, the search for new stress tests remains an important task in the diagnostics of coronary heart disease (CHD).
Aim. To assess the potential of squatting stress EchoCG in the diagnostics of CHD.
Material and methods. In total, 53 men (mean age 53,2±0,93 years) underwent stress EchoCG. At coronary angiography, the CHD diagnosis was verified in 37 men (mean age 54,1±1,2 years), while in the other 16 men (mean age 51,0±1,4 years), myocardial ischemia was not confirmed. All participants underwent standard stress EchoCG with dobutamine, as well as supine and squatting EchoCG. The myocardial ischemia criterion was the development of additional asynergy zones in left ventricular myocardium.
Results. The test was performed in all patients, without any complications. Disturbed local contractility was observed at the time of squatting and rapidly disappeared while standing up. The sensitivity and specificity of squatting stress EchoCG in the CHD diagnostics were 94,6% and 81.3%, respectively.
Conclusion. Therefore, we have demonstrated a high diagnostic value of squatting stress EchoCG for diagnosing myocardial ischemia. This value was comparable to that of stress EchoCG with dobutamine.

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Key words: stress echocardiography, squatting stress test, left ventricular longitudinal myocardial deformation, peak systolic strain, coronary angiography, left ventricular local contractility.
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ANGIOGENIC PROPERTIES OF ADIPOSE TISSUE-DERIVED MULTIPOTENT MESENCHYMAL STROMAL CELLS IN PATIENTS WITH CORONARY HEART DISEASE

Dzhoyashvili N. A.[1], Efimenko A. Yu.[1], Akchurin R. S.[2], Tkachuk V. A.[1,2], Parfenova E. V.[1,2]

Abstract
Aim. To compare angiogenic properties of adipose tissue (AT) derived multipotent mesenchymal stromal cells (MMSC) in patients with or without coronary heart disease (CHD) and to investigate potential effects of concomitant Type 2 diabetes mellitus (DM-2) on these properties.
Material and methods. To extract AT MMSC, subcutaneous adipose tissue samples were obtained during a surgical intervention in 19 controls (individuals without cardiovascular disease or DM-2), 28 patients with CHD and DM-2, and 32 CHD patients without DM-2. Angiogenic properties of AT MMSC were assessed by the length of capillary-like structures formed by endotheliocytes on Matrigel in the presence of the conditioned AT MMSC medium. Growth factor gene expression was measured using the real-time polymerase chain reaction. Growth factor levels in the conditioned AT MMSC medium were measured using the enzyme-linked immunosorbent assay (ELISA).
Results. In CHD patients, the total length of capillary-like structures, formed by endotheliocytes in the presence of the conditioned AT MMSC medium, was twice as low as in controls. However, there was no marked difference between CHD patients with or without DM-2. CHD patients did not demonstrate a reduction in the levels of main angiogenic factors, measured in the conditioned AT MMSC medium. On the contrary, the levels of some factors (VEGF, HGF, and PIGF) were elevated, as well as the levels of PAI-1.
Conclusion. Angiogenic activity of secretion end-products of AT MMSC was reduced in CHD patients, compared to CHD-free individuals. The presence of concomitant DM-2 did not affect angiogenic properties of AT MMSC in CHD patients. Reduced angiogenic activity of AT MMSC could be due to increased PAI-1 production. PAI-1 suppresses the activity of plasminogen activators and, therefore, may have angiogenic effects. To confirm this hypothesis, further research is needed.

Russ J Cardiol 2013, 5 (103): 27–34
Key words: angiogenesis, coronary heart disease, Type 2 diabetes mellitus, adipose tissue-derived stromal cells, paracrine function.
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LEFT CARDIAC CHAMBERS AFTER IMPLANTATION OF MITRAL VALVE PROSTHESES “MIX”, “MEDINGE-2”, “KEMCOR”, AND “PERICOR”

Rogulina N. V., Sizova I. N., Gorbunova E. V.

Abstract
Aim. To compare ultrasound parameters of left cardiac chambers after the implantation of mitral valve prostheses “MIX”, “MEDINGE-2”, “KemCor”, and “PeriCor”, using the 10-year follow-up data.
Material and methods. We analysed 2,543 echocardiography protocols of patients with mitral valve disease, who in 1995–2008 underwent the implantation of mitral valve prostheses “MIX” (n=122), “MEDINGE-2” (n=67), and biological prostheses “KemCor” or “PeriCor” (n=306). The exclusion criteria were aortal valve prosthesis, prosthesis dysfunction, and age under 18 years.

Results and conclusion. In the early post-intervention period, left ventricular (LV) ejection fraction tended to decrease (p>0,10); however, by the end of the first year, it was normalised. The use of biological prostheses resulted in a significant (p≤0,05) reduction in linear dimension of left atrium and in systolic pulmonary artery pressure, which was observed immediately after the intervention and persisted for several years. The dynamics of linear and volume LV parameters after mitral valve prosthesis implantation did not depend on the prosthesis type.

Russ J Cardiol 2013, 5 (103): 35–39
Key words: mechanical cardiac valve prosthesis, biological cardiac valve prosthesis, mitral valve disease, left atrium, left ventriculum, pulmonary artery pressure.
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RADIOMETRY OF WATER-CONTAINING MYOCARDIAL TISSUE IN PATIENTS WITH ARTERIAL HYPERTENSION

Terekhov I. V.[1], Solodukhin K. A.[1], Nikiforov V. S.[2], Lomonosov A. V.[3]

Abstract
Aim. To study the water-containing myocardial tissue in patients with arterial hypertension (AH), using the ultra-high frequency (UHF) radiometry method, in order to assess myocardial function parameters.
Material and methods. In total, echocardiography was performed in 30 patients, aged 40–60 years, with Stage I–III AH and Functional Class I–III chronic heart failure. Myocardial radiometry was performed with the diagnostic complex "Aquatone", which assesses the status of water-containing tissues using the resonance probe radio emission (1 GHz) and stimulated tissue emission (65 GHz).
Results. There was a strong negative correlation between the radio signal intensity and left ventricular posterior wall thickness (r=–0,96), myocardial mass index (r=–0,82), and end-systolic dimension (r=–0,66), as well as a strong positive correlation with end-diastolic dimension (r=0,55) and ejection fraction (r=0,73).
Conclusion. The results obtained suggest the presence of pronounced changes in myocardial radio-physical characteristics in AH patients, as manifested in the disturbed myocardial ability to transform the external probe emission into the stimulated one.

Russ J Cardiol 2013, 5 (103): 40-43
Key words: myocardial hypertrophy, arterial hypertension, radiometry.
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GLYCOPROTEIN INTEGRIN ALPHA POLYMORPHISM AND ACUTE CEREBROVASCULAR EVENTS IN THE FAMILIES OF PATIENTS WITH ATRIAL FIBRILLATION

Aksyutina N. V.[1], Nikulina S. Yu.[1], Shulman V. A.[1], Nazarov B. V.[1], Maksimov B. V.[2], Bezruk A.P.[1], Balog A.I.[3], Poplavskaya E. E.[1], Bespalov A. V.[1], Kotlovskyi M. Yu.[1], Chernova A. A.[1]

Abstract
Aim. To assess the associations between the polymorphism of the glycoprotein integrin alpha (Iα) gene and acute cerebrovascular events (ACerVE) in the families of patients with atrial fibrillation (AF).
Material and methods. In total, 43 probands with chronic AF and ACerVE in medical history (25 women and 18 men) and their 54 first, second, and third-degree relatives (37 women and 17 men) were examined. The control group included 188 people free from cardiovascular disease (96 women and 92 men). All participants underwent standard medical examination, lectrocardiography (ECG), echocardiography, and genetic analysis. In addition, the relatives of probands underwent 24-hour Holter ECG monitoring and physical stress test, in order to detect paroxysmal cardiac arrhythmias.
Results. CC genotype of the glycoprotein Iα 807C>T polymorphism was significantly less prevalent in patients with AF and ACerVE, compared to the control group (23,3% vs. 43,1%; p=0,026; odds ratio (OR) 0,40; 95 confidence interval (CI) 0,19–0,86%). In contrast, CT genotype of the glycoprotein Iα 807C>T polymorphism was significantly more prevalent among participants with AF and ACerVE, compared to the controls (62,8% vs. 42,6%; p=0,026). Overall, genotypes with T allele (CT+TT) were significantly more prevalent in AF patients with ACerVE than in controls (76,8% vs. 57,0%; p=0,026; OR 0,40; 95% CI 0,19–0,86%). In three relatives of probands, AF was detected, and two relatives had ACerVE in their medical history. Among the relatives with AF and ACerVE, CT genotype of the glycoprotein Iα 807C>T polymorphism was also registered.
Conclusion. This study has demonstrated that CT genotype of the glycoprotein Iα 807C>T polymorphism is associated with ACerVE in the families of AF patients. Individuals with TT genotype of the glycoprotein Iα 807C>T polymorphism might benefit from the administration of acetylsalicylic acid, while in people with CC and CT genotypes, anticoagulants might be more effective.

Russ J Cardiol 2013, 4 (102): 6-10
Key words: glycoprotein Iα gene, acute cerebrovascular event, atrial fibrillation.
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PREVENTIVE MYOCARDIAL REVASCULARISATION BEFORE ABDOMINAL AORTIC INTERVENTIONS: LONG-TERM RESULTS

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Abstract
Aim. To assess the effects of preventive myocardial revascularisation on the longterm results of abdominal aortic interventions.
Material and methods. The retrospective analysis of the data from patients examined before planned abdominal aortic interventions was performed. Group I included 86 patients (mean age 59,4±7,7 years) who were operated at the Kemerovo Cardiology Centre clinic. Group II included 32 patients (mean age 53,5±6,2 years) who were operated at the Novokuznetsk City Clinical Hospital No. 29. Before abdominal aortic interventions, the majority of Group I patients underwent coronary angiography (CAG) and, if indicated, preventive myocardial revascularisation. The long-term results were assessed 4–6 years later.
Results. In Group I, CAG was performed in 77 (89%) patients, and preventive myocardial revascularisation was performed in 23 (27%) patients. Among Group I patients, fatality was 1,2% (n=1) in the long-term post-intervention period, with the level of total mortality of 3,5%. In Group II patients, the respective figures were 31,2% (n=10) and 34,4% (p<0,001). In univariate analyses, the main predictor of total morality was the absence of preventive myocardial revascularisation (odds ratio, OR, 14,49; 95% confidence interval (CI) 3,65–57,49; p<0,001). Clinical manifestations of angina (p=0,063) and myocardial infarction in medical history (p=0,105) failed to demonstrate statistical significance as mortality predictors. The factors associated with a reduction in the risk of fatal outcomes were β-blocker therapy (OR 0,06; 95% CI 0,01–0,31; p<0,001) and ACE inhibitor therapy (OR 0,35; 95% CI 0,11–1,10; p=0,070).
Conclusion. Preventive myocardial revascularisation significantly improved the longterm survival after abdominal aortic interventions. In logistic regression analyses, the absence of preventive myocardial revascularisation was associated with reduced.
long-term survival after abdominal aortic interventions, while β-blocker therapy was linked to improved long-term survival.

Russ J Cardiol 2013, 6 (104): 11-16
Key words: coronary angiography, abdominal aortic interventions, preventive revascularisation, survival.
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ENDOTHELIAL DYSFUNCTION MARKERS IN PATIENTS WITH NON-ST ELEVATION ACUTE CORONARY SYNDROME AND MULTIFOCAL ATHEROSCLEROSIS

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Abstract
Aim. To investigate the association between endothelial dysfunction markers and multifocal atherosclerosis in non-ST elevation acute coronary syndrome (NSTE- ACS).
Material and methods. The study included 82 patients with NSTE-ACS, who underwent coronary angiography, colour duplex ultrasound of brachiocephalic arteries (BCA) and lower extremity arteries (LEA), and a complex assessment of endothelial function during their hospitalisation. Vasodilating endothelial function was assessed by endothelium-dependent vasodilatation (EDVD) in a reactive hyperemia test. Vasoconstrictory and adhesive endothelial function was assessed by the blood levels of endothlin-1, sP-selectin, and sE-selectin in a solid-phase enzyme immunoassay. Statistical analyses were performed using the STATISTICA 6.0 software package.
Results. Isolated coronary artery (CA) atherosclerosis was registered in 46,3% of the patients, while isolated BCA atherosclerosis was observed in 9,7%, and the combination of CA and peripheral artery atherosclerosis was registered in 19,5%. No cases of isolated LEA atherosclerosis were observed. According to the visualisation results, 24,3% of the patients had no signs of atherosclerotic stenosis (>30%) in any vascular basin. The highest levels of endothelin-1 were registered in patients with isolated BCA atherosclerosis and with the combination of peripheral and CA atherosclerosis. No significant differences were observed between the groups by the blood levels of sP-selectin and sE-selectin; moreover, these levels were within the reference range. All groups demonstrated similar levels of vasodilating endothelial function.
Conclusion. In NSTE-ACS patients, vasoconstrictory endothelial function was clearly associated with the atherosclerosis parameters. At the same time, there was no link between the atherosclerosis severity and localisation and the parameters of vasodilating and adhesive endothelial function. Endothelin-1, as a vasoconstriction marker, was most informative in patients with peripheral and multifocal atherosclerosis.

Russ J Cardiol 2013, 6 (104): 17-22
Key words: non-ST elevation acute coronary syndrome, endothelial dysfunction.
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METABOLIC PLATELET STATUS IN PATIENTS WITH STABLE ANGINA

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Abstract
Aim. To study the activity of NAD- and NADP-dependent platelet dehydrogenases in patients with various functional classes of angina.

Material and methods. The study included 91 men with Functional Class II–IV angina, aged 45–72 years. In all participants, the bioluminescent method was used to measure the activity of the following enzymes: glucose-6-phosphate dehydrogenase (G6PD), glycerol-3-phosphate dehydrogenase (GPDH), NADPmalate dehydrogenase (NADP-MDH), NAD- and NADH-dependent lactate dehydrogenase reaction (LDH and NADH-LDH, respectively), NAD- and NADHdependent malate dehydrogenase reaction (MDH and NADH-MDH, respectively), NADP- and NADPH-dependent glutamate dehydrogenase (NADP-GDH and NADPH-GDH, respectively), NAD- and NADH-dependent glutamate dehydrogenase (NAD-GDH and NADH-GDH, respectively), NAD- and NADP-dependent isocitrate dehydrogenase (NAD-IDH and NADP-IDH, respectively), and glutathione reductase (GR).
Results. The metabolic platelet status was associated with the functional class of angina. In patients with Functional Class II angina, minimal platelet changes, linked to the inhibition of plastic processes, were observed. Patients with Functional Class III angina demonstrated an inhibition of lipid metabolism and an increase in glycolytic activity. In Functional Class IV angina, the metabolic disturbances were most pronounced and manifested in inhibited plastic processes and lipid catabolism, together with activated anaerobic reactions.
Conclusion. In stable angina patients, the changes in intracellular metabolic activity of platelets mirror the increase in the functional class of angina. Modification of platelet metabolism could be one of the methods of decreasing the receptor and, therefore, aggregation platelet activity.

Russ J Cardiol 2013, 6 (104): 23-27
Key words: angina, platelets, NAD- ad NADP-dependent dehydrogenases, intracellular metabolism.
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A NON-INVASIVE MARKER OF INSULIN RESISTANCE IN PATIENTS WITH OBESITY

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Abstract
Insulin resistance (IR) and hormone activity of visceral fat are the main pathogenetic mechanisms which link obesity and cardiovascular complications. Until recently, the association between epicardial adiposity and IR has been understudied.
Aim. To investigate the association between the thickness of epicardial fat tissue (tEFT) and IR and to determine the predictive value and threshold levels of tEFT for the diagnostics of IR.
Material and methods. The study included 186 men (mean age 54,4±9,1 years) with the mean body mass index of 34,23±3,97 kg/m². IR was assessed by the levels of insulin and HOMA-IR index. The echocardiography measurement of tEFT (mm behind the free right ventricular wall) was performed in a systole, in a parasternal position on the long and short left ventricular axis.
Results. Mean tEFT levels in the IR-positive group were significantly higher (7,0 (7,0;9,0)) than in the IR-negative group (5 (4,0;6,0); p<0,001). In the logistic regression analyses, the proportion of accurate predictions was 91%, and the Somers' D-value was 0,837. The optimal cut-off for tEFT, as a non-invasive IR marker, was ≥7 mm (sensitivity 91,5% and specificity 90,6%).
Conclusion. The tEFT parameter could be used as a non-invasive marker of IR, which might facilitate the identification of obese patients with high levels of cardiovascular risk and the early start of preventive interventions.

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Key words: insulin resistance, metabolic syndrome, epicardial adiposity.
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LUNG DIFFUSION CAPACITY AND NON-SPECIFIC INFLAMMATION MARKERS IN PATIENTS WITH CORONARY HEART DISEASE AND DIABETES MELLITUS

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Abstract
Aim. To assess the differences in the lung diffusion capacity and non-specific inflammation markers among patients with coronary heart disease (CHD) and the combination of CHD and Type 2 diabetes mellitus (DM-2).
Material and methods. The study included 70 CHD patients: with DM-2 (n=40; 57,1%) and without DM-2 (n=30; 42,9%). Lung diffusion capacity (DIco) was assessed with the single-breath method and subsequent correction by haemoglobin levels (DIco cor). The levels of the following non-specific inflammation markers were also assessed: IL-1β, IL-12, TNF-α, IFN-γ, MMP-9, and CRP.
Results. In all participants, DIco levels were within the reference range. However, in patients with CHD and DM-2, they were significantly lower (–6,3%). Moreover, in DM-2 patients, the levels of inflammation markers, such as CRP (p=0,006), MMP-9 (p<0,001), and TNF-α (p=0,01), were significantly higher than in non-diabetic CHD patients. A reduction in DIco levels correlated with an increase in the activity of nonspecific systemic inflammation, assessed by the levels of CRP (r=–0,39; p=0,020), MMP-9 (r=–0,66; p=0,013), TNF-α (r=–0,72; p=0,02); with decompensated carbohydrate (for HbA1 and DIco cor, r=–0,32; p=0,043) and lipid metabolism (for total cholesterol and DI cor, r=–0,29; p=0,025; for low-density lipoprotein cholesterol and DIco cor, r=–0,45; p=0,003; for triglycerides and DIco cor, r=–0,43; p=0,021); and with the duration of DM-2 (r=–0,65; p=0,014).
Conclusion. In patients with CHD and DM-2, respiratory dysfunction, manifested in decreased levels of DIco cor, is associated with increased levels of inflammation markers (CRP, MMP-9, and TFN-α). The decrease in DIco cor is linked to increased activity of non-specific systemic inflammation (assessed by the levels of CRP, MMP-9, and TFN-α), decompensated carbohydrate and lipid metabolism, and a longer duration of DM-2.

Russ J Cardiol 2013, 6 (104): 33-38
Key words: lung diffusion capacity, diabetes mellitus, coronary heart disease.
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THYROID STATUS COMPENSATION AND CARDIOVASCULAR PARAMETERS IN PATIENTS WITH PRIMARY HYPOTHYREOSIS

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Abstract
Aim. To investigate the effects of primary hypothyreosis (PHT) compensation on cardiac remodelling, aortic elasticity, and vasomotor endothelial function.
Material and methods. In total, 28 women with PHT were examined (age 42–78 years; median age 59,5 years). All patients underwent echocardiography and the assessment of aortic elasticity and vasomotor endothelial function using the method by Cleremajer et al. (1992). The examination took place twice, during the PHT decompensation and its compensation due to the treatment with levothyroxine sodium (on average, 3 months after the beginning of the therapy).
Results. The PHT compensation was associated with a reduction in the levels of thyrotrophic hormone from 18,8 (95% confidence interval 10,7–27,0) to 2,6 (2,1–3,1) mIU/l ($p<0,001$) and an elevation in the levels of free thyroxin from 10,8 (9,2–12,44) to 13,7 (12,7–14,7) pmol/l ($p<0,005$). Left ventricular myocardial mass decreased from 192,4 (182,0–202,8) to 171,4 (160,9–181,9) g. The proportion of patients with left ventricular diastolic dysfunction decreased from 92,9 (77,4–98,0) to 71,4 (54,7–88,2)% ($p<0,05$), while the proportion of patients with right ventricular diastolic dysfunction decreased from 82,1 (64,4–92,1) to 25,0 (9,0–41,0)%
($p<0,001$). Aortic wall thickness reduced from 5,26 (4,90–5,62) to 4,53 (4,28–4,78) mm, aortic elasticity index increased from 2,26 (1,60–2,92) to 5,26 (4,36–6,15) mm 2/mm Hg, and pulse wave velocity decreased from 12,8 (11,4–14,3) to 8,42 (6,59–10,3) m/s. Relative increase in brachial artery diameter in the reactive hyperemia test, as a marker of vasomotor endothelial function, changed from 2,91 (1,69–4,14) to 9,13 (7,84–10,4)% (all p-values <0,001).
Conclusion. PHT compensation is associated with reduced left ventricular myocardial mass, improved left and right ventricular function, increased aortic elasticity, and improved vasomotor endothelial function.

Russ J Cardiol 2013, 6 (104): 39-42
Key words: primary hypothyreosis, cardiac remodelling, aortic elasticity, endothelial dysfunction.
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ASSOCIATION BETWEEN OXIDATIVE-ANTIOXIDANT MODIFICATIONS OF LOW-DENSITY LIPOPROTEINS AND CORONARY HEART DISEASE IN A MALE POPULATION OF NOVOSIBIRSK

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Abstract
Aim. To investigate the association between potentially atherogenic oxidativeantioxidant modifications of low-density lipoproteins (LDL) and coronary heart disease (CHD) in a male population.
Material and methods. A population-based survey included 1024 male residents of Novosibirsk City, aged 47–73 years. The participants underwent a questionnaire survey, a standard cardiologic survey, anthropometry, blood pressure measurement, and electrocardiography. "Definite CHD" (Functional Class II–IV stable effort angina) was registered in 223 men (21,8%), according to validated epidemiologic, clinical, and functional criteria. Blood biochemistry analyses focused on the levels of total cholesterol (TCH), triglycerides (TG), high-density lipoprotein cholesterol (HDL–CH), high-sensitivity C-reactive protein (hsCRP), glucose, baseline levels of lipid peroxidation (LPO) products and fat-soluble antioxidants (alpha-tocopherol, retinol, beta-carotene, and xanthines) in LDL, LDL oxidation resistance in vitro, and an concentration of autoantibodies to oxidised LDL (oxLDL).
Results. There were positive correlations and independent associations between the oxidative LDL modifications, in particular between reduced LDL oxidation resistance and CHD. On the other hand, there were negative correlations between the antioxidant LDL modifications (such as reduced alpha-tocopherol levels in LDL) and CHD. The prevalence of CHD was higher in participants with baseline levels of LPO products in LDL >0,8 nM MDA/mg LDL protein and with reduced LDL oxidation resistance (baseline levels >5,4 nM MDA/mg LDL protein vs. levels >13,2 nM MDA/mg LDL protein at later stages of LDL oxidation). However, the prevalence of CHD was lower in individuals with LDL levels of alpha-tocopherol >1,06 mg/mg LDL protein.
Conclusion. These findings agree with the previously obtained data on the key role of oxidative LDL modifications in the pathogenesis of atherosclerosis and CHD.

Russ J Cardiol 2013, 6 (104): 43-47
Key words: population study, coronary heart disease, low-density lipoproteins, oxidation resistance, antioxidants.
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FIVE-YEAR DYNAMICS OF CIRCADIAN BLOOD PRESSURE PROFILE IN FAR NORTH WORKERS WITH ARTERIAL HYPERTENSION

Zapesochnaya I. L., Avtandilov A. G.

Abstract

Aim. In a prospective study, to assess the dynamics of circadian profiles of blood pressure (BP) in Far North workers with arterial hypertension (AH) and different shift working patterns.

Material and methods. In the first phase of the study (2003–2005), 95 patients with Stage 1–2 AH were examined. Group I included 53 patients who worked only day shifts; Group II included 42 patients who worked alternating day and night shifts. In the second phase (2007–2011), both groups were examined, including 24-hour BP monitoring, and two subgoups (treated vs. untreated AH) were defined.

Results. In Far North workers with AH, there was a negative dynamics in circadian BP profile, particularly among night shift workers. AH patients require antihypertensive combination therapy irrespective of their shift working patterns.

Russ J Cardiol 2013, 6 (104): 48-53

Key words: arterial hypertension, Far North, night shifts, circadian blood pressure profile.

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CLINIC AND PHARMACOTHERAPY

WHEN THE BODY DOES NOT COLLABORATE: PHARMACOLOGICAL TREATMENT OF OBESITY

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Abstract

The paper presents the modern evidence on pharmacological treatment of patients with obesity and comorbidities, who try to modify their lifestyle, but are unsuccessful due to metabolic disturbances. The main and recently discovered additional effects of orlistat are discussed.

Russ J Cardiol 2013, 4 (102): 70-72

Key words: obesity, dyslipidemia, arterial hypertension, anti-cancer.

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ALGORITHM FOR DIFFERENTIAL ADMINISTRATION OF COMBINATION ANTIHYPERTENSIVE THERAPY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract

Aim. To compare the effectiveness of three variants of long-term combination antihypertensive therapy (AHT), based on two methods of renin-angiotensinaldosterone system (RAAS) inhibition (angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor antagonists (ARAII)) or on calcium channel blockade with a dihydropyridine calcium channel blocker (CCB), all of which were administered in order to achieve target levels of blood pressure (BP). To develop an algorithm for differential administration of combination AHT in patients with arterial hypertension (AH) and Type 2 diabetes mellitus (DM-2).

Material and methods. The study included 71 patients (mean age 56,8±6,5 years) with AH and DM-2, but without clinically manifested nephroangopathy. The therapy course (30–32 weeks) was completed by 69 patients. All participants were randomised into three groups. The ACEI+CCB group (n=22) received perindopril (5–10 mg/d), indapamide SR (1,5 mg/d), and amlodipine (5–10 mg). The ARAII+CCB group (n=25) was administered valsartan (80–160 mg/d), indapamide SR, and amlodipine. The CCB+BAB group (n=22) received amlodipine (5–10 mg/d), indapamide SR, and metoprolol succinate (50–100 mg/d). The doses of AHT were increased stepwise. At baseline and after 30–32 weeks of the treatment, 24-hour BP monitoring (BPM), renal artery ultrasound and Doppler ultrasound, carbohydrate and lipid metabolism assessment, and 24-hour albumin excretion measurement were performed.

Results. Target BP levels were achieved in the majority of patients from all three groups. For the two-component combination AHT, target BP levels were achieved more often with the combination of RAAS inhibitors and indapamide SR, compared to the combination of CCB and indapamide SR. Most patients receiving the latter combination required additional administration of a third medication, in order to achieve adequate BP control. The combination of CCB and BAB increased intrarenal vascular resistance and less effectively controlled night-time systolic AH, compared to the combination of RAAS inhibitors and CCB. The combination of ACEI and CCB, compared to the ARAII+CCB combination, was associated with improved glycemic control, effective reduction of the duration of night-time diastolic AH and night-time heart rate, and normalisation of initially elevated intrarenal vascular resistance at the level of segmental intrarenal arteries. These findings were used for the development of the algorithm for differential administration of combination AHT in patients with AH and DM-2.

Conclusion. In DM-2 patients, long-term combination AHR with ACEI and CCB demonstrates more beneficial effects on the metabolic and neurohumoral regulation processes, compared to the combination of ARAII and CCB. These benefits are particularly pronounced in patients with inadequate glycemic control and increased intrarenal vascular resistance. The combination of CCB and BAB inadequately controls night-time systolic AH and does not improve renal hemodynamics.

Russ J Cardiol 2013, 4 (102): 74-82
Key words: diabetes mellitus, arterial hypertension, target blood pressure, combination antihypertensive treatment, intrarenal vascular resistance, glycemic control.
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PLEIOTROPIC EFFECTS OF TRIMETAZIDINE

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Abstract
Aim. To investigate potential pleiotropic effects of trimetazidine (Preductal MB) in patients with stable effort angina.
Material and methods. This randomised controlled clinical study included 95 patients with Functional Class I–III stable effort angina and Stage 2–3 arterial hypertension. Clinical effectiveness of pharmacological therapy was assessed by expert-evaluated subjective and objective criteria, with the calculation of the treatment effectiveness index (%) (Patent No. 58859 A [8], Ukraine).
Results. The complex pharmacological therapy of coronary heart disease (CHD) was twice as effective after the addition of trimetazidine, due to increased antianginal action and exercise capacity. Trimetazidine also reduced energy deficiency and tissue hypoxia in myocardial ischemia. Pleiotropic effects of trimetazidine (antiatherosclerotic, anti-inflammatory, and stress-limiting) could justify the extended indications for this medication.
Conclusion. In a randomised clinical trial including patients with stable effort angina, the effectiveness of complex pharmacotherapy was doubled by additional administration of trimetazidine (Preductal MB 35 mg twice per day for 6 weeks), due to increased antianginal effects and exercise capacity.

Russ J Cardiol 2013, 4 (102): 83-87
Key words: coronary heart disease, stable angina, metabolism, patients, pleiotropic effects, trimetazidine (Preductal MB).
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EXPERIENCE OF USING A FIXED-DOSE COMBINATION OF PERINDOPRIL AND AMLODIPINE IN THE CLINICAL PRACTICE SETTINGS: A REAL-WORLD OPPORTUNITY TO INCREASE ANTIHYPERTENSIVE THERAPY EFFECTIVENESS

Ostroumova O. D., Guseva T. F., Bondarets O. V.

Abstract
The paper presents the results of the studies on effectiveness and safety of a fixeddose combination of perindopril A and amlodipine (Prestans) in the real-world clinical practice settings in Russia and other countries. The focus is on the evidence of fast and strong antihypertensive action of this medication, its excellent tolerability, and increased therapy compliance. The evidence presented justifies a wider use of this fixed-dose combination of perindopril A and amlodipine in order to improve blood pressure control in hypertensive patients.

Russ J Cardiol 2013, 5 (103): 44–49
Key words: arterial hypertension, fixed-dose combinations of antihypertensive agents, calcium antagonists, amlodipine, angiotensin-converting enzyme inhibitors, perindopril.
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ANTIHYPERTENSIVE COMBINATION THERAPY EFFECTS ON CARDIAC REMODELLING IN ELDERLY PATIENTS

Gadzhieva L. Kh.[1], Masuev K. A.[2], Ibragimova M. I.[2]

Abstract
Aim. To investigate potential regression of left ventricular (LV) remodelling in elderly patients receiving antihypertensive combination therapy.
Materials and methods. The study included 80 patients (23 men, 57 women) with arterial hypertension (AH) and different levels of cardiovascular risk, aged 60–86 years (mean age 72,4±6,5 years; median age 72 years; interquartile range 69,5–76 years). The mean AH duration was 19,6±6,8 years. All patients underwent echocardiography at baseline and 6 months after the beginning of antihypertensive combination therapy: fixeddose combinations of an ACE inhibitor and a diuretic (perindopril + indapamide), or an ACE inhibitor plus a calcium antagonist (lisinopril + amlodipine). Statistical analyses were performed using “Statistica-6.0” software package (StatSoft Inc., 1984–2001).
Results. The study participants had high and very high levels of cardiovascular risk. Six patients (7,5%) had Stage II AH, while 72 (92,5%) had Stage III AH. In 60 patients (75,0%), AH was combined with coronary heart disease (CHD), in 2 (2,5%) with diabetes mellitus (DM), in 16 (20%) with CHD and DM. Isolated systolic AH (ISAH) was registered in 35 patients (44%). At baseline, echocardiography parameters were similar across clinical groups. After 6 months of combination therapy, positive dynamics of echocardiography parameters was observed: for example, left atrium size was significantly lower in patients treated with perindopril

and indapamide, compared to patients who received lisinopril and amlodipine or controls. Similar findings were obtained for end-diastolic dimension and interventricular septum thickness. In contrast to the other two groups, the control group did not demonstrate any significant dynamics of end-systolic dimension (p>0,05). Patients treated with perindopril and indapamide showed the best dynamics of LV myocardial mass index (from 121,6±16,42 to 111,0±13,59) and LV myocardial mass (from 229,2±47,91 to 204,7±51,01). In all groups, there was an improvement in diastolic function, which manifested in a significant E/A reduction.
Conclusion. In elderly AH patients with high and very high cardiovascular risk, antihypertensive combination therapy was associated with a significant regression in LV remodelling. The optimal combination included an ACE inhibitor and a diuretic (perindopril arginine and indapamide).

Russ J Cardiol 2013, 5 (103): 50–55
Key words: left ventricular remodelling, arterial hypertension, antihypertensive combination therapy, elderly patients.
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INDAPAMIDE RETARD AS THE MEDICATION OF CHOICE IN ELDERLY PATIENTS WITH ARTERIAL HYPERTENSION

Chukaeva I. I., Spiryakina Ya.G.

Abstract
The modern society faces a steady increase in the numbers of elderly people, which is associated with a range of social and medical problems. Age-related aspects of body anatomy and physiology, multiple comorbidity, and cognitive decline restrict the choice of medications in elderly patients. The paper discusses the need for the agreement between the choice of antihypertensive agents in elderly patients and the importance of organoprotection. From the evidence-based medicine standpoint, indapamide retard is considered as the medication which meets all the requirements for arterial hypertension treatment in elderly patients.

Russ J Cardiol 2013, 5 (103): 56–60
Key words: elderly patients, arterial hypertension, organoprotection, indapamide retard.
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TRIMETAZIDINE MB ROLE IN THE OPTIMISATION OF THE ACUTE CORONARY SYNDROME TREATMENT: EFFECTS ON ENDOTHELIAL DYSFUNCTION AND SYSTEMIC INFLAMMATION

Davydov S. I., Titova V. V., Gordeeva M. A., Tarasov A. A., Babaeva A. R.

Abstract
Aim. To study the effects of trimetazidine MB therapy on the clinical manifestations and markers of endothelial dysfunction and systemic inflammation in patients with acute coronary syndrome (ACS).
Material and methods. This open, comparative, randomised parallel-group study included 60 patients with a verified ACS diagnosis (34 men and 26 women, aged 40–84 years). All participants were randomised into two treatment groups: the main group receiving trimetazidine MB (Preductal MB) 35 mg twice a day, and the control group receiving standard therapy but not trimetazidine MB. The examination included electrocardiography (ECG), echocardiography, 24-hour ECG monitoring, and chest X-ray.
Results. After 3 months of the treatment, the main group demonstrated a significant reduction in the incidence and duration of anginal attacks (–58% and –42%, respectively), as well as in the weekly nitrate intake (–66%). There was a nonsignificant (possibly, due a relatively small sample size) tendency towards a reduction in the severity of anginal attacks (–36%). The control group demonstrated a less prominent dynamics of clinical parameters: the incidence of anginal attacks decreased by 21%, the weekly nitrate intake by 20%, and the duration and severity of anginal attacks only by 6%.
Conclusion. The combination of trimetazidine MB with the standard ACS therapy improves the treatment effectiveness, in terms of the anginal syndrome manifestations and endothelial function stabilisation, as suggested by a significant reduction in von Willebrand factor and endothelin levels, compared to the control group.

Russ J Cardiol 2013, 6 (104): 54-61
Key words: endothelial dysfunction, systemic inflammation, coronary heart disease, angina, anginal attack, trimetazidine MB (Preductal MB).
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ANTIISCHEMIC AND ANTIARRHYTHMIC EFFECTS OF SIMVASTATIN IN PATIENTS WITH DIASTOLIC HEART FAILURE

Pinchuk T. V.[1], Fedulaev Yu.N.[1], Khayretdinova G. A.[2]

Abstract
Aim. To assess the dynamics of antiischemic and antiarrhythmic effects of the 6-month simvastatin therapy (20 mg/d) in patients with ischemic chronic heart failure (CHF), arterial hypertension, and preserved left ventricular (LV) ejection fraction.
Material and methods. The study included 125 patients with diastolic dysfunction (impaired relaxation and pseudonormalisation): 66 patients receiving standard CHF treatment and simvastatin (the main group), plus 59 patients receiving only standard CHF

treatment (the control group). Within the main group, antiischemic and antiarrhythmic effects of simvastatin were compared by the type of diastolic LV dysfunction. At baseline and after 6 months of the treatment, all participants underwent 24-hour electrocardiography monitoring.
Results. According to the analyses of qualitative and quantitative parameters of transient myocardial ischemia, the main group demonstrated a reduction in the ischemia duration (–32,7%; p<0,001), the ST segment displacement area (–35,7%; p<0,001), and the number of ischemic episodes (–30,3%; p<0,001). Within the main group, a significant dynamics of these parameters was observed only among patients with impaired relaxation (–44,5%, —43,9%, and –36,2%, respectively; p<0,001). QTDc significantly decreased in the main group (–17,9%; p<0,05), with a non-significant tendency towards reduction in the control group (–13,3%; p>0,05). In patients with Type I and Type II diastolic heart failure (DHF), the QTDc reduction was similar (p<0,05). The number of supraventricular and ventricular extrasystoles significantly decreased in the main group (–24,5% and –27,9%, respectively; p<0,05), exclusively among patients with Type I DHF, in contrast to the control group. Pathologic values of heart rate turbulence (HRT) were observed in one-third of the patients from both groups. The simvastatin therapy was associated with a significant decrease (–20%) in the number of patients with pathologic HRT values, irrespectively of the DHF type. The TWA index significantly decreased only in the main group (–25,9%; p<0.05), with no marked difference by the DHF type. In the main group, parasympathetic parameters of heart rate variability significantly increased, while in the control group, these parameters significantly decreased.
Conclusion. Simvastatin therapy was associated with a significant improvement of the key qualitative and quantitative parameters of transient myocardial ischemia, as well as with a marked antiarrhythmic effect.

Russ J Cardiol 2013, 6 (104): 62-67
Key words: diastolic left ventricular dysfunction, simvastatin, chronic heart failure, myocardial ischemia, antiarrhythmic effect.
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LITERATURE REVIEWS

COMBINATION ANTIHYPERTENSIVE THERAPY IN PATIENTS WITH ARTERIAL HYPERTENSION AND CORONARY HEART DISEASE

Morozova T. E., Andrushchishina T. B.

Abstract
The leading positions in the treatment of patients with arterial hypertension (AH) and coronary heart disease (CHD) are held by angiotensin-converting enzyme (ACE) inhibitors and beta-adrenoblockers (BAB), which have demonstrated their effectiveness in terms of improved patients' survival. In patients with AH and CHD, the rational, pathogenetic pharmacotherapy using a combination of an ACE inhibitor zofenopril and a highly cardio-selective and vasodilating BAB nebivolol demonstrates antihypertensive and antiischemic action, decreases the risk of potential adverse cardio-metabolic effects, reduces the severity of endothelial dysfunction, and, consequently, improves quality of life.

Russ J Cardiol 2013, 4 (102): 88-94
Key words: arterial hypertension, coronary heart disease, beta-adrenoblockers, nebivolol, ACE inhibitors, zofenopril.
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CHRONIC KIDNEY DISEASE: DEFINITION, CLASSIFICATION, DIAGNOSTICS, AND TREATMENT

Kobalava Zh.D., Villevalde S. V., Efremovtseva M. A.

Abstract
Cardiovascular disease (CVD) is the leading cause of death in patients with chronic kidney disease (CKD). At the same time, CKD is an independent risk factor of CVD and mortality. CVD and CKD share common conventional risk factors (such as arterial hypertension, diabetes mellitus, obesity, and dyslipidemia). The combination of CVD and CKD is associated with such non-conventional renal risk factors as hyperhydratation, anemia, phosphorus and calcium metabolism disturbances, systemic inflammation, and hypercoagulation, which can also influence the development and pathogenesis of CVD. High prevalence of renal dysfunction and adverse prognostic role of reduced glomerular filtration rate (GFR) and albuminuria justified the development of the universal therapeutic strategy for CKD patients. The latest version of these recommendations was published in 2013, as a part of the KDIGO (Kidney Disease Improving Global Outcomes) initiative. The latest KDIGO recommendations classify CKD not only by GFR categories, but also by albuminuria levels, which provides an opportunity to stratify patients by their complication risk. The new classification is based on the evidence demonstrating that the risks of total and cardiovascular mortality, acute renal damage, and CKD progression substantially differ by the levels of urinary albumin excretion, regardless of GFR values. The need for early diagnostics of renal and cardiovascular dysfunction, in order to stratify risk levels and define the therapeutic strategy and tactics, is also reflected by the updates of the national and international recommendations on arterial hypertension, atherosclerosis, and cardiovascular prevention.

Russ J Cardiol 2013, 4 (102): 95-103
Key words: cardiovascular risk, chronic kidney disease, glomerular filtration rate, albuminuria.
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MODERN OPPORTUNITIES OF HEART RATE REGULATION IN CORONARY HEART DISEASE

Zagidullin N. Sh.[1], Gareeva D. F.[1], Zagidullin B. I.[2], Travnikova E. O.[1], Zulkarneev R. Kh.[1], Zagidullin Sh.Z.[1]

Abstract
It has been demonstrated that high heart rate (HR) levels are an independent risk factor of cardiovascular events and mortality from coronary heart disease and chronic heart failure (CHF). Recently, the so-called If-inhibitors which selectively block the pacemaker current in sinoatrial node cells (ivabradine, or CoraxanR) have been introduced to clinical practice. The latest large randomised clinical trials, such as SHIFT and BEAUTIFUL, have shown that in patients with stable effort angina, CHF, and HR >70 bpm, ivabradine reduces the incidence of cardiovascular end-points: myocardial infarction, coronary interventions, hospitalisations, and other events. These results justified the inclusion of ivabradine in the international clinical guidelines.

Russ J Cardiol 2013, 5 (103): 61–65
Key words: heart rate, heart failure, ivabradine, coronary heart disease.
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DIAGNOSTICS AND TREATMENT OF CHRONIC KIDNEY DISEASE IN MODERN CLINICAL GUIDELINES: WHAT DO PRACTITIONERS NEED TO KNOW?

Skibitskyi V. V., Fendrikova A. V.

Abstract
Chronic kidney disease (CKD), widely prevalent in real-world clinical practice settings, is associated with an increased risk of cardiovascular and renal complications. Modern clinical guidelines on the management of CKD patients provide recommendations on the early diagnostics of renal functional and structural pathology, as well as on the adequate treatment which prevents or postpones the progression of these pathological changes. Currently, the assessment of glomerular filtration rate and albuminuria severity is considered obligatory in the CKD diagnostics. These criteria are reflected in the CKD classification, presented in the modern clinical guidelines. The presence of CKD requires the administration of effective treatment, including renin-angiotensin-aldosterone system (RAAS) blockers. At the same time, most CKD patients also require antihypertensive combination therapy, which includes RAAS blockers, diuretics, and/or calcium antagonists. The choice of antihypertensive agents is defined by the specific clinical situation. One of the effective calcium antagonists with proven nephroprotective activity is lercanidipine. The treatment of CKD patients should also include adequate glycemia control and lipid-lowering agents.

Russ J Cardiol 2013, 5 (103): 66–72
Key words: chronic kidney disease, renal function, albuminuria.
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L-CARNITINE IN CARDIOLOGY: REALITY AND PERSPECTIVES

Aronov D. M.

Abstract
Carnitine is a substance close to vitamins B, which participates in the mitochondrial energy synthesis. L-carnitine controls the rate of the long-chain fatty acid oxidation and acts as a specific co-factor facilitating their tr ansport via the internal mitochondrial membrane. It also participates in the elimination of long-chain fatty acid excess from mitochondria and cytoplasm. These effects prevent cytotoxicity. This review presents the results of the studies which comply with the standards of evidence-based medicine.
It has been shown that in patients with acute myocardial infarction (AMI), L-carnitine therapy was associated with a reduction in myocardial necrosis and an improved clinical course of AMI (end-point incidence in the main and control groups was 15,6% and 26%, respectively). In the first 5 days of L-carnitine therapy, there was a significant reduction in mortality in the main group of AMI patients. In patients with stable angina, L-carnitine reduces the risk of all-cause mortality, repeat AMI, and ventricular arrhythmias. In patients with intermittent claudication, L-carnitine significantly increases the pain-free walking distance. This medication is well tolerated, with no registered major adverse effects.

Key words: L-carnitine, acute myocardial infarction, intermittent claudication.
Russ J Cardiol 2013, 5 (103): 73–80
N. I. Pirogov Russian National Medical Research University, Moscow, Russia.

ACETYLSALICYLIC ACID IN PRIMARY PREVENTION AMONG PATIENTS WITH ARTERIAL HYPERTENSION

Melekhov A. V., Ryazantseva E. E.

Abstract
Arterial hypertension (AH) remains one of the most prevalent cardiovascular diseases (CVD) and is an important risk factor of severe, often fatal complications. CVD prevention in AH patients is a complex task, including not only blood pressure reduction, but also targeting additional risk factors. The HOT study was the first attempt to assess the effects of acetylsalicylic acid (ASA) on CVD risk in AH patients. It was shown that ASA reduced the risk of major cardiovascular events (non-fatal acute myocardial infarction (MI), non-fatal stroke, and cardiac death) by 15% (p=0,03). The risk of MI was reduced by 36% (p=0,02). In order to implement the HOT

study results in the clinical practice, additional data analyses were performed, which demonstrated that ASA benefits were the most pronounced in patients with creatinine levels >150 mmol/l. The evidence from the HOT study, including the subgroup analysis results, has been included in the latest guidelines on AH management.

Russ J Cardiol 2013, 5 (103): 81–87
Key words: acetylsalicylic acid, arterial hypertension, essential arterial hypertension, primary prevention, cardiovascular complications, HOT study.
Hospital Therapy Department No. 2, N. I. Pirogov Russian National Medical Research University, Moscow, Russia.

STAGES OF ATHEROSCLEROTIC PLAQUE DEVELOPMENT AND UNSTABLE PLAQUE TYPES: PATHOPHYSIOLOGIC AND HISTOLOGIC CHARACTERISTICS

Ragino Yu.I.[1], Volkov A. M.[2], Chernyavskyi A. M.[2]

Abstract
This literature review focuses on the modern views on the problem of atherosclerotic plaque, its developmental stages (from the lipid steak to unstable atherosclerotic plaque), and various types of plaque instability (lipid, inflammatory, and degenerative-necrotic). Pathophysiologic (mechanisms of formation and development) and pathomorphologic (illustrated histologic description) characteristics of the process are also discussed.

Russ J Cardiol 2013, 5 (103): 88–95
Key words: atherosclerotic lesions of coronary arteries, unstable plaque, instability types, pathophysiology, histology.
[1]Institute of Internal Medicine, Siberian Branch, Russian Academy of Medical Sciences, Novosibirsk; [2]Academician E. N. Meshalkin Novosibirsk State Research Institute of Circulation Pathology, Novosibirsk, Russia.

SALT CONSUMPTION. KIDNEYS AS THE TARGET ORGAN. PART IV

Poteshkina N. G.

Abstract
The paper is focused in the salt consumption effects on renal system during the development and progression of arterial hypertension. The factors facilitating the transformation of normal hemodynamic profile into the hypertensive one are discussed. The author presents the results of experimental and clinical studies which confirm negative effects of excessive salt consumption on the morphology and function of kidneys as the key organ regulating blood pressure levels. These effects are due to both hemodynamic and non-hemodynamic mechanisms of the salt sensitivity phenomenon. The evidence of the low-salt diet effectiveness in the prevention of kidney pathology, as the target organ damage in arterial hypertension, is presented.

Key words: arterial hypertension, salt consumption, renal system, target organ.
Russ J Cardiol 2013, 5 (103): 68-75
N. I. Pirogov Russian National Medical Research University, Moscow, Russia.

PROBLEMS IN PHARMACOTHERAPY OF RESISTANT ARTERIAL HYPERTENSION

Teplova N.V., Taratukhin E.O.

Abstract
The paper focuses on the problems in the treatment of patients with resistant arterial hypertension. The relevant recommendations from the European guidelines are presented. Angiotensin receptor antagonists are considered as a group of antihypertensive agents with additional benefits and good tolerability. The evidence on antihypertensive combination therapy is also presented.

Russ J Cardiol 2013, 6 (104):76-79
Key words: resistant arterial hypertension, combination therapy, diuretics, calcium antagonists, olmesartan.
Hospital Therapy Department No. 1, Therapy Faculty, N.I. Pirogov Russian National Medical Research University, Moscow, Russia.

PRESS RELEASE

ATHEROSCLEROSIS 2013: CONTROVERSIAL ASPECTS OF LIPID-LOWERING THERAPY IN THE CARDIOLOGIC PRACTICE

Russ J Cardiol 2013, 6 (104): 85-90

JUBILEE

Evgenyi V. Kolpakov
Russ J Cardiol 2013, 5 (103): 96

Sergey S. Yakushin
Russ J Cardiol 2013, 6 (104): 91
Vladimir L. Gabinskiy
Russ J Cardiol 2013, 6 (104): 91

AD MEMORIAM

VIKTOR A. LUSOV: DOCTOR, SCIENTIST, LEADER, AND TEACHER

Gordeev I. G., Shaidyuk O. Yu., Luchinkina E. E., Taratukhin E. O.

Abstract
The paper is focused on the importance of Viktor A. Lusov, as well as the department he had been heading for many years, for the Russian cardiology. The biographical information and the data on Professor Lusov's students and colleagues are presented. The authors emphasise the important role of the clinical school maintained by Viktor A. Lusov — a talented doctor, scientist, leader, and teacher.
Based on the materials of the History Session, the Russian National Cardiology Congress

Russ J Cardiol 2013, 6 (104): 80-84
Key words: cardiology, thrombolysis, myocardial infarction, department, hospital therapy.
Hospital Therapy Department No. 1, Internal Medicine Faculty, N. I. Pirogov Russian National Medical Research University, Moscow, Russia.

Russian Journal of Cardiology is currently issued since 1996. It is official journal of the Russian Society of Cardiology (RSC).

Editor-in-Chief: Prof. Eugene V. Shlyakhto, Academician of Russian Academy of Sciences, President of RSC.

The target audience of this peer-reviewed journal is cardiologists and internal disease specialists. The journal is primarily focused on original studies, cardiac surgery, and cardiac pharmacotherapy. It also publishes lectures and literature reviews on various problems of modern cardiology, reports on new diagnostic methods, and other information which is important for the practitioners. The aim of the journal is both scientific and practical, also with referring to organizing matters of the RSC. The best of all cardiological research in Russia is submitted to Journal.

The language of publication is Russian, with contents and abstracts of all the articles presented in English. The Journal also accepts manuscripts from foreign authors and publishes them in English with abstracts in Russian.

Journal is peer-reviewed, with multistage editing. Editorial board is presented by the leading cardiologists from different cities of Russia (http://roscardio.ru/en/editorial-council-and-board-rjc.html).

The Russian Journal of Cardiology aims to ensure that its publications fulfil the requirements of international publishing standards, such as the Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, by the International Committee of Medical Journal Editors, ICMJE (http://www.icmje.org), and the recommendations by the Committee on Publication Ethics, COPE (http://www.publicationethics.org.uk).

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Russian Index of Scientific Citation (RCI-2012) — 0,502.

Complete versions of all issues are published into Scientific Electronic Library (http://www.elibrary.ru) /

It is authorized by RSC for publication of Russian and ESC Guidelines on cardiovascular disease diagnosis and therapy.

ISSN 1560–4071, circulation — 7.000 copies, periodicity — 12 issues per year.

Publisher: "Silicea-Poligraf": http://roscardio.ru/en/, E-mail: cardiojournal@yandex.ru, cardio.nauka@yandex.ru

Russian Journal of Cardiology pages:

– http://www.roscardio.ru/en/russian-journal-of-cardiology.html

– http://www.scardio.ru/en/publication/russian_journal_of_cardiology/

Manuscript publication rules in the Russian Journal of Cardiology:

http://roscardio.ru/en/information-for-authors-rjc.html

Subscription: http://roscardio.ru/en/subscription.html

MANUSCRIPT PUBLICATION RULES IN THE *RUSSIAN JOURNAL OF CARDIOLOGY*

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The *Russian Journal of Cardiology* accepts the following manuscripts:

1. Original papers present the results of clinical studies. The word limit is 3,000 (including references, tables, and figure legends). The maximal number of references is 15. The structured abstract should contain 5 sections (***Aim***, ***Material and Methods***, ***Results***, ***Conclusion***, and ***Key words***), and be no longer than 300 words.

2. Lectures, or clinically oriented reviews, are written by experts in broader areas of medicine. Lectures could be focused on epidemiology, pathophysiology, diagnostics, treatment, and prevention. The word limit is 5,000 (including references, tables, and figure legends). The maximal reference number is 80. The unstructured abstract is no longer than 150 words.

3. Literature reviews are focused on more specific topics, compared to lectures. The word limit is 4,500 (including references, tables, and figure legends). The maximal reference number is 50. The unstructured abstract is up to 150 words.

4. Clinical case is a brief report on a complex diagnostic problem and its solution, or a description of a rare clinical observation. The word limit is 600 (including references, tables, and figure legends). The maximal number of references is 5. No abstract is required.

5. Editorial should be no longer than 1,500 words (including references, tables, and figure legends). The maximal reference number is 15. The unstructured abstract is no longer than 150 words.

6. Clinical opinion informs the readers on the topics of cardiovascular medicine and related disciplines. The word limit is 2,500 (including references, tables, and figure legends). The maximal number of references is 15.

7. Letters to the Editor discuss a specific publication by the *Russian Journal of Cardiology* and have a word limit of 500.

PART 1: OFFICIAL DOCUMENTS

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Manuscripts should be accompanied by a cover letter, which should include the following information: 1) the manuscript is not being considered for publication by any other journal; 2) it has not been published previously; 3) potential conflict of interests has been fully disclosed; 4) all authors have read and approved the manuscript; 5) and the authors are responsible for the validity and integrity of the work as a whole. The cover letter should also contain the contact details of the corresponding author.

If the manuscript is a part of a dissertation/thesis, the proposed defense time should be specified.

The cover letter is presented on a separate page.

Authorship information

The authorship information is provided on a separate page and should contain the following: authors' names, institutional affiliations, and positions. For at least one author, the contact details are specified, including e-mail address, telephone number, and mailing address. This address will be used after the publication of the manuscript, for sending 1 (one) respective issue of the journal to the authors.

If the list of authors includes more than 4 people, the individual contribution should be specified for each author. When the manuscript is authored by a group of authors, all the group members should fully qualify for the authorship. Authorship credit could be based on: 1) contributions to conception and design of the study, or analysis and interpretation of the data; 2) drafting the article or revising it critically for important intellectual content; 3) final approval of the version to be published.

Conflict-of-interest notification page

This separate page contains the authors' disclosure of any potential financial and personal relationships which can lead to conflicts of interests related to the submitted

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Conflict of interest exists when an author (or the author's institution), reviewer, or editor has financial or personal relationships that inappropriately influence their actions and decisions. Not all relationships represent true conflict of interest.

The potential for conflict of interest can exist regardless of whether an individual believes that the relationship affects his or her scientific judgment. Financial relationships (such as employment, consultancies, stock ownership, honoraria, and paid expert testimony) are the most easily identifiable conflicts of interests and the most likely to undermine the credibility of the journal, the authors, and of science itself. However, conflicts can occur for other reasons, such as personal relationships, academic competition, and intellectual passion.

Authors should describe the role of the study sponsor, if any, in study design; collection, analysis, and interpretation of data; writing the report; and the decision to submit the report for publication. If the sponsors had no such involvement, the authors should so state.

Acknowledgements

All contributors who do not meet the criteria for authorship should be listed in Acknowledgements. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, or a departmental chairperson who provided only general support. Financial and material support should also be acknowledged. Groups of persons who have contributed to the paper, but whose contributions do not justify authorship, may be listed under such headings as "clinical investigators" or "participating investigators". Their function or contribution should be described — for example, "served as scientific advisors", "critically reviewed the study proposal", "collected data", or "provided and cared for study participants". Because readers may infer their endorsement of the data and conclusions, these persons must give written permission to be acknowledged. The word limit for Acknowledgements is 100 words.

Ethical considerations

The journal accepts the articles describing Phase 3 and 4 clinical studies. Inclusion of women and ethnic minorities in clinical studies and analytical reviews is encouraged. The studies should be performed in accordance with Law 61 "On Circulation of Pharmaceuticals" from April 12th 2010 (if they were fully or partly performed in the Russian Federation), and/or with Good Clinical Practice principles. The participants should be informed about the aims and major features of the study before providing written informed consent. Authors should clarify the procedure of obtaining informed consent while describing the study protocol in the ***Material and Methods*** section. The approval of the study protocol by the Ethics Committee should also be mentioned. If study methods include X-ray exposure, detailed description and exposure doses should be presented in ***Material and Methods***.

Patients have a right to privacy, therefore, identifying information, including images, names, initials, or hospital record numbers, should not be published. If is information is essential for scientific purposes, the patient (or parent or guardian) should give written informed consent for its publication in print or electronic media. If necessary, the journal may request this written informed consent from the authors.

Example:

The study was performed according to the Good Clinical Practice guidelines and the Declaration of Helsinki. The study protocol was approved by the Ethics Committees of all the study centres involved. Written informed consent was obtained from all participants prior to their inclusion in the study.

Overlapping publications

In the cover letter, the author (s) should inform the Editor about all previous submissions of the manuscript, including:

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2) Redundant publication and acceptable secondary publication. Redundant (or duplicate) publication is publication of a paper that overlaps substantially with one already published in print or electronic media.

A paper might be considered if: it is particularly important for public health and contains a complete reference to the primary publication; it was rejected by another journal; it represents a complete report that follows publication of a preliminary report.

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Misappropriation of the ideas of others.

Violation of generally accepted research practices: serious deviations from accepted practices in carrying out research; or deceptive statistical or analytical manipulations.

Failure to comply with legislative and regulatory requirements: repeated, willful violations of applicable local regulations and law involving the study performance, use of funds, pharmaceuticals, recombinant products, new devices, or various biologically active materials.

Inappropriate behavior: unfunded or knowingly false accusations of misconduct; failure to report known or suspected misconduct; withholding or destruction of information relevant to a claim of misconduct and retaliation against persons involved in the allegation or investigation.

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Plagiarism is the use of others' published or unpublished ideas or words (or other intellectual property) without attribution or permission, and presenting them as new and original, rather than derived from an existing source.

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PART 2: MANUSCRIPT PREPARATION AND SUBMISSION

Title page

Article title should be capitalized and presented without word hyphenation, in semi-bold font (Times New Roman BOLD, 12 pt). Family names and initials of authors are italicized: *Ivanov I. I., Petrov P.* P.

The full name of the institution (s) where the study was conducted should be followed by the name of the city and country. The footnotes are presented as Arabic numerals, after the author's family name and after the name of the respective institution.

The first page of the manuscript (with the title and the beginning of the text) should be signed by all authors.

Abstract

The abstract form is defined by the manuscript type: a structured abstract has 5 sections (***Aim***, ***Material and Methods***, ***Results***, ***Conclusion***, and ***Key words***), while an unstructured abstract contains a brief work description and ***Key words***.

The maximal number of ***Key words*** is 6.

Text

Original articles should be structured into the following sections: ***Introduction***, ***Material and Methods***, ***Results***, ***Discussion***, and ***Conclusion***. Reviews and lectures can be formatted differently.

All manuscript pages should be single-sided and printed on A4 paper, using font size 12, 1.5 interval, all margins of 2.0 cm, and left alignment. The data should be reported using SI units. Between a percentage symbol and a preceding digit, there should be a space character; *p* value is reported with decimal points ($p<0{,}0001$). The text should be carefully edited and proofread by the author (s). Footnotes for the quotations should specify the original source (author (s), year). Authors are responsible for the accuracy of quotations, reported medication doses, and other presented information.

All the pages should be numbered consecutively, beginning with title page.

Statistics

All published manuscripts are reviewed by a statistical expert and should comply with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (*Ann Intern Med* 1997 126: 36–47). It is also recommended to follow specialised guidelines, such as the ones by the *European Heart Journal*:

http://www.oxfordjournals.org/our_journals/eurheartj/for_authors/stat_guide.html

Statistical methods should be described in detail in the ***Material and Methods*** section.

Abbreviations and the list of abbreviations

Abbreviations should be standard and clear to the readers. Authors must avoid using abbreviations which could have more than one meaning.

The list of abbreviations and their definitions should follow the standards for research publications. Abbreviations are used for medical terms frequently used in the manuscript (for example, AH, CHF, or FC) and for clinical trial names (such as SOLVD, TIMI, or HOPE).

Illustrations (figures)

Illustrations (diagrams, charts, or figures) are accepted in electronic formats MS Excel, Adobe Illustrator, Corel Draw, or MS PowerPoint. Photographs should have a minimal resolution of 300 pixels per inch. The name of each illustration file should include the family name of the first author (in Latin characters) and the illustration number, according to its order of citation in the text.

Titles and legends for illustrations are printed on a separate page. The duplication of information in tables and illustrations should be avoided.

Tables should capture information concisely and display it efficiently. Each table is printed on a separate page, together with its number, title, and explanatory information (footnotes and abbreviations).

All tables should identify the measurement units and specify the data presentation (for example, M±m; M±SD; median; mode; percentiles, etc.). All numbers, totals, and percentages should be double-checked and correspond to the respective part of the text. If necessary, authors should place explanatory matter in footnotes. The following symbols should be used for footnotes, in sequence: *, †, § , ‖, ¶, #, **, ††, etc. Abbreviations should be listed alphabetically in the table footnote.

Every first mention of each illustration and table in the text should be highlighted in yellow. If the reference to the illustration or table is a part of a sentence, it is spelled-out as "Figure 1" or "Table 1"; the reference in brackets is abbreviated as (Fig. 1) or (Tab. 1).

References

References are printed on a separate page, using 1.5 interval. All references in the text should also be in the list of references, and *vice versa*. Citing unpublished or old (over 10 years) work is not permitted; an occasional exception could be made for selected highly informative sources.

The reference should contain up to three family names of the authors; the following names are abbreviated as "и др." for Russian sources, or "et al." for international sources. For journal articles, the reference contains family names and initials of the authors; article title; journal title; publication year; volume and issue; and page numbers. For articles from proceedings, it contains family name and initials; article title; proceedings title; publication place; publication year; and page numbers.

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Authors are responsible for the accuracy of the references.

The references should comply with the format recommended by the American National Information Standards Organization (NISO), adapted by the National Library of Medicine (NLM; http://www.nlm.nih.gov/citingmedicine) for its databases (Library's MEDLINE/PubMed database). The titles of journals should be abbreviated according to the format accepted by a specific journal; this information could be found on the journal website, or in the Index Medicus.

Citation examples:

Article:

Smith A, Jones B, Clements S, et al. Clinical transplantation of tissue-engineered airway. Lancet 2008; 372:1201–09.

Transliterated Russian article:

Bart BYa, Larina VN, Brodskyi MS. Cardiac remodelling and clinical prognosis in patient with chronic heart failure and complete left bundle branch block. Russ J Cardiol 2011; 6: 4–8. Russian (Барт Б.Я., Ларина В.Н., Бродский М.С. Ремоделирование сердца и прогноз больных с хронической сердечной недостаточностью при наличии полной блокады левой ножки пучка Гиса. Российский кардиологический журнал 2011, 6:4–8).

Book:

Shlyakhto EV, Konradi AO, Tsyrlin VA. The autonomic nervous system and hypertension. SPb.: Meditsinskoe izdatel'stvo; 2008. Russian (Шляхто Е.В., Конради А.О., Цырлин В.А. Вегетативная нервная система и артериальная гипертензия. СПб.: Медицинское издательство; 2008).

Chapter:

Nichols WW, O'Rourke MF. Aging, high blood pressure and disease in humans. In: Arnold E, ed. McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles. 3rd ed. London/Melbourne/Auckland: Lea and Febiger; 1990. p.398–420.

Russian chapter:

Diagnostics and treatment of chronic heart failure. In. National clinical guidelines 4th ed. Moscow: Silicea-Poligraf; 2011. pp.203–293. Russian (Диагностика и лечение хронической сердечной недостаточности. В кн: Национальные клинические рекомендации. 4-е издание. М.: Силицея-Полиграф; 2011.сс.203–296).

Webpage:

Panteghini M. Recommendations on use of biochemical markers in acute coronary syndrome: IFCC proposals. eJIFCC 14. http://www.ifcc.org/ejifcc/vol14no2/1402062003014n.htm (28 May 2004)

PART 3: MANUSCRIPT SUBMISION CHECK-LIST

The check-list for submitting a manuscript to the *Russian Journal of Cardiology* includes the following:

1. Cover letter.
2. Manuscript.
2.1. Title page.
2.2. Structured abstract and key words.
2.3. List of abbreviations.
2.4. Main text.
2.5. Acknowledgements (if applicable).
2.6. References.
2.7. List of illustrations, tables, diagrams, or photocopies, in the order of their appearance in the text.
2.8. Illustrations, tables, or diagrams.
3. Information about the authors.
4. Information about potential conflicts of interest/funding sources.
5. Information about compliance with ethical standards.

All electronic documents should be named as follows: family name and initials of the first author; and a brief description of the document.

For example: "IvanovII.Letter", "IvanovII.Title page", "Ivanov II.Text", "IvanovII.Figure1", "IvanovII.Authors", "IvanovII.Conflict", and "IvanovII.Ethics".

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This section regulates the relationship between the editorial office of the *Russian Journal of Cardiology* (referred to as "Editor"), the publishing house Silicea-Poligraf ("Publisher"), and the author (s) submitting their manuscript to the *Russian Journal of Cardiology* ("Author").

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PART 5: MANUSCRIPT REVIEWING

An electronic version of the manuscript should be sent to the Editor: cardiojournal@yandex.ru The manuscript format should comply with the above-mentioned submission requirements by the journal.

If the manuscript fully complies with all requirements, it is assigned a unique registration number for further editorial use. The Author receives a confirmation letter, which states that the manuscript has been received, and contains the respective registration number.

All manuscripts must undergo primary screening. The Editor reserves a right to reject the manuscript, or specify the corrections which must be made by the Author before the reviewing.

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Reviewing is confidential for both the Author and the reviewers. The reviewer receives the manuscript which does not include authors' names or institutions.

The Editor informs the Author about the reviewing results in an e-mail.

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