Importance of Further Recognition of Atherosclerotic Patients Candidate for CABG: Predisposing Factors for Postoperative Stroke

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A B S T R A C T

Given the common pathogenesis of atherosclerotic coronary and carotid diseases, increasing attention has been paid by cardiovascular surgeons for detection, evaluation and treatment of carotid artery stenosis in patients undergoing Coronary Artery Bypass Graft (CABG). Coronary artery bypass is a frequent surgery with a global scope; it has been proven that the presence of carotid artery stenosis in these patients increases the risk of ischemic stroke before surgery resulting in reduced quality of life and increased mortality, as well as disability of patients and increased costs and hospitalization. In fact, preoperative strokes account for about 3% of the CABG complications. Given that cardiac surgery patients with carotid artery stenosis are at high risk for surgery-associated neurological events, therefore, the key points in facing with these patients are introduced in this pilot study, to help treat them better and with a proper prognosis.

INTRODUCTION

Atherosclerosis:

Atherosclerosis is an epidemic in most developed countries, with a less prevalence in Central and South America, Africa and Asia. Premenopausal women compared with same age men are at lower risk for atherosclerosis, but the incidence becomes equal in men and women in postmenopausal women (Thomas, G., & Robert, 2010).

In industrialized countries, atherosclerosis often begins in the first few decades of life. So that one out of every 6 suddenly died American adolescents aged 13-19 has pathological evidence of atherosclerotic coronary arteries. Accumulation of lipoproteins, endothelial damage and inflammation are of numerous processes that contribute to the initiation and progression of atherosclerosis (DOV, M., et al., 2000).

The pathogenesis of atherosclerosis:

In the early stages of atherosclerosis, small particles of lipoproteins penetrate the vascular endothelium; they are oxidized there and accumulate in the tunica intima. This process is accelerated at the site of endothelial damage. The damage may arise from hypertension, hypercholesterolemia, smoking, or excessive shear forces (tangential). Lipid accumulation in the tunica intima leads to the expression of adhesion molecules on the luminal surface of endothelial cells and thereby allows them to attach the circulating monocytes (e.g., macrophages) (Alamowitz, S., et al., 2001; Sabeti, S., et al., 2001; Khairi, H.S., M.C. Crowson, 1995; Tarzamani, M.K., 2007). The monocytes swallow lipoproteins and changes to fat-accumulated monocytes or foam cells. Accumulation of these foam cells is the first visible evidence of atherosclerosis. Foam cells multiply and lead to continuation of local inflammation and thus degradation of endothelium through releasing proinflammatory mediators. Accumulation of fat in foam cells results in their necrosis, but fat remains at the center of the plaque. Macrophages and mast cells release enzymes such as metalloproteinase (such as collagenase and gelatinase) which degrade collagen and the proteins of extracellular matrix adjacent to the plaque. While, T cells inhibit collagen formation by vascular smooth muscle cells through secreting cytokines (e.g., interferon alpha) (Durand, D.J., et al., 2004; Hennerici, M., et al., 1987). Increased degradation and

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reduced formation of collagen predispose the plaque to corrosion and tear. Activated platelets also release some substances (such as thromboxane, serotonin) which stimulate vasoconstriction and expansion of thrombus. When the extent of platelet aggregation and thrombus formation in sufficient to halt blood flow (either partial or full), an acute coronary event occurs (such as unstable angina, non-ST elevation myocardial infarction [NSTEMI] or ST elevation myocardial infarction [STEMI]) (Berens, S., et al., 1992; Kobayashi, H., et al., 2010).

**Risk factors for atherosclerosis:**

Several risk factors have been identified for development of atherosclerosis. Unrecoverable risk factors include older age, male gender, and family history of premature atherosclerosis. Other modifiable risk factors and their treatment may reduce the risk of atherosclerosis. These factors include hyperlipidemia, hypertension, diabetes mellitus, metabolic syndrome, smoking, obesity, sedentary lifestyle, and excessive alcohol consumption. As a marker of inflammation, CRP may increase the risk of plaque rupture or contribute to clot formation. Increased serum levels of CPR, if measured by very sensitive methods, is strongly associated with risk of MI, stroke, peripheral arterial disease, and sudden death. Coronary artery calcification is also a typical manifestation of coronary atherosclerosis and is associated with the presence and severity of CAD (David Sutton, Roger Gregson, H.S., 2003).

**Carotid Artery:**

The common carotid artery originates from the brachiocephalic artery at right and the aortic arch at left. The artery is divided into internal and external carotid arteries at the upper rim of the thyroid cartilage. The external carotid artery supplies the structures in neck, face, skull, tongue and cheeks. The internal carotid artery supplies the brain, eyes, forehead, and a part of the nose (David Sutton, Roger Gregson, H.S., 2003; Durand, D.J., et al., 2004).

**Carotid Artery Stenosis:**

Approximately 730 thousand strokes occur in the United States per year, which impose a cost of more than $40 million. Half of these strokes are the consequence of carotid artery atherosclerosis (Alamowitch, S., et al., 2001).

The signs depend on the brain area involved. Many patients are asymptomatic and stenosis may be detected during an examination. The disease may present itself as loss of vision, weakness and tingling in the extremities, muffled speech, inability to articulate words, or eventually coma. In such situations, an emergency consultation with a physician is essential to avoid a real stroke.

History of cerebrovascular accident, hypertension, smoking, diabetes, obesity, high cholesterol (especially LDL), age over 60, female gender, and severe coronary artery disease are the most common risk factors associated with the occurrence of carotid artery stenosis (Sabeti, S., et al., 2001; Khairi, H.S., M.c. Crowson, 1995).

As mentioned, carotid artery stenosis has been highly reported in females (Durand, D.J., et al., 2004) as well as in patients with rheumatoid arthritis compared with patients without rheumatoid arthritis, because cardiovascular mortality and morbidity increase in rheumatoid arthritis (Selnes, O.A., et al., 2012).

This disease is treated based on being symptomatic or asymptomatic and may include the followings:

1. Medical procedures or medications
2. Endarterectomy: surgical removal of plaque from the vessel
3. Repair with open surgery

**The Relationship between Stroke and Carotid Arteries Stenosis:**

Stroke is a severely debilitating disease, which extra cranial atherosclerotic disease, specifically carotid artery stenosis, is its major causes. Atherosclerotic plaques are most often formed in the proximal internal carotid artery; however, the common carotid artery is also the culprit at times. In patients who have had a carotid endarterectomy, the distal common carotid artery is a frequent location for plaque formation. Generally, stroke occurs as the first symptom of the disease, and often a carotid bruit is the only sign that can be seen on physical examination (Branthwaite, M.A., 1975).

**Carotid Artery Stenosis Detection Techniques:**

The two main predictors for stroke are previous symptoms (transient ischemic attack and recent stroke) and severity of stenotic lesions. For this reason, diagnosis is critical for the prevention of stroke. Several imaging modalities can be used in this regard. CTA has excellent spatial and contrast resolution for plaque detection. It is able to detect plaque at the bifurcation of the internal and external carotid arteries, and is used to define vascular anatomy proximal and distal to a stenotic plaque. CT, however, is not used as the initial screening test.
Vascular ultrasound is easily accessible and can be brought to the patient's bedside. It is inexpensive, risk-free, and excellent for the evaluation of carotid anatomy and determination of flow dynamics. B-mode ultrasound is used for the anatomic determination of the arteries, whereas severity of plaques is evaluated by Doppler, which can measure the velocity and pressure gradients across a lesion (Branthwaite, M.A., 1975). Doppler sonography is formed from a combination of real time B-mode images and waveform analysis of Doppler wave. The old Doppler systems were limited to black and white images, but the recent progresses and the possibility of color images generation have turned Doppler sonography into a powerful instrument for the evaluation of vascular disorders (Shirani, S., et al., 2006). There are limitations of Doppler imaging, which can give false measurements. Any factor that decreases the velocity of the blood from the heart to the carotid arteries can interfere with accurate estimation of carotid stenosis. Most commonly, severe LV dysfunction, valvular heart disease, and aortic disease are the culprits. Highly calcified plaques also may cause artifact on ultrasound that may interfere with accurate assessment. Magnetic resonance angiography (MRA) is another tool for carotid artery assessment. It is more expensive than the previous two modalities, but it is relatively safe and determines the anatomy well in plaque morphology. Black-blood imaging is a magnetic resonance sequence in which blood is black and vessel walls are enhanced, which contribute to determination of plaque morphology. Angiography can be performed without gadolinium contrast by using time-of-flight sequence, which provides high-density signals for flowing blood. In addition, PC imaging also can give blood flow velocity pressure information across stenotic lesions. In general, CT and MRI are used only in the cases where vascular ultrasound is limited or when a patient requires carotid endarterectomy for carotid artery stenosis.

Coronary Blood Flow:

Anatomy:

Most people have two coronary arteries that originate from the left aortic sinus and right aortic sinus in turn. The left main coronary artery differs in the length before the left anterior descending artery (LAD) and left circumflex artery (LCX) branches arise from it. In most cases, LAD coronary artery supplies blood to nearly 50% of the left ventricular mass (approximately 150gr), which includes two-thirds of the intraventricular septum and the left ventricular anterior wall. The right coronary artery supplies blood to more than 30% of left ventricular mass (about 90gr), which includes one-third of the posterior interventricular septum and half of the posterior wall. The remaining 20% of the left ventricular mass is supplied by LCX coronary artery (Rosa Mp, Portal Vl., 2010).

B-3-2 Mechanical Determinants of Coronary Blood Flow: Coronary Perfusion Pressure:

Like other perfusion circulations, coronary myocardial blood flow is dependent on existing pressure. In physiological conditions, the diastolic aortic pressure becomes the input pressure of the coronary perfusion. On the other hand, the aortic diastolic pressure, along with cardiac dimensions, determines after load of the left ventricular, and consequently are myocardial oxygen consumption. Therefore, any reduction in aortic pressure not only increases coronary perfusion pressure but also increases metabolic needs of coronary blood flow. In elderly patients with reduced arterial compliance which leads to an increase in systolic and diastolic blood pressure and reduction of its dialectic pressure, especially in relation with arterial hypertension, the created condition will not be quite suitable for matching coronary blood flow to myocardial oxygen consumption. Similarly, aortic stenosis (which causes increased left ventricular systolic pressure and relative decrease of the aortic diastolic pressure) and aortic regurgitation (which causes decreased aortic diastolic pressure) are conditions that lead to mismatch between coronary blood flow and myocardial oxygen consumption. In the presence of coronary stenosis, the post-stenotic coronary pressure becomes the input pressure of the myocardial perfusion (Ebadi, Ahmad, et al., 2014; Firoozabadi, Mehdi Dehghani, and Ebadi. A., 2014; Firoozabadi, Mehdi Dehghani, et al, 2014).

Coronary artery bypass graft (CABG):

The number of patients who undergo CABG has increased greatly in recent years, so that it is the most common major surgery performed in the United States today, partly due to advances in heart surgery which in turn reduce the risk of mortality. Following decreased mortality, morbidity becomes increasingly more important because of its fundamental role in improving the outcome of surgery and postoperative quality of life. CABG improves survival in patients with significant left main coronary artery disease (CAD), 3-vessel CAD, and ventricular dysfunction. CABG also improves the quality of life in patients with “left main equivalent” CAD (proximal left anterior descending and proximal left circumflex), but does not protect them from the risk of subsequent infarction. In patients who were candidates for CABG, the severity of angina pectoris reduced 90% after surgery. The most important mechanism of improvement of survival and left ventricular function after CABG is restoration of achievable perfusion but without or with negligible contraction of myocardium. The rates of hospital mortality for coronary bypass surgery in low risk patients can be less than 1%. Myocardial
Concomitant carotid and coronary artery disease:

Although the number of patients with concomitant carotid and coronary disease is not too high, they are at high risk in comparison to patients with only carotid or coronary disease. CABG is the treatment of ischemic heart disease. Advances in the field of conservation, CBP technology, and postsurgical care during the past three decades have been related with reduced CABG-associated morbidity and mortality. However, stroke is remained as the major non-cardiac complication of CABG and affects patient’s quality of life, economic status, and survival. Although the overall incidence of CABG-related stroke is approximately 2%, the role of extra cranial carotid disease on stroke remains unclear. In various studies, the incidence and morbidity of CVA in patients undergoing CABG is about 2.1-5.2% and 0-38%, respectively, and regardless of mortality, CVA is the most serious complication of surgery which disables patients and increases the costs and hospitalization (Ebadi, Ahmad, et al., 2014). There are several mechanisms which can cause perioperative stroke in patients undergoing CABG. Embolism can arise from a variety of sources, such as arrhythmias, left ventricular thrombus, dissection of aorta, microemboli, aortic arch, fragile aorta due to its closure, and aortic catheterization, fat and air (Firoozabadi, Mehdi Dehghani, and Ebadi, A., 2014). In a study, the following risk factors (with odds ratios) are presented for CABG perioperative stroke; preoperative factors including carotid stenosis (%5.3), history of subcortical small vessels ischemia (%4.1), history of cerebrovascular disease (including transient ischemic attack or stroke) (%2.1), history of diabetes (%2.8), atherosclerotic ascending aorta (%2.0), history of peripheral vascular disease (%2.0), hypertension (%1.8), smoking (%1.6), previous cardiac surgery (%1.4), and history of high pulse pressure (1.1 for every 10 mm Hg increase); intraoperative factors including hypotension (*8.4), manipulation of atherosclerotic ascending aorta (%1.8), cardiopulmonary bypass for more than 2 hours (%1.4); and postoperative factors including atrial fibrillation (0.6 and 2.6 in two different studies) (denotes the adjusted odds ratios) (Firoozabadi, Mehdi Dehghani, et al., 2014). Concurrent endarterectomy (CEA) and CABG was first introduced by Bernhard et al. in 1972 to reduce the risk of mortality and disability from concomitant carotid and coronary disease. Recent attention paid again to this strategy is arisen from controlled trials which show the benefits of combined CEA in both asymptomatic and symptomatic carotid artery severe stenosis. The post-CABG causes of stroke are multifactorial. Univariate analysis of systematic review of CABG-associated stroke has been identified the following factors; carotid stenosis 80% or higher, carotid occlusion, previous stroke or transient ischemic attack (TIA), peripheral vascular disease, post-infarction angina, female gender, prolonged CPB, aging, previous CEA, diabetes, smoking, hypertension and carotid bruit (Branthwaite, M.A., 1975). Brent et al. proposed that simultaneous operation of coronary artery graft and CEA in patients with concomitant coronary and carotid artery disease can reduce mortality and morbidity in these patients (Rockman, C.B., et al., 2004). Detection of significant stenosis by auscultation is unreliable. Carotid bruit may be heard with the smallest carotid stenosis or not heard even when the lumen is only 1-2 mm. Combination of carotid artery ultrasound and risk factors may have predictive value for patients who are at risk of post-CABG stroke (Berens, E.S., et al., 1992; Auastasiadis, K., et al., 2009; Szabol, S.Z., et al., 1994; Ikuof, Seigo G., S. Jun, 2000; Rath, P.C., et al., 2001). Carotid artery disease should be considered in all patients with ischemic heart disease. Faggieri et al. reported the incidence of carotid artery disease, which is defined as carotid stenosis, as 75% in patients older than 60 years; this was reported 11% in patients who underwent CABG. Recently, ultrasound has shown higher incidence of patients with severe carotid and coronary disease than previous studies.

Conclusion:

Carotid disease should be evaluated with ultrasound in patients who undergo CABG, because it was shown that 20% of them may have unilateral or bilateral carotid stenosis. Major systemic studies on stroke and CABG pointed out the relationship between increase in stroke and higher degrees of carotid stenosis (Branthwaite, M.A., 1975). But in order to further identify risk factors and inflammatory complications, it is recommended to perform further clinical trials in this field (Iewis, B., et al., 1995; Rashid, S., et al., 1996; Zayde, H., et al., 2009; Akhtar, W., et al., 2009; Shuzou, T., et al., 2005).

REFERENCES


