In the name of God

The Journal of Tehran Heart Center
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New concepts in Aortic Arch Repair. Are we Heading in the Right Way?

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The standard approach for repair of type A aortic dissection includes repair or replacement of the aortic valve, the ascending aorta and the arch, alone or in combination with direct vision under hypothermic circulatory arrest. Although type A dissection usually extends into the distal thoracoabdominal aorta, the descending thoracic aorta is usually left alone. During the follow-up, surgeons will sequentially and periodically evaluate the patients looking for aneurysmal dilatation of the untreated aorta for an eventual late open surgical or endovascular repair.

Surgery of the aorta continues to be a surgical challenge. Aortic disease and surgery are dynamic as new ideas are continuously brought up in terms of surgical approach, extension of repair and characterization of patients. Technology also plays an important role nowadays. Since the early days of high-porosity vascular grafts, until today where vascular grafts are being coated with albumin or collagen, results have dramatically changed in terms of control of hemorrhage and related intraoperative death. The inception of endovascular therapy seems to change the perception of patients suffering from descending thoracic aortic aneurysms and chronic dissections.1 Acute type B dissections are still a matter of concern regardless of the attempted therapy.

Type A dissection routinely involves the aortic arch. Operation-related morbidity and mortality is still high. Some questions are still unanswered; like the need of performing complex combined resections of the arch and how to treat the descending aorta. To save the patient first has always been our major surgical standard and we believe this must always be priority in the critical decision-making process.

Here we will have a quick look at evolving concepts, ideas and technologies, asking some questions for the near future.

Where are we?

As stated, the currently accepted gold standard for treatment of acute type a dissection is the radical management of the proximal tear regardless of its location. Most of the times, the tear is located in the supracoronary region of the ascending aorta. Due to a frequently associated tear in the arch or extended dissection to the arch or descending thoracic aorta, it is mandatory to explore the arch under hypothermic arrest. This carries significant technical difficulty and higher risk of mortality. All types of techniques have been evaluated including simple hypothermic arrest at 18-20°C.2 In recent years retrograde cerebral perfusion through the superior vena cava and antegrade cerebral perfusion through the neck vessels has been advocated trying to reduce the incidence of neurological damage.3,4 However, surgical trauma and perioperative morbidity continues to be a major limiting factor for a complete single-stage repair when needed. Therefore, the classical strategy to approach the ascending aorta, arch and descending thoracic aorta still consists of a two-operation approach through median sternotomy and left lateral thoracotomy. There are also some additional limitations for a second operation, namely the increased age of surgical candidates.

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after primary anterior repair and the associated comorbidity, especially of pulmonary origin. Not to be neglected is the still significant risk of paraplegia related to operations on the thoracoabdominal aorta regardless of the surgical approach and technique used. Mortalities in the range of 20-30% are common even in the best hands.5

What can be offered today?

This type of surgery is still a matter of controversy. Previous attempts to decrease risks and make operations simple are not new. An important modification of the surgical technique was the operation designed by Borst et al more than twenty years ago and well known today as the “elephant trunk” repair.6 Even though there is an agreement that this technique performs well, its major drawback is the need for a second operation provided the descending thoracic aortic is left untouched or there are different levels of involvement. New applications are being explored with excellent results.7

As stated, a significant proportion of patients will eventually require additional procedures for acute or chronic dissections or atherosclerotic aneurysms. The advent of endovascular stent-grafting has actually modified our perception of the patient1 and has greatly facilitated the approach to complex patients although we still lack sufficient follow-up to clearly define true indications and possible pitfalls. Actually only midterm results regarding descending endovascular retrograde repair of thoracic aneurysms have been reported.8 Something important to consider are the continuous changes in the stent-graft technology. Acute aortic dissections will continue to be a challenge for a number of years due to its pathophysiology and characteristics.

New developments are on the horizon. All of them try to overcome the associated morbidity and mortality, to decrease the need for late reoperations and to facilitate single-stage repair of both dissections and aneurysms if feasible. Technological advances are looked as the eventual panacea and this has to be looked at with care. Recently, some modifications of the “elephant trunk” technique are seen as promising. Antegrade deployment of nitinol stent-grafts appear to be of interest. Initial reports using conventional stent-grafts for retrograde deployment9,10 have led to the identification of some problems and the need to reapproach this issue with new stent-grafts especially designed for antegrade deployment.

Some new devices are currently available in the market like the Chavan-Haverich11 and the E-Vita Open (Jotec, Hechingen, Germany) integrated stent-grafts, however global experience is still scanty.12-14 These devices consist of stent-grafts with an integrated conventional Dacron graft that will be used to repair the arch and ascending aorta during surgical repair. A common fact seems to be the immediate thrombosis of the false lumen after surgery in the case of aortic dissection and this is regarded as a very positive issue.

Mid- and long-term results are needed to ascertain what will the real role of these devices be.15

Hybrids?

This sounds like an attractive word. Some patients might benefit from a hybrid approach combining retrograde transfemoral deployment of stent-grafts in the treatment of chronic complex aortic disease, associated with arch debranching through median sternotomy.16 Some suffering from more complex disease may benefit from procedures that involve the use of newer devices such as those integrated stent-grafts designed for antegrade deployment during circulatory arrest.12-14 What will work better is yet to be defined. The key point will be an exhaustive collection of data, the use of judicious indications, avoiding biases in patient selection and lack of more favorable results to skew the balance in its favor. This has always been our surgical standard. And please, do not forget old techniques that still work.

References

Current Applications of Coronary and Cardiac Multidetector Computed Tomography

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Abstract

Cardiovascular disease remains the principal cause of death in the modernized world. Several novel noninvasive imaging techniques have been recently developed to improve diagnosis of cardiac and coronary disease. Of these advances, multidetector computed tomographic (MDCT) angiography has evolved most dramatically to transform computed tomography from a single-slice trans-axial modality to a three-dimensional volumetric technique. Current generation 64-detector row CT scanners allow for large volume coverage with submillimeter spatial and sub-second temporal resolution. These advances enable important new applications for MDCT in the assessment of cardiac and coronary anatomy. In this report, we discuss in depth potential appropriate uses of cardiac and coronary MDCT angiography.

Keywords: Coronary CT angiography • Non-invasive cardiac imaging • Coronary atherosclerosis

Cardiovascular disease (CVD) is the principal cause of morbidity and mortality in the modernized world, accounting for the deaths of more than 16 million individuals per year. Epidemiologic studies suggest that CVD is occurring at earlier ages and at higher costs, somewhat paradoxically related to improved economic conditions worldwide, and associated changes in diet and physical activity. We are facing an epidemic of obesity and metabolic syndrome and an increasing incidence of CVD. These disquieting data necessitate improved and earlier detection and better characterization of CVD. Numerous non-invasive imaging modalities have been extensively studied for the diagnosis of CVD and for directing patient-specific therapies. These techniques include magnetic resonance imaging, single photon emission computed tomography, echocardiography and multidetector computed tomography.1,4 Recently, advances in computed tomography (CT) technology have permitted the emergence of the use of current generation 64-detector CT scanners as an imaging modality with the ability to comprehensively evaluate both coronary and cardiac structure and function.1,9 At its introduction in the early 1970s, CT technology possessed certain limitations (including limited spatial and temporal resolution) that precluded its use for cardiac imaging. The

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small diameter of the coronary arteries requires high spatial resolution, while perpetual coronary artery motion demands high temporal resolution. It was not until the late 1990s when CT achieved submillimeter spatial resolution, therapy permitting the acquisition of data of an isotropic nature, namely that each voxel (or data element) is of equal resolution in the x-, y- and z-planes. Furthermore, at this time, CT achieved sub-second temporal resolution, thereby permitting acquisition of virtually motion artifact-free data. Today, with the recent introduction of 64-slice MDCT scanners, rapid volume coverage can now be achieved which, when coupled with high spatial and temporal resolution, results in exquisite cardiac and coronary artery imaging.

The purpose of this report is to review appropriate potential uses for cardiac and coronary MDCT imaging. The potential uses are primarily based on the recently released ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR Appropriateness Criteria for Cardiac Computed Tomography and Cardiac Magnetic Resonance Imaging. In case where the authors’ opinion of the clinical utility of cardiac MDCT imaging diverges from the appropriateness criteria set forth, it will be noted.

Perhaps the greatest optimism for the successful integration of cardiac MDCT into daily clinical practice lies rooted in the detection of symptomatic coronary artery disease. Within this indication, numerous subsets of patients can be delineated (Table 1).

Although there is great hope for MDCT to be able to successfully diagnose and stratify risk in symptomatic patients presenting with chest pain, there is in fact little data to support its incremental clinical value above and beyond more traditional non-invasive imaging modalities. Nonetheless, preliminary positive studies examining the role of MDCT in the evaluation of chest pain in patients without known coronary artery disease are beginning to emerge.

In a study evaluating 31 symptomatic emergency department patients with chest pain for≥30 minutes, non-diagnostic electrocardiograms and normal cardiac enzyme levels, MDCT coronary angiography (utilizing 4- and 16-slice CT scanners) was able to detect significant disease in 21 individuals who were ultimately diagnosed with an acute coronary syndrome. The sensitivity and specificity were 95.5% and 88.9%, respectively. This early study, utilizing primarily older generation scanners with inferior temporal and spatial resolution, lent initial credence to the value of MDCT in the evaluation of symptomatic patients. It may be reasonable to assume that with the introduction and more widespread use of newer, improved 64-detector scanners, the results of this study may be expanded to larger populations.

In a similar study, 69 individuals who presented to the emergency department with chest pain were evaluated with 16-slice chest MDCT angiography to determine whether MDCT might provide incremental value in the assessment of chest pain.

<table>
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<tr>
<th>Table 1. Appropriateness Criteria for Coronary CTA</th>
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<td><strong>Detection of CAD: Symptomatic—Evaluation of Chest Pain Syndrome (Use of CT Angiogram)</strong></td>
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<tr>
<td>• Intermediate pre-test probability of CAD</td>
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<td>• ECG uninterpretable OR unable to exercise</td>
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<td><strong>Detection of CAD: Symptomatic—Evaluation of Intra-Cardiac Structures (Use of CT Angiogram)</strong></td>
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<tr>
<td>• Evaluation of suspected coronary anomalies</td>
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<tr>
<td><strong>Detection of CAD: Symptomatic—Acute Chest Pain (Use of CT Angiogram)</strong></td>
</tr>
<tr>
<td>• Intermediate pre-test probability of CAD</td>
</tr>
<tr>
<td>• No ECG changes and serial enzymes negative</td>
</tr>
<tr>
<td><strong>Detection of CAD with Prior Test Results—Evaluation of Chest Pain Syndrome (Use of CT Angiogram)</strong></td>
</tr>
<tr>
<td>• Uninterpretable or equivocal stress test (exercise, perfusion, or stress echo)</td>
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<tr>
<td><strong>Structure and Function—Morphology (Use of CT Angiogram)</strong></td>
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<tr>
<td>• Assessment of complex congenital heart disease including anomalies of coronary circulation, great vessels, and cardiac chambers and valves</td>
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<tr>
<td>• Evaluation of coronary arteries in patients with new onset heart failure to assess etiology</td>
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<tr>
<td><strong>Structure and Function—Evaluation of Intra- and Extra-Cardiac Structures (Use of Cardiac CT)</strong></td>
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<tr>
<td>• Evaluation of cardiac mass (suspected tumor or thrombus)</td>
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<tr>
<td>• Patients with technically limited images from echocardiogram, MRI, or TEE</td>
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<tr>
<td>• Evaluation of pericardial conditions (pericardial mass, constrictive pericarditis, or complications of cardiac surgery)</td>
</tr>
<tr>
<td>• Patients with technically limited images from echocardiogram, MRI, or TEE</td>
</tr>
<tr>
<td>• Evaluation of pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation</td>
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<tr>
<td>• Noninvasive coronary vein mapping prior to placement of biventricular pacemaker</td>
</tr>
<tr>
<td>• Noninvasive coronary arterial mapping, including internal mammary artery prior to repeat cardiac surgical revascularization</td>
</tr>
<tr>
<td><strong>Structure and Function—Evaluation of Aortic and Pulmonary Disease (Use of CT Angiogram)</strong></td>
</tr>
<tr>
<td>• Evaluation of suspected aortic dissection or thoracic aortic aneurysm</td>
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<tr>
<td>• Evaluation of suspected pulmonary embolism</td>
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*Non-gated, CT angiogram which has a sufficiently large field of view for these specific indications

At a one month follow-up, the summation of clinical history, physical examination, any subsequent cardiac
workup and MDCT were evaluated. Of the 69 individuals who presented, 13 individuals (19%) were diagnosed with significant MDCT findings above and beyond “standard” workup. Ten of thirteen of these findings were cardiac, while 3 were non-cardiac. The three non-cardiac significant findings included pericarditis with pericardial effusion, pneumonia, and pulmonary embolism. The inclusive sensitivity and specificity for all causes of chest pain (cardiac and non-cardiac) were 87% and 96%, respectively.

While there is not an abundance of data examining the role of MDCT coronary angiography for the evaluation of symptomatic chest pain, there is nevertheless a large body of data that demonstrates that high-row (16- and 64-slice) MDCT angiography is highly accurate in the detection of obstructive coronary artery lesions (Figure 1 and 2).

Figure 1. CTA (curved reformatted image) of left anterior descending coronary artery. Arrows indicate regions of mild, non-obstructive atherosclerotic plaque with no significant stenosis

Figure 2. CTA of left anterior descending coronary artery. Arrows indicate regions of significant, obstructive atherosclerotic plaque

The earliest demonstration of reliable non-invasive coronary angiography with 16-slice MDCT was published by Nieman and colleagues in 2002. They studied 59 primarily male patients in whom obstructive coronary artery disease was suspected for whom cardiac catheterization had been planned. Prior to conventional coronary angiography, these patients underwent MDCT coronary angiography. MDCT scans were compared to quantitative coronary angiography (QCA). In this study, only 231 of 332 coronary segments (69%) could be properly evaluated by MDCT. In evaluable segments, detection of an obstructive stenosis (defined as >50% by QCA) exhibited a sensitivity, specificity and negative predictive value of 95%, 86% and 97%, respectively. This study was noteworthy for numerous reasons. First, this study demonstrated feasibility of non-invasive coronary angiography with MDCT. Moreover, the study underscored several important factors that affect overall accuracy of MDCT angiography. Twenty arteries were incorrectly assigned by MDCT as stenotic, each exhibiting significant vessel calcification. This limitation has been repeated time and again in MDCT angiography studies, and highlights the importance of the partial volume averaging effect of calcific plaque in the over-estimation of coronary artery stenosis.

In a similar study employing 16-slice MDCT coronary angiography, Ropers et al. found 38 of 308 vessel segments to be unevaluable and thus excluded these segments from final analysis. The design of their study consisted of a per-vessel analysis rather than a per-segment analysis. This issue is central to the accuracy of MDCT angiography because, as the authors correctly noted, a high-grade proximal stenosis may likely affect downstream image in the distal affected vessel. Employing this strategy, the sensitivity and specificity for the detection of obstructive stenosis (defined as >50%) was 92% and 93%, respectively.

The accuracy of MDCT coronary angiography has also been examined in a population with a high prevalence of coronary artery disease. In a study of 60 patients with a mean coronary artery calcium score of 506, there was an inverse relationship between coronary calcification and accuracy of stenosis detection with MDCT. In all patients, the sensitivity for stenosis detection was 72% and specificity was 97%. When individuals with coronary artery calcium scores >1000 were excluded, the sensitivity and specificity rose to 98% for both. In addition to evaluation of coronary artery segments by MDCT, the investigators in this study also examined per-patient characteristics of coronary MDCT. When an individual was examined as a whole for the presence or absence of a significant obstructive stenosis, the correct identification of significant coronary artery stenosis could be made in 97% of patients.

The largest and most successful study utilizing 16-detector row MDCT prospectively evaluated 103 consecutive patients undergoing both invasive coronary angiography and coronary CTA. On a per-segment-basis, the sensitivity, specificity and positive and negative predictive value of MDCT was 95%, 98%, 87%, and 99%, respectively. On a per-patient basis, the positive predictive value increased to 98%.

Raff and colleagues published the first study of the
diagnostic accuracy of 64-detector CT scanners.\textsuperscript{17} They studied 70 individuals, examining the exactness by which 64-detector CT scanners could correctly classify coronary artery lesions on a per-segment, per-vessel, and per-patient analysis. In comparison to quantitative coronary angiography, Raff’s group reported sensitivity, specificity, and positive and negative predictive values on a per-patient analysis of 90%, 95%, 93%, and 93%, respectively. In a careful analysis of mitigating variables in MDCT angiography, higher coronary artery calcium burden, increasing body mass index, and faster heart rate were associated with worsening scan quality and reduced accuracy of detection of significant coronary artery disease (Figure 3).

Figure 3. Heavily calcified coronary arteries preclude accurate assessment of coronary stenosis (right hand panel). Coronary angiography (left hand panel) shows no obstruction in area of heavy calcification, but a tight proximal lesion, not seen on CTA, is present in the proximal segment.

Since Raff’s initial investigation with 64-detector row CT, several other studies have been published examining MDCT against conventional coronary angiography.\textsuperscript{18-23} With one lone exception, the sensitivity, specificity and negative predictive value of these studies have well exceeded 90%. It has now become widely accepted that current generations of CT scanners are highly accurate in the detection of obstructive coronary artery stenosis.

These landmark studies and others examining the accuracy of coronary CTA are important and share many lessons. In chronology, the sensitivity, specificity, and positive and negative predictive values of high-detector row MDCT for the identification of obstructive coronary artery stenosis demonstrated improvement over time. It is likely that this progression in test performance is due, in part, to a learning curve that is intrinsic to the use of any new and developing technology. Moreover, the increased volume coverage with 64-row versus 16-row scanners results in much less cardiac motion misregistration artifact, thereby permitting enhanced diagnostic accuracy. Another lesson learned is that higher calcium scores result in reduced accuracy for detection of stenosis. This is likely explained by partial volume averaging of calcium which results in decreased MDCT accuracy compared to QCA. Furthermore, the importance of low heart rate and normal body mass index for enhanced accuracy has been reliably demonstrated in these investigations. It is noteworthy to mention that these studies uniformly included only individuals undergoing subsequent invasive coronary angiography. Therefore, the extrapolation of these results to individuals without a clinical indication for cardiac catheterization may not necessarily be appropriate. Indeed, individuals without a clinical need for conventional coronary angiography (and thereby with a lower pre-test likelihood of coronary artery disease) might likely possess lower levels of calcific coronary plaque such that the accuracy of coronary CTA in these individuals may be enhanced.

While deemed “uncertain” for appropriate use by the recently introduced guidelines, MDCT coronary angiography has nonetheless been extensively evaluated for the assessment of patients with coronary artery bypass grafts (CABGs) as well as those with intracoronary stents. Given their generally larger size and minimal mobility, coronary artery bypass grafts are theoretically easier to image than native coronary arteries (Figure 4).

Figure 4. Three-dimensional volume rendered image of a patient following coronary artery bypass grafting, patent vein graft from the aorta to the right coronary artery (VG), and patent but small left internal mammary graft to the left anterior descending coronary artery. (LIMA)

In a systematic review of 985 patients with 2200 bypass grafts, 16-slice MDCT angiography demonstrated 99% sensitivity and 98% specificity for the detection of bypass graft patency.\textsuperscript{23} Moreover, MDCT angiography identified significant bypass graft stenoses with 88% accuracy.

In patients who have undergone coronary artery bypass grafting who require repeat operation, MDCT angiography is useful for evaluation of grafts not only for patency but also for surgical planning. In a small study of fifteen patients, MDCT angiography delineated significant narrowings of the internal mammary arteries, adherence of vascualr and cardiac...
structures to the sternum and severity of calcifications of the aorta. These findings resulted in the cancellation of two patients in whom a re-operation was considered to be associated with unnecessarily high risk. In a larger study of 202 patients, MDCT angiography was useful in determining the mean distances of the internal mammary artery grafts to the sternum at three points that traversed the thoracic cavity.

These important findings prior to repeat operations are easily depicted by noninvasive MDCT angiography. Intracoronary stents have also been evaluated using MDCT angiography. Different intracoronary stents exhibit different partial volume averaging effects. When 111 consecutive stents were evaluated in 65 individuals utilizing a 40-slice MDCT scanner, detection of moderate or severe restenosis was associated with a sensitivity, specificity, and positive and negative predictive values of 88.9%, 80.6%, 47.1%, and 97.4%, respectively (Figure 5).

In a similar study evaluating 51 individuals with coronary stents and utilizing 16-slice MDCT angiography, the sensitivity, specificity, and positive and negative predictive value for the assessment of ≥50% restenosis of an intracoronary stent were 88.3%, 98.5%, 83.3%, and 97.3%, respectively.

MDCT coronary angiography has also been studied in patients with stable angina pectoris. In a study of 128 patients with stable angina scheduled for invasive coronary angiography, Mollet et al. focused on “revascularizable” coronary segments, or those > 2mm in diameter. In this group, there were 18 obstructive lesions identified by QCA, of which 14 were identified by MDCT. Of the four coronary lesions not correctly identified, two lesions exhibited severe calcification and two exhibited significant motion artifact. The sensitivity, specificity, and positive and negative predictive value of 16-detector coronary CTA for the detection of significant stenosis were 92%, 95%, 79%, and 98%, respectively.

Given MDCT angiography’s value for the detection of significant CAD, some groups have proposed the combination of MDCT coronary anatomic evaluation with stress test functional evaluation. While no current studies currently exist that examine the incremental diagnostic benefit of MDCT coronary angiography following stress testing, the practice is nonetheless becoming commonplace. As noted in recent guidelines, MDCT angiography is considered appropriate for use in stress tests considered to be equivocal or suspected to be inaccurate. Direct comparison of combination MDCT and stress testing to either modality alone is necessary to further delineate the role of either in the evaluation of patients at risk for coronary heart disease.

Current use of MDCT coronary angiography has been primarily limited to symptomatic individuals. Non-invasive coronary evaluation by way of stress testing is commonly employed for cardiac risk stratification in high-risk asymptomatic individuals undergoing non-cardiac surgery. MDCT coronary angiography is finding increasingly use in this patient population, and may provide a better evaluation of overall coronary plaque burden in the patient undergoing surgery. Recently, fifty-five consecutive patients with severe aortic stenosis were evaluated with 16-slice MDCT prior to coronary angiography. In this study, the sensitivity of detecting significant stenosis was 100% compared to invasive coronary angiography. Comparing the sensitivities with high (>1000) and low (<1000) calcium scores, MDCT could permit avoidance of conventional angiography in 80% of low-calcium cases but in only 6% of high-calcium cases. From these data, the authors concluded that MDCT may serve as an alternative to conventional cardiac catheterization in patients undergoing elective aortic valve replacement.

To this point, the discussion of the use of coronary CT angiography has focused primarily on the detection of coronary artery disease. The use of contrast-enhanced CT angiography for the demarcation of anomalous coronary artery origins and courses has been well validated as early as the introduction of the 4-slice CT scanners (Figure 6).
In perhaps the largest review of 1758 individuals who had undergone either 4- or 16-detector coronary CT angiography, 28 individuals (1.6%) were found to have coronary artery anomalies. Of these patients, 13 anomalies were considered “malignant” forms because of their path between the aortic root and pulmonary trunk. The majority of these “malignant” anomalies were of the right coronary artery (11 of 13). MDCT coronary angiography is superior to conventional cardiac catheterization for the identification of coronary anomalies, as 11 of 20 invasive angiograms performed on individuals suspected of having coronary artery anomalies either resulted in inadequate cannulation of the anomalous artery or ability to render a definitive diagnosis.

MDCT angiography may be useful for the delineation of other congenital abnormalities. Certain atrial septal defect types, such as sinus venosus defects, are sometimes not well visualized by echocardiography. CT angiography has been shown effective in identifying atrial septal defects of varying types as well as for delineating their borders in patients undergoing percutaneous closure (Figure 7).

Perhaps the greatest hope for MDCT angiography in the evaluation of patients presenting with chest pain is the “triple rule out” of acute coronary syndrome, pulmonary embolism and thoracic aortic dissection.

While no formal investigations to date have evaluated the accuracy of MDCT angiography for this collective purpose, MDCT has nonetheless been demonstrated to be highly accurate in the detection of both pulmonary emboli and aortic dissection. The PIOPED II investigators evaluated 824 patients with 4-, 8- and 16-slice MDCT scanners. Excluding MDCT scans of poor image quality, the sensitivity and specificity of MDCT for the diagnosis of pulmonary emboli was 83% and 96%, respectively. When combined with venous phase imaging, the sensitivity increased to 90% with specificity remaining constant at 95% (Figure 8).

Similarly, even with the use of older-generation CT scanners, the sensitivity for the detection of acute aortic dissection has been high, ranging between 88-100%. Cardiac MDCT angiography may also be employed for evaluation of cardiac structure and function. In this vein, MDCT angiography may have great potential in the evaluation of individuals presenting with new-onset heart failure. MDCT angiography can provide comprehensive assessment of left and right ventricular ejection fraction and volume as well as determining the extent of coronary artery disease. This may render this modality useful for the distinction between ischemic and nonischemic cardiomyopathies. Although systemic evaluation of cardiac CT has not yet been performed for the distinction of non-ischemic versus cardiomyopathy, it is not unreasonable to consider its use. In the absence of significant left main, proximal left anterior descending, or three-vessel coronary artery disease, the physician may be able to confidently conclude that ventricular dysfunction may be due to a cause other than coronary artery disease.

In our own laboratory, we reconstruct twenty phases of the cardiac cycle in 5% increments of the R-R interval. Using this protocol, appraisal is possible for both overall ventricular systolic function as well as for segmental wall motion. The accuracy of MDCT cardiac imaging for these purposes has been well validated. Cardiac MDCT imaging has been compared to cardiac magnetic resonance imaging (MRI) and echocardiography. In a study of 52 patients, the correlation between MDCT and MRI was high for left ventricular end diastolic volume (r=0.83), left ventricular systolic volume (r=0.90), ejection fraction (r=0.88), and myocardial mass (r=0.84). The correlation of echocardiography to MRI was low for left ventricular end diastolic volume (r=0.05), end systolic volume (r=0.59) and ejection fraction (r=0.24). These data suggest that cardiac MDCT imaging may be more useful for evaluation of ejection fraction in individuals and thus, may be considered in the evaluation of individuals with technically limited echocardiograms.

In a binary analysis of 616 myocardial segments for the presence or absence of segmental wall motion abnormalities,
there was an 89% agreement between MDCT cardiac imaging and transthoracic echocardiography. In this study, only five phases of the cardiac cycle (0%, 40%, 50%, 70%, and 80%) were reconstructed. It is undoubtedly true that agreement between MDCT and echocardiography would be enhanced by the addition of more phases of the cardiac cycle. A potential advantage of cardiac MDCT over transthoracic echocardiography in the evaluation of individuals with heart failure may lie in the enhanced ability of MDCT to visualize both the left and right ventricles. As the right ventricular size and function has historically been difficult to assess with echocardiography, identification of a noninvasive method for quantifying function of both ventricles accurately may be valuable to understand an individual’s heart failure etiology as well as to guide its treatment. In a study of twenty patients evaluated by both MDCT cardiac imaging and first-pass radionuclide angiography, agreement between methods was good (R= 0.854, p=0.001) with reconstructions of only two phases of the cardiac cycle. Moreover, MDCT cardiac imaging was able to provide right ventricular end-diastolic and end-systolic volumes as well as right ventricular mass, which is not possible with radionuclide angiography.

Cardiac MDCT angiography is also useful for evaluation of non-coronary cardiovascular anatomy. It is well documented that muscular tissue within the pulmonary veins are often the origin of arrhythmogenic foci that serve as an important cause of atrial fibrillation. Numerous surgical and more recently, percutaneous techniques have been developed to disconnect electrically the pulmonary veins from the left atrium, thereby providing a cure to the arrhythmia. As the anatomy of pulmonary vein is different amongst individuals, noninvasive imaging of the pulmonary veins and left atrium in individuals prior to atrial fibrillation ablation is essential (Figure 9).

Specific examples of pulmonary vein variation include a common left or right pulmonary vein (in 2.4-25% of individuals imaged) as well as accessory pulmonary veins. These findings have obvious implications at the time of ostial segmental pulmonary vein isolation. MDCT cardiac imaging has been embraced with increasing use for the three-dimensional reconstruction of pulmonary veins and left atrium. In our own laboratories, we routinely create MDCT renderings of left atria and pulmonary veins in patients prior to segmental pulmonary vein isolation. These pulmonary vein and left atrium surface-shaded three-dimensional models are created using CardEP software (GE Healthcare, Milwaukee, WI) or EBW software (Philips Medical Systems, Cleveland, Ohio) and can be easily merged with the Carto system (Figure 10).

In this way, pulmonary vein ostial diameters as well as their length to first branchpoint can be easily measured. The fusion between the CT and electroanatomic data results in an accuracy to 2.1 mm in distance between the mapping points and the MDCT surface.

New developments in software technology now permit co-registration of three-dimensional surface-shaded cardiac MDCT images with projection images acquired by fluoroscopy. In twenty patients placed in the same position, co-registration of MDCT images and fluoroscopic images of the left atrium demonstrated a mean registration error of only 1.4 mm. This technique will undoubtedly result in improved navigation and localization of intracardiac catheters during atrial and ventricular arrhythmia ablations. MDCT cardiac imaging is also useful for evaluation of the left atrial appendage for the presence or absence of thrombus. Prior studies utilizing older generation scanners with inferior temporal resolution have demonstrated MDCT’s ability to identify thrombus. With current generation 64-slice MDCT scanners with improved temporal resolution, thrombus as well as thrombus-in-formation (non-clearing spontaneous echo contrast) can be successfully identified (Figure 11).
Focal pulmonary vein stenosis as a complication of atrial fibrillation ablation is widely recognized, occurring as a result of hyperplasia of the venous vascular wall. MDCT cardiac imaging can reliably demonstrate focal pulmonary vein stenosis and is useful for the follow-up of patients who develop symptoms after atrial fibrillation ablation.

The coronary venous system is being increasingly utilized for percutaneous treatment of patients with advanced left ventricular systolic dysfunction. The coronary sinus and lateral marginal veins are often cannulated with a transvenous lead in the placement of biventricular pacemakers in patients with mechanical dyssynchrony. Successful placement of the transvenous left ventricular lead in an appropriate location within the coronary venous system is estimated to be 88-95%. This number may be lower in less experienced institutions and underscores the fact that 5-12% of individuals will undergo an invasive procedure without successful lead implantation. MDCT angiography is highly successful in defining coronary vein anatomy prior to any invasive procedure. In 37 individuals, MDCT angiography has been shown to be successful for the illustration of the coronary sinus and its tributaries. In these individuals, identification of coronary vein variants was noted, including separate insertion sites of the coronary sinus and cardiac veins, linking the anterior and posterior coronary veins at the crux cordis, and incomplete connection of the posterior vein to the contralateral sinus. These findings may provide explanations for cases where successful left ventricular lead implantation via the coronary sinus cannot be achieved or aid in the pre-procedural planning of where a left ventricular lead is to be placed.

Similar hybrid imaging systems are being developed to use CTA mapping of the coronary arteries in the cardiac catheterization laboratory to assist in performing real time angiography. Coronary CTA, inherently three dimensional, is useful in selecting angiographic views and avoiding foreshortening artifacts present in silhouette imaging produced by conventional fluoroscopy.

**Conclusion**

With the introduction of current generation scanners which can provide rapid volume coverage with improved spatial and temporal resolution, the utility of MDCT for cardiac and coronary imaging is experiencing exponential growth. MDCT angiography of the coronary arteries is useful for the evaluation of symptomatic individuals with and without known coronary artery disease, with high accuracy. The utility of MDCT cardiac imaging extends to non-coronary indications that aid the cardiac specialist in applications of electrophysiology, echocardiography, heart failure, and nuclear cardiology. The evolution of MDCT has been rapid; further evidence supporting these and many more applications can be expected, as investigators in many centers around the world are excited by the many opportunities for clinical research presented by this new technology.

**Reference**


Figure 11. CTA showing left atrial thrombus (arrow)
Current Applications of Coronary...


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Methylenetetrahydrofolate Reductase (MTHFR) Gene C677T Polymorphism Is Associated with Coronary Atherosclerosis Disease in a Sample of Iranian Patients

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2Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Background: Several studies showed that elevated plasma homocysteine level is a risk factor for coronary artery disease (CAD). A common polymorphism C677T of methylenetetrahydrofolate reductase (MTHFR) gene is reported to be associated with decreased enzyme activity and increased blood homocysteine level.

Methods: This study evaluated the association between C677T polymorphism and blood homocysteine level with CAD in 100 patients compared to 100 normal controls.

Results: Higher prevalence of the C677T polymorphism as well as elevated level in blood homocysteine were observed in Iranian CAD cases compared to the normal control. The C677T MTHFR common polymorphism was significantly associated with CAD, supported by a P value 0.032 and Chi-square equal to 6.87.

Conclusions: The TT genotype of MTHFR gene was attributed to increased blood homocysteine level in patients compared to T/C and C/C genotypes in studied Iranian cases. This study shows the advantage of testing C677T polymorphism in affected patients as a risk factor for coronary artery disease.

Keywords: MTHFR • Coronary artery disease • Folate • Folic acid • Homocysteine

Introduction

Homocysteine is a thiol-containing amino acid produced from methionine metabolism. Elevated plasma homocysteine is generally accepted as an independent risk factor for cardiovascular disease and venous thrombosis.1-5 Enhanced risk associated with a 5μmol/l elevated total homocysteine was estimated to be the same as that associated with a 0.5 μmol/l increased total cholesterol in CAD patients.6 Homocysteine is involved in two main metabolic pathways; transsulfuration in which homocysteine is catalyzed to cysteine by cystathionine β synthase and Vit B6 and remethylation in which homocysteine is converted to methionine in a reaction catalyzed by methionine synthase. The methyl donor in the second reaction is methylenetetrahydrofolate (MTHF) which is converted by methylenetetrahydrofolate reductase enzyme (MTHFR).7

Common polymorphism of C to T substitution at the nucleotide position 677 of MTHFR gene causes alanine to valine substitution and produces thermolably sensitive form of enzyme. This polymorphism reduces enzyme activity and increases thermolability in lymphocyte extract. It is
associated with high plasma homocysteine level and has been involved in development of early atherosclerotic and thrombotic vascular diseases.8-13 Thermolabile MTHFR however accounts for mild hyperhomocysteinemia in approximately 25% of patients with vascular disease.7,14,15 The aim of this study was to assess the prevalence of the C677T MTHFR polymorphism and its association with plasma homocysteine level among CAD patients diagnosed in Tehran Heart Center.

Methods

Sampling

This study was carried out on 100 reetnelovpatients aged 32 to 56, who had angiography in Tehran Heart Center with angiographically documented CAD, at least 50% coronary artery stenosis (left anterior descending, circumflex or right coronary artery) or a history of coronary angioplasty or surgical revascularization. A cardiologist consulted all chosen families. A control group consists of 100 randomly chosen normal volunteers, aged 32 to 55, without a history of CAD. Informed consent was obtained from all participants and the study was approved by the ethics committee of the center. Five milliliter of blood sample was obtained from cases and controls. Total fasting plasma homocysteine was measured for all patients and 100 controls using homocysteine measuring kit (Axis homocysteine enzyme immunoassay, Germany). For DNA analysis, standard salting out DNA extraction procedure was used to extract DNA from 200 collected blood samples for as previously described in Miller et al 1988.16

Polymorphism analysis of MTHFR gene

Hundred CAD patients and 100 healthy normal controls were tested for common C677T MTHFR polymorphism. A Pair of primers were designed to amplify a 254 bp fragment of MTHFR gene containing codon 677 forward and reverse primers were (5´GCC TCT CCT GAC TGT CAT CC3´) and (5´GGA GCT TAT GGG CTC TCC TG3´) respectively. PCR thermal cycle was performed in 32 cycles. Each cycle consisted of 95°C denaturation for 30 seconds, 60°C annealing for 1 minute and 72°C extension for 30 seconds. The thermal cycles began with an initial denaturation of 95°C for 5 minutes followed by a final extension of 72°C for 10 minutes. PCR product was exposed to restriction enzyme digestion with HinfI (Roche, Germany). The presence of the C677T Polymorphism within the MTHFR gene creates a HinfI restriction site that is detected by appearance of a 147 and 108 base pair fragments on a 10% polyacrylamide PAGE gel electrophoresis, visualized with silver staining (Figure 1).17

Statistical analysis

The predicted number of subjects required for meaningful analysis was determined based on the following assumptions: the predicted mean ± standard deviation homocysteine plasma concentration in healthy subjects (10.5±2.8 μmol/L), difference in the homocysteine level between patients and controls (10%) and the level of significance 0.05. Allele frequencies were calculated for each genotype by allele counting. Descriptive values were expressed as the mean ±SD. Comparisons of allele frequencies between case and control groups were determined using a Pearson χ² test using SPSS for windows version 9.0 (Chicago, Illinois) software. Differences between patient and control group were assessed by student t test for continuous variables (Homocysteine). Fisher exact test was used when the number of observation in any group was less than or equal to 5. All tests were two-tailed and p<0.05 was considered as significant.

Results

Hundred CAD cases and 100 normal controls were genotyped for common polymorphism C677T MTHFR and blood homocysteine level to determine their association with CAD disease. The mean age of case and control was 48.2 and 47.8 respectively, from whom 30% were female. The frequency of mutated C677T MTHFR polymorphism
was 33.5% among 100 cases and 22% among 100 normal controls (Table 1).

Table 1. Distribution of C677T polymorphism of the MTHFR gene and its genotype frequencies among CAD cases and normal controls

<table>
<thead>
<tr>
<th>Groups</th>
<th>Normal (C/C)</th>
<th>Heterozygote (T/C)</th>
<th>Mutant (T/T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>43.0 (34.0%)</td>
<td>47.0 (47.0%)</td>
<td>10.0 (10.0%)</td>
</tr>
<tr>
<td>Control</td>
<td>61.0 (61%)</td>
<td>34.0 (34.0%)</td>
<td>5.0 (5.0%)</td>
</tr>
</tbody>
</table>

The frequencies of the C/C, C/T, and T/T genotypes among control group were 61.0%, 34.0% and 5.0% respectively whereas the corresponding frequencies among the patients with CAD syndrome were 43%, 47% and 10% respectively. The incidence of the thermolabile C677T MTHFR in 100 patients with CAD and 100 controls was compared (Table 1). The difference between the two groups was significant ($\chi^2 = 6.87$ and $P=0.032$). There was no significant difference in the level of thermolabile MTHFR among male and female in either patient ($\chi^2 = 1.32$, $P=0.420$) or control ($\chi^2 = 4.9$, $P=0.08$), as well as for age in either patient ($\chi^2 = 3.6$, $P=0.162$) or control ($\chi^2 = 5.9$, $P=0.380$) groups.

The level of plasma homocysteine was compared among patients and controls. The proportion of homocysteine was substantially higher among patients with CAD than that among the controls. The difference of blood homocysteine level between two groups was significant (14.93±5.23 versus 11.81±5.75 and $P<0.05$). The correlation between MTHFR genotypes T/T, C/T and C/C and homocysteine level in cases was 18.75, 15.32 and 14.93 in comparison to 13.68, 11.07 and 13.68±5.70 for the control group ($P<0.05$).

Individuals homozygous for T/T genotype were associated with higher levels of plasma homocysteine level than C/T and C/C genotypes. There was a small increase in homocysteine levels in patients with C/T genotype. This data is in line with several previous studies that have found elevated plasma homocysteine concentration in CAD patients with T/T genotypes. It is in accordance with previous studies that suggest folate abnormalities appear to play a major role in the pathogenesis of increased homocysteine level in older persons.

Numerous studies have demonstrated a significant relationship among C677T polymorphism, homocysteine concentration and CAD, however some reports have suggested no relationship between risk of CAD and C677T polymorphism. Kluijtmans and Whitehead performed a meta-analysis of the first 10 studies that argued an increase risk of CAD in patients with TT genotype. They demonstrated a 30% increased risk of CAD associated with TT and CT genotypes (OR 1.27, 95% CI 1.11-1.44).

In a report from the Polish population, which included 100 patients after MI and 100 healthy volunteers, no significant relationship was shown between MTHFR genotype and age where the MI happened. However, different results were obtained in the Turkish population where 96 males who suffered MI below the age of 45 with TT genotype showed almost six-fold higher risk of MI than other genotypes found in 100 healthy volunteers who had 5% incidence of TT genotype.

On the other hand, some workers who found no relationship between polymorphism and CAD had studied older patients. Payne and colleagues have suggested an obscuring of the correlation of the polymorphism with premature onset of CAD in selected patients that achieved a negative relationship. Our study highlights the potential prognostic significance of the C677T substitution in MTHFR gene in patients with coronary artery disease in a sample of Iranian patients.
Acknowledgment

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Relation Between Capillary Wedge Pressure Measured by Echocardiography Through Tissue Doppler Imaging (TDI) Method and Catheterism in Patients with Mitral Valve Stenosis

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Abstract

Background: Considering suggested formula in the references and PCWP measured by catheterism, in the present study the relation between pulmonary capillary wedge pressure (PCWP) measured the flow velocity of mitral valve and mitral annulus motion through tissue doppler imaging is evaluated

Methods: 52 cases of severe MS were admitted for Balloon Mitral Valvolotomy (BMV) are included in this study. Mean age was 35±5 years consisting of 40 females and 12 males. Valve area, Pulmonary artery systolic pressure (PAP), E (Maximum Velocity of mitral valve at the beginning of diastole) & Em (Maximum rate of mitral annular motion at the beginning of diastole which is recorded through septal or lateral wall annulus site) velocity and left atrial (LA) size were also measured by echocardiography and PCWP & PAP through catheterism. All patients had normal ejection fraction (EF) and coronary arteries; there was no other valvular diseases and shunts.

Results: There was a significant correlation between PAP in echocardiography and catheterism. Mean PAP was 53±19 mmHg in echocardiography and 53.9±17.8mmHg in catheterism. There wasn’t any correlation between PCWP in echocardiography and catheterism (P=0.33) and also no relation between PCWP and mitral valve area (MVA) or LA size (P=0.2). E/Em ratio increased in severe MS cases.

Conclusion: E/Em ratio and suggested formula would overestimate the wedge pressure so echocardiography is not a reliable method for measuring PCWP in severe MS. Em velocity and E/Em ratio may be used for estimating MS severity.

Keywords: Mitral stenosis • Pulmonary capillary wedge pressure • Tissue Doppler imaging

Introduction

The prevalence of Valvular disease is changing with the health care promotion and technological progress, but in developing countries, valvular rheumatismal diseases such as mitral stenosis (MS) are still common. According to the development of noninvasive methods, the evaluation of myocardial and valvular function or PAP is limited to those who are candidates for BMV. Echocardiography is a noninvasive method for evaluating...
myocardial and valvular function. The results of Doppler studies had good correlation with invasive methods such as catheterism.

New methods such as Echocardiography, (TDI) or Tissue Doppler echocardiography are safe and acceptable. They are accurate methods for assessment of end diastolic pressure and valvular annular motion.2,3

The assessment of end diastolic pressure in left ventricle or LA pressure which reflects capillary wedge pressure and diagnosing myocardial systolic dysfunction is one of the TDI applications.2,3

Wedge pressure is calculated as follows:

\[ PCWP = 1.9 + 1.24 \times \frac{E}{Em} \]

\( E = \) Maximum Velocity of mitral valve at the beginning of diastole (cm/s)

\( Em = \) Maximum rate of mitral annular motion at the beginning of diastole which is recorded through septal or lateral wall annulus site (cm/s). Similar findings about PCWP are reported by echocardiography and catheterism.5

E/Em ratio is also related to PCWP.7 E/Em>10 predicts PWCP> 15 mmhg with the sensitivity and specificity of 92% and 80% respectively.8

The objective of this study is comparing echocardiography and catheterism findings in PCWP measurement, because PWCP has an important role in MS management. PWCP has already been measured by catheterism, but nowadays, non invasive methods such as 2D or Doppler and TDI can assess PCWP.9 But the question is, whether echocardiography can be an alternative for catheterism in PCWP measurement in MS patients or not?

**Methods**

52 severe MS cases, who were candidate for BMV by INOU balloon, were included in this study. They were 15-65 years old and their mean age was 35±5. This study was done during APR 2005 to Feb 2006. The female and male cases were 40(76.9%) and 12(23.1%) respectively. Demographic data and clinical signs were recorded (Table1). All the patients were studied after their own consent and obtaining the approval of Ethnic Committee of Ghaem Hospital. Patients underwent 2D, M mode, Doppler and TDI echocardiography by (Norway 'C Horton 'C VIVID3) 24 hours before BMV and catheterism.

All parameters were assessed according to ASE guidelines. 64.4% of the patients had AF rhythm and 35.4% had sinusal rhythm. All factors that may alter PCWP or may increase LA pressure such as EF ≤ 45%, MR ≥ 3°, other valvular involvement, AI ≥ 3°, shunts and coronary artery diseases in angiography were excluded. Finally we selected severe MS cases who were candidate of BMV regardless to TR severity.

Echocardiography was done by VIVID3 with 2.5-3MHZ probe in left lateral position and some parameters were evaluated including:

1. Mitral valve area (MVA) by PHT, planimetery, PISA method and continuity equation, as well as Peak E velocity. 2. Valvular anatomical study (PTMC score)
3. LA, LV and RV size and LV, RV function, and LA area by planimetry in 4-ch view
4. TR severity and pulmonary artery pressure (PAP)
5. TDI of mitral annulus and Peak velocity of Em at the medial-side of annulus were measured in 4-chamber view with real time online method, FPS 20-40 /s and evaluation of PCWP through the suggested formula in text.7,10
6. In AF patients, all parameters were measured 4-5 times and then for mean evaluation, average of all measures were obtained.
7. Sample volume size was the same at all measurements. All patients underwent catheterism in 24 hours after echocardiography.

<table>
<thead>
<tr>
<th>N</th>
<th>52</th>
<th>52</th>
<th>49</th>
<th>51</th>
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<td>6.4</td>
<td>55.6</td>
<td>40.7</td>
<td>53</td>
<td>53.9</td>
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<tr>
<td>Median</td>
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<td>22</td>
<td>6</td>
<td>56</td>
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<td>12</td>
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<td>103</td>
<td>130</td>
<td>100</td>
<td>129.6</td>
<td>70</td>
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MVA, mitral valve area; E, Early diastolic flow velocity of mitral valve; Em, Early diastolic flow velocity of mitral annular motion by tissue Doppler study; LA, left atrium; PA, pulmonary artery systolic pressure; ECHO, Echocardiography; CATH, Catheterization; PCWP, pulmonary capillary wedge pressure.
Coronary angiography was also done in patients older than 40 years or those with more than two coronary artery disease risk factors or suspicious to coronary artery disease.

PCWP, PA pressure, Right ventricle (RV), LV and Aortic pressures were measured by right and left catheterism. LV and Aortic injection were also done.

**Statistical analysis**

Data are presented as mean±SD. Regression analysis is used to relate PCWP with echocardiography measurements. Chi square test was used for comparison of sex and age with our parameters. Levene test was performed for the equality of variances. Pair wise multiple comparison were performed by Independent T test method and Pearson.

Correlations were taken in to considerations. P<=0.05 was considered significant.

**Results**

52 cases were studied, among of which 40 cases were female (76.9%) and 12 were male (23.1%). So the number of females was significantly more than males (P<0.005).

Mean age was 35±5 years (15-65). Mean mitral surface area was 0.9cm² (0.4-1.3). Mean E velocity was 210.3 cm/sec (60-510). Mean Em velocity was 6.4cm/sec (3-12). Mean E/Em ratio was 40.7 (7-103). Mean LA size in long axis parasternal view was 55mm (21-80). Mean of EF was 55%. Mean LA area is about 28-34cm²

Mean echocardiographic wedge pressure was 53.8 mmHg (10.1-129). Mean catheterism wedge pressure was 23.5 (12-35). Mean echocardiographic PA pressure was 53 mmHg (25-130) and mean catheterism PA pressure was 53.9 mmHg (26-100) (Table 2).

Comparing PA pressure in echocardiography and catheterism had got a meaningful correlation.

Also, there wasn’t any relation between wedge pressure in echocardiography and catheterism (P=0.167).

There was a significant statistical correlation between age and wedge pressure in catheterism but it was lower in older patients. (P<0.05)

Mean E/Em ratio was 40.7 (7-103) and there was a significant relation between the E/Em ratio and mitral valve area. Less MVA was reported in those with more E/Em ratio. (P=0.05)

There wasn’t any significant relation between E/Em ratio and LA size (P=0.78), but there was significant correlation between LA area and E/Em (p=0.00). Em was significantly related with MVA (P=0.05) and less Em was seen in those with less MVA.

There wasn’t any correlation between LA size and wedge pressure in catheterism (P=0.13), but there was significant relation between LA area and wedge pressure in catheterism (P=0.004) and wedge pressure in echocardiography (P=0.00).

There was a negative correlation between aging and PA pressure in echocardiography. (P=0.05) There wasn’t any significant difference between PA pressure in catheterism in men and women (53±15.7 in men and 51.6±9.6 in women) (Table 3).

There wasn’t any significant correlation between Em and LA size (P=0.34). Pressure in catheterism and a higher incidence of AF rhythm was reported in those with upper PA pressure (P=0.005).

There wasn’t any correlation between MVA and wedge pressure in catheterism (P=0.5) as a meaningful correlation was reported between cardiac arrhythmia and wedge well as between PA pressure and PCWP (P=0.33).

<table>
<thead>
<tr>
<th>echocardiography</th>
<th>Catheterism</th>
<th>t-test for equality of means</th>
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<tr>
<td></td>
<td>n</td>
<td>mean±SD</td>
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<tr>
<td>Wedge pressure (mm Hg)</td>
<td>47</td>
<td>53.8±28.4</td>
</tr>
<tr>
<td>PA pressure (mm Hg)</td>
<td>52</td>
<td>53±19.3</td>
</tr>
</tbody>
</table>

PCWP, pulmonary capillary wedge pressure; PAP, pulmonary artery systolic pressure; PA, pulmonary artery; df, degree of freedom

**Discussion**

Wedge pressure of MS cases in catheterism and echocardiography were not the same in this study but we can accurately predict PA pressure by echocardiography.

Higher E/Em ratio indicates more severe MS. PCWP was also correlated significantly with E/Em ratio.10,11
Table 3. Data analysis according to P. value and Pearson correlation

<table>
<thead>
<tr>
<th></th>
<th>Pearson</th>
<th>P. value</th>
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<tr>
<td>Correlation Cath Wedge, Em</td>
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<td>0.167</td>
</tr>
<tr>
<td>Cath Wedge, age</td>
<td>-0.239</td>
<td>0.04</td>
</tr>
<tr>
<td>Echo Wedge, MVA</td>
<td>-0.279</td>
<td>0.05</td>
</tr>
<tr>
<td>MVA, Cath Wedge</td>
<td>0.97</td>
<td>0.50</td>
</tr>
<tr>
<td>Cath Wedge, Cath PA</td>
<td>0.141</td>
<td>0.33</td>
</tr>
<tr>
<td>Cath Wedge, LA size</td>
<td>0.221</td>
<td>0.136</td>
</tr>
<tr>
<td>Cath Wedge LA area</td>
<td>-0.24</td>
<td>0.004</td>
</tr>
<tr>
<td>E/Em ,Echo Wedge</td>
<td>0.962</td>
<td>0.00</td>
</tr>
<tr>
<td>E/Em ,MVA</td>
<td>-0.27</td>
<td>0.05</td>
</tr>
<tr>
<td>E/Em ,LA size</td>
<td>0.43</td>
<td>0.789</td>
</tr>
<tr>
<td>E/Em LA area</td>
<td>-0.26</td>
<td>0.00</td>
</tr>
<tr>
<td>Em, MVA</td>
<td>0.328</td>
<td>0.19</td>
</tr>
<tr>
<td>Em, LA</td>
<td>-0.142</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Cath, Catheterization; Echo, Echocardiography; MVA, mitral valve area; E, Early diastolic flow velocity of mitral valve; Em, Early diastolic flow velocity of mitral annular motion by tissue Doppler study; LA, left atrium; PA, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure.

They considered E/Em>10 as a predictor of PCWP>15 (PCWP>1.55±1.47 E/Em), but in this study, ischemic heart disease and heart failure (HF) cases without mitral valve involvement were assessed. Patients with HF (NYHA III, IV) were studied in the other trial and better correlation was reported in patients without significant mitral stenosis.12-13

No there wasn’t any difference between PA pressure and PCWP in both genders. This had also been reported in previous studies.12 No significant correlation between E/A ratio, deceleration time (Dct) and LVEDP was reported in the other studies for patients with severe mitral regurgitation (MR).13,14,15 In our study, there was also a non-significant correlation between PCWP and mitral valve flow velocities in severe MS cases (with or without AF).

The lack of such correlation may be due to the LV relaxation, stiffness and dismotility of basal portion of LV in rheumatismal MS and the influence of mitral valve area. The higher E velocity and lower Em velocity in these cases cause higher E/Em ratio and overestimation of PCWP by using the suggested formula.

But E/Em ratio, PHT and DT are used to predict MS severity. This has been proven in a trial done in Jun 200514 but MR wasn’t reported in our patients. All of them had moderate to severe rheumatismal MS.

In this study, we found that in older patients, PCWP increased less may be due to greater compliance of LA. Previous studies reported limits for assessment of LA pressure in multi valvular disease by using E/Em14 and this was also proven in patients with MR.14,15

In the other comparison made in 2005,15,16 it was also mentioned that in organic or primary MR cases we can not predict filling pressure by E/Em ratio because it’s so difficult to estimate LV filling pressure in patients with severe MR and normal EF.

Comparing PA pressure in catheterism and echocardiography, significant correlation was seen. We may use PA pressure in echocardiography to estimate accurately PA systolic pressure, even in rheumatismal MS cases with tricuspid insufficiency.

Age and PCWP hadn’t already been compared.

In this study, we suggested that E/Em ratio predicts MS severity. E/Em>40±7 was reported in severe MS cases but there wasn’t any relation between E/Em and PCWP or LVEDP.

In this article, lower Em was also reported in those with more severe MS. Almost similar results were reported for patients with AF in other articles. It was found that the raise of PA pressure may increase AF incidence.

This may be explained by the increase of RVEDP and RAP that may be led to atrial repolarisation abnormalities.

This study was done on MS cases only because catheterism was routinely done in candidates of BMV. So we missed MR cases with LV dysfunction. We have studied annular motion in the medial side of septum to assess Em, but it also deems necessary to study lateral septal Em in severe MS cases.

**Conclusion**

We may estimate MS severity by using E and E/Em ratio but we can’t predict PCWP accurately which needs further studies on larger populations.

We saw that PCWP measured by TDI method of echocardiography is overestimated with respect to catheterism data.

On the other hand, Echocardiography is an appropriate method to predict systolic PA pressure in MS cases and may be an alternative for catheterism.

**Acknowledgements**

The authors wish to thank to the echocardiography and the catheterism laboratory of Cardiology Department of Ghaem Hospital.

**References**


Induced Myocardial Infarction Using Ligation of the Left Anterior Descending Coronary Artery Major Diagonal Branch: Development of an Ovine Model

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Received 25 May 2006; Accepted 3 July 2006

Abstract

Background: We report experimental myocardial infarction by occluding coronary arteries in ovine models.

Methods: Twelve ewes were included in the study. After the chest was opened by left lateral thoracotomy incision, the second diagonal branch of the left anterior descending coronary artery was ligated at a point approximately 40% distant from its base. Prophylactic antiarhythmics were administered. Animals were mechanically ventilated during surgery and stayed in the ICU for 24h afterwards. Experiments were then evaluated by echocardiographic, electrocardiographic, hemodynamic, serologic and morphologic investigations. Echocardiographic measurements were repeated after two months and animals were then sacrificed for postmortem cardiac examinations.

Results: All animals survived the surgical procedure. Cyanotic discoloration and hypokinesia in the cardiac tissue in an area of 3×4 cm plus ST-segment elevations was detected immediately after vessel ligation. Moreover, there were pathologic Q-waves 2 months later. Echocardiographic evaluations revealed an average of 22% relative decrease in cardiac ejection fraction. Wall motion analysis demonstrated anteropapical hypokinesia and akinesia in all animals one day and two months after operation. Thin walled infarcted areas with tissue fibrosis were evident in pathologic investigations two months after surgery.

Conclusion: In conclusion, we developed a practical and safe method of producing myocardial infarction in large animal models.

Keywords: Myocardial infarction • Animal models • Sheep • Coronary arteries

Introduction

Today, acute myocardial infarction (MI) is the major cause of mortality in many countries. Using large animal models for cardiovascular research has recently become an issue of interest mainly due to their, similarity to human anatomic and physiopathologic characteristics, despite a few drawbacks like substantial resources for housing and care.1-7 Coronary artery ligation to induce myocardial infarction in these models is now considered as a widely used and an attractive method for experimental research because of its clinical relevance.5-12 How ever, there are only few published studies describing
the procedure in detail. Here in the present study, we report a detailed guide for induction of MI in ovine models by ligation of the main diagonal branch of the left anterior descending (LAD) coronary artery (namely homonymous artery in sheep) with echocardiographic, electrocardiographic, hemodynamic, serologic and morphologic evaluations.

**Methods**

**Animal care and selection**

The study was approved by the ethical committee of Tehran University of Medical Sciences. All experiments received humane care in accordance with the “Guide for the Care and Use of Laboratory Animals” published by the US National Institute of Health (NIH Publication NO. 85-23, revised 1996). Twelve Iranian ewes weighing 50±10 kg were used. During the study, the animals were held in metabolic cages, had free access to water, and were fed with a mixed diet of hay and sheep pellets. All animals were housed for one week in the animal house for adaptation. They were examined by a veterinarian and a cardiologist both clinically and echocardiographically and excluded from the study if any serious morbidity was detected.

**Surgical preparation**

The sheep were NPO (nil per os) 24h prior to surgery. Animals received intramuscular xylazine, 0.2 mg/kg, to become sedated for shaving and instrumentation. Body hair was shortened and then shaved in the chest area. The saphenous vein was cannulated with a #20 gauge (pink) intravenous catheter. A central venous cannula was placed in the jugular vein using the Seldinger technique. Intravenous infusion of lactated Ringer’s solution (20 cc/kg in 1h) was delivered before anesthesia which was maintained at a rate of 10 cc/kg per hour. The urethra was catheterized by a #10 Foley catheter connected to a urine bag. A pulse oximeter transducer was connected to the ear to monitor O2 saturation. Five electrocardiogram (ECG) electrodes were connected to the extremities and on the chest. Anesthesia was induced by intravenous injection of sodium thiopental, 5 mg/kg, and maintained by halothane (2.0- 3.0 vol. %) in oxygen. Animals were then immediately intubated by a 7.5mm endotracheal tube and mechanically ventilated (Draeger Ventilog3®) with 100% O2 at a respiratory rate of 12-14/min, with an endotracheal tube and mechanically ventilated (Draeger Ventilog3®) with 100% O2 at a respiratory rate of 12-14/min.

Successful ligation was confirmed by myocardial cyanosis plus ST- segment changes on electrocardiogram became evident, the thoracotomy was closed (pericardium with 5-0 Prolene™, muscles and skin with 2-0 Vicryl™ sutures) and a chest tube was placed. For antiarrhythmic prophylaxis, lidocaine was given as an intravenous bolus dose just before ligation of the diagonal branch (2mg/kg) & 15-20 minutes afterwards (1mg/kg).

Post-operative analgesia was provided by 50 mg pethidine given intramuscularly. Cases stayed at animal ICU for 24h after surgery and then were discharged if there were no perioperative morbidities.

**Evaluation**

The experiments were evaluated by echocardiographic, electrocardiographic, hemodynamic, serologic, gross macroscopic and microscopic histopathologic parameters. Cardiac function was evaluated pre-operation and on the 1st day post-operation using trans-thoracic color Doppler ultrasonography (Toshiba model SSA380A); left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), fractional shortening (FS) and ejection fraction (EF) were measured. FS was defined as LVESD-LVEDD/LVEDD and EF was defined as LVEDD2-LVEDD2/LVEDD2. Electrocardiograms were continuously displayed on a monitoring system (SPACELAB™), and intermittently obtained on a paper chart record. By peripheral cannulation of an artery in the ear, systemic arterial pressure was continuously monitored. The left jugular vein was cannulated with a heparin coated catheter (Arrow International, Inc.) and the central venous pressure (CVP) was measured. Measurements were recorded pre-ligation and one hour post-infarction. Serologic examinations were performed by measuring serum specific proteins CTnI, and CK-MB before operation and 24-48h after it. Successful ligation was confirmed by myocardial cyanosis and hypokinesia with bulging and ST- changes on the ECG. After a predetermined 2-month interval, the echocardiographic and electrocardiographic evaluations were repeated and samples were then euthanized with an overdose of sodium thiopental (35mg/kg) for postmortem autopsy of their hearts. Heart specimens were examined for any infarct areas, aneurysms, etc. and then sliced into cross sections for Masson’s tri-chrome staining and microscopic evaluations.
Statistical analysis

Data analysis was performed by SPSS® software version 12.0. Each variable was evaluated by Student paired t test. P values <0.05 were considered statistically significant. All data are presented as mean± standard error of mean (SEM) unless otherwise specified.

Results

All surgeries were performed without any major morbidity or mortality. The anatomy of coronary vasculature was readily recognized. Ischemic bluish discoloration and hypokinesia in the cardiac tissue in an area of 3×4 cm was easily speculated immediately after coronary artery ligation (figure 1).

More over, acute ST-segment elevations were apparent shortly after vessel ligation (figure 2.A) with pathologic Q-waves observed two months later (figure 2.B).

Echocardiographic evaluations showed an average of ~22% relative decrease in EF with P values<0.001 (table 1). Wall motion analysis demonstrated variable degrees of anterioapical hypokinesia and akinesia in all animals one day and two months after operation. There was also a finding of mural dyskinesia in one specimen at 2-month post operational evaluation.

Table 1. Echocardiographic variables (n=12)*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preligation</th>
<th>24h after ligation</th>
<th>2 months after ligation</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD(mm)</td>
<td>47.7±6.40</td>
<td>59.0±6.54</td>
<td>50.8±8.26</td>
</tr>
<tr>
<td>LVESD(mm)</td>
<td>13.1±1.48</td>
<td>29.0±3.98**</td>
<td>21.8±4.19**</td>
</tr>
<tr>
<td>FS(%)</td>
<td>40±1</td>
<td>27±1**</td>
<td>31±3**</td>
</tr>
<tr>
<td>EF(%)</td>
<td>71.6±1.52</td>
<td>49.6±2.35**</td>
<td>58.7±3.94**</td>
</tr>
</tbody>
</table>

LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; FS, fractional shortening; EF, ejection fraction
* Data are stated as mean±SE
** Statistically significant (p<0.05) compared with preligation

Hemodynamic measurements revealed statistically significant rise in CVP (P<0.05) one hour after ligation (table 2).

Table 2. Hemodynamic variables (n=12)*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preligation</th>
<th>1h after ligation</th>
<th>2 months after ligation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR(beats/min)</td>
<td>78.7±14.7</td>
<td>85.2±15.9</td>
<td>72.8±16.2</td>
</tr>
<tr>
<td>CVP(mm Hg)</td>
<td>4.3±1.3</td>
<td>5.6±0.8**</td>
<td>6.2±1.2**</td>
</tr>
<tr>
<td>SAP(mm Hg)</td>
<td>56.0±5.1</td>
<td>49.1±6.7</td>
<td>51.2±6.4</td>
</tr>
</tbody>
</table>

HR, heart rate; CVP, central venous pressure; SAP, systemic arterial pressure
* Data are stated as mean±SE
** Statistically significant (p<0.05) compared with preligation

There was also a meaningful rise in serum cardiac specific proteins CTnI and CK-MB 24-48h after surgery (table 3).

Table 3. Cardiac enzyme mean levels (n=10)

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Preligation</th>
<th>24-28h after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTnI (ng/ml)</td>
<td>&lt;0.1</td>
<td>7.19</td>
</tr>
<tr>
<td>CK-MB (IU/L)</td>
<td>&lt;35</td>
<td>1498</td>
</tr>
</tbody>
</table>

CTnI, cardiac Troponin I; CK-MB, Creatine Kinase isoenzyme MB

Post-mortem pathologic examinations two months after surgery showed thin walled infarcted areas (figures 3, 4) with tissue fibrosis (figure 5).
Shahram Rabbani et al

Discussion

Coronary artery occlusion and hence inducing myocardial infarction in large animal models is a practical method for examining novel therapeutic protocols in cardiovascular research. However, these animals such as sheep lack good coronary collateral circulation which may lead to a remarkable incidence of fatal arrhythmias due to myocardial ischemia during such procedures.6,7

In the studies done by MT Rademaker, et al.12, RWJ Milner, et al.1 and LJ Markovitz, et al.4, the LAD artery was ligated at a point approximately 40% of the distance from the apex to the base of the heart with the simultaneous ligation of the diagonal vessel at a point that was nearly in line with the point at which the LAD artery was ligated. Animals in our pilot experience and also in experiments accomplished by WG Kim et al.7, died during such operation as of intractable arrhythmias following myocardial ischemia. WG Kim et al.7,11 performed a modified method with sequential ligation of the LAD artery and its diagonal branch; i.e., they ligated the LAD artery first and then its diagonal branch one hour later. We also failed to perform this method successfully in three cases, but ligation of the major diagonal branch of the LAD artery proved to be safe and yet practical for inducing MI documented by paraclinical investigations.

Two other pilot experiments in which antiarrhythmic prophylaxis was not administered, subjects failed to survive due to intractable ventricular fibrillations. Hence, we recommend prophylactic use of antiarrhythmic medications such as intravenous lidocaine (2 mg/kg as pre-ligation bolus dose and 1mg/kg 15 minutes afterwards) as it is also emphasized in previous studies.3,4,7,12

In conclusion, inducing myocardial infarction by coronary artery occlusion in animal experiments is a practical method for cardiovascular research examining therapeutic protocols for the Ischemic heart. However, development of fatal intractable arrhythmias is much more common in larger animals like sheep which have a similar anatomy to human circulatory system. We introduced a practical, reliable, and yet safe ovine model of inducing myocardial infarction in this study.

Acknowledgment

This study was performed in and technically supported by Tehran Heart Center- Tehran University of Medical Sciences.
Induced Myocardial Infarction Using Ligation ...

References

2. Frink RJ, Merrick B. The sheep heart: coronary and conduction system anatomy with special reference to the presence of an os cordis. Anat Rec 1974;179:189-200
The National Survey of Cardiac Pacemakers and Cardioverter Defibrillators

Saeed Oraii, MD*, Mahmood Eftekharzadeh, MD, Mehrdad Mirmasoumi, MD, Alireza Ghorbani Sharif, MD, Mohammad Kazem Taraghi, MD, Mehdi Hasanzadeh, MD, Hassan Javadzadegan, MD, Mohammad Javad Zibaenejad, MD, Jalal Zamani, MD, Gholamreza Shafieian, MD, Reza Poorbahador, MD, Bijan Shad, MD, Mitra Azadi, MD, Ahmad Bolouri MD, Mohammad Hosein Dashiti, MD, Keyghobad Behdin, MD, Shahroo Sanii, Shahrbano Davoodabadi, RN

Tehran Arrhythmia Clinic, Tehran, Iran.

The Journal of Tehran Heart Center, V 1, N 2 (2006) 95-99

Abstract

Background: Permanent pacemakers provide effective relief of symptoms and are life-saving in patients with symptomatic heart block. Implantable cardioverter defibrillators (ICD) are also increasingly recognized as life-saving tools in various groups of patients with malignant ventricular tachyarrhythmias.

Methods: As part of the "world survey on pacemaker and ICD implantations", a survey of all device implantations in Iran during the year 2001 was performed. Data was collected and cross-checked through three sources i.e. direct contact with implanting physicians, pacemaker companies and the governmental pacemaker distributing body.

Results: During the year studied, 1635 patients received permanent pacemakers. 88% were new implants at an estimated rate of 24 per million population. The mean age of patients was 65 years and 56.2% were male. 40 cardiologists and 19 surgeons implanted the pacemakers at 27 centers throughout the country. Complete heart block was consistently the most common indication at all centers (mean 56.1%), sick sinus syndrome being the next most common one (mean 20.8%). 69% of the pacemakers were single chamber pacemakers. Transvenous insertion of bipolar steroid-eluting passive fixation leads was the predominant practice at most centers. A total of 60 ICDs were implanted at 7 centers by 9 cardiologists. 45% of ICD implants were dual chamber devices.

Conclusion: The survey is the only one available right now and provides useful information about the prevailing pacemaker and defibrillator implantation practice in Iran. Future surveys would be facilitated if a standardized implant registry such as that used in Europe were established in this country.

Keywords: Pacemaker • Implantable defibrillator • Survey • Iran

Introduction

Pacing is a field of rapid clinical progress and technologic advances. Pacemakers and implantable cardioverter defibrillators (ICD) are increasingly recognized as efficient tools for the management of cardiac rhythm disorders. Clinical progress in the 1990s have included the refinement of indications for pacing as well as the use of pacemakers for new, non-bradycardiac indications, such as the treatment of cardiomyopathies and congestive heart failure.1-3 Important

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published data and studies are shedding new lights on issues such as pacing indications and pacing mode selection, and they have influenced practice patterns significantly. Pacemaker surveys are reported from countries around the world and some countries are conducting nationwide surveys on a regular basis. No reliable data have, however, been available about the implantation rates for devices or the prevailing implantation practices in Iran. Unfortunately, the only reported data about this country contains inaccurate and contradictory data. An accurate and comprehensive survey could provide useful insights into trends and differences in pacemaker and defibrillator practices. Rigorous and expert analysis of the available data can also provide the decision makers with helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and impact the overall cost of care favorably by focusing resources on the most effective strategies. As part of the World Survey on Pacemaker and ICD Implantation, a survey of all device implantations in Iran during the year 2001 was performed. This data was presented along with the data collected by other investigators from other parts of the world at XII World Congress on Cardiac Pacing and Electrophysiology, Feb. 2003 and it was published at PACE journal at July 2004.

Methods

During the year 2001, all hospitals, university or private, involved in pacemaker implantation were identified. A list of all cardiologists active in pacemaker implantation was compiled. Those with sufficient interest in pacemaker and ICD to invest time and effort necessary to gather the necessary data were selected from each center and/or city and contacted. A response was obtained from 9 physicians (36%), for whom the survey questionnaire form was sent. At some areas physicians involved in pacemaker programming and follow-up were summoned for help. The questionnaire soliciting 26 pieces of information was a modification of the XIIth World Congress: World Survey form (kindly provided by Dr. Harry G. Mond) for collecting the whole country data.

Information was also obtained independently from the representatives of the two pacemaker manufacturers providing pacemaker and ICD devices (Medtronic and St. Jude) as well as a governmental agency (Exchange Board of Trustees) that was the sole distributor of pacemaker and ICD devices to the governmental hospitals at the time. The data collected from the three sources of information were cross checked and verified.

The compiled data from the whole country are analyzed and reported. However, it should be pointed out that the results of a few high volume centers were different in some respects from the others and for some measured variables affected the whole data.

Results for pacemakers

Demographics

A total of 1635 pacemakers were implanted in the whole country of which 1439 (88%) were new implants. The number of new implants per million population was estimated as 24/ million for the whole country but no estimates were possible for different regions of the country as implantation facilities were not available at all areas and patients had been referred to other centers. Overall, 56.2% of the patients were reported to be males with an average age of 65.4 years. Females (43.8%) had a similar average age of 66 years. Age distribution is depicted at Figure 1.

![Figure 1. Distribution of age groups](image)

<table>
<thead>
<tr>
<th>Age Groups, years</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;13</td>
<td>1.5</td>
</tr>
<tr>
<td>13-60</td>
<td>25.5</td>
</tr>
<tr>
<td>61-80</td>
<td>59.1</td>
</tr>
<tr>
<td>&gt;80</td>
<td>13.9</td>
</tr>
</tbody>
</table>

Implanting centers

27 centers were identified as implanting pacemakers, though less than 5 pacemakers per year were implanted in 6 hospitals. 57% of pacemakers were implanted in Tehran. One third of the centers were private non-governmental hospitals but they only implanted 9.6% of all the implants during that period. A review of implanting physicians identified 59 doctors (40 cardiologists, 19 surgeons). 72.5% of implantations throughout the country were performed by cardiologists. Median duration of admission varied greatly between the studied centers from 1 day to 11 days. For the whole country it was estimated to be 5 days.

Indications

Complete heart block was the most common indication at all centers (mean 56.1%) with sick sinus syndrome comprising the next most common one (mean 20.8%). Table 1 describes the mean proportion of indications for the whole country. Pacemaker implantation for newer indications (the last 3 groups of table 1) was reported only from a few centers.
Table 1. Indication for initial implant

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unspecified</td>
<td>Unknown</td>
<td>4.2</td>
</tr>
<tr>
<td>AV Block</td>
<td>1^ st/ 2^ st heart block</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Complete heart block</td>
<td>56.1</td>
</tr>
<tr>
<td>Bundle Branch Block</td>
<td>All combinations (No AV block)</td>
<td>2.7</td>
</tr>
<tr>
<td>Sick Sinus Syndrome</td>
<td>Bradycardia</td>
<td>10.4</td>
</tr>
<tr>
<td></td>
<td>Bradycardia/ tachycardia</td>
<td>5.8</td>
</tr>
<tr>
<td></td>
<td>Chronic AF + bradycardia</td>
<td>4.6</td>
</tr>
<tr>
<td>Carotid Sinus/</td>
<td></td>
<td>0.2</td>
</tr>
<tr>
<td>Neurocardiogenic syncope</td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>AV Ablation</td>
<td></td>
<td>0.4</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>Hypertrophic</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**Pacemaker types**

Great divergence of practice in different centers was evident at this area. VVI/VVIR was the only mode at initial implant at some centers, while it comprised less than 50% of new implants at the others (39% at one center). For the whole country, 31% of all implants were dual chamber pacemakers (including single pass VDD) even though this was greatly influenced by the results of a few centers. Data

About pacemaker modes are presented in table 2.

Table 2. Proportion of pacing modes at initial implant

<table>
<thead>
<tr>
<th>Pacing Mode</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>VVI</td>
<td>28.7</td>
</tr>
<tr>
<td>VVIR</td>
<td>40.3</td>
</tr>
<tr>
<td>AAI/ AAIR</td>
<td>0</td>
</tr>
<tr>
<td>VDD</td>
<td>17.2</td>
</tr>
<tr>
<td>DDD</td>
<td>2.1</td>
</tr>
<tr>
<td>DDDDR</td>
<td>11.7</td>
</tr>
</tbody>
</table>

**Pacing leads**

There was not much difference in practice patterns in this area. For the whole country, transvenous leads were used in 97.8% and Epicardial leads in 2.2%. Other data about pacing leads are summarized in table 3.

Table 3. Characteristics of pacing leads

<table>
<thead>
<tr>
<th>Lead Type</th>
<th>Atrium</th>
<th>Ventricle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transvenous (%)</td>
<td>97.8</td>
<td>95.2</td>
</tr>
<tr>
<td>Epi-myocardial (%)</td>
<td>2.2</td>
<td>4.8</td>
</tr>
<tr>
<td>Electrode Configuration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bipolar (%)</td>
<td>87.4</td>
<td>79.4</td>
</tr>
<tr>
<td>Unipolar (%)</td>
<td>12.6</td>
<td>20.6</td>
</tr>
<tr>
<td>Lead Fixation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active fixation (%)</td>
<td>12.6</td>
<td>4.2</td>
</tr>
<tr>
<td>Passive fixation (%)</td>
<td>87.4</td>
<td>95.8</td>
</tr>
<tr>
<td>Electrode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroid-Eluting (%)</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>Non-steroid (%)</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Lead Insertion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Introducer (%)</td>
<td>99.4</td>
<td>98.6</td>
</tr>
<tr>
<td>Venous cut down (%)</td>
<td>0.6</td>
<td>1.4</td>
</tr>
</tbody>
</table>

**Results for ICDs**

60 ICDs were implanted during the year 2001. Devices were implanted at 7 centers (4 university and 3 private hospitals) by 9 cardiologists. 45% of implants were dual chamber devices and 5% were ICDs with biventricular pacing capabilities. All were new implants.

**Discussion**

Little data had been available on pacemaker and ICD implantation practices in Iran. This survey was the first attempt at collecting genuine and reliable information from the whole country. Although we had a low response rate from implanting physicians (36%), the data was collected and verified from other sources to ensure the collection of comprehensive and reliable information. The comparison of this data with that of other countries can be useful for elucidating the current obstacles and drawbacks in this life saving therapeutic field and to be optimistic, can be used by policymakers to implement future strategies aimed at better provision of health care for the community.

Our nationwide rate of 24 new implants per million population was much lower than what was reported from most developed countries (median of 283/million in
Europe) and may be indicative of lack of access to medical care or lack of knowledge in the medical community about indications for pacemaker implantation. The younger age of our population may, on the other hand, have played a role. This is also reflected in a lower proportion of our patients at the above-80 age group (14%) vs. most developing countries (Japan 20%, Australia 25%, Canada 28%).

Age may also be a reason why the most common indication for pacemaker implants in virtually all surveyed areas was reported to be complete heart block (average 56%). Sick sinus syndrome, increasing in incidence with advancing age, is a more common cause in many other parts of the world. Other causes may be under-detection or fewer tendencies to implant pacemakers in milder cases of sick sinus syndrome.

An interesting difference with the data of other countries is in the near zero incidence of single chamber atrial pacemakers and a proportionally high rate of implantation for single pass VDD pacemakers (average 17%). The latter figure is among the highest reported in the world. VDD mode was the one chosen for 34% of implants at one of the high volume centers. In appropriately selected cases single pass VDD pacemakers may be a suitable, less costly alternative to DDDR devices.

On the other hand, the high proportion of VDD implants accompanied by a near zero rate of AAI/AAIR pacemaker implants may reflect a lack of experience in atrial lead placement or lack of self-confidence in operators.

Inappropriate selection of the cases for VDD mode and failure to check for an adequate atrial sensing may end up in a pacemaker working practically in VVI mode with its known adverse consequences. A low rate of implantation of AAI/AAIR pacemakers may also imply a concern over long-term safety with the possible emergence of complete heart block.

A concerning issue is, however, the low proportion of physiological pacing (VDD or DDD/DDDR) at many implanting centers. VVI/VVIR was the only mode implanted at 7 centers and comprising over 80% of implants in 6 others. Although the survival advantage of physiological pacing is questioned, a higher incidence of atrial fibrillation, congestive heart failure and stroke is reported with VVI pacing in several large trials. Various presentations of pacemaker syndrome may also occur in 20-60% of patient with VVI/R pacing and the necessity for an upgrade or reprogramming to DDDR is reported in 26% of cases in some trials. Cost problems appear to play a role. It looks, however, that unfortunately some physicians who refer patients for pacemaker implantation and some of those who implant them, are unaware of the advantages of physiological pacing systems and/or may not be experienced in implanting them.

An analogous problem lies in deciding when to implant an ICD or even deciding between a pacemaker alone versus a cardioverter defibrillator with pacing capabilities for patients with the substrate for the development of a malignant ventricular tachyarrhythmia. Rates of ICD implantations in this country are among the lowest reported in the world and the greatest problems appear to be both in financial allocations and lack of knowledge in the medical community.

The decision about the type of pacemaker or ICD and various programming details may also be a tough one and may have a great impact on patient outcome, both in terms of mortality and quality of life. It is anticipated that these decisions will become even more compelling as the field advances and implantation techniques look easier to learn. Paradoxically, the modernization of implant and monitoring techniques will also bring up more implanters who are not electrophysiologists. Many of these individuals have an inadequate level of training or Commitment to the field to make correct diagnostic and therapeutic decisions, or to provide adequate surveillance, programming and follow-up for the patients in whom devices are implanted.

Lack of facilities and expertise for lead extraction in this country is an embarrassing issue that needs careful scrutiny. Everybody practicing in the field has encountered patients operated on several times for pacemaker infections, still carrying extruded leads or generators along with scars from the previous palliative procedures. Lead extraction is a demanding procedure that needs the necessary equipments as well as experience with an adequate case load. It is the responsibility of referral university hospitals to gather the required facilities and expertise for this costly service and financial incentives are not supposed to direct their management policies. Unfortunately, this does not appear to be the case.

So as usually happens in medicine, it is left to the physician to be the primary one caring for his patient. In this context, it means that the physician, independent of financial, bureaucratic, logistical, or any other extraneous factors must decide which patients need pacemakers or ICDs and what kind they should get. Education is also the key; that is, doctors who make this decision must have an in-depth understanding of the technology, its limitations, and its applications. They must also be aware of the clinical trial data that are relevant to the issue, acknowledging that trial data do not always exactly correlate with the patient under consideration and that “extrapolation is a way of life”. When they don’t know, they have to consult more knowledgeable colleagues for guidance. It is well established with coronary interventional procedures but sometimes forgotten in pacemaker and ICD fields that only a high level of education, training and practice will bring up the necessary competence and guarantee a favorable outcome. The increasing involvement in pacemaker insertion and follow-up by electrophysiologists should curtail the problem, although definitive data to prove better use by this “subspecialized” group are yet to emerge.

A survey is ongoing to collect the data for the year 2005, both for Iran and the other countries of the world but it will not be available until the year 2007. The current data is the
only one available right now and despite being published worldwide, in summary and along With the data of the other countries, had not been published in detail before. During the following years some important changes may have occurred. A great achievement has been made in changing the view of the cardiology community toward the pacemaker and electrophysiology field from a far-fetched, undesirable, complex and complicated procedure to a more easily understood and well-desired one with a high rate of success and nil rates of complications. Many centers have now developed or are willing to develop the necessary electrophysiology settings and many cardiologists are now interested in getting subspecialty training in this field. Devices are more frequently implanted by trained cardiologists than surgeons and this will hopefully have an impact on patient selection, appropriate device selection and procedure outcomes. It looks that physiologic pacing systems are more frequently implanted. The implantation of biventricular devices appear to have especially grown markedly and more ICDs are being implanted. Implantation practices regarding lead selection, site of access etc. also appear to have changed somewhat but we should wait for the results of the year 2005 to make firm conclusions. We hope that when the data for the year 2005 are ready, their comparison with the current data and the study of the trends would pave the way for further progress in the future.

References

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Prophylactic Effect of Theophylline in Renal Contrast Nephropathy after Coronary Angiography

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Abstract

Background: Contrast nephropathy will increase mortality up to 30% following angiographic procedures. Adenosine is a crucial mediator of contrast-induced nephropathy. The purpose of this study was to investigate whether the adenosine antagonist Theophylline reduces the incidence of CN after coronary angiography.

Methods: In this randomized, double-blind, placebo-controlled clinical trial study, carried out from February 2004 to September 2005 at the Fatemeh Zahra Hospital, 70 patients who were undergoing coronary angiography were divided into two groups. Case group (n=35) received oral Theophylline 200 mg bid. 24 h before and for 48 h after angiography. The control group (n=35) received placebo. Serum Na+, K+, blood urea nitrogen (BUN), creatinine, glomerular filtration rate (GFR) were measured before and after angiography.

Results: In the case group there were no significant change in serum creatinine (0.90±0.7 vs. 0.92±0.3 mg/dl), BUN (17.76±7.8 vs. 19.35±9.6 mg/dl), GFR (83.01±26.7 vs. 81.36±24.9 ml/min) Na+ (139.08±3.6 vs. 138.54±2.7 mEq/l) and K+ (4.30±0.4 vs. 4.19±0.3 mEq/l). In the control group, there was a significant fall in GFR after angiography (86.10±34.8 vs. 80.7±30.4 ml/min, P=0.03). Following angiography, there were no significant difference in serum creatinine, BUN, GFR, Na+ and K+ level between the two groups. None of the patients in either group faced contrast induced nephropathy.

Conclusion: Theophylline does not appear to add a protective role in preventing against contrast induced nephropathy in patients undergoing angiographic procedures.

Keywords: Acute renal failure • Angiography • Radio-contrast induced nephropathy • Theophylline

Introduction

Contrast-induced nephropathy (CN) is an important cause of renal failure and is related to greater mortality and morbidity rates and health care costs.1 It is the third leading cause of ARF in hospitalized patients.2 The incidence of CN, varies from 0 to 23% in patients undergoing cardiac catheterization and angiography, depending on the definition of CN used and the risk profile of the patient population included in the study.3 CN increases mortality up to 30% following angiographic procedures.4 Usually, CN is defined as a rise in serum creatinine of 25%, or 50% of the baseline value, and appears to be the result of a synergistic combination of direct tubular epithelial cell toxicity and alterations in renal hemodynamics with renal modularity ischemia.5 Although the mediators of these changes are still not very clearly defined, but alterations in the metabolism of prostaglandins, nitric oxide, endothelin, and adenosine may play a role. Various preventive strategies have been employed to reduce the incidence of CN, which include administration of intravenous fluids, frusemide, mannitol, low-dose dopamine, atrial natriuretic peptide (ANP), and calcium-channel blockers.6-13 However, the results of most studies are conflicting, and more evidence is required before any therapeutic measures can be recommended for routine
use. Since adenosine may have a role in the pathogenesis of CN, hence an adenosine antagonist (Theophylline) has been investigated as a means for reducing the risk of CN.12 16-18 However; data on use of oral Theophylline for this purpose is scant and inconsistent. The purpose of this prospective study was to determine whether alterations in renal function after administration of radio contrast agents can be prevented by oral Theophylline.

**Methods**

This study was a randomized, double-blind, placebo-controlled clinical trial about the role of Theophylline in contrast induced nephropathy as compared with placebo. The study was carried out from February 2004 to September 2005 at the Fatemeh Zahra Hospital, affiliated with Mazandaran University of Medical Sciences, Iran. The study protocol was approved by the institutional ethics Committee and informed written consent was obtained from all the patients under study.

**Patients**

Patients were the Iranian male and female living in southern coastline of the Caspian Sea who met the inclusion criteria of the study. We prospectively studied 70 consecutive patients who were referring to the Institute for coronary angiography. All of them were at high risk of CN (had at least one of the following factors: age>65 years, diabetes mellitus, history congestive heart failure, recent use of NSAIDS or ACE inhibitors or amino glycoside drugs). Exclusion criteria included, pre-existing renal failure with serum creatinine 3.0 mg/dl, maintenance dialysis, a history of acute myocardial infarction, left ventricular ejection fraction (EF) <25%, allergy to contrast media, pregnancy, diuretic therapy and using of Theophylline until one week before angiography.

**Study Procedures**

Prior to angiography, in all patients, the serum level of Na+ and K+ (Medica, USA), blood urea nitrogen (BUN) and creatinine (CIBA-Corning, USA) was measured. Glomerular filtration rate (GFR) was calculated using Cockcroft-Gault formula. The patients were randomly divided in two groups as following: case group (n=35), who underwent routine coronary angiography, and received oral Theophylline (pharmashimi, Iran) 200 mg bid. 24 hours pre to 48 hours post angiography. Control group (n=35), received placebo (prepared in pharmacology institute of Mazandaran University of Medical Science) with the same procedure. The placebo was prepared in identical size and color packages. The Two groups matched for age and diabetes mellitus. In addition, all patients received intravenous normal saline (1 ml/kg/h) commencing 12 hours before and continued for 12 hours after the procedure. Coronary angiography was performed using a high-osmolar contrast medium, 100 cc of 76% Urograffin (Schering AG, Berlin, Germany). All laboratory tests were repeated 72 hours after angiography. All of the follow up evaluations and laboratory tests were done by individuals who were blind to the Theophylline and control groups.

**Statistical analysis**

Statistical analysis of all the qualitative results of this study was done by chi-square test. All data are expressed as mean±SD. The significance of a difference between two groups was calculated using independent t-test with \( P < 0.05 \) used as the significant level.

**Results**

A total of 70 patients entered this study according to the inclusion criteria and were randomly allocated in either Theophylline (21 male and 14 female, mean age 62.1±9 years) or control group (22 male and 13 female, mean age 61.3±10 years). There was no difference between the groups in terms of mean age. Prior to angiography, the two groups had comparable serum creatinine (0.90±0.7 mg/dl in Theophylline group vs. 0.93±0.3 mg/dl in control group) and BUN (17.76±10.9 vs. 19.04±10.9 mg/dl). There were no significant differences in serum creatinine and BUN. There were also no significant differences in serum Na+ (139.08±3.6 vs. 140.02±3.5) and K+ (4.3±0.4 vs. 4.3±0.5). The mean GFR as estimated by the plasma method was also not significantly different between the two groups (83.01±34.8 vs. 86.10±34.8 ml/min) (Table 1).

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Control group</th>
<th>Theophylline group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=19 (54%)</td>
<td>61.3±10</td>
<td>62.1±9</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>n=18 (51%)</td>
<td>0.90±0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>19.04±10.9</td>
<td>0.90±0.7</td>
<td>NS</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>140.02±3.5</td>
<td>139.08±3.6</td>
<td>NS</td>
</tr>
<tr>
<td>Serum sodium (mEq/l)</td>
<td>4.3±0.5</td>
<td>4.3±0.4</td>
<td>NS</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>86.10±34.8</td>
<td>83.01±26.7</td>
<td>NS</td>
</tr>
</tbody>
</table>

BUN, Blood Urea Nitrogen; GFR, Glomerular Filtration Rate; NS, Non Significant

* Data are stated as mean ± SD
Following angiography, there were no significant differences in serum creatinine concentrations (0.92±0.3 mg/dl in Theophylline group vs. 0.96±0.3 mg/dl in control group) and BUN levels (19.35±9.6 vs. 20.35±9.2 mg/dl). The mean GFR did not differ significantly, either (81.36±24.9 vs. 80.70±30.4 ml/min). Mean of serum Na+ (138.54±2.7 vs. 139.58±3.3) and K+ (4.19±0.3 vs. 4.29±0.6) were also similar in the two groups. On the other hand, there were no significant changes in serum creatinine concentrations, BUN, Na+ and K+ levels in the Theophylline group after angiography. The mean GFR did not change significantly in this group as compared with pre-angiographic values. In contrast, in the control group, there was a significant fall in GFR following angiography (86.10±34.8 vs. 80.7±30.4 ml/min, P=0.03) (Table 2). None of the patients in either group faced contrast induced nephropathy (more than a 25% rise in serum creatinine).

Table 2. Renal parameters in the case and the control groups

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Theophylline group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.93±0.3</td>
<td>0.96±0.3</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>19.04±10.9</td>
<td>20.35±9.2</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>86.10±34.8</td>
<td>80.70±30.4</td>
</tr>
<tr>
<td>Serum sodium (mEq/l)</td>
<td>140.02±3.5</td>
<td>139.58±3.3</td>
</tr>
<tr>
<td>Serum potassium (mEq/l)</td>
<td>4.30±0.5</td>
<td>4.29±0.6</td>
</tr>
</tbody>
</table>

BUN, Blood Urea Nitrogen; GFR, Glomerular Filtration Rate; NS, Non Significant
*Data are stated as mean ± SD

**Discussion**

Renal insufficiency presents a challenge in patients with acute coronary syndromes. Nephrotoxicity due to the administration of radio contrast agents is a common but preventable cause of acute renal failure. Various strategies for the prevention of contrast-induced nephropathy (CN) have been studied, which had conflicting results. Adenosine has been shown to reduce renal blood flow and glomerular perfusion pressure by means of A1-receptor-mediated renal afferent arteriolar vasoconstriction and A2-receptor-mediated efferent arteriolar vasodilation. The administration of contrast in human subjects is known to reduce renal blood flow and glomerular filtration rate. Theophylline completely prevented the fall in creatinine clearance within 24 hours after non-ionic contrast and reduced the level approximately in half. Another study, however, using 810 mg oral Theophylline, indicated that it did not offer any benefit over routine saline hydration for the prevention of CN in patients with serum creatinine 1.5 mg/dl receiving contrast media. In our study, the increase of serum creatinine level didn’t indicate contrast induced nephropathy and no patient required hemodialysis. The reason can be the exclusion of patients with moderate to severe renal failure ($\text{Cr} \geq 3$) from the study and the fact that all patients received adequate saline hydration. Although the difference of GFR among the two groups was not statistically significant, but estimation of GFR in the control group demonstrated a reduction, following angiography. It suggests the role of Theophylline in prevention of some functional kidney changes and contrast induced nephropathy.

We didn’t observe any contrast induced nephropathy. Further studies are required to compare the efficacy of Theophylline monotherapy with that of saline hydration for changes in renal function in any of the patients under study. Abizaid et al. in the study comparing saline hydration, saline hydration plus dopamine, and saline hydration plus intravenous Aminophylline infusion, reported that neither dopamine nor Aminophylline reduced the incidence of CN. Data on oral Theophylline in the prevention of CN is scant and contradictory. Katholi et al. studied the effect of 2.88 mg/kg oral Theophylline (every 12 hour, four doses) compared with placebo in the prevention of CN. They reported that although serum creatinine did not change significantly, but Theophylline completely prevented the fall in creatinine clearance within 24 hours after non-ionic contrast and reduced the level approximately in half. Another study, however, using 810 mg oral Theophylline, indicated that it did not offer any benefit over routine saline hydration for the prevention of CN in patients with serum creatinine 1.5 mg/dl receiving contrast media. In our study, the increase of serum creatinine level didn’t indicate contrast induced nephropathy and no patient required hemodialysis. The reason can be the exclusion of patients with moderate to severe renal failure ($\text{Cr} \geq 3$) from the study and the fact that all patients received adequate saline hydration. Although the difference of GFR among the two groups was not statistically significant, but estimation of GFR in the control group demonstrated a reduction, following angiography. It suggests the role of Theophylline in prevention of some functional kidney changes and contrast induced nephropathy.

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the prevention of contrast nephropathy.

References

Periodontal Disease as a Risk Factor for Coronary Artery Disease

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Received 26 May 2006; Accepted 4 August 2006

Abstract

Background: Coronary artery disease is recognized as one of the three major causes of mortality around the world. The role of inflammation in producing coronary artery disease has been established in previous studies. Since periodontal disease, which is highly prevalent, is considered as a cause of inflammation, its influence on producing coronary artery disease was investigated in the present study considering its four main indices.

Methods: In this case-control study, 60 patients with angiographically proven coronary artery disease were selected as case group. After matching for some baseline characteristics including educational level, age, sex, and some established risk factors for coronary artery disease, 60 healthy individuals were selected as control group from a population in whom coronary artery disease had been angiographically ruled out. Then, the existence of periodontal diseases was compared with statistical methods in these two groups, considering four different dental indices.

Results: The mean plaque index (PI) was 57.82±2.92% in cases vs. 35.73±2.53% in controls (p<0.05). Mean bleeding on probing (BOP) was 36.3±3.38% in cases versus 18.6±2.6% in controls, while mean Attachment Loss>4mm was 35.14±3.89% and 15.48±2.79% in cases and controls, respectively (P<0.05). The mean loss of teeth (LOT) was not significantly different in cases and controls (5.08±0.52 versus 5.38±0.53, P>0.05). Therefore, except for the number of lost teeth, there was a statistically significant difference between these two groups. For an evaluation of independent variables, multiple logistic regression analysis was used. Odds ratio was 1.02 for attachment loss and 2.2 for BOP.

Conclusion: Periodontal diseases may be counted as a risk factor for coronary artery disease and it is essential to study the effects of control and management of these diseases as primary and secondary prevention for coronary artery disease in future studies.

Keywords: Periodontal disease • Dental plaque index • Coronary artery disease

Introduction

Periodontal diseases are one of the most common chronic diseases with an infectious origin, which cause inflammatory destruction of periodontal tissues. This condition is caused after contact of periodontium with dental plaques, which contain more than 400 bacterial species. Destruction of periodontium is caused by the release of toxic agents and enzymes from specific species of plaques and host response to bacteria and their products.1 Because of the wide spectrum of microbial plaques associated with, and chronicity of periodontal diseases, presence of local and systemic immune responses, and the development of inflammation, this condition may also affect the course of some systemic diseases.
diseases. For example, inflammation has an established role in the development and exacerbation of coronary artery disease, which is one of the most important causes of mortality in most communities. Interestingly, the classic risk factors such as hypertension and cigarette smoking count for only two-thirds of cardiovascular events. Therefore, other factors may also contribute to the pathogenesis of this disease. According to some studies, the prevalence of mortal cardiovascular events is 1.5 to 2 times greater in patients with periodontal diseases. This issue has been discussed and reemphasized in newly-published studies, too. However, most of the data about this relationship has been regarded as inconclusive. With regards to the lifestyle, oro-dental healthcare status and high prevalence of periodontal and cardiovascular diseases in Iran, we decided to evaluate the relationship between these two conditions in a case-control study.

Methods

Sampling

This analytical, case-control study was conducted on patients with angiographically-proven coronary artery disease. Toothless patients, patients suffering from immune diseases and diabetes mellitus, and patients receiving chemotherapy or hormones were excluded from the study. The characteristics of 60 patients were obtained through interviews, completion of fixed questionnaires (including age, sex, educational level, positive family history and other risk factors for coronary artery disease) and physical examination (measurement of body weight and height, blood pressure and blood sugar). Thereafter, 60 healthy individuals were selected as the control group from a population in whom coronary artery disease had been ruled out according to angiography. They were matched with the control group, according to some baseline characteristics, as much as possible. Finally, these two groups were similar in age, sex, educational level, serum levels of cholesterol and triglyceride, hypertension, hyperlipidemia, positive family history, smoking, and body mass index (BMI).

Oral Examination

A dentist examined teeth in both case and control groups on hospital beds with mirror, Williams probe and cotton role. Periodontal tissues in teeth were examined in patients. Teeth were selected according to Ramford and oral hygiene index (OHI). The degree of attachment, plaque index (O’leary), BOP (bleeding on probing) and the number of lost teeth (without considering the third molar) were measured. Measurement of AL was done with regard to cementoenamel junction (CEJ) of teeth. Measurement of AL>4mm was done in 6 areas of each tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, distolingual). In order to measure BOP, the probes were slightly intruded into the sulcus of gums in each tooth. The occurrence of bleeding after 30 seconds in O’leary chart was registered and calculated according to this formula:

\[
BOP = \frac{\text{Bleeding areas}}{\text{Total areas}} \times 100
\]

In order to calculate plaque index, patients were given plaque-enhancing pills. The colored areas were calculated in 4 areas in O’leary chart according to this formula:

\[
PI = \frac{\text{Colored areas}}{\text{Total tooth areas}} \times 100
\]

T-test and chi-square and multiple logistic regression tests were used for data analysis. Data were analyzed with SPSS software.

Results

The characteristics of case and control groups are shown in tables (1 to 3).

Table 1. Distribution of relative frequency of age in case and control groups as divided by sex

<table>
<thead>
<tr>
<th>Age group</th>
<th>Cases *</th>
<th>Controls *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>30-50 Y</td>
<td>8 (13.3%)</td>
<td>8 (13.3%)</td>
</tr>
<tr>
<td>≥ 50 Y</td>
<td>32 (53.3%)</td>
<td>12 (20%)</td>
</tr>
<tr>
<td>Total</td>
<td>40 (66.7%)</td>
<td>20 (33.3%)</td>
</tr>
</tbody>
</table>

Data are presented as the number (%) of patients

Table 2. Distribution of frequency of educational level in case and control groups

<table>
<thead>
<tr>
<th>Educational Level</th>
<th>Cases *</th>
<th>Controls *</th>
</tr>
</thead>
<tbody>
<tr>
<td>No education</td>
<td>7 (11.7%)</td>
<td>5 (8.3%)</td>
</tr>
<tr>
<td>Under diploma</td>
<td>22 (36.7%)</td>
<td>20 (33.3%)</td>
</tr>
<tr>
<td>Diploma</td>
<td>17 (28.3%)</td>
<td>21 (35%)</td>
</tr>
<tr>
<td>Associate degree</td>
<td>8 (13.3%)</td>
<td>6 (10%)</td>
</tr>
<tr>
<td>Bachelor and over</td>
<td>6 (10%)</td>
<td>8 (13.3%)</td>
</tr>
</tbody>
</table>

Data are presented as the number (%) of patients

*Non-significant P values
Table 3. Frequency of family history of coronary artery disease, cigarette smoking, level of triglyceride, cholesterol and blood pressure in cases and controls

<table>
<thead>
<tr>
<th></th>
<th>Cases*</th>
<th>Controls*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Family history</td>
<td>22 (36.7%)</td>
<td>17 (28.3%)</td>
</tr>
<tr>
<td>Cigarette Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 pack/ year</td>
<td>7 (11.7%)</td>
<td>5 (8.3%)</td>
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<tr>
<td>&gt;10 pack/ year</td>
<td>8 (13.3%)</td>
<td>8 (13.3%)</td>
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<tr>
<td>Level of Triglyceride</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG &lt; 200</td>
<td>42 (70%)</td>
<td>48 (80%)</td>
</tr>
<tr>
<td>200 &lt; TG &lt; 400</td>
<td>15 (25%)</td>
<td>11 (18.3%)</td>
</tr>
<tr>
<td>TG &gt; 400</td>
<td>3 (5%)</td>
<td>1 (1.6%)</td>
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<tr>
<td>Level of Cholesterol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>chol &lt; 200</td>
<td>20 (33.3%)</td>
<td>27 (45%)</td>
</tr>
<tr>
<td>200 &lt; chol &lt; 240</td>
<td>23 (38.3%)</td>
<td>22 (36.7%)</td>
</tr>
<tr>
<td>chol ≥ 240</td>
<td>17 (28.3%)</td>
<td>11 (18.3%)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
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<tr>
<td>Normal</td>
<td>48 (80%)</td>
<td>45 (75%)</td>
</tr>
<tr>
<td>High</td>
<td>12 (20%)</td>
<td>15 (25%)</td>
</tr>
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TG, triglyceride; chol, cholesterol
Data are presented as the number (%) of patients
*Non-significant p values

T-test showed no significant difference in age, gender, level of cholesterol and triglyceride and BMI between these 2 groups (P>0.05). U. Mann-Whitney and X² were used for comparison of educational level, hypertension and family history, which showed no significant difference between cases and controls (P>0.05).

The results of orodental examination in patients and controls according to 4 indices, including the number of lost teeth, BOP, PI and percentage of AL ≥ 4mm are as follows:
1. The mean number of lost teeth was 5.08±0.52 in cases and 5.38±0.53 in controls, which did not show a significant difference. (P>0.05)
2. There was a significant difference in BOP between cases (36.3±3.38%) and controls (18.6±2.63%). (P<0.05)
3. There was a significant difference in PI between cases and controls (57.82±2.92% vs. 35.73±2.53%), (P<0.05)
4. The mean attachment loss ≥ 4mm was 35.14±3.89% and 15.48±2.79% in cases and controls, respectively. (P<0.05)

For an evaluation of independent variables, multiple logistic regression analysis was used. Odds ratio was 1.02 for attachment loss and 2.2 for BOP (table 4).

Table 4. Indices of oro-dental health in cases and controls

<table>
<thead>
<tr>
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<th>Cases</th>
<th>Controls</th>
<th>P value</th>
<th>Odds Ratio</th>
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<tbody>
<tr>
<td>LOT (n)</td>
<td>5.08 ± 0.52</td>
<td>5.38 ± 0.53</td>
<td>&gt; 0.05</td>
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<tr>
<td>BOP (%)</td>
<td>36.03 ± 3.38</td>
<td>18.6 ± 2.63</td>
<td>&lt; 0.05</td>
<td>2.2</td>
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<tr>
<td>PI (%)</td>
<td>57.82 ± 2.19</td>
<td>35.73 ± 0.53</td>
<td>&lt; 0.05</td>
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<tr>
<td>AL &gt; 4 (%)</td>
<td>35.14 ± 3.89</td>
<td>15.48 ± 2.79</td>
<td>&lt; 0.05</td>
<td>1.02</td>
</tr>
</tbody>
</table>

LOT, Loss of Teeth; BOP, Bleeding On Probing; PI, Plaque Index; AL, Attachment Loss
* Results are expressed as mean ± standard deviation

Discussion

This study was aimed to evaluate the association between periodontal diseases and coronary artery disease. Our findings show that mean plaque index in the case group was twice as much as in the control group, which indicated bad health care in patients. The index of gum bleeding and records of the number of AL ≥ 4mm was used for the evaluation of periodontal status and gum inflammation. In some studies, this finding has been used as an index for increased chance of coronary artery disease. In 1999, Arbes divided the percentages of the areas with AL ≥ 3mm as to 0 to 33%, 33% to 67% and over 67%, with increased risk of coronary artery disease as 1.4, 2.3, and 3.8, respectively. Elter et al showed that individuals with both high rates of attachment loss and tooth loss had elevated odds for prevalent coronary artery disease compared to individuals with low attachment loss and low tooth loss. In a study that was done in 2000 in Shahid Beheshti University of Medical Sciences, dentistry school, the association between ischemia and gum inflammation was evaluated. The odds ratio for this disease was 11.7, which was much higher than similar studies done outside Iran. In our study, too, the mean percentage of AL ≥ 4mm in cases was 2.5 times as much greater as in controls.

The other index for gum inflammation was the mean amount of BOP which was twice as much in patients. This correlated with Gulnur’s studies in 2000. This was regarded as another reason for the prevalence of coronary artery disease in patients who do not have a good oro-dental health care. In a newly-published work, Briggs et al showed that higher proportion of sites examined in cases had plaque and bleeding on probing compared to controls.

The mean number of lost teeth did not show a significant difference between cases and controls, which was consistent with Destefano’s study in 1993. Another research done by Karimi in Iran also showed the same results, which showed a significant difference with Moghaddasi’s study. Similar to Moghaddasi et al, Briggs et al showed that cases with coronary artery disease had an average of three teeth less than the controls.
Conclusions

Since 3 main indices out of 4 indices for periodontal diseases correlated with increased risk of ischemia in our research and most other studies, periodontal disease may be regarded as an independent risk factor for coronary artery disease. Hence, programs for public education and increase of health facilities must be considered for control of these diseases. The effect of this management on prevention of coronary artery diseases should be evaluated in future studies.

References

Percutaneous Repositioning of Dislodged Atrial Pacing Lead

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Abstract

The overall rate of atrial pacing lead dislodgement is estimated to be about 3%. These leads are generally repositioned via a second operation through opening the pacemaker pocket.

Some operators have introduced percutaneous techniques using snare system or deflectable catheters for this purpose.

In this article we present our experience with five cases of percutaneous lead repositioning. Three cases were performed using deflectable ablation catheters and in two cases we used a specially designed urologic basket. The procedural success rate was 100% at the beginning but the long term success rate was 60%.

Keywords: Atrial pacing lead • Dislodgement • Urologic basket • Percutaneous repositioning

Introduction

Lead dislodgement requiring reoperation is a complication that raises the costs of pacemaker implantation surgery while adding to patient’s discomfort. Migration of a dislodged atrial lead can present with undersensing, loss of atrial capture, loss of atrial kick in patients who need AV synchrony and rarely phrenic nerve stimulation or improper RV stimulation. Once detected, the dislodged lead should be immediately repositioned.1,2

In recent years, percutaneous transcatheter repositioning of displaced permanent pacemaker leads has been advocated before consideration of surgical repositioning. The procedure is easy and safe, allowing a reduction in the need for surgical lead revision and the associated morbidity and costs.3,5 In this article we introduce five cases of dislodged atrial leads. In three cases we tried repositioning with deflectable ablation catheter and in two cases we used a specially designed urologic basket.

Methods

Cases performed by deflectable ablation catheters

Three patients, who had atrial lead dislodgment and were diagnosed early in post implantation follow up, were selected for this procedure.

In two cases the atrial lead was dislodged to SVC. In both cases we were able to reposition the lead successfully but in one of them the lead migrated again into SVC.

In the third case, the tip of atrial lead was dislodged to the ventricular side of the anterior leaflet of tricuspid valve. It was repositioned successfully.

In the follow up period (which is 9 months up to now), the leads remain stable in RA.

*Corresponding Author: Ahmad Yamini Sharif. Associate professor of cardiology, Tehran University of Medical Sciences. Tehran Heart Center, Jalal Al Ahmad & North Kargar Cross, Tehran, Iran 1411713138. Tel: +98-21-88029600-69. Fax: +98-21-88029731. E-mail: yaminisharif.a@doctor.com
Cases performed by specially designed urologic basket

Case 1

A 68-year-old man was admitted in January 2006 with dyspnea, mild dizziness and evidence of pacemaker malfunction due to atrial lead dislodgement. He had a history of CABG in 1985 and PCI (implantation of 7 stents in two stenotic SVG grafts) in 2003. In 2004 he experienced an inferior MI, after which he had transient complete heart block accompanied by respiratory arrest and cardiogenic shock, which was treated medically and the block resolved. In the next admission (4 months later) he had first degree AV block and episodes of complete heart block accompanied by dizziness and exacerbation of dyspnea. ECG showed narrow complexes and old inferior MI. In the last echocardiographic study ejection fraction was 40% and there was no evidence of significant dysynchrony, therefore we decided to implant a dual chamber pacemaker for him.

The implantation was successful and the patient was discharged with good condition in November 2005. During follow up study, pacemaker analysis showed no atrial sensing and pacing. Programming the pacemaker to VVIR mode did not relieve symptoms and the patient was scheduled for repositioning of atrial lead which was performed with this specially designed urologic basket on February 2006.

More description on specially designed urologic basket (Cardiac pacing lead hook)

This device is specially designed based on the nonmetallic urologic stone basket known as Dormia basket, used for removal of stones that are located in the "lower ureter".

By making certain changes, its functionality is changed so that instead of forming a basket, the operator can construct a hook around the cardiac pacing lead by pulling the steerable inner line of the device. (Figure 1).

In the next step the operator is able to reposition the lead by some traction of the device.

To remove the hook, the operator releases the inner line, this will allow the hook to be reshaped and straightened as it once more enters the delivery system (Mullins sheath).

To perform repositioning of atrial pacing lead, the patient was brought to catheterization laboratory in the post absorptive nonsedated state. Mullins sheath was placed around the atrial lead of pacemaker and by using deflectable ablating catheter, the Mullins sheath was positioned over the loop of the atrial pacing lead (Figure 2).

Figure 2. This figure shows how to position the Mullins sheath (single arrow head) over the loop of dislodged atrial lead of pacemaker (double arrow head)

After removing the ablating catheter, the specially designed urologic basket was sent over the loop of j-shaped atrial lead. The deflectable part of this basket was passed through the tip of the Mullins sheath which was positioned over the loop of the dislodged pacemaker lead. By deflecting the tip of basket, we made a hook around the lead (Figure 3, A to C).
Percutaneous Repositioning of...

Case 2

A 68-year-old man was admitted in January 2003 with dyspnea and dizzy spells. His ECG showed complete heart block. In echo study, ejection fraction was 40%. In coronary angiography, borderline lesions (about 50%) were found in LAD and circumflex artery. A dual chamber pacemaker was implanted for him and the patient was discharged from the hospital. Four weeks later he came to our pacemaker clinic because of diaphragmatic stimulation. He announced that his diaphragmatic stimulation started after severe sneezing. His chest x ray revealed migration of atrial lead to superior vena cava (SVC). By changing the Pacemaker mode to VVIR, diaphragmatic stimulation was terminated but the patient showed signs of pacemaker syndrome. So we decided to perform repositioning of the dislodged atrial lead with specially designed urologic basket. The dislodged atrial lead was repositioned into the right atrium but one day later this J-shaped passive fixation atrial lead migrated into the SVC once again and the patient preferred reoperation. In the second operation session another atrial lead (an active fixation lead) was inserted into right atrial auricle.

Results

Percutaneous repositioning of dislodged atrial lead was possible in all 5 cases but in two cases the leads migrated again, therefore our long-term success rate was 60%.

Discussion

This experience highlights the feasibility of non surgical repositioning of pacemaker atrial leads while introducing a new device. The procedure is possible when a passive fixation J-shaped atrial lead is used. There are some reports about repositioning of dislodged atrial pacing leads by snare systems, or deflectable catheters. We used the deflectable catheter in 3 cases which we diagnosed the lead dislodgment early in post implantation period. The procedure was successful and easily performed but in one case the lead migrated to SVC again.

To reposition the dislodged atrial pacing lead by snare system, the tip of the dislodged atrial pacing lead should move freely in the right atrium or superior vena cava (SVC). There are some devices such as Needle’s Eye®snare, designed to grasp objects without free end but these devices are used for percutaneous retrieval of cardiac leads and to our knowledge, they are not used for lead repositioning.

When the tip of dislodged atrial pacing lead is attached to the wall of atrium, SVC or tricuspid valve, deflectable catheters could be used but if the tip of displaced lead is tightly fixed to atrial wall or SVC it is impossible to detach...
the lead.

By using this new device (cardiac pacing lead hook), the operator is able to reposition the lead. Therefore we used our new device in two cases diagnosed with dislodgment later in follow up.

**Conclusion**

The results of this experience encourage us to try percutaneous repositioning of dislodged atrial leads in more cases and evaluate the results. We prefer to use the deflectable ablation catheters for the dislodged leads which are diagnosed early. For those who are diagnosed later we use our newly invented device, “The cardiac pacing lead hook”.

**References**

Case Report

Left Ventricular Non-Compaction Associated with WPW Syndrome

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Abstract

Noncompaction of the ventricular myocardium is an embryonic cardiomyopathy that is increasingly being recognized. Noncompaction of LV myocardium, right ventricular myocardium, or both can occur in isolation, in congenital heart diseases, in valvular heart diseases, in neuromuscular disorders, skeletal abnormalities and in endocrinologic abnormalities. Clinical manifestations of ventricular non-compaction include congestive heart failure, arrhythmia, sudden cardiac death and embolic events. This report is illustrative of non-compaction left ventricle associated with WPW syndrome in a 12-year-old girl presented with aborted sudden cardiac death and heart failure.

Keywords: Left ventricular non-compaction • WPW syndrome • Echocardiography

Introduction

Noncompaction of the ventricular myocardium is an embryonic cardiomyopathy that is thought to be a consequence of intrauterine arrest of compaction.1 It is characterized by deep trabeculations in the LV endocardium in association with left ventricular hypertrophy, dilation or hypertrophy and dilation. The definition of non-compaction includes thickened myocardium with a two layered structure consisting of compaction epicardial and noncompaction endocardial myocardium (maximum end-systolic ratio noncompaction to compaction more than 2) with a meshwork of perfused intertrabeculation recesses and regional hypokinesia.2-6 Noncompaction of LV myocardium, right ventricular myocardium, or both can occur in isolation, in congenital heart diseases, in valvular heart diseases, in neuromuscular disorders, skeletal abnormalities and in endocrinologic abnormalities.3,5

Clinical manifestations of ventricular non-compaction include congestive heart failure, arrhythmia, sudden cardiac death and embolic events.3

Case report

A 12-year-old girl was referred to our hospital with diagnosis of hypertrophic cardiomyopathy and heart failure. Review of past medical history, demonstrated an aborted sudden cardiac death last year, which was complicated with dysarthria and spastic paresis. On physical examination there was spastic paresis of lower extremity, soft S1, normal S2 and S4, systolic murmur III/VI in left sternal border and apex. Electrocardiography (ECG) showed severe left ventricular (LV) hypertrophy pattern, ST – T change (strain pattern), left atrial abnormality, short PR intervals and delta
waves (negative in V1 and inferior leads) representing Wolf-Parkinson-White (WPW) syndrome (Figure 1).

Chest radiography revealed cardiomegaly with prominent pulmonary artery branches. On Holter monitoring there was normal heart rate variability and infrequent PACs.

Electrophysiology study showed left lateral accessory pathway.

Transthoracic echocardiography (TTE) was performed and revealed severe LVH with asymmetrically involved septum (Figure 2).

There was severe global hypokinesia and moderate to severe LV systolic dysfunction (EF=25-30%) and severe diastolic dysfunction (restrictive pattern), left atrial pressure was estimated about 25 mmHg. There was mild mitral regurgitation and moderate tricuspid regurgitation, with moderate pulmonary hypertension.

Left lateral accessory pathway was ablated successfully and ICD was implanted to prevent sudden cardiac death. The patient discharged with ASA, diuretic and ACE inhibitor.

**Discussion**

**Pathogenesis**

Several pathogenic concepts have been proposed for LV non-compaction.2-5 1) Persistence of embryonic sinusoids and an arrest in the compaction process of the myocardium2-8 2) an attempt of an impaired myocardium to grow and, thus, try to overcome an inborn error. 3) the result of an adaptation to special hemodynamic conditions, 4) the consequence of an impaired adhesion of cardiac myocytes as a result of malfunction of gap junctions,2 and 5) cardiac neuropathy, a disturbance associated with the cardiac conduction system comprising His-Purkinje fibers.5 several mutations have been describes, including G25 gene encoding a protein family called the tafazzines.8 LVNC is a morphologic abnormality with genetic heterogeneity.

**Clinical Manifestations**

Patient may be asymptomatic or presented with congestive heart failure, sudden cardiac death, such as our case, arrhythmia or embolic events.2 Congestive heart failure is the most common presenting condition.2,4 CHF can be a result of either systolic or diastolic ventricular dysfunction. Diastolic dysfunction is probably a result of the abnormal ventricular trabecular structure causing impaired relaxation and filling.2 The cause of systolic dysfunction is less clear, chronic myocardial ischemia due to coronary microcirculatory dysfunction has been recently suggested as a
possible mechanism. Arrhythmogenic mechanisms in LVNC include sympathetic nerve dysfunction and abnormalities in cardiac conduction system.

Among the noncardiac abnormalities associated with LVNC, neurologic abnormalities are the most frequent (29% reported in one study).2-6

**Diagnosis**

Chest radiographs show an enlarged heart and signs of pulmonary congestion. ECG abnormalities are frequent. In many patients, ECG features include biventricular hypertrophy with extreme QRS voltages, noted to be similar to those seen in Pompe’s disease; isolated or diffuse T-wave changes; WPW with premature atrial and ventricular contractions.

Prominent left ventricular trabeculations have been reported in 68% of normal hearts12 and can also be observed in hypertrophic hearts secondary to valvular, hypertrophic or dilated cardiomyopathy.13 The echocardiographic examination must be performed with special care to avoid false diagnosis of the disease.

The echocardiographic examination must be performed with special care to avoid false diagnosis of the disease. The echocardiographic criterion are 1) the presence of more than 3 trabeculations within one imaging plane, apically from the insertion of papillary muscle in the inferior and lateral wall,5 2) markedly thickened LV wall presenting as two layered myocardium with noncompaction/compaction ratio of 2/1 at end systole obtained in parasternal short axis view,2,5,6 3) deep intertrabecular recesses filled with blood from LV cavity visualized with color Doppler echocardiography, and 4) hypokinesia of the affected and possibly adjoins segments.2,6

In our case the presence of significant asymmetrical hypertrophy of the basal portion of anteroseptal segment results in false diagnosis of hypertrophic cardiomyopathy, but the correct diagnosis was made by the presence of a two layered myocardium located preferentially in LV apex and mid-ventricle distal to papillary muscles in inferolateral walls.

**Prognosis and Treatment**

The prognosis a of patient with LVNC is assessed controversially.2-5,11 In earlier reports, LVNC was reported to be associated with high mortalities as a result of heart failure and sudden cardiac death. In the meantime, many cases of LVNC have been published with a better. This difference in prognosis can be explained with improvement in medical and surgical therapy for heart failure as a result of β Blocker agents,5,11,14 ACE inhibitors, implantation of cardioversion/ defibrillators and heart transplantations. Patients with LVNC and atrial fibrillation should receive oral anticoagulation. LVNC associated with rhythm disorder is primarily treated with antiarrhythmic drugs while some patients require ICD implantation.

Therapy in patients with LVNC and neuromuscular disorder is limited to physiotherapy use of orthoses and symptomatic therapy of pain from muscle cramps, sensorimotor polyneuropathy and Non cardiac. Non neurologic disorders comprises the established therapy used for specific disorder.2-6

**References**

International Cardiovascular Meetings and Congresses Calendar 2007

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<td>Chicago, IL, United States</td>
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Information for Authors

Scope of the journal
“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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Review of manuscripts
All manuscripts correctly submitted to will first be reviewed by the Editors. Some manuscripts will be returned to authors at this stage if the paper is deemed inappropriate for publication in “The Journal of Tehran Heart Center”, if the paper does not meet submission requirements, or if the paper is not deemed to have a sufficiently high priority. All papers considered suitable by the Editors to progress futher in the review process will undergo appropriate peer review and all papers provisionally accepted for publication will undergo a detailed statistical review.

Preparation of manuscripts
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.
Style and spelling
Authors whose first language is not English are requested to have their manuscripts checked carefully before submission. This will help expedite the review process and avoid confusion. Abbreviations of standard SI units of measurement only should be used.
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

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