

# Iranian Heart Journal

OFFICIAL QUARTERLY PUBLICATION OF THE IRANIAN HEART ASSOCIATION

Volume 10, Number 1  
Spring, 2009

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# **European National Society Cardiovascular Journals: Background, Rationale and Mission Statement of the “Editors’ Club” (Task Force of the European Society of Cardiology)**

Fernando Alfonso, MD, PhD, FESC \*, Giuseppe Ambrosio, MD, PhD, FESC \*\*, Fausto J. Pinto, MD, PhD, FESC \*\*\*, Ernst E. van der Wall, MD, PhD, FESC (Chairman of the Task Force) \*\*\*\* Anesti Kondili MD, Djamaledine Nibouche MD, Karlen Adamyan MD, Kurt Huber MD, Hugo Ector MD, Izet Masic MD, Rumiana Tarnovska MD, Mario Ivanusa MD, Vladimír Staněk MD, Jørgen Videbæk MD, Mohamed Hamed MD, Alexandras Laucevicius MD, Pirjo Mustonen MD, Jean-Yves Artigou MD, Ariel Cohen MD, Mamanti Rogava MD, Michael Böhm MD, Eckart Fleck MD, Gerd Heusch MD, Rainer Klawki MD, Panos Vardas MD, Christodoulos Stefanadis MD, József Tenczer MD, Massimo Chiariello MD, Joseph Elias MD, Halima Benjelloun MD, Olaf Rødevand MD, Piotr Kułakowski MD, Edvard Apetrei MD, Victor A. Lusov MD, Rafael G. Oganov MD, Velibor Obradovic MD, Gabriel Kamensky MD, Miran F. Kenda MD, Christer Höglund MD, Thomas F. Lüscher MD, René Lerch MD, Moufid Jokhadar MD, Habib Haouala MD, Vedat Sansoy MD, Valentin Shumakov MD, Adam Timmis MD (European National Society Cardiovascular Journals Editors, see Appendix for complete affiliations) Carlos Daniel Tajer MD, Kathleen Coard MD, Rachel Hajar MD, Chu-Pak Lau MD, H K Chopra MD, Seyed Abdolhossein Tabatabaei MD, Manlio Márquez MD, Abdus Samad MD, Javier Galeano MD, Anton Doubell MD, Chi-Tai Kuo MD, Rungroj Krittayaphong MD, Kaduo Arai MD (ESC Affiliated National Society Cardiovascular Journals Editors, see Appendix for complete affiliations) Fernando Bacal MD, Luis Guzmán MD (Other cardiac societies with official journal endorsing this document)

Editors-in-Chief:

(\*) Revista Española de Cardiología, published by the Spanish Society of Cardiology

(\*\*) (former Editor) Giornale Italiano di Cardiologia, published by the Italian Federation of Cardiology

(\*\*\*) Revista Portuguesa de Cardiologia, published by the Portuguese Society of Cardiology

(\*\*\*\*) Netherlands Heart Journal, published by the Netherlands Society of Cardiology

**This manuscript will be simultaneously published in all Affiliated National Societies Journals that consented to publication (*Iranian Heart Journal 2009; 10 (1):6-15*).**

Cardiovascular scientific production in Europe is growing both in quantity and in quality. Promoting high-quality research is a major goal of the European Society of Cardiology (ESC)<sup>1-3</sup>. The ESC has two highly respected official general journals, namely the *European Heart Journal* and *Cardiovascular Research*, devoted to clinical and basic research respectively.<sup>1-3</sup>

The ESC also publishes several sub-speciality official journals covering the full spectrum of cardiovascular diseases and related techniques. Most European countries, however, also have their own cardiovascular journals. National Society Cardiovascular Journals (NSCJ) are time-honoured and classically disseminate high-quality scientific research mainly originating from each particular European country.

They also play a major role in education and harmonisation of clinical practice. Most NSCJ are published in local languages but many of them also incorporate English editions. Altogether, NSCJ provide a highly effective means to disseminate cardiovascular research produced in Europe. Scientific knowledge, however, has no barriers and many of these journals have gained an undisputed international profile. Some NSCJ, however, are just emerging and would benefit from networking support. It became clear that enhancing collaboration among NSCJ Editors would facilitate advancement in knowledge and further diffusion of scientific and educative contents.

Developing a "Constitution Document" and "Mission Statement" was considered desirable to set the basis of future collaboration among NSCJ Editors. We assumed this responsibility in recognising the crucial role of NSCJ in Europe. Our target was to produce and issue a core document with fundamental principles upon which all NSCJ Editors would agree. Common goals will be identified and agreed-on measures will be pursued. The constitution document presented herein was therefore developed to formalise the NSCJ Editors' Club Task Force.

#### ***National Society Cardiovascular Journals: Background and Basic Data***

All Editors-in-Chief of the official cardiovascular journals of the ESC National Societies are *de facto* members of the Editors' Club. On April 2007, during the "spring days" at the Heart House in Nice, the ESC Board formally approved the initiative and the Editors' Club Task Force was officially launched. The organisation of the Task Force consists of a Nucleus of NSCJ Editors and remains within the membership division of the ESC, coordinated by the ESC vice-president. Further involvement of the ESC publishing department will be also considered as required.

The initial steps of the Editors' Club Task Force moved in the direction to gain further insights on who we are and where we are now. Accordingly, several proactive measures were taken:

Upon request of this Task Force, the portal on the ESC web page for the NSCJ was modified to increase its visibility. Currently, this site may be reached, not only from the area corresponding to members and National Societies, but also directly from the scientific area of the ESC.<sup>4</sup> It is clear that NSCJ significantly contribute to the enormous scientific input provided by the ESC as a whole and appropriate recognition to this fact should be granted.

Electronic communication brings the scientific community closer together. Therefore, direct links to NSCJ have been updated and implemented.<sup>4</sup> This would further stimulate exchange of scientific research amongst European authors, researchers and readers. Submission of high quality original research articles should be encouraged by NSCJ Editors, establishing efficient networking tools connecting all European journals.

As a final preliminary step, the Task Force strived to obtain detailed editorial and organisational data from all corresponding journals. Accordingly, feedback was directly requested from the NSCJ Editors and Presidents of the National Societies. A comprehensive structured questionnaire (23 items), was devised. Corporate mailing and subsequent collection of all editorial data were guaranteed with the help of the ESC membership department. Consistency checks were performed and, when required, data confirmation was directly obtained from the corresponding national Editor. Fully detailed results of this survey are currently freely available from the ESC web page (metafile of national journals).<sup>4</sup> This posted material will be updated annually.

Main results of the survey are as follows. A total of 40 National Societies responded to the structured questionnaire including a total of 34 journals. Eight National Societies have no official journal, the 3 Baltic countries share the same Journal and 3 National Societies have more than 1 journal. The oldest cardiovascular journal in Europe is *Archives des Maladies du Cœur et des Vaisseaux* founded in 1908. Overall, 11 journals have more than 30 years of existence, 2 are older than 20 years and 12 have been published for more than a decade. In addition to NSCJ in local languages, 12 journals are also available in English (full text) and 27 journals systematically include English abstracts. Thirty-three journals include original papers whereas 1 exclusively consists of review papers or state of the art articles. Thirteen journals are published monthly. The journals print run varies from 1 000 to 9 000 copies (mean 3 135 copies). A system of "peer review" is selected to evaluate manuscripts by 31 journals and 23 journals adhere to the requirements of the International Committee of Medical Journals Editors. Twenty nine journals are indexed (*Index Medicus*), 18 appear in PubMed (MEDLINE) and 5 have obtained an impact factor in

2006. In addition to the print edition, 26 journals have an electronic edition, and 13 have also implemented an electronic system for manuscript submission. A dedicated web page is offered by 25 journals whereas 26 publications are directly accessible via the web page of the corresponding national society.<sup>4</sup>

### **General Editorial Considerations**

Both, technical and ethical considerations should be addressed.<sup>5-8</sup> Promoting editorial quality standards is of paramount importance to increase the attractiveness of our publications in the globalised and highly competing field of academic cardiovascular medicine. In this regard the Task Force believes that every effort should be made to follow the uniform recommendations initially issued by the International Committee of Medical Journal Editors (ICMJE) nearly 30 years ago. These recommendations have been recently updated (6<sup>th</sup> edition) and the emphasis has shifted from the original technical requirements (focused on unifying technical and formal aspects of manuscript preparation), to general principles of editorial ethics and global policies that should govern biomedical publishing.<sup>5,8</sup> Technical requirements are indeed important to guaranty clarity, precision and to facilitate dissemination of medical studies. In turn, implementation and strict compliance with these requirements eventually raises the overall quality of research. In this regard, the suggestions provided by the CONSORT (CONSolidated Standards Of Reporting Randomised Trials) group should be followed to improve presentation of randomised clinical trials.<sup>9</sup> These studies should comply with special requirements, including a check list and flow diagram. We should keep in mind that cardiology is one of the medical disciplines where performance of randomised trials has more clearly fructified and the concept of evidence-based medicine is widely embraced.

Currently, online editions represent the most efficient means for disseminating the information that journals publish. Visits to electronic editions are ever-increasing and full article downloads grow exponentially.<sup>3,10</sup> Therefore, electronic connectivity should be facilitated so that online journal editions are made more visible to readers and, if possible, freely available. In this regard, a provocative novel index, known as the “web impact factor”, has been proposed and the field of *webometrics* is just emerging.

On the other hand, ethical considerations directly affect the credibility of the scientific content. Therefore, they should ensure transparency, trust and honesty in the scientific process involved in performance and publication of research.<sup>5-8</sup> The final purpose is to protect the process of scientific exchange. It should be acknowledged that a sizable bulk of corporative research has recently moved from academic and university centres to close agreements between

sponsors and private contract research organisations. Accordingly, explicitly disclosing the role of the sponsor in designing, conducting, analysing, interpreting and writing the trial is becoming increasingly relevant. Other concepts such as Editorial Freedom and Editorial Independence have been recently emphasised by the ICMJE, WAME (Word Association of Medical Editors) and CSE (Council of Science Editors).<sup>5-8</sup> Authority and autonomy are critical to ensure appropriate editorial decisions. In this regard, NSCJ Editors should jealously safeguard the editorial independence of their respective national journals.

The peer review process - despite its limitations - has been enthroned at the highest level and it is now currently identified as an essential part of the editorial scientific process. Therefore, standards for peer review excellence should be developed. This requires both fairness in judgement and expertise in the field. Editors are responsible for monitoring and ensuring fairness, timeliness, and thoroughness in this process.<sup>5-8</sup>

Other issues such as conflicts of interest (for authors, reviewers and editors) and requirements for authorship are also intended to protect the credibility of the scientific information. Disclosure of potential conflicts of interest should be enforced. Disclosure on data accessibility and accepting a full responsibility for accurate data presentation and interpretation are key considerations. Confidentiality and agreed-on embargos should be maintained. Publication bias (selective reporting of positive findings and lack of publication of studies with negative results) should be prevented by NSCJ Editors. The whole publication process is based on the credibility, trust, authenticity and scientific honesty.<sup>5-8</sup> To further preserve scientific credibility, NSCJ Editors should harmonise their policies regarding scientific misconduct and scientific fraud.<sup>11-16</sup> The HEART Group (Heart Editors Action Round Table) of cardiovascular editors issued a consensus document focused on redundant publication.<sup>12</sup> Eventually, publishing “expression of concern” notes or even retraction of published material should be considered. *Salami slicing* and *shot gunning* publication strategies should be discouraged and, at least, disclosed.<sup>11-16</sup> Secondary publications, even in different languages, should follow the ICMJE requirements.<sup>5</sup>

Finally, stimulating bibliometric indexes is of clear interest to gain international recognition. The impact factor (*Journal Citation Reports*) represents a widely accepted means to evaluate the scientific prestige of journals. However, flaws in the impact factor calculation should be acknowledged and research or scholarly merits should not be rewarded based on the impact factor of the journal in which articles are eventually published.<sup>2,17-19</sup> Padding the impact factor should be discouraged. However, NSCJ Editors should develop common policies to stimulate diffusion of

European studies exclusively based on scientific quality and clinical relevance criteria. This would overcome current citation biases, particularly against non-English biomedical journals.<sup>17</sup> Joint support of European research by increasing recognition of European scientific and editorial quality is considered, therefore, highly advisable.

### ***Rationale for the Editors' Club***

European NSCJ are heterogeneous and, above all, are published in different languages. This highlights that cooperation among NSCJ Editors is crucial to avoid "Tower of Babel" phenomena precluding efficient dissemination of scientific information across Europe. Even relatively humble journals should not be condemned to ostracism but rather considered highly successful providing they have a broad dissemination and are deeply appreciated by their readers. We should break boundaries and set free scientific knowledge from any constrictions generated by language, logistic, bureaucratic or economic barriers. Cross-links between European Journals are highly advisable. Cross-references should be stimulated but only when based on strict criteria of scientific quality. A minimal list of important issues should be developed with principles that all NSCJ Editors could agree upon. Common goals, priorities and challenges should be readily identifiable. Finally, proactive global decisions should be made in order to capture a wider audience.

All the above described editorial recommendations, however, leave enough room for specific editorial policies that shape the particular interest of every specific journal. Room for diversity should be jealously maintained as the focus and scope of different national journals actually differ. Nevertheless, advancement in knowledge is founded in the exchange of novel information by investigators, and NSCJ Editors have full responsibility for stimulating cooperation among European researchers.

Here, we would like to present three typical examples where these collaborative efforts could be applicable:

1. Novel recommendations suggesting to register all clinical trials prior to definitive publication should be discussed on the light of currently available administrative national laws and recent European directives (EudraCT). Proposals for a uniform European "Repository" of clinical trials fulfilling not only administrative and regulatory issues but also editorial requirements (including free public access) should be considered.<sup>20,21</sup> This will allow early recognition of undue trial design changes or methodological flaws. Eventually, most NSCJ Editors could joint uniform recommendations and common editorial policies and platforms might be devised at a European level.

2. Collaboration among NSCJ Editors is essential to further disseminate and promote clinical application of ESC clinical practice guidelines. After endorsement by National Societies, translation of these guidelines into national local languages should facilitate their implementation into clinical practice.<sup>22-27</sup> Foot notes, incorporating comments of local experts, are pivotal in this regard. Publication of these guidelines in NSCJ should follow the general rules for "secondary publication", after primary publication in the European Heart Journal has been granted. Nevertheless, time matters, and this detailed and rigorous editorial process (typically affecting uniquely long documents) should be expedited to streamline the translation process and to monitor its accuracy. Implementation of an "early translation process" would be desirable. A full collaboration between NSCJ Editors and the ESC committee of practice guidelines is, therefore, of paramount importance. The circle of knowledge will be closed when the corresponding feedback is ensured by dissemination of selected national activity registries unraveling local practices in patient care.<sup>28,29</sup> This will help to elucidate success, viability and implementation of different ESC initiatives at the national level. Hopefully, this bidirectional exchange in knowledge will promote widespread implementation of these recommendations and harmonisation of cardiovascular practices across Europe. Eventually, uniform and consistent clinical practices should translate into improvements in patient care.

1. Boosting dissemination of official ESC late breaking clinical trials, by readily translating their abstracts into local languages and publishing the main results of these important studies, while paying maximal attention to preserve accuracy and scientific integrity, remains a challenge.<sup>30,31</sup> This final proposal will require, once more, a close coordination between ESC scientific bodies, ESC publishing department and NSCJ Editors

### ***Mission Statement:***

1. To *increase collaboration among NSCJ Editors*. The main purpose of this Task Force is to foster interaction among NSCJ Editors. Selected editorial topics will be discussed and addressed using a systematic and comprehensive approach. Standing and "ad hoc" committees will be created. Common editorial policies should be developed. As needed, editorials, uniform requirements, and consensus documents will be issued. Regular meetings (annual ESC Congress and others) will be scheduled and a formal agenda will be proposed.

2. To *promote editorial excellence*. A major objective of the Task Force is to devise means to

improve the scientific standards of NSCJ. Scientific content, quality requirements, credibility, and editorial and research ethics will be promoted.<sup>5-8</sup>

3. To *improve diffusion* of scientific knowledge. Coordination of editorial initiatives among NSCJ and also official ESC journals will further facilitate diffusion of editorial and scientific content. To develop common strategies to increase awareness of the high quality scientific research generated in Europe which, in turn, would positively affect bibliometric indicators. Recognition and diffusion of European cardiovascular research, ESC clinical practice guidelines and other scientific or education initiatives should be promoted. Distribution of common academic material, core curriculum, and additional teaching tools should be also facilitated. Fostering of electronic editions should be encouraged to increase diffusion and NSCJ visibility.

4. To *share technical editorial information*, experiences, initiatives, publishing resources and technical tools among NSCJ Editors. To address common issues regarding free access to scientific content. To foresee common strategies to advance into the dynamic field of standardised platforms for manuscript submission. To adopt common policies aimed to increase efficiency in the publication process. To promote parallel electronic and English-editions in an increasing number of NSCJ and, eventually, sharing copy-editing resources. To develop joint efforts to more efficiently tackle the problem of finite editorial resources, and finally, to ensure economic viability of NSCJ.

5. To *provide an operative framework and dataset* that will enable future joint ventures and comprehensive European publishing initiatives. To further stimulate collaboration between NSCJ Editors and the ESC scientific bodies and publishing department. In this way, promotion of spotlight, theme or monographic issues, covering burning cardiovascular topics, might be nicely coordinated.

6. *Public relations*. To provide a common voice when issues concerning NSCJ arise. To serve as a *liaison* in the relations with governmental bodies, professional or scientific organisations, industry, the media and the public.

7. To *foster collaboration between National Societies and the ESC*. To close the gap between ESC official journals and NSCJ. To promote European incentives to stimulate publication of quality research.

### **Final Remarks**

All the information presented in the present document set the basis to support this exciting editorial initiative. NSCJ Editors should be committed to progressively adapt their local policies, including instructions to authors, to follow general editorial recommendations.<sup>5-8,32,33</sup> The main challenge of the Editors Club will be to foster consensus and agreements upon strategic priorities among NSCJ. The breadth and quality of articles should be improved and strategic actions should be aimed to foster inclusion of most NSCJ in well respected international bibliographic databases and electronic search systems. Joint efforts should aim to broaden distribution and dissemination of these journals and to consolidate their prestige and recognition by the international scientific community. The main goals of this pioneering effort are, therefore, already quite clear: to increase collaboration among NSCJ Editors, enhance editorial standards, improve quality requirements, preserve publication ethics, guarantee scientific credibility and expand dissemination of scientific knowledge. Commitment of NSCJ Editors to achieve these objectives is crucial and this Editors' Club emerging forum should provide a unique opportunity to foster global editorial policies. Overtime, the results and implications of these ambitious editorial initiatives should be critically evaluated.

### **Acknowledgements**

The continuous help of Anne Mascarelli (ESC) deserves special recognition

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**Appendix:**

*Journal names (by alphabetic order of Country of origin) and Members (Editors-in-Chief) of the Editors' Club Task Force:*

<b>National Society Name</b>	<b>National Society Journal</b>	<b>Chief-Editor</b>
Albanian Society of Cardiology	Revista Shqiptare e Kardiologjisë	Anesti Kondili
Algerian Society of Cardiology	Journal de la Société Algérienne de Cardiologie	Djamaleddine Nibouche
Armenian Cardiologists Assoc.	Armenian Journal of Cardiology	Karlen Adamyan
Austrian Society of Cardiology	Journal für Kardiologie *	Kurt Huber
Belgian Society of Cardiology	Acta Cardiologica	Hugo Ector
Association of Cardiologists of Bosnia and Herzegovina	Medicinski Arhiv	Izet Masic
Bulgarian Society of Cardiology	Bulgarian Journal of Cardiology	Rumiana Tarnovska
Croatian Cardiac Society	Kardio List	Mario Ivanusa
Czech Society of Cardiology	Cor et Vasa	Vladimír Staněk
Danish Society of Cardiology	Cardiologisk Forum	Jørgen Videbæk
Egyptian Society of Cardiology	Egyptian Heart Journal	Mohamed Hamed
Estonian Society of Cardiology	Seminars in Cardiovascular Medicine **	Alexandras Laucevicus
Finnish Cardiac Society	Sydänääni (Heart Beat)	Pirjo Mustonen
French Society of Cardiology	Archives des Maladies du Cœur et des Vaisseaux	Jean-Yves Artigou
Georgian Society of Cardiology	Archives of Cardiovascular Diseases	Ariel Cohen
German Cardiac Society	Scientific-Practical Journal	Mamanti Rogava
	Clinical Research in Cardiology	Michael Böhm
	Clinical Research in Cardiology Supplements	Eckart Fleck
	Basic Research in Cardiology	Gerd Heusch
	Cardio News	Rainer Klawki
Hellenic Cardiological Society	Hellenic Journal of Cardiology	Panos Vardas
		Christodoulos Stefanadis
Hungarian Society of Cardiology	Cardiologia Hungarica	József Tenczer
Italian Federation of Cardiology	Journal of Cardiovascular Medicine (English)	Massimo Chiariello
	Giornale Italiano Di Cardiologia (Italian)	Leonardo Bolognese
Latvian Society of Cardiology	Seminars in Cardiovascular Medicine**	Aleksandras Laucevicus
Lebanese Society of Cardiology	Heart News	Joseph Elias
Lithuanian Society of Cardiology	Seminars in Cardiovascular Medicine **	Aleksandras Laucevicus
Moroccan Society of Cardiology	Revue Marocaine de Cardiologie	Halima Benjelloun
Netherlands Society of Cardiology	Netherlands Heart Journal	Ernst E. Van der Wall
Norwegian Society of Cardiology	HjerteForum	Olaf Rødevand
Polish Cardiac Society	Kardiologia Polska -Polish Heart Journal	Piotr Kułakowski
Portuguese Society of Cardiology	Revista Portuguesa de Cardiologia	Fausto J. Pinto
Romanian Society of Cardiology	Romanian Heart Journal	Eduard Apetrei
Russian Fed Society of Cardiology	Russian Journal of Cardiology	Victor A. Lusov
	Cardiovascular Therapy and Prevention	Rafael G. Oganov
	Rational Pharmacotherapy in Cardiology	Rafael G. Oganov
Cardiology Society of Serbia	Kardiologija	Velibor Obradovic
Slovak Society of Cardiology	Kardiológia/Cardiology	Gabriel Kamensky
Slovenian Society of Cardiology	Slovene Cardiology	Miran F. Kenda
Spanish Society of Cardiology	Revista Española de Cardiología	Fernando Alfonso
Swedish Society of Cardiology	Svensk Cardiologi	Christer Höglund
Swiss Society of Cardiology	Kardiovaskuläre Medizin	Thomas F. Lüscher
		René Lerch
Syrian Cardiovascular Association	Heart Forum	Moufid Jokhadar
Tunisian Society of Cardiology	Cardiologie Tunisienne	Habib Haouala
Turkish Society of Cardiology	Archives of the Turkish Society of Cardiology	Vedat Sansoy
Ukrainian Society of Cardiology	Ukrainian Journal of Cardiology	Valentin Shumakov
British Cardiovascular Society (UK)	Heart	Adam Timmis

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# ASSESSMENT OF MYOCARDIAL VIABILITY: THE VALUE OF 24-HOUR THALLIUM-201 (<sup>201</sup>Tl) REDISTRIBUTION IMAGING TO ENHANCE VIABILITY DETECTION IN STRESS REINJECTION PROTOCOL

Mahdi Mogharrabi MD, Aref Hooman MD, Hadi Malek\* MD, Fereidoon Rastgoo MD\*  
 and Isa Neshanar Asli MD

## Abstract

**Background-** To assess the value of 24-hour redistribution imaging after <sup>201</sup>Tl reinjection for the detection of myocardial viability, we compared the results of <sup>201</sup>Tl reinjection imaging with those obtained 24 hours after reinjection.

**Methods-** In total, 35 patients aged 57±8 years (mean ± SD) who showed one or more persistent perfusion defects on stress reinjection images after myocardial infarction were assessed for myocardial viability. After pharmacological stress and 4-hour reinjection imaging, 25 patients who showed non-viable segments at reinjection image underwent 24-hour redistribution imaging. The stress, reinjection, and 24-hour redistribution images were analyzed quantitatively. Criteria for viability definition were: 1) segments which showed at least

50% uptake of peak activity of normal regions at stress phase and 2) segments with less than 50% uptake at stress image which showed at least 20% redistribution at the later phases.

**Results-** Of the 102 abnormal myocardial regions on the stress images, 19 segments at reinjection images and another 17 segments at 24-hour redistribution images demonstrated redistribution. On the other hand, 24-hour imaging showed viability in 17 out of 83 segments (20.4%), which were considered non-viable regions at reinjection image, occurring in 8 out of 25 patients.

**Conclusion:** In stress reinjection protocol by <sup>201</sup>Tl, 24-hour redistribution imaging is proposed to be performed in patients who show significant non-viable myocardial tissue at 4-hour reinjection imaging for a better recognition of viable myocardium (*Iranian Heart Journal 2009; 10 (1):16-20*).

**Key words:** nuclear medicine ■ viability ■ Thallium 201 ■ redistribution ■ myocardial infarction

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**M**ycocardial viability testing for the recognition of viable myocardium at high risk, including ischemic, stunned, and hibernating tissue is important for predicting the clinical benefits of revascularization as well as prognosis in patients with coronary artery disease.<sup>1</sup>

Thallium-201 (<sup>201</sup>Tl) redistribution imaging has been widely used for the identification of myocardial ischemia and

Received April 2, 2007; Accepted for publication May 2, 2008.

From the Nuclear Medicine Department, Taleghani Hospital, Shaheed Beheshti University of Medical Sciences, Tehran, and the \*Department of Nuclear Medicine, Shahid Rajaie Cardiovascular Medical and Treatment Center, Tehran, Iran

Corresponding author: M.Mogharrabi, MD, Nuclear Medicine Assistant of Shahid Beheshti University of Medical Sciences, Department of Nuclear 5<sup>th</sup> Azar Hospital, Department of Nuclear medicine, Golestan University of Medical Sciences, Gorgan, Iran

Email: [dr\\_mahdimogharrabi@yahoo.com](mailto:dr_mahdimogharrabi@yahoo.com)

Tel: +98171-2220561

Fax: +98171-2228363

viability after myocardial infarction. A standard imaging protocol that includes stress and redistribution images with <sup>201</sup>Tl reinjection as necessary will

provide most of the viability information that can be obtained from <sup>201</sup>Tl imaging. One other approach to assess myocardial viability while saving time involves the routine reinjection of <sup>201</sup>Tl 3-4 hours after stress, without acquiring redistribution images; however, some studies have shown that in a small subset of patients the reinjection images may underestimate viability.<sup>2</sup>

Bonow et al., who advocated thallium uptake quantification as an index for viability detection for the first time, showed that most irreversible segments at stress redistribution <sup>201</sup>Tl imaging that show more than 50% of peak activity of normal regions are viable on the basis of FDG uptake, which is the standard method for viability detection.<sup>3</sup> On the other hand, although segments with a fixed defect tracer activity equal to or greater than 50% do not often show functional improvement following revascularization, revascularization of these segments may prevent remodelling and be important for long-term prognosis.<sup>4</sup> Therefore, we only investigated the viability of segments with less than 50% uptake at stress phase. If these segments showed at least 20% redistribution at a later 24-hour image, they were defined as viable.

The purpose of this study was to evaluate the potential advantage of the 24-hour redistribution <sup>201</sup>Tl imaging in stress-reinjection protocol to estimate viable myocardium in patients with myocardial infarction.

### **Methods**

Thirty-nine patients with myocardial infarction, diagnosed on the basis of confirmatory case histories, clinical manifestations, electrocardiogram, cardiac markers, and/or coronary angiogram, underwent imaging tests. Fourteen patients with complete viability at reinjection imaging were excluded from study; the remaining 25 patients received the 24-hour redistribution imaging.

All medications that interfere with dipyridamole (methylxanthines...) were withheld 24 hours before the test and caffeine on the morning of the imaging and were resumed after the completion of the first phase of imaging. Written informed consent was obtained from all the patients.

For pharmacological stress, all the patients received 56mg/kg dipyridamole intravenously in 4 minutes, and after 3 minutes, 3-3.5 mCi <sup>201</sup>Tl was administered. Forty-five minutes later, the patients underwent <sup>201</sup>Tl single photon emission computed tomography (SPECT). After 4 hours, all the patients were reinjected with 1-1.5 mCi <sup>201</sup>Tl and were imaged 30 minutes later. 24-hour redistribution imaging was performed if reinjection images revealed at least one segment without viability criteria (equal or more than 20% redistribution).

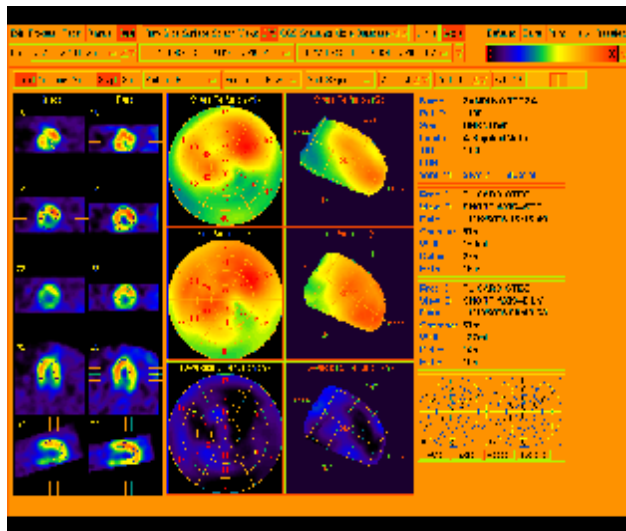
All images were obtained by a single-head SPECT camera (ADAC GENESYS series) equipped with a low-energy all-purpose collimator. The acquisitions were performed using <sup>201</sup>Tl energy windows of 76±10% kev and 167±10% kev, with matrix size of 64×64 and zoom factor of 1.3. Imaging was performed in 180° circular arc (RAO to LPO) at 6° intervals. The acquisition time was 30 and 40 seconds for the first two and the last images, respectively. Myocardial images were reconstructed using filtered back projection method with Butterworth filter, and displayed as a series of short-axis, horizontal, and vertical long-axes slices. The slice thickness was 4 mm (Fig. 1).

Images were analyzed quantitatively by Autoquant software. All segments with radiotracer uptake less than 50% maximum uptake in stress images were re-evaluated in reinjection; and if they did not

show viability criteria, 24-hour redistribution phase was performed. These segments were defined as viable if they showed at least 20% redistribution.

### Statistical analysis

Results were analysed by SPSS 15 software. All parameters were expressed as mean  $\pm$  SD. Paired T-test was used to compare the number of viable and non-viable segments as well as thallium uptake at the infarcted and peri-infarct segments at the three mentioned phases of the study. P-values  $<0.05$  were considered statistically significant.



**Fig. 1.** Reinjection image as compared to 24-hour image showing considerable increase in viability detection

### Results

Twenty-five patients aged  $57 \pm 8$  years (17 male and 8 female) who showed persistent defect after stress reinjection images were assessed for myocardial viability after myocardial infarction. The total number of abnormal segments on the initial study was 102. At 4-hour reinjection images, 19 (18.6%) segments and at 24-hour redistribution imaging, an additional 17 (20.4%) segments showed viability. The redistribution image in 8 (32%) patients and 17 (20.4%) segments increased the detection of viable segments in comparison with reinjection imaging ( $p < 0.05$ ). In 15 patients, there was no significant change between the two phases of imaging; and 2 cases revealed reverse redistribution. The mean thallium uptake at infarcted and peri-infarct segments at the redistribution images was higher than that in the reinjection images (51.8% vs. 47.7%), which was statistically significant ( $p < 0.05$ ).

### Discussion

The concept of hibernation has been challenged in recent years and an alternative concept has been proposed, that of persistent left ventricular dysfunction caused by repeated episodes of myocardial ischemia leading to repetitive stunning.<sup>5,6</sup> Independent of the mechanism, which is difficult to determine clinically, the important clinical issue is that viable but dysfunctional myocardium in patients with chronic coronary artery disease will improve in function only if identified and revascularized. At present, several clinically reliable physiological markers of viability can be used for this purpose. These include indexes of regional coronary blood flow, regional wall motion, and regional systolic wall thickening. These are accurate markers of viability when they are normal or nearly normal but have limitations in the identification of viable myocardium when severely reduced or absent. In the setting of hibernating myocardium by definition, indexes of regional perfusion and systolic function will be severely reduced or absent despite the maintenance of tissue viability.<sup>7,8</sup> Thus these indices are imprecise in differentiating hibernating myocardium from

myocardial scar. During the past decade, numerous studies have demonstrated that nuclear cardiology techniques involving single photon methods as well as positron emission tomography (PET) also provide critically important information about viability. Imaging agents that reflect regional myocardial blood flow and membrane integrity should provide excellent information regarding tissue viability.<sup>8,9</sup>

Because of poor negative predictive accuracy, it is now accepted that standard stress–redistribution thallium scintigraphy does not satisfactorily increase the precision in differentiating hibernating myocardium from fibrotic myocardium. It is well established that modification in imaging protocols in thallium considerably enhances the ability of thallium imaging to depict viable myocardium.<sup>2,10,11</sup> These include late redistribution imaging and thallium reinjection techniques. An imaging protocol that includes stress and redistribution images with thallium reinjection as necessary will provide most of the viability information that can be obtained from thallium imaging. Dilsizian et al. believed that rarely do late redistribution images after reinjection provide important additional information not achieved with the earlier three-image acquisition image.<sup>12</sup> However this protocol requires two sets of images at the redistribution and then reinjection phases. Thus it is suboptimal from the point of view of patient convenience and time consuming in the setting of a busy laboratory. Therefore, several modifications of the reinjection technique to streamline the imaging protocol are currently in clinical practice. One of these involves the routine reinjection of thallium 3-4 hours after stress without acquiring redistribution images. This approach improves efficiency and helps with the identification of viable myocardium in most patients in whom redistribution images would have been misleading by showing persistent defects. As was mentioned above, hibernation refers to a segment which shows hypoperfusion at rest,<sup>13</sup> and differentiating between scar and hibernating tissue is the aim of viability detection studies. There has been a gradual evolution and refinement of thallium imaging protocol in recent years to study myocardial viability. Quantification of relative thallium uptake in the left ventricle, as an important development in viability detection studies, was first advocated by Bonow et al., who showed that most myocardial segments with at least 50% of the maximal left ventricular uptake were demonstrated to be viable at FDG PET.<sup>3</sup> In our study, we investigated the segments with less than 50% of maximal uptake at stress phase. If these segments showed at least 20% redistribution in later phases, they were considered viable. We concluded that 20.4% of segments (17 out of 83 segments), which remained persistently hypoperfused at reinjection, showed viability at 24-hour redistribution imaging. The mechanism of this phenomenon has been proposed in previous studies:<sup>2-13</sup> reinjection of thallium at rest increases thallium uptake in the normally perfused territories to a greater extent than in hypoperfused territories, resulting in the appearance of relative thallium washout compared with the redistribution image. This differential uptake of thallium results in a defect on stress images that improves or normalizes on the redistribution images but then reappears on the reinjection images.<sup>14</sup>

In such patients, the reinjection image may mirror the stress image; and it is the redistribution image, not the reinjection image, that provides the important information regarding reversibility of the defect, hence, viability.

In this subset of patients, the elimination of redistribution data creates uncertainties regarding the interpretation of an irreversible defect when a stress–reinjection protocol is used.<sup>2-13</sup> Antanopolous et al. compared early post-exercise images with delayed 4 and 24-hour redistribution and revealed that delay imaging showed 11% improvement in the detection of viable segments.<sup>15</sup>

This value was 20.4% in our study; however, patient selection, stress, and imaging protocol as well as viability detection criteria were different.

We believe that our study not only does not overestimate the value of delay imaging for viability detection but also may underestimate it because of our strict criteria for viability definition.

### **Conclusion**

In patients with previous myocardial infarction who are referred for viability detection and undergo stress 4-hour reinjection imaging, 24-hour delay imaging is recommended if reinjection images reveal considerable non-viable segments.

### **Conflict of Interest**

No conflicts of interest have been claimed by the authors.

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## **Coronary Flow Reserve Before and After Coronary Artery Bypass Surgery**

H. R. Salehi MD†, M. Maleki MD\*, M. Hajaghaei MD\*\*\*, Z. Ojaghi MD\*\*  
and F. Noohi MD\*

## Abstract

**Background-** The coronary sinus (CS) blood flow can be used as a non-invasive measure of cardiac perfusion. Besides transesophageal echocardiography, transthoracic echocardiography with Doppler flow measurement has been introduced as a feasible and reproducible method to determine the CS blood flow. The purpose of this study was to assess the coronary flow reserve (CFR) by transthoracic imaging of the CS flow in patients with coronary artery disease before and after coronary artery bypass graft surgery (CABG).

**Methods-** Twenty-nine patients with coronary artery disease who were candidates for CABG were evaluated in this study. CFR was measured using the CS flow profile. Twenty-one patients, comprised of 15 men and 6 women at a mean age of  $56.7 \pm 9.1$  years, were evaluated. All the patients had a pre-operative increase in their coronary blood flow during the dipyridamole stress test (mean CFR/beat= $1.38 \pm 0.2$ , mean CFR/min= $1.54 \pm 0.18$ ).

**Results-** CFR was significantly higher in post-operative status (mean CFR/beat= $2.25 \pm 0.45$ , mean CFR/min= $2.55 \pm 0.43$ ,  $p < 0.001$ ).

**Conclusion-** Our study, in accordance with previous studies, denotes that a transthoracic measurement of CFR can be used as a feasible and reproducible method to monitor the changes in cardiac perfusion after revascularization (*Iranian Heart Journal 2009; 10 (1):21-26*).

**Key words:** coronary flow reserve ■ coronary artery disease ■ coronary sinus ■ coronary artery bypass graft

Coronary flow reserve (CFR) is defined as the maximal (hyperemic) to resting ratio of the coronary blood flow. CFR is an important physiologic parameter of coronary circulation and depends on the patency of the epicardial coronary arteries and the integrity of the microvascular circulation.

CFR measurement has such various clinical applications as functional assessment of the intermediate stenosis, detection of the critical stenosis, monitoring of the coronary flow in the post-angioplasty period, and assessment of the post-infarct blood flow.

It has been proposed that the coronary sinus (CS) blood flow can be used as a feasible and reproducible measure of cardiac perfusion. However, the standard

or digital coronary angiography) or the use of radioisotope dyes (argon technique or xenon scintigraphy). New methods in the field of echocardiography that have been recently introduced to determine CFR include direct visualization of the coronary arteries (mostly left anterior descending artery) by transesophageal echocardiography.<sup>1,2,3</sup> Nevertheless, the images do not have sufficient clarity for an accurate measurement of the vessel diameter; as a result, only coronary blood velocity can be measured.<sup>5-14</sup>

Recently, Alexander and colleagues described reduced coronary flow reserve in the CS as a predictor of hemodynamically significant stenosis of the left coronary artery territory.<sup>14</sup> More recently, transthoracic

Received April 23, 2007; Accepted for publication May 2, 2008.

\* Professors in Cardiology \*\* Assistant Professor in Cardiology \*\*\* Fellow of Echocardiography + Cardiology

From the Department of Cardiology, Shaheed Rajaei Cardiovascular Medical and Research Center, Tehran, Iran..

Correspondence to H.R. Salehi, M.D., Department of Echocardiography, Shaheed Rajaei Cardiovascular Medical and Research Center, Mellat Park, Vali Asr Avenue, Tehran, Iran. E-mail: [hr\\_salehi@med.mui.ac.ir](mailto:hr_salehi@med.mui.ac.ir) Tel: (021) 22055594

methods for CFR measurement are expensive, invasive, and require cardiac catheterization (intravascular Doppler flow wire, thermodilution wire,

imaging of the CS to measure CFR has been presented and its validity and reproducibility has been confirmed compared with standard invasive techniques.<sup>15,16</sup>

In this study, we used transthoracic echocardiography to determine CFR in the CS in patients who were candidates for coronary artery bypass graft surgery (CABG) before and one month after surgery.

### Methods

Obtaining an acceptable imaging of the CS was possible for 21 of the 29 selected patients (age=56±9.1; 15 male, 6 female). The baseline characteristics of the patients are summarized in Table I.

**Table I. Baseline characteristics of the study group**

No.	21
Age	56.7±9.1
Male/Female	15/6
HTN	9
DM	5
HLP	7
Smoking	8
LVEF	47.1±6.1
Single vessel	2
Two vessel	5
Three vessel	14
Left main disease	1

All of the 29 patients had sinus rhythm without a significant valvular disease. Patients with unstable angina (i.e., angina at rest), significant valvular disease, and history of asthma were excluded from the study. All drugs were continued to prevent acute symptoms. Eight patients were excluded due to poor image quality,<sup>5</sup> occurrence of chest pain during the test,<sup>2</sup> and poor follow-up.<sup>1</sup> Dipyridamole was used as the vasodilator agent mostly because of its prolonged action compared with adenosine.<sup>17-19</sup>

Echocardiography was done with a GE Vivid 7 system with a 2.5-MHz transducer. The CS was visualized in the long axis view from modified RV inflow view, and efforts were made to reduce the  $\theta$  angle for an accurate Doppler measurement of the flow. Color Doppler was carried out to confirm the flow within the CS. The CS blood flow velocity was identified via pulse-wave Doppler recordings as systolic and diastolic waves. The sample was placed at the CS ostium. The peak velocity and time-velocity integral (TVI) of the CS were measured by outlining the antegrade phase of the flow velocity signal in the CS moving into the right atrium. The CS was then imaged in the apical 4-chamber view with the posterior tilting of the transducer (Fig. 1).



**Fig. 1. Systolic and diastolic waves in the transthoracic imaging of the coronary sinus**

M-mode echocardiography of the CS at its entry point to the right atrium was used to obtain its diameter. The average of the measurements over 3 cardiac cycles was used as the major diameter of the CS.<sup>23</sup>

Assuming that the cross-sectional area (CSA) of the CS is an ellipse and that the major diameter is double the length of the minor diameter, the CSA of the CS was calculated as:  $0.39$  (the major diameter)

The CS blood flow was then calculated as:

$$(\text{CS TVI}) \times (\text{CS CSA}) \times (\text{HR})$$

TVI: Time Velocity Integral, CSA: Cross-Sectional Area, HR: Heart Rate

To determine the flow/beat, HR was omitted.

After the baseline measurement of the CS diameter and flow, dipyridamole (0.56 mg/Kg) was infused over a 4-minute period to obtain an increase in the heart rate (10% from baseline status).

After the termination of the infusion, a Doppler profile of the CS was continuously recorded up to 10 minutes for the detection of the hyperemic flow. The CS diameter was measured 3 - 5 minutes after the termination of the infusion. Blood pressure and heart rate were automatically measured.

Echocardiography was repeated nearly one month after surgery (28 to 36 days). This measurement was done in the baseline and then in the hyperemic phase for the calculation of CFR both before and after CABGs.

CFR was calculated as the ratio of the volumetric hyperemic blood flow to the volumetric baseline blood flow. The level of CFR <2 was used for the diagnosis of low CFR according to the previous studies (sensitivity=89%, specificity=77%).<sup>14</sup>

### Results

All the parameters were expressed as mean and standard deviation (SD). Comparisons between the

parameters recorded before and after revascularization were made with the paired Student's *t*-test (Table II). Statistical significance was accepted when confidence intervals were >95% ( $p < 0.05$ ). The baseline heart rate did not differ before and after CABGs.

**Table II. Echocardiographic data before and after surgery**

There was a significant increase in the CS diameter in the post-CABG status ( $9.4 \pm 1.2$  vs.  $8.6 \pm 1.05$ ) compared to the baseline status. Also, there was a trend for increase in the CS diameter in the hyperemic phase before CABGs; this increase was higher in the post-operative status (mean value of increase CS diameter: 0.5 mm before and 1.5 mm after surgery).

Before surgery, there was an increase in the coronary blood flow during the stress test (mean CFR/beat =  $1.38 \pm 0.2$ , mean CFR/min =  $1.54 \pm 0.18$ ). CFR was significantly higher in the post-operative status (mean CFR/beat =  $2.25 \pm 0.45$ , mean CFR/min =  $2.55 \pm 0.43$ ).

Comparing the similar values before and after surgery showed meaningful differences in the values before and after revascularization ( $p < 0.0001$ ). There was a significant increase in the systolic velocity ratio (hyperemic/baseline) after surgery (mean systolic velocity ratio before surgery =  $1.21 \pm 0.1$ , mean systolic velocity ratio after surgery =  $1.34 \pm 0.15$ ,  $p = 0.007$ ). This was also true about the systolic TVI ratio (mean systolic TVI ratio before surgery =  $1.23 \pm 0.15$ , mean systolic TVI ratio after surgery =  $1.57 \pm 0.17$ ,  $p < 0.001$ ). Similarly, there was a significant increase in the diastolic TVI ratio (mean diastolic TVI ratio before surgery =  $1.27 \pm 0.15$ , mean diastolic TVI ratio after surgery =  $1.68 \pm 0.33$ ,  $p < 0.001$ ).

In contrast to the previous values, there was an insignificant increase in the diastolic velocity ratio (mean diastolic velocity ratio before surgery =  $1.21 \pm 0.19$ , mean systolic velocity ratio after surgery =  $1.36 \pm 0.28$ ,  $p = 0.054$ ).

### Conclusion

Several studies have demonstrated that revascularization in patients with coronary artery disease produces remarkable improvement in the cardiac function, symptoms, and exercise tolerance.

However, an objective measurement of the expectable CS blood flow has traditionally required invasive studies.

By using this noninvasive method of measuring the CS blood flow by TTE, we were able to show a statistically significant increase in the coronary artery flow after revascularization procedures, a finding previously established by invasive studies. One limitation of this study is that we did not compare our data with those of an invasive technique.<sup>2,3</sup>

In the coronary arteries, CFR measurement by Doppler echocardiography is limited to the coronary blood velocity. The flow velocity variation is proportional to

Variable	Preop	Postop	P value	
HR	Resting	66.8±5.2	68.8±4.2	0.117
	Stress	75.5±5.9	78.7±4.2	0.117
CS diam	Resting	8.6±1.06	9.4±1.21	0.001
	Stress	9.1±1.04	10.97±0.92	<0.001
CFR/beat	1.38±0.2	2.25±0.43	<0.0001	
CFR/min	1.54±0.18	2.55±0.43	<0.0001	
S velocity ratio	1.21±0.1	1.34±0.15	<0.007	
D velocity ratio	1.21±0.19	1.36±0.28	<0.054	
S TVI ratio	1.23±0.15	1.57±0.17	<0.001	
D TVI ratio	1.27±0.15	1.68±0.33	<0.001	

the total blood flow if the vessel lumen is kept constant. So an estimation of CFR can be accurate if the coronary artery functions only as a conduit.<sup>4,5</sup>

CFR and CF velocity are closely correlated, because most of vasodilatation is located in the microcirculation and the arterioles. Nonetheless, in this study a measurement of blood velocity and TVI was done on the venous side of the coronary system. Similar to other veins, the CS has a thin wall and highly extensible structure; and in this point, the coronary blood velocity is no longer closely related to CFR.<sup>15</sup>

As a result, for the measurement of CFR from the CS, a measurement of the CS diameter at baseline and hyperemic phases is mandatory; and ignoring this step may lead to significant errors in the estimation of CFR. In another study with a focus on the CS diameter before and after CABGs, there was an insignificant increase in the CS diameter in the post-surgery status.<sup>23</sup> Another difference in the CFR estimation on the arterial and the venous side is based on the different shape of the flow in the cardiac cycle. In the coronary arteries, there is a predominantly diastolic flow (peak diastolic velocity:  $28 \pm 9$  cm/sec and peak systolic velocity  $17 \pm 4$  cm/sec) with a gradual diastolic slope in the CS. However, the pattern of the flow is also related to the right atrial pressure wave, and there are two distinct systolic and diastolic waves. In the healthy subjects, the systolic wave is dominant.<sup>16</sup>

A simple CFR assessment via the diastolic velocity ratio in the coronary arteries is, therefore, used with reasonable accuracy.<sup>5-8</sup> This is not, however, true in the CS; and there is a significant difference between CFR and the diastolic velocity ratio in our study.

Another variable of the coronary blood flow is heart rate. As was mentioned, we calculated CFR using 2 formulas to obtain CFR/beat and CFR/min. There is a close relation between these two parameters leading to CFR/min higher than CFR/beat in all cases.<sup>23</sup>

In summary, our study demonstrated that TTE could be used to measure the CS blood flow in patients after CABG. This statistically significant finding, in accordance with previous invasive studies, suggests that TTE may be used as a noninvasive modality to monitor the changes in the CS blood flow and to determine coronary perfusion in patients after revascularization, especially when it is added to the findings of regional wall motion abnormalities in the stress echo lab.<sup>20-22</sup>

### Conflict of Interest

No conflicts of interest have been claimed by the authors.

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## **Neurocognitive Complications after Off-Pump and On-Pump CABG**

Ali Sadeghpour Tabae MD\*, Alireza Rostami MD\*\*, Soheila Arefi, MD\*\*\*  
and Ali Sadeghi MD+

### **Abstract**

**Background-** Neurocognitive dysfunction after cardiac surgery with cardiopulmonary bypass (CPB or “pump”) is a common complication, reported in up to 53% of patients. In many patients this morbidity is only mild and transient, but in 5% of cases, it is severe.

**Method-** In this prospective study from June 2002 to July 2004, 186 cases underwent coronary artery bypass graft surgery (CABG) using CPB or off-pump CABG (OPCAB), and they were evaluated for neurocognitive complications by mini-mental status examination.

**Results-** The average age of the patients was 56±6.2 years, 62% were male and 38% were female. 121 operations were performed with CPB (on-pump) and 65 operations were done off-pump. Mini-mental status test was normal in 50% of off-pump CABGs and in 43% of on-pump CABGs, very mild disturbance was seen in 48% of off-pump CABGs and in 54% of on-pump CABGs ( $p$  value=0.192, NS), mild disturbance was seen in 2% of off-pump CABGs and in 3% of on-pump CABGs ( $p$  value 0.392, NS), and moderate or severe disturbance was not seen in either group.

**Conclusion-** In our study, there was no significance difference in the frequency of postoperative neurocognitive complications between off-pump and on-pump CABG patients (*Iranian Heart Journal 2009; 10 (1):27-30*).

**Key words:** coronary artery bypass graft ■ cardiopulmonary bypass ■ neurocognitive complication ■ OPCAB

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Cardiopulmonary bypass (CPB) is one of the causes of brain damage during coronary artery bypass graft surgery (CABG). Neurologic complications after cardiac surgery may be categorized as: 1) neurologic deficits, and 2) neurocognitive dysfunction.

Dysfunction of the nervous system after surgery is further classified in three groups: 1) CNS complications, 2) psychological complications, and 3) peripheral neurologic complications.

~~Generalized neuro-psychological function including intelligence, problem solving, concentration, learning and memory are among the cognitive functions of the brain.~~

The presence of atheroma in the aorta and previous history of stroke are two causes of neurologic deficits. The incidence of neurocognitive disorders increases with the use of hypothermia and total

Received Oct. 2, 2007; Accepted for publication May 2, 2008.

\*Associate Professor of Cardiovascular Surgery; \*\* Resident of Cardiovascular Surgery, Shaheed Rajaie Cardiovascular Medical and Research Center, Mellat Park, Vali Asr Ave. Tehran, Iran, \*\*\* Assistant Professor of Reproductive Endocrinology Department, Avicenna Research Center, Shaheed Beheshti University of Medical Sciences, Evin, Tehran, Iran, +Professor of Cardiac Anesthesia, Shaheed Rajaie Cardiovascular and Research Medical Center, Mellat Park, Vali Asr Ave. Tehran, Iran.

Correspondence to: Ali Sadeghpour Tabaee MD; Dept. of Cardiovascular Surgery; Shaheed Rajaie Cardiovascular Medical and Research Center, Mellat Park, Vali Asr Ave. Tehran, Iran. Tel: 02123922589

circulatory arrest. Old age is a major risk factor for neurocognitive disorders.

In this study, neurocognitive complications after off-pump and on-pump CABG are evaluated and compared. Neurocognitive complications (intelligence, problem solving, concentration, learning, memory, error free performance and dexterity) after cardiac surgery with CPB is a common complication (reported in up to 53% of patients).<sup>1</sup> CPB itself may cause brain damage during cardiac surgery, the mechanism responsible for which possibly being microemboli formation and hypoperfusion. Disorders in concentration and memory have been reported in about 50% of patients who have underwent CABG with CPB.<sup>1</sup>

## Methods

In this prospective study from June 2002 to July 2003, the patients at our center who were operated as off-pump CABG were evaluated and demographic data such as age, sex, degree of hypothermia, number of grafts, etc. were collected. For each off pump patient, two patients who were operated on pump were evaluated.

Neurocognitive complications after discharge from the ICU were evaluated (3-5 days after the operation). They were analyzed in a questionnaire as mini-mental status test and were scored as follows: (normal score: 30, very mild: 28-29; mild: 26-27; moderate: 24-25; severe dysfunction: below 24). The results were analyzed with SPSS 11 software. For ethical concerns, informed consent was received from all the patients in the study.

## Results

Totally, 133 patients were evaluated in this study. Fifty-two percent of patients were male and 42% female; patients were in the age range of 55-69 years old; 53% were operated on pump and 39% were operated with off-pump technique.

In the study population, 41% were in the normal group, 53% in the very mild and 6% in the mild dysfunction group, according to their scores of neurocognitive disorders.

In the first row of Table I, the distribution of the neurocognitive disorders is demonstrated according to use of the pump. There was no significant difference between the two groups. ( $P=0.192$ ). Also, there was no significant difference in the incidence of neurologic complications between males and females ( $p=0.392$ ).

The frequency of neurocognitive complications in accordance with the type of complication and age are demonstrated in the third row of Table I, which shows that with increasing age, the rate of neurocognitive complications increases after CABG.

**Table I. The distribution of neurocognitive complications in the study population.**

Neurocognitive score		Normal	Very mild	Mild	Total
Type of operation (p=0.192)	On-pump	50% (32)	48% (48)	2% (7)	100% (87)
	Off-pump	37% (23)	55% (22)	8% (1)	100% (46)
Sex (p=0.392)	male	46% (38)	48% (40)	6% (5)	100% (83)
	female	34% (17)	60% (30)	6% (3)	100% (50)
Age group (P=0.007)	40-54	58% (30)	38% (20)	4% (2)	100% (52)
	55-69	34% (22)	61% (39)	5% (3)	100% (64)
	Over 70	18% (3)	65% (11)	17% (3)	100% (17)
Study population		41% (55)	53% (70)	6% (8)	100% (133)

## Discussion

In this study we evaluated the neurocognitive complications in patients who underwent CABG as on-pump and off-pump technique.

The age of the patients influenced the incidence of neurocognitive complications in off-pump and on-pump groups. With increasing age, the incidence of such complications increases (p=0.007).

In the study of Pukas, Hernandez and Sabick, there was no significant difference in the incidence of neurologic events and postoperative stroke between off-pump and on-pump CABG patients. In one study, cognitive performances of candidates for bypass were significantly lower than those of a healthy control group.<sup>1</sup> In our study there was no significant difference for neurocognitive complications between males and females. There was no significant difference in incidence of neurocognitive complications between off-pump and on-pump surgery, similar to that reported in the study of Vedin.<sup>4</sup>

With increasing age in the on-pump group, the rate of neurocognitive complications increases.

In another study patients undergoing on-pump surgery have a significant relative reduction in prefrontal activation, which correlates with intraoperative cerebral microembolic load.<sup>2</sup> In a study of 52 patients by Stroodant et al., it was demonstrated that off-pump surgery leads to a reduction in intraoperative cerebral microembolization.<sup>3</sup>

In Vedin's study in 2006, there were no differences in postoperative cognitive function after on-pump compared to off-pump CABG.<sup>4</sup>

Although neurocognitive decline after CABG is mostly transient, memory impairment can persist for months.<sup>5</sup>

In another study, long-term cognitive function and MRI evidence of brain injury were similar after off pump and on pump coronary artery bypass grafting surgery.<sup>6</sup>

Cognitive decline after cardiac surgery is a function of underlying patient factors rather than perioperative ischemic events alone.<sup>7</sup> In one study the harmful effects of CPB were not permanent,<sup>15</sup> contrary to the results of Newman's study.<sup>16</sup>

## Conclusion

According to this study, we conclude that the use of pump has not influenced the incidence of neurocognitive disorders, and there is no significant difference for this complication between males and females. However with increasing age, the incidence of neurocognitive disorders increases, thus off pump CABG may have a beneficial role in older patients.

### Conflict of Interest

No conflicts of interest have been claimed by the authors.

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## Acute Myocardial Infarction in Women

Toba Kazemy MD and Gholam Reza Sharifzadeh MSc

## Abstract

**Background-** Epidemiological evidence shows that among women the incidence of acute myocardial infarction (AMI), risk factors of cardiovascular disease, and mortality rate of AMI are different. The objective of this study was to compare the baseline characteristics, risk factors, medical care, and mortality of AMI between women and men.

**Methods-** In this descriptive-analytical study, we examined data from medical charts and administrative files of patients that were hospitalized with AMI between 1994 and 2003 in Birjand hospitals. Questionnaires were completed by two educated nurses under the supervision of a cardiologist and the data were analyzed with SPSS software.

**Results-** From 918 patients, 71.9% were male (M) and 28.1% were female (F). The women were older than the men (mean age  $65.62 \pm 10.56$ yr in F vs.  $58.98 \pm 12.11$ yr in M) and had a greater incidence of hypertension (50% in F vs. 24.6% in M,  $p < 0.001$ ) and diabetes mellitus (17% in F vs. 9.8% in M,  $p < 0.006$ ), but smoking was more common in the men (13.7% in F vs. 36.3% in M,  $p < 0.001$ ). Intra-hospital mortality was higher in the women but not significantly (10.4% in F vs. 8.6% in M,  $p = 0.42$ ). Fasting blood sugar (FBS), cholesterol level, and diastolic blood pressure (DBP) were significantly higher amongst the women.

**Conclusion-** Women with AMI had older age and higher incidence of diabetes and hypertension. Thus designing interventional programs for reducing these risk factors by education in women is needed (*Iranian Heart Journal 2009; 10 (1):31-34*).

**Key words:** acute myocardial infarction ■ female ■ risk factors

Acute myocardial infarction (AMI) is the single most common cause of death in both women and men in large parts of the world.<sup>1</sup> AMI accounts for a great number of deaths in Iran<sup>2</sup> and in Birjand<sup>3</sup> as well.

Several studies have shown that the incidence of AMI in men is higher than that in women.<sup>4-8</sup> In recent years, not only has the incidence of AMI in women increased, but also the burden of AMI on the mortality of women has also increased.<sup>4-6</sup>

Previous studies have suggested differences in the epidemiology of AMI in women.

Women, on average, were older than men and had a

The diagnosis of AMI was based on the criteria proposed by Braunwald:<sup>12</sup> dynamic changes of electrocardiography indicating the development of AMI and changes of cardiac enzyme activity in the blood stream. The medical records of the selected patients were reviewed by two trained nurses; and information was obtained on the patients' age, risk factors, use of pharmacologic agents, and mortality in the men and women.

The data were then entered into SPSS software, and data analysis was performed using the chi-square ( $X^2$ ) and t-test at  $\alpha = 0.05$ .

Received Oct. 23, 2007; Accepted for publication June 2, 2008.

From the Department of Cardiology, Vali Asr Hospital, Birjand University of Medical Sciences, Birjand, Iran.

Address for correspondence: Toba Kazemi MD, Assistant Professor of Cardiology, Vali Asr Hospital, Birjand University of Medical Sciences, Ghaffari St, Birjand, Iran. Fax: 0561-4447746, Email: med\_847@yahoo.com

higher prevalence of hypertension (HTN), diabetes mellitus (DM), dyslipidemia, and in-hospital mortality.<sup>7-8</sup>

However in other studies, no difference was seen in long-term mortality after myocardial infarction between men and women.<sup>9-11</sup>

In the present study, we assessed the incidence, risk factors, mortality, and use of pharmacological agents between men and women in a cross-sectional study of all AMI patients admitted to Birjand hospitals between 1994 and 2003.

### Methods

This is a descriptive study conducted between 1994 and 2003 in Birjand, a city in the East of Iran. We obtained lists of all patients who were hospitalized in Birjand with AMI.

### Results

From 1994 to 2003, 918 patients were hospitalized with definite AMI in Birjand. 71.9% of the subjects were men with a mean age of  $58.9 \pm 12.1$  years, and 28.1% were women with a mean age  $65.6 \pm 10.6$  years ( $p < 0.001$ ).

The prevalence of cardiac risk factors between the men and women is compared in Table I.

**Table I. Frequency distribution of risk factors in men and women with definite AMI**

Risk Factor	Women	Men	P-value
Mean age (years)	$65.6 \pm 10.6$	$58.9 \pm 12.1$	$< 0.001^*$
Hypertension	129 (50%)	161 (24.4%)	0.001*

Diabetes	44 (17%)	65 (9.8%)	0.002*
Dyslipidemia	49 (19%)	128 (19.4%)	0.88
Cigarette smoking	35(17.6%)	240 (36.4%)	0.001*
Positive family history	11 (4.3%)	28 (4.2%)	0.99

Total: men=660, women=258 \*statistically significant

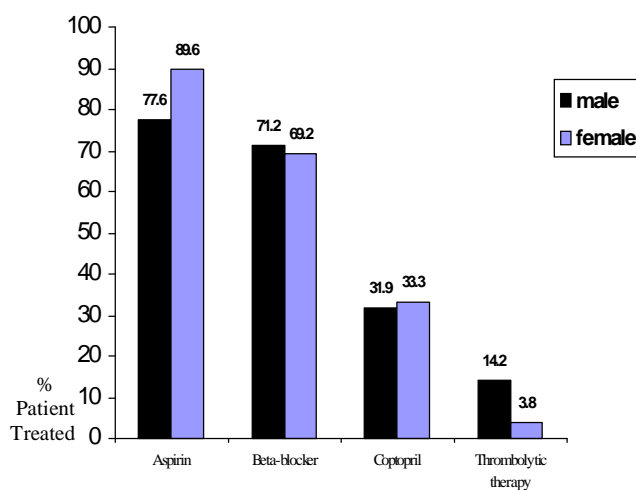
Table II presents the mean level of fasting blood sugar (FBS), serum lipids, and blood pressure in the men and women.

**Table II. Comparison of mean levels of FBS, serum lipids, and blood pressure in women and men**

Object	Women	Men	P-value
FBS (mg/dl)	138.4±75.4	122.2±52.6	0.001*
Cholesterol(mg/dl)	214.7±61.7	199.6±49.5	<0.001*
Triglyceride (mg/dl)	138.8±69.8	138.4±103.7	0.95
SBP (mmHg)	125.3±25.9	121.5±26.1	0.07
DBP (mmHg)	87.6±15.5	75.6±16.3	0.01*

SBP: systolic blood pressure, DBP: diastolic blood pressure

Comparisons revealed a statistically significant difference between blood sugar, cholesterol, and diastolic blood pressure in the two groups. Acute medical care of the patients is presented in Figure 1.



**Fig. 1.** Comparisons of acute care of men and women with definite AMI

Only the frequency of the administration of thrombolytic therapy was significantly lower in the women (3.8% in women vs. 14.2% in men,  $p<0.001$ ).

Intra-hospital mortality of women was higher than that of the men, but not significantly (10.4% in women vs. 8.7% in men,  $p=0.42$ ).

## Discussion

In our study, 28.1% of the patients hospitalized with a definite diagnosis of AMI were women, and the women on average were older than the men. The results of other studies are in agreement with this finding.<sup>4-6</sup> The lower prevalence of AMI in the women may be due to the protective effect of estrogen in women.<sup>13</sup>

In accordance with other studies, the prevalence of hypertension and diabetes mellitus was higher (statistically significant) in the women than that in the men and the prevalence of smoking in the men was three-times that of the women.<sup>11-14</sup>

In our study, there was increased in-hospital mortality among the women compared with the men, but not significantly. In the majority of reports, in-hospital mortality of women was higher than that of the men<sup>7,8</sup> but in other studies, for example in Yazd (2000-2001), there was no difference between male and female in-hospital mortality from AMI.<sup>9-11</sup>

Medical care has an important role in reducing the mortality of patients. In a recent publication from the Neufeld Cardiac Research Institute<sup>7</sup>, Gotllieb et al. noted that women were less likely to be treated with aspirin, beta-blockers, captopril, and thrombolytics, but in our study the medical management was similar except for thrombolysis.

In our study, thrombolytics were used significantly less frequently in the women (three-times lower in women). One of the most important reasons for a poorer prognosis of AMI in the women in our study may be due to this lower use of thrombolysis in the men.

Several earlier studies also have noted that women are less likely to receive thrombolysis therapy due to older age, co-morbid conditions, and late arrival.<sup>15-17</sup>

## Conclusion

Sex differences in the management, risk factors, and outcome of AMI in Birjand are similar to those in other parts of the world. Despite the low prevalence of AMI in the women, in-hospital mortality in the women was higher, which may be due to older age, greater co-morbidity (especially DM and HTN), and especially, less use of thrombolysis in the women. We compared only the in-hospital differences in management, risk factors, and outcome after AMI in women and men. We unfortunately did not assess sex-based differences in management, risk factors, and short- and long-term

mortality after AMI in the present study. Further studies are required to clarify these issues.

### Acknowledgments

We are indebted to all physicians and nurses in the cardiac wards in Birjand. We are also grateful to Miss Assiabani and Talebi for data collection.

### Conflict of Interest

No conflicts of interest have been claimed by the authors.

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# Evaluation of Right Ventricular Function before and after Dobutamine Stress Echocardiography in Healthy Individuals

Niloufar Samiei MD, Fariba Bayat MD, Zahra Ojaghi Haghghi MD, Mojgan Parsaei MD, Feridoon Noohi MD\* and Ahmad Mohebbi MD\*

## Abstract

**Background-** Several well-established echocardiographic parameters such as tricuspid annular plane systolic excursion (TAPSE), right ventricular outflow tract (RVOT) fractional shortening (FS), myocardial performance index, and Doppler tissue imaging have been used for the assessment of right ventricular (RV) performance. The aim of this study was to evaluate the response of various parameters of RV function to dobutamine infusion in healthy individuals.

**Methods-** Thirty-eight participants with negative dobutamine stress testing for the left ventricle and with a mean age of 57 years (range: 40-85 yrs) underwent echocardiography, including measurement of TAPSE, fractional shortening (FS), and TDI (S velocity, strain and strain rate of base, mid, and apex) of the right ventricle at rest and after dobutamine infusion according to standard dobutamine stress testing (DSE) for the evaluation of changes in RV function after DSE.

**Results-** There were significant increases in S velocity (61.1%,  $P < 0.001$ ), FS (19.7%,  $P < 0.001$ ), TAPSE (6.4%,  $PV = 0.026$ ), strain rate (SR) in base (201%), apex (114%) and mid-wall (71%, all  $P < 0.001$ ), and strain in the apical portion (21%,  $PV = 0.001$ ) after dobutamine. There was no significant difference in SR between the RV free wall segments, but strain at mid-segment was more than that in the apical and basal segments at rest.

**Conclusion-** All RV performance parameters increased with the infusion of dobutamine. The mean values for strain rate were homogenous in basal, mid, and apical segments at rest and significantly increased in all the segments. This was in marked contrast to mean strain values, which were greatest in the mid part of the RV free wall at rest and increased only in the apical segment after DSE (*Iranian Heart Journal 2009; 10 (1):35-39*).

**Key words:** dobutamine ■ stress echocardiography ■ ventricular function

**R**ight ventricular (RV) function is an important independent predictor of exercise capacity and mortality in patients with heart failure or pulmonary hypertension, independent of left ventricular function.<sup>1,2</sup> However, despite increasing interest in the echocardiographic estimation of RV function

during routine assessment of cardiac function,

and detection of patients with decreased RV reserve in valvular or congenital heart disease.

The aim of this study was to evaluate RV function by various parameters, especially TDI, before and after dobutamine stress testing in healthy individuals.

RV function can be quantified by various echocardiographic indices such as the RV index of myocardial performance, tricuspid annular plane

Received Feb. 10 2007; Accepted for publication May 2, 2008.

From the Department of Echocardiography and \*Cardiology, Shaheed Rajaei Cardiovascular Medical and Research Center, Tehran, Iran.

Correspondence to: Niloufar Samiei, MD Department of Echocardiography, Shaheed Rajaei Cardiovascular Medical and Research Center, Tehran, Iran. Tel: 23922494

estimation of RV reserve in healthy individuals during stress test has not been fully evaluated. It can be helpful in the assessment of pathologic RV response

systolic excursion (TAPSE), RV outflow tract (RVOT) fractional shortening (FS), and pulsed wave Doppler tissue imaging (DTI).<sup>3-9</sup>

There are several publications on DTI of the LV, whereas the application of DTI on the RV is limited especially after DSE.

## Methods

### Study population

In total, 38 individuals were included in our study from patients referred for an evaluation of ischemia to our center. They were eligible for inclusion in the study if they had visually and echocardiographically normal RV and LV systolic function at rest, negative DSE for ischemia in LV segments, and had no other disease that could be associated with RV dysfunction.

### Resting echocardiography

Echocardiography was performed in the left lateral position. Two-dimensional (2D) and color Doppler myocardial imaging (CDMI) were performed (Vivid 7, GE, Horten, Norway, 3 MHz probe) and stored digitally for subsequent analysis. Study of TAPSE by M-mode and tricuspid annular velocity at the junction of the tricuspid annulus was done in the apical 4-chamber view by TDI and the RV lateral wall strain and strain rate by SI. RV out flow tract fractional shortening was measured in the parasternal short axis view.

For the assessment of regional longitudinal function, real time 2D CDMI-derived velocities were recorded from the RV free wall using apical 4-chamber views. High frame rate acquisition was used. Careful attention was taken to make the ultrasound beam parallel to the direction of wall motion. CDMI data were analyzed offline using specialized software (TVI, GE Vingmed Medical System) as previously described.<sup>10,11</sup>

Timing information was added using PW Doppler traces of the pulmonary and tricuspid valve for RV analysis.

From the velocity data, longitudinal SR and strain were estimated in the base, mid, and apical segments of the RV free wall.

### Dobutamine stress echocardiography

Graded dobutamine infusion was administered through a peripheral arm vein in 3-minute stages at infusion rates of 5, 10, 20, 30, and 40  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ . When necessary, atropine 0.25 mg was added during peak dobutamine infusion, maximally three times at 2-minute intervals, in an attempt to increase heart rate to a target of 85% of the age-predicted maximal level (220-age). Reasons for termination of infusion were achievement of target heart rate, maximal drug infusion

level at a lower heart rate, development of ventricular tachycardia or ventricular fibrillation, and severe adverse effects and symptoms including angina pectoris. All of the parameters measured at rest were repeated at peak dobutamine infusion. All the analyses were performed by two observers (double checked), and the average of three measurements of each parameter was used for statistical analysis.

### Statistical analysis

Values are presented as mean  $\pm$  1 SD. Comparison between the base and the mid and apical segments at rest and after DSE was performed using the repeated measure ANOVA model.

Percent changes in various parameters of RV function before and after DSE were measured via the paired *t*-test.

Evaluation of age and sex effects on RV function parameters was conducted by linear regression model and *t*-test, respectively.

A *P*-value  $<0.05$  was considered statistically significant.

## Results

### Baseline data

The study group included 38 patients (with negative DSE for LV ischemia and normal hyperdynamic response). The mean age was 57 (range: 40 - 85 years), and 27 of the patients (71%) were female and 11 (28.9%) were male.

The mean value of TAPSE at baseline was  $22.9 \pm 4$  mm, and there was a significant negative correlation between age and TAPSE ( $PV=0.01$ ). The mean value of baseline tricuspid annular velocity was  $12.9 \pm 2.9$  cm/sec, and no significant correlation with age and sex was seen.

The mean value of fractional shortening was  $62 \pm 12\%$ , with no correlation with age ( $PV=0.17$ ) but with correlation with sex, as it was higher in the females ( $PV=0.05$ ).

The mean values of RV strain in the basal, mid, and apical portions were  $-17.7 \pm 7.9\%$ ;  $-27.5 \pm 7.8\%$ , and  $-22.9 \pm 10.1\%$ , respectively. There was a significantly higher mean strain value in the mid segment of the RV free wall ( $PV<0.001$ ).

The mean values of RV strain rate in the basal, mid, and apical portions were  $-1.43 \pm 0.68$ ,  $-1.81 \pm 0.75$ , and  $-1.64 \pm 0.7$ , respectively, which were higher in the mid segment but there was no statistically significant difference and there was relatively homogenous strain rate in all the RV segments ( $PV=0.59$ ). No correlation was seen between strain and strain rate with age and sex.

The baseline characteristics are listed in Table I.

### Results after dobutamine stress test

The mean value of RV peak systolic tissue velocity at peak DSE was  $19.7 \pm 5$  cm/s, which significantly increased (61.1%,  $PV < 0.001$ ) compared with resting S velocity.

The mean value of TAPSE was  $23.8 \pm 3.7$  mm with a statistically significant (6.4%,  $PV = 0.026$ ) increase compared to the resting value.

The mean value of FS was  $72.8 \pm 11.9$ , with 19.7% increase with stress test ( $PV < 0.001$ ).

The mean values of RV strain in the base, mid, and apical segments were  $-20.6 \pm 10.3\%$ ,  $-27.6 \pm 6.9\%$ , and  $-28 \pm 9.7\%$ , respectively, with 27.3%, 5%, and 21% increase compared with baseline RV strain, which was statistically significant only in the apical segment ( $PV = 0.001$ ) by the paired *t*-test, but a significant change in strain was seen overall by the repeated measure ANOVA model in all the myocardial segments after DSE ( $PV = 0.019$ ).

The mean values of RV strain rate in the base, mid, and apical segments were  $-3.5 \pm 5.3$ ,  $-3.2 \pm 1.1$ , and  $-2.8 \pm 0.87$  (l/s), respectively, with a significant (201%, 71%, and 114%,  $PV < 0.001$ ) increase compared with the resting values, and homogenous values in all the segments were seen.

Echocardiographic parameters after dobutamine stress testing and percent changes are listed in Table I.

**Table I. Echocardiographic parameters before and after dobutamine stress testing**

Variable	Mean±SD (baseline)	Mean±SD (after DSE)	Percent change (%)	P value
S velocity (cm/s)	$12.9 \pm 2.9$	$19.7 \pm 5$	61.1	<0.001
TAPSE (mm)	$22.9 \pm 4$	$23.8 \pm 3.7$	6.4	0.026
RVOT Fractional shortening (%)	$62 \pm 12.8$	$72.8 \pm 11.9$	19.7	<0.001
RV strain in base segment (%)	$-17.7 \pm 7.9$	$-20.6 \pm 10$	27.3	0.136
RV strain in mid segment (%)	$-27.5 \pm 7.8$	$-27.6 \pm 6.9$	5.8	0.933
RV strain in apical segment (%)	$-22.9 \pm 10$	$-28 \pm 9.7$	21.9	0.001
RV strain rate in base segment (l/s)	$-1.43 \pm 0.68$	$-3.5 \pm 5.3$	201	0.019
RV strain rate in mid segment (l/s)	$-1.81 \pm 0.75$	$-3.2 \pm 1.1$	71	<0.001
RV strain rate in apical segment (l/s)	$-1.64 \pm 0.7$	$-2.8 \pm 0.87$	114	<0.001

### Discussion

Sutherland et al. in a review article<sup>11</sup> showed that radial SR/strain values were difficult to measure from the normal thin (<6mm) RV free wall, as the small computational distance, combined with near field imaging artifacts and only longitudinal maximal systolic velocities/SR/strain can be reliably derived

from the basal, mid, and apical segments of the RV free lateral wall. They showed<sup>11</sup> SR/strain profiles obtained were inhomogeneous. The mean values for SR/strain were lowest in the basal segments and increased toward the apex, that is, in contrast to regional peak velocities that decrease from base to apex.

In another study by Marwick et al.,<sup>12</sup> strain measurements of RV were higher than strain index measurements of LV and increased from base to apex. Weidmann et al.<sup>13</sup> found higher systolic strain and SR in the mid-wall segment of the RV. In our study, we showed that mean strain values were higher in the mid-wall segments and SR values were homogenous in all the RV segments. The fact that the RV sinus contributes most of the stroke volume<sup>14</sup> may explain the higher strain values in the RV sinus (mid-wall) segments; therefore, the measurement of RV strain in the mid-wall is better for evaluation in this part and lesser affected by annular movement compared to the RV basal parameters.

RVOT FS, TAPSE, and peak systolic velocity of the tricuspid annulus have been shown to be closely related to RV ejection fraction.<sup>4,5,16</sup> We have reported the mean value of TAPSE, S velocity, and RVOT FS in healthy individuals as 22.9mm, 12.9 cm/s, and 62%, respectively, which is in concordance with findings in earlier studies.<sup>16,17</sup>

Kjaergaard et al. showed little or no variation with age and sex in the estimates of RV function in healthy individuals.<sup>15</sup> In our study, there was a reverse correlation between age and TAPSE and also fractional shortening correlated with sex; and there was no significant correlation between age, sex, and other parameters of RV function.

After dobutamine stress echocardiography (DSE), there were significant increases in RVOT FS (19%), S velocity of TV annulus (61%), and TAPSE (6%). The least change was seen in TAPSE, which may be due to the decreased longitudinal TV annulus movement toward the apex in higher heart rates and more circumferential shortening.

The mean values of strain rate increased significantly in a homogenous pattern at all the segments, but the strain values increased only in the apical segment. Nevertheless, with more analysis using the ANOVA model, an overall increase in all the myocardial segments strain was significant.

Strain and SR response to DSE was relatively similar to the left ventricular response to DSE. In normal myocardium, increasing doses of dobutamine are associated with increasing SR throughout the study, but in contrast, myocardial strain initially increases and then decreases as heart rate increases.<sup>18</sup>

### Conclusion

This study showed significant increases in RV function parameters after dobutamine infusion, indicating significant RV reserve in normal right ventricular function. This may be helpful in the assessment of pathologic RV reserve in valvular and congenital heart disease.

### Conflict of Interest

No conflicts of interest have been claimed by the authors.

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## C - Reactive Protein and Coronary Calcium Score Association in Coronary Artery Disease

Ali Hosseinsabet, Bahram Mohebbi, Ahmad Mohebbi  
and Alireza Almasi

### Abstract

**Objectives-** Both high-sensitivity C-reactive protein (hs-CRP) and spiral computed tomography coronary artery calcium score are valid markers of cardiovascular risk. It is unknown whether hs-CRP is a marker of atherosclerotic burden or whether it reflects a process leading to acute coronary events.

**Methods-** We studied the association of high-sensitivity C-reactive protein and coronary calcium score in 143 patients that were candidates for coronary artery bypass graft surgery.

**Results-** In our cross sectional study we found no significant association between high-sensitivity C-reactive protein and coronary calcium score in bivariate ( $p=0.162$ ) and multivariable ( $p=0.062$ ) analysis, but in patients who did not use statins, this association was significant and positive in bivariate ( $p=0.001$ ) and in multivariate analysis this association was negative and significant ( $p=0.008$ ).

**Conclusion-** High-sensitivity C-reactive protein was not associated with coronary calcium score. The relation between C-reactive protein and clinical events might not be related to atherosclerotic burden. Measures of inflammation, such as C-reactive protein, and indices of atherosclerosis, such as coronary calcium score, are likely to provide distinct information regarding cardiovascular risk (*Iranian Heart Journal 2009; 10 (1):40-47*).

**Key words:** coronary calcification ■ C-reactive protein ■ inflammation ■ atherosclerosis ■ risk factors

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Much evidence exists to suggest that inflammation plays a major role in the development of atherosclerosis and its clinical manifestations.<sup>1,2</sup> In some studies, plasma levels of inflammatory markers, particularly C-reactive protein (CRP), predict myocardial infarction and cardiovascular death.<sup>3-8</sup> However, CRP is associated with many established risk factors, including dyslipidemia, cigarette smoking, hypertension, diabetes and obesity<sup>9-15</sup> and the relation between CRP and coronary artery disease (CAD) has been significant in some studies,<sup>16-18</sup> but in others it has not been significant<sup>17,19-27</sup> and has even been significantly negative in others.<sup>28,29</sup>

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Received April 2, 2007; Accepted for publication May 2, 2008.

From the Department of Cardiology, Shaheed Rajaie Cardiovascular Medical and Research Center, Tehran Iran.

Correspondence to: A. Mohebbi, MD, Department of Cardiology Shaheed Rajaie Cardiovascular Medical and Research Center, Tehran Iran.

Tel: + (9821) 23912580

The extent to which CRP levels predict clinical events depends on the relation of CRP to the burden of underlying atherosclerosis or the milieu leading to plaque rupture and thrombosis, and is unknown. Given that CRP levels predict clinical events, it is of substantial interest to dissect the pathophysiology of this relation. In contrast to clinical events, an independent association between CRP levels and coronary<sup>19-29</sup> or carotid<sup>27,30-36</sup> atherosclerosis has not been established clearly. Coronary artery calcification (CAC), measured by electron beam tomography (EBT) or spiral computed tomography, might be useful in identifying novel risk factors for coronary atherosclerosis in asymptomatic subjects.

The amount of CAC at EBT is correlated with the burden of atherosclerosis at both autopsy and coronary angiography,<sup>37,38</sup> and studies suggest that CAC is a predictor of clinical CAD events in both symptomatic<sup>39</sup> and asymptomatic<sup>40,41</sup> subjects. Studies of CAC might permit differentiation of factors associated with coronary atherosclerosis from those related to plaque rupture or thrombosis.

Studies of CRP and CAC in healthy subjects have produced conflicting results. While some studies have found no association between CRP and CAC,<sup>17-29</sup> others have reported a weak relation.<sup>16-18</sup> It is unclear whether these conflicting reports reflect the limitations of study design and analysis, or real differences in the pathophysiology of CAC, a measure of coronary atherosclerotic burden, and elevated CRP, a marker of inflammation.

Some support the concept that CAC scores and plasma CRP levels might provide independent and complementary information regarding the risk of cardiovascular events.<sup>22,42</sup>

## Methods

The study population comprised 143 patients with coronary artery disease admitted to our center, an academic tertiary referral center, from December 2006 to March 2007 for coronary artery bypass graft (CABG) surgery. When patients were admitted to our center for CABG, medical history and physical examination were completed and patients were excluded from study if they had a history of the following conditions:

- 1-myocardial infarction or unstable angina during the previous month,
- 2-aortic valve replacement or mitral valve replacement surgery,
- 3- CABG surgery or coronary stenting.

All study participants gave written informed consent. The protocol was approved by the Research Committee of the Iran University of Medical Sciences, Tehran. Age, cardiac risk factors including hypertension, dyslipidemia, diabetes mellitus, family history of coronary disease, smoking status, and drug history were determined by interview (self-reported), and body mass index (BMI) by examination. Blood sampling was done for lipid profile, creatinine<sup>44-46</sup> and hs-CRP and frozen at -70° C for four months. Hs-CRP measurement was done by commercial kits (Pars Azmun Co.), by latex immunoturbid assay and by a single laboratory technician blinded to all clinical and radiologic data. Routine lab data included lipid profile and creatinine, and coronary calcium scoring was done by 10-slice spiral CT scan (Siemens Somatom Sensation 10). Calcium score of the coronary arteries was expressed according to Agston et al.,<sup>43</sup> as previously explained. A total CAC score was determined from the sum of individual scores of the 4 major epicardial coronary arteries. All scans were interpreted by a single radiologist blinded to all clinical and serologic data.

Data were analyzed by SPSS 15 software and reported as mean  $\pm$  SD if they were continuous and as proportions if they were categorical.

Because some variables did not have normal distribution, we transformed them to logarithmic for normalization of data and because some patients had CCS=0, log (CCS+1) was substituted.

Firstly, we assessed the association between coronary calcium score [log CCS+1] and log (hs-CRP) overall by Pearson correlation coefficient, and then in the presence of any risk factors and any drug use in both sexes by this method.

Because almost all patients used aspirin and beta- blockers, and a negligible percents of patients used calcium channel blockers or gemfibrozil, we did not include them in our analysis. Secondly, we assessed this correlation by multivariable linear regression (enter mode) overall and then according to statins use.

We entered age, BMI, drug history, all risk factors and lipid profile and creatinine in the multivariate analysis.

**Results**

Table I shows demographic characteristics, CRP levels, and CCS scores in the sample (n=143). Bivariant analysis of CRP and CCS in all patients and subgroups is presented in Table II.

**Table I. Characteristics of the study sample.**

<b>Age, years</b>	57.7± 9.4
<50	18.2
50-59	39.2
60-69	30.8
>70	11.9
<b>BMI, kg/m2</b>	27.2± 3.5
<24.99	29.4
25-29.99	49
>30	21.6
<b>Tg, mg/dl</b>	153.6± 78.2
<b>Cholesterol, mg/dl</b>	171.4± 48.8
<b>LDL, mg/dl</b>	94.0 ±31.4
<b>HDL, mg/dl</b>	41.0± 37.9
<b>CR, mg/dl</b>	1.37± 0.95
<b>hs-CRP, mg/dl</b>	2.89± 3.43
<b>CCS</b>	366.4± 586.7
<b>Male</b>	74.1
<b>HTN</b>	32.2
<b>DLP</b>	45.5
<b>DM</b>	32.9
<b>C/S</b>	35
<b>FH</b>	14
<b>ACEI/ARB</b>	51.7
<b>Statins</b>	62.2

Values are mean±SD, or percent. BMI=body mass index, Tg=triglyceride, LDL=low density lipoprotein, HDL= high density lipoprotein, CR=creatinine, hs-CRP=high sensitivity CRP, CCS=coronary calcium score, HTN=hypertension, DLP=dyslipidemia, DM=diabetes mellitus, C/S=cigarette smoking, FH=family history of coronary artery disease, ACEI/ARB=angiotensin converting enzyme inhibitor/ angiotensin receptor blocker

This correlation was not significant overall (r=-0.118, P=0.162), and was significant in 60-69 year-old patients (r =0.327, P=0.031) and in patients who did not use statins (r=0.442, P=0.001), this correlation was moderate and significant. In other subgroups this correlation was not significant. Table III shows factors which were associated with CCS, when C - reactive protein is not included in a fully adjusted multivariable linear regression. Age, male sex and family history of coronary artery disease were positive predictors of CCS.

**Table II. Correlation of log (hs-CRP) and log (CCS+1) in all cases and subgroups.**

\* (+) is presence of the condition and (-) is absence of the condition.

GROUP	R		P
MALE	0.122		0.213
FEMALE	0.037		0.828
HTN (+)	0.144		0.339
HTN (-)	0.118		0.248
	B	SD	P
(Constant)	1.173	1.323	0.427
DM (+)	0.176		0.236
DM (-)	0.034	0.096	0.008
SEX (+)	0.101		0.673
SEX (-)	-0.409	0.191	0.033
FH (+)	0.101		0.267
FH (-)	0.304	0.144	0.177
C/S (+)	0.110		0.988
C/S (-)	0.019	0.163	0.980
ACEI/ARB (+)	0.091		0.442
ACEI/ARB (-)	0.121	0.165	0.287
STATIN (+)	0.470	0.212	0.028
STATIN (-)	0.442		0.001
Age <50	0.058	0.172	0.934
ACEI/ARB 60-69	-0.069	0.153	0.630
ACEI/ARB 60-69	0.327		0.031
STATIN >70	-0.146	0.157	0.195
BMI <24.99	0.000	0.003	0.558
BMI 25-29.99	0.080		0.632
LogHDL >30	0.138	0.184	0.355
LogHDL >30	0.323		0.081
LogTG	0.182	0.159	0.257
ALL CASES	-0.18		0.162
LogCRP	-0.134	0.252	0.598
BMI	-0.014	0.021	0.514

**Table III. Multivariate analysis of factors associated with coronary calcium score when C-reactive protein is not included in the analysis.**

\*Results of linear regression (log of (CCS+1) as the dependent variable) are presented when CRP is not included in analysis, as the change log(CCS+1) for a specific change in risk factor. Models were adjusted for the following variables; age, sex, history of hypertension, history of dyslipidemia, diabetes mellitus, family history of coronary artery disease, smoking, use of the following medications: statins, ACEI/ARB ,LDL[log LDL] ,HDL[logHDL], TG[logTG] ,CR[logCR], body mass index.

Factors which were associated with CCS, when C - reactive protein is included in the fully adjusted multivariate linear regression are shown in Table IV. Age was the only predictor of CCS in the presence of CRP, and sex and family history of coronary artery disease were not predictors of CCS after adjustment for CRP level.

**Table IV. Multivariable analysis of factors associated with coronary calcium score when C- reactive protein is included in the analysis.**

	B	SD	P
(Constant)	1.046	1.312	0.427
AGE	0.037	0.008	0.000
SEX	-0.343	0.193	0.078
HTN	0.293	0.176	0.099
DLP	-0.005	0.161	0.977
DM	0.141	0.164	0.392
FH	0.395	0.213	0.067
C/S	0.068	0.170	0.688
ACEI/ARB	-0.032	0.153	0.834
STATIN	-0.204	0.158	0.200
LDL	0.001	0.003	0.657
LogHDL	0.089	0.184	0.630
LogTG	-0.169	0.158	0.288
LogCRP	-0.063	0.253	0.802
BMI	-0.013	0.021	0.542
LogCRP	-0.115	0.061	0.062

\*Results of linear regression (log of (CCS+1) as the dependent variable) are presented when CRP is included in analysis as the change log(CCS+1) for a specific change in risk factor. Models were adjusted for the following variables; age, sex, history of hypertension, history of dyslipidemia, diabetes mellitus, family history of coronary artery disease, smoking, use of the following medications: statins, ACEI/ARB ,LDL[log LDL] ,HDL[logHDL] TG[logTG] ,CR[logCR], body mass index and CRP [logCRP].

Because in bivariate analysis the association of log (CRP) and log (CCS+1) was significant in patients who did not use statins, we analyzed this association in patients in fully adjusted, multivariate linear regression. Table V shows this analysis. Male sex and family history of coronary artery disease are positive predictors of CCS, and CRP was negative predictor of CCS (P=0.008) in patients who did not use statins.

**Table V. Multivariable analysis of factors associated with coronary calcium score and C - reactive protein in patients not using statins.**

	B	SD	P
(Constant)	3.774	1.682	0.031
AGE	0.021	0.012	0.088
SEX	-0.653	0.262	0.017
HTN	0.318	0.259	0.227
DLP	0.086	0.243	0.724
DM	0.250	0.226	0.276
FH	0.682	0.318	0.038

C/S	-0.346	0.275	0.215
ACEI/ARB	0.191	0.231	0.414
LDL	0.004	0.004	0.294
LogHDL	0.188	0.219	0.396
LogTG	-0.261	0.241	0.285
LogCR	-0.531	0.292	0.077
BMI	-0.068	0.037	0.077
LogCRP	-0.278	0.100	0.008

\*Results of linear regression (log of (CCS+1) as the dependent variable) are presented in patients that not use statin, as the change log (CCS+1) for a specific change in risk factor. Models were adjusted for the following variables; age, sex, history of hypertension, history of dyslipidemia, diabetes mellitus, family history of coronary artery disease, smoking, use of the following medications: statins, ACEI/ARB ,LDL[log LDL] ,HDL[logHDL] ,TG[logTG] ,CR[logCR] , body mass index and CRP [logCRP]

## Discussion

CCS measured at spiral CT might be useful for identifying novel risk factors and exploring the relation of risk factors with coronary atherosclerosis. We have examined the association between plasma CRP and CCS in patients who were candidates for CABG. In previous studies, subjects of the study were suspected to have coronary artery disease without any documentation as proof, but in our study we selected patients who had coronary artery disease documented and confirmed by selective coronary artery angiography. We found no evidence of a positive association between hs-CRP and calcium scores. Indeed, if anything, these data suggest an inverse relationship between hs-CRP levels and coronary calcium in patients who did not use statins.

Nonetheless, we believe the lack of a positive association between hs-CRP and coronary calcium score deserves careful consideration. The lack of correlation in the current data between spiral CT score and hs-CRP suggests that calcification may be less likely to reflect inflammation per se; spiral CT-detected calcification may predominantly be a marker for mature and hence stable atherosclerotic plaque, and thus only be an indirect marker for the presence of uncalcified rupture-prone lesions, which may be more likely markers for future cardiac events, but a correlation between soft, noncalcified plaque was not confirmed.<sup>24</sup> Deposition of calcium in atherosclerotic lesions has been shown to be an active process analogous to the formation of bone spicules.<sup>47</sup> Furthermore, it appears to involve cells of special embryonic lineage.

Thus, coronary calcification may not merely be a direct consequence of atherogenesis but rather may depend upon the presence of specific determinants independent of the central processes involved in plaque formation. The reasons for the lack of association between CRP and CCS, in contrast to a more consistent association between CRP and clinical events, are unclear. However, this finding supports the concept that CRP levels might not be related to atherosclerosis per se, distinct from being a marker of plaque rupture and thrombosis. Therefore, CRP might not be useful in identifying the underlying mechanisms of atherosclerosis initiation or progression. The present findings suggest that the relationship between higher CRP levels and incident cardiovascular events may reflect the composition, morphology, and stability of plaque rather than overall atherosclerotic burden.<sup>48</sup> Because CCS are associated with risk for subsequent cardiovascular events and provide a measure of disease processes distinct from CRP, these two measures may be complementary rather than competitive for risk prediction.<sup>42</sup>

This study, demonstrating that hs-CRP is unrelated to the presence and severity of clinical calcified atherosclerosis, suggests that serologic inflammatory markers are principally a measure of the athero-inflammatory disease process and are not an index of the extent of coronary atherosclerotic plaque. The independent prognostic utility of quantifying calcified atherosclerosis and systemic inflammation suggests that disease and process markers of atherosclerosis may be complementary tools in coronary heart disease prediction.

We used a validated commercial assay for the measurement of hs-CRP, but variability in commercial assays may limit the validity of these data. We used CCS as a surrogate for coronary atherosclerotic plaque burden on the basis of the well-established relationship between CCS and the extent of histologic plaque.<sup>37</sup> However, atherosclerosis in vascular beds other than the coronary arteries could also contribute to the level of hs-CRP.<sup>49</sup>

## Funding Sources

*This research was done with financial support from Iran University of Medical Sciences.*

## Conflict of Interest

No conflicts of interest have been claimed by the authors.

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## Effect of Periodontal Diseases on Plasma Level of LDL, HDL and Total Cholesterol in Rats

Hamidreza Rashidinejad MD, Houman Mehrizi DDS, Amin Arsalan DDS,  
Mohammad Reza Rahmani MS and Jafar Ahmadi MD

### Abstract

**Introduction-** Cardiovascular diseases (CVD) are known as the major life-threatening factors and the most common causes of mortality around the world, especially in developed countries. Many risk factors for CVD are well known, like dyslipidemia, diabetes mellitus, cigarette smoking, hypertension, positive family history, and aging. However, there is evidence recently showing a relation between periodontal diseases (PD) and increased risk of CVD. The basis of this study was to determine any relation between PD and serum levels of total cholesterol, LDL, and HDL so as to investigate whether periodontal disease can facilitate coronary atherosclerosis due to dyslipidemia.

**Methods-** In this experimental study, 20 healthy male rats weighing 200 – 250 grams were divided into case and control groups. In the case group (10 rats), we injected 0.6 ml of complete Freund's adjuvant in the mid-buccal area of both upper and lower jaws; and a sample of blood was taken from all 20 rats to measure the LDL, HDL, and cholesterol. After two weeks, the injection was repeated in the same areas with the same amount of drug; and at the end of the 4<sup>th</sup> week, blood sampling was repeated in both groups. The inflammation in the case group was confirmed with direct clinical observation and based on histological study at the end of the 4<sup>th</sup> week. Finally, the serum levels of LDL, HDL, and total cholesterol were compared between the two groups using the independent samples t-test.

**Results-** The statistical tests did not show any significant difference between the two groups. Also, we found no significant difference between the lab test values before and after the study procedure.

**Conclusion-** There was no certain relation between PD and cardiovascular diseases, except for their common risk factors. However, if any relation exists, it might be due to a mechanism other than the serum cholesterol level (*Iranian Heart Journal* 2009; 10 (1):48-51).

**Key words:** cardiovascular disease ■ periodontal disease ■ total cholesterol ■ LDL ■ HDL

which is related to the local collection of lipids. High amounts of serum LDL will lead to an increased accumulation of LDL in the AP and can result in coronary vascular accidents.

**T**he major pathology of coronary artery disease (CAD) is atherosclerotic plaque (AP) formation,

health. All the rats were kept in similar environmental

Received Aug. 12, 2007; Accepted for publication Sept. 2, 2008.

From the Dept. of Cardiology , Afzalipour Hospital, Kerman University of Medical Sciences, Kerman Iran.

Address for Correspondence: H. R. Radhidinejad MD, Assistant Professor of Cardiology, Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran.

Tel: 0341-3222762

The importance of dyslipidemia and especially high levels of LDL in AP formation is clearly defined; and other factors such as cigarette smoking, arterial hypertension, diabetes mellitus, positive family history, and aging are also the main risk factors of atherosclerosis.<sup>1</sup>

The relation between inflammation and atherosclerosis and cardiovascular diseases (CVDs) has been proven<sup>2,3</sup> and some evidence recently depicts a role for oral infections in atherosclerosis.<sup>4</sup> It seems that a probable mechanism via inflammatory mediators and increase in WBC and platelet count accelerates the process of AP formation.<sup>5,6</sup>

Periodontitis is a bacterial infection classified as a chronic local infection and caused by anaerobic gram negative microorganisms originating from dental plaque, which leads to inflammation due to entering lipo-polysaccharides and other microbial components into the gums.<sup>7,8</sup> The pathogenesis of inflammation in gums is the increase of pre-inflammatory cytokines, resulting in the damage of the periodontal ligaments and alveolar bone.<sup>8</sup> Many CAD risk factors are assumed as risk factors for periodontal diseases (PD) as well; in other words, there might be many common risk factors for PD and cardiovascular diseases.<sup>5,8</sup> Hypercholesterolemia, especially increased LDL, is determined as a main risk factor for atherosclerosis; instead increased HDL cholesterol is related with a decreased risk of CAD.<sup>8,10</sup>

A relation between periodontitis and hyperlipidemia has been shown in some animal laboratory studies,<sup>11</sup> and some human studies have shown that the periodontal state is worse in patients with hypercholesterolemia and CVDs<sup>8</sup> and the amount of periodontal damage is related to the serum cholesterol level.<sup>12</sup>

There are still controversies about the relation between PD and CVDs in certain studies, and researchers have mentioned a need for more experimental results to clarify the exact relationship between these factors.<sup>13</sup>

The main aim of this study was to assess the effect of PD on serum levels of total cholesterol, LDL, HDL, and dyslipidemia in rats.

**Methods**

In this experimental case-control study, we entered 20 healthy male rats weighing between 200 – 250 grams after an initial clinical examination by a periodontist and a physiologist to confirm their periodontal

conditions (daylight, temperature) during the study period and had free access to a single kind of food.

First, we randomly divided the rats into two groups and took a blood sample from their periorbital vessels using hematocrit glass pipes. Then, the serum was separated with a centrifuge and after coding, the samples were sent to a lab. All the rats were identified with color marks on their bodies and codes of their blood samples. On the same day, we injected 0.06cc of complete Freund’s adjuvant, a drug proven to cause chronic inflammation, into the midbuccal area of the upper and lower jaws of the rats in the case group. In the control group, we did not perform any injection. During the study, we induced general anesthesia in all the rats in a closed glass container with ether-inoculated cotton. Ethical considerations in working with animals were observed at all times.

After the procedures, the rats were moved to animal rooms in the laboratory; and after 14 days, we repeated the injection in the same regions with the same amount of drug. On the 28<sup>th</sup> day, blood sampling was done; and the serum levels of LDL, HDL, and total cholesterol were measured with an auto-analyzer.

To compare the mean of variables, the paired samples t-test and independent samples t-test at the 0.05 significance level were performed using SPSS® for Windows software.

The existence of inflammation in the case group was determined by direct clinical observation during the study period and confirmed in a microscopic examination of the histologic samples by a pathologist.

**Results**

In the case group (10 rats), the means of serum total cholesterol, LDL, and HDL levels were not significantly different from those in the control group in the first day of the study (Table I).

**Table I. Comparison of the means of total cholesterol, LDL and HDL in rats of case and control groups.**

Variable	Group	Before (1 <sup>st</sup> Day)		After (28 <sup>th</sup> Day)		P Value **
		Mean±SD	P Value *	Mean±SD	P Value *	
Cholesterol	Case	98.25±4.99	NS	78.11±10.2	NS	NS
	Control	98.40±4.31		71.62±8.78		
LDL	Case	49.80±4.20	NS	42.00±6.98	NS	NS
	Control	48.20±1.44		37.87±4.58		

HDL	Case Control	41.80±1.72 43.00±1.24	NS	33.33±3.31 32.00±4.44	NS	NS
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\* Independent Samples t-test for equality of means in two groups

\*\* Paired Samples t-test for equality of means before and after

One rat in the case group and two in the control group died during the study. There was no significant difference between the case and control groups at the end of the 28<sup>th</sup> day according to the independent samples t-test.

The Kolmogorov-Smirnov test was performed first and showed that the variables were normally distributed. Because of losing 3 rats, we controlled the loss bias with a sensitivity analysis method.

### Discussion

The results of the current study are similar to those in previous studies in some aspects, although due to a lack of a specifically similar study we could not compare all the results together. Because of ethical limitations, many studies on humans are cross-sectional and the researchers cannot induce PD; therefore, assessing the association between CVDs and PD is not clearly applicable. Consequently, an assessment of the coexistence of PD with CVDs or some predisposing factors of CVDs has been considered in several studies (Losche et al. 2000; Emingil et al. 2000; Katz et al. 2001; Katz et al. 2002; Ancabazile et al. 2002; Jeffrey et al. 2002; Scott et al. 2002 and Lopez et al. 2002<sup>14-18</sup>). The coexistence of the two diseases has been noted apart from other risk factors,<sup>1,7,8,19-22</sup> and in other studies, no evidence has emerged to define a relation between them.<sup>23,24</sup> Also, in certain studies, the researchers have evaluated the relation of the two diseases without considering the common risk factors like cigarette smoking.<sup>23,24</sup>

The results of the current study cannot precisely define a coexistence and relation between PD and plasma lipid levels. Also, there is no evidence in favor of a cause-and-effect relationship between the two phenomena. In fact, our results support studies which question the relation between PD and cardiovascular problems, apart from other risk factors.

Based on our present knowledge and the results, a lack of a proven cause-and-effect relationship between PD and plasma lipid levels can lead to two conclusions. Either there is no relation between PD and CVD and previous studies might have methodological errors or biased positive results; or the physiological mechanism in cardiovascular problems related with PD is not due to the effect of PD on plasma lipids (especially cholesterol, LDL, and HDL levels).

### Conflict of Interest

No conflicts of interest have been claimed by the authors.

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# *Case Reports*

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## **Multiple Coronary Aneurysms**

M.M. Peighambari MD, H.R. Sanati MD and L. Zahedi MD

### **Abstract**

Coronary artery aneurysm is a relatively infrequent abnormality but its diagnosis has been increased after the advent of coronary angiography. Atherosclerosis accounts for the majority of cases of coronary aneurysms. Other etiologies include congenital aneurysms, dissection, infection, vasculitis, and some other inflammatory conditions. We describe a 41-year-old woman who presented with typical chest pain and dyspnea and had multiple small and large coronary aneurysms associated with stenotic segments (*Iranian Heart Journal 2009; 10 (1):52-54*).

**Key words:** coronary artery aneurysm ■ Kawasaki disease

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**Case report**

The patient was a 41-year-old female referred to our hospital with exertional chest pain and dyspnea. A review of her past medical history did not demonstrate any risk factor for coronary artery disease.

On physical examination, the only positive finding was S4, heard on the apical zone of the chest wall. At presentation, she had normal stable blood pressure, heart rate, temperature, and respiratory rate. Laboratory data showed normal complete blood counts, as well as renal and liver function tests. An electrocardiogram did not show any important abnormality other than nonspecific ST-segment changes in leads V3 to V6. Transthoracic echocardiography showed systolic dysfunction with an EF of 35 to 40%, mild MR, mild TR, mild PI, high normal pulmonary artery pressure, grade I diastolic dysfunction, and regional wall motion abnormalities in multiple segments. Transesophageal echocardiography demonstrated a huge LCX aneurysm with mural thrombosis (Fig.1).

**Fig. 1.** Transesophageal echocardiography showing a huge LCX aneurysm with mural thrombosis

Myocardial perfusion imaging revealed anteroseptal and inferolateral ischemia. Based on these findings, she was candidate for coronary angiography, which showed severely tortuous coronary arteries with multiple small and large aneurysms and

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Received April 23, 2007; Accepted for publication May 2, 2008.

From the Department of Cardiology, Shaheed Rajaei Cardiovascular Medical and Research Center, Tehran, Iran.

Correspondence to: HR. Sanati MD, Department of Cardiology, Shaheed Rajaie Cardiovascular Medical and Research Center, Tehran, Iran.

Tel: 23922580

## **Atrial Septal Aneurysm Concomitant with Severe Mitral Stenosis**

Saeed Hosseini MD, Mehdy Hadadzadeh MD, Alireza Alizadeh Ghavidel MD,  
Rostam Esfandiari MD

### **Abstract**

An atrial septal aneurysm is an uncommon abnormality and may be the origin of thromboembolic events. We would like to present an unusual case of the septal abnormality with mitral stenosis and history of thrombo-embolic cerebrovascular accident (*Iranian Heart Journal 2009; 10 (1):55-57*).

**Key words:** atrial septal aneurysm ■ cerebrovascular accident

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Atrial septal aneurysm (ASA) is a rare but well-recognized cardiac abnormality of uncertain clinical significance.<sup>1-6</sup> ASA has been reported as an unexpected finding during autopsy<sup>1</sup> but may also be diagnosed in living patients by echocardiographic techniques.<sup>2</sup> ASA formation can be secondary to interatrial pressure differences but may also be a primary malformation involving the region of the fossa ovalis or the entire septum. ASA may be an isolated abnormality but is often found in association with other structural cardiac abnormalities, e.g., mitral valve prolapse<sup>7,8</sup> or atrial septal defects.<sup>9</sup>

Several reports suggest a possible link between ASA and cardiogenic embolism in patients with otherwise unexplained ischemic stroke. We present an uncommon association of ASA with severe mitral stenosis (MS) and stroke.

## Case report

A 44 year-old lady presented with shortness of breath for 3months.

Received May 8, 2008; Accepted for publication Aug. 21, 2008.

From the Dept. of Cardiovascular Surgery and Cardiology, Shaheed Rajaee Cardiovascular Medical Center, Mellat Park, Vali Asr Ave. Tehran, Iran; Correspondence to: S. Hosseini, MD, Dept. of Cardiovascular Surgery, Shaheed Rajaee Cardiovascular Medical Center, Mellat Park, Vali Asr Ave. Tehran, Iran.  
Tel : +982123922589

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until 2 years ago, when a thromboembolic cerebrovascular accident (CVA) occurred. Her past medical history was negative for other medical diseases.

Her vital signs were HR: 102/min. irregular, BP: 100/60 mm Hg, RR: 16/min. The positive findings in physical examination included an opening snap, mid-diastolic decrescendo murmur, S3 and right arm plegia grade 3. Preoperative laboratory values were within normal limits and the electrocardiogram showed atrial fibrillation (AF). No abnormality was found in chest X-ray. Transthoracic and transesophageal echocardiographies (TTE and TEE) revealed severe mitral stenosis (MS) with an estimated valve area of 0.9 cm<sup>2</sup> and some degrees of leaflet and annular calcification (echocardiographic score: 8-9). The left atrium (LA) was moderately enlarged (5 x 4.5 cm). In addition, the 2-D echocardiographic windows showed a large atrial septum aneurysm (29 x 26 mm) without any septal defect (Fig.1).



**Fig. 1.** Pre-operative transesophageal echocardiographic view.

During the diastolic phase the aneurysm bulged into the right atrium. No other pathology in the other heart valves or chambers was revealed. Estimated left ventricular ejection fraction was 45%, pulmonary artery pressure was 40mmHg and right ventricle function was reported as being within normal range. Selective coronary angiography showed normal coronary arteries.

## Surgical Technique

Under general anesthesia, a standard median sternotomy was done and the pericardium was opened. After heparin infusion (3mg/kg), ascending aorta and bicaval cannulation was performed. After establishment of total cardiopulmonary bypass under normothermia, cardiac arrest was induced using antegrade and retrograde blood cardioplegia. Left and right atriotomies were done and the mitral valve, atrial chambers and septum were evaluated precisely. The mitral valve was involved with a rheumatic process and the thickened, calcified and destroyed mitral leaflets precluded the possibility of mitral repair. The atrial septum was aneurysmal and protruded into the right atrium. The base of the aneurysm was 25mm. After excision of both mitral

leaflets, a 29mm mechanical prosthesis was inserted using interrupted sutures. After excision of septal tissue involved with aneurysm, the resultant defect (30 x 30mm) was repaired with a fresh non-treated autologous pericardial patch using running 4-0 polypropylene sutures. The heart chambers were de-aired and atriotomy incisions repaired. The patient was weaned from CPB without inotropic support.

After hemostasis and leaving two drains in the mediastinal cavity and pericardial sac, the sternum was closed. The patient was extubated eight hours after arrival in the ICU. She made an uneventful recovery thereafter and hospital stay was 8 days. The function of the mitral prosthesis was normal on post-operative echocardiography and there was no residual ASD. Trans-mitral mean gradient was 2mmHg and LVEF was estimated at 45%.



**Fig. 2.** Surgical view of the IAS aneurysm.

### Discussion

Since the first report by Gallet et al.<sup>5</sup> in 1985, several echocardiographic studies have suggested that an ASA may behave as a possible cardioembolic source leading to ischemic stroke, particularly when it is associated with a patent foramen ovale (PFO).<sup>6-10</sup> ASA is an uncommon lesion, with a prevalence of 0.22% in a large prospective study with TTE<sup>6</sup>, 3%–8% in studies with TEE<sup>8,10</sup> and 1% in autopsies.<sup>12</sup> ASA is often associated with other cardiac abnormalities, including PFO, mitral valve prolapse, and atrial septal defect.<sup>9</sup> Because an interatrial shunt, such as a small ASD or a PFO, has been noted in 54%–85% of patients with ASA,<sup>9,10</sup> paradoxical embolism may be one potential mechanism related to stroke. Another possible mechanism is that an ASA itself may be thrombogenic because a thrombus within the ASA has occasionally been visualized by TEE.<sup>8,9</sup> As mentioned above, ASA is often associated with PFO and mitral valve prolapsed, but in the present case it was accompanied with severe MS. So the history of CVA in our patient may be related to AF cardiac rhythm and underlying MS and not necessarily to the septal aneurysm.

In conclusion, the ASA is not a rare abnormality and we should keep it in mind in every patient with an embolic event with unknown origin. The surgical indication of ASA depends on the concomitant abnormality or pathology.

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