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Address

North Kargar Street, Tehran Heart Center, Tehran, Iran 1411713138. Tel: +98-21-88029720. Fax: +98-21-88029702. Web Site: http://jthc.tums.ac.ir. E-mail: jthc@tums.ac.ir.
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“The Journal of Tehran University Heart Center”

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Heart and Athlete

Mohammad Alasti, MD1*, Bita Omidvar, MD2, Mohammad Hossein Jadbabaei, MD2

1Imam Khomeini Hospital, Jondishapour University of Medical Sciences, Ahwaz, Iran.
2Golestan Hospital, Jondishapour University of Medical Sciences, Ahwaz, Iran.

Abstract

Regular participation in intensive physical exercise is associated with electro-morphological changes in the heart. This benign process is called athlete’s heart. Athlete’s heart resembles few pathologic conditions in some aspects. So differentiation of these conditions is very important which otherwise may lead to a catastrophic event such as sudden death. The most common causes of sudden death in young athletes are cardiomyopathies, congenital coronary anomalies, and ion channelopathies. The appropriate screening strategy to prevent sudden cardiac death in athletes remains a challenging issue. The purpose of this review is to describe the characteristics of athlete’s heart and demonstrate how to differentiate it from pathologic conditions that can cause sudden death.

Keywords: Athletes • Electrocardiography • Heart • Death, sudden, cardiac

Introduction

The athlete’s heart syndrome refers to the electro-morphological remodeling which occurs to varying extents dependent upon the sporting discipline.1 It has been a subject of many studies over decades as the ability to differentiate a pathologic process from a physiologic process is of critical importance to the clinician and patient.

Regular participation in intensive physical exercise is associated with central and peripheral cardiovascular adaptations that facilitate the generation of a large and sustained cardiac output and enhance the extraction of oxygen from exercising muscle for aerobic glycolysis.2

Sports are classified according to their types, dynamic (isotonic) or static (isometric). Briefly, dynamic exercise involves changes in muscle length and joint movement with rhythmic contractions which develop a relatively small intramuscular force. Static exercise induces development of a large intramuscular force with little or no change in muscle length or joint movement. These two types of exercises should be thought of as the two opposite poles of a continuum, with most physical activities involving both static and dynamic components.3

During progressive dynamic exercise, cardiac output components (heart rate and stroke volume) are increased. The increase in stroke volume is achieved by both increasing of end-diastolic volume (Frank-Starling mechanism) and decreasing of end-systolic volume (increased contractile state). Total peripheral resistance deeply decreases. Thus, systolic and mean blood pressure increase moderately and diastolic blood pressure is maintained or decreases slightly. By contrast, static exercise induces a small increase in VO2, heart rate, and cardiac output without changing of stroke volume. Total peripheral resistance does not decrease. The rising of systolic, mean, and diastolic blood pressure is linked to the muscle mass involved, the percent of maximal
Preserved systolic and diastolic function and regression of structural abnormalities with deconditioning are consistent with physiologic adaptation to training. Several studies evaluating transmural flow by Doppler echocardiography have shown higher early peak diastolic filling velocity and higher ratios of early (E) to late (A) filling velocities (E/A ratio usually 1.5 to 1.9) in trained athletes when compared with control subjects, suggesting supranormal diastolic function. Increased cardiac mass is a common finding in trained athletes who have an increased left ventricle (LV) size. LV mass usually falls within the accepted normal limits for age-and sex-matched control subjects. Left atrial (LA) enlargement is another common morphologic finding. LA enlargement is usually mild to moderate. Increased diameter of the left atrium, found more commonly in athletes who have demonstrable changes in LV morphology and in those individuals active in ultra-endurance sports like cycling and marathon running, is believed to be secondary to increased volume load. Mild-to-moderate structural changes of the right ventricle (RV) with preserved contractile function are the other finding in the athlete’s heart syndrome. These include increased end-diastolic volume, wall thickness, and mass.

The differential diagnosis for individuals with clearly abnormal RV includes dilated cardiomyopathy, hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and myocarditis. The heart of a trained individual usually falls within accepted normal limits, including the following measurements: LV end diastolic dimension less than 6.0 cm, LV wall thickness less than 1.3 cm, septal-posterior wall thickness ratio less than 1.3, and LV mass less than 294 g in men and 198 g in women. However, there can be significant overlap between the upper limits of normal in the athlete’s heart with other forms of structural cardiac disease.

Athletes with concomitant adaptive cardiac hypertrophy have less left-sided and more right-sided regurgitation than physically active healthy subjects with smaller hearts. The increases in the frequency and severity of tricuspid regurgitation (TR) and pulmonary regurgitation (PR) should be kept in mind when examining athletes with physiologic hypertrophy.

Some factors can affect the magnitude of morphologic changes following exercise. Endurance disciplines, such as cycling, cross-country skiing, and rowing/canoeing have the greatest effect on LV cavity dimensions. Other disciplines such as soccer, basketball, handball, and other team ball sports (which include aerobic and anaerobic exercise training) show a moderate impact on LV cavity dimension. Finally, technical disciplines such as equestrian sports or yachting have only a minimal effect on cardiac dimensions.

For years, it has been believed that predominantly isotonic (aerobic) training leads to more significant changes in LV cavity dilatation, wall thickness, and mass. This is in contrast to athletic activities in which the training is predominantly isometric (strength) in nature, like weight lifting and wrestling, in which there may be only increased wall thickness. Interestingly, a recent study showed that the most extreme increases in LV wall thickness had been observed in those athletes training in rowing and cycling. Of note, strength training was associated with only a mild increase in wall thicknesses (although often disproportionate to cavity size), whereas absolute values uncorrected for body surface area usually remained well within the accepted normal range (<12 mm).

Body size, sex, and race are the other factors that can affect the response of the heart to exercise. In general, larger male athletes have greater absolute increases in LV wall thickness, cavity dimension, mass, and left atrial dimension. Although some of the differences between males and females seem to be related to different body size, other mechanisms are the lower increasing of absolute blood pressure during peak exercise in women and their lower level of natural androgenic hormones.

It seems that a larger proportion of African-American athletes compared with Caucasian athletes have an LV wall thickness exceeding upper normal limits. The exact stimulus to the disproportionate LV wall thickening in African-American athletes remains unknown. However, there is a significant degree of variability among athletes that cannot be explained by these factors alone. Other genetic and environmental factors are believed to have a significant role in the cardiac structural changes in athletes.

**Differentiation from cardiovascular diseases**

The differential diagnosis of physiologic LV enlargement in trained athletes is based on the presence of normal LV systolic/diastolic function and absence of segmental wall motion abnormalities. Indeed, LV cavity dilatation in normal athletes is associated with superior physical performance as assessed by cardiopulmonary testing. An athlete with left ventricular hypertrophy (LVH) between 12 and 16 mm presents a grey zone between the extremes of physiological adaptation and mild expression of HCM. The identification of LVH in a female athlete, any adolescent athlete aged <16 years old, and any athlete participating in low intensity endurance sports is highly indicative of HCM. Physiological LVH is homogeneous and symmetrical. Athletes rarely exhibit differences of >2 mm between adjacent LV myocardial segments, and the ratio of the interventricular wall thickness to the LV posterior wall thickness in end-diastole is <1.5:1. In contrast, almost any pattern of hypertrophy is possible.
in HCM. Most individuals (60%) with HCM demonstrate asymmetrical septal hypertrophy and 10% reveal hypertrophy confined to the LV apex. The LV cavity size is the most important discriminator between physiological LVH and HCM. Almost all athletes with physiologically LVH have concomitant enlargement of the LV cavity. Typical values of LV cavity size in athletes with LVH range between 55 and 65 mm. Most individuals with HCM have a small LV cavity (<45 mm). Approximately, 25% of individuals with HCM exhibit basal, dynamic LV outflow tract obstruction and up to 70% develop obstruction with exercise. Early rapid LV filling is impaired as evidenced by the demonstration of a reversed E/A ratio, prolonged E-deceleration time (>240 ms), isovolumic relaxation times (>90 ms), and reversed systolic to diastolic wave (S/D) ratio during pulmonary vein Doppler. Measurement of myocardial velocity gradients from digitized M-mode colour Doppler reveals that individuals with HCM exhibit impaired myocardial filling during the rapid filling phase of diastole and display reduced LV posterior wall myocardial velocity gradients compared with athletes.\(^2\)\(^3\)\(^4\)

Assessment of longitudinal cardiac function with pulsed tissue Doppler at the level of the mitral valve annulus has demonstrated that individuals with morphologically mild HCM exhibit lower early diastolic velocities (Ea). An Ea of <9 cm/s in lateral mitral annulus favours pathological LVH with a sensitivity approaching 90%. The E/Ea ratio may also be useful in differentiating physiological LVH from HCM. An E/Ea >12 is indicative of high left atrial filling pressures, a hallmark of HCM; however, most trained athletes exhibit a E/Ea <8.\(^2\)\(^3\)\(^4\)

In patients with HCM, strain and strain rate are abnormal even in the absence of myocardial fibrosis on cardiac MRI.\(^2\)\(^3\)\(^4\) Also, athletes have a synchronous activation pattern in the left and right ventricle. In contrast, the HCM patients have significant inter and intraventricular activation delays.\(^2\)\(^4\)

Pulsed tissue Doppler studies have shown that many HCM patients exhibit impaired longitudinal systolic function. So, finding of a mitral valve annular peak systolic velocity of <9 cm/s in an athlete with LVH should raise the suspicion of underlying pathology.\(^2\)\(^4\) Sherrid et al. measured the diastolic flow in septal perforator coronary arteries of patients with HCM by transthoracic echocardiography. The peak diastolic flow in these individuals was significantly increased compared to both healthy controls and individuals with hypertrophy caused by arterial hypertension.\(^2\)\(^5\)

MRI has a potential value for diagnosing HCM by virtue of its superiority over echocardiography in identifying segmental hypertrophy in the anterolateral LV free wall or at the apex.\(^2\)\(^6\)

In active athletes presenting with LV hypertrophy, abnormal amino terminal pro-brain natriuretic peptide (NT-pro BNP) levels indicate HCM, whereas normal values are inconclusive.\(^2\)\(^7\)

Commercial laboratory genetic testing is now available in HCM but it is costly and the diagnostic yield is only 60-70%. Therefore, a negative gene test does not exclude HCM.\(^2\)\(^9\)\(^2\)\(^1\)

The measurement of peak oxygen consumption during an exercise test is another method of differentiating physiological LVH from HCM. A peak oxygen consumption of >50 mL/kg/min in an athlete with mild LVH favours physiological adaptation.\(^2\)\(^9\) Stopping the sport discipline has no effect on LVH in patients with HCM; but even in highly trained Olympic athletes, a substantial reduction (by 2-5 mm) will occur after a 3-month deconditioning period.\(^2\)\(^7\)

Both athletes and ARVC patients demonstrate RV enlargement compared to controls; nonetheless, RV cavity size is not significantly larger in ARVC patients than in athletes, whereas right ventricle outflow tract (RVOT) diameter is significantly larger in ARVC subjects compared to athletes. Furthermore, all ARVC patients show localized RV wall motion abnormality, an abnormality not detected in athletes and controls.\(^2\)\(^8\)

The differentiation from dilated cardiomyopathy (DCM) is generally easily made because of the absence of LV systolic dysfunction in athlete’s heart, absence of familial history of DCM, and absence of arrhythmias.\(^2\)\(^9\)

In trained athletes, LV cavity enlargement is associated with consistent enlargement of the RV; indeed, the physiologically dilated LV cavity maintains the ellipsoid shape, with the mitral valve normally positioned and without mitral regurgitation.\(^3\)\(^0\)\(^3\)\(^1\)

**Electrocardiogram in athletes**

Abnormal Electrocardiograms (ECGs) are common in athletes. Athletes of African descent and athletes participating in endurance sports (cycling, rowing, and triathlons) or sports with high peak levels of activity (football, basketball, track, and soccer) tend to have a higher incidence of abnormal ECG. Conversely, female athletes and athletes participating in more technically oriented sports (judo and equestrian sports) have a relatively lower incidence of abnormal ECG findings.\(^3\)\(^2\)\(^3\)\(^3\)

The spectrum of abnormalities includes sinus bradycardia, first and second-degree heart block, early repolarization, and LV hypertrophy. Certain ECG abnormalities are associated with heart disease and an increased risk of sudden cardiac death (SCD). These abnormalities include the pseudo-infarct pattern seen in HCM (septal Q-waves) and Wolff-Parkinson-White (WPW) syndrome (inferior Q-waves).\(^3\)\(^4\)

The ECGs of trained athletes often exhibit pure voltage criteria (based only on QRS amplitude measurements) for LVH that reflect physiological LV remodelling with increased LV wall thickness and chamber size. Isolated QRS voltage criterion for LVH is an unusual pattern in patients with HCM, in whom pathologic hypertrophy is characteristically
associated with additional ECG abnormalities such as left atrial enlargement, left axis deviation, delayed intrinsicsoid deflection, T-wave inversion, and pathologic Q waves.\textsuperscript{35}

Thus, systematic echocardiographic evaluation of athletes fulfilling isolated QRS voltage criteria at preparticipation screening is not justified, unless such subjects have other ECG changes, relevant symptoms, abnormal physical examination, or positive family history for cardiovascular diseases or premature SCD.\textsuperscript{30, 35, 36}

The presence of T-wave inversion of 2 mm or more in at least 2 adjacent leads in an athlete is a non-specific but warning ECG sign of a potential cardiovascular disease. The significance of flat or minimally inverted (<2 mm) T waves (mostly inferior and/or lateral leads) is unclear. These changes usually revert to normal with exercise and are considered a benign ECG phenomenon resulting from increased vagal tone. However, such minor T-wave abnormalities are uncommonly encountered in the athlete heart, but are common in cardiomyopathy. This indicates that they may have a pathologic basis and should be cautiously investigated and followed up over time.\textsuperscript{37, 38}

In asymptomatic white adolescent athletes aged less than 14 years, the presence of T-wave inversions in leads V\textsubscript{1}-V\textsubscript{4} should not justify further investigations in the absence of symptoms or a family history of premature heart disease or SCD. In contrast, T-wave inversions beyond V\textsubscript{4} (even beyond V\textsubscript{6}) are uncommon in post-pubertal athletes and their rarity probably warrants further investigation.\textsuperscript{39}

The identification of deep T-wave inversions in the anterior and/or lateral leads is a recognized feature of apical HCM. Detailed assessment of the left ventricular apex at echocardiography and the use of a contrast agent to define the endocardial borders should, therefore, be considered.\textsuperscript{37}

The prevalence of incomplete right bundle branch block (RBBB with QRS duration <120 ms) has been estimated to range from 35 percent to 50 percent in athletes compared with 10 percent in young healthy controls. The ECG pattern is more often noted in athletes engaged in endurance sports, with a striking male preponderance. It has been suggested that it is caused by the enlarged RV cavity size or increased cardiac muscle mass and the resultant conduction delay. Incomplete RBBB does not require further tests in the presence of a negative family/personal history and physical examination. The RBBB morphology has been shown to be reversible with deconditioning. An underlying ARVD should be suspected when the pattern of incomplete RBBB is associated with disproportionate extent of T-wave inversion (beyond V\textsubscript{6}) or in the presence of premature ventricular beats with a LBBB morphology.\textsuperscript{32, 37}

The early repolarization ECG pattern is another common finding among highly trained athletes, in whom it is observed in 50-80 percent of resting ECGs. The most notable ECG feature is the elevation of the QRS-ST junction (J point) of at least 0.1 mV from baseline, often associated with notching or slurring of the terminal QRS complex. Early repolarisation may vary on location, morphology, and degree. It is most often localised in precordial leads, with the greatest ST-segment elevation in mid-to-lateral leads (V\textsubscript{5}-V\textsubscript{6}). Maximal ST-segment displacement may also occur more laterally (leads V\textsubscript{8}, V\textsubscript{10}, L\textsubscript{3} and aVL), inferiorly (L\textsubscript{2}, L\textsubscript{3} and aVF), or anteriorly (leads V\textsubscript{3}-V\textsubscript{6}). Slowing of the heart rate exaggerates ST-segment elevation, whereas sinus tachycardia occurring during exercise or after isoproterenol administration reduces and often eliminates early repolarisation changes. In athletes presenting with syncope or cardiac arrest which remains unexplained after a detailed clinical work-up, an ECG pattern of early repolarisation in the inferior and/or lateral leads, with a prominent terminal QRS slurring, should raise the suspicion of an underlying idiopathic ventricular fibrillation. The characteristics of benign early repolarization that differentiate it from potentially pathological ST-segment elevation include diffuse ST-segment elevation, upward concavity of the initial portion of the ST segment, notching or slurring of the terminal QRS complex, and concordant large amplitude T waves. Also, athletes exhibit an up-sloping ST segment with a mean ST/ST\textsubscript{80} ratio <1, whereas patients with the Brugada syndrome show a down-sloping ST segment with a ST/ST\textsubscript{80} ratio >1.\textsuperscript{32, 37}

As opposed to the common occurrence of ST-segment elevation in athletes, the presence of ST-segment depression is rare and should warn the clinician to pursue pathologic causes.\textsuperscript{35}

**Arrhythmia in athletes**

Sinus bradycardia is a common finding on the ECG of a highly trained athlete. Variable degrees of atrioventricular (AV) block are also not uncommon. The most common are first-degree (10%) and second degree Mobitz type I (8%). Although second-degree Mobitz type II and even third-degree heart block have been reported, they are exceedingly rare. Resolution of (asymptomatic) first-degree or second-degree atrioventricular (AV) block with hyperventilation or exercise confirms its functional origin and excludes any pathologic significance.\textsuperscript{37}

Escape junctional beats or rhythm may be recorded in athletes with more severe bradycardia and result in functional AV dissociation. Sinus arrhythmia that disappears during exercise has also been reported.\textsuperscript{37}

Most ventricular tachyarrhythmias (including non-sustained ventricular tachycardia) occurring in highly trained athletes are not associated with adverse clinical consequences and are usually abolished or substantially reduced after relatively brief periods of deconditioning.\textsuperscript{13, 26, 40}

But complex and frequent ventricular tachyarrrhythmias should raise the possibility of disease states such as myocarditis. Periods of forced deconditioning may not be useful
in resolving the differential diagnosis of myocarditis versus athlete’s heart since detraining is associated with reduction (and even abolition) of ventricular tachyarrhythmias in athletes with or without underlying pathologic substrates.13, 31

The risk of lone atrial fibrillation (AF) is higher in athletes compared with controls.41, 42 According to a recent study, frequency of vigorous exercise was associated with an increased risk of developing AF in young men and joggers. This risk decreased as the population aged and was offset by known beneficial effects of vigorous exercise on other AF risk factors.43

Another study showed the elderly athlete may not be as healthy as believed: among former athletes, sinus node dysfunction occurred significantly more often compared with age-matched controls.24

**Syncope in athletes**

Syncope in young individuals is usually benign; however, syncope can be a warning of impending SCD. In the athlete with syncope, an echocardiogram is necessary in all but the most classic neurocardiogenic syndromes.34, 44

Syncope that occur during exertion are more likely to be life-threatening than those that occur at rest. What is called exercise-induced neurocardiogenic syncope is in fact syncope that occurs after exercise or during pauses in exertion. Post-exertional syncope is not likely to be life-threatening, but is likely to be caused by vasodilatation and corresponding hypotension. Syncope without prodromal symptoms is more troubling than a gradual onset of syncope. Syncope that occurs only with upright posture is less likely to be arrhythmic than that occurring during sitting or lying down. Syncope with clear and reproducible triggers of stress, excitement, or fear is more likely to be neurocardiogenic than arrhythmic. Injury secondary to syncope is more often seen in arrhythmic disorders and rarely seen in neurocardiogenic syncope. Frequent episodes of presyncope and lightheadedness are less likely to be arrhythmic in origin than occasional episodes of syncope. In individuals with this family history of inherited cardiac condition, syncope is more concerning.34

**Cardiovascular causes of sudden cardiac death**

The exact incidence of SCD in young athletes is unknown. In Italian competitive athletes (age 14-35 years), the incidence was found to be 3.6/100 000 and in US athletes, the incidence was lower (0.5/100 000).45

The combined prevalence of cardiovascular diseases that predispose to SCD in the general athletic population is estimated at 0.3%.30

SCD in athletes is more common in men (men/women ratio ranging from 5:1 to 9:1).21 The risk of SCD in athletes significantly increases with age.30 Sudden collapse usually occurs with physical exertion, predominantly in the late afternoon and early evening hours, corresponding to the peak periods of competition and training, and particularly in organized team sports.21 The most common cardiovascular cause of SCD in young athletes in US is hypertrophic cardiomyopathy, accounting for about 35% of such events.21

Second in frequency to HCM is a variety of congenital malformations of the coronary arteries, the most common of which is anomalous origin of the left main coronary artery from the right sinus of Valsalva. Young individuals with anomalous left main coronary artery may die suddenly as the first manifestation of their disease, although a minority experience angina, syncope, or even acute myocardial infarction. The vast majority of these events are related to exertion. Indeed, occurrence of one or more episodes of exertional syncope in a young athlete necessitates exclusion of this coronary anomaly. In athletes it may be possible to identify anomalous left main (or right) coronary artery using two-dimensional or transesophageal echocardiography, which can then lead to definitive confirmation with coronary arteriography or CT angiogram. Other unusual variants of coronary arterial anatomy, including hypoplasia of some portion of the coronary circulation, left anterior descending, or right coronary artery emanating from the pulmonary trunk, have been reported.21 Arrhythmogenic right ventricular dysplasia (ARVD) is the most common underlying organic heart disease in Italy but its frequency is in the range of less than 5% in US.21

Understanding of commotio cordis has increased in recent years, and it is presently an important cause of SCD in athletes. Commotio cordis is frequently caused by projectiles which are implements of the game, and strike the chest at a broad range of velocities. Chest barriers with proven efficacy in preventing commotio cordis are not yet available and commercially available chest protectors have proven ineffective in preventing ventricular fibrillation.21 Sudden unexpected death in a young athlete can be attributed to illicit substance abuse (cocaïne, anabolic steroids, or dietary and nutritional supplements).21

Less common causes of sudden death in young athletes (accounting for 3%-8%) include myocarditis, dilated cardiomyopathy, aortic dissection and rupture (usually caused by Marfan syndrome), sarcoidosis, valvular heart disease (mitral valve prolapse or aortic valve stenosis), and atherosclerotic coronary artery disease. Also, a small number of athletes die suddenly without evidence of structural cardiovascular disease, even after careful gross and histologic examination of the heart. It is likely that some are caused by previously unidentified WPW syndrome, ion channelopathies, and catecholaminergic polymorphic ventricular tachycardia (CPVT), or possibly, undetected
Preparticipation screening

Preparticipation cardiovascular screening is the systematic practice of evaluating athletes before participation in sports for the purpose of identifying abnormalities that may predispose to SCD. History taking and physical examination are the cornerstone of screening protocols. Personal history of exertional chest discomfort, unexplained syncope or near-syncope, unexplained dyspnea or fatigue associated with exercise, prior recognition of a heart murmur, elevated systemic blood pressure, family history of cardiac death before age 50 years, disability from heart disease in a close relative < 50 years of age, specific knowledge of certain cardiac conditions in family members (hypertrophic or dilated cardiomyopathy, ion channelopathies and Marfan syndrome) should be inquired.48

Physical examination should include dynamic auscultation for heart murmur, palpation of femoral pulses to exclude aortic coarctation, evaluation for the physical stigmata of the Marfan syndrome, and measurement brachial artery blood pressure in sitting position.49, 50 In athletes, the LV may be prominent to feel and displaced laterally. Third and fourth sounds are permissible, as is a soft mid-systolic flow murmur.48

In Italy, screening usually starts at the beginning of competitive athletic activity (age 12-14 years) and is repeated on a regular basis. First-line examination includes history taking, physical examination, and 12-lead ECG. The addition of 12-lead ECG has the potential to enhance the sensitivity of the screening process for the detection of cardiovascular diseases. In fact, ECG is abnormal in up to 95% of patients with HCM, which is the leading cause of sudden death in athletes. Likewise, ECG abnormalities have also been documented in the majority of athletes who died from ARVC, proven at autopsy.35

The screening method recommended by the American Heart Association states that 12-lead ECG is not cost-effective for screening large populations of young athletes because of its low specificity.30, 35 Additional tests are requested only for subjects who have positive findings at the initial evaluation. Despite different preparticipation screening strategies, athlete sudden death rates in demographically similar regions of the United States and Italy have not differed significantly in recent years. These data do not support a lower mortality rate associated with preparticipation screening programs involving routine electrocardiography and examinations by specially trained personnel.31

Cardiovascular disease and sport

When a cardiovascular abnormality is identified in a competitive athlete several considerations arise: (1) level of risk for SCD if participation in organized sports continues; (2) likelihood that risk would be reduced if systematic training and competition were terminated; and (3) criteria to formulate appropriate eligibility or disqualification decisions.21

Athletes with radiofrequency cure of supraventricular tachycardias can resume competitive athletics after 4 weeks. Athletes with first-degree or Mobitz I heart block, which does not worsen with exercise, do not need restriction of competitive athletics. However, athletes with Mobitz II or complete heart block generally require pacing. Those athletes with permanent pacemakers should not participate in competitive athletics with a danger of bodily collision.21

Only low intensity competitive athletics is permitted in athletes with structural heart disease and sustained ventricular arrhythmias, without regard to the method of treatment.21

In patients with ARVD, moderate and high level competitive athletics are contraindicated. This recommendation is independent of age, gender, and phenotypic appearance and does not differ for those athletes without symptoms or for those treated with drugs, surgery, catheter ablation, or an implantable defibrillator.6, 21, 28

In individuals with HCM, competitive athletics should be prohibited. Young athletes with the unequivocal diagnosis of HCM are discouraged from competitive athletic participation, with the exception of low-intensity sports like golf, billiards, and bowling.6, 21 Annual serial echocardiography is recommended throughout adolescence in athletes with a family history of HCM.36

Because of the potential for SCD, competitive athletics are not recommended in the Brugada syndrome.28 Athletes with a clinical diagnosis of myocarditis should be temporarily excluded from competitive and amateur-leisure time sport activity. This recommendation does not differ for athletes with only mild symptoms or under treatment with drugs. After resolution of the clinical presentation (at least 6 months after the onset of the disease), clinical reassessment is indicated before the athlete re-enters a competitive sport lifestyle.52

Athletes with a clinical diagnosis of DCM should be excluded from most competitive sports, with the possible exception of those of low intensity. This recommendation does not differ for those athletes without symptoms, those with prior treatment with drugs or major interventions with surgery, or those with an implantable cardioverter defibrillator (ICD).52 All patients with CPVT are restricted...
from participation in competitive athletics, with the possible exception of low intensity sports.6

Restriction from competitive sports in patients with long QT syndrome is recommended for those with syncpe or resuscitated SCD, and for those with QTc above 470 in males and 480 in females.23 Asymptomatic patients with prolonged QTc should be restricted to low-intensity competitive sports.6

Return to sport after a commotio cordis event should be on a case-by-case basis. There is concern that patients undergoing a commotio cordis event are more vulnerable to recurrent events.9

Athletes with an anomalous coronary anomaly associated with exercise-related sudden cardiac death should be excluded from athletic activities until the anomaly is surgically corrected.46

In athletes with coronary artery disease and ventricular arrhythmias, only low intensity competitive athletics are permitted. Athletes with documented vasospasm should also undergo atherosclerosis risk factor management because underlying atherosclerosis contributes to abnormal coronary vasomotion. Recommendations for athletic activity should be based on evidence that exercise produces vasospasm in the athlete, the ability to control symptoms with medications, and the presence of underlying atherosclerosis. Consensus guidelines favour marked restriction of physical activity in them.46

In patients who have hypertension and are about to engage in intense (although amateur) exercise training, a medically supervised peak or symptom limited exercise test with electrocardiography and blood pressure monitoring is warranted. Athletes with hypertension should be treated according to the general guidelines for the management of hypertension. Diuretics and beta-blockers are not recommended for first-line treatment in patients engaged in competitive or high-intensity endurance exercise.53

An ICD disqualifies an athlete for competitive sports, except those with a low cardiovascular demand. In addition to underlying disease, there are other reasons to stop participation in intensive sports: (1) physical activity is a likely trigger for ventricular arrhythmias; (2) transient impaired consciousness can be dangerous during certain sports; and (3) the efficacy of the ICD to interrupt malignant ventricular arrhythmias during intense exercise is probably suboptimal.54

Extreme ipsilateral arm movements should be avoided to prevent lead fracture, such as during volleyball, basketball, racket sports, swimming, or gymnastics. The risk of subclavian crush should be the reason for implanting single-lead devices and with a lead preferably with only one shocking coil. Sudden onset discriminator in these patients should be used carefully because ventricular arrhythmias may develop during sinus tachycardia, reducing the specificity of this parameter.54

Leisure-time sports resumption is allowed from 6 weeks after implant, preferably after a control stress test. When appropriate or inappropriate ICD interventions occur, a 6-week period refraining from sports should be reconsidered to evaluate the effect of changes in medical therapy or ICD programming.54

Conclusion

Differentiating a pathologic condition from the physiologic process in athletes is very important because the inability to diagnose the underlying heart disease can lead to sudden death during exercise, which is a catastrophic event. For all the advances, finding the appropriate screening strategy to prevent SCD in athletes still remains a challenging issue.

References


Role of Surgeon in Length of Stay in ICU after Cardiac Bypass Surgery

Mahdi Najafi, MD*, Hamidreza Goodarzynejad, MD, Mahmood Sheikhfathollahi, PhD, Hossein Adibi, MD

1Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran.
2Endocrine and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Background: We presumed that the surgeon himself has an impact on the results after coronary artery bypass grafting (CABG) as there is no unique protocol for the discharge of post-operative cardiac patients at our institution. Therefore, we examined whether the surgeon himself has an impact on the intensive care unit (ICU) stay of isolated CABG patients.

Methods: We prospectively studied a total of 570 consecutive patients undergoing elective CABG. Length of stay in the ICU was defined as the number of days in the ICU unit post-operatively. Seven operating surgeons were classified in 3 categories on the basis of the mean hospital stay of their patients (1, 2 and 3 if the mean total patients' stay in hospital was <8 days, between 8 to 10 days, and longer than 10 days; respectively). Using a multivariable regression model, we determined the independent predictors of length of stay in the ICU (> 48 hours) and examined the role of surgeon in this regard.

Results: Incidence of post-operative arrhythmia and length of ICU stay were higher in the patients of surgeon category 3 than those of surgeon categories 1 and 2. Surgeon category 3 also operated on patients with higher EuroSCOREs than did surgeon categories 1 and 2. With the aid of a multivariable stepwise analysis, three variables were identified as independent predictors significantly associated with ICU length of stay: age, history of cerebrovascular accident, and surgeon category.

Conclusion: Surgeon category may independently predict a prolonged length of stay in the ICU. We suggest that a unique discharge protocol for post-CABG patients be considered to restrict the role of surgeon in the ICU stay of these patients.

Keywords: Intensive care units • Length of stay • Coronary artery bypass

Introduction

Despite major improvements in peri-operative management, a remarkable proportion of cardiac surgery patients are monitored in the intensive care unit (ICU) for a period of time longer than usual recovery period. A prolonged length of stay (LOS) in the ICU following cardiac surgery is linked with poor patient outcomes and possibly restricts the overall number of performed procedures. Prolonged hospitalization also considerably increases the expenditure of health resources. Thus, to improve care efficiency, institutions often need to identify patients that possibly need a longer period of high dependency care after cardiac surgery. Among cardiac surgeries, coronary artery bypass grafting (CABG) has received particular attention in this regard because it is an expensive and commonly performed procedure. Furthermore, increased ICU stay in cardiac surgery patients has been related to a significant reduction in long-term survival; therefore, the ability to precisely predict the duration of stay in the ICU and patient outcome is of
essential importance.

Many studies have reported the factors affecting the length of post-operative ICU stay, but since a large number of variables could be considered,7 disparity in study results exists. Moreover, there is not a unique protocol for discharging the post-operative patients at our institution, so we presumed that surgeon himself has an impact on the results after CABG surgery as well as on the ICU stay and costs.

We, therefore, undertook this prospective study to determine pre-operative and intra-operative predictors contributing to prolonged LOS in the ICU with a special focus on the role of individual surgeons in influencing surgery outcomes.

Methods

From May to September 2006, we prospectively studied a total of 570 consecutive patients undergoing elective CABG at Tehran Heart Center. Patients who underwent CABG combined with a heart valve repair or replacement, resection of a ventricular aneurysm, or other surgical procedures were excluded. Written informed consent was obtained from all the patients, and the study was approved by the local hospital ethics committee.

Patient data, risk factors, operation, and outcome data were prospectively recorded on a structured paper form as described previously.4 Briefly, during the patient’s admission by interview and physical examination the following variables were collected: age, gender, body mass index (BMI), New York Heart Association (NYHA) function class, the number of diseased vessels, and left ventricular ejection fraction (LVEF). History of myocardial infarction, smoking, diabetes, hypercholesterolemia, hypertension, peripheral vascular disease, cerebrovascular disease, respiratory failure, and renal failure were also noted. Pre-operative medical characteristics were collected by research general practitioners, and operation data were detailed by the surgeons and perfusionists. The data were entered into the SPSS software by a single operator at a later date.

LOS in the ICU was defined as the number of days in the ICU unit post-operatively. Patients who stayed in the ICU for more than 2 consecutive days on the initial admission were classified as having a prolonged ICU stay. The study outcomes were the pre-operative and intra-operative risk factors of prolonged LOS in the ICU, and the occurrence of post-operative complications in the ICU.

Patients who currently smoked cigarettes or who had quit smoking for less than 1 month were considered smokers. Any cerebral neurological deficit induced by both cerebrovascular accident (CVA) and transient ischemic attacks or previous cerebral surgery was defined as cerebrovascular disease. Peripheral vascular disease (PVD) was defined as history or any evidence of aneurysm or occlusive peripheral vascular disease on physical examination.

The amount of inotropic support and arterial blood gas parameters (base excess and pH in plasma) were recorded within and up to 24 hours after surgery. A wound infection was any wound infection in the sternum or leg incision following surgery. Post-operative arrhythmia was defined as all observed rhythms except for normal sinus rhythm.

The operations were performed by seven surgeons. Surgeons, in terms of mean total in-hospital duration of stay for patients of each individual surgeon, were classified into 3 groups as follows:

1. if mean total patients’ stay in hospital was <8 days; 2, if mean total patients’ stay in hospital ranged between 8 to 10 days; and 3, if mean total patients’ stay in hospital was longer than 10 days.

The numerical variables were presented as mean±SD and were compared using the One-Way ANOVA test, while the categorized variables were summarized by absolute frequencies and percentages and were compared using the chi-square test. A multivariable stepwise logistic regression models for risk factors predicting LOS in ICU was constructed. Variables were included into the multivariable model if the p value was found to be less than or equal to 0.20 in the univariable analysis as well as their clinical significance. The associations of the independent predictors of LOS in ICU in the final model were expressed as odds ratios (OR) with 95% confidence intervals (CIs). Model discrimination was measured using the c statistic, which is equal to the area under the ROC (Receiver Operating Characteristic) curve. Model calibration was estimated using the Hosmer-Lemeshow (HL) goodness-of-fit statistic (higher p values imply that the model fit the observed data better). For the statistical analysis, the statistical software SPSS version 13.0 for Windows (SPSS Inc., Chicago, IL) and the statistical package SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA) were used. All the p values were 2-tailed, with statistical significance considered as p value ≤ 0.05.

Results

The baseline characteristics and pre-operative data of the CABG patients according to individual surgeon categories are presented in Table 1. There were 7 operating surgeons classified in 3 categories on the basis of the mean hospital stay of their patients as explained in the method section.

Surgeon category 3 operated on patients with higher EuroSCOREs than did surgeon categories 1 and 2. There were also some differences noted between surgeon categories with respect to the number of grafts performed, inotropic drug use, and time on pump.

The overall in-hospital mortality rate was 0.5%. As seen in Table 2, all 3 deaths occurred in surgeon category 3 operations (2.9% compared to no mortality for patients in surgeon categories 1 and 2; p value = 0.001). Incidence
of post-operative arrhythmia and length of ICU stay were higher in patients of surgeon category 3 than those of surgeon categories 1 and 2 (Table 2).

Age, sex, BMI, surgeon category, EuroSCORE, hypertension, diabetes, prior CVA, history of PVD, prior MI, NYHA function class, LVEF, number of diseased vessels, and creatinine were the variables entered into the logistic regression model based on their statistical significance in univariable analyses (entering criterion p value ≤ 0.20) as well as their clinical significance.

Table 3 shows the independent predictors of LOS at ICU in patients undergoing CABG. The multivariable stepwise analysis helped identify three variables as independent predictors significantly associated with ICU length of stay:

<table>
<thead>
<tr>
<th>Predictors</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgeon category*</td>
<td>1**</td>
<td>1 -</td>
<td>0.017</td>
</tr>
<tr>
<td>Age</td>
<td>1.020</td>
<td>1.000-1.041</td>
<td>0.048</td>
</tr>
<tr>
<td>Prior CVA</td>
<td>2.593</td>
<td>1.082-6.215</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Hosmer-Lemeshow goodness-of-fit test: p value=0.86
Area under the ROC curve (AUC): c=0.64

*Reference category
CVA, Cerebrovascular accident; OR, Odds ratio; CI, Confidence interval
age, history of CVA, and surgeon category. The table also shows that the predictive performance of the risk model assessed by using the area under the ROC curve (AUC) was acceptable (c = 0.64), and so was the calibration of the risk model.

Discussion

We studied pre-operative and intra-operative variables in a multivariable regression model to predict LOS in the ICU after bypass surgery for 570 CABG patients at our center. Three variables, namely age, prior CVA, and surgeon category, were found to be the independent predictors of an ICU length of stay greater than 48 hours.

Over the past 2 decades, a considerable number of reports have been published on the predictors of LOS in ICU following CABG surgery. However, a great disparity in type and number of independent variables analyzed has been reported. Tuman et al. found 11 pre-operative variables to be significantly associated with LOS in the ICU, including emergency surgery, age, pre-operative renal dysfunction, prior MI, cerebrovascular disease, type of surgery, congestive heart failure, and left ventricular dysfunction. Although they developed a model for predicting illness after cardiac surgery, the study has been shown to predict only the mean LOS in the ICU.

In a similar study on pre-operative variables, Tu et al. suggested that LOS following cardiac surgery could be predicted by a multivariate predictive index. Five variables were found to be the independent predictors of prolonged LOS in the ICU (age, female sex, left ventricular function, urgency of surgery, and type of surgery). Nonetheless, the authors accepted that the model had a poor predictive ability and LOS in the ICU could not be predicted with certainty. Mounsey et al. found only left ventricular end diastolic pressure and number of diseased coronary vessels to be beneficial in predicting LOS in ICU. Michalopoulos et al. studied elective procedures taking into account not only pre-operative variables, but also significant variables related to both the operative and immediate post-operative period such as number of inotropes administered and blood transfusion. They found that age, pre-operative left ventricular ejection fraction, bypass time, aortic cross-clamp time, number of inotropic agents used, and blood transfusions to be predictors of an extended LOS in the ICU.

Deoring et al. suggested that a significant portion of the variance in the ICU length of stay following CABG could be attributed to five variables, including pre-operative mortality risk (Parsonnet score), intubation hours, presence of arrhythmias, early hemodynamic instability, and 12-hour fluid balance. Finally, in a newly published study, Rosenfeld and co-workers found age > 70 years, urgency of surgery, pump time, and chronic obstructive pulmonary disease to be the independent pre-operative predictors for a prolonged ICU stay in CABG patients.

Such disparity in study results may be due to the fact that the majority of these studies have not included the operative or immediate post-operative variables and have just taken into account events which affect patient outcome during the pre-operative period. Other explanations for the differences in study findings may be due to various study populations and treatment protocols, different cut-off used to define a prolonged stay in the ICU (from ≥ 2 to 10 days), and differences in variables definitions, and the large number of variables that can be considered.

Chiming with other studies that have suggested age to be an independent predictor of the ICU stay ≥48 hours, ≥3 days, and ≥ 6 days, age was also a significant predictor of LOS in ICU in our study. A longer stay in the ICU in older patients may be justified by higher pre-operative comorbidity rates and severity of illness. However, because of improvements in operative and anesthetic techniques, mortality and morbidity in the elderly have been declined recently. Gender was not a significant predictor in our study. In a recently published study, Ranucci et al. also reported that female gender was not an independent risk factor for mortality or prolonged ICU stay, which is consistent with our results.

In a previous study, the variable of ‘previous history of CVA’ was independently associated with atrial fibrillation after cardiac surgery. It can be assumed that prior CVA may prolong LOS following CABG surgery by increasing the risk of atrial fibrillation arrhythmia as suggested by our current study.

The main difference between our study and those described above is that we took into account surgeon category as a variable. We found that the surgeon could potentially influence the duration of a patient’s ICU stay and that there were differences in the average LOS in ICU between surgeons at our hospital. Particularly, we found that patients in surgeon category one as a reference, had higher LOS compared to category 2 and lower LOS compared to category 3. It may indicate the necessity of using a unique protocol for discharging post-operative patients.

This study was observational and limited by its inherent restrictions and by the fact that we did not evaluate the contribution of individual intra-operative variables such as blood transfusion and cross-clamp time. However, it has previously been shown that compared with pre-operative and post-operative variables, intra-operative factors are less indicative of ICU duration of stay when all factors are considered together. Moreover, as all our patients were elective, the conclusions are limited to this study population and do not include emergent patients.
Role of Surgeon in Length of Stay in ICU after Cardiac Bypass Surgery

Conclusion

Detection of high-risk patients may help in more careful peri-operative management to decrease the possibility of prolonged hospitalization and its related morbidity and mortality. More studies with larger sample sizes are warranted to identify other factors contributing to ICU stay in CABG which have not been studied to date. In addition to age and other pre-operative variables, surgeon category may predict an extended LOS in the ICU. We suggest that a unique protocol for discharging post-operative patients be considered to restrict the role of surgeon in ICU stay after bypass surgery.

Acknowledgment

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References


Abstract

Background: Cardiac involvement in systemic sclerosis (SSc) is more prevalent than previously thought. In this study, the frequency and severity of cardiovascular involvement were assessed in SSc patients referred to Firouzgar Hospital.

Methods: Fifty-eight patients with SSc, selected from the data bank of SSc patients, were reviewed for the frequency and severity of 8 organ involvements in this case series.

The preliminary severity scale, published by international SSc study groups, was employed for the determination of the severity grade in the cardiovascular system. In the cardiac scoring scale, grade 0 represents normal heart (no cardiac involvement), grade 1 denotes mild involvement [electrocardiography (ECG) conduction defect and a left ventricular ejection fraction (LVEF) of 45-49%], grade 2 signifies moderate involvement (arrhythmia, LVEF = 40-44%), grade 3 indicates severe involvement (LVEF <40%), and grade 4 stands for end stage (congestive heart failure and arrhythmia requiring treatment).

Results: In this study, 24 (41.4%) patients were in the diffuse cutaneous (dcSSc) subset. The female to male ratio was 10.5:1, and the mean duration from symptom onset to diagnosis was 7.35 years for the dcSSc subset and 8.41 years for the limited cutaneous (lcSSc) subset of disease, there being no significant difference. Cardiac involvement in this series was seen in 13 (22.4%) cases, and there was no significant difference in terms of frequency and severity between the two disease subgroups (p value = 0.96 and p value = 0.46 respectively).

Conclusion: Our findings showed that the cardiac involvement in this series was infrequent and that there was no significant difference in the severity of cardiovascular involvement between the two subtypes of SSc in the late stage of the disease.

Keywords: Scleroderma, systemic • Connective tissue diseases • Heart

Introduction

Systemic sclerosis (SSc) is a connective tissue disorder characterized by vascular lesion and widespread fibrosis in organs such as skin, gut, lung, heart, and kidneys. Clinically, there is a broad spectrum of symptoms from widespread
severe skin thickening (diffuse) to skin thickening limited to distal extremities and/or face (limited). In the diffuse form, skin involvement is limited to hands, body, and face; whereas in the limited form, skin involvement is limited to hands and extremities lower than elbows and knees.

Cardiac involvement in SSc seems to be more prevalent than previously thought, as shown by improved invasive and non-invasive diagnostic techniques for detecting heart disease. Cardiopulmonary, renal, and extensive skin involvement is poor prognosis and the leading cause of early death in SSc.

To determine the abundance of cardiac involvement, the present study drew upon such different modalities as autopsy, exercise test, radionuclide scan, chest X-ray, ECG, and echocardiography. The severity of cardiac disease is usually determined using the two scoring methods of Clement and Medsger. The former is currently less favored in clinical trials, but the latter is regarded as more practical and is accepted by international SSc study groups.

The present study was designed to address the dearth of data on the severity and frequency of cardiac involvement in SSc patients in Iran.

**Patients and methods**

The SSc data bank in Firouzgar Hospital Rheumatology Department contains information on 67 patients (Until January 2007). Patients fulfilling the preliminary criteria of the American Rheumatism Association were recruited into this study, and 4 patients diagnosed as having SSc overlap with other connective tissue disease in addition to 5 patients whose cardiac involvement was secondary to pulmonary involvement were excluded. In total, 58 patients were included in the study.

During a 6-month period after the first visit to our clinic, core set variables of all the patients in this case series were assessed to define each organ system involvement. For cardiac involvement, traditional criteria hinging on the presence of 1 or more dichotomous variables, i.e. presence or absence of cardiomegaly, pericardial effusion, ventricular arrhythmias, conduction disturbances, axis deviations, and pathological Q waves (myocardial necrosis), were employed. For cardiac severity, the preliminary severity scale, published by international SSc study groups, was utilized and the patients’ files were reviewed retrospectively. The preliminary severity scale introduced by Medsger proposes a 9-organ disease severity scale for SSc, with “severity” defined as the total effect of the disease on the organ function. The scale has both irreversible (damage) and reversible components (activity), and the severity grading for each organ system ranges from 0 (no document) to 4 (end-stage disease).

In the cardiac scoring scale, grade 0 represents normal heart (no cardiac involvement), grade 1 denotes mild involvement [electrocardiography (ECG) conduction defect and a left ventricular ejection fraction (LVEF) of 45-49%], grade 2 signifies moderate involvement (arrhythmia, LVEF = 40-44%), grade 3 indicates severe involvement (LVEF <40%), and grade 4 stands for end stage (congestive heart failure and arrhythmia requiring treatment).

For the cardiac severity scale, each variable was primarily attributed to SSc rather than to another disorder. For example, if patients with mild (grade 1) cardiac involvement developed superimposed bacterial pneumonia with transient severe dyspnea and fibrillation (grade 2, moderate) due to hypoxia, the cardiac score was evaluated after pneumonia had resolved.

The relationship between cardiac involvement severity (cardiac scoring) and disease stage was assessed by analyzing the time periods in two disease subsets: early and late stages of the disease. Early stage was defined as diffuse cutaneous (dcSSc) < 3 years and limited cutaneous (lcSSc) < 5 years.

The analyses were performed using SPSS software version 9 released for microcomputers. The chi-square test was used for the detection of any correlation between cardiac severity and the two subsets of scleroderma, and the Fisher exact test was employed for the comparison of cardiac severity in the early and late stages of the 2 disease subsets. The Kendall Tau correlation coefficient was used to assess the correlation between cardiac severity and severity of other organ involvement.

**Results**

Table 1 depicts the general characteristics of the patients. There were 58 patients with a mean age ± SD of 40.9±13.7 years and a female to male ratio of 53/5, of whom 24 (41.4%) patients were in the dcSSc subset. The mean total skin score in all the patients was 16.6, based on the modified Rodnan scoring system, and the mean duration from symptom onset to study entry was 7.3±8.5 years for the dcSSc and 8.4±8.2 years for the lcSSc subsets; there was no statistically significant difference (p value = 0.638).

Table 2 illustrates the characteristics of cardiac involvement in the patients. Cardiac involvement was detected in 13 (22.4%) and conductive disturbance in 6 (10.3%) out of the
58 SSCa study patients. Axis deviation was found in 6 (10.3%) patients, all with left axis deviation. Additionally, abnormal Q waves and arrhythmia were found in 1 (1.7) and 2 (3.5) patients, respectively.

Cardiomegaly on chest x-ray, echocardiography, or ECG was found in 10 (17.2%) patients: 4 in the limited and 6 in the diffuse disease subtypes. Echocardiography revealed pericardial effusion in 9 (15.5%) patients, with a moderate-to-severe degree of pericardial effusion in 3 (5.1%) persons. As Table-3 demonstrates, there was no difference in terms of cardiac involvement between the 2 forms of scleroderma.

### Table 2. Cardiac characteristics of the patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>lcSSc subset</th>
<th>dcSSc subset</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal axis</td>
<td>29 (85.3)</td>
<td>22 (95.7)</td>
<td>51 (87.9)</td>
</tr>
<tr>
<td>LAD</td>
<td>5 (14.7)</td>
<td>1 (4.3)</td>
<td>6 (10.3)</td>
</tr>
<tr>
<td>RAD</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>1 (2.9)</td>
<td>1 (4.3)</td>
<td>2 (3.5)</td>
</tr>
<tr>
<td>Abnormal Q-wave</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Conduction defect</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>29 (85.3)</td>
<td>21 (91.3)</td>
<td>50 (86.2)</td>
</tr>
<tr>
<td>LLBB</td>
<td>1 (2.9)</td>
<td>1 (4.3)</td>
<td>2 (3.4)</td>
</tr>
<tr>
<td>LAHB</td>
<td>3 (8.8)</td>
<td>0</td>
<td>3 (5.2)</td>
</tr>
<tr>
<td>RBBB + LAHB</td>
<td>1 (2.9)</td>
<td>0</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Complete hemi block</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>4 (11.8)</td>
<td>6 (25)</td>
<td>10 (17.2)</td>
</tr>
</tbody>
</table>

### Table 3. Severity grade and stage of the disease in two subsets of systemic sclerosis (SSc)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Severity</th>
<th>lcSSc subset</th>
<th>dcSSc subset</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>Normal</td>
<td>5</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Late</td>
<td>Normal</td>
<td>13</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Numbers in the parenthesis are the related percentages

 lcSSc subset, Limited cutaneous subset; dcSSc subset, Diffuse cutaneous subset; LAD, Left axis deviation; RAD, Right axis deviation; LLBB, Left bundle branch block; LAHB, Left anterior hemiblock; RBBB, Right bundle branch block

With respect to the cardiac severity scoring of the patients, 45 (77.6%) patients scored zero (normal heart); cardiac involvement in 13 of the 58 (22.4%) patients was detected. Seven and 5 patients in the limited and diffuse disease subsets, respectively, had mild cardiac involvement (grade 1); moderate to severe cardiac involvement was not observed in either of the two subsets; and only 1 patient with diffuse skin involvement had end-stage cardiac involvement. A comparison of the limited and diffuse subsets of patients with no cardiac involvement as group 1 and the others with mild-to-severe involvement as group 2 yielded no statistically significant difference (p value = 0.96).

In regard to the relationship between the severity of cardiac involvement and that of other systems, cardiac severity showed no correlation with the severity of dermal, peripheral vascular, renal, tendinous, muscular, and gastrointestinal systems. There was, however, a significant correlation between cardiac severity and pulmonary severity (Kendall Tau = 0.27, p value = 0.04). The relationship between cardiac severity (cardiac scoring) and disease stage in the two disease subsets was evaluated, and the time scales were analyzed in the two disease subsets in terms of early and late stages; early stage was defined as dcSSc < 3 years and lcSSc < 5 years. There were 8 (23.5) patients with the dcSSc subtype in the early disease stage < 3 years (Table 3). There was no difference in the severity grade of the two disease subtypes between the early and late stages (in early stage: p value = 0.136 and $\alpha^2 = 3.564$; in late stage: p value = 0.433 and $\alpha^2 = 0.332$).

### Discussion

The female to male ratio in the present study population at a mean age±SD of 40.9±13.7 years was 53/5, which does not chime in with the results of pervious epidemiological studies of SSc reporting that the disease is 3-4 times more common in women. Nonetheless, the onset of SSc in this study is in the fourth and fifth decades of life as is the case in other similar studies. The mean disease duration from onset to entry in the lcSSc and dcSSc subtypes was 8.4 and 7.3 years, respectively. This means that the patients referred for treatment in the late disease stages, contributing to sample collection bias in the present study.

From a total of 58 SSc patients, 13 (22.4%) persons were found to have cardiac involvement and most of these patients (12/13 [92%]) showed mild severity of involvement. In the Janosik et al. study, pathological involvement of the pericardium was observed in 70%-80% of the patients at autopsy, while clinical manifestation was present in 7%-20% of the study subjects. They reported an association between pericardial effusion and cardiac involvement; pericardial effusions were small or large and had developed rapidly in some cases due to renal failure.

Echocardiography revealed pericardial effusion in 9 (15.5%) patients, moderate-to-severe pericardial effusion in 3 (5.1%) patients, and no renal failure in our study population.
It is deserving of note that echocardiography tends to be abnormal in 50% of patients and includes evidence of pericardial thickening or fluid, while clinical presentations of pericarditis and of tamponade are infrequent. In this series, we found axis deviation in 6 (10.3%) patients, all with left axis deviation. Arrhythmia and abnormal Q waves were present in 2 and 1 patient in each disease subset. In the Kostis J.B. et al. study, electrocardiography abnormalities, including arterial and ventricular arrhythmias and conduction disturbances by ambulatory electrocardiography study, confirmed a high prevalence of both supraventricular and ventricular tachyarrhythmia. In our study, cardiomegaly on chest x-ray, echocardiography, or ECG were found in 10 (17.2%) patients: 4 in the limited and 6 in the diffuse disease subtypes. In the Clements P. J. et al. study of 90 patients, 44 (49%) patients were found with cardiac involvement, which was comprised of arrhythmia in 4 (4.4%), cardiomegaly in 16 (17.8%), conduction defect in 9 (10%), pericardial effusion in 9 (10%), axis deviation in 18 (20%), and pathological Q wave in 12 (13.3%). The SD of the duration of SSc prior to entry was 6.6±7.8 years, and 39 patients entered the study within 3 years of disease onset. In a study of cardiac involvement by Geirsson A. J. et al., 40 patients with SSC and disease duration of 6 years were included in study. Cardiomegaly and arrhythmia at rest were 57% and 7.5% in the diffuse and CREST syndrome, respectively.

There were 9 (15.5%) patients with mild-to-severe pericardial effusion in our study as opposed to the 17.6% figure in the Pittsburgh study; the incidences of pericarditis were, however, similar. In the MC Whorter et al. study, the incidence of pericardial effusion was 50% and that of tamponade was not high as well. Coronary involvement was evaluated via non-invasive procedures in the present study, and no serological correlation with specific auto-antibodies was done, which can be deemed a limitation of our study.

Forty-five (77.6%) of our study population scored zero for cardiac involvement (normal heart). As was mentioned above, evidence for cardiac involvement was relatively infrequent; a comparison between the limited and diffuse subsets of patients with no cardiac involvement as group 1 and the others with mild-to-severe involvement as group 2 yielded no difference in terms of frequency between the two groups (P value = 0.46).

An assessment of the relationship between the severity of cardiac involvement (cardiac scoring) and lung involvement showed no correlation with the severity of skin involvement. Visceral involvement in the diffuse subset patients was high in the early disease stage and skin stiffness was low in the late stage. Visceral involvement gradually decreased but did not cure spontaneously. In the existing literature, the incidence of visceral involvement in the limited form is similar to that of the diffuse form except for renal and dermal involvement, which is gradual. By contrast, 66.7% of the patients in the diffuse subset in the present study were in the late disease stage, denoting the lack of a relationship between skin involvement and severity of lung and cardiac disease. On the other hand, skin severity is not a good indicator of the severity of visceral organ involvement, especially in the late stage. This is concordant with the results of the Ferri C et al. study.

We found no difference in the severity of cardiac involvement between the two disease subsets in the early and late stages. This result may be in consequence of either the low incidence of cardiac involvement, rendering the number of cases in each disease stage insufficient to divulge any difference, or collection bias as the patients were recruited into the study long after the disease onset.

In the Furst et al. study, patients with progressive SSC were matched for sex, age, and disease duration and the results showed a relationship between muscle involvement and severity of skin disease.

A point of significance is that the present study represents only a small group of SSC patients in Iran. Furthermore, the fact that the majority (55%) of our patients were in the late disease stage precludes any generalization of the results.

**Conclusion**

The present study represents a baseline estimate of the occurrence and severity of cardiac involvement in a small group of Iranian SSC patients. In this case series of 58 patients, a low incidence of cardiac involvement was detected. Our study also demonstrates the relative ease and applicability of severity scale measures for an assessment of cardiac involvement in SSC sufferers. The existing literature bears testament to the importance of such instruments in clinical trials.

Future studies are required to shed further light on the correlation between cardiac involvement and severity and specific auto-antibodies in scleroderma.

**Acknowledgment**

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**References**


Electrocardiogram Abnormalities and Coronary Calcification in Postmenopausal Women

Siamak Sabour, MD, PhD1,2*, Diederick Grobbee, MD, PhD1, Annemarieke Rutten, MD3, Mathias Prokop, MD, PhD3, Marie-Louise Bartelink, MD, PhD1, Yvonne van der Schouw, PhD1, Michiel Bots, MD, PhD1

1Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands.
2Faculty of Health and Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran.
3Radiology Department, University Medical Center Utrecht, Utrecht, The Netherlands.

Abstract

Background: An electrocardiogram (ECG) can provide information on subclinical myocardial damage. The presence, and more importantly, the quantity of coronary artery calcification (CAC), relates well with the overall severity of the atherosclerotic process. A strong relation has been demonstrated between coronary calcium burden and the incidence of myocardial infarction, a relation independent of age. The aim of this study was to assess the relation of left ventricular hypertrophy (LVH) and ECG abnormalities with CAC.

Methods: The study population comprised 566 postmenopausal women selected from a population-based cohort study. Information on LVH and repolarization abnormalities (T-axis and QRS-T angle) was obtained using electrocardiography. Modular ECG Analysis System (MEANS) was used to assess ECG abnormalities. The women underwent a multi detector-row computed tomography (MDCT) scan (Philips Mx 8000 IDT 16) to assess CAC. The Agatston score was used to quantify CAC; scores greater than zero were considered as the presence of coronary calcium. Logistic regression was used to assess the relation of ECG abnormality with coronary calcification.

Results: LVH was found in 2.7% (n = 15) of the women. The prevalence of T-axis abnormality was 6% (n = 34), whereas 8.5% (n = 48) had a QRS-T angle abnormality. CAC was found in 62% of the women. Compared to women with a normal T-axis, women with borderline or abnormal T-axes were 3.8 fold more likely to have CAC (95% CI: 1.4-10.2). Similarly, compared to women with a normal QRS-T angle, in women with borderline or abnormal QRS-T angle, CAC was 2.0 fold more likely to be present (95% CI: 1.0-4.1).

Conclusion: Among women with ECG abnormalities reflecting subclinical ischemia, CAC is commonly found and may in part explain the increased coronary heart disease risk associated with these ECG abnormalities.

Keywords: Atherosclerosis • Hypertrophy, left ventricular • Myocardial ischemia • Women • Postmenopause

Introduction

With an electrocardiogram (ECG), information can be obtained on subclinical myocardial damage. The frontal T-axis has been postulated to be a general marker of ventricular repolarization abnormality and has been shown
to be a strong and independent risk indicator of fatal and non-fatal cardiac events in the elderly.\(^1\) In addition, the spatial QRS-T angle, which is defined as the angle between the directions of ventricular depolarization and repolarization,\(^4\) has been shown to be an important determinant of diagnosis and prognosis in patients presenting with acute chest pain.\(^5\) The presence of spatial QRS-T angle relates to increased risk of cardiac death for coronary heart disease in postmenopausal women.\(^6\) Findings from autopsy and clinical angiographic studies have suggested a link between left ventricular hypertrophy (LVH) and severity of coronary atherosclerosis.\(^10\), \(^11\) Clear associations between echocardiographically assessed LVH and coronary atherosclerosis risk factors have been reported\(^12\), \(^13\) and LVH has been shown to predict future cardiovascular disease.\(^14\), \(^15\)

Coronary atherosclerosis can be non-invasively assessed in a valid and reproducible manner by the measurement of coronary calcium using coronary computer tomography.\(^16\) High coronary artery calcium (CAC) scores independently predict coronary heart disease (CHD).\(^10\), \(^14\), \(^17\) It may also reflect the presence of subclinical ischemia.

We set out to investigate whether morphological cardiac abnormalities (LVH) and ECG parameters (T-axis and QRS-T angle) that reflect potential ischemic abnormalities related to CAC in postmenopausal women.

**Methods**

We used data from a cross-sectional study among 566 postmenopausal healthy women as has been detailed earlier.\(^18\) In short, these women were selected from participants of the PROSPECT study, one of the two Dutch cohorts participating in the European Prospective Investigation into Cancer and Nutrition (EPIC).\(^19\) In PROSPECT 17, 357 healthy participants of a nationwide population-based breast-cancer screening program, aged 49-70 years, living in Utrecht and surroundings were enrolled between 1993 and 1997. Between October 2002 and April 2004, 1996 women were randomly selected from 5844 participants of the PROSPECT study who were postmenopausal and did not use contraceptives or hormone replacement therapy, and 1000 agreed to participate. Of these 1000 women, a random selection of 566 underwent a multislice CT examination at a second visit between January and December 2004.

At the first re-examination visit, smoking behavior and family history of coronary heart diseases (CHD) were assessed using a questionnaire. Age was calculated from birth date and date of investigation. Height and weight were measured and body mass index (BMI) was calculated as weight divided by height squared (kg/m\(^2\)). Waist-to-hip ratio (WHR) was assessed. Systolic and diastolic blood pressure (SBP & DBP) were measured at both arms with an automated and calibrated blood pressure device (DINAMAP\(^\text{TM}\) XL, Critikon, Johnson & Johnson, Tampa, Florida, USA) with the subject in supine position. A venous blood sample was drawn after an overnight fast of at least eight hours. Plasma total cholesterol, plasma triglycerides, and plasma glucose were measured using standard enzymatic procedures. High-density lipoprotein (HDL) cholesterol was measured via the direct method (inhibition, enzymatic). Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula. We defined hypertension as either using anti-hypertensive therapy or a systolic blood pressure > 140 mmHg or a diastolic blood pressure > 90 mmHg. Pulse pressure (PP) was defined as SBP - DBP.

The participants underwent a multi-detector computed tomography (MDCT) examination for the assessment of CAC. The amount of calcium in the coronary arteries was assessed with a MDCT scanner (Mx 8000 IDT 16, Philips Medical Systems, Best, The Netherlands). The subjects were positioned within the gantry of the MDCT scanner in supine position. During a single breath hold, images of the heart, from the level of the tracheal bifurcation to below the base of the heart, were acquired using prospective ECG triggering at 50-80\% of the RR-interval, depending on the heart rate. Scan parameters were 16 × 1.5 mm collimation, 205 mm field of view (FOV), 0.42 s rotation time, 0.28 s scan time per table position, 120 kVp and 40-70 mAs (patient weight < 70 kg: 40 mAs; 70-90 kg: 55 mAs; > 90 kg: 70 mAs). Scan duration was approximately 10 seconds, depending on heart rate and patient size.

Quantification of coronary calcium was performed on a separate workstation with software for calcium scoring (Heartbeat-CS, EBW, Philips Medical Systems, Best, The Netherlands). All regions with a density over 130 Hounsfield units were identified as potential calcifications. After completing a training-program, a trained scan reader, blinded for electrocardiographic results of the women, manually selected only the calcifications within the coronary arteries (left main, left anterior descending, left circumflex, right coronary artery, or posterior descending artery). To reduce the influence of noise, the minimum size of a calcified lesion was set at 0.5 mm\(^2\). The peak density in Hounsfield units and the area in mm\(^2\) of each selected region were calculated. The Agatston\(^20\) calcium score was obtained by multiplying the area by a weighting factor that is dependent on the peak signal anywhere in the lesion. The scores of individual lesions were added to obtain the Agatston calcium score for the entire coronary tree. Calcium presence was defined as score > 0. We performed reproducibility studies, in which 199 scans were read in duplicate, showing Intraclass correlation coefficients (ICCC) of > 0.95 for the duplicate readings. Another reproducibility study in which in 73 women a duplicate MDCT scan was made within three months of the first scan showed ICCC between repeat scans of > 0.90.\(^21\)

A standard 12-lead electrocardiogram was recorded with the women lying in supine position using Cardio Perfect...
equipment (Cardio Perfect Resting ECG, Welch Allyn Cardio Control, Delft, The Netherlands). ECGs were recorded at a sampling frequency of 300 Hz and stored digitally. All ECGs were processed by the Modular ECG Analysis System (MEANS) as described and evaluated in detail earlier. The program was extensively validated, and the outcomes of MEANS in population-based research were at least as good as ECG interpretation by a trained research physician except for myocardial infarction (cases of AM1 and IM1 are correctly diagnosed in only 43% and 54% of the cases, respectively). MEANS as a well-known method introduced more than a decade ago computes a representative averaged beat for each of the 12 leads from which ECG measurements and a diagnostic interpretation are derived. Mean QRS and T axes were computed from vectorcardiographic X, Y and Z leads, which can, in good approximation, be constructed from the standard ECG leads. The mean spatial axes are based on the areas of the wave components of the QRS complex and the T wave. The mean frontal T-axis is the angle between the X axis and the projection of the mean spatial T-axis on the frontal XY plane. The spatial QRS-T angle is the angle between the mean spatial QRS axis and the mean spatial T-axis. Electrocardiographic LVH was defined by using voltage and repolarization criteria, in which the age-adjusted Sokolow criterion pulse pressure (PP) was defined as SBP-DBP.

Women with T-axis 15-75 were considered “normal”, -15 thru 14 as “borderline” and finally both -180 thru 16 and 106 thru 180 as “abnormal”. Furthermore, we also combined borderline categories in abnormal and considered ECG abnormalities as dichotomized variables in part of our analysis.

The outcome variable for this analysis was total CAC, and the primary predictor variables were LVH and ECG abnormalities. The following covariates as potential confounders were used in the analysis: age, BMI, WHR, cigarette smoking status, SBP, DBP, PP, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, glucose, and family history of CHD. ECG abnormalities were divided into two categories 1: normal and 2: borderline or abnormal to assess the relation between ECG abnormalities and CAC. Logistic regression models were used to evaluate the associations under study. Odds ratio (OR) for CAC and 95% confidence intervals (CI) were determined. A significance level of 0.05 was used for all the analyses. Data analysis was performed using SPSS for Windows version 13.0.

Results

Table 1 lists the characteristics of the study population in terms of the presence or absence of CAC. The prevalence of LVH was 2.7%, of T-axis abnormality 6%, and of QRS-T angle abnormality 8.5%. Sixty-two percent of the women had a coronary calcification score greater than zero.

Table 2 shows the associations between vascular risk factors and CAC as well as ECG parameters. Factors that were related to CAC were increased age, WHR, SBP, DBP,
CAC was reported. A study among 159 young to middle-aged postmenopausal women the presence of LVH and the presence of CAC had a significantly larger left ventricular mass than did those without CAC, independent of other important atherosclerosis risk factors, with a parallel, but insignificant, trend in women. A study in 2,724 young African-American and white adults age African-American participants without hypertension or overt ischemic heart disease showed that men with CAC had a significantly larger left ventricular mass and higher left ventricular mass index than did those without CAC, independent of other important atherosclerosis risk factors, with a parallel, but insignificant, trend in women. A study in 2,724 young African-American and white adults who participated in the CARDIA study reported that left ventricular mass was significantly associated with the extent of CAC among subjects who were positive for CAC, but not those who were negative for CAC. Combining results from individual studies indicating that ECG abnormalities predict events, and our current findings suggest that part of the increased risk through ECG abnormalities may be attributable to the presence of coronary atherosclerosis and vice versa. Studies showing that CAC predicts future events results from combining results from individual studies indicating that ECG abnormalities predict events, and our current findings suggest that part of the increased risk through ECG abnormalities may be attributable to the presence of coronary atherosclerosis and vice versa.

A few studies have examined the association of LVH and CAC. In a Turkish population among 249 asymptomatic hypertensive patients, a positive association between concentric LVH and CAC was reported. A study among 159 young to middle-aged postmenopausal women the presence of LVH and the presence of CAC had a significantly larger left ventricular mass than did those without CAC, independent of other important atherosclerosis risk factors, with a parallel, but insignificant, trend in women. A study in 2,724 young African-American and white adults who participated in the CARDIA study reported that left ventricular mass was significantly associated with the extent of CAC among subjects who were positive for CAC, but not those who were negative for CAC. Combining results from individual studies indicating that ECG abnormalities predict events, and our current findings suggest that part of the increased risk through ECG abnormalities may be attributable to the presence of coronary atherosclerosis and vice versa.

Table 2. Age adjusted relation of coronary calcification, left ventricular hypertrophy and ECG abnormalities with clinical covariates

<table>
<thead>
<tr>
<th></th>
<th>CAC</th>
<th>LVH</th>
<th>T-axis</th>
<th>QRS-T angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>1.12 (1.08-1.16)*</td>
<td>1.04 (0.95-1.14)</td>
<td>1.04 (0.98-1.11)</td>
<td>1.05 (1.00-1.11)*</td>
</tr>
<tr>
<td>Body mass index (Kg/m²)</td>
<td>1.02 (0.98-1.06)</td>
<td>1.01 (0.90-1.13)</td>
<td>1.04 (0.96-1.12)</td>
<td>1.08 (1.01-1.15)*</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>1.84 (1.40-2.43)*</td>
<td>1.31 (0.65-2.67)</td>
<td>1.79 (1.11-2.87)*</td>
<td>1.68 (1.11-2.54)*</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>1.01 (1.00-1.02)*</td>
<td>1.03 (1.01-1.05)*</td>
<td>1.01 (0.99-1.03)</td>
<td>1.02 (1.01-1.03)*</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>1.04 (1.02-1.06)*</td>
<td>1.03 (0.98-1.09)</td>
<td>1.01 (0.98-1.05)</td>
<td>1.04 (1.01-1.07)*</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>1.01 (1.00-1.02)*</td>
<td>1.05 (1.02-1.08)*</td>
<td>1.01 (0.99-1.04)</td>
<td>1.02 (1.01-1.04)*</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>1.78 (1.24-2.56)*</td>
<td>3.87 (1.06-14.12)*</td>
<td>2.34 (1.08-5.07)*</td>
<td>2.63 (1.34-5.16)*</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>1.13 (0.94-1.36)</td>
<td>0.78 (0.45-1.35)</td>
<td>0.78 (0.54-1.12)</td>
<td>1.07 (0.80-1.45)</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>1.24 (1.01-1.52)*</td>
<td>0.87 (0.47-1.54)</td>
<td>0.79 (0.53-1.18)</td>
<td>1.07 (0.78-1.49)</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>0.56 (0.34-0.93)</td>
<td>0.46 (0.08-2.45)</td>
<td>0.35 (0.11-1.10)</td>
<td>0.89 (0.37-2.10)</td>
</tr>
<tr>
<td>Triglyceride (mmol/l)</td>
<td>1.32 (0.97-1.79)</td>
<td>0.75 (0.27-2.05)</td>
<td>1.41 (0.85-2.32)</td>
<td>1.19 (0.75-1.89)</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>1.35 (1.05-1.72)*</td>
<td>1.16 (0.75-1.79)</td>
<td>1.39 (1.08-1.86)*</td>
<td>1.26 (0.98-1.61)</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>6.16 (2.90-13.09)*</td>
<td>0.56 (0.07-4.40)</td>
<td>2.71 (1.16-6.32)*</td>
<td>1.45 (0.61-3.41)</td>
</tr>
<tr>
<td>Former smoking (%)</td>
<td>1.12 (0.78-1.60)</td>
<td>0.62 (0.21-1.85)</td>
<td>0.87 (0.43-1.77)</td>
<td>0.81 (0.44-1.48)</td>
</tr>
<tr>
<td>Family history of  CHD in either parent</td>
<td>1.96 (1.09-3.53)*</td>
<td>1.30 (0.28-5.99)</td>
<td>1.11 (0.37-3.31)</td>
<td>0.34 (0.08-1.46)</td>
</tr>
</tbody>
</table>

* p < 0.05

ECG, Electrocardiogram; CAC, Coronary artery calcification; LVH, Left ventricular hypertrophy; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; CHD, Coronary heart diseases

Discussion

In the present study, we showed that in healthy postmenopausal women the presence of LVH and of subclinical myocardial damage as assessed by T-axis and QRS-T abnormalities related to the presence of coronary calcifications.

A few studies have examined the association of echocardiographically assessed LVH with CAC. In a Turkish population among 249 asymptomatic hypertensive patients, a positive association between concentric LVH and CAC was reported. A study among 159 young to middle-aged postmenopausal women the presence of LVH and the presence of CAC had a significantly larger left ventricular mass than did those without CAC, independent of other important atherosclerosis risk factors, with a parallel, but insignificant, trend in women. A study in 2,724 young African-American and white adults who participated in the CARDIA study reported that left ventricular mass was significantly associated with the extent of CAC among subjects who were positive for CAC, but not with the presence of CAC after multivariable adjustment. Our findings expanding the evidence to women are in principle in agreement with these reports. However, we did not find a statistically significant relation between LVH and CAC. The lack of reaching statistical significance can most likely be attributed to a relatively small sample size in combination of a relatively modest sensitivity of the ECG to assess LVH. We feel that a lack of statistical significance does not rule out the existence of a relation in a larger study with more sensitive measurement to assess LVH.

Information on the relation between T-axis and QRS-T angle abnormalities and coronary calcification is absent. A Pub Med search (February 24, 2008) on terms as ‘coronary calcium or coronary calcification’ and ‘T-axis or QRS-T angle’ indicated no studies. Combining results from individual studies showing that CAC predicts future events results from studies indicating that ECG abnormalities predict events, and our current findings suggest that part of the increased risk through ECG abnormalities may be attributable to the presence of coronary atherosclerosis and vice versa.

One aspect of our study that may need consideration is the conclusion to be drawn from analyses adjusted for various
risk factors. One may argue that after our multivariate analyses, the statistical significance of the relations between ECG abnormalities and CAC was lost and our conclusions are, therefore, overstated. Alternatively, since these risk factors most likely causally relate to both the occurrence of ECG abnormalities and CAC and that ECG abnormalities and CAC both reflect stages of subclinical vascular damage, one may also argue that adjusted models indicate that the risk factors for these two conditions are similar. We support the latter reasoning.

Conclusion

We found that among women with ECG (T-axis and QRS-T angle) abnormalities, reflecting subclinical ischemia, CAC is commonly found. Our finding may in part explain the increased coronary heart disease risk associated with these ECG abnormalities.

Acknowledgment

This study was supported by grant 2100.0078 from The Netherlands Organization for Health Research and Development. The Medical Ethics Committee of the University Medical Center Utrecht approved the study and written informed consent was obtained from all the participants before enrolment. The first author was supported by the Health Ministry of Iran.

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Screening of Carotid Artery Stenosis in Coronary Artery Bypass Grafting Patients

Abbas Salehiomran, MD*, Shapour Shirani, MD, Abbasali Karimi, MD, Hossein Ahmadi, MD, Mehrab Marzban, MD, Namvar Movahedi, MD, Naghmeh Moshtaghi, MD, Seyed Hesameddin Abbasi, MD

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

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Abstract

Background: We sought to evaluate the routine echo-Doppler screening of carotid artery stenosis in patients undergoing coronary artery bypass grafting.

Methods: A total of 2179 consecutive patients who underwent coronary artery bypass grafting alone or with other cardiac surgery at Tehran Heart Center, Tehran-Iran, between January 2005 and January 2006 were included in this retrospective study. Carotid Doppler was performed for 1604 (81.48%) of these patients.

Results: The patients’ age ranged between 20 and 84 years (mean: 58.33, SD: 10.08 years). Of the 1604 patients studied, 1186 (73.9%) were men, 592 (36.9%) had diabetes, 598 (37.3%) were smokers, and 194 (12.1%) cases had significant left main stenosis. Twenty-one (1.3%) patients had significant carotid stenosis (> 60% stenosis), which constituted 0.9% of all the bypass surgery candidates. Post-operative cerebrovascular accident was not detected in any of the patients with significant carotid stenosis, but cerebrovascular accident occurred in 22 (1.4%) of the patients without carotid stenosis. Magnetic resonance angiography (MRA) was conducted in 15 patients. In our univariate analysis, female gender (p value = 0.023), hypertension (p value = 0.055), peripheral vascular disease (p value < 0.001), and age (p value = 0.001) were significant in the development of carotid stenosis.

Conclusion: Pre-operative duplex carotid screening seems to be necessary in patients when there is hypertension, peripheral vascular disease, female gender, and advanced age.

Keywords: Carotid stenosis • Stroke • Ultrasonography, Doppler

Introduction

Coronary artery bypass grafting (CABG) is one of the most common operations in the field of cardiovascular surgery today. Despite the increasing number of high-risk patients among CABG candidates, a decrease in mortality in CABG has been observed in recent years. Unfortunately, this improvement does not encompass patients with acute coronary syndrome. With all this, morbidity of stroke after CABG remains relatively high due to advanced age and diffuse atherosclerotic disease in candidates for CABG. Advanced age, peripheral vascular disease, prior history of cerebral ischemia and atherosclerosis of the ascending aorta have been identified as risk factors for cerebral infarction after CABG.

Excluding intra-operative death, stroke is the most dreaded peri-operative complication in patients undergoing coronary bypass surgery. The incidence of stroke is 2.1-5.2% in bypass
surgery patients with a mortality of 0-38%.7 The profound impact of stroke after cardiac surgery is demonstrated by a nearly fivefold increase in hospital mortality (19% versus 4%) and a length of intensive care unit stay reaching more than twice that of uncomplicated operations.8,9

The shedding of debris from carotid or aortic atherosclerotic plaques, embolization of the intracardiac clot, and decrease in perfusion pressure to < 60 mmHg are the etiologic causes of stroke associated with bypass surgery.10 Moreover, there is still a lack of guidelines as regards pre-operative vascular investigations in patients undergoing CABG: whereas some authors tend to limit pre-operative vascular investigations to patients with symptoms and/or clinical signs of associated vascular disease (e.g. carotid bruit or peripheral pulse losses),11 others are liable to routinely opt for pre-operative Echo-Doppler screening of carotid vessels.12

The present study sought to investigate the routine Echo-Doppler screening in all patients undergoing CABG.

**Methods**

A total of 2179 consecutive patients who underwent CABG alone or with other cardiac surgery at Tehran Heart Center, Tehran-Iran, between January 2005 and January 2006 were included in this retrospective analysis of prospectively collected data. For 1604 (81.48%) cases of these patients, carotid Doppler was performed by an expert radiologist who had been practicing Doppler studies on a daily basis for over 5 years. The device utilized was a Toshiba Eccocree with linear 7.5-MHZ and convex 3.75-MHZ transducers. A standard protocol based on the Nicolaides criteria was applied to all the patients.13 In keeping with the American Heart Association (AHA), in this study significant carotid stenosis was considered > 60%.14

The patients’ data included the following variables: age, sex, smoking, hyperlipidemia (whether the patient had a history of hyperlipidemia diagnosed and/or treated by a physician and/or patient had been assured previously of (a) TG > 200, (b) LDL ≥ 130, (c) HDL < 30, and (d) admission cholesterol > 200 mg/dl), hypertension, peripheral vascular disease (whether the patient had peripheral vascular disease as indicated by claudication either on exertion or at rest, amputation for arterial insufficiency, aorto-iliac occlusive disease reconstruction, peripheral vascular bypass surgery, angioplasty, or stent), diabetes mellitus (defined as a history of diabetes regardless of the duration of disease or need for anti-diabetic agents), left main coronary artery stenosis ≥ 50%, peri-operative cerebral vascular accident (whether or not the patient had a post-operative stroke), and in-hospital mortality (death occurred within 30 days after CABG). The study protocol was approved by the Ethics Committee of Tehran Heart Center.

The numerical variables were presented as mean±SD, and the categorized variables were summarized by percentages. Univariate and multivariate analyses were performed. The groups were assessed according to the following statistical tests: Student’s t-test to compare normally distributed continuous variables, Mann-Whitney’s U test to compare non-normally distributed variables, and chi-square or Fisher’s exact test to compare categorical variables. Predictors exhibiting a statistically significant relation with sternal wound infection (SWI) in the univariate analysis were taken for a multivariate step-wise logistic regression analysis to investigate their independence as predictors. Odds ratio (OR) and 95% confidence interval (CI) were evaluated; p values of 0.05 or less were considered statistically significant. All the statistical analyses were carried out using SPSS 13.0 and SAS 9.1 for Windows.

**Results**

The patients’ age ranged between 20 and 84 years (mean: 58.33, SD: 10.08 years). All the patients were coronary bypass candidates; however, some were concomitantly undergoing another surgery. Of the 1604 patients studied, 1186 (73.9%) were men, 592 (36.9%) had diabetes, 598 (37.3%) were smokers, and 194 (12.1%) cases had significant left main stenosis. Other variables are listed in Table 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>n = 1604 (81.48%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>26.1%</td>
</tr>
<tr>
<td>Smoking</td>
<td>37.5%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>36.9%</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>76.1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>66.0%</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>4.1%</td>
</tr>
<tr>
<td>Family history</td>
<td>30.4%</td>
</tr>
<tr>
<td>Left main disease</td>
<td>12.1%</td>
</tr>
<tr>
<td>Age (mean±SD) (y)</td>
<td>61±8.80</td>
</tr>
<tr>
<td>Ejection fraction (mean±SD)</td>
<td>48.47±10.92</td>
</tr>
</tbody>
</table>

In patients with atheromatous plaques, 3 had total occlusion of the left internal carotid and 4 had occlusion of the right internal carotid artery. In total, 21 (1.3%) patients had significant carotid stenosis (> 60% stenosis), which constituted 0.9% of all the bypass surgery candidates. Of these patients, 19 had unilateral and 2 had bilateral significant stenosis. Post-operative cerebrovascular accident (CVA) was not detected in any of the patients with significant carotid stenosis, but CVA occurred in 22 (1.4%) of the patients without carotid stenosis. Among these 21 patients, carotid stenting was done in one case pre-operatively. Brain magnetic resonance angiography (MRA) was obtained in 15 patients, but in the remaining cases (n=6) MRA was not considered...
because the patients showed no neurological symptoms in their neurological consultation session. In these 15 patients, carotid stenosis was confirmed by MRA. Endarterectomy was not done because of total occlusion of the carotid artery in 7 cases and neurological consultation in 4 patients. Carotid stenting was conducted in 4 cases. In the univariate analysis, female gender (p value = 0.023), hypertension (p value = 0.055), peripheral vascular disease (p value < 0.001), and age (p value = 0.001) were significant in the development of carotid stenosis (Table 2).

Table 2. Characteristics of patients with and without carotid stenosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1* (n = 1583)</th>
<th>Group 2** (n = 21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD) (y)</td>
<td>60.97±8.79</td>
<td>67.24±7.75</td>
<td>0.001</td>
</tr>
<tr>
<td>Female</td>
<td>25.8%</td>
<td>47.6%</td>
<td>0.023</td>
</tr>
<tr>
<td>Smoking</td>
<td>37.6%</td>
<td>28.6%</td>
<td>0.396</td>
</tr>
<tr>
<td>Diabetes</td>
<td>37%</td>
<td>28.6%</td>
<td>0.426</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>76.1%</td>
<td>76.2%</td>
<td>0.994</td>
</tr>
<tr>
<td>Hypertension</td>
<td>65.8%</td>
<td>85.7%</td>
<td>0.055</td>
</tr>
<tr>
<td>PVD</td>
<td>3.3%</td>
<td>61.9%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Left main disease</td>
<td>11.9%</td>
<td>23.8%</td>
<td>0.165</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>1.6%</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>LVEF (mean±SD)</td>
<td>48.44%±10.89</td>
<td>50.48±13.13</td>
<td>0.396</td>
</tr>
<tr>
<td>CVA</td>
<td>1.4%</td>
<td>0</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*Without significant carotid stenosis
**With significant carotid stenosis
PVD, Peripheral vascular disease; LVEF, Left ventricular ejection fraction; CVA, Cerebrovascular accident

**Discussion**

An association between carotid and coronary artery disease is well recognized. Routine pre-operative duplex carotid screening of all coronary surgery patients, albeit common, may delay surgery and increase cost. In our study of patients with significant carotid artery stenosis, CVA did not occur in any of the patients; an adequate focused history and physical examination could, therefore, identify patients at risk for the presence of significant carotid disease and obviate the need for a costly routine scanning of all CABG patients. On the other hand, female gender, age, hypertension, and peripheral vascular disease were significant risk factors for developing carotid stenosis (p value ≤ 0.05) in our univariate analysis. Interestingly, the factors that other studies deem significant, namely cigarette smoking and left main disease, had no influence on the developing of carotid stenosis in our patients.

Nicolaiides et al. demonstrated that the advantages of Duplex US, including absence of complications, relatively low costs, and widespread availability, were weakened by the lack of standards for quantifying degrees of stenosis. Screening of carotid arteries for stenosis combined with endarterectomy reduces peri-operative as well as post-operative stroke. Screening also helps to discover and follow significant carotid artery stenosis cases without neurological symptoms. The presence of significant carotid artery stenosis can change the bypass schedule to a bypass with endarterectomy or endarterectomy and then bypass surgery. In light of our results, it seems that the presence of factors such as hypertension, peripheral vascular disease, female gender, and advanced age renders pre-operative duplex carotid screening necessary.

**Conclusion**

It is deserving of note that in our patients, CVA occurred only in cases that had no significant carotid artery stenosis. This may be partially due to more precaution exercised by the cardiac surgeon in patients with significant stenosis during surgery such as high perfusion pressure, prevention of aggressive manipulation of the aorta, or use of side-biting clamp (Satinsky) of the ascending aorta. Overall, it seems that peri-operative CVA is multifactorial and has no direct (linear) relationship with stenosis of the carotid artery. We would, therefore, recommend that carotid Doppler study be carried out in selected patients to save time and reduce cost.

**Acknowledgment**

This study was approved and supported by Tehran Heart Center, Tehran University of Medical Sciences.

**References**


Non-Invasive Assessment of Coronary Artery Stenosis with Estimation of Myocardial Wall Stress

Hassan Moladoust, PhD1, Manijhe Mokhtari-Dizaji, PhD1*, Zahra Ojaghi-Haghighi, MD2, Fereidoon Noohi, MD2

1Department of Medical Physics, Tarbiat Modares University, Tehran, Iran.  
2Shaheed Rajaie Heart Center, Iran Medical Sciences University, Tehran, Iran.

Abstract

Background: More diagnostic techniques require a better understanding of the forces and stresses developed in the wall of the left ventricle. The aim of this study was to differentiate significant coronary artery disease (CAD) patients using a non-invasive quantification of myocardial wall stress in the diastole phase.

Methods: Sixty male subjects with sinus rhythm (30 patients with significant and 30 with moderate left anterior descending coronary artery stenosis in the proximal portion) as well as 35 healthy subjects as the control group were recruited into the present study. By two-dimensional, pulsed wave, and tissue Doppler echocardiography, the average end-diastolic wall stress was calculated at the left ventricle anterior and interventricular septum wall segments using regional wall thickness, meridional and circumferential radii, and non-invasive left ventricular end-diastolic pressure.

Results: A comparison of the calculated end-diastolic myocardial wall stress between the patients with significant and moderate coronary stenosis on the one hand and the healthy subjects on the other showed statistically significant differences in the anterior and septum wall segments (p value < 0.05). The patients with significant left anterior descending coronary artery stenosis had higher end-diastolic myocardial wall stress than did those with moderate stenosis and the healthy group in all the anterior and septum wall segments.

Conclusion: It is concluded that non-invasive end-diastolic myocardial wall stress in coronary artery disease patients is an important index in evaluating myocardial performance.

Keywords: Coronary artery disease • Echocardiography • Diagnosis

Introduction

Coronary artery disease (CAD) is the number one killer in the world. As a case in point, each year 650,000 previously asymptomatic patients present in the United States with an acute coronary event as the initial presentation of CAD.1 Approximately, one-third of individuals dying annually from sudden cardiac death possess no identifiable Framingham risk indices that would predict a future hard cardiac event.2 Therefore, the detection of coronary heart disease early in its course is of great potential importance.

More advanced diagnostic techniques require that one gain a better understanding of the mechanics and performance of the myocardium, and this in turn calls for an analysis of the forces and stresses developed in the wall of the left ventricle (LV).3 Systolic and diastolic wall stress has been previously determined by combining simultaneous measurements of LV pressures with angiographic and echocardiographic...
measurements of the LV radius and wall thickness.\textsuperscript{4,7} This method, in addition to being cumbersome and time-consuming, requires invasive procedures. The non-invasive assessment of LV end-diastolic pressure provides important information on the hemodynamic status\textsuperscript{8} and may be an important clinical tool in these patients, taking advantage of non-invasive quantification of myocardial wall stress in end-diastole. Recently, we demonstrated\textsuperscript{7} the role of Color-Tissue Doppler imaging (TDI) in the estimation of LV end-diastolic pressure (LVEDP) in patients with CAD. We concluded from our study that the ratio of the early transmitral filling velocity (E) to the early-diastolic mitral annular velocity (Ea) as an interesting application of TDI\textsuperscript{9} provided an index of LVEDP.

The aim of the present study was to estimate and compare the non-invasive regional myocardial wall stress in the diastolic phase between patients with significant coronary stenosis, moderate coronary stenosis, and healthy subjects.

**Methods**

Sixty male CAD patients with sinus rhythm (30 with significant and 30 with moderate left anterior descending coronary artery (LAD) stenosis in the proximal portion, aged 53±5 and 52±5 years old, respectively) as well as 35 healthy volunteers aged 51±8 years old were enrolled in the study. Significant and moderate stenosis was defined as more than 70% and between 50-70% stenosis determined by coronary angiograms, respectively. Exclusion criteria included a history of cardiovascular surgery, LV hypertrophy, pacemaker rhythm, severe valvular disease, and diabetes. All the healthy subjects had a normal physical examination, electrocardiography (ECG), normal echocardiography, and no history of cardiovascular disease, angina, hypertension or diabetes, and medication. Blood pressure was recorded in the left radial artery with the patient in supine position using a semiautomatic device (Riester 0124, Germany) before the measurement of the echocardiographic studies. All the subjects gave their informed consent prior to their participation in the study. This study was performed from June 2007 to January 2009 through random sampling and was approved by the ethics committee of Tarbiat Modares University and Shaheed Rajaie Cardiovascular and Research Center.

Invasive coronary angiography was performed by expert cardiologists through the femoral approach, using standard Judkin’s technique with 6F catheters. Selective injection of left and right coronary arteries was performed in multiple orthogonal views. The culprit lesion was identified by angiographic criteria for the severity of stenosis. The percent luminal diameter stenosis was derived using the caliper technique by comparing the diameter of the stenosis with that of the most normal appearing region proximal to the stenosis. Images were acquired and digitally recorded in at least two orthogonal optimal projection angles at 25 frames per second (Siemens Medical Systems, Germany). Between 1 and 2 days after the angiography, transthoracic conventional and tissue Doppler echocardiography examinations were performed.

All the echocardiography studies were conducted with a Vivid\textsuperscript{7} digital ultrasound scanner (GE, Milwaukee, WI, USA) equipped with an M3S transthoracic sector transducer with harmonic capability. The images were acquired with the subjects at rest and lying in the lateral decubitus position. Two-dimensional ECG was superimposed on the images and end-diastole was considered at the peak R-wave of the ECG. LV ejection fraction (LVEF) was measured using Simpson’s biplane method by measuring end-diastolic and endsystolic volumes in two-dimensional 2(D) images. TDI was performed using standard transthoracic apical two- and four-chamber views according to the guidelines of the American Society of Echocardiography (ASE).\textsuperscript{10}

The sample volume of the pulsed wave Doppler was placed between the tips of the mitral leaflets with the ultrasonic beam aligned to flow in the apical four-chamber view and early transmitral flow velocity was obtained. Color Doppler myocardial imaging (CDMI) was performed by adjusting the signal filters until they reached a Nyquist limit of 16 cm/s. The CDMI raw data were recorded at a depth of 16 cm, frequency of 2.4 MHz, and frame rates higher than 150 frames per second throughout the three cardiac cycles and stored digitally as cine-loop format on the memory of the scanner. Off-line analysis was carried out by the quantitative analysis software equipped to obtain regional myocardial velocity. Digital 5 mm sample volumes were placed within the lateral mitral annulus\textsuperscript{7, 11, 12} and tissue velocity curves were acquired. The wall filter settings were adjusted to exclude high-frequency signals and the gain was minimized, so the onset of the early-diastolic mitral annular velocity could be reliably identified. Echocardiographic analysis was performed by an experienced observer who was unaware of the patient’s angiographic outcomes. All the Doppler data were measured at end-expiration, and the average of three cardiac cycles was taken into account for analysis in this study.

The force per unit area of myocardium, or wall stress, is proportional to the LV intra-cavity pressure and LV cavity dimension and inversely proportional to wall thickness.\textsuperscript{13} In this study, the radii and thickness of the LV segments were measured from the apical four- and two-chamber echocardiograms at end-diastole. In these echocardiograms, the septal and anterior wall radii and thickness quantities were measured at base, mid, and apical segments respectively by averaging three consecutive heartbeats. Endocardial meridional and circumferential radii were determined for each wall segment by considering each region to be locally ellipsoidal as described in detail elsewhere (Figure 1).\textsuperscript{4}

The average end-diastolic wall stress ($\sigma$) was calculated
Non-Invasive Assessment of Coronary Artery Stenosis with Estimation of Myocardial Wall Stress

Figure 1. A diagram depicting the variables used to calculate wall stress. An illustration of how local left ventricular (LV) wall geometry can be described by wall thickness ($h$), endocardial circumferential radius of curvature ($r_\theta$) and endocardial meridional radius of curvature ($r_\phi$) using the formula proposed by Deanda et al.\textsuperscript{14, 15} taking into account regional wall thickness ($h$), mid-wall meridional ($R_\phi$) and circumferential ($R_\theta$) regional radii of the curvature at the equator of each segment and LVEDP:

$$\sigma = 1.332 \times LVEDP \times \frac{R_\phi}{h} \left(3 - \frac{R_\phi}{R_\theta}\right)$$

Where $R_\phi$ and $R_\theta$ are endocardial circumferential radius ($r_\theta + \frac{h}{2}$) and endocardial meridional radius ($r_\phi + \frac{h}{2}$), respectively. In this study, non-invasive LVEDP was estimated with lateral early-diastolic color-TDI annular velocity, combined with mitral early velocity by pulsed Doppler echocardiography (lateral E/Ea ratio) as follows by averaging three consecutive heart beats:\textsuperscript{7}

$$LVEDP = 1.44 + \left[1.36 \times \text{(lateral E/Ea)}\right]$$

It has been demonstrated that the correlation coefficient between LVEDP and lateral E/Ea is higher and its limit of agreements (LOA) is lower than those of other mitral segments;\textsuperscript{2, 11, 12} therefore, in this study we applied only lateral E/Ea ratio to the estimation of LVEDP and quantification of myocardial wall stress.

All the data are expressed as mean±standard deviation (SD). The data were tested for normal distribution and homogeneity of variance by the Kolmogorov-Smirnov test (K-S) and Levene test respectively. Maximum sample size was estimated on 23 samples with a confidence level of 95% and power of test of 90% in each group. One-way analysis of variance (ANOVA) was used to test the hypothesis that the means of the three study groups were equal and the Post Hoc least significant differences (LSD) test was used for multiple comparisons. The p values were obtained using Student’s t-test whenever two groups were compared. P values less than 0.05 were chosen as the levels of statistical significance.

Intraobserver and interobserver variabilities were the differences between the measurements expressed as a percentage of the error of the means. All the statistical analyses were performed using the SPSS software package (SPSS Inc. Chicago, IL, USA).

**Results**

The demographic and echocardiographic characteristics of the 95 subjects are presented in Table 1 as Mean±SD. The subjects were divided into three groups according to the presence of diameter narrowing as follows: 1) Healthy: no diameter narrowing; 2) Moderate LAD coronary artery stenosis in the proximal portion: diameter narrowing of between 50-70% stenosis (61±3% of stenosis); and 3) Significant LAD coronary artery stenosis in the proximal portion: diameter narrowing of more than 70% (90±3% of stenosis). The groups were comparable as regards age, heart rate, and body mass index (BMI) (p = non significant).

In Figure 2, radial systolic and diastolic blood pressures are shown for the three groups with significant and moderate LAD stenosis in the proximal portion and healthy subjects. The statistical analysis of the systolic and diastolic blood pressure showed that there were no significant differences between the groups. The reason is that patients with stenosis usually use hypertension drugs (60%) (p value < 0.05).

The results of LVEF\% are presented in Figure 3. With the progression of stenosis, the LVEF\% was decreased by 11% and 25% compared with that of the healthy group, respectively. There were significant LVEF\% differences between the study groups (p value < 0.05).

At the end-diastole phase, the anterior and the septal wall radii (meridional and circumferential radii) and wall thickness quantities measured at base, mid, and apical segments are depicted in Table 2 for the groups with significant and moderate LAD coronary artery stenosis and the healthy subjects.

The statistical analysis of the anterior and the septal wall radii (meridional and circumferential radii) and wall thickness quantities measured at base, mid, and apical segments showed no significant differences between the groups except for the anterior wall thickness in the base, mid, and apex regions, septal wall thickness in the base and mid regions, and the septum meridional radius in the apex region.

Comparisons between the groups (using Student’s t-test) demonstrated that the healthy and significant LAD coronary artery stenosis groups were significantly differentiable with the septal wall meridional radius in the mid and apex regions, the septal wall circumferential radius in the base, mid, and apex regions, and hence the anterior wall meridional radius in the base region and the anterior wall circumferential radius in the apex region.

Also, there were significant differences between the healthy and significant LAD coronary artery stenosis groups.
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Table 1. Characteristics of the subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Healthy N = 35</th>
<th>Moderate LAD coronary artery stenosis N = 30</th>
<th>Significant LAD coronary artery stenosis N = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>51±8</td>
<td>52±5</td>
<td>53±5</td>
</tr>
<tr>
<td>Stenosis (%)</td>
<td></td>
<td>61±3</td>
<td>90±3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25±2</td>
<td>25±2</td>
<td>24±2</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>72±8</td>
<td>74±18</td>
<td>79±14</td>
</tr>
</tbody>
</table>

*Data are presented as mean±SD

LAD, Left anterior descending coronary artery

The statistical analysis of LVEDP demonstrated significant differences between the groups (p value < 0.05). The least significant difference (LSD) analysis of LVEDP parameter to test the significance between the two groups showed that the healthy group was significantly differentiable with significant and moderate LAD coronary artery stenosis, but there was no significant difference between the moderate and significant LAD coronary artery stenosis groups.

The average end-diastolic wall stress ($\sigma$) was calculated using regional wall thickness ($h$), mid-wall meridional ($R_o$), and circumferential ($R_\theta$) regional radii of the curvature at the equator of each segment and LVEDP. The comparisons of the calculated anterior and septum wall stresses between the patients with significant and moderate stenosis and the healthy subjects are shown in Figures 5 (a) and (b), respectively.

The results showed an increase in the end-diastolic myocardial wall stress relating to the progression of LAD coronary artery stenosis. The patients with significant LAD coronary artery stenosis had higher end-diastolic myocardial wall stress than did those with moderate stenosis and the healthy group in all the anterior and septum wall segments (p value < 0.05).

The end-diastolic wall stress averages of the anterior and septum walls in the moderate stenosis and significant stenosis groups were approximately 10% and 40% greater,
respectively, compared with the healthy coronary artery group.

The LSD analysis showed no significant differences between the wall stress of the healthy controls and the patients with moderate coronary stenosis; however, due to the high wall stress of the patients with significant coronary stenosis, the overall ANOVA was significantly different. There were significant differences between the healthy controls and the patients with significant coronary stenosis and also between the patients with moderate and significant coronary stenosis (p value < 0.05). Intraobserver and interobserver variability of the wall stress (taking into account regional wall thickness, regional radii of curvature, and LV pressure) was in the range of 4.1-7.6% and 4.8-8.5%, respectively.

**Discussion**

CAD or atherosclerotic heart disease is the end result of the accumulation of atheromatous plaques within the walls of the coronary arteries that supply the myocardium with oxygen and nutrients. The importance of the assessment of the properties of LV and ventricular muscle and their quantification has been evaluated in terms of myocardial wall stress and these calculations have been used in the investigation of various heart diseases. Wall stress may be calculated at the diastolic phase of the cardiac cycle; however, this calculation requires invasive measurements of LV blood pressure in the cardiac catheterization laboratory during retrograde left heart catheterization. In our previous study, we concluded from our experience that non-invasively obtained Doppler E/Ea ratio as an interesting application of TDI provided an index of LVEDP, which could be measured using color Doppler myocardial imaging. In that study, based on very encouraging initial results (LVEDP related strongly to lateral E/Ea, r = 0.85; p value < 0.001), we applied lateral E/Ea for the purpose of non-invasive estimation of LVEDP and therefore non-invasive quantification of myocardial diastolic wall stress.

The average end-diastolic wall stress was calculated at the LV anterior and interventricular septum wall segments using the formula proposed by Deanda et al. and taking into account LV pressure, regional wall thickness, and meridional and circumferential regional radii of the curvature. The stress calculated by this formula represents the mean value of the average stress across the thickness of the LV wall, with

<table>
<thead>
<tr>
<th>Segments</th>
<th>Healthy (N=35)</th>
<th>Moderate LAD coronary artery stenosis (N=30)</th>
<th>Significant LAD coronary artery stenosis (N=30)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meridional Radius (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base</td>
<td>29.3±2.0</td>
<td>30.0±3.6</td>
<td>30.8±2.2</td>
<td>0.086</td>
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<tr>
<td>Mid</td>
<td>29.0±2.8</td>
<td>28.9±3.8</td>
<td>30.5±3.9</td>
<td>0.148</td>
</tr>
<tr>
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<td>21.5±2.6</td>
<td>22.1±3.1</td>
<td>22.7±2.5</td>
<td>0.261</td>
</tr>
<tr>
<td>Circumferential radius (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base</td>
<td>26.5±2.4</td>
<td>30.1±3.6</td>
<td>30.8±2.2</td>
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</tr>
<tr>
<td>Mid</td>
<td>28.7±2.7</td>
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<td>28.9±3.8</td>
<td>0.385</td>
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<tr>
<td>Apex</td>
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<td>22.1±3.1</td>
<td>0.071</td>
</tr>
<tr>
<td>Wall thickness (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base</td>
<td>10.2±1.3</td>
<td>11.1±1.3</td>
<td>10.9±2.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Mid</td>
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<td>11.2±2.8</td>
<td>0.012</td>
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<tr>
<td>Apex</td>
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<td>10.8±1.1</td>
<td>10.2±2.1</td>
<td>0.028</td>
</tr>
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<td>Septal wall</td>
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</tr>
<tr>
<td>Meridional Radius (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base</td>
<td>23.1±1.9</td>
<td>23.5±2.7</td>
<td>24.3±2.9</td>
<td>0.206</td>
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<tr>
<td>Mid</td>
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<td>Apex</td>
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<td>19.6±3.6</td>
<td>20.9±2.4</td>
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<tr>
<td>Circumferential radius (mm)</td>
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</tr>
<tr>
<td>Base</td>
<td>22.0±2.0</td>
<td>22.7±2.8</td>
<td>30.5±2.2</td>
<td>0.112</td>
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<tr>
<td>Mid</td>
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<td>20.9±2.4</td>
<td>30.5±4.0</td>
<td>0.104</td>
</tr>
<tr>
<td>Apex</td>
<td>18.0±1.5</td>
<td>18.2±3.5</td>
<td>22.7±2.5</td>
<td>0.051</td>
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<tr>
<td>Wall thickness (mm)</td>
<td></td>
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</tr>
<tr>
<td>Base</td>
<td>9.2±1.2</td>
<td>10.8±1.4</td>
<td>10.2±1.7</td>
<td>0.000</td>
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<tr>
<td>Mid</td>
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<td>11.0±1.0</td>
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<td>0.006</td>
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<tr>
<td>Apex</td>
<td>10.0±1.3</td>
<td>10.5±1.3</td>
<td>10.0±1.6</td>
<td>0.180</td>
</tr>
</tbody>
</table>

*p value* LAD, Left anterior descending coronary artery

The average end-diastolic wall stress was calculated at the LV anterior and interventricular septum wall segments using the formula proposed by Deanda et al. and taking into account LV pressure, regional wall thickness, and meridional and circumferential regional radii of the curvature. The stress calculated by this formula represents the mean value of the average stress across the thickness of the LV wall, with
In this study, we estimated regional end-diastolic myocardial wall stress in the anterior and septum walls for base, mid, and apex segments. The results showed that the variations of end-diastolic myocardial wall stress in atherosclerotic patients were significantly greater than those of the healthy group (p value < 0.05).

We are cognizant of the fact that invasive coronary angiography is the standard clinical means for depicting the coronary arteries and is the gold standard for diagnosing CAD, but angiographic coronary stenosis does not always reflect the potential alteration in the regional myocardial perfusion. The relationship between stenosis severity and physiological reduction in the coronary flow is quite variable even when there are no imaging limitations, for example eccentric stenosis or obscure areas due to thrombus. Radionuclide methods would be more accurate than coronary angiography in defining ischemic myocardial wall segments, and the accuracy of wall stress may be different when compared with this perfusion technique.

One of the reasons for investigating relationships between the mechanical parameters of the myocardial tissues and coronary stenosis is to find possibilities for remotely characterizing the conditions of normal and diseased tissues. The main focus in most previous studies of tissue characterization has been on elasticity acoustic parameters. More recently, progress has been made in making use of the great sensitivity of strain properties of tissues to their pathological condition: the so-called ultrasonic strain rate imaging. The relation between forces acting upon an object and the resulting deformation is described by Hooke’s law, which states that forces and deformation are linked by the elasticity. This relation remains valid when applied to the myocardium; be that as it may, in order to describe the total deformation of the myocardium, all forces acting on it have to be taken into account.22

The clinical assignment of patients and healthy subjects in the present study may have been biased by their referring physicians. However, we observed no significant differences in age, gender, and body mass index between the groups, indicating an excellent match of the three groups.

Annular velocities may vary with the site of sampling, and thus the utility of this method is dependent on the location of the sample volume. Tissue Doppler recordings were obtained only from the lateral mitral annulus, and the other mitral segments were not evaluated in this study. We chose the lateral aspects of the mitral annulus because this site is easy to obtain from the apical window and, in contrast to the parasternal window, the velocities should not be influenced by anteroposterior translation.23 The main disadvantage of color-TDI is the requirement for an offline analysis for quantifying myocardial velocities and inability to provide instantaneous display of the Doppler information, which can be time-consuming. In this study, E/Ea was calculated using color-TDI and was used to estimate wall stress non-invasively. Further studies are required to compare E/Ea calculated using pulsed-TDI and E/Ea calculated using color-TDI to non-invasively estimated LVEDP and resulted wall stress. In this study, the non-invasive indices of regional wall stress were calculated from the non-invasive estimation of LVEDP and echocardiographic segmental LV diameter and wall thickness in the LAD at risk regions and further studies are required to calculate wall stress for other coronary
arteries at risk regions.

**Conclusion**

In conclusion, non-invasive evaluations of diastolic function constitute an important role of clinical echocardiography and research setting. Our results underscore the importance of end-diastolic myocardial wall stress in CAD patients as an index in the non-invasive evaluation of myocardial performance.

**Acknowledgment**

We wish to thank Dr A. Khaledifar and Dr A. Khajavi for their invaluable technical assistance. This study was approved by the Institutional Review Board and Ethics Committee of Tarbiat Modares University. The first author, Hassan Moladoust, is currently affiliated with the Department of Medical Physics, Guilan Medical Sciences University, Rasht, Iran.

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Timely Diagnosis of Left Ventricular Posterior Wall Rupture by Echocardiography: A Case Report

Maryam Esmaeilzadeh, MD, FCAPSC*, Ahmad Mirdamadi, MD, Majid Kiavar, MD, Gholamreza Omrani, MD, FCAPSC

Shaheed Rajaei Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran.

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Abstract

Left ventricular free wall rupture is responsible for up to 10% of in-hospital deaths following myocardial infarction. It is mainly associated with posterolateral myocardial infarction, and its antemortem diagnosis is rarely made.

One of the medical complications of myocardial infarction is the rupture of the free wall, which occurs more frequently in the anterolateral wall in hypertensives, women, and those with relatively large transmural myocardial infarction usually 1-4 days after myocardial infarction.

We herein present the case of a 66-year-old man suffering inferior wall myocardial infarction with abrupt hemodynamic decompensation 9 days after myocardial infarction. Emergent transthoracic echocardiography revealed massive pericardial effusion with tamponade, containing a large elongated mass measuring 1 × 8cm suggestive of hematoma secondary to cardiac rupture. In urgent cardiac surgery, the posterior wall between the left coronary artery branches was ruptured.

Keywords: Heart rupture • Pericardial effusion • Cardiac tamponade

Introduction

Left ventricular (free wall) rupture is the major culprit in up to 10% of in-hospital deaths following acute myocardial infarction (MI), usually between 3 to 6 days after the infarction. It typically involves the anterior or lateral wall, at the terminal region of the left anterior descending coronary artery distribution. It is associated with transmural infarctions involving at least 20% of the left ventricle (LV), and it rarely occurs in areas with good collateral blood supply.1, 2 The local factors that beget myocardial rupture are thinness of the apical wall at the terminal end of blood supply, poor collateral flow, and shearing effect of muscular contraction against an inert and stiffened necrotic area.

Occurring more frequently in elderly, female,2, 3 and hypertensive patients,1, 4 myocardial rupture is detected more often in the LV than in the right ventricle (RV)1 and tends to strike between day 1 and week 3 but more commonly within 1 to 4 days post infarction.1 In addition, it is known to happen most commonly in patients with delayed hospital admission and its concomitant maintained physical activity.5

Rupture of the LV free wall usually gives rise to hemopericardium and death from cardiac tamponade. The course of rupture varies from a catastrophic event, with an acute tear leading to immediate death (acute rupture), to a slow and incomplete tear causing a late rupture (subacute rupture). An incomplete rupture may occur when the thrombus and hematoma together with the pericardium seal the rupture of the LV and may develop into a diverticulum or a false aneurysm. The clinical recognition of the rupture is often first suggested by the development of profound RV failure and shock progressing to electromechanical dissociation. Immediate pericardiocentesis will temporarily...
relieve tamponade, followed by cardiopulmonary bypass and coronary artery bypass graft surgery to repair the wall.

Although there is often insufficient time for diagnostic tests in patients in whom an acute LV free wall rupture is suspected, echocardiography is the examination of choice. Echocardiography may demonstrate a pericardial effusion and typical findings of cardiac tamponade. Be that as it may, identification of the rupture site is rarely possible.

Case report

A 66-year-old man with a history of systemic hypertension was admitted to our hospital due to neglected inferior wall MI (6 days before) and recurrent chest pain. Physical examination was unremarkable. Initial twelve-lead electrocardiogram displayed q wave and ST segment elevation in leads II, III, aVF, and V₆, while cardiac markers showed elevated creatine kinase (CKMB = 54 Iu/L) and cardiac troponin I (11.4 μg/l). Chest pain was controlled by medical treatment. Transthoracic echocardiography (TTE) showed normal LV size with moderate concentric hypertrophy and moderate LV systolic dysfunction (ejection fraction = 40%); hypokinesia of the base and mid septal, base and mid inferior, and mid posterior segments; mild to moderate RV dysfunction; and no pericardial effusion. On the third day after admission, the patient suddenly developed hypotension; his blood pressure dropped to 90/50 mmHg and he exhibited cold perspiration, tachycardia, and paleness. ECG showed no new ischemic changes.

Emergent bedside TTE revealed severe LV systolic dysfunction (LVEF = 25%) and akinesia of the base and mid inferior, base and mid septal, and mid posterior segments as well as large pericardial effusion associated with diastolic collapse of the RV, RV outflow tract, and right atrium (Figures 1 & 2). Over and above the massive effusion in the pericardial space, an elongated echo-dense mass measuring 1 × 8cm was detected over the right atrium and RV, suggestive of hematoma. The patient, therefore, underwent emergent coronary angiography followed by urgent cardiac surgery with the diagnosis of myocardial rupture.

During surgery, one liter bloody effusion was initially drained from the pericardial space, and the site of the cardiac rupture at the posterior wall between the left coronary artery branches was repaired so that coronary artery bypass grafting could be performed.

The patient’s post-operative course was uneventful, and he was discharged one week after cardiac surgery.

Discussion

One of the fatal complications of MI, myocardial rupture accounts for up to 10% of in-hospital deaths in the wake of acute MI.¹ The course of rupture varies from catastrophic, with an acute tear leading to immediate death, to sub-acute, accompanied by nausea, hypotension, and pericardial type of chest discomfort.³ Factors contributing to this complication are delayed hospital admission and the resultant maintenance of physical activity as well as recurrent and intense chest pain.⁵

Our patient was hypertensive with delayed hospital admission. His inferior wall was involved and cardiac rupture had already occurred without the preceding chest discomfort. Fortunately, however, the timely diagnosis and emergent cardiac surgery brought about the successful sealing of the rupture site with the hemopericardium and the patient’s life was saved.

The prognosis of a cardiac rupture is very poor even when...
surgical therapy is contemplated;\textsuperscript{1} we would, therefore, maintain that patients may fare better if they are afforded early diagnosis and management of this frequently fatal condition.

**Conclusion**

The case presented here highlights the merit of TTE as regards the early diagnosis of LV rupture. Echocardiography can be performed at bedside; consequently, it has the potential to identify this catastrophic condition in patients with acute MI and to determine the next course of action.

**References**

Case Report

Cervical Mass Following Carotid Attempt at Intervventional Repair of Aortic Coarctation: a case report

Ali Dabbagh, MD*, Manuchehr Hekmat, MD, Arash Ghanavati, MD, Abdolrahim Ghasemi, MD

Shahid Modarres Hospital, Shahid Beheshti University of Medicine (SBMU), Tehran, Iran.

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Abstract

A 4-month-old boy was admitted to our hospital following an unsuccessful attempt at interventional repair of aortic coarctation via the right carotid artery, which seemed to have given rise to the formation and growth of a cervical mass overlying the entry site. Despite the initial anticipation of difficulty during intubation due to the pressure effect of the mass, anesthesia progressed uneventfully, the mass, which was a hematoma, was evacuated, and the coarctation was repaired. The patient was discharged after the operation. At three weeks’ follow-up, there was no significant lesion in the neck and transthoracic echocardiography demonstrated no residual coarctation.

Keywords: Neck • Aortic coarctation • Carotid arteries

Introduction

Penetrating carotid artery trauma may occur in consequence of incidental puncture during a number of procedures like the insertion of central venous catheters, which, if not performed meticulously, could give rise to a number of untoward complications.1 Penetrating carotid artery trauma may also happen during many rare instances when the carotid artery is used as a portal for angiography, interventional angioplasty, extracorporeal membrane oxygenation (ECMO), etc.

This manuscript presents a case of neck hematoma in the wake of carotid artery trauma sustained during an unsuccessful attempt at interventional repair of aortic coarctation. The complication was treated surgically under general anesthesia, during which the cervical mass was evacuated and the coarctation was repaired.

Case presentation

A 4-month-old boy was admitted to our university hospital due to an enlarged cervical mass following carotid attempt at interventional repair of aortic coarctation diagnosed via transthoracic echocardiography. The patient had previously been referred to the pediatric catheterization lab for the definite repair of the coarctation as well as pressure gradient correction; however, initial attempts at introducing the guidewire into the arterial system (first femoral, then brachial, and finally right carotid) failed. The patient was thereafter transferred to the ward for further treatment, but his parents chose to take him home. Three weeks later, the patient was admitted to the operating room for an emergency operation to evaluate and possibly evacuate the mass and also to assess and repair the carotid artery rupture and coarctation (Figures 1 and 2). Before the decision for surgery had been made, a Doppler examination of the carotid...
artery ruled out a pseudoaneurysm of the carotid artery under the hematoma. Volatile anesthetics, supplemented with ketamine, were planned for the patient; and under standard non-invasive monitoring, 3mg/Kg intramuscular ketamine plus 1.5% halothane was administered. With the patient breathing spontaneously under deeper levels of anesthesia, laryngoscopy showed that the glottis was not difficult for intubation. A peripheral intravenous line was established for muscle relaxants, and the trachea was intubated without any need for extra devices. Additionally, an arterial line in the right brachial artery was established to commence invasive arterial monitoring. The left subclavian approach was chosen for the insertion of the central venous line at the first attempt, which demonstrated the central venous pressure waveform.

The patient was operated on in the supine position with a roll below the neck to extend the neck gently and produce a "thyroid position". The surgical approach was initially based on making the proximal and distal control of the right external carotid, but the hugeness of the cervical mass rendered it impossible. The skin over the mass was, therefore, gradually dissected and the mass, which was a hematoma around and inside the sternocleidomastoid muscle, appeared (Figures 3 and 4). The hematoma was evacuated and the bleeding site, the punctured right external carotid, was repaired by direct suturing. Subsequently, the sternocleidomastoid muscle was repaired, a hemovac drain was inserted, and the overlying skin was sutured.

The patient was then placed in the right lateral decubitus position for a thoracotomy approach both to repair the coarctation of the aorta with a subclavian flap angioplasty and to close the patent ductus arteriosus (PDA). After this surgical procedure, the pressure gradient at the level of the coarctation was corrected, the left lung was re-expanded, the thorax was closed, and the skin was sutured.

The patient was transferred to the pediatric cardiac intensive care unit and was extubated the following day. Transthoracic echocardiography was indicative of no significant gradient across the repaired site of the coarctation, and the patient was discharged to the ward after 3 days. At three weeks’ follow-up, there was no significant lesion in the neck and transthoracic echocardiography demonstrated no residual coarctation.
Discussion

Carotid artery trauma in the existing medical literature is categorized as penetrating and blunt. Arterial interventions or angiography through the carotid artery, albeit not commonly practiced, may be utilized in rare cases in which the clinician has no good portal for arterial entry, e.g. in patients with weak pulses; though it is not as much common as traumatic arterial complications in other arteries.2 Interventional repair of aortic coarctation is one of these rare situations. Inadvertent puncture of the common carotid artery is the most frequent complication of central venous catheter insertion and may result in central nervous system injury or airway compromise.3

One of the main untoward effects of carotid rupture, which is fortunately not common, is the effect of the enlarging mass on the upper airway. This effect may lead to gross mass effect, eventual fatal airway obstruction, and airway compromise.4 5 The case presented herein was a typical case of penetrating carotid artery trauma leading to a mass effect and a partially displaced airway. As a result, the coarctation was repaired in the next step after the repair of the carotid artery while the patient was in a stable situation. It is worthy of note that using the carotid artery for interventions or angiography in such cases may beget a number of deleterious effects;1, 4-6 it is mandatory that this approach be taken cautiously with respect to the angiography catheter entry portal. If there is a no other arterial choice except for the carotid artery in diagnostic and interventional repair therapies of the aortic coarctation, the clinician should increase his/her attention for the possibility of post-procedure events. The reason is that in such cases, the blood pressure in the upper limb is increased due to the pathophysiology of the aortic coarctation; the blood leakage from the ruptured artery is, therefore, much more severe than that in normal cases. Such surgical cases require much more sophisticated cautious interventions on the part of the anesthesiologist, surgeon, and interventionist.

Conclusion

This case demonstrated that a penetrating carotid artery puncture could lead to a number of life-threatening complications; especially in a newborn with aortic coarctation.

References

Management of Iatrogenic Rupture of Profunda Femoris Artery after Femoral Fracture Fixation with Stent Graft Implantation

Hamidreza Varastehravan, MD, Hossein Nough, MD, Zahra Ansari, MD*

Afshar Hospital, Shaheed Sadoughi Medical University, Yazd, Iran.

Received 09 August 2008; Accepted 24 December 2008

Abstract

Vascular injuries with acute or chronic arterial hemorrhage after femoral shaft fractures are a rare but a life-threatening complication. We observed a case of iatrogenic rupture of the profunda femoris artery after the internal fixation of a femoral shaft fracture. The pseudoaneurysm, presenting with painful expansile swelling and hemodynamic instability, together with the rupture was evident on femoral angiography. Endovascular stent graft placement was performed successfully, and there was no sign or symptom at 9 months' follow-up.

Keywords: Stents • Pseudoaneurysm • Iatrogenic disease

Introduction

Acute or late rupture of arteries after femoral fracture is rare and usually caused by iatrogenic trauma or rarely by bone spikes. The profunda femoris pseudoaneurysms following various orthopedic surgical procedures have previously been described. The diagnosis is usually delayed because of nonspecific clinical features such as pain, anemia, fever, and hematoma. Management of a profunda femoris artery pseudoaneurysm has changed from surgical intervention to radiological intervention because of difficult access to the deep muscle compartment of the thigh, where the profunda femoris artery is located.

Case report

An 18-year-old man with a close fracture of the mid shaft of the right femur, sustained in a car accident, underwent an open reduction internal fixation. On physical examination, the distal pulses and sensation of the right leg were normal and there were no signs of nerve or artery damage.

After surgery, the patient was discharged with normal vital signs. On the same day, however, the patient returned to the hospital with a markedly painful, expansible swelling at the medial aspect of his right thigh as well as anemia (Hb = 7). This was initially diagnosed as a post-operative hematoma, so the patient underwent surgical hematoma drainage. The following day, the patient’s clinical condition exacerbated with the painful swelling recurring; he was referred for angiography in the cath lab in conscious state.

Selective arteriography of the superficial artery and profunda femoris artery via the contralateral approach showed a pseudoaneurysm of the right thigh with a maximum...
Figure 1. Arteriography of the superficial and profunda femoris arteries via the contralateral approach. The arrow shows the rupture of the profunda femoris and dye jetting from the rupture before stenting. The pseudoaneurysm of the right thigh, originating from the pinpoint perforation of the distal right profunda femoris artery and dye jetting into the pseudoaneurysm, is shown diameter of 9 cm, originating from a pinpoint perforation of the distal right profunda femoris artery with a diameter of about 3 mm and jetting of the dye to the pseudoaneurysm (Figure 1). The superficial femoral artery and run-off were normal.

Given the potential difficulties of open surgical repair, the patient was candidated for transcatheter stent graft placement, to be performed simultaneously with angiography in the cat lab and without anesthesia. After selective engagement of the right SFA via the contralateral approach with a multi-purpose 6F guiding catheter and administration of 5000 U IV Heparin and 2 gr IV Keflin, a 0.018 v-18 control wire was passed along the right profunda femoris. The diameter of the artery was estimated at 3 mm; a 3.25 × 16 mm Jomed coronary graft stent was, therefore, passed through in order to cover the perforation and it was subsequently inflated at 14 atm. Injection into the right profunda femoris artery showed the sealing and complete cessation of the blood and dye jetting from the profunda into the pseudoaneurysm (Figure 2). In Figure 1, dye is jetting from the rupture but in Figure 2 after stent graft inflation there is no dye jetting. Aspects of the pseudoaneurysm are marked in Figure 2.

Heparin was not reversed, and 325 mg Aspirin and 600 mg Plavix were prescribed stat with Keflin 1 gr IV QID for 24 hours and Aspirin 80 mg/d and Plavix 75 mg/d for one month. The patient’s general condition and vital signs rapidly improved, and sonography 2 days later was indicative of a reduction in the mass diameter in the right thigh (about 3-4 cm) with the patency of the right profunda femoris artery. After discharge on the fourth day, the patient was prescribed Aspirin (80 mg/day) and Plavix (75 mg/day) for one month. At one month’s follow-up, sonography was completely normal and there was no sign or symptom on physical examination.

Figure 2. The arteriography of the superficial and profunda femoris arteries via the contralateral approach after stenting. The arteriogram shows complete cessation of the blood and dye jetting from the profunda into the pseudoaneurysm. The arrow shows the aspects of the pseudoaneurysm

**Discussion**

The profunda femoris artery is the largest branch of the femoral artery. Injuries to the proximal part of the profunda femoris artery may cause external hemorrhage because of the artery’s superficial location. But more distal injuries such as injuries due to mid-shaft fracture of the femur may produce silent lesions on account of the fact that peripheral pulses are not affected unless the superficial femoral artery is injured or compromised by a compressing hematoma. Pseudoaneurysms and arteriovenous fistulae are the probable complications of these silent lesions.

Iatrogenic pseudoaneurysms of the femoral artery after the fracture of the femur are rare. Detection of pseudoaneurysms tends to be delayed usually because a progressive swelling is painless in most cases, unless hemodynamic instability and high clinical suspicion of active bleeding prompts a diagnosis of the rupture of the artery and pseudoaneurysm. Pain, hematoma, swelling, occasional fever, unexplained anemia, and hemodynamic instability are non-specific clinical signs. It is worthy of note that the thigh compartment syndrome has also been observed after pseudoaneurysm formation.

Planning the line of management in cases with the rupture of the artery or pseudoaneurysms depends on the length and size of lesions. Also in such cases, open surgical repair is rendered difficult by the presence of a hematoma. Moreover, active bleeding reduces access to the deep muscle compartment of the thigh, where the profunda femoris artery is located adjacent to the proximal femoral shaft. A review of the existing medical literature shows that the successful transcatheter treatment of penetrating injuries to the profunda femoris artery has already been reported.
Conclusion

Profunda femoris artery rupture is a rare iatrogenic complication of femoral shaft fracture fixation. Clinical suspicion can be confirmed by angiography. Be that as it may, whereas the surgical treatment of such cases is usually hampered by the relative inaccessibility of the anatomical compartment involved, transcatheter stent graft placement performed simultaneously with angiography is now the first of choice of management.

References

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<td>Website: <a href="http://www.valvesymposium.com/">http://www.valvesymposium.com/</a></td>
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<td></td>
<td>Brussels, Belgium</td>
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<td>ISHAC - International Symposium on the Hybrid Approach to Congenital</td>
<td>1-3 September 2010</td>
<td>Website: <a href="http://www.hybridsymposium.com">http://www.hybridsymposium.com</a></td>
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<tr>
<td>Heart Disease</td>
<td>Columbus, OH United States</td>
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<td>24th EACTS Annual Meeting</td>
<td>11-15 September 2010</td>
<td>Website: <a href="http://www.eacts.org">http://www.eacts.org</a></td>
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<td></td>
<td>Geneva, Switzerland</td>
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<td>Perfusion Safety &amp; Best Practices</td>
<td>6-9 October 2010</td>
<td>Website: <a href="http://www.amsect.org/sections/education/index.html">http://www.amsect.org/sections/education/index.html</a></td>
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<td></td>
<td>Toronto, ON Canada</td>
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<tr>
<td>&quot;Congenital Heart Disease&quot;(1st Day: Sequential Segmental Analysis of</td>
<td>14-15 October 2010</td>
<td>Website: <a href="http://www.boerhaavenet.nl/">http://www.boerhaavenet.nl/</a></td>
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<tr>
<td>Malformed Hearts, 2nd Day: Borderline Hypoplastic Left Ventricle)</td>
<td>Leiden, Netherlands</td>
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<tr>
<td>20th World Congress of The World Society of CardioThoracic Surgeons</td>
<td>20-23 October 2010</td>
<td>Website: <a href="http://www.wscts2010.com">http://www.wscts2010.com</a></td>
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<tr>
<td>combined with 6th Global Forum on Humanitarian Medicine in Cardiopace</td>
<td>Chennai, India</td>
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<td>&amp; Cardiac Surgery</td>
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<tr>
<td>Turkish Cardiovascular Surgery Society 11th Annual Meeting</td>
<td>27-31 October 2010</td>
<td>Website: <a href="http://www.tkmdc2010.org/">http://www.tkmdc2010.org/</a></td>
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<td></td>
<td>Antalya, Turkey</td>
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# INTERNATIONAL CARDIOVASCULAR MEETING AND CONGRESSES CALENDER (2010-2011)

<table>
<thead>
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<th>Title</th>
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<tr>
<td>Preceptorship in Intraoperative Transesophageal Echocardiography</td>
<td>Durham, NC, United States</td>
<td>11 January 2010</td>
<td>13 January 2010</td>
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<tr>
<td>1st International Cardiovascular Pharmacotherapy Conference</td>
<td>Riyadh, Saudi Arabia</td>
<td>12 January 2010</td>
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<tr>
<td>XXes Journées Européennes de la Société Française de Cardiologie</td>
<td>Paris, France</td>
<td>13 January 2010</td>
<td>16 January 2010</td>
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<td>World Cardiology, Metabolism and Thrombosis Congress (WCMTC)</td>
<td>Sao Paulo, Brazil</td>
<td>20 January 2010</td>
<td>23 January 2010</td>
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<tr>
<td>13th Society for Cardiovascular Magnetic Resonance (SCMR) Annual Scientific Sessions</td>
<td>Phoenix, AZ, United States</td>
<td>21 January 2010</td>
<td>24 January 2010</td>
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<td>29th Belgian Society of Cardiology Annual Scientific Meeting</td>
<td>Brussels, Belgium</td>
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<td>31st Annual Meeting of The American Academy of Cardiovascular Perfusion (AACP)</td>
<td>Nashville, TN, United States</td>
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<tr>
<td>35th Annual Cardiovascular Conference at Snowbird</td>
<td>Snowbird, UT, United States</td>
<td>3 February 2010</td>
<td>6 February 2010</td>
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<td>Leuven Symposium on Myocardial Velocity and Deformation Imaging</td>
<td>Leuven, Belgium</td>
<td>4 February 2010</td>
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<td>10th Annual International Symposium on Congenital Heart Disease</td>
<td>St. Petersburg, FL, United States</td>
<td>6 February 2010</td>
<td>9 February 2010</td>
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<tr>
<td>2nd National Chronic Heart Failure and Hypertension</td>
<td>London, England, United Kingdom</td>
<td>11 February 2010</td>
<td>12 February 2010</td>
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<tr>
<td>Heart to Heart 3</td>
<td>Cape Canaveral, Florida, United States</td>
<td>13 February 2010</td>
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<tr>
<td>The 2nd World Congress on Controversies in Cardiovascular Disease</td>
<td>Istanbul, Turkey</td>
<td>18 February 2010</td>
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<tr>
<td>(C-Care)</td>
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<tr>
<td>Cardiovascular Topics at Johns Hopkins</td>
<td>Baltimore, MD, United States</td>
<td>18 February 2010</td>
<td>20 February 2010</td>
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<tr>
<td>Diagnostic and Interventional Radiology</td>
<td>London, United Kingdom</td>
<td>18 February 2010</td>
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<tr>
<td>Cardiovascular Disease Prevention 2010: Eighth Annual Comprehensive</td>
<td>Coral Gables, Florida, United States</td>
<td>18 February 2010</td>
<td>20 February 2010</td>
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<td>Symposium</td>
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<tr>
<td>Preceptorship in Intraoperative Transesophageal Echocardiography</td>
<td>Durham, NC, United States</td>
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<td>Arrhythmias &amp; the Heart Symposium</td>
<td>Maui, HI, United States</td>
<td>22 February 2010</td>
<td>25 February 2010</td>
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<tr>
<td>15th Annual Cardiology at Cancun - Advances in Clinical Cardiology</td>
<td>Cancun, Mexico</td>
<td>22 February 2010</td>
<td>26 February 2010</td>
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<td>and Multi-Modality Imaging</td>
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<tr>
<td>International Stroke Conference 2010</td>
<td>San Antonio, TX, United States</td>
<td>23 February 2010</td>
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<td>International Conference on Early Disease Detection and Prevention</td>
<td>Munich, Germany</td>
<td>25 February 2010</td>
<td>28 February 2010</td>
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<td>(EDDP 2010)</td>
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<td>9th Genoa Meeting on Hypertension, Diabetes and Renal Diseases</td>
<td>Genoa, Italy</td>
<td>25 February 2010</td>
<td>27 February 2010</td>
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<tr>
<td>First International Meeting on Cardiac Problems in Pregnancy</td>
<td>Valencia, Spain</td>
<td>25 February 2010</td>
<td>28 February 2010</td>
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<td>International Congress of Cardiology (ICC)</td>
<td>Hong Kong, Hong Kong</td>
<td>26 February 2010</td>
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<td>Keystone Symposia: Cardiovascular Development and Repair (X2)</td>
<td>Keystone, CO, United States</td>
<td>28 February 2010</td>
<td>05 March 2010</td>
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<td>Vascular Care 2010: Current Management of Peripheral Vascular Disease</td>
<td>Truckee, CA, United States</td>
<td>28 February 2010</td>
<td>03 March 2010</td>
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<td>Consensus and Controversies</td>
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<td>International Congress XXIII on Endovascular Interventions</td>
<td>Scottsdale, AZ, United States</td>
<td>28 February 2010</td>
<td>04 March 2010</td>
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<tr>
<td>4th Middle East Cardiovascular Congress</td>
<td>Kish Island, Iran</td>
<td>03 March 2010</td>
<td>05 March 2010</td>
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<td>3rd International Conference on Hypertension, Lipids, Diabetes &amp;</td>
<td>Berlin, Germany</td>
<td>04 March 2010</td>
<td>06 March 2010</td>
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<tr>
<td>Stroke Prevention</td>
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<tr>
<td>The Future of Genomic Medicine III</td>
<td>San Diego, CA, United States</td>
<td>05 March 2010</td>
<td>06 March 2010</td>
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<tr>
<td>Interventional Cardiology 2010: 25th Annual International Symposium</td>
<td>Snowmass Village, United States</td>
<td>07 March 2010</td>
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<tr>
<td>10th Annual Spring Meeting on Cardiovascular Nursing</td>
<td>Geneva, Switzerland</td>
<td>12 March 2010</td>
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<td>American College of Cardiology (ACC) 59th Annual Scientific Session</td>
<td>Atlanta, GA, United States</td>
<td>14 March 2010</td>
<td>16 March 2010</td>
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<tr>
<td>Preceptorship in Intraoperative Transesophageal Echocardiography</td>
<td>Durham, NC, United States</td>
<td>15 March 2010</td>
<td>17 March 2010</td>
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<td>VIII Congress of the Italian Society of Cardiovascular Prevention (SIPREC)</td>
<td>Rome, Italy</td>
<td>18 March 2010</td>
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<td>XI International Forum for the Evaluation of Cardiovascular Care</td>
<td>Prague, Czech Republic</td>
<td>18 March 2010</td>
<td>20 March 2010</td>
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<td>The Houston Aortic Symposium: Frontiers in Cardiovascular Diseases, The Third in the Series</td>
<td>Houston, TX, United States</td>
<td>25 March 2010</td>
<td>27 March 2010</td>
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<td>Athens Cardiology Update 2010</td>
<td>Athens, Greece</td>
<td>25 March 2010</td>
<td>27 March 2010</td>
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<td>22nd International Meeting 'Cardiology Today'</td>
<td>Nicosia, Cyprus</td>
<td>27 March 2010</td>
<td>28 March 2010</td>
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<td>Saudi Hypertension Conference 2010</td>
<td>Jeddah, Saudi Arabia</td>
<td>29 March 2010</td>
<td>31 March 2010</td>
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<td>The 14th Annual Scientific Meeting of the Egyptian Hypertension Society</td>
<td>Cairo, Egypt</td>
<td>07 April 2010</td>
<td>09 April 2010</td>
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<td>Vascular Laboratory 2010: Advanced Topics for Vascular Specialists and Other Health-Care Professionals</td>
<td>Sacramento, CA, United States</td>
<td>10 April 2010</td>
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<td>Preceptorship in Intraoperative Transesophageal Echocardiography</td>
<td>Durham, NC, United States</td>
<td>12 April 2010</td>
<td>14 April 2010</td>
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<td>7th Mediterranean Meeting on Hypertension and Atherosclerosis</td>
<td>Nevsehir, Turkey</td>
<td>14 April 2010</td>
<td>18 April 2010</td>
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<td>The Tenth International Conference of the Jordan Cardiac Society</td>
<td>Amman, Jordan</td>
<td>20 April 2010</td>
<td>22 April 2010</td>
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<td>5th Cardiac MRI &amp; CT Clinical Update 2010</td>
<td>Cannes, France</td>
<td>23 April 2010</td>
<td>25 April 2010</td>
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<td>New Zealand Resuscitation Council Conference 2010</td>
<td>Auckland, New Zealand</td>
<td>30 April 2010</td>
<td>01 May 2010</td>
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<td>EuroPRevent 2010 - Cardiovascular Prevention: a Lifelong Challenge</td>
<td>Prague, Czech Republic</td>
<td>05 May 2010</td>
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<td>5th European Cardiology Conference for General Practitioners</td>
<td>Dubrovnik, Croatia</td>
<td>07 May 2010</td>
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<td>Controversies in Cardiovascular Disease: Practical Approaches to Complex Problems: Medical and Surgical</td>
<td>St. Paul, MN, United States</td>
<td>08 May 2010</td>
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<td>7th Metabolic Syndrome, Type II Diabetes and Atherosclerosis Congress (MSDA)</td>
<td>Marrakesh, Morocco</td>
<td>12 May 2010</td>
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<td>Preceptorship in Intraoperative Transesophageal Echocardiography</td>
<td>Durham, NC, United States</td>
<td>17 May 2010</td>
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<td>3rd Cardiovascular CT, Concord Conference 2010</td>
<td>Sydney, Australia</td>
<td>21 May 2010</td>
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<td>EuroPCR</td>
<td>Paris, France</td>
<td>25 May 2010</td>
<td>28 May 2010</td>
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<td>Heart Failure Congress 2010</td>
<td>Berlin, Germany</td>
<td>29 May 2010</td>
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<td>9th Asian-Pacific Congress of Cardiovascular &amp; Interventional Radiology (APCCVIR 2010)</td>
<td>Seoul, South Korea</td>
<td>01 June 2010</td>
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<td>International Conference on Pulmonary Circulation 2010</td>
<td>Prague, Czech Republic</td>
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<td>05 June 2010</td>
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<td>Preceptorship in Intraoperative Transesophageal Echocardiography</td>
<td>Nice, NC, United States</td>
<td>07 June 2010</td>
<td>09 June 2010</td>
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<td>World Congress of Cardiology</td>
<td>Beijing, China</td>
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<td>International Workshop on Complications during Cardiac Interventions: Management and Prevention</td>
<td>Düsseldorf, Germany</td>
<td>16 June 2010</td>
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<td>Cardiostim 2010-17th World Congress in Cardiac Electrophysiology and Cardiac Techniques</td>
<td>Nice, France</td>
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<td>The 7th Tunisian and Europeans Days of Cardiology Practice</td>
<td>Port El Kantaoui, Tunisia</td>
<td>17 June 2010</td>
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<td>Multidisciplinary European Endovascular Therapy (MEET 2010)</td>
<td>Marseille, France</td>
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<td>20th European Meeting on Hypertension</td>
<td>Oslo, Norway</td>
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<td>78th European Atherosclerosis Society Congress</td>
<td>Hamburg, Germany</td>
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<td>Ehra Europace</td>
<td>Madrid, Spain</td>
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<td>6th Asian Interventional Cardiovascular Therapeutics Congress</td>
<td>Singapore, Singapore</td>
<td>01 July 2010</td>
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<td>21st International Congress on Thrombosis 2010</td>
<td>Milan, Italy</td>
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<td>iCi - Imaging in Cardiovascular Interventions</td>
<td>Frankfurt, Germany</td>
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<tr>
<td>CSI - Congenital &amp; Structural Interventions</td>
<td>Frankfurt, Germany</td>
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<td>Berlin, Germany</td>
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<td>The 26th International Pediatric Association Congress of Pediatrics (IPA 2010)</td>
<td>Johannesburg, South Africa</td>
<td>04 August 2010</td>
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<td>ESC Congress 2010</td>
<td>Stockholm, Sweden</td>
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<td>19th EUROCHAP 2010 European Chapter Congress of the</td>
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<td>International Union of Angiology</td>
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<td>65th Brazilian Congress of Cardiology</td>
<td>Belo Horizonte, Brazil</td>
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<td>Valencia, Spain</td>
<td>02 October 2010</td>
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<tr>
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<tr>
<td>26th Annual Echocardiography in Pediatric and Adult</td>
<td>Rochester, MN, United States</td>
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<td>Copenhagen, Denmark</td>
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<td>2010 Cardiometabolic Health Congress</td>
<td>Boston, MA, United States</td>
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<td>8th Annual World Congress on Insulin Resistance, Diabetes, and</td>
<td>Los Angeles, CA, United</td>
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<td>The 3rd International Conference on Fixed Combination in the</td>
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<td>Treatment of Hypertension, Dyslipidemia and Diabetes Mellitus</td>
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<td>13th British Society for Heart Failure Annual Meeting</td>
<td>London, United Kingdom</td>
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<td>International Symposium on Progress in Clinical Pacing</td>
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<tr>
<td>Euro echo 2010</td>
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<td>Heart, Vessels &amp; Diabetes - The European Conference</td>
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Information for Authors

The first three consecutive issues of “The Journal of Tehran University Heart Center” were published under the title of “The Journal of Tehran Heart Center” with ISSN: 1735-5370. From the fourth issue onward, however, the journal has been entitled “The Journal of Tehran University Heart Center” with ISSN:1735-8620.

Scope of the Journal

“The Journal of Tehran University 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 University Heart Center” is an international, English language, peer reviewed journal concerned with Cardiovascular Medicine. It is an official journal of the Cardiovascular Research Center of the Tehran University of Medical Sciences (in collaboration with the Iranian Society of Cardiac Surgeons) 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.

Article Categories

The Journal of Tehran University Heart Center accepts the following categories of articles:

- Guest Editorial
- Original Article
- Clinical and pre-clinical papers based on either normal subjects or patients and the result of cardiovascular pre-clinical research will be considered for publication provided they have an obvious clinical relevance.
- Brief communication
  - Case report
  - Review Article
- “The Journal of Tehran University Heart Center” publishes a limited number of scholarly, comprehensive reviews whose aims are to summarize and critically evaluate research in the field addressed and identify future implications. Reviews should not exceed 5000 words.
- Letter to editor
  - Letters to the editor must not exceed 500 words and should focus on a specific article published in “The Journal of Tehran University Heart Center” within the preceding 12 weeks. No original data may be included. Authors will receive pre-publication proofs, and the authors of the article cited invited to reply.

Submission of Manuscripts

Four double spaced copies on 8 1/2 × 11 in. paper should be sent to:

Dr. A. Karimi, Editor in Chief,
“The Journal of Tehran University Heart Center”,
Tehran Heart Center,
North Kargar Street,
Tehran, Iran
1411713138

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Acknowledgements

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

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![Graph showing drug load and efficacy](image)

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<table>
<thead>
<tr>
<th></th>
<th>1-year HR</th>
<th>2-year HR</th>
</tr>
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<tbody>
<tr>
<td>Xience V</td>
<td>0.33</td>
<td>0.55 [0.38, 0.80]</td>
</tr>
<tr>
<td>TAXUS</td>
<td>p=0.0014</td>
<td>p=0.0014</td>
</tr>
</tbody>
</table>

**Graph showing ischemic MACE (%)**

- Xience V: 9.7% Δ4.7%, 12.3%
- TAXUS: 5.0% Δ5.2%, 9.1%