In the name of God

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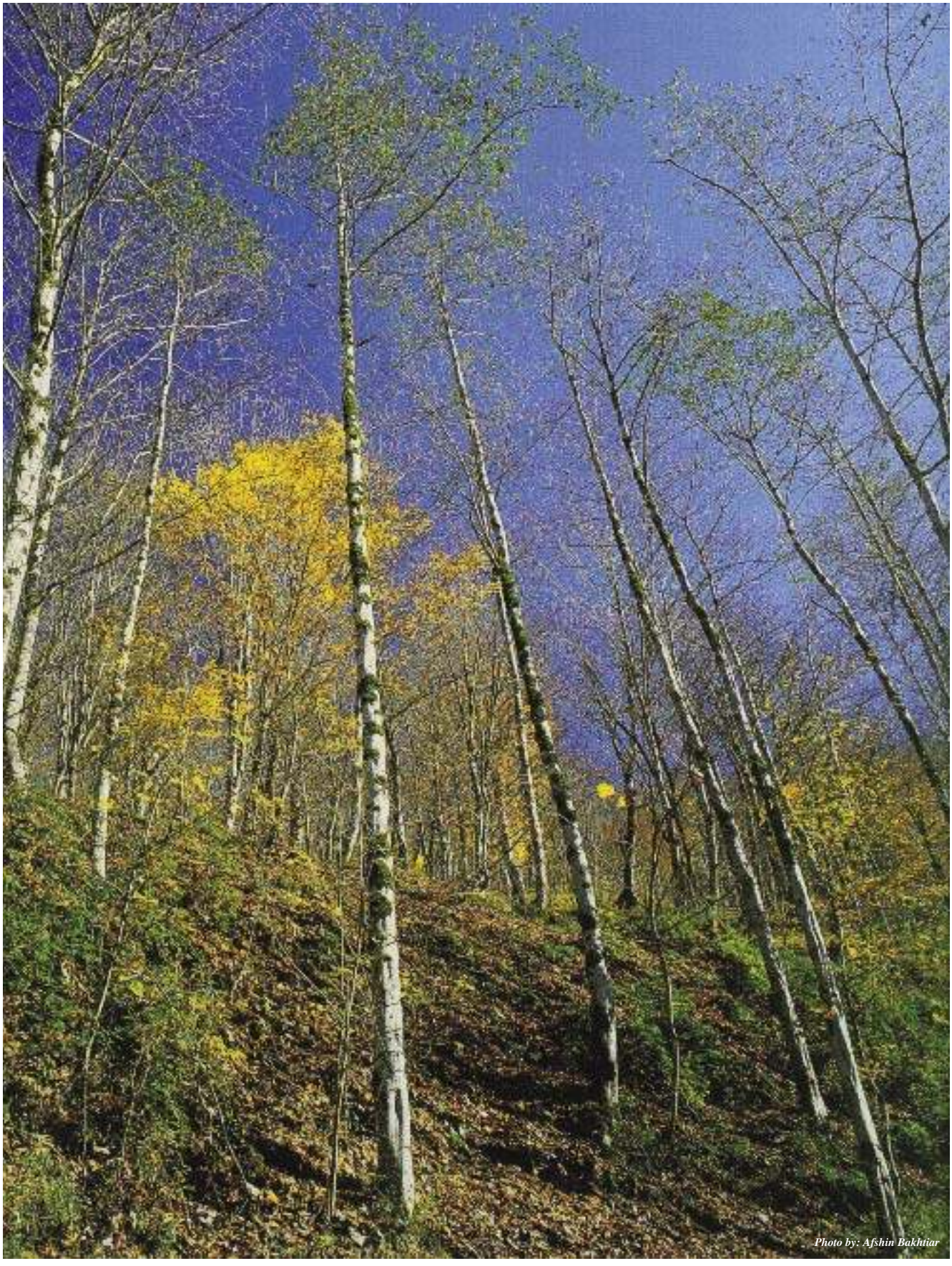

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Editorial

An Insight into Laser Revascularization of the Heart

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The notion to revascularize the ischemic myocardium from left ventricular cavity is not a new concept. The possibility was first proposed by Wearn in 1933.1

The work by mechanical means was followed by Walter, Massimo and later on by Sen.2-5 The fundamental concept was based on two factors; first a reptilian heart model and second the heart muscle structure which possesses a spongy character, en-meshed by sinusoids bathing the myocytes.

The Vineberg operation6 consisted of the insertion of a mammary artery into the heart muscle to establish a connection between the small capillaries (angiogenesis) and heart circulation in hopes of alleviating angina in ischemic heart disease.

In reptile hearts, the coronary arteries play a minor role in the perfusion of myocardium. Their circulation is supplied by canals from left and right ventricular cavities. So, ligation of coronary branches does not produce myocardial infraction (Figure 1-3).

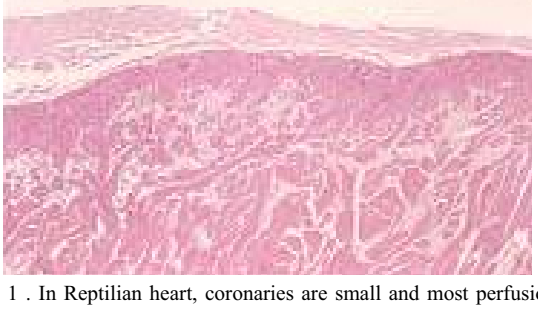

Figure 1 . In Reptilian heart, coronaries are small and most perfusions of the heart muscle is by way of channels directly from the ventricular cavity (Histology of snake heart muscle).

Figure 2. Schematic drawing of Reptile heart with channels from ventricular cavity and small size of coronaries

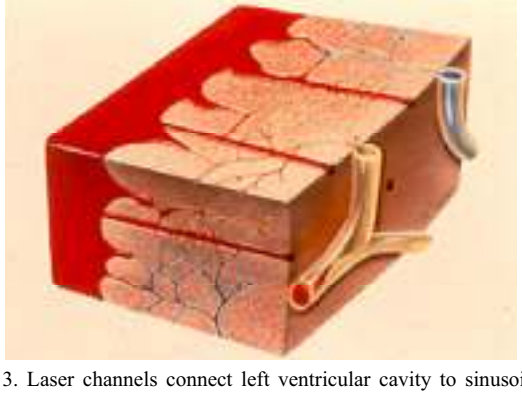

Figure 3. Laser channels connect left ventricular cavity to sinusoids and perfuse the myocardium (A schematic drawing)

The mechanical recanalization had a serious drawback. These channels were closed due to initial trauma, causing inflammatory reaction cell infiltration, fibrosis and eventual closure of the channels.

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The discovery of laser (light Amplification by Stimulated Emission of Radiation) in early 1960 by Nobel Laureate, Dr Theodor Maimon inspired our team to examine the hypothesis of recanalizing the ischemic myocardium with CO2 laser7,8 (Figure 4).

Figure 4. Nobel Prize winner and inventor of laser Dr. T. Maimon

Our primary reason for selecting this wave length (10.6 micron) was because its excellent absorption by the water content of myocardium (80% of myocardium is water by weight). We were also encouraged because CO2 laser could be made to deliver pulses of short duration in order of milli seconds and of very high energy density.

Since the thermal relaxation time of myocardium is about 30 milli seconds and pulses of this order can be made, the thermal injury was very minimal and almost non existent (Mass conversion to energy photons and water vapor) ($E=mc^2$).

Consequently the channels would stay open and perfuse the myocardium.

This high powerful laser was loaned to us by scientist Dr. Polayni from the American optical company Boston. Mass. USA9,10 (Figure 5).

Figure 5. Original CO2 laser for TMLR puts approximately two million watts continuous wave, triggered electronically by P-R interval of ECG, with milliseconds Pulse duration (1970)

This laser with short pulse duration could produce channels in myocardium clean and without thermal injury (Figure 6).

Figure 6. Thermal injury to myocardium was very small (less than one layer of cell)

With the help of my wife Mary Cayton, we worked in the laboratory (VA Center, Medical College of Wisconsin Milwaukee. Wis. USA), at nights, weekends and on holidays for over 24 years.11-15

The expenses were paid by my own practice of cardiovascular surgery and some by the philanthropic foundation of St. Lukes Medical Center Milwaukee, USA.

The theory was proven to be correct and we published our work in 1970 in the Journal of Micro Surgery. This was a carefully randomized study on animals. The patency of the channels and their protection of ischemic myocardium were demonstrated in these animals after ligation of a major coronary artery.

As a matter of fact, we had one animal (a dog) in which all coronaries were ligated and she was lived for 2 years, kept in a kennel in rural area of Wisconsin.

Unfortunately, she died by being hit by a truck while chasing the vehicle. Since bringing this large laser equipment to an operating room for clinical trial was impossible, we designed a smaller co2 laser and experimented on cold cardioplegic heart.

Patency of these canals was also proven before clinical trail was allowed by Institutional Review Board Committee of St lukes medical center.

The initial trial was on 12 patients in combination with CABG.

The laser channels were made in areas that bypass was not possible, either due to total occlusion of the vessel or severe diffuse disease of the coronary.

Ischemic area was demonstrated prior to surgery by nuclear scan. Channels were made (one channel per each square centimeter). One of the pioneering patients expired 5 years later due to metastatic cancer of the Lung.

Patency of laser channels were demonstrated by tissue microscopy. These channels were covered by endothelium which proved to be true endothelium by DNA immunoperoxidose studies (Figure 7).

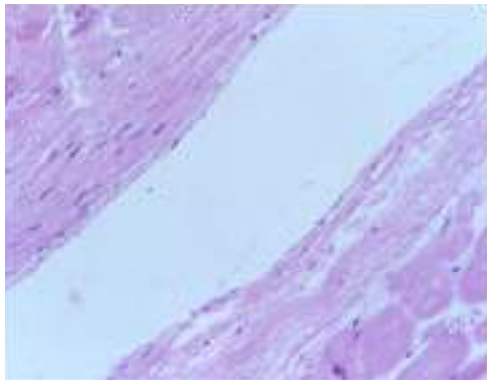

Figure 7. Patency of laser channels is demonstrated 51/2 years post of (autopsy specimen). The channels are covered by true Endothelium as proven by DNA immuno peroxides studies.

In some cases, ventricologram showed patency of the channels (Figure 8).

The work was published in Annals of Thoracic Surgery in 1984, and later on in Journal of clinical laser medicine and surgery. Our laser laboratory noted that the laser pulse could produce arrhythmias (ventricular tachycardia and ventricular fibrillation) if pulse hits at ST segment of ECG in animals.

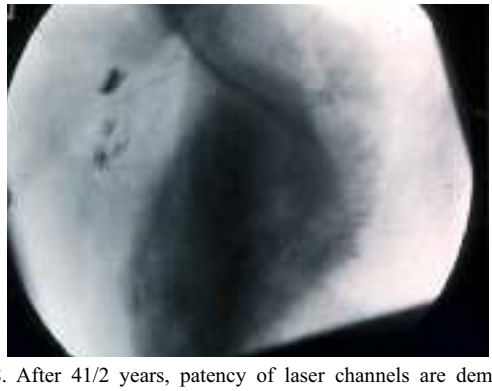

Figure 8. After 41/2 years, patency of laser channels are demonstrated by special technique of ventriculography during systole and diastole (Appreciation to General Electric Co. Milwaukee, U.S.A)

Therefore we synchronized the laser pulse at P-R intervals so the pulse would arrive at up stroke of R Wave.

This has two major advantages: 1. Prevents arrhythmias and 2. Laser arrives during diastole of cardiac cycle and the energy is quickly absorbed by the water content of blood; therefore it does not travel to the other side nor does it damage the interior of the left ventricular valves and cardio tendonae.

During the last several years, numerous articles and even book chapters have been published presenting various techniques such as percutaneous, per catheter- by endoscopic and electromechanical imaging. Also different lasers and different wave lengths have been applied.

The TMLR (Trans–Myocardial Laser Revascularization) has been in the Armamentarium of the surgeon.

The alleviation of angina in end-stage coronary artery disease is proven.

Randomized multicenter studies conducted under auspices of FDA proved that this technique is superior to medical treatment in this group of patients. It relieves and drops angina class from class 4 or class 3 at least two classes and quality of life is also improved.16

The technique is used either as sole therapy or combined procedure with coronary bypass surgery.

One should keep in mind that the commercial lasers which are available do not meet the original standard on patency of the channels.

The channels usually close in a few weeks. The effect of laser at relieving pain is attributed to angiogenesis triggered by the laser channels.

The alleviation of angina is long lasting and some of our patients are 20 years past surgery. Therefore, placebo effect can not be considered. As a matter of fact, perfusion of myocardium in many patients has improved and demonstrated by nuclear scan and MRI; ejection fraction in a few patients has markedly increased.16

Since the commercial parties have rushed the production of this product and its presentation to the market without my personal approval, one could state with honesty that the final chapter in TMLR is not closed.

The goal should be to produce a laser like the first laser, to avoid thermal injury to myocardium in order to assure patency of laser channels and give patients the security of receiving the full-benefit of TMLR, the initial intention of this technique.

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Review Article

Clinical Applications of Cardiovascular Magnetic Resonance Methods

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Abstract

The application of magnetic resonance to diagnostic medical imaging stands as one of the great scientific achievements in the past 50 years. Magnetic resonance techniques are easily applied to organs which remain stationary during the imaging procedure, such as the brain and musculoskeletal system. Imaging of moving heart structures and circulating blood is considerably more difficult. Clinical application of magnetic resonance to the cardiovascular system remains challenging but continuing technological innovations have enabled cardiovascular specialists to more effectively utilize magnetic resonance in clinical practice as well as for innovative research. Cardiovascular magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) are now being used with increasing frequency for the assessment of patients with cardiovascular disease. This paper will introduce clinicians to the current applications of these flexible and robust tools. A brief introduction will be given to the physics of MRI, the instrumentation and the imaging strategies. The main focus of the article, however, is to review how these techniques are being applied by clinicians in routine daily care.

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Introduction

Terminology can be a stumbling block for clinicians being introduced to the study of magnetic resonance methods. In conventional parlance, the term cardiovascular MRI is used to describe imaging of the heart and blood vessels which is accomplished without using contrast agents. The term cardiovascular magnetic resonance angiography (MRA) is most commonly used when blood vessel imaging is accomplished with the use of intravenous contrast agents. MRA techniques increase the conspicuity of blood vessels and aid in defining vascular pathology (Figure 1).

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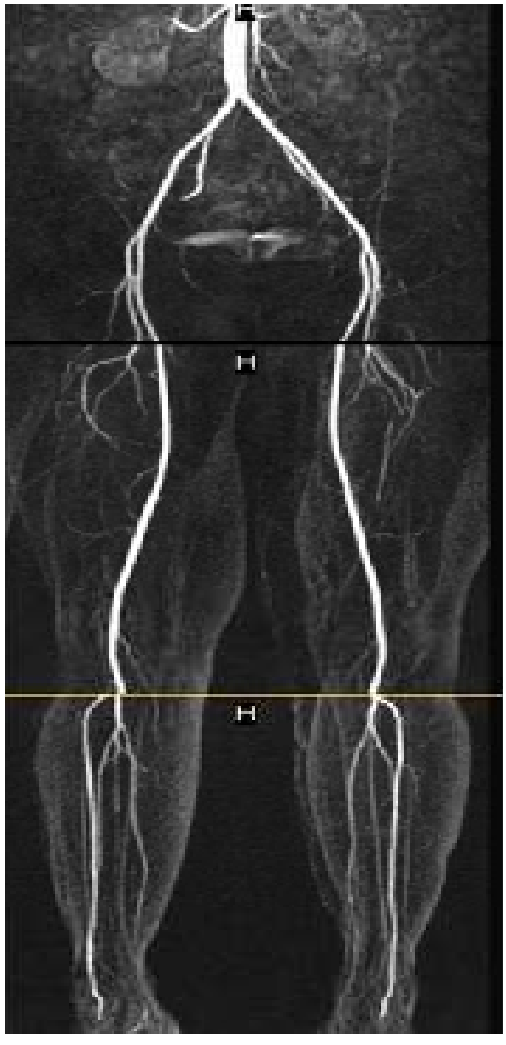

Figure 1. Magnetic resonance angiography (MRA) of the abdominal aorta, iliac arteries and lower extremities in a normal patient. This image was acquired following the intravenous administration of gadolinium contrast

The term contrast enhanced magnetic resonance imaging (CE-MRI) is used to describe imaging of the myocardium and soft tissues, as opposed to blood vessels, following contrast agent infusion. CE-MRI is most commonly used to assess myocardial viability, myocardial perfusion or to aid in soft tissue characterization (e.g. assessment of cardiac masses or thrombi).

The physics of magnetic resonance can be daunting but, a relatively simple working knowledge of how images are formed using magnetic resonance is all that is required to facilitate informed clinical application. Recall that most clinical cardiologists are not expert in the physics of ultrasound, nuclear pharmacy or X-rays yet can quite ably apply echocardiography, nuclear stress imaging and cardiac catheterization techniques within their practice. In an analogous fashion, armed with basic principles, the clinician can also apply magnetic resonance methods within their practice.

Basic Principles

Magnetism arises as a result of the motion of charged particles.[1] Many materials exhibit magnetic properties but, in medicine we exploit the hydrogen nucleus to generate images. The hydrogen nucleus, which is abundantly distributed throughout the body primarily in the form of water molecules, both spins and possesses an electric charge. Accordingly, the hydrogen nucleus creates magnetism. When the human body is placed in the external magnetic field of a commercial magnetic resonance instrument a small net magnetic force is produced by the hydrogen nuclei. This net magnetic force can be manipulated and localized in space forming an image which represents the distribution of the aforementioned nuclei. When one looks at a typical magnetic resonance image, one is simply looking at a map of hydrogen nuclei, primarily in the form of water, in the area being interrogated.

A crucial point in magnetic resonance methods is to understand that the magnetic behavior of hydrogen nuclei is highly dependent on the local environment in which they are concentrated. The human body, with its complex latticework of tissues and organs, has a variable distribution and concentration of hydrogen nuclei in solid organs and in the vasculature. Each tissue has 2 unique signatures which describes how the hydrogen nuclei behave in a magnetic field after they have been perturbed by a radiofrequency pulse of appropriate energy. The magnetic behavior within the overall lattice that the nuclei are located is referred to as T1 relaxation (spin-lattice relaxation). The magnetic behavior between adjacent hydrogen nuclei is referred to as T2 relaxation (spin-spin relaxation). T1 and T2 values for typical tissues are well established. The signal produced by hydrogen nuclei and detected by magnetic resonance instruments can be made to be dependent on T1 and T2 characteristics of the area interrogated. With this background, it can now be appreciated that image appearance in MRI is dependent on hydrogen nuclei density, T1 characteristics, T2 characteristics and motion (including blood flow). Although complex, it is just this complexity which can be manipulated by magnetic resonance methods, with and without contrast agents, to provide unparalleled insight into form and function in both normal and pathological states.

Instrumentation

The components of a commercial MR scanner include:

(1) A large superconducting magnet which is always on and provides a continuous and stable field strength.

(2) A series of smaller magnets, referred to as gradient coils, which surround the main magnet. These gradient magnets are switched on and off quite rapidly and transiently create a "gradient" of field strengths in 3 dimensions.

(3) Radiofrequency transmission and receiver coils

(4) A computer to process the information and generate the typical image display.[2]

To acquire an image, the patient must lie still in the main bore of the magnet. The local magnetic environment is manipulated through the rapid application of the magnetic "gradients" which, as noted above, surround the main magnet. Radiofrequency energy is applied and absorbed within the imaging area of interest. The combination of gradient application and radiofrequency energy perturbation allows a 3-dimensional signature to be given to the hydrogen nuclei within the imaging plane. The timing chosen for the image field perturbation and the timing chosen for detection are software parameters programmed into the instrument (see Imaging Sequences section below). These techniques facilitate localization and image contrast which result in the generation of medical images capable of exquisite temporal and spatial resolution.

Most MR instruments in clinical use throughout the world operate at field strengths of 0.5 to 1.5 Tesla. For perspective, the earth's magnetic field is less than 1 Gauss (1 Tesla = 10,000 Gauss). The workhorse instrument for general imaging use is the 1.5 Tesla instrument. Recently, scanners have become commercially available that operate at a field strength of 3 Tesla. For the highest quality CV applications, standard bore configuration magnets are required. It should be noted that scanners are available which do not have a bore configuration (open magnets) but, these instruments are not adequate for most cardiovascular applications. Figure 2 shows the 1.5 Tesla magnet used in our laboratory.

Imaging Sequences

There are myriad ways that an MR instrument can be made to interact with tissues of interest. The set of instructions given by the computer to the gradient coils and radiofrequency coils during acquisition is referred to as an imaging sequence. The basic imaging sequences have been designed to highlight a tissue of interest. The blood pool can be made to appear either dark or bright and the acquisition can also be designed to highlight anatomic information or flow information. Spatial resolutions ranging from several millimeters to sub-millimeter can be achieved in any desired plane to highlight anatomy. Very low temporal resolutions can be achieved to highlight function. Cardiac gating is required for cine imaging and in a typical acquisition used to assess ventricular function, cine images with a temporal resolution in the range of 15-30 milliseconds are routinely obtained. Commercially available sequences can provide limited information about tissue characteristics. Further, as will be described later, clinically important information about tissue vascularity and myocardial viability can be obtained following the infusion of MRI contrast agents.

A detailed treatment of imaging sequences is a complex topic which is beyond the scope of this paper but can be found in many standard references. Suffice it to say that imaging sequences are continually being developed by software programmers and many of the new and exciting developments in cardiovascular magnetic resonance methods are being made possible by innovations in this area.

Figure 2. 1.5 Tesla MRI instrument optimized for cardiovascular applications from the authors lab

Contrast Agents

Agents have been developed which significantly alter the magnetic field behavior of hydrogen nuclei and thereby alter tissue contrast. Most currently available MR contrast agents are chelates of the rare earth metal gadolinium. Gadolinium is not imaged directly, rather the images obtained are a representation of the effect that gadolinium has on adjacent hydrogen nuclei. Gadolinium is effective because hydrogen nuclei in close proximity to gadolinium have a T1 relaxation time that is dramatically lowered when compared to hydrogen nuclei not in proximity to gadolinium. Accordingly, imaging sequences can be chosen to highlight differences in T1 relaxation and these differences can produce excellent tissue contrast. Bolus administration and early imaging, while the gadolinium chelate is still within the vasculature, is used to produce high quality angiograms (MRA). The normally used MR contrast agents diffuse rapidly into the extracellular space and images can be obtained after the infused agent has left the vascular compartment and distributed into the tissues (CE-MRI).

Gadolinium is highly toxic in its elemental state but, gadolinium chelates have been devised with remarkable safety

profiles. There have been rare but, well described, systemic side effects including anaphylactoid reactions. Serious toxic effects have also recently been reported in patients with renal failure and advanced renal failure should be regarded as a strong relative contraindication to contrast MRI. Despite the small risks associated with their use, gadolinium based agents have been used safely in patients of all ages and contrasted images have greatly improved the diagnostic power of magnetic resonance imaging. The development of improved contrast agents for clinical applications is an area of intense research in laboratories throughout the world.

Safety

A major advantage of MRI is that imaging is performed without exposing the patient to ionizing radiation or iodinated contrast material. Accordingly, as currently applied, MRI is devoid of any known destructive biophysical effects in appropriately selected patients.

There are, however, important safety considerations for MR imaging and many excellent resources are available which deal with safety.[3,4] An excellent web based resource is http://www.mrisafty.com/ Standard contraindications include cardiac pacemakers, defibrillators, ferromagnetic intracranial aneurism clips, and various implanted or magnetically activated devices. Most orthopedic hardware can be imaged safely although image degradation is likely to occur if the region of interest is in close proximity to the metallic hardware. Sternal wires, coronary stents, and artificial heart valves can be safely imaged in almost all situations. There is an increasing body of literature describing the safety of imaging some cardiac pacemaker patients in a carefully monitored protocol.[5] These preliminary results are exciting, and may expand the use of MRI but, imaging of patients with pacemakers is investigational and can not be recommended at this time.

Clinical Applications

Indications

A unique strength of magnetic resonance methods is the ability to obtain anatomic, functional and perfusion information with a single method. Vascular and nonvascular anatomy can be imaged with excellent resolution and, since MRI techniques are inherently 3 dimensional, images can be acquired in any plane. As long as the patient can cooperate with lying still and occasional breath-holding instructions (to reduce respiratory motion) high quality images can be obtained in most patients. Table 1 lists the current clinical uses for MRI. Resources are now available from international organizations which highlight clinical indications as well as appropriateness criteria.[6-8]

Table 1. Indications for cardiovascular magnetic resonance imaging assessment of right and left ventricular volumes, ejection fraction and mass

Ischemic Heart Disease
- (a) Ventricular morphology, volumes and ejection fraction
- (b) Myocardial perfusion at rest and following pharmacologic stress
- (c) Myocardial viability following contrast administration (delayed CE-MRI)
- (d) Phosphorous spectroscopy (investigational – not a current clinical tool)

Valvular Heart Disease
- (a) Serial assessment of ventricular volumes, ejection fraction and mass
- (b) Valvular morphology (echo techniques are first line)
- (c) Quantitative flow, measuring stenotic gradients and regurgitant fractions

Myocardial Disease Primarily Involving the Left Ventricle
- (a) Ventricular morphology, volumes and ejection fraction
- (b) Assessment of patterns of hypertrophy (hypertrophic cardiomyopathy)
- (c) Delayed CE-MRI as an aid in recognizing the etiology of cardiomyopathy (e.g. dilated or ischemic cardiomyopathy, myocarditis, sarcoid, amyloid)

Right Ventricular Cardiomyopathy

Pericardial Disease
- (a) Constrictive pericardial disease
- (b) Atypical pericardial effusions (echo techniques are first line)

Congenital Heart Disease
- (a) Morphology of the heart, central pulmonary arteries and aorta
- (b) Right and left ventricular morphology and function
- (c) Assessment of intracardiac shunts
- (d) Assessment of post-surgical results

Assessment of Cardiac and Paracardiac masses (echo techniques are first line)

Diseases of the Thoracic and Abdominal Aorta

Peripheral and Cerebrovascular Angiography

Coronary Artery Imaging
- (a) Assessment of anomalous coronary arteries
- (b) Kawasaki's disease

Ventricular Function

Validation of the accuracy of MR methods for assessing volume, function and mass dates back to the early days of cardiovascular MRI.[9-14] In the opinion of most authorities, MRI now represents the gold standard for assessing right

and left ventricular function. Unlike other modalities, MRI can accurately and reproducibly assess ventricular function and mass independent of geometric assumptions. In our lab, we routinely assess ventricular function using several single plane long axis images and a stack of serial short axis images proscribed to encompass the entire heart from base to apex. To acquire a 2 chamber plane (RAO equivalent), a 4 chamber plane (LAO equivalent) and an LVOT plane requires a total of 3 EKG-gated, breath-hold scans each lasting only ~5 to 10 seconds. Using these views, standard area-length ejection fraction calculations can be obtained which are quick and accurate, particularly in patients with normal regional wall motion. The serial short axis series usually requires 4 to 6 separate breath-hold scans. Accurate ejection fraction and volume calculations can be made using a Simpson's rule algorithm. Results obtained using these inherently 3 dimension data sets are reproducible and accurate even in patients with regional wall motion abnormalities. A comprehensive assessment of ventricular function can be obtained in ~10 minutes from the time the patient lies down in the scanner until the results are obtained. MRI has the added benefit of being able to measure wall thickness, wall thickening and LV mass. Patients, such as those with chronic valvular pathology, in who chamber dilatation and ejection fraction influence prognosis and the timing of surgical intervention, can be accurately followed. The benefits of MRI can also be exploited in the research community, particularly in the area of drug therapy and development. Studies can be designed that involve fewer patients and can be accomplished in a more cost effective and shorter time frame using MRI methods.

Cardiomyopathy

MRI is useful for the assessment of patients with cardiomyopathy since treatment algorithms are often based on the etiology and severity of myocardial dysfunction. Defining an ischemic etiology may lead to additional testing in the hope of identifying treatable coronary artery obstruction. Accurate assessment of ejection fraction can influence the appropriate use of device therapy in the form of biventricular pacing and/or implantable defibrillators. Facilitating proper patient selection for device therapy is an issue of clinical and economic importance.

Contrast enhanced MRI (CE-MRI) techniques have been used to accurately distinguish between ischemic and nonischemic etiologies for cardiomyopathy. Patients with prior myocardial infarction (ischemic etiology) demonstrate a characteristic endocardial to transmural pattern of contrast enhancement following gadolinium infusion (see section on Ischemic Heart Disease). In comparison, patients with a nonischemic etiology typically do not show this pattern. In ground-breaking work from the laboratory of Dr. Dudley Pennell at the Royal Bromptom Hospital in London, McCrohon et al. showed that patients with nonischemic dilated CE-MRI often demonstrate a pattern of mid-wall enhancement. Their work was the first to suggest that delayed CE-MRI may become a useful alternative to invasive coronary angiography in the work-up of patients with cardiomyopathy.[15] This is a complicated and somewhat controversial area and continued research is to be expected.[16-17]

Abnormal contrast uptake has been seen in patients with acute myocarditis using several acquisition techniques although the findings can be variable.[18-21] Ventricular function assessment, chamber morphology, valvular function, quantitative flow measurements and CE-MRI make possible a comprehensive evaluation of known or suspected hypertrophic cardiomyopathy.[22-26] Figure 3 is an example of asymmetric septal hypertrophy in a patient with hypertrophic cardiomyopathy. MRI may be uniquely useful in less common variants such as apical hypertrophic cardiomyopathy which can be missed by echocardiography.[24] MRI findings in sarcoid and amyloid heart disease have been described by MRI, although the findings can be variable and nonspecific.[27-28]

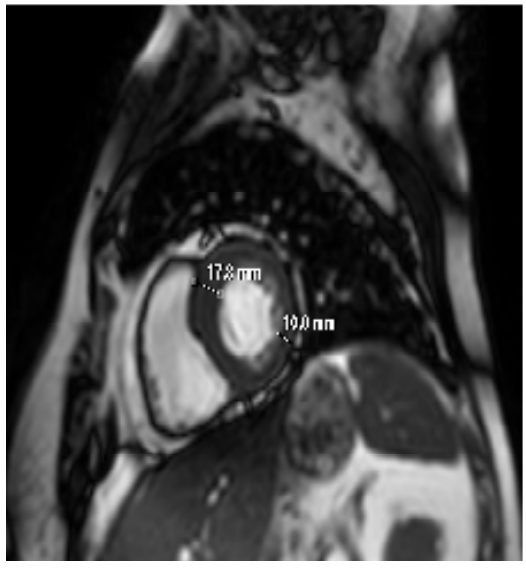

Figure 3. Basal slice from a cine MRI study demonstrating asymmetric septal hypertrophy in a patient with hypertrophic cardiomyopathy

Cardiomyopathy associated with thalassaemia can be evaluated by MRI.[29] These patients often receive multiple blood transfusions during their lifetime resulting in iron overload and cardiomyopathy with subsequent death due to arrhythmia or heart failure. There is no consistent relation between serum iron and myocardial dysfunction. Nor does liver iron consistently predict myocardial iron content. Some authors have demonstrated the usefulness of the MRI T2* studies in diagnosing such cases. It is hoped that diligent follow-up may prevent myocardial scarring and irreversible cardiomyopathy in this select population.

Right ventricular cardiomyopathy is difficult to evaluate

and requires the combination of a strong clinical suspicion and the strict application of clinical and imaging criteria. Since the right ventricle is poorly evaluated by echo, nuclear and catheterization techniques MRI has assumed an important role in the imaging criteria. Helpful parameters include right ventricular dilation, focal contractile abnormality, trabecular disarray and fat infiltration of myocardium.[30-32]

Ischemic Heart Disease

Left ventricular size and function is a major determinant of prognosis in patients with ischemic heart disease. As noted above, the accuracy of MRI for assessing both the myocardium (mass, wall motion, regional wall thickening) and the blood pool (chamber volumes and ejection fraction) is quite helpful. MRI pharmacologic stress testing can be performed using dobutamine or adenosine. The spatial resolution of MRI stress testing is superior to conventional nuclear studies but, stress testing in the MR environment can be cumbersome and therefore, is not widely used.

MRI can also be used to assess myocardial viability. The usual protocol includes assessment of cardiac anatomy and function and delayed imaging of the myocardium following the infusion of gadolinium contrast (delayed CE-MRI). The gadolinium chelates in routine clinical use are primarily extracellular agents which diffuse into the interstitial space. Normal myocytes exclude gadolinium while areas of myocardial scar, which don't contain normal myocytes, accumulate gadolinium over time. When imaged with a specialized inversion recovery sequence normal myocardial tissue is nulled and made to appear dark (black). Figure 4 is an example of a normal delayed CE-MRI study.

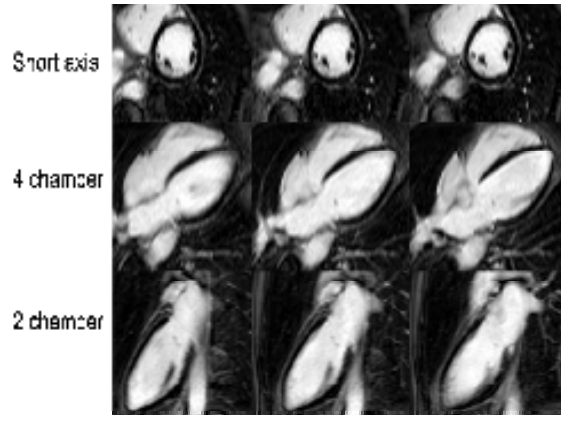

Figure 4. Delayed contrast enhanced magnetic resonance imaging (CE-MRI) demonstrating normal myocardial viability. Note the excellent nulling of the myocardium (normal myocardium appears dark) and the absence of any areas of abnormal hyperenhancement within in the myocardium

In contradistinction, abnormal areas of high gadolinium concentration are made to appear bright (white). The easily remembered adage in MR myocardial viability imaging is: "bright is dead". Figure 5 is an example of a localized myocardial infarction from our lab.

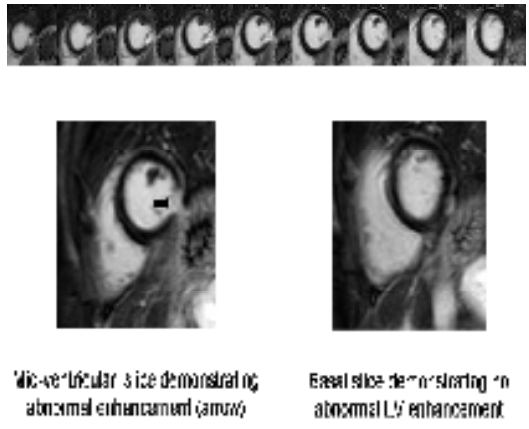

Figure 5. The top row shows a series of short axis slices from a delayed contrast enhanced magnetic resonance imaging (CE-MRI) acquisition. This patient presented with chest pain, malignant ventricular ectopy and enzyme evidence of a small myocardial infarction. The bottom left image is a magnified image from the mid-ventricle and shows a discrete transmural infarction (arrow). The bottom right image is a magnified image from the base of the heart showing normal myocardium

The spatial resolution of MRI is approximately 40-fold superior to conventional nuclear viability imaging and its accuracy has been validated in both animal and human studies. Pioneering work was done by Dr. Raymond Kim and associates and has been corroborated and expanded through the work of others.[33-40] The exquisite resolution of MRI facilitates a full thickness evaluation of myocardial infarction. Small subendocardial infarcts can be identified as well as extensive transmural infarctions.[41-42] The extent of infarction has been precisely correlated with improvement of regional myocardial function following surgical revascularization in humans.[34] Recent research is being directed at making the techniques even quicker and more patient friendly.[43] Most authorities now consider delayed CE-MRI to represent a gold standard for the clinical assessment of myocardial viability.

A combined LV function and viability study can be performed in less than 20 minutes and requires no additional equipment. In labs that combine the above with stress testing, a comprehensive physiologic evaluation of ischemic heart disease can be achieved in 30-45 minutes but, requires specialized drug infusion equipment and the presence of trained medical personnel. Combining stress perfusion imaging with an assessment of myocardial viability appears to improve clinical utility.[44-45]

Valvular Heart Disease

Transthoracic and transesophageal echocardiography are excellent techniques for assessing fine morphologic detail of

heart valves. However, MRI is complementary for assessing valve morphology and, is a superior technique for assessing the physiologic consequences of valvular pathology. Subjective assessments can be obtained using cine gradient echo techniques which highlight the disturbed flow patterns characteristic of valvular stenosis and regurgitation. Reproducible objective assessments can be obtained using quantitative flow and volumetric MR techniques. Aortic and mitral valve gradients and valve areas can be rapidly calculated in a manner analogous to echocardiography.[46-48] Regurgitant flow and volume can be reproducibly assessed in both mitral and aortic regurgitation.[49-51]

Magnetic resonance methods are uniquely helpful in identifying patients with pathology of the aortic valve and ascending aorta. It has been recognized that patients with a congenitally abnormal aortic valve (bicuspid) often have associated pathology of the aortic wall (aneurysm or coarctation). A high index of suspicion is required to tailor the diagnostic imaging strategy and guide appropriate therapy. In these patients, MRI is used to assess anatomy and ventricular function, quantitative flow methods are used to assess stenotic and/or regurgitant lesions and MRA is used to assess the entire aorta. Figure 6 is an example of a patient from our lab that was accurately diagnosed by MR methods and underwent successful surgical therapy.

Prosthetic valves can be imaged safely but, morphologic detail at valve level valve cannot be assessed due to local artifacts from the metallic components of the valves. Eccentric regurgitant jets and quantitative flow can still be assessed.

Pericardial Disease

MRI is accurate for diagnosing pericardial effusions. Echocardiography is the initial choice for assessing pericardial pathology but, MRI is complementary and is particularly useful for assessing loculated effusions. MRI can also contribute to the evaluation of suspected constrictive pericardial disease by allowing accurate measurement of pericardial thickness and assessment of the physiologic sequelae of constriction such as RV chamber distortion and RA enlargement. Calcium produces an MRI signal void and its presence can only indirectly be inferred by MRI. Computed tomography (CT) is another tool that can be used since CT very accurately assesses pericardial calcium content. A comprehensive assessment of pericardial disease often requires a multimodality approach.[52]

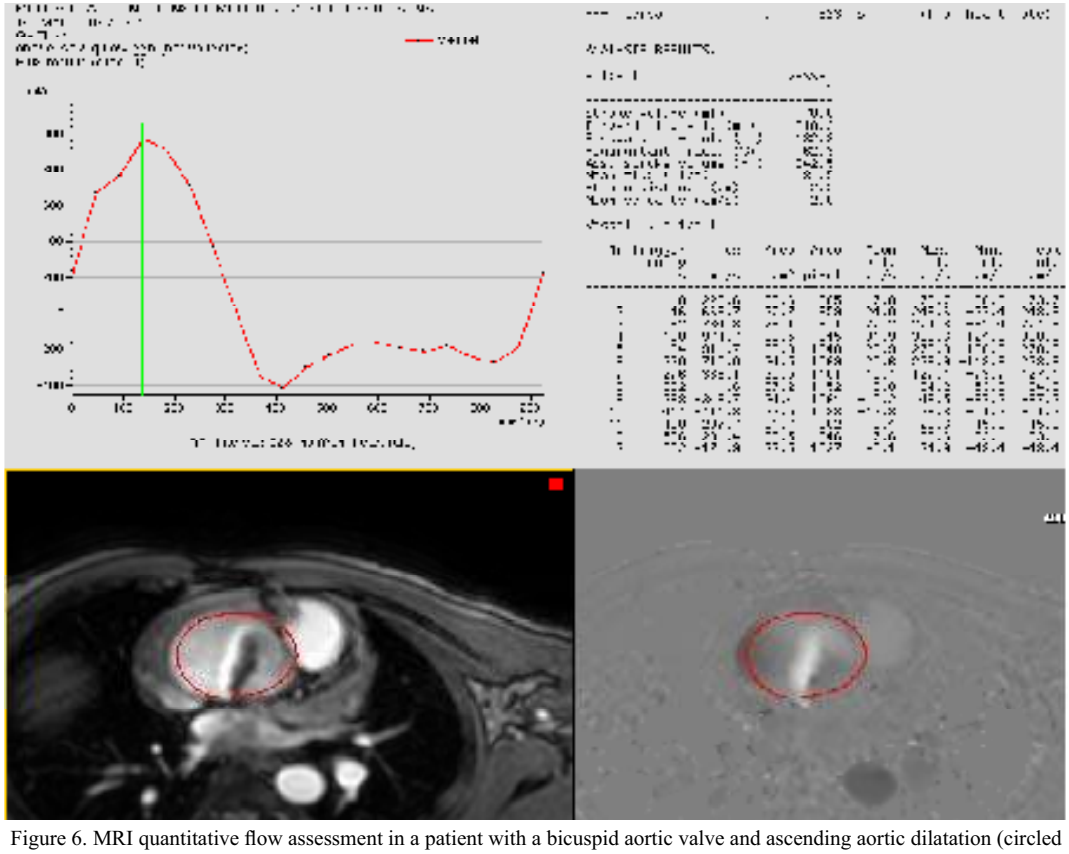

Figure 6. MRI quantitative flow assessment in a patient with a bicuspid aortic valve and ascending aortic dilatation (circled region of interest in the bottom frames). The top left frame is a graphic representation of flow across the region of interest at the level of the aortic valve. The top right frame demonstrates volumes and flow velocities in tabular form. This patient was shown to have increased velocities and severe aortic regurgitation. He underwent successful replacement of his aortic root and aortic valve

Cardiac and Paracardiac Masses

Echocardiography is the first line imaging strategy for evaluation of cardiac masses but MRI is an important complementary tool. The large field of view can precisely assess size and the relationship to cardiac and noncardiac structures. The flexibility of imaging sequences (e.g. T1-weighted, T2-weighted and fat suppression techniques) permits some insight into tissue composition. Finally, image appearance following contrast infusion facilitates assessment of vascularity. Left ventricular thrombi, even small apical thrombi, can be reliably imaged using MRI techniques (Figure 7).

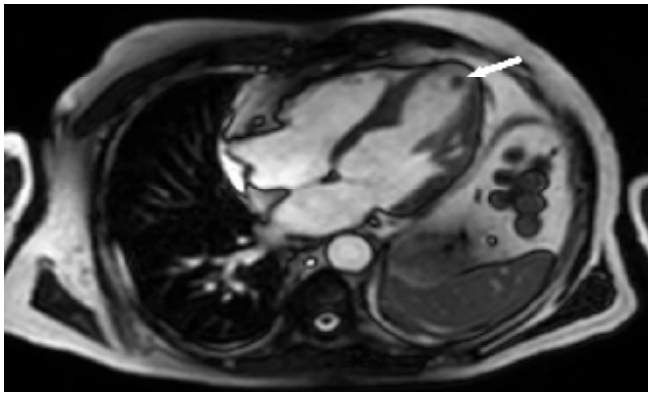

Figure 7. Cine MRI demonstrating a small apical thrombus (arrow)

Congenital Heart Diseases and Post Surgical Follow Up

Advances in medical and surgical techniques have created an increasing population of patients with congenital heart disease surviving in to adulthood. Echocardiography is an excellent tool in most young children. However, MRI is of great complementary utility in complex congenital heart anomalies in the adult. The absence of radiation or nephrotoxic iodine administration is important in the younger population. The wide field of view facilitates the systematic assessment of cardiac morphology as well as the status of venous return, the central pulmonary arteries and the thoracic aorta.[6,53,54] Quantitative flow techniques can be used to noninvasively calculate systemic and pulmonary blood flow and, thereby identify the presence of any shunt. Figure 8 is an example of an atrial septal defect with a significant left-to-right shunt identified in our lab.

In the post-surgical population, surgically created conduits can be notoriously difficult to locate and interrogate. MRI is useful to follow patients after surgery and to look for complications or residual defects. The wide field of view of MRI and the ability to perform quantitative flow assessment in any imaging plane can be helpful.

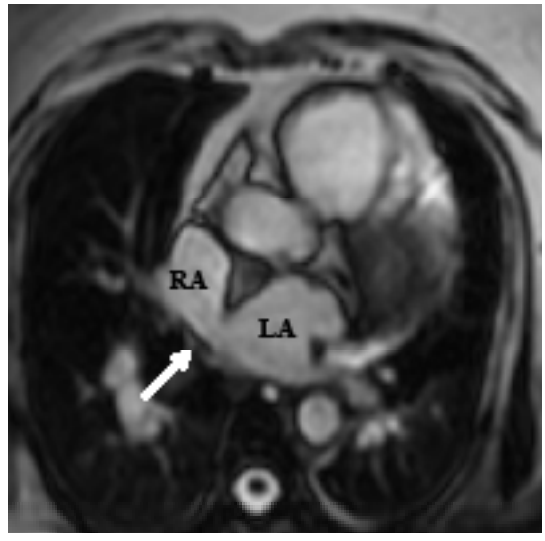

Figure 8. Cine MRI of a sinus venosus atrial septal defect (arrow). RA, Right atrium; LA, Left atrium

Coronary Artery Imaging

A significant body of research has been done on MR coronary angiography and in carefully selected patients diagnostic images can be obtained. A preliminary early report was published many years ago by Dr. Warren Manning and associates comparing MR coronary angiography with conventional angiography.[55] Figure 9 is an example of an MR coronary angiogram obtained in our lab. It must be recognized that the technical requirements are considerable and long acquisition times are required. Accordingly, MR coronary artery imaging is seldom used clinically in the detection of atherosclerotic coronary artery disease.

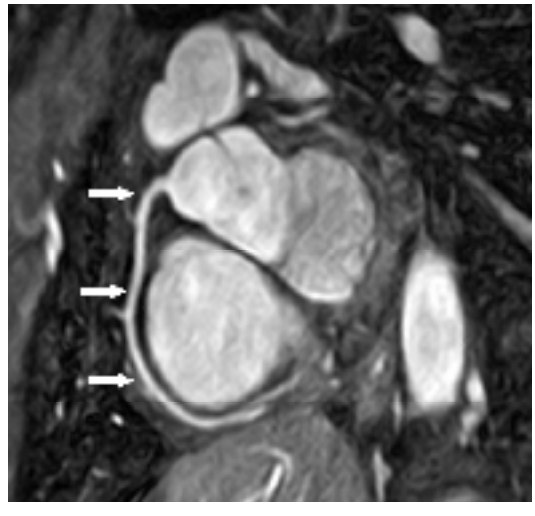

Figure 9. MR coronary angiogram of a normal right coronary artery (arrows)

A niche clinical use of MR coronary imaging is for the detection of congenital coronary anomalies involving the origin and course of the proximal vessels.[56] In young patients, where the desire to avoid radiation is of greatest relevance, MRI is often used as the first line test. Coronary artery aneurysms, such as those seen in Kawasaki's disease, can be followed-up via MRI (Figure 10). In the current state of development, CT coronary angiography is much faster, has superior spatial resolution and is the preferred noninvasive strategy for coronary imaging in most situations. Research using magnetic resonance to characterize not only the lumen of the epicardiac coronary arteries but to assess plaque morphology continues.

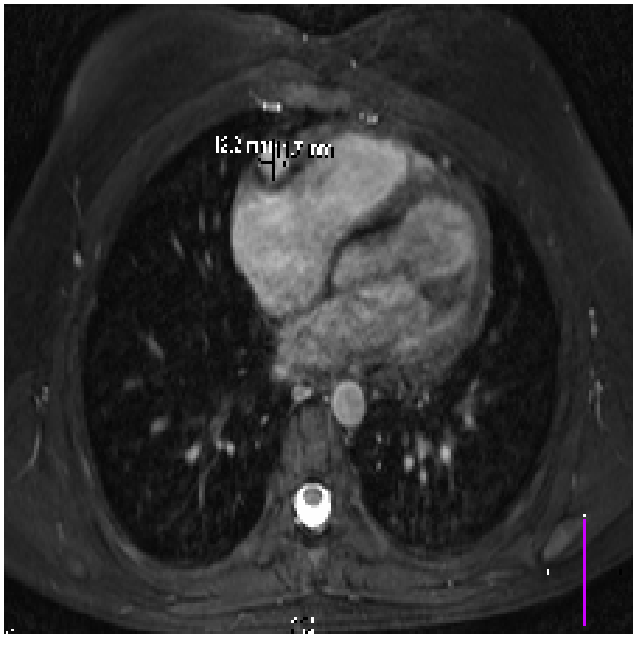

Figure 10. Magnetic resonance image of a 12.2 mm x 11.7 mm right coronary artery aneurysm in a young patient with Kawasaki's disease

Magnetic Resonance Angiography

Magnetic resonance imaging is inherently sensitive to flow and early investigators recognized the potential for noninvasive MR angiography. The earliest efforts were done by manipulating imaging sequences in order to highlight natural flow phenomena and contrast. However, it wasn't until the widespread use of MR contrast agents that MRA became sufficiently accurate and reproducible for clinical use. Magnetic resonance angiography has revolutionized the diagnostic evaluation of patients with aortic disease (Figure 11), renovascular disease (Figure 12), cerebrovascular disease, and upper and lower extremity peripheral vascular disease (Figure 13). In the past, most of these patients required invasive angiography to assess their status. Currently, in state-of-the-art labs, almost all diagnostic angiography is accomplished noninvasively with MRA or, recently, CT angiography. The invasive angiography suite remains valuable to arbitrate an equivocal or nondiagnostic noninvasive angiography study. Fortunately, the major role of the invasive angiography suite has shifted to the performance of therapeutic interventions.

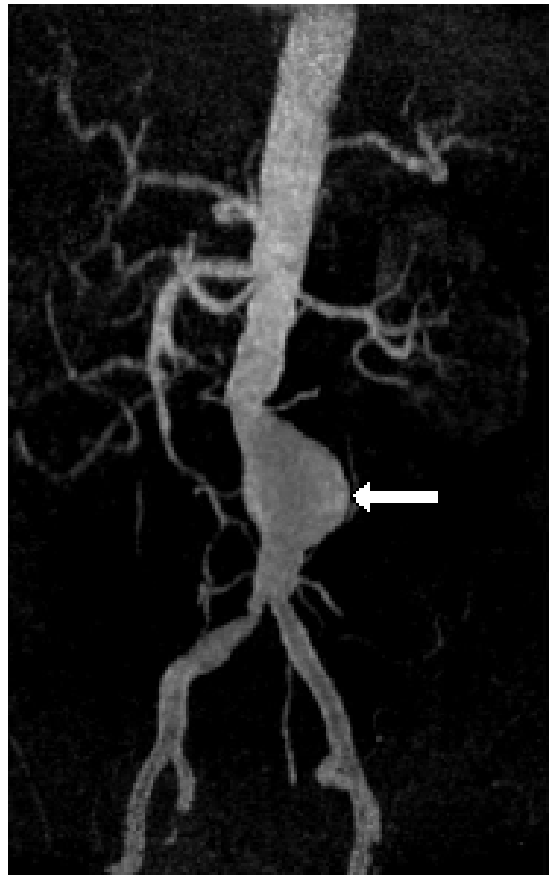

Figure 11. MR angiogram demonstrating an infrarenal abdominal aortic aneurysm (arrow)

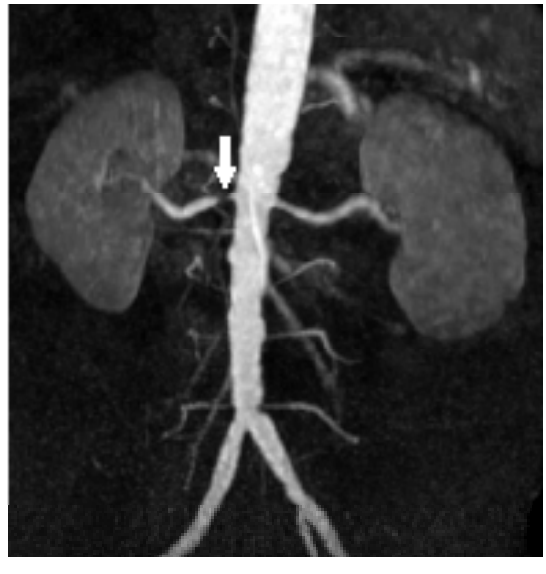

Figure 12. MRA of right renal artery stenosis (arrow)

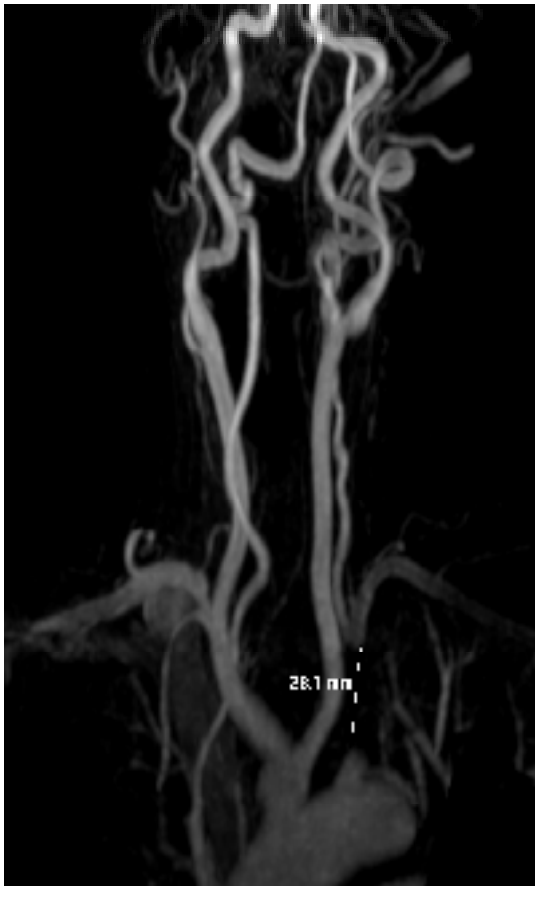

Figure 13. MRA of the aortic arch and neck arteries demonstrating 100% occlusion of the left subclavian artery

Future Considerations

The field of cardiovascular magnetic resonance is well established for the clinical applications described above. This field is far from mature and new developments are being reported regularly. Accurate definition of atherosclerotic plaque composition and burden would be of enormous clinical utility and is an area of active and promising research.[61,62] Work continues to be pursued in the area of MR coronary angiography. A potential role for MR spectroscopy has been described and is the subject of ongoing basic science investigation.[63] The disciplines of interventional MRI and high field strength (3 Tesla) MRI are also in their early stages.

Conclusions

Magnetic resonance methods are assuming an increasingly prominent role in the evaluation of patients with cardiovascular disease. The contemporary clinician should acquire a working knowledge of the technology available and how to apply these techniques in a cost effective manner. It is to be expected that the uses of cardiovascular MR will proliferate as promising new avenues of research are explored.

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Original Article

Usefulness of Dipyridamole Myocardial Perfusion SPECT in Patients with Left Bundle Branch Block

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Abstract

Background: *Diagnosis of coronary artery disease (CAD) in patients with left bundle branch block (LBBB) is considered as a challenge in cardiology due to the low accuracy of noninvasive methods such as basal and stress electrocardiography (ECG). This diagnostic challenge can be reduced but not eliminated using dipyridamole as a stress method instead of exercise. The aim of this study was to assess the diagnostic value of dipyridamole stress Tc-99m Sestamibi single photon emission computed tomography (SPECT) myocardial perfusion imaging in patients with complete LBBB.*

Methods: *We studied 40 patients with permanent and complete LBBB using Tc-99m Sestamibi SPECT and dipyridamole stress to evaluate CAD. Perfusion defect was considered fixed when there was no difference between rest and stress score, while reversible defect was defined as a segment with higher score on stress images. All patients underwent coronary angiography.*

Results: *Eleven patients (27.5%) had normal myocardial perfusion SPECT and 29 patients (72.5%) had reversible perfusion defects. Angiography was positive in 30 patients, while 10 cases showed normal angiography. The sensitivity, specificity, positive predict value and negative predict value of our study for detecting >50% coronary stenosis was 86.6%, 70%, 89% and 64% respectively.*

Conclusion: *We found 33 (82.5%) patients with concordant angiography and myocardial perfusion SPECT results (p=0.002). Angiography was positive in 90% of patients with reversible perfusion defects on myocardial perfusion SPECT. In summary, Tc-99m Sestamibi SPECT in patients with LBBB showed high accuracy (82.5%) in detecting >50% coronary stenosis.*

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Keywords: *Left bundle branch block • Myocardial perfusion imaging• SPECT• Technetium-99m Sestamibi• Dipyridamole*

Introduction

Noninvasive diagnosis of coronary artery disease (CAD) in patients with left bundle branch block (LBBB) continues to be a challenge in nuclear cardiology. Basal and stress ECG has persistently shown low sensitivity and specificity in

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diagnosing of CAD in this group of patients. Since the 1990s, several studies acknowledged the diagnostic value of Thallium-201 (Tl-201) myocardial perfusion imaging in patients with complete LBBB.[1-4] Stress scintigraphy is not specific for the frequent occurrence of septal, anterior and apical defects in the absence of CAD. This diagnostic challenge can be reduced but not eliminated using dipyridamole as a stress method instead of exercise.[5] Good results have been reported using exercise (+dipyridamole) SPECT with technetium compounds both in Non-LBBB patients and LBBB patients with no previous acute myocardial infarction.[6]

Confirming CAD has obvious implications for management. Several studies have shown greater cardiac mortality in the presence of LBBB. Generally, a good prognosis has been found in patients with LBBB and normal or near-normal myocardial perfusion scintigraphy.[7] Noninvasive diagnosis of CAD in patients with LBBB will help in stratifying this group according to cardiovascular morbidity and mortality risks, thus allowing clinicians to provide early treatment especially to patients in the high risk category. The purpose of this study was to assess the diagnostic value of Tc-99m Sestamibi SPECT myocardial perfusion imaging and dipyridamole in patients with complete LBBB.

Methods

We studied 40 patients with permanent and complete LBBB (QRS with ≥ 0.12 sec) on surface electrocardiograms. Patients were referred to dipyridamole stress perfusion SPECT imaging with Tc-99m Sestamibi for evaluation of CAD from March 2004 to December 2005. Indication for performing myocardial SPECT imaging was chest pain syndrome. Patients with significant valvular disease, previous myocardial infarction, pulmonary edema, active asthma and history of revascularization were excluded from the study. All patients gave their informed consent and signature and the study was approved by the Institutional Ethics committee.

0.56 mg/kg dipyridamole was infused over a period of 4 minutes. No patient had obstructive lung disease, took Theophylline, or drank coffee within the previous 12-24 hours. Tc-99m Sestamibi was injected intravenous (IV) 3 minutes after the end of dipyridamole IV infusion. A 12-lead ECG was recorded prior to and every minute during infusion. Heart rate and blood pressure were recorded at 1-minute intervals during infusion. All patients underwent same-day rest/stress Tc-99m Sestamibi SPECT perfusion imaging protocol. A rest dose of 296 MBq (8 mCi) was used. A high-fat snack (milk) was provided to facilitate hepatobiliary tracer elimination of Tc-99m Sestamibi. Rest imaging was carried out 1 hour after injection. Stress dose of 814 MBq (22 mCi) was used. Stress imaging was done 1 hour after stress dose. SPECT scintigraphy images were obtained on an ADAC dual head gamma camera equipped with high resolution collimators. An energy window was set at symmetric 20% over 140 kev photopeak; 32 images at 30 sec/stop were obtained and stored in 64×64 matrix over 180 from RAO (right anterior oblique) 45º. Zoom factor was 1.3, while slice thickness was 5mm/pixel. Images were processed to obtain short and long axis sections perpendicular to cardiac axes. Tomograms were divided into 25 segments for qualitative and quantitative interpretation. Myocardial perfusion status was scored as follows: 0=normal radiotracer uptake; 1=mildly reduced uptake; 2=moderately reduced tracer uptake; 3=severely reduced tracer uptake; and 4=absent radiotracer uptake. Perfusion defect was considered fixed when there were no differences between rest and stress score, while reversible defect was defined as a segment with higher score on stress images. Ischemia was defined as a change of one or more grades between rest and stress images. Interpretation of tomographic images was done by consensus of two experienced observers unaware of other patient data.

All patients underwent coronary angiography within 3 months after myocardial perfusion imaging. Patients were considered having significant coronary stenosis if > 50% reduction of luminal diameter was present. All angiograms were reviewed by attending physicians in the cardiac catheterization

laboratory without knowledge of myocardial imaging results. Data were expressed as mean values ± standard deviation (SD). Chi-square with Yates correction was used to compare differences among patient groups. For statistical analysis, we used SPSS version 10 (SPCC, Inc., Chicago, IL, USA); P value< 0.05 was considered statistically significant.

Results

Forty patients were studied; their mean age was 62±10 years (39-76 years), 17 (42.5%) were men and 23 (57.5%) women. Eleven patients (27.5%) had a normal myocardial perfusion SPECT. Fixed defect of septum without extension to the other walls was considered as normal scan. Twenty nine patients (72.5%) had reversible perfusion defects. Multiple perfusion defects were observed in two or more than two walls in 20 cases, while single perfusion defect was noted in 9 cases (2 in lateral wall and 7 in anteroseptal and anterior walls). Thirty patients had positive angiography (12 cases with 3VD, 8 cases with 2VD and 10 cases with 1VD). Among the patients with one vessel disease, 6 had LAD lesions lesion and LCX stenosis was observed in 4 other cases.

Four patients showed normal myocardial perfusion scan with positive angiography where all vessels had less than 70% stenosis (3 LCX lesions and 1 LAD lesion). Three patients had reversible defects on myocardial perfusion SPECT, while their angiography was normal. Normal angiography and myocardial perfusion scan was observed in 7 cases (figure 1).

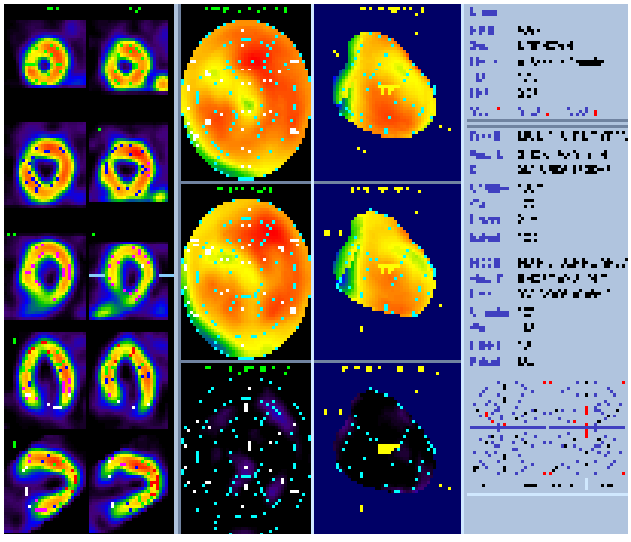

Figure 1. Fixed defect of septum in patient with normal angiography and perfusion scan

The results of both studies were positive in 26 patients (figure 2).

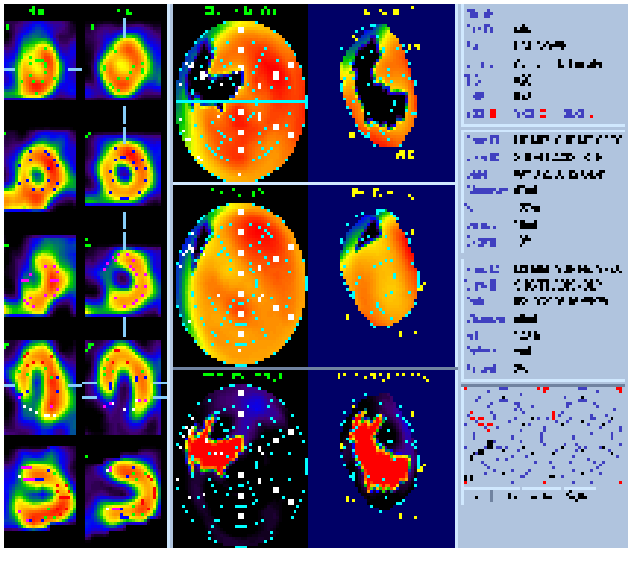

Figure 2. Reversible defect in anteroseptal and apical walls on myocardial perfusion SPECT

Overall, we found 33 patients (82.5%) with concordant angiography and MPS results (P=0.002). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of our study for detecting>50% coronary stenosis was 86.6%, 70%, 89%, 64%, and 82.5% respectively (table 1).

Table 1. Angiography and MPI findings in patients with LBBB

Angio \ MPI	Positive	Negative	Total
Positive	26	4	30
Negative	3	7	10
Total	29	11	40

Angio, Angiography; MPI, Myocardial Perfusion Imaging; LBBB, Left Bundle Branch Block

Discussion

Patients with LBBB often have high prevalence of perfusion abnormalities, especially in the anteroseptal region even in the absence of CAD or LAD disease.8-11 Thus, noninvasive assessment of LAD disease in patients with LBBB remains a challenge in nuclear cardiology, even in the era of advanced technology. Various reports2,3 have confirmed the prevalence of LAD disease by coronary angiography within the range of 45-48% among patients with LBBB referred for dipyridamole or exercise Thallium-201 scintigraphy.

Our results using Tc-99m Sestamibi and SPECT showed higher prevalence of anteroseptal perfusion abnormalities (62.5%). Its reason is that we studied LBBB patients with chest pain syndrome. The probability of CAD in this group of patients is usually high.12

Reversible perfusion defects were present in 72.5% of our patients. Angiography was positive in 90% of these patients, confirming the results of MPI. Our results agreed with those of Knapp et al.13 who reported that 14 of 15 patients with significant LAD stenosis showed reversible changes in septum using Tc-99m Sestamibi.

Exercise-induced septal perfusion defects in the presence of LBBB did not necessarily indicate CAD, however it may have reflected functional ischemia due to asynchronous septal contraction14, metabolic abnormalities in myocardium15, or reduced coronary flow reserve.16 However, reversible changes in LAD distribution remain suggestive of significant LAD stenosis even in the presence of LBBB.

Several recently reported series of exercise stress planar or SPECT imaging in patients with LBBB showed sensitivity from 27 to 100% and specificity from 14 to 79% using different indices.2,3,17 O'Keefe et al.18 reported that adenosine Tl-201 SPECT achieved significantly higher overall accuracy (93%) than exercise Tl-201 imaging (68%) in detection of LAD disease. False-positive rate was 5% in adenosine group vs. 35% in exercise group. The authors proposed using pharmacologic stress perfusion imaging as the preferred method for CAD evaluation in patients with LBBB. Our study was not designed to test the differences between exercise and dipyridamole stress scintigraphy, but

the false-positive rate in our study was 10% which is similar to the above mentioned adenosine group.

Conclusion

Our data showed that reversible perfusion defects in MPI have high sensitivity (86.6%), specificity (70%), and accuracy (82.5%) in detecting >50% coronary stenosis. One can appreciate the fact that myocardial perfusion scan and coronary angiography should be considered complementary tools in evaluation of patients with LBBB and coronary artery disease.

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Original Article

Echocardiographic Characteristics Including Tissue Doppler Imaging After Enhanced External Counterpulsation Therapy

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Abstract

Background: *The aim of this study was to echocardiographically assess the effects of EECP (Enhanced External Counterpulsation Therapy) therapy on systolic and diastolic cardiac function.*

Methods: *LVEF (left ventricular ejection fraction), ESV (end-systolic volume), EDV (end-diastolic volume), Sm (myocardial systolic wave), Ea (myocardial early diastolic wave), Vp (propagation velocity), E/Ea (peak early diastolic transmitral flow velocity/Ea), E/Vp and diastolic function grade were studied in twenty-five patients before and after 35 hours of EECP.*

Results: *EECP reduced ESV and EDV and increased EF significantly (p=0.018, 0.013, 0.002, respectively) in patients with baseline LVEF≤50%, but not in patients with baseline LVEF>50%. Patients with E/Ea≥14 had a significant reduction in EDV and ESV (p=0.038 and 0.32, respectively) and an increase in LVEF (p=0.007) after EECP, whereas patients with baseline E/Ea<14 had no significant change in these parameters. Similarly, EECP significantly improved ESV, EDV and LVEF (p=0.014, 0.032, 0.027 respectively) in patients with grades II and III of diastolic dysfunction (decreased compliance) at baseline, but not in patients with normal diastolic function or grade I diastolic dysfunction (impaired relaxation). Patients with Ea<7 cm/sec prior to EECP showed significant improvement in EDV, ESV and LVEF after therapy (p=0.024, 0.015, 0.001), while patients with Ea≥7cm/sec showed no significant change. Similarly, patients with Sm<7cm/sec prior to EECP showed significant improvement in EDV, ESV and LVEF after EECP (p=0.016, 0.017, 0.006), while patients with Sm ≥7cm/sec did not.*

Conclusion: *These results provide new insight into the hemodynamic effectiveness and potential clinical applications of EECP.*

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Keywords: *EECP• Echocardiography• TDI*

Introduction

Enhanced External Counterpulsation Therapy (EECP) has been studied for 45 years as a noninvasive method for the

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treatment of ischemic heart disease.1,2 Recently, EECP has been used successfully as therapy for patients with chronic stable angina inadequately controlled with medication and unsuitable for PCI (percutaneous coronary intervention) or CABG (coronary artery bypass graft surgery).3-5 EECP increases time to exercise-induced ischemia, reduces angina frequency and nitroglycerin use, and improves Canadian Cardiovascular Society classification (CCS) and quality of life.3,4,6-9 It has been reported that up to 15% of patients with angina meet the criteria for refractory angina.10

Although EECP is known to decrease symptoms in patients with angina, its role in patients with heart failure has only recently been investigated. Recent studies suggest EECP increases exercise capacity by increasing peak oxygen uptake and exercise duration and improving functional status and quality of life in patients with heart failure. With the help of these studies, FDA cleared the EECP therapy for treatment of heart failure in 2002.11-16

EECP is associated with an immediate and long-lasting increase in the blood flow of coronary arterial circulation,17,18 increasing endothelial shear stress19 and enhancing endothelial function by stimulating the release of the vasodilatory mediator nitric oxide and reducing the release of vasocontractile endothelin-1.20-22 Also, EECP stimulates collateral blood vessel development not only by increasing the release of angiogenesis factors such as vascular endothelial growth factor,23,24 basic fibroblast growth factor, and hepatocyte growth factor,20,24 but also by increasing monocyte chemoattractant protein 1 (a proinflammatory cytokine).

The present study sought to evaluate the effects of EECP on the echocardiographic parameters of systolic and diastolic function before and after a 35-hour course of EECP.

Study population

Twenty-five consecutive patients with refractory chronic, stable angina met the following inclusion criteria: (1) age>18 years; (2) symptoms of angina consistent with Canadian Cardiovascular Society classification II or III; (3) angiographically proven CAD; and (4) deemed a poor candidate for PCI or CABG.

Patients were excluded if they had any of the following: (1) unstable angina; (2) myocardial infarction in the preceding 6 weeks; (3) LV ejection fraction <25%; (4) significant valvular disease; (5) overt heart failure; (6) left main lesion>50%; (7) blood pressure >180/100mmHg; (8) a permanent pacemaker or ICD (Internal Cardiac Defibrillator); (9) AF (Atrial Fibrillation) rhythm or frequent PVC (Premature Ventricular Contraction) that interfered with EECP triggering; (10) severe peripheral vascular disease, phlebitis or deep vein thrombosis; and (11) bleeding diathesis or warfarin use with INR > 2.0.

Medication usage remained unchanged during this study and patients underwent echocardiography before and after EECP therapy.

Methods

EECP

All patients were treated with an EECP therapy system (Vasomedical, Inc., Westbury, New York), comprised of an air compressor, computer console, treatment table and an integrated cuff set with three pairs of pneumatic cuffs. Before treatment, the cuffs are wrapped around the calves and the lower and upper thighs of the patient, and ECG leads are placed. In synchrony with the patient's cardiac cycle, the EECP system inflates the cuffs with air in rapid sequence from the calves to the buttocks in early diastole, compressing blood vessels in the lower extremities and displacing venous and arterial blood towards the heart. At the end of diastole, the compressed air is released from all the cuffs simultaneously to rapidly remove the externally applied pressure and allow the vessels to reconform. Inflation increases diastolic blood pressure (diastolic augmentation) and venous return during diastole, while deflation reduces vascular impedance and cardiac workload during the subsequent systole. The EECP was applied in 35 hours divided into 60-minute sessions five days per week. During each session, the change in the patients' blood pressure wave was monitored by finger plethysmography. A cuff pressure of approximately 0.04 Pascal was applied so that the ratio of plethysmographically-measured diastolic peak pressure to systolic peak pressure was 1.5 times or higher.

Echocardiography

Standard echocardiography examinations were carried out in accordance with the recommendations of the American Society of echocardiography using a digital ultrasound machine (Vivid 3, GE Medical Systems, Inc.) with the patient in the left, lateral decubitus position. A variable frequency phased-array transducer (2.5-3.5-4.0MHZ) was used for two-dimensional, M-mode and Doppler imaging. All measurements were analyzed using the average of ≥3 cardiac cycles. Two-dimensional (2D) measurements of left ventricular (LV) volume were obtained from the apical 4-chamber view at end-diastole and end-systole, and left ventricular ejection fraction (LVEF) was calculated using the modified Simpson method.

Pulsed Doppler assessment of LV inflow was performed in the apical 4-chamber view with the sample volume placed at the level of the valve tips. The following measurements of global LV diastolic function were determined: peak velocity of the of E and A waves and the E/A ratio; deceleration time of the E wave (msec); and isovolumic relaxation time (msec), measured as the time interval occurring between the end of systolic output flow and transmittal E-wave onset by placing pulsed Doppler sample volume between the outflow tract and the mitral valve.

Pulsed Doppler myocardial imaging

Pulsed doppler myocardial imaging (DMI) was performed by spectral pulsed Doppler signal filters by adjusting the Nyquist limit within 15-20 cm/sec (close to myocardial velocities) and using minimal optimal gain. In the apical 4-chamber view, a 3.5-mm pulsed Doppler sample volume was placed on the basal septum of the LV at the level of mitral annulus. Myocardial systolic wave (Sm) and early diastolic wave (Ea) were measured.

Diastolic function grading

Normal LV diastolic function was diagnosed if the peak early diastolic transmitral flow velocity (E)/peak late diastolic transmitral flow velocity (A) ratio was between 0.75 and 1.5 and the E/Ea ratio was <10. Mild LV diastolic dysfunction was diagnosed if the E/A ratio was <0.75 regardless of the E/Ea ratio. Moderate LV diastolic dysfunction was diagnosed if the E/A ratio was between 0.75 and 1.50 and the mitral E/peak early diastolic myocardial velocity (Ea) ratio was >10. Severe LV diastolic dysfunction was diagnosed if the E/A ratio was >1.5 and the E/Ea ratio was >10.

Color Doppler M-mode imaging

Mitral inflow propagation velocity was evaluated from the apical 4-chamber view using color flow imaging to place a color M-mode cursor parallel to mitral inflow in the center of the flow stream. The aliasing velocity of 0.5 to 0.7 m/sec and signal was recorded at a fast sweep speed (100-200 mm/sec). The slope of the first aliasing velocity from the mitral valve to LV was measured.

Statistical analysis

All values were expressed as mean±SD. The paired t-test method was used to compare pre-treatment with post-treatment values and statistical significance was determined at a level of $p<0.05$.

Results

Twenty-five consecutive patients presenting for EECP therapy were enrolled in this study. Mean age of the patients was 57.8±9 years (range: 42 to 82 years) and eighteen were men (72%). Eighteen patients (72%) had three vessels and six patients (24%) had two-vessel disease, one patient (4%) had single vessel disease. Sixteen patients had history of CABGS (64%) (Table 1).

Table 1. Baseline characteristics

Mean age, range (years)	57.8, 42-82
Gender (men / women)	18
Coronary artery disease factors and revascularization status	
3VD	18(72%)
2VD	6(24%)
1VD	1(4%)
Left ventricular ejection fraction	
EF>50%	12(48%)
EF=31%-50%	8(32%)
EF<31%	5(20%)
Prior PCI	2(8 %)
Prior CABG surgery	16(64%)
Angina CCS class	
I	5 (20%)
II	13 (52 %)
III	7 (28 %)
IV	0

CAD, Coronary artery disease; CABG, Coronary artery bypass grafting; PCI, Percutaneous coronary intervention; CCS, Canadian cardiovascular society classification

Mean baseline end-diastolic volume (EDV) was 125.08±67.5 ml and end-systolic volume (ESV) was 73.6±60 ml, both of which reduced significantly after EECP therapy to 105±58.4 ml and 59.8±47.2 ml, respectively (both $p<0.01$). Mean LVEF was 46%±12.6% at baseline, which increased significantly to 51.5%±12% ($p<0.01$). Mean baseline Ea and Sm were 10±5.7 cm/sec and 9±5.44 cm/sec, respectively, and showed no significant change after EECP. Mean propagation velocity, E/Ea, and E/Vp before treatment were 42.40±13.79, 15.6±7.46, 2.05±0.90, respectively, and showed no change after EECP therapy. Mean diastolic function grade was 2.24±1.26 pre-treatment, and exhibited no significant change after therapy (Table 2).

Table 2 Changes in left ventricular function after EECP*

	Pre-EECP	Post-EECP	P value
LVEF (%)	46±12.6	51.5±12	<0.01
LVEDV (ml)	125.08±67.5	105±58.4	<0.01
LVESV (ml)	73.6±60	59.8±47.2	<0.01

*Data are stated as mean±SD

EECP, Enhanced external counterpulsation; LVEF, Left ventricular ejection fraction; LVEDVI, Left ventricular end diastolic volume; LVESV, Left ventricular end systolic volume

In a secondary set of analyses, patients were divided according to whether their baseline values fell above or below prespecified thresholds. EECP reduced ESV and EDV while it increased LVEF significantly (p=0.018, 0.013, 0.002, respectively) in patients with baseline LVEF≤50%. There was no such change in those with baseline LVEF>50%.

Patients with E/Ea<14, who were expected to have low left atrial pressure, had no improvement in EDV, ESV, and LVEF after EECP treatment, whereas those with E/Ea ≥14, who were expected to have elevated LAP, had a significant reduction in EDV and ESV (p=0.038 and p=0.032, respectively) and an increase in LVEF (p=0.007). Similarly, patients with normal diastolic function or mild diastolic dysfunction (impaired relaxation) had no significant change in EDV, ESV, and LVEF after EECP treatment, while patients with moderate to severe diastolic dysfunction (decreased LV compliance) had significantly improved ESV, EDV, and LVEF (p=0.014,0.032,0.027 respectively).

Patients with Ea<7 cm/sec prior to EECP showed a significant improvement in EDV, ESV, and LVEF after therapy (p=0.024, 0.015, 0.001), while those with Ea≥7cm/sec exhibited no significant change. Similarly, patients with baseline Sm<7cm/sec showed a significant improvement in EDV, ESV, LVEF after EECP (p=0.016, 0.017, 0.006), while those with Sm≥7cm/sec showed no significant change after EECP.

Discussion

The present study is one of the first echocardiographic studies of patients treated with EECP for chronic stable refractory angina pectoris focusing on tissue Doppler imaging. Findings in this study demonstrated that EECP significantly increases LVEF and decreases EDV and ESV. Therefore, systolic function and LV volumes improve after EECP therapy.

Urano et al. reported that EECP treatment improved not only LV dilation, but also myocardial blood flow.22 EECP treatment is also associated with an immediate increase in blood flow in multiple vascular beds, including the coronary arterial circulation.16 As a result, EECP increases endothelial shear stress by increasing blood flow,10 which enhances endothelial function7 by stimulating the release of vasodilatory mediator nitric oxide and reducing the release of vasocontractile endothelin-1.19,20,23 These changes are progressive during the course of therapy24 and serve to explains improved coronary perfusion and vasodilation after EECP.

The result of this study shows no significant change in diastolic function parameters such as Ea, propagation velocity, E/Ea, E/Vp, and diastolic function grade. Similarly, in a recent study, no significant change in fractional shortening and diastolic function was observed. There was a reduction in the area of inducible ischemia at dobutamine stress echocardiography after EECP; nevertheless, perhaps due to a small sample size, it was not significantly different.25

It was noted that the patients with lower LVEF (≤50%) and Sm velocity of the septal annulus (<7cm/sec) had more significant changes in LVEF, EDV, and ESV than the patients with higher E/Ea (≥14) and lower Ea velocity of septal annulus (<7cm/sec). Therefore, in our study the patients with more advanced systolic and diastolic dysfunction, and higher LV end diastolic pressure and left atrial pressure, had more improvement in LVEF, EDV, and ESV, which is in accordance with results reported by Novo et al. regarding a trend that patients who benefited most were those with worse systolic function and severely compromised segmental kinesis.25

Results from this study provide new insight into the hemodynamic effects of EECP therapy in patients with coronary artery disease and either preserved or impaired left ventricular function. Effects of this safe, noninvasive therapy in individual patients can be more readily anticipated and clinical application of EECP may hold the promise of being more specifically prescribed in the near future.

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Original Article

Impact of Dialysis on Open Cardiac Surgery

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Abstract

Background: *Dialysis patients frequently have coronary artery disease but are regarded as high risk patients for coronary artery bypass grafting (CABG).*

Methods: *Between February 2002 and September 2006, seventeen dialysis-dependent patients underwent isolated CABG at our center. CABG was performed under cardiopulmonary bypass (CPB) for all the patients. All cases had been maintained on hemodialysis and the duration of preoperative hemodialysis ranged from 6 to 24 months (mean 13.4±6.4). The patients' characteristics, clinical and operative data as well as perioperative and mid-term outcome were reviewed.*

Results: *All patients were men with a mean age of 53±8.4 years. Mean preoperative ejection fraction was 45.5%±10.4% (range 25 to 60%). One internal mammary graft was used in 16 (94.1%) patients. Cardiopulmonary bypass and aortic cross-clamp times were 71.3±18.7 and 40.5±8.3 minutes respectively. The more frequent complication was prolonged mechanical ventilation in 2 (11.7%), there was no perioperative mortality. In mid-term follow-up (mean time: 11.8±9.5 months) the mid-term mortality rate was 20% (3 patients).*

Conclusion: *CABG in chronic renal dialysis patients can be accomplished with acceptable short and mid-term morbidity and mortality.*

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Keywords: *Coronary artery bypass grafting• Dialysis • Mortality*

Introduction

Dialysis treatment is one of the great technical achievements of 20th century medicine; it provides the chance of prolonged life in end-stage renal disease patients.[1] Cardiac disease is the cause of death in 44% of long-term dialysis patients.[2] Renal transplantation has been documented to lessen complication associated with renal failure. The underlying coronary artery disease must frequently be addressed to allow uncomplicated dialysis. It is imperative that it be considered before kidney transplantation as well, to assure a successful result.2 Although there has been tremendous advancement in the use of percutaneous transluminal coronary angioplasty (PTCA) for treatment of coronary artery disease, coronary

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artery bypass grafting (CABG) remains the gold standard for revascularization.[3]

The goal of this study was to describe perioperative and mid-term results of CABG in end-stage renal disease (ESRD) patients.

Methods

Seventeen patients with ESRD maintained on chronic hemodialysis who underwent elective, isolated CABG procedure at Tehran Heart Center from February 2002 through September 2006 were retrospectively analyzed.

Patients' data included the following variables: age, gender, coronary risk factors (such as hypertension, diabetes mellitus, hyperlipidemia, and cigarette smoking) as well as New York Heart Association class (NYHA), Canadian Cardiovascular Society angina class (CCS), preoperative angiographic profiles (total number of significantly diseased coronary arteries and ejection fraction). All variables were based on definitions of the Society of Thoracic Surgeons and were regularly reported to the national cardiac database.

We also reviewed operative data including number of distal anastomosis, use of internal mammary artery (IMA), cardiopulmonary bypass, aortic cross clamp time and quality of coronary arteries, as well as postoperative complications and mortality.

The mean time of preoperative hemodialysis was 13.4±6.4 months (6 to 24 months). Surgical procedure details included median sternotomy, cardiopulmonary bypass (CPB) at normothermia or mild hypothermia, with the use of a roller pump (flow rate, 1.8–2.4 L/min/m2) and membrane oxygenator. Hemofiltration was used for all cases. All patients received Cloxacillin 1.5 g every 6 hours and Ceftizidim 1 g intravenously every 12 hours for antimicrobial prophylaxis from 30 minutes before surgery to 72 hours postoperatively. All patients underwent hemodialysis on the day prior to surgery and patients underwent their usual hemodialysis postoperatively. One internal mammary graft was used in 16 out of 17 patients. In the case of arteriovenous fistula, free IMA was used. All other grafts were saphenous vein.

All patients were evaluated for a follow-up period of 1 to 34 months (mean 11.8±9.5). Follow-up was accomplished by phone and use of the last out patient fills. Mid-term result evaluation included changes in anginal class (CCS), NYHA class, mortality, morbidity and successful kidney transplantation.

Continuous variables were expressed as mean±standard deviation. Discrete variables were presented as percentages.

Results

Patients' characteristics, risk factors and pre operative profiles are shown in table 1.

Table 1. Demographics and preoperative factors

Patients Characteristics	Value
Age (Y) (mean±SD)	53 ± 8.4
Male sex	17 (100%)
Diabetes Mellitus	10 (58.8%)
Hypertension	8 (47.1%)
Hyperlipidemia	10 (58.8%)
Smoker	7 (41.2%)
Triple vessel disease	13 (76.5%)
Ejection fraction (%) (mean±SD)	45.5 ± 10.4
CCS class (mean±SD)	2.0 ± 0.7
NYHA class (mean±SD)	1.8 ± 0.8

CCS, Canadian Cardiovascular Society Angina class; NYHA, New York Heart Association class

All patients were men with a mean age of 53±8.4 years. Three patients (17.6%) had documented myocardial infarction. Mean preoperative ejection fraction was 45.5%±10.4% (range 25 to 60 %).

Total number of distal anastamosis was 3.7±0.7. The qualities of coronary arteries were severely diseased in 8 (42.1%), moderate in 7 (41.2%) and good in 2 (11.8%) of the patients. Cardiopulmonary bypass time and aortic cross-clamp times were 71.3±18.7 and 40.5±8.3 minutes respectively.

The postoperative profiles are shown in table 2.

Table 2. Postoperative factors*

Variable	Value
Mechanical ventilation time (hours)	15.9 ± 10.1
ICU stay (hours)	69.5 ± 46.8
Hospital stay (days)	10.94 ± 3.4
Perioperative mortality	0
Mid-term mortality	3 (20%)

* Data are stated as mean±SD

Mean duration of mechanical ventilation was 15.9±10.1 hours. Length of stay in intensive care was 69.5±46.8 hours. The complications were as follow: prolonged mechanical ventilation in two patients (11.7%), atrial fibrillation in one (5.9%) and pericardial effusion in one. Persistent bleeding or tamponade were not seen.

All postoperative patients were able to undergo dialysis on early and late follow-up without interfering angina. We did not have perioperative mortality (30 days after operation) in our group. During mid-term follow-up of 11.8±9.5 months, the mortality rate was 20% (3 patients). Two patients died 3 months after surgery because of infection and renal failure and one patient 1.5 years after surgery because of

renal failure. Mean preoperative CCS class changed from 2.0±0.7 to 1.5±0.7 in a mid-term follow-up but NYHA class did not show any change (1.8±0.8 to1.8±0.5). Five out of seventeen patients (29.4%) underwent kidney transplantation successfully after CABG.

Discussion

Although dialysis prolongs the lifespan and life quality of patients with ESRD, dialysis still has only an overall 5-year survival rate of 55% to 60%.4 It is widely accepted that patients with end-stage renal disease have an accelerated rate of atherosclerosis and an increased mortality rate from CAD.1 The higher incidence of CAD in this patient population can be attributed to the presence of comorbid conditions that include hypertension, hyperlipidemia, renal anemia and fluid overload by arteriovenous shunt, heterotopic calcification due to secondary hyperparathyroidism and abnormal carbohydrate metabolism that leads to accelerated atherosclerosis.1,5 Both renal dysfunction (RD) and ESRD are important risk factors for patients undergoing cardiopulmonary bypass. Despite this risk, increasing number of patients with RD and ESRD are being referred for coronary revascularization and CABG in particular.[6]

In our study, for all the patients who underwent CABG, perioperative mortality was not seen. Previous studies have suggested a survival benefit for CABG in dialysis patients.3,7 Cooper et al.6 reported operative mortality rose inversely with declining renal function, from 1.3% for those with normal renal function to 9.3% with severe RD not on dialysis and 9.0% for those who were dialysis dependent.

None of our 17 patients required a balloon pump for cardiopulmonary bypass weaning. Perioperative complications in our group were as follow: prolonged mechanical ventilation, atrial fibrillation, and pericardial effusion. There is no cerebrovascular accident (CVA) in our patients which is not paralleled in similar reports: Kaul and coworkers,8 11%, Blum et al.9 8% and Franga and associates,2 7%.

In previous studies actuarial overall survival at 5 years was 32.0% ± 12%2 and the adjusted 8-year survival rates were 44.8% with CABG.10 Our mid-term mortality in mid-term follow up was 20%. Causes of death were unrelated to cardiac problems (infection and end-stage renal failure).

A frequent indication for operation was angina interfering with routine hemodialysis and the great majority of patients enjoyed excellent relief of angina immediately after operation.2

In the present study, all our patients were able to undergo dialysis on early and mid-term follow-up without interfering angina postoperatively and 29.4% of the patients underwent kidney transplantation successfully after CABG.

The low numbers of hemodialysis cases along with short follow-up period were the study limitations.

Conclusion

Although dialysis-dependent patients are understood to be a high risk group for cardiac operative outcomes, but CABG can be performed in them with acceptable short and mid-term morbidity and mortality.

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Original Article

Acute Rheumatic Fever in the North East of Iran: A Study of 80 Cases

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Abstract

Background: *To evaluate the frequency, clinical presentation and cardiac involvement of children with RF in the North-East of Iran.*

Methods: *A case series analysis was conducted on 80 patients with acute rheumatic fever (ARF), who were hospitalized at Ghaem hospital in Mashad between 1994 and 2000, were studied. Laboratory tests and results from echocardiographic examinations, and clinical findings were analyzed. All patients received standard care for children with ARF. The X^2 test was used for comparison of binary data.*

Results: *When compared to similar studies from developed countries, our study demonstrates a decreased frequency of RF in North-East Iran over the past few years. However, it is still a major health problem and the most common cause of acquired heart disease in childhood. The distribution of the major modified Jones criteria in our study is slightly different from that described in the literature, with a higher incidence of carditis.*

Conclusion: *It appears that carditis is endemic in this region. Considering the high morbidity and complications involved in this disease, there is an immediate need for effective preventive programs for the initiating cause streptococcal infections, especially since it is treatable.*

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Keywords: *Rheumatic fever • Developing country • Children • Carditis*

Introduction

In 1994, WHO estimated the annual incidence of Rheumatic Fever/Rheumatic Heart Disease (RF/RHD) as approximately 10 million individuals throughout the world, accounting for 400 000 deaths per year; the majority are from the Asia-Oceania region. It also estimated that the carrier rates of Group A Beta hemolytic streptococcal infection (GABHS) in different regions is 7.5-39% among school age children. This global issue has been the subject of many international studies and has prompted WHO to reintensify its RF/RHD program with the participation of 16 countries from five regions, namely Africa, the Americas, Eastern Mediterranean, South-East Asia and Western Pacific. The long-term objective of this program is to reduce the morbidity and mortality associated with RF/RHD through primary health care efforts.1

Rheumatic fever (RF) is the most common cause of acquired heart disease in children and young adults in developing countries.2 Although the incidence of ARF has declined in the United States and Western Europe, it has remained high in developing countries.3-6 Known suspected contributing factors include low socio-economic status, overcrowding, malnutrition,

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and low government health subsidy.1

Carditis is the most important and serious manifestation of the disease because it can be lethal or lead to the development of permanent heart disease.6-9 In order to evaluate the clinical presentation and cardiac involvement of children with RF, we conducted a case series study in children admitted to our hospital with the diagnosis of acute RF from 1994 to 2000.

Methods

This was a case series analysis conducted on patients less than 16 years of age with the discharge diagnosis of ARF. These patients were admitted to Ghaem hospital, the largest tertiary referral center and a major teaching hospital in Mashad.

All patients were admitted with the diagnosis of ARF. Diagnostic criteria was based on the modified Jones criteria.2 63 of the patients (79%) were experiencing their first attack and the remaining 9 cases (11%) were admitted due to disease recurrence.

Eight cases (10%) were suspected to be recurrences, but there was no scientific proof.

Information on sex, age, preceding history of pharyngitis, family history of RF, and demographic distribution of the patients was collected. An initial diagnostic evaluation consisted of a full blood count, erythrocyte sedimentation rate (ESR), C-reactive protein, streptococcal serology, throat and blood cultures, midstream urine, ECG and chest x-ray. M-mode, two-dimensional and color Doppler echocardiography was done for all of patients.

Initial clinical assessment consisted of daily measurements of heart rate (awake and asleep), temperature, joint involvement, and presence or absence of rash, chorea, or nodules. The blood parameters assessed weekly, included: ESR, C-reactive protein, and streptococcal serology. Quiescence of disease activity was ascertained when ESR was below 30 mm/h, joint symptoms disappeared clinically and relief of cardiac disease was assured at serial evaluations. Cardiac evaluation consisted of standard clinical and echocardiograph assessment.

Valvular regurgitation was graded as mild, moderate and severe. Mild regurgitation was considered subclinical but pathological regurgitation. A massive holodiastolic (aortic regurgitation) or holosystolic (mitral regurgitation) color jet in Doppler echocardiography was the criterion for pathological regurgitation. Mitral regurgitation was considered moderate if the jet filled half or less of the left atrium; any amount greater than that accounted as severe. A jet diameter less than 30% of the diameter of the left ventricular outflow was considered moderate while greater amounts were classified as severe aortic insufficiency. On the basis of this grading, about one fourth of the patients had mild, one half had moderate and another one fourth had severe valvular regurgitation.

All patients received standard care for children with ARF. The X^2 test was used for comparison of binary data.

Results

Population

In this article we have studied Clinical data from 80 patients with ARF, who were hospitalized at Ghaem hospital in Mashad between 1994 and 2000.

There was a slight male predominance (56% of the patients were males). The mean age on hospitalization was 10.29±2.55 years (mean ± SD), and ranged from 5 to 16 years. Twenty percent of patients were less than 8 and 80% were less than 12 years of age.

There was a positive family history of RF in 14% of patients. A preceding history of pharyngitis was reported in 78% of the patients.

Laboratory Findings

The most common laboratory findings were as follows; leukocytosis in 84% of the patients, anemia in 62%, elevated erythrocyte sedimentation rate (ESR) (>40 mm/hr) in 90% and positive C-reactive protein (CRP) in 85% of patients. Anti-streptolysin O (ASO) titers were elevated in 87% of patients. Positive Throat cultures for GABHS infection, scarlet fever and both raised ASOT and positive throat culture was 3.5%, 3.5% and 90.5% respectively.

Demographic Distribution

Sixty-one percent of the hospitalized patients were from Mashad's urban areas, and the rest were from rural areas. The socioeconomic status of 78 patients (86%) was low. Eighty one percent of patients were in families with 4 to 8 members. Most of our patients (63%) were admitted in winter and spring (figure1).

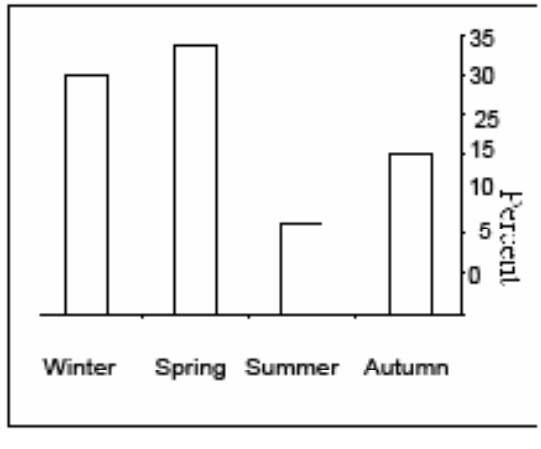

Figure1: Frequency of patients with acute rheumatic fever in each season

Incubation period was less than 30 days in 85% of patients. The frequency of ARF declined from 19 patients in 1994 to 5 patients in the year 2000 (figure 2).

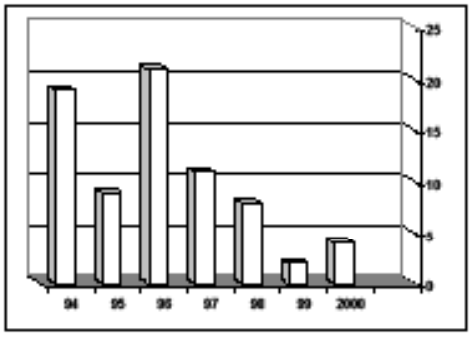

Figure 2: Frequency of acute rheumatic fever in mashad between 1994-2000

Jones Criteria

Carditis occurred in 81%, Arthritis in 69%, Sydenham's chorea in 8%, and erythema marginatum in 3% of patients. Subcutaneous nodules were present only in one patient. Fever occurred in 71% and arthralgia in 76% of patients.

Cardiac Manifestations

Valvulitis occurred in 80% of patients with cardiac involvement. MR was the most common presentation of valvulitis (75%). Aortic insufficiency was seen in 13% of patients. Tricuspid insufficiency and Mitral stenosis developed in 1.3%and 5% of patients respectively. Carditis, valvulitis and cardiomegaly was significantly more common in female patients (p=0.03, p=0.01, p=0.02 and p=0.04 respectively). Pericardial effusion occurred in 2.5% of patients. Acute congestive heart failure (CHF) on first presentation occurred in 5% of patients.

ECG & X-Ray findings

The least prevalent minor criteria was prolonged P-R interval which was seen in 15% of the studied population; the most common ECG finding was sinus tachycardia (50%). ST and T changes were seen in 2.5% and 1.3% of patients respectively. The most common X-Ray findings were cardiomegaly (37%). Atrial enlargement was seen in 16.5% of patients.

Medical Treatment

Non-steroidal anti-inflammatory therapy was used in 86% of cases. Steroid was used for 42% and digoxin for 11% of patients with carditis.

Discussion

Ironically, in many instances, the first attack of RF is highly treatable with primary prophylaxis and the recurrences with valvular damage are highly preventable by adherence to secondary prophylaxis.

Unfortunately, preventive programs for eradicating GABHS are beyond the realm of many healthcare systems. In underdeveloped countries, the prevalence rate of RF/RHD remains an unacceptably high 12.6 cases per 1000 school children in Zambia, 10.2 cases per 1000 school children in Sudan, and 7.9 cases per 1000 school children in Bolivia.10

WHO estimation reveals that therapy of 1000 sore throats prevents a single case of RF. In Asia, with the exception of industrialized countries like Japan and Singapore, RF and RHD continues to drain human and government resources with millions of dollars in secondary prevention. Thus RF/RHD continues to be one of the health priorities in countries with limited resources.1

When our study was compared to the reported series of RF in the literature, there were both similarities and differences.3,6-8,11-13 When compared to similar studies from developed countries, our study showed that the frequency of RF has decreased in recent years in North East of IRAN probably due to earlier diagnosis and treatment of streptococcal pharyngitis. The age of hospitalized patients (10.3+2.5 years) was similar to the Lebanon study (11.1+2.9 years).14 The gender predominance was also the same (slight male predominance). The majority of our patients came from large low-income families. 81% of patients belonged to large families with 4-8 members. Most of our patients were from Mashad and its peripheral areas (that are relatively urban areas), which is probably a referral bias. About 50% of our patients were from poor socio-economic conditions (workers and farmers). This finding highlights the need for an urgent control program and early detection and treatment of streptococcal infections in this group. Most of our patients (63%) were admitted in winter and spring, probably due to higher stereptococcal infections of upper respiratory tract. About 44% of our patients had a history of antibiotic therapy for pharyngitis before admission.

The incidence of arthritis and carditis were 69% and 81% respectively. Comparison of this study with similarly designed studies5,15-18 shows that in our study the incidence of carditis is more frequent than arthritis. It seems that carditis may be endemic to the east of Iran, thus rheumatic heart disease prevention programs should remain the central goal. The mitral and aortic valve involvement in this study (MR in 75% and AI in 13%) were comparable to that reported in the literature.5,15,17,19,20 MR, vulvulitis and increased PR interval were significantly and indefensibly more common in female gender (p value<0.05).

Conclusion

Due to the established high morbidity and severe complications of ARF, this study reaffirms the need for

effective preventive programs for streptococcal infections, especially since this cause is treatable. Public health education by all available media especially through video films is also recommended. Although the incidence of ARF is declining in comparison to previous years, this study showed that ARF is endemic in this area. This study confirmed that the incidence of ARF is high in low socio-economic groups and highlights the need for an urgent control program. Greater effort should be made in the early detection and treatment of streptococcal infections.

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Original Article

Predictors of Long-term Outcome in Patients with Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention: A single center registry (THCR)

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Abstract

Background: *This study sought to access differences in long-term (9 months) outcomes between Acute Coronary Syndrome (ACS) patients who undergo early intervention compared to Percutaneous Coronary Intervention (PCI) in stable and refractory conditions.*

Methods: *Data originated from Tehran Heart Center Registry- interventional cardiology (THCR-IC) and consisted of 1267 patients divided into two categories; 227 patients had features corresponding to acute coronary syndromes (17.9%) and 1040 patients suffered from stable angina (82.1%). They were admitted between April 3, 2003 and April 25, 2004.*

Results: *The clinical success rate of PCI was higher in ACS (97% vs. 94%; P=0.037), while In-hospital complications were similar in both groups. During the follow-up period, clinical restenosis was not significantly different and the overall number of re-interventions caused by restenosis or progression was not more frequent in ACS patients. Also, 1.3% of ACS and 0.4% of SA patients died, but the difference was not statistically significant (P=0.16). Finally, Major Adverse Cardiac Events (MACE) showed no significant difference (5.2% vs. 3.9%; P=0.42). Multivariate analysis showed that female sex (OR=25.6; P=0.003) and previous history of PCI (OR=8.4; P=0.016) were the only strong independent risk factors for major adverse cardiac events. Analyzing ACS patient outcomes using Mantel-Hanzel analysis showed that the female sex was the only factor which strongly increased the incidence of MACE.*

Conclusion: *Both ACS and SA patients who underwent coronary intervention had similar in-hospital and composite major adverse cardiac events, nevertheless female gender must be considered as an independent risk factor for major adverse cardiac events especially in patients with acute coronary syndrome who undergo PCI.*

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Keywords: *Acute coronary syndrome • PCI • Outcome*

Introduction

Patients with Acute Coronary Syndromes are at risk for adverse cardiac events.1 In a patient with unstable angina, the risk of acute myocardial infarction or death is high: 20% of patients within 30 days after the onset of symptoms and 25% in 6 months.2 Mortality in this group of patients varies from 1.5 to 2.5 after six weeks to 7-10% after a year.3 The

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general term "Acute Coronary Syndrome" encompasses a wide variety of symptoms in patients with variable history and varying pathophysiological mechanisms.

Since it's inception in 1977, Percutaneous Coronary Intervention (PCI) has become the most common method for coronary revascularization. Randomized trials have demonstrated that patients presenting with an acute coronary syndrome (ACS) who subsequently undergo routine angiography and revascularization, predominantly by PCI, have improved outcomes compared with patients not treated with a routine invasive strategy.4-6

It seems that PCI for ACS patients has been associated with worse procedural, in-hospital and long term outcomes compared PCI under stable angina and elective conditions. A slightly lower success rate and higher peri procedural complication rate has been well documented in literature.7

Despite this fact, PCI especially under protection of platelet glycoprotein (GP) IIb/IIIa receptor inhibitors is a widely adopted treatment strategy for acute coronary syndromes without persistent ST-segment elevation (NSTACS).8

A consequence of PCI, however, is restenosis. There have been reports that restenosis rates with unstable angina are higher than rates with stable angina,9-11 although others demonstrated no difference.12,13 However, the exact relation between restenosis and the effect of timing of PCI in ACS is largely unknown.

It seems to be most important for an interventionist to recognize-as main predictor (the elements that are more effective on individual patient outcome). With this awareness, an operator can decide efficiently about the treatment strategy; whether PCI as an early invasive management is suitable for the operation at hand.

These matters promoted us to perform the present study in Tehran heart center Interventional cardiology registry to assess the short and long-term outcomes and related predictors in acute coronary syndrome (ACS) and to compare those to the outcomes of stable angina patients undergoing PCI with the same conditions.

Methods

Design and setting

The present retrospective study was performed in Tehran Heart Center Registry of Interventional cardiology (THCR-IC); that is a single center registry which contains demographic and clinical features plus previous medical antecedents such as risk factors, procedural details and follows up data.

Study population

During the period April 3, 2003 to April 25, 2004, 1406 patients underwent PCI. 139 patients were excluded due to Primary PCI in the setting of acute ST-elevation MI (n=36), incomplete follow-up (n=103). 1267 patients remained in our study. Of these, 1040 (82.1%) were classified as the stable angina (SA) group and 227 (17.9%) as acute coronary syndrome (ACS) group.

Definitions

Acute Coronary Syndrome (ACS) is clinically defined as ST-elevation Myocardial Infarction (STEMI), non-ST elevation myocardial Infarction (NSTEMI) and unstable angina of high and low risk types. In the setting of our present study, we selected patients who had the features of ACS within two weeks of PCI.

Unstable angina was defined according to Braunwald classification and described as the sudden appearance and/or worsening of angina, with more frequent and prolonged attacks occurring at rest or on efforts that were previously well tolerated.14 Stable angina was defined according to the Canadian Cardiovascular Society classification (classes 1 through 4); patients displaying effort symptoms according to class I-III were classified as SA group.15

Acute myocardial Infarction (AMI) included patients with a history of NSTEMI in the last two weeks or ST-elevation myocardial infarction from 24 hours to two weeks after the acute event.

Baseline and clinical characteristics

These characteristics included age, sex, and other demographic data, patients' medical history such as previous history of AMI, previous systemic hypertension, diabetes mellitus and other risk factors. Also, lab data and echocardiographic features as well as the diagnosis of stable or unstable angina pectoris were considered.

Angiographic and procedural characteristics

Lesion morphology was classified according to the modified American Heart Association/ American Collage of Cardiology (AHA/ACC) classification taskforce.16 Reference vessel diameter, present degree of stenosis and lesion lengths were estimated visually. It was the responsibility of the operators to select the treatment strategy and record selected device, procedural complications and outcome on detailed forms. Stent placement procedures were performed according to standard methods; the size of the balloon and the pressure used during dilation were dependent on the operator's discretion.

Angioplasty procedure

PCI was carried out with the aid of the standard techniques and pharmacotherapy, as applicable at the time. Routine

preprocedure medication included: ASA 100-325 mg daily and Clopidogrel (Plavix) 600 mg (either 75mg per day for 5 days, 300mg 24 hours before or 600mg 4-6 hours before the procedure), Intravenous Heparin 7500-10000U during procedure and in selected patients, for 12-24 hours following angioplasty. Other medications before, during, as well as after the procedure were administrated according to the clinical situation and concomitant disorders at the discretion of the attending cardiologist.

Follow-up

Follow-up data were obtained from hospital charts through the follow up clinic and supplemented by a structured telephone interview with the patients or one of his or her immediate relatives conducted by an educated general practitioner.

Endpoints

The primary endpoint of this study was In-hospital complications including death, Q or non-Q-wave MI or need for emergency bypass surgery. With due attention to this definition, we descript success rate in our study. Angiographically, success is residual stenosis less than 30% in the target vessel and clinical success is defined as angiographically successful PCI without any severe In-hospital complication. Secondary endpoints consisted of Major Adverse Cardiac events (MACE) including death, non-fatal myocardial infarction and target vessel revascularization (CABG or Repeated PCI in the target vessel).

Statistical analysis

Continuous variables are expressed as mean±SD, and dichotomous variables as frequencies. Categorical variables were compared using the chi-square test and continuous variables by using student t test and p values < 0.05 were considered statistically significant. The impact of different baseline characteristics on outcome was first tested using a simple regression model. Those variables that were significantly associated with any of the measured outcomes were then evaluated with mantel-Hanzel statistics and multiple stepwise regression models using the Cox proportional hazards model. The impact on outcome was expressed as odds ratios with 95% confidence intervals.

Results

The study population consisted of 1267 patients who underwent PCI, of which 227 (17.9%) had the features of acute coronary syndrome and 1040 (82.1%) experienced only stable angina.

Baseline clinical and demographic characteristics of patients have been detailed in Table 1.

Table 1. Baseline clinical and demographic characteristics

	Acute coronary Syndrome	Stable Angina	P value
No of cases (%)	227(17.9)	1040(82.1)	
Age	58.26±0.71	56.97±0.32	0.092
Female Gender	78 (34.3)	293 (28.1)	NS
Clinical characteristics			
Renal insufficiency(Cr>1.5 mg/dl)	27 (11.8)	88 (8.4)	NS
MVD	75 (33)	448 (43.07)	NS
EF< 40%	44 (0.4)	150 (14.4)	NS
Positive Family History	70 (30.8)	236 (22.6)	0.009
Hyperlipidemia	88 (38.7)	479 (46)	0.045
Hypertension	93 (40.9)	320 (30.7)	0.003
Diabetes mellitus	56 (24.6)	230 (22.1)	NS
History of smoking	81 (35.6)	376 (36.1)	NS
History of Unstable Angina	168 (74)	253 (24.3)	<0.001
History of MI	106 (46.6)	356 (34.2)	<0.001
Prior CABGs	9 (3.9)	30 (2.8)	NS
Prior PCI	15 (6.6)	60 (5.7)	NS

Categorical variable are expressed as N (%) & continuous variable are expressed as mean±SD
MVD, Multi vessel disease; EF, Left ventricular ejection fraction; CABG, Coronary artery bypass grafting; PCI, Percutaneous coronary intervention

According to this, many/most patients with ACS had a previous experience of myocardial infarction; also more ACS patients had positive family history of CAD and suffered from hypertension. However, hyperlipidemia was significantly more common in SA patients. Furthermore, a larger number of patients with ACS had impaired left ventricular function. Except these findings, the two groups were similar in clinical and demographic characteristics.

Angiographic and lesion characteristics

As demonstrated in table 2, of the 1754 treated lesions, 301 lesions were in ACS and 1453 lesions were in SA patients. According to American Heart Association (AHA/ ACC) classification, lesions with type B2 and C, eccentric and thrombotic lesions were more frequent in ACS patients. Diseased vessel in ACS patients had significantly greater diameter (RVD), while lesion length was often similar in both groups.

Table 2. Angiographic and lesion characteristics

	Acute Coronary Syndrome	Stable Angina	P value
No of arteries	301(17.1)	1453(82.9)	
RVD(mm)	3.02±0.41	2.95±0.40	0.006
Lesion length(mm)	15.64±7.07	15.42±7.28	NS
Target territory			
LAD	159 (52.8)	761 (52.3)	NS
LCX	61 (20.2)	339 (23.3)	NS
RCA	73 (24.2)	323 (22.2)	NS
Lesion Characteristics			
Type B2 and C	149 (49.5)	633 (43.5)	0.004
Ostial	13 (4.3)	64 (4.4)	NS
Proximal	69 (22.9)	387 (26.6)	NS
Long (11-20mm)	135 (44)	693 (47)	NS
Diffuse (>20mm)	40 (13.2)	199 (13.6)	NS
Calcification	5 (1.6)	15 (1.0)	NS
Bifurcation	23 (7.6)	109 (7.5)	NS
Eccentric	73 (24.2)	278 (19.1)	0.043
Thrombus	17 (5.6)	25 (1.7)	<0.001
Total occlusion	29 (9.6)	143 (9.8)	NS

Categorical variable are expressed as N (%) & continuous variable are expressed as mean±SD
RVD, Reference vessel diameter; LAD, Left anterior descending artery; LCX, Left circumflex artery; RCA, Right coronary artery

Procedural and early outcomes

As detailed in table 3, length and diameter of stents used in ACS patients compared with stable angina patients were significantly higher. Also, the percent of preprocedural stenosis was higher in ACS while SA patients had more residual stenosis. The clinical success rate of PCI was higher in ACS while In-hospital complications were similar in both groups.

Table 3. Procedural variables

	Acute Coronary Syndrome	Stable Angina	P value
Preprocedural stenosis (%)	91.38±8.6	88.1±10.2	<0.001
Post procedural stenosis (%)	2.90±0.70	5.54±0.45	0.015
Stent diameter (mm)	3.06±0.37	3.00±0.36	0.015
Stent length (mm)	16.98±5.57	16.11±5.36	0.018
Success rate	292 (97)	1366 (94)	0.037
In-hospital complications	22 (7.3)	79 (5.43)	NS

Categorical variable are expressed as N (%) & continuous variable are expressed as mean±SD

Following up and late outcomes

Follow up data (table 4) were available in 1130 (89%) patients from among the 1267 studied (92% of ACS and 88% of SA patients). Follow up duration was slightly more in SA patients which does not seem to be clinically significant (8.9±2.3 months in SA and 8.5±2.4 in ACS). Clinical restenosis was not significantly different in the two groups and the overall number of re-interventions caused by restenosis or progression, as well as the repeat PCI or CABG was not more frequent in ACS patients. During the follow up, 1.3% of ACS and 0.4% of SA patients died, but the difference was not statistically significant (P=0.16). MACE showed no significant difference (5.2% vs. 3.9%) during the follow-up period.

Table 4. Follow-up data

	Acute Coronary Syndrome	Stable Angina	P value
Follow up duration (m)	8.52±2.45	8.95±2.31	0.019
Nonfatal MI	0	7 (0.6)	NS
TVR	9 (3.9)	31 (2.9)	NS
CABG	6 (0.4)	14 (1.3)	NS
Repeated PCI	3 (1.3)	20 (1.9)	NS
TLR	3 (1.3)	12 (1.1)	NS
Death	3 (1.3)	5 (0.4)	NS
Any MACE	12 (5.2)	41 (3.9)	NS

Categorical variable are expressed as N (%) & continuous variable are expressed as mean±SD
MI, myocardial infarction; TVR, Target vessel restenosis; TLR, Target lesion restenosis; CABG, Coronary artery bypass grafting; PCI, Percutaneous coronary intervention; MACE, Major adverse cardiac events

The repeat PCI or CABG was not more frequent in ACS patients. During the follow up, 1.3% of ACS and 0.4% of SA patients died, but the difference was not statistically significant (P=0.16). The Major Adverse Cardiac Events (MACE) showed no significant difference (5.2% vs. 3.9%) during the follow-up period.

Multivariate analysis

In view of the fact that differences were encountered in baseline, lesion and procedural characteristics, which might confound the long term outcomes especially the major adverse cardiac events, the Mantel-Hanzel and multivariate logistic stepwise regression analysis was carried out. After considering all factors which might have an effect in MACE, we found that female sex (OR=25.6; P=0.003) and previous history of PCI (OR=8.4; P=0.016) were the only strong

independent risk factors for major adverse cardiac events. Additional statistical analysis with Mantel-Hanzel method showed that the female sex was the only factor which strongly increased the incidence of MACE. It must be considered that female gender frequency and prevalence of previous PCI were not different between the two groups.

Discussion

PCI is an attractive therapeutic option in ACS that is fraught with risk not seen in patients with stable angina. Injured, 'unstable' plaque, intraluminal white, platelet-rich thrombus, systemic coagulation and fibrinolytic disturbances create a very specific situation. Thus, lower clinical success and higher complication rates in ACS patients undergoing PCI is not unexpected.7,17 Unlike some studies, the present study demonstrated higher clinical success and similar in-hospital complication rates in ACS patients.

Surprisingly, we found no difference concerning early outcome in ACS compared to SA patients. A higher incidence of restenosis after PCI in patients with ACS was described by many investigators, but not all.18-20 In our experience, clinical restenosis rate (TLR and TVR) is not significantly more frequent in ACS patients. Also, the present study showed no difference in other long-term outcomes such as need for revascularization, death and composite of major adverse cardiac events between ACS and SA patients, while according to some studies acute coronary syndrome is an independent risk factor for worse outcome of PCI.

However, the optimal timing of PCI in these patients remains uncertain. The question remains: to what extent should the patient be stabilized before the procedure? Recent guidelines suggest a relatively early intervention, especially in high risk patients with ACS,14,15 after various reports demonstrated a reduction in myocardial infarction (MI) and possibly death for invasively treated versus conservatively treated patients.13,16

In five large, randomized trials (Veterna affairs Non-Q-wave Infarction strategy in hospital (VANQWISH]),18 Fragmin and Fast revascularization during instability in coronary artery disease(FRISC II),6 Treat Angina with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction 18 (TACTICS-TIMI 18),16 TIMI IIIB,19 and the third randomized Intervention treatment of Angina (RITA-3)20 a routine, early invasive strategy (early angiography followed by revascularization, depending on angiographic findings) was compared with a "Conservative" strategy (angiography and subsequent revascularization only if medical therapy failed or substantial residual ischemia was documented). An early invasive strategy was shown to be beneficial in the FRISCII, TACTICS-TIMI 18, and RITA-3 studies, especially in the subgroup of high risk patients, such as those presenting with an elevated cardiac Troponin level.

As may be concluded from the earlier reports, result of PCI is better in stabilized angina than in refractory ones.9,21,22 In VANQWISH trial,18 early invasive therapy brought even worse results than the initially conservative strategy. Numerous objections have been put forward with respect to this trial. Nevertheless, some recent studies have clearly proven the superiority of the early invasive strategy over the more conservative approach.

RITA-3 randomized trial concluded that in patients presenting with unstable coronary artery disease, an interventional strategy is preferable to a conservative strategy, mainly because of the significant reduction in refractory or severe angina, and with no increased risk of death or myocardial infarction. FRISCII and TACTICS-TIMI18 have demonstrated similar results. According to these studies, in ACS, the early invasive approach leads to a sustained reduction in mortality, cardiac morbidity, need for repeat hospital admissions and late revascularization procedures. The latest ICTUS trial23 study concluded that either optimized medical therapy and selective invasive strategy or early invasive strategy in an ACS without ST-segment elevation leads to similar results and did not show superiority for either one of them. These could be inferred from the recent investigations in the stent era, the low-molecular-weight heparin and aggressive antiplatelet therapy, including IIb/IIIa receptor inhibitors. The initial 'cooling off' therapy improves the results of coronary interventions.24-27

Several factors may confound our results about long-term outcomes of ACS patients, predominantly the differences in baseline, lesion and procedural characteristics. Logistic stepwise regression analysis clearly showed that female gender and history of prior PCI were independent risk factors for major adverse cardiac events; also Mantel-Hanzel analysis demonstrated that female gender must be considered an important predictor of major adverse cardiac events in ACS patients. In a prospective study,28 it was demonstrated that women treated with very early aggressive revascularization with coronary stenting of and

culprit lesion as the primary revascularization strategy had a better long-term outcome as compared with men. Female gender independently reduced the risk of death or MI like results derived from TACTICS-TIMI1816 study, whereas subgroup analysis in FRISCII study29 showed a worse in-hospital and long-term outcome in women compared with men who were treated similarly, confirmed by our findings in the present study.

The association between a prior PCI and outcome following PCI in ACS has not been previously examined in detail. In a pooled analysis of three randomized ACS trials (GUSTOIIB, PURSUIT, and PARAGONE-B),30 it was concluded that patients with prior PCI had a lower mortality rate compared with patients without prior PCI. Furthermore, patients with prior PCI had a higher incidence of MI compared with patients without prior PCI, however no difference was observed in the composite of death or myocardial infarction between these

patients. Another study showed a significantly lower event-free survival at 9-month follow up despite similar in-hospital complication in patients with prior PCI.31

Conclusion

Although both ACS and SA patients treated with aggressive revascularization with coronary intervention had similar in-hospital and composite of major adverse cardiac events as a long-term outcome, female gender must be considered as an independent risk factor for major adverse cardiac events in patients with ACS who undergo PCI.

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TEHRAN HEART CENTER

Original Article

Predictive Factors for ICU and Ward Stay After CABG

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Abstract

Background: *To determine factors that predicts ICU and ward stay during hospitalization for coronary artery surgery.*

Methods: *Data were collected retrospectively from 200 patients. ICU and ward stay time was divided into two groups and compared by X2 and t test and variables with a p value of less than 0.1 were included in logistic regression model. Specificity and sensitivity of tests were examined by ROC curve.*

Results: *Mean time of ICU and ward stay (day) was 3.89 and 11.07 days respectively. The mean volume of transfused blood in group 1 (ICU stay ≤ 3 day) was 694 ml and in group 2 (>3 day) was 1231 ml where the difference was significant (p<0/05) and this correlation between stay time and transfusion was not seen in ward stay. In univariate analysis, factors such as transfused volume, maximum flow, Chronic obstructive pulmonary disease (COPD), Ejection fraction (EF), Intra aorta pump (IABP) and drainage volume were different between two groups of ICU stay times and such factors in ward stay were transfused volume, minimum flow, COPD, reoperation due to bleeding, and amount of 24 hours bleeding. In logistic regression model variables such as age, pump time, transfused volume and COPD were predictors of ICU stay and only drainage volume was predictor of ward stay.*

Conclusion: *Transfusion of blood is associated with long ICU stay time. Mechanism of this increased time is depression of immune system and increased rate of infection. Volume of bleeding from chest tube in 24 hours is associated with long hospital stay, because chest tube dose not pull out until drainage volume reduced to 50 ml in 24 h.*

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Keywords: *Ward stay• ICU stay • Coronary artery risk factors • Open heart su*

Introduction

Despite recent efforts to bypass ICU (intensive care unit) stay,[1] cardiac surgery patients are invariably monitored in the ICU for a period of time that varies from 1 to several days. Prolonged stay in the ICU not only increases the overall costs of cardiac surgery but it may also limit the number of operations performed. Therefore, the ability to accurately predict the duration of stay in the ICU and patient outcomes is important. One study investigated the influence of blood derivatives on the acquisition of severe postoperative infection and ICU stays. The influence of blood derivatives on infection and stay was assessed for RBC (red blood cell) concentration, plasma and platelets. After multivariate analysis, the variables associated with long hospital stay were re-intubation, dehiscence, long mechanical ventilation and

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transfusion. Vamakas investigated the independent association of allogenic blood transfusion with longer hospital stay and longer hospital charges after adjustment for the effects of confounding factors that are related to both these outcomes and the receipt of a perioperative transfusion. In this study, the postoperative length of hospitalization, the postoperative length of stay in ICU and the length of endotracheal intubation after operation were used as surrogate measures of morbidity. This study confirmed the previously reported association between transfusion of blood and hospital stay.[2] The scoring system used to predict a patient's stay in these studies and in general ICU have not been useful in the postoperative cardiac surgery with special applicability to cardiac surgery patients. However, the majority of reported models are complex, impractical for inter center use and have modest predictive ability.[3-5] This may result partly from the fact that all studies analyzed pre operative variables and ignored variables related to the operation itself. In this study we have assessed determinants for ICU stay in post operative coronary artery bypass graft (CABG) surgery patients by analyzing preoperative, intraoperative and immediate post operative variables. This approach has enabled us to develop a simple model predictive of ICU and ward stay.

Method

From Jan 2004 to Feb. 2006, we retrospectively studied 200 consecutive patients undergoing elective CABG (on-pump) surgery in our hospital. We recorded variables such as age, gender, weight, atrial fibrillation, diabetes, BSA(basal surface area), ejection fraction (EF), post operative myocardial infarction (MI), aortic cross clamp time, pump time, transfusion volume, post operative 24-hour's bleeding, consumed platelet, cryoprecipitate and plasma, duration of CPB (cardiopulmonary bypass), hypotension (BP<40 mm/Hg), Cardiopulmonary bypass (CPB) flow (minimum and maximum), COPD (chronic obstructive pulmonary disease), inotropic drug use, IABP (intra aortic balloon pump) use, renal failure, ICU and ward stay. The patients with off-pump CABG, coronary-valvular surgery and tracheostomy patients (cared in post ICU unit) excluded from study.

Collection of data in no way interfered with care of patient (retrospective) and therefore patients' consent was not required. The amount of blood transfused in the operating room, during the ICU stay after operation and using of inotropic drug was recorded. Blood transfusion was given when the patient's Hct (hematocit) or Hb (hemoglubin) was reduced to 34% or 10gr, respectively. For this analysis, prolonged stay in the ICU was defined as greater than 3 days and for ward stay greater than 7 days. Duration of mechanical ventilation, atelectasia pneumothorax, pneumonia and reintubation were recorded for all patients. Patients with missing data were excluded and duration of ICU stay and ward stay divided into two time periods [(≤3and>3) and (≤7and>7)] and analyzed by X^2 or t test (Continuous variables compared by t test and categorical or discrete variables compared by X^2). To assess the ability of independent variables in predicting dependent variables, we used a logistic model and the odd ratio was calculated. Furthermore, the data were subject to logistic regression analysis where ICU stay constituted binary dependent variable (3≤vs> 3 days) and ward stay (7≤vs >7 days). The fit of the above test was assessed by the Roc (receiver under curve) curve. Data are reported as mean and were considered significant when $P< 0.05$.

Results

For all patients, mean ICU stay was 3.89±1.4 days, mean duration of ward stay was 11.07±2.2 days and mode was 3.39 days. Minimum time of ICU stay was zero (expired in operating Room) and its maximum was 30 days. Of all patients, 85% were discharged in less than 2 weeks from the word (Cumulative percent).

Of all patients, 68% were discharged in less than 3 days from ICU. From these numbers,

96% were discharged in less than 6 days and 4 percent stayed more than 6 days, all of which had acute respiratory distress with clinical and laboratory signs such as reduced saturation of PO2 and increased PCO2, pneumonia and ARDS (acute respiratory distress syndrome). Two patients with tracheotomy had received 30 and 25 units of blood production. Patients were divided into two groups with respect to amount of blood transfusion (≤750 ml and >750 ml). The two groups differ in plasma transfusion, use of PEEP (positive end expiratory pressure), COPD, reintubation, atelectasia, cross clamp time, pump time, amount of 24 hour bleeding and ICU stay ($P<0.05$); however, this difference was not seen with respect to ward stay ($P>0.05$). The mean volume of transfused blood 655 ml for group A (ICU stay≤3 days) and 1132 ml for group B (ICU stay>3 days).

This correlation was not seen in ward stay (table 1, 2).

Table 1. Comparison of two time periods (for ward stay)*

Variable	≤7 day	>7 day	P value
Blood transfusion (ml)	915±415	1247±102	0.05
Minimum pump flow (ml/min)	4094±824	4037±501	0.05
COPD	8%	4%	<0.01
Reoperation for bleeding	0.01	0.07	<0.01
Amount of 24 hour bleeding (ml)	503±268	737±595	0.02

* Data are presented as mean±SD

Table 2. Comparison of two time periods (for ICU stay)*

Variable	3 day≤	>3 day	P value
Blood transfusion (ml)	694±107	1231±795	0.04
Cryoprecipitate usage (ml)	450±100	150±50	0.04
Amount of 24 hour bleeding (ml)	606±50	739±46	0.06
PCO_2 after extubation (mmHg)	32±5	36±6	0.02
COPD	4%	6.5%	<0.01
Reintubation	1.5%	9.1%	<0.01
Atelectasia	7%	12.4%	<0.01
Ejection fraction (%)	50±10	35±7	<0.01
Pump time (min)	77±17	89±20	<0.01
Maximum Flow (ml/min)	46032±425	4369±1204	0.04
Balloon pump (%)	4.2	9.4	0.02
Use of inotropic drugs (%)	5.6	15	0.04

* Data are presented as mean±SD

In univariate analyses (X^2 and t test), factors such as volume of transfusion, maximum flow in pump, COPD, EF, IABP and amount of 24h bleeding and reoperation for bleeding were significant ICU stay, (table 2) (P<0.05). In table 3, there was no difference with regards to demographic variables such as age, sex, basal surface area (BSA) and weight. The two groups were matched with regard to demographic variables.

Table 4 shows the result of a forward stepwise selection of variables put into the logistic model with variables entered based on their statistical significance (entering criterion P< 0.1). A forward step selection procedure led to a set of 4 variables in the model i.e., COPD, amount of transfused blood age and pump time (P<0.05, odd ratio were 3.2, 7.4, 5.1, 4.2, respectively). The results of variable selection into the logistic model with ward stay as binary variables (ward stay≤7 and>7 day) showed the only variable that predict ward stay was the amount of chest tube drainage (P<0.05). Age and sex do not affect duration of ward stay**.**

Table 3. Comparison of demographic variables in two time periods of ICU stay*

Variable	3 day≤	>3 day	P value
Age (Y)	54±10.7	59±7.9	0.06
Body surface area	1.7±0.2	1.73±0.3	0.07
Weight (Kg)	72.6±5.1	75±4.6	0.06
Female/Male	40%	43%	<0.01

* Data are presented as mean±SD

Table 4. Predicting factors for ICU stay time with logistic regression model

Variable	P value	Odds ratio	Confidence interval
Pump time	0.015	4.2	3.98-4.45
Age	0.042	5.1	4.87-5.26
Amount of transfused blood	0.045	7.4	7.13-7.59
COPD	0.041	3.2	3.03-3.31

Discussion

This study included both preoperative, Intraoperative and Immediate postoperative variables in a logistic regression model to determine variables that predict duration of stay in ICU and ward after CABG. We found that patients who had long pump time, older age, COPD and received a large number of blood units remained in the ICU for a longer period than usual. Other factors significant in univariate analysis, did not turn out to be significant predictors for ICU or ward stay period.

Among all variables examined, volume of drainage was the only factor that predicted duration of ward stay (odd ratio 6.7). The volume of blood administered in the operating room and in the ICU was the most important predictor of stay in the ICU. We believe that this correlation between transfusion and ICU stay is related to complications of transfusion, because clear evidence links blood transfusion with alteration in immune function.[6]

Higgins and Eric[7-8] published one of the first reports linking transfusion with an increased incidence of complications such as infection, and documented a model for predicting hospital stay. Goodnovgh[9] found an association between respiratory complication and blood transfusion; while walker[10] reported that patients receiving preoperative allogenic blood transfusion have longer hospital stays. Examining a similar group of patients (who do not receive transfusion) our work confirms such findings as shown in figure 2. The main problem with increased length of stay was a higher incidence of respiratory complication and infection. In two separate studies,[11-12] increased incidence of postoperative respiratory complications were noted in transfused patients undergoing surgery. Carren,[13] investigated RBC transfusion and postoperative length of stay in the hospital or ICU among patients undergoing CABG and the effect of perioperative blood transfusion on stay. The variation was calculated after adjustment for the effect of 10 confounding factors that pertained to severity of illness and infection. The post operative stay averaged 8±0.3 days in the hospital and 50±4.1 hours in ICU. The postoperative length of hospitalization increased by 0.83 percent per unit transfused and the postoperative stay in the ICU increased by 0.87 percent per RBC unit. This independent association may

be due to a relationship between blood transfusion and a higher incidence of septic complication of cardiac surgery or it may reflect the function of blood transfusion as surrogate marker for severity of illness. Graves et al.[14] found a linear trend between the number of units of blood transfused and incidence of multiorgan failure. This association is very important, because most mortality in our patients correlated to multiorgan failure. Many questions related to blood transfusion remain to be answered; for example: what are the precise indications for blood transfusion in cardiac surgery? Herbert et al.[15] suggested that for most critically ill patients, hemoglobin level of less than 7 g/l is a trigger for blood transfusion but we believe in ICU, erythropoietin should be given to CABG patients besides transfusing blood.

Should transfusion practice be altered such that only leukocyte depleted blood is used for transfusion? Heal[16] made a powerful biological and economic argument that this practice would save lives and money. Regarding age of blood, there are questions about the efficacy of RBC stored>15 days, because of the reduced ability of this RBC to improve tissue oxygenation. This is the mechanism of respiratory failure in our patients. RBC stored>15 days loses ATP (adenosine tri phosphate), thus causing a decrease in deformability and reduced transportation of oxygen in microcirculation. We also found that post operative bleeding is associated with prolonged wards stay (not ICU stay) because patients with drainage from chest tube are discharged to the ward until the 24 hour drainage is reduced to 50 ml/24 h, the chest tube isn't pulled out. We also found that age and pump time prolonged ICU stay, confirming results documented by other studies.[17-18] In logistics model, variables such as age, pump time, transfusion volume, and COPD were predictors of ICU stay and only drainage volume was a predictor of ward stay.

Conclusion

Transfusion of blood is associated with long intensive care stay time. Other factors such as age, COPD and pump time correlated with this period. Volume of bleeding in 24 hours is associated with long hospital stay. We emphasized that complications like respiratory failure links to blood transfusion and were responsible for the length of ICU stay after CABG. The results of this and similar investigations strongly suggest that transfusion is associated with long ICU stay. We believe that transfusion is associated with altered immune function, infection, and mortality, therefore randomized, prospective studies to further investigate these finding should be undertaken.

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Berif Communication

Interventional Closure of Patent Foramen Ovale (PFO) with Amplatzer PFO Occluder in Patients with Paradoxical Cerebral Embolism

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Abstract

Background: *Percutaneous transcatheter closure has been proposed as an alternative to surgical closure or long-term anticoagulation in patients with presumed paradoxical embolism and patent foramen ovale (PFO).*

Methods: *There were two symptomatic patients (29 and 47 years old) who underwent percutaneous transcatheter closure of PFO after at least two events of cerebral ischemia; one embolic event had occurred under anti-platelet therapy. For both patients, Amplatzer PFO occluder measuring 25 mm in diameter were used. In both cases, complete occlusion by color Doppler and transesophageal contrast echocardiography investigation was achieved after the procedure and lasted at least up to 3 months after implantation as determined by our follow up. Mean fluoroscopy time was 16.7 minutes.*

Results: *Percutaneous transcatheter closure was technically successful in both patients (100%). No residual shunt was seen at the end of the procedure or in follow-ups. In-hospital follow-up was uneventful. At a mean follow-up of 3 months, no recurrent embolic neurological events were observed.*

Conclusion: *Transcatheter closure of PFO with Amplatzer PFO occluder devices is a safe and effective therapy for patients with previous paradoxical embolism PFO. Percutaneous closure is associated with a high success rate, low incidence of hospital complications, and freedom of cerebral ischemic events.*

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Keywords: *Patent foramen ovale • Amplatzer PFO occluder • Cerebral emboli*

Introduction

Patency of the foramen ovale (PFO) has been identified as a potential risk factor for paradoxical embolism potentially followed by cerebral ischemic events.[1-5] Cryptogenic stroke (with no detectable source of embolism) accounts for about 40% of strokes in young adults.[6-7] Although the underlying mechanism by which PFO accounts for the phenomenon is not entirely elucidated yet, transseptal passage of emboli from the right- to the left-sided chambers of the heart appear to play an important role.[8] Moreover, patients with documented PFO and previous embolism are at increased risk of recurrent thromboembolic events in up to 4.2% even under therapeutic anticoagulation.3,[9-11] Thus, long-term management of

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PFO remains controversial. Oral anticoagulation9,[12-14] and surgical closure[15,16] are options to help prevent recurrent neurological events. However, both therapeutic strategies are associated with significant morbidity. As an alternative nonsurgical transcatheter closure using various devices has shown promising potential in small series.[17-19]

Methods

Patient population

From Aug. 2005 to Sep. 2005 two consecutive patients underwent transcatheter closure of a documented PFO; patients qualified after the occurrence of at least one transient ischemic attack (TIA) or stroke documented by PFO and detected by transoesophageal echocardiography (TOE). The diagnosis of ischemic stroke was based on symptoms and signs of a suddenly occurring neurologic deficit, and the corresponding findings on computer tomography or magnetic resonance imaging scans. TIA was defined as a focal neurologic deficit resolving completely within 24 hours. An ischemic event was considered to be resulting from paradoxical embolism when the following criteria were met: (1) presence of PFO with or without atrial septal aneurysm (ASA) and spontaneous or provocable right-to-left shunt on contrast TOE. (2) clinically and/or morphologically diagnosed TIA or stroke by a neurologist; and (3) exclusion of any other likely cause of systemic arterial embolism.

Morphology and Laboratory Examinations

A standardized neurological physical examination, cerebral computed tomography (CT) or magnetic resonance imaging (MRI) was performed before interventional device closure. A 12-lead electrocardiogram and contrast enhanced and color Doppler TOE with and without Valsalva maneuver were used to document right-to-left atrial shunt in all patients. Standard blood testing and screening for evidence of hypercoagulable states (proteins C and S, antithrombin III, lupus anticoagulant, anticardiolipin, factor V Leiden) completed the periinterventional laboratory panel in all patients.

Definitions

According to the present guidelines, a PFO was defined as a functional dehiscence between septum primum and septum secundum without evidence of an anatomic defect in the septa on TOE. An atrial septal aneurysm was defined as an abnormally redundant atrial septum with an excursion of ≥ 15 mm to either side of the septum.[20,21]

The degree of right-to-left shunt was quantified by the number of microbubbles in the left atrium on a still frame image during contrast TOE (saline solution); grade 0 = none; grade 1 = minimal (1-5 bubbles); grade 2 = moderate (6-25 bubbles); grade 3 = severe (>25 bubbles).[21]

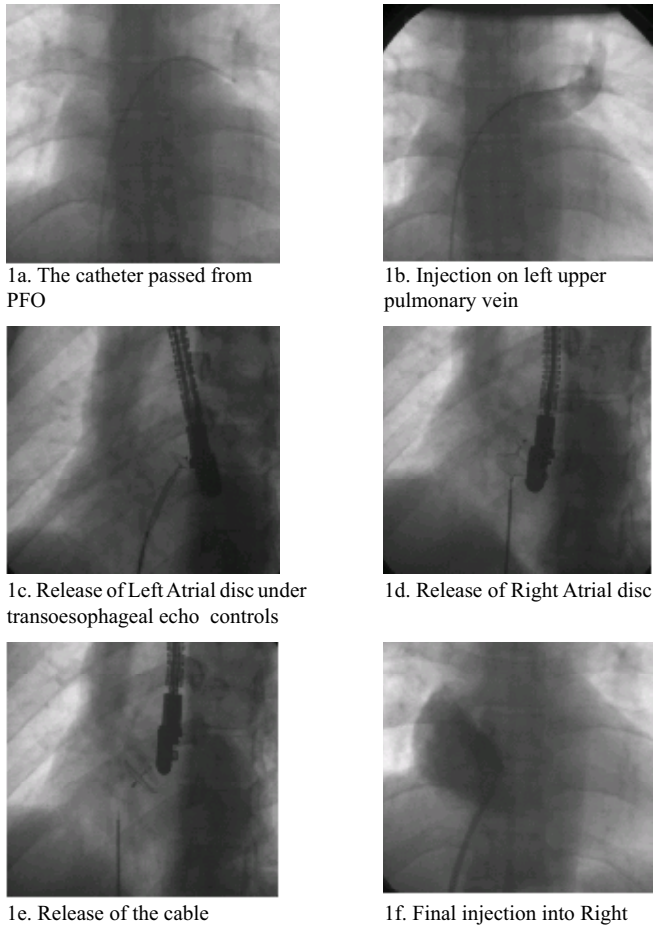
Implantation Procedures

PFO closure was performed with the Amplatzer PFO occluder (AGA Medical, Golden Valley, MN) (Figure 1). Design and technical details of the device and the technique of transcatheter implantation of the device across the intraatrial septum have been described previously.[21]

Periinterventionally, all patients received one IV doses of 1 gr cefazolin and 5,000 units of intravenous heparin during the intervention.

Postinterventional Care

Postinterventional care included 100 mg of oral aspirin per day for 6 months and 75 mg of oral Clopidogrel for 3 months. Standard prophylaxis for bacterial endocarditis was recommended for 6 months according to the guidelines of the American Heart Association.[22]



1a. The catheter passed from PFO

1b. Injection on left upper pulmonary vein

1c. Release of Left Atrial disc under transoesophageal echo controls

1d. Release of Right Atrial disc

1e. Release of the cable

1f. Final injection into Right Atrium which showed no shunt

Figure 1. Sequential stages of device implantation

Postprocedural Control and Follow-Up

Patients were monitored overnight and discharged the following day. A transthoracic contrast echocardiogram (TTE) examination was performed within 24 hours of percutaneous closure in all patients. There months after discharge patients were referred to the outpatient clinic for a physical follow-up exam and contrast echocardiography. Thereafter, patients were followed up by telephone interview and/or by contacting the referring physician.

Results

Patient Characteristics

Between Aug. 2005 and Sep. 2005, percutaneous transcatheter closure of a PFO was successfully performed in two consecutive patients with cryptogenic cerebral ischemia using an Amplatzer PFO occluder. Indications for transcatheter PFO closure included TIA in patients and multiple paradoxical embolisms had occurred in both patients. The first patient was 29 years old man with one syncope and TIA before anticoagulant therapy and one TIA under ASA therapy. The second patient was a 47 years old man with two TIA that one was under ASA therapy. None of patients had any incidence of hypercoagulable state.

Procedural Success and Complications

We used the Amplatzer PFO occluder of 25-mm diameter in both patients. None had echocardiographic evidence of atrial septal aneurysm. General anesthesia was not required in patients. Mean fluoroscopy time was 16.7 minutes and device implantation was successfully accomplished in all patients. Complete occlusion by virtue of totally abolished transseptal flow was present in all patients immediately after device deployment as assessed by angiography.

During the intervention, no deaths or systemic thromboembolic events were noted in our patients. No any persistent arrhythmia occurred during or after the procedure. There were no peri-interventional thromboembolic events in these patients and no evidence of thrombus formation on subsequent follow-up echocardiograms.

Follow-up

The mean follow-up period was 3 months. No patient suffered from any recurrent cerebral event after successful implantation of the Amplatzer PFO occluder. Thus, the rate of recurrent neurological events was zero during the follow-up.

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Case Report

Myocardial Infarction in a Patient with Prosthetic Aortic Valve

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Abstract

A 45- year old man with a history of Aortic Valve replacement presented with acute chest pain which was diagnosed to be anterior wall myocardial infarction. He received thrombolytic therapy with streptokinase. Echocardiography and fluoroscopy showed normally functioning ball and cage aortic prosthesis. Coronary arteriography showed globular filling defect in midportion of left anterior descending coronary artery, most probably embolized thrombus. The patient underwent medical treatment especially warfarin with higher range of INR without any intervention. He had a smooth in-hospital course and uneventful recovery.

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***Keywords**: Aortic prosthesis • Myocardial infarction • Ball and cage valve*

Introduction

Approximately 6 percent of all patients with STEMI do not have coronary atherosclerosis demonstrated by coronary angiography or at autopsy. Many of these cases are caused by coronary artery spasm and or thrombosis; perhaps with underlying endothelial dysfunction or small plaques that are not apparent on coronary angiography. One of the additional causes includes coronary emboli (perhaps from small mural thrombosis, a prolapsed mitral valve or a myxoma).1

We report the case of a patient with myocardial infarction caused by an uncommon etiology that was an embolized clot.

Case Report

A 45-year-old man, with a 20-year history of aortic valve replacement and under occasional treatment with warfarin 5mg and INR (about 2), was admitted because of acute, severe chest pain which was initiated 10 hours before presentation. He had clinical scenario of acute coronary syndrome and 12-lead- ECG showed ST-Elevation and T- wave Inversion on v2-v6, a characteristic of acute anterior wall MI. The diagnosis was documented with increase in Troponin level and creatine kinase MB.

The echocardiography showed akinesia in apical segments and normally functioning ball and cage valve in aortic position. Thrombolytic therapy was done with streptokinase infusion. After a good hospital course, the patient was discharged and was referred to our hospital, which is a tertiary center. The perfusion scan with technetium 99 showed stress induced perfusion defect in the apical segment: so coronary angiography was planned. Fluoroscopy revealed normally functioning Starr-Edward, Aortic prosthesis. In selective coronary arteriography, Right coronary and left circumflex

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coronary arteries were normal. Left anterior descending artery was free of atherosclerotic plaques but there was a globular filling defect in mid to distal portion of LAD after major diagonals (Figure 1). This filling defect was most probably an embolized thrombus from ball and cage valve. The case was presented at the weekly conference of our center and general consensus about him was medical treatment and continuation of warfarin with higher levels of INR and intermittent follow up. He had excellent and uneventful in hospital course and discharge. In a follow up visit after 3 months, the patient was good without symptoms of myocardial ischemia.

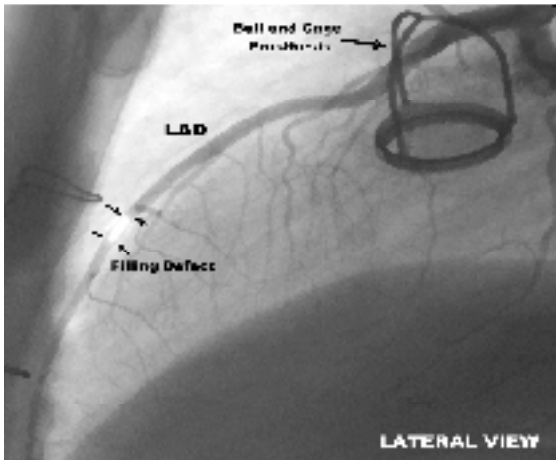

Figure 1. Coronary angiography of the patient in lateral view which shows globular filling defect in the mid-part of left anterior descending artery

Discussion

Embolic complications due to prosthetic heart valves are common. One report documented a left main coronary artery thrombus extending from a Starr – Edward's aortic valve prosthesis 22 years after its placement. It resulted in unstable angina and a small myocardial infarction. This rare complication illustrates the importance of adequate anticoagulation.2 The most common etiology for obstructive prosthetic heart valve thrombosis (PVT), is thrombus formation due to inadequate anticoagulation.3 A short course of thrombolytic therapy may be considered first line therapy for PVT.4 In a necropsy observation of 20 patients Who died after AVR with a Hufnagel trileaflet prosthesis, it was revealed that four of seven patients dying early had extensive PVT causing obstruction of one coronary arterial ostium on both sides.5 Some emboli seemed triggered by the valve prosthesis.6 Acute coronary syndrome might be caused by isolated thrombus on aortic prosthetic valve without any insufficiency of prosthesis and embolic finding due to thrombosed valve.7 Therefore, we must take into account any embolized clot in any patient with acute coronary syndrome and prosthetic valve.

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International Cardiovascular Surgery Meetings Calender (2007-2008)

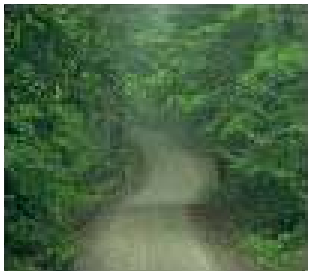



Congress	Time-Location	Address
Singapore LIVE 2007 (16th Annual Live Interventions in Vascular Endotherapy)	January 22-24, 2007, Singapore	Email: contact@singlivecourse.com Website: http://www.singlivecourse.com/
43rd Annual Meeting of The Society of Thoracic Surgeons (STS)	January 29 – 31, 2007, San Diego, California, USA	Email: sts@sts.org Website: http://www.sts.org/
53rd Annual conference of the Indian Association of Cardio Vascular Thoracic Surgeons (CTCON 2007)	February 8 – 11, 2007, Jaipur, Rajasthan, India	Email: email-info@ctcom2007.com Website: http://www.ctcon2007.com/
7th Indian Society of Extra-Corporeal Technology (ISECT CON 2007)	February 9 – 10, 2007, Jaipur, Rajasthan, India	Tel: 91 0935 135 2897 Email: info@ctcon2007.com
37th Annual Meeting of the Japanese Society for Cardiovascular Surgery (JSCVS)	Feburary 21 – 23, 2007, Tokyo, Japan	Email: JSCVS37@hij.twmu.ac.jp Website: jscvs37.umin.jp
25th International Cardiovascular Surgical Symposium Annual Meeting	March 3–10, 2007, Zürs, Arlberg, Austria	Email: congress@herzchirurgie.at Website: http://www.asian-annals.org/general/www.surgery-zur.at
71st Annual Scientific Meeting of the Japanese Circulation Society	March 15 – 17, 2007, Kobe, Japan	Email: 71junkan@congre.co.jp Website: www.congre.co.jp/jcs71
CREF 27 - The San Diego Cardiothoracic Surgery Symposium: Science and Techniques of Perfusion	March 15 – 18, 2007, San Diego, California, USA	Email: info2007@amainc.com Website: http://www.amainc.com/

Congress	*Time-Location*	*Address*
First Annual Florida Valve Symposium — Current Controversies in Valve Management	March 28–30, 2007, St. Petersburg, Florida, USA	Email: siestavc@aol.com Website: http://www.floridavalvesymposium.com/
Valves in the Heart of the Big Apple: Evaluation Management of Vascular Disease 2007	April 12 –14, 2007, New York, USA	Email: info@heartvalvesocietyofamerica.org Website: http://www.heartvalvesocietyofamerica.org/
5th Vienna Interdisciplinary Symposium on Aortic Repair (VISAR)	April 19–21, 2007, Vienna, Austria	Email: visar@ieurocongress.org Website: http://www.eurocongress.org/
27th Annual Meeting and Scientific Sessions of the International Society for Heart and Lung Transplantation (ISHLT)	April 25–28, 2007, San Francisco, California, USA	Email: meeting@ishlt.org Website: http://www.ishlt.org/
1st Meeting of the World Society for Pediatric and Congenital Heart Surgery	May 3–4, 2007, Washington, DC, USA	Email: contacts@wspchs.org Website: http://www.wspchs.org/
87th Annual Meeting of the American Association for Thoracic Surgery (AATS)	May 6 – 9, 2007, Washington, D.C., USA	Email: aats@prri.com Website: http://www.aats.org/
15th Annual Meeting of the Asian Society for Cardiovascular Surgery (ASCVS)	May 17–20, 2007, Beijing, China	Email: ASCVS2007@cma.org.cn Website: http://www.ascvs2007.com/
Euro PCR — 2007 (The Paris Course on Revascularization)	May 22–25, 2007, Barcelona, Spain	Email: europa@europa-organisation.com Website: http://www.europa-organisation.com/
15th European Conference on General Thoracic Surgery (ESTS)	June 3–6, 2007, Leuven, Belgium	Email: sue@ests.org.uk Website: http://www.ests.org/
10th Annual Scientific Meeting of the International Society for Minimally Invasive Cardiothoracic Surgery (ISMICS)	June 6–9, 2007, Rome, Italy	Email: ismics@prri.com Website: http://www.ismics.org/
12th European Congress on Extracorporeal Circulation Technology	June 6–9, 2007, Kyiv, Ukraine	Email: congress.fecect@reedbusiness.nl Website: http://www.fecect.org/
4th Biennial Meeting of the Society for Heart Valve Disease (SHVD)	June 15–18, 2007, New York, USA	Email: secretariat@shvd.org Website: w02-0566.web.dircon.net/biennial2007
7th International Congress on Complications during Coronary Intervention: Management and Prevention	June 20–22, 2007, Lausanne, Switzerland	Email: coronarycomplications@eurocongress.org Website: http://www.coronarycomplications.org/
XXVth Meeting of the Society of Cardiac Surgeons	June 21–23, 2007, Pamplona, Navarra, Spain	Email: jherreros@unav.es Website: http://www.cardiasurgeons.ca/

Congress	*Time-Location*	*Address*
17th World Congress of the World Society of Cardio-Thoracic Surgeons (WSCTS)	July 11–13, 2007, Kyoto, Japan	Email: wscts2007@congre.co.jp Website: http://www.wscts2007.com/
21st Annual Meeting of the European Association for Cardio-Thoracic Surgeon (EACTS)	September 15–19, 2007, Geneva, Switzerland	Email: info@eacts.co.uk Website: http://www.eacts.org/
19th Annual Meeting of the Mediterranean Association of Cardiology and Cardiac Surgery (MACCS 2007)	September 27–30, 2007, Opatija, Croatia	Email: info@alphastudio.it Website: http://www.maccs2007.org/
7th International Congress on Coronary Artery Disease - From Prevention to Intervention	October 7–10, 2007, Venice, Italy	Email: coronary@kenes.com Website: www.kenes.com/cad7
VIII Annual International Symposium on Advances in Understanding Aortic Diseases	October 13–14, 2007, Tokyo, Japan	Email: ctstokyo-ikyoku@umin.ac.jp
60th Annual Scientific Meeting of the Japanese Association for Thoracic Surgery (JPATS)	October 17 – 20, 2007, Sendai, Japan	Email: jats-adm@umin.ac.jp Website: http://www.asian-annals.org/general/www.jpats.org
Eighth Biennial Congress of the Syrian Cardiovascular Association	November 1-3, 2007 Damascus, Syria	E-mail: scva@scs-net.org Tel/Fax: 00963 94 27 27 55
18th Biennial Congress of the Association of Thoracic & Cardiovascular Surgeons of Asia (ATCSA)	November 25–28, 2007, Bali, Indonesia	Tel/Fax: 62 21 566 5993
ISMICS Winter Workshop 2007	November 28–December 2, 2007, Antalya, Turkey	Email: oztekinoto@oztekinoto.com
Pioneering Techniques in Cardiac Surgery, the Fifth in the Series	December 6–7, 2007, Leipzig, Germany	Email: blaeser@medizin.uni-leipzig.de
4th Asian Pacific Congress of Heart Failure (APCHF)	January 31–February 3, 2008, Melbourne, Australia	Email: apchf@tourhosts.com.au Website: http://www.apchf.com.au/
38th Annual Meeting of the Japanese Society for Cardiovascular Surgery (JSCVS)	February 20–22, 2008, Fukuoka, Japan	Email: JSCVS38@med.kurume-u.ac.jp Website: square.umin.ac.jp/jscvs
16th Annual Meeting of the Asian Society for Cardiovascular Surgery	May 2–4, 2008, Singapore	Email: mice@themeetinglab.com Website: http://www.ascvs2008.com/
Endoscopic & Laparoscopic Surgeon of Asia 2008 (ELSA 2008)	September 2 – 6, 2008, Yokohama, Japan	Email: elsa2008@convention.co.jp Website: www2.convention.co.jp/elsa2008

International Cardiovascular Meetings and Congresses Calender (2007-2008)

Title	City	Start Date	End Date
XVII Annual Meeting of the French Society of Cardiology	France, Paris	17 January 2007	20 January 2007
Singapore 2007 Live, 16th Annual Live Interventions in Vascular Endotherapy	Singapore, Singapore	22 January 2007	24 January 2007
39th Annual Business Meeting of the Finnish Cardiac Society and 33rd Progress Report Meeting	Finland, Nilsiä	26 January 2007	27 January 2007
Annual Meeting of the Norwegian Society of Cardiology (Winter Meeting)	Norway, Lillehammer	26 January 2007	28 January 2007
26th Annual Scientific Meeting of the Belgian Society of Cardiology	Belgium, Brussels	01 February 2007	03 February 2007
1st European Forum, Heart Exercise & Prevention	France, Paris	02 February 2007	03 February 2007
Cardiology Update 2007: Educational Programme	Switzerland, Davos	12 February 2007	16 February 2007
Annual Meeting of the Belorussian Scientific Society of Cardiologists	Belarus, Minsk	15 February 2007	16 February 2007
34th Annual Congress of the Egyptian Society of Cardiology	Egypt, Cairo	20 February 2007	23 February 2007
International Summit on Syncope: State of the Art 2007	United States of America, Amelia, Florida	23 February 2007	25 February 2007
Acute Coronary Syndromes: from Plaque to Imagery	Luxembourg	03 March 2007	03 March 2007
7th Annual Spring Meeting on Cardiovascular Nursing: "Changing Practice to Improve Care"	United Kingdom, Manchester	23 March 2007	24 March 2007

Title	City	Start Date	End Date
6th International Workshop on Interventional Pediatric Cardiology	Italy, San Donat Milanese (Milan)	28 March 2007	31 March 2007
13th Annual Transoesophageal Echocardiography Course	United Kingdom, London	29 March 2007	30 March 2007
The 3rd Local Annual Meeting of the Libyan Cardiac Society	Libyan Arab Jamahiriya, AL Baida	30 March 2007	01 April 2007
73nd Annual Meeting of the German Cardiac Society	Germany, Mannheim	12 April 2007	14 April 2007
8th International Congress of Cardiology and Cardiac Surgery	Lebanon, Beirut	18 April 2007	21 April 2007
The 54th Annual Conference of the Israel Heart Society together with the Israel Society of Cardiothoracic Surgery	Israel, Tel Aviv	18 April 2007	19 April 2007
EuroPrevent 2007	Spain, Madrid	19 April 2007	21 April 2007
XXVIII Annual Congress of the Portuguese Society of Cardiology	Portugal, Vilamoura	21 April 2007	25 April 2007
Annual Meeting of the Swedish Society of Cardiology	Sweden, Gothenburg	25 April 2007	27 April 2007
4th Global CardioVascular Clinical Trialists Forum	France, Cannes	26 April 2007	28 April 2007
Spring Meeting of the Netherlands Society of Cardiology	Netherlands, Amsterdam	26 April 2007	27 April 2007
8th International Conference of Nuclear Cardiology - ICNC8	Czech Republic, Prague	29 April 2007	02 May 2007
Annual Meeting of the Norwegian Society of Cardiology (Spring Meeting)	Norway, Oslo	03 May 2007	05 May 2007
Cardiology and Vascular Medicine - update and perspective	Netherlands, Rotterdam	07 May 2007	09 May 2007
Annual Scientific Congress of Cardiology of the Hugarian Society of Cardiology	Hungary, Balatonfüred	09 May 2007	12 May 2007
15th Alpe-Adria Cardiology Meeting	Czech Republic, Brno	11 May 2007	13 May 2007
1st All Africa Conference on Heart Disease, Stroke and Diabetes	Kenya, Nairobi	13 May 2007	16 May 2007
IV Congress of Cardiologists and Angiologists	Bosnia and Herzegovina, Mostar	17 May 2007	19 May 2007
EuroPCR 2007	Spain, Barcelona	22 May 2007	25 May 2007
25th Anniversary Meeting of the Slovenian Society of Cardiology	Slovenia, Radenci	24 May 2007	26 May 2007
VI Annual Congress of the Armenian Cardiologists Association	Armenia, Yerevan	24 May 2007	26 May 2007
Annual Meeting of the Austrian Society of Cardiology "Jahrestagung 2007"	Austria, Salzburg	30 May 2007	02 June 2007

Title	City	Start Date	End Date
Annual Meeting of the Danish Society of Cardiology	Denmark, Nyborg	31 May 2007	02 June 2007
11th Danubian Forum of Cardiac Surgery	Romania, Timisora	01 June 2007	02 June 2007
Annual Meeting of the Estonian Society of Cardiology	Estonia, Tallinn	01 June 2007	02 June 2007
Annual Meeting of the Italian Association of Hospital Cardiologists (ANMCO)	Italy, Florence	03 June 2007	06 June 2007
Annual Scientific Conference of the British Cardiovascular Society	United Kingdom, Glasgow (Scotland)	04 June 2007	07 June 2007
Heart Failure 2007	Germany, Hamburg	09 June 2007	12 June 2007
76 th Congress of the European Atherosclerosis Society	Finland, Helsinki	10 June 2007	13 June 2007
Annual Congress of the Swiss Society of Cardiology	Switzerland, Geneve	13 June 2007	15 June 2007
17th Scientific Meeting of the European Society of Hypertension	Italy, Milan	15 June 2007	19 June 2007
RHYTHM 2007- ARRHYTHMIAS AND HEART FAILURE: pharmacological and non- pharmacological therapies	France, Cannes	15 June 2007	17 June 2007
Mayo International Vascular Symposium in Iceland, June 2007	Iceland, Reykjavik	19 June 2007	23 June 2007
Europace 2007	Portugal, Lisbon	24 June 2007	27 June 2007
The 34th International Congress on Electrocardiology	Turkey, Istanbul	27 June 2007	30 June 2007
The Annual Interventional Cardiology Conference - CARDIOALEX	Egypt, Bibliotheca Alexandrina	27 June 2007	29 June 2007
World Heart Federation Teaching Seminar on CVD 2007	Norway, Sommarøy	20 August 2007	01 September 2007
ESC Congress 2007	Austria, Vienna	01 September 2007	05 September 2007
The 46th National Congress of Cardiology of the Romanian Society of Cardiology	Romania, Sinaia	15 September 2007	18 September 2007
43rd EASD Annual Meeting 2007	Netherlands, Amsterdam	17 September 2007	21 September 2007
XI International Congress of the Polish Cardiac Society	Poland, Wroclaw	20 September 2007	22 September 2007
Bleeding Complications in the treatment of Acute Coronary Syndrome	Sweden, Lund	03 October 2007	05 October 2007
XVI International Symposium on Drugs Affecting Lipid Metabolism	United States of America, New York	04 October 2007	07 October 2007
XII Congress of the Slovak Society of Cardiology	Slovak Republic, Bratislava	04 October 2007	06 October 2007

Title	City	Start Date	End Date
7th International Congress on Coronary Artery Disease - from Prevention to Intervention	Italy, Venice	07 October 2007	10 October 2006
Venice Arrhythmias 2007 - Tenth International workshop on Cardiac Arrhythmias	Italy, Venice	07 October 2007	10 October 2007
National Cardiology Congress of the Society of Cardiology of the Russian Federation	Russian Federation, Moscow	09 October 2007	11 October 2007
Annual Autumn Meeting of the Finnish Cardiac Society	Finland, Helsinki	10 October 2007	12 October 2007
European Conference on Myocardial and Pericardial Diseases with focus on heart diseases in women	Germany, Marburg	11 October 2007	14 October 2007
Annual General Meeting of the Irish Cardiac Society	Ireland, Holywood (Co. Antrim)	11 October 2007	13 October 2007
Wonca Europe 2007	France, Paris	17 October 2007	20 October 2007
Annual Meeting of the Spanish Society of Cardiology	Spain, Madrid	17 October 2007	20 October 2007
XXIII National Cardiology Congress of the Turkish Society of Cardiology	Turkey, Antalya	20 October 2007	23 October 2007
Autumn Meeting of the Netherlands Society of Cardiology	Netherlands, Ermelo	25 October 2007	27 October 2007
The 8th biennial meeting of the Syrian Cardiovascular Association	Syrian Arab Republic, Damascus	01 November 2007	03 November 2007
Cardio Lipid 2007 Egypt	Egypt, Ain Sokhna - Red Sea	15 November 2007	17 November 2007
National Meeting of the Algerian Society of Cardiology	Algeria, Algiers	07 December 2007	09 December 2007
4th Asian Pacific Congress of Heart Failure	Australia, Melbourne	31 January 2008	03 February 2008
16th Annual Meeting of the Asian Society For Cardiovascular Surgery (ASCVS 2008)	Singapore,	13 March 2008	16 March 2008
The 4th International Annual Meeting of the Libyan Cardiac Society	Libyan Arab Jamahiriya, Benghazi	21 March 2008	23 March 2008
XVI World Congress of Cardiology	Argentina, Buenos Aires	18 May 2008	21 May 2008
ESC Congress 2008	Germany, Munich	30 August 2008	03 September 2008
National Congress of the Latvian Society of Cardiology	Latvia, Riga or Jurmala	26 September 2008	27 September 2008

Information for Authors

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"The Journal of Tehran Heart Center" aims to publish the highest quality material, both clinical and scientific, on all aspects of Cardiovascular Medicine. It includes articles related to research findings, technical evaluations, and reviews. In addition, it provides a forum for the exchange of information on all aspects of Cardiovascular Medicine, including educational issues. "The journal of Tehran Heart Center" is an international, English language, peer reviewed journal concerned with Cardiovascular Medicine. It is an official journal of the Tehran Heart Center and is published quarterly. Papers submitted to this journal which do not adhere to the Instructions for Authors will be returned for appropriate revision to be in line with the Instructions for Authors. They may then be resubmitted. Submission of an article implies that the work described has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis), that it is not under consideration for publication elsewhere, that its publication is approved by all Authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, without the written consent of the publisher.

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Original Article

Clinical and pre-clinical papers based on either normal subjects or patients and the result of cardiovascular pre-clinical research will be Considered for publication provided they have an obvious clinical relevance.

Brief communication

Case report

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Letters to the editor must not exceed 500 words and should focus on a specific article published in "The Journal of Tehran Heart Center" within the preceding 12 weeks. No original data may be included. Authors will receive pre-publication proofs, and the authors of the article cited invited to reply.

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All submitted manuscripts must not exceed 5000 words, including References, Figure Legends and Tables. The number of Tables, Figures and References should be appropriate to the manuscript content and should not be excessive.

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Declaration of Helsinki

The Authors should state that their study complies with the Declaration of Helsinki that the locally appointed ethics committee has approved the research protocol and that informed consent has been obtained from the subjects (or their guardians).

Section of the manuscript

Original articles should be divided into the following sections: (1) Title page, (2) Abstract and Keywords, (3) Introduction, (4) Methods, (5) Results, (6) Discussion, (7) Conclusion, (8) Acknowledgements, (9) References, (10) Figure legends, (11) Tables, (12) Figures.

General format

Prepare your manuscript text using a word processing package. Submissions of text in the form of PDF files are not permitted. Manuscripts should be double –spaced, including text, tables, legends and references. Number each page. Please avoid footnotes; use instead, and as sparingly as possible, parenthesis within brackets. Enter text in the style and order of the Journal. Type references in the correct order and style of the journal. Type unjustified, without hyphenation, except for compound words. Type headings in the style of the journal. Use the TAB key once for paragraph indents. Where possible use Times New Roman for the text font and Symbol for the Greek and special characters. Use the word processing formatting features to indicate Bold, Italic, Greek, Maths, Superscript and subscript characters. Clearly identify unusual symbols and Greek letters. Differentiate between the letter o and zero, and the letters I and i and the number 1. Mark the approximate position of each figure and table. Check the final copy of your paper carefully, as any spelling mistakes and errors may be translated into the typeset version.

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The title page should include the following: (1) the title, (2) the name (s) of authors and their highest degree (no more than 12 authors are acceptable), (3) the institution (s) where work was performed, (4) institution, and location of all authors, (5) the address, telephone number, fax number and e-mail address of the corresponding author.

Abstract

All abstracts may not contain more than 250 words and should also be submitted as a separate file. The abstract should be formatted with the following heading: (1) Background, (2) Methods, (3) Results, (4) Conclusion.
A maximum of six Keywords may be submitted.

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Figures should be saved in TIFF format at a resolution of at least 300 pixels per inch at the final printed size for colour figures and photographs, and 1200 pixels per inch for black and white line drawings. Although some other formats can be translated into TIFF format by the publisher, the conversion may alter the tones, resolution and contrast of the image. Digital colour art should be submitted in CMYK rather than RGB format, as the printing process requires colours to be separated into CMYK and this conversion can alter the intensity and brightness of colours. Therefore authors should be satisfied with the colours in CMYK (both on screen and when printed) before submission. Please also keep in mind that colours can appear differently on different screens and printers. Failure to follow these guides could result in complications and delays.. Photographs: Photographs should be of sufficiently high quality with respect to detail, contrast and fineness of grain to withstand the inevitable loss of contrast and detail inherent in the printing process. Please indicate the magnification by a rule on the photograph. Colour figures: There is a special charge for the inclusion of colour figures.. Figure legends: These should be on a separate, numbered manuscript sheet grouped under the heading “Legends” on a separate sheet of the manuscript after the References. Define all symbols and abbreviations used in the figure. All abbreviations and should be redefined in the legend.

Tables

Tables should be typed with double spacing, but minimizing redundant space and each should be placed on a separate sheet. Tables should be submitted, wherever possible, in portraits, as opposed to landscape, layout. Each Table should be numbered in sequence using Arabic numerals. Tables should also have a title above and an explanatory footnote below. All abbreviations and should be redefined in the Footnote.

Acknowledgements

All sources of funding and support, and substantive contributions of individuals, should be noted in the Acknowledgements, positioned before the list of references.

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