The Effect of Cardiovascular Risk Factors and Coronary Atherosclerosis Severity on Long Term Graft Patency Rate in Patients Who Underwent Coronary Artery Bypass Graft Surgery

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ABSTRACT

Introduction: The postoperative success of coronary artery bypass grafting depends on graft patency rate. The atherosclerotic process goes on in native arteries and bypass grafts of patients who underwent coronary artery bypass graft surgery. In this study, we aimed to investigate the effect of preoperative cardiovascular risk factors and the extensity of atherosclerosis detected by coronary angiography on long-term graft survival after the operation.

Patients and Methods: We included 974 patients (738 males, 236 females, mean age 57.9 ± 9.0 years) who underwent isolated coronary artery bypass graft surgery between the years 1990-2010 and coronary angiography due to various reasons during their follow-ups. The cardiovascular risk factors of the patients were detected and the extensity of coronary artery disease in the pre-operative coronary angiographies was determined by calculating Gensini Score Index. The effect of these results on graft patency was analyzed.

Results: As a result of coronary angiography, overall graft patency rates were found to be 52.6%, 64.6%, and 38.4% in the 1st, 5th and 10th years, respectively. Arterial grafts showed better patency rates than venous grafts in both short-term (1st year) and long-term (5th and 10th years). Independent cardiovascular risk factors were age (beta: 0.006, p= 0.001), smoking (beta: 0.101, p= 0.003), and family history (beta: 0.063, p= 0.03) for all occluded grafts. Diabetes mellitus (beta: 0.03, p= 0.02) and Gensini Score Index (beta: 0.01, p= 0.03) were associated with occluded left internal mammary artery graft. Age (beta: 0.05, p= 0.002), smoking (beta: 0.073, p= 0.002), and Gensini Score Index (beta: 0.001, p= 0.002) were associated with occluded saphenous vein graft. Smoking (beta: 0.047, p= 0.001), family history (beta: 0.033, p= 0.013), and Gensini Score Index (beta: 0.001, p= 0.001) were associated with occluded right internal mammary artery graft.

Conclusion: According to short and long-term results of a large group of patients, graft atherosclerosis was associated with cardiovascular risk factors, the extensity of coronary atherosclerosis, type and duration of graft. Today, primary and secondary cardiovascular risk factors should be improved to achieve higher long-term graft patency rates.

Key Words: Coronary artery disease; heart disease risk factors; coronary artery bypass grafting.

Koroner Arter Baypas Greft Cerrahisi Yapılan Hastalarda Kardiyovasküler Risk Faktörlerinin ve Koroner Ateroskleroz Ciddiyetinin Uzun Dönem Greft Açıklık Oranına Etkisi

ÖZ

Giriş: Koroner arter baypas greft cerrahisi sonrası başarı, greft açıklığı ile doğru orantılıdır. Koroner arter baypas greft operasyonu geçiren hastalarda nativ arterler ve baypas greftlerinde aterosklerotik süreç devam eder. Bu çalışmanın amacı, koroner arter baypas greft cerrahisi öncesinde belirlenen kişiye ait kardiyovasküler risk faktörlerinin ve koroner anjiyografide saptanan ateroskleroz yaygınlığının operasyon sonrası uzun dönemde greft ömrüne etkisini araştırmaktır.

Hastalar ve Yöntem: Çalışmaya 1990-2010 yılları arasında izole koroner arter baypas greft cerrahisi uygulanan ve takiplerinde çeşitli nedenlerle koroner anjiyografileri yapılan toplam 974 hasta (738'i erkek, 236'sı kadın, yaş ortalaması 57.9 ± 9.0 yıl) dahil edildi. Hastalara ait kardiyovasküler risk faktörleri saptandı ve operasyon öncesi koroner anjiyografilerdeki koroner arter hastalığının yaygınlığı Gensini skor indeksi hesaplanarak belirlendi. Tüm bunların uzun dönem greft açıklık oranına etkisi analiz edildi.

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Bulgular: Koroner anjiyografi sonucunda; tüm greftlerde açıklık oranı birinci yılda %52.6, beşinci yılda %64.6, 10. yılda %38.4 olarak bulunmuştur. Açıklık oranları hem erken (birinci yıl) hem de geç dönemlerde (5 ve 10. yıl) arteryel greftlerde, venöz greftlerden daha iyiydi. Kardiyovasküler risk faktörlerinden yaş (beta: 0.006, p= 0.001), sigara (beta: 0.101, p= 0.003) ve aile hikayesi (beta: 0.063, p= 0.03) tüm greftlerin tıkanıklığında bağımsız risk faktörü olarak bulunmuştur. Tıkalı sol internal mammary arter ile diabetes mellitus (beta: 0.03, p= 0.02) ve Gensini skor indeksi (beta: 0.01, p= 0.03); tıkalı safen ven greft ile yaş (beta: 0.05, p= 0.002), sigara (beta: 0.073, p= 0.002), Gensini skor indeksi (beta: 0.001, p= 0.002); tıkalı sağ internal mammary arter grefti ile sigara (beta: 0.047, p= 0.001), aile hikayesi (beta: 0.033, p= 0.013), Gensini skor indeksi (beta: 0.001, p= 0.001) ilişkili bulunmuştur.

Sonuç: Geniş ölçekli bir hasta grubunda kısa ve uzun dönem sonuçların araştırıldığı bu çalışmada, greft aterosklerozu kardiyovasküler risk faktörleri, koroner aterosklerozun yaygınlığı, greft tipi ve greft süresi ile ilişkili bulunmuştur. Uzun dönem greft açıklık oranlarını artırmada günümüzde temel hedef, primer ve sekonder kardiyovasküler risk faktörlerinin iyileştirilmeye çalışılması olmalıdır.

Anahtar Kelimeler: Koroner arter hastalığı; kalp hastalığı risk faktörleri; koroner arter baypas greft.

INTRODUCTION

Coronary artery disease (CAD) is the most significant cause of mortality and morbidity in the world[1]. Atherosclerosis is the most critical and common reason for CAD[2]. Many risk factors are known to cause CAD. By controlling these risk factors in CAD, nonfatal coronary cases can drop, and cardiovascular deaths can also be reduced by half[1]. So, risk factors should be identified, and action should be taken against preventable risk factors.

Coronary artery bypass graft (CABG) surgery is a safe and effective treatment method and it has been used to treat multivessel disease for many years[3]. The atherosclerotic process goes on in native arteries and by-pass grafts after CABG surgery, and the postoperative success depends on graft patency rate[4]. In studies, many cardiovascular risk factors and biochemical parameters were reported to be critical initiating events of coronary atherosclerosis; however, the results of the impact of these risk factors on atherosclerosis progression after CABG and percutaneous coronary intervention (PCI) were contradictory[5].

In our study, we aimed to retrospectively investigate the effect of preoperative CV risk factors and the atherosclerosis severity detected by coronary angiography on long-term postoperative graft survival.

PATIENTS and METHODS

Hospital health records and computer-stored patient medical records from 1990 to 2010 were retrospectively reviewed for the study. Our study includes a total of 974 patients who underwent coronary angiography due to various reasons in our hospital after CABG surgery. Preoperative cardiovascular risk factors, demographic data, echocardiographic and biochemical parameters of the study population were recorded. The severity of CAD was determined based on the stenosis obtained in preoperative coronary angiography by calculating the Gensini score index (GSI)[6]. The year and reason of the postoperative coronary angiography and the rates for graft occlusion/stenosis were recorded.

Patients with moderate and severe valvular heart disease, cardiomyopathy, hepatic insufficiency, and malignancy and who underwent valvular surgery were excluded from the study.

Gensini Scoring System

Gensini score index (GSI) was calculated multiplying the Gensini severity coefficient determined for stenosis ratio (stenosis rates were 0-25%, 25-50%, 50-75% 75-90%, 90-99%, and complete occlusion, and the Gensini scores were 1, 2, 4, 8, 16, and 32, respectively) by the coefficient determined according to the functional importance of myocardial region supplied by the stenosed artery[6]. Accordingly, left main coronary artery (LMCA), proximal left anterior descending artery (LAD), proximal circumflex artery (Cx), and LAD medium segment were multiplied by 5, 2.5, 2.5, and 1.5, respectively, and right coronary artery (RCA), distal LAD, posterior descending artery (PDA), optus marginal (OM) artery were multiplied by 1, and the others were multiplied by 0.5. The number of grafts and the bypass graft information were obtained from medical records of the surgery.

Ethical Statement

The design of the study, prepared in accordance with the principles stated in the Helsinki Declaration, was approved by the local Clinical Research Ethics Committee.

Statistical Analysis

Mean + standard deviation was used for normally distributed continuous variables, and median (max-min) values were used for non-normally distributed continuous variables. Pearson correlation coefficient was used to calculate the relationship between continuous variables, and Spearman's correlation was used for non-continuous variables. The correlation coefficient (r) was calculated for the correlation analysis. The degrees of correlation coefficients were determined as follows: a low degree was between |0 and 0.25|, a moderate degree was between |0.25 and 0.50|, a strong degree was between |0.50 and 0.75|, and a very strong degree was between |0.75 and 1|. Linear regression analysis was used for multivariate analysis. $p< 0.05$ was statistically significant. SPSS 15.0 "Statistical Package for Social Sciences" software was used for all calculations.

RESULTS

Preoperative demographic and clinical variables of 974 patients are shown in Table 1. These patients first underwent isolated CABG surgery and then at least one year after the operation, they underwent angiography during their follow-ups. Of all the patients, 24.2% were female, and the mean age was 57.9 ± 9.0 years. Preoperative coronary angiographies showed that 20% had single-vessel disease, 35% had two-vessel disease, 45% had multiple vessel disease, and the mean GSI of the patients was 66.7 ± 33.3.

The information regarding the grafts used in surgeries of the study population was obtained from operation records. The rates of left internal mammary artery-left anterior descending (LIMA-LAD), saphenous vein graft-obtuse marginal artery (SVG-OM), and saphenous vein graft-right coronary artery (SVG-RCA) grafts used in the operations were 80.1%, 41.4%, and 29.4%, respectively.

The mean number of years that the patients had angiography was 5.2 ± 2.89 years with a minimum of 1 year and a maximum of 10 years. The coronary angiography was performed due to stable angina pectoris in 458 patients (47%), unstable angina pectoris in 82 patients (8.4%), non-ST myocardial infarction (MI) in 16 patients (1.6%), ST-elevation MI in 4 patients (0.4%), and atypical chest pain, dyspnea, heart deficiency, positive cardiac stress test, ventricular arrhythmia, and ischemia in thallium in 414 patients (42.5%).

As a result of the coronary angiography, graft patency was calculated in terms of years. The LIMA graft patency rates were 90.1%, 94.6%, and 95.3% in the 1st, 5th, and 10th years, respectively. The SVG patency rates were 73.6%, 83.5%, and 61.5% in the 1st, 5th, and 10th years, respectively. The right internal mammary artery (RIMA) graft patency rates were 92.9%, 93.6%, and 93.8% in the 1st, 5th, and 10th years, respectively.

Multivariate linear regression analysis revealed that age (beta: 0.006, p= 0.001), smoking (beta: 0.101, p= 0.003), prior MI (beta: 0.097, p= 0.02), prior PCI (beta: 0.078, p= 0.02), and family history (beta: 0.063, p= 0.03) were independent risk factors for all the occluded grafts (Table 2). Diabetes mellitus (DM) (beta: 0.03, p= 0.02), prior MI (beta: 0.038, p= 0.04), and GSI (beta: 0.01, p= 0.03) were independent risk factors for occluded LIMA graft (Table 3). Age (beta: 0.05, p= 0.002), smoking (beta: 0.073, p= 0.002), prior PCI (beta: 0.080, p= 0.02), ejection fraction (EF) (beta: 0.101, p= 0.004), and GSI (beta: 0.001, p= 0.002) were independent risk factors for occluded SVG (Table 4). Smoking (beta: 0.047, p= 0.001), family history (beta: 0.033, p= 0.013), peripheral artery disease (PAD) (beta: 0.059, p= 0.002), and GSI (beta: 0.001, p= 0.001) were independent risk factors for occluded RIMA graft (Table 5).

Table 1. Baseline demographic and clinical variables of the study population

Age (year)	57.9 ± 9.0	
Sex (male/female), n (%)	%75.8/%24.2	
BMI (kg/m^2)	28.1 ± 3.2	
Type 2 diabetes mellitus, n (%)	398 (%40.9)	
Hypertension, n (%)	858 (%88.1)	
Smoking status, n (%)	479 (%49.2)	
	Minimum (mg/dL)	**Maximum (mg/dL)**
Total cholesterol	99	429
Triglycerides	50	1111
HDL cholesterol	23	99
LDL cholesterol	33	338
Creatinine (mg/dL)	0.96 ± 0.6	
Family history	438 (%45)	
Peripheral vascular disease, n (%)	202 (%20.7)	
Prior myocardial infarction, n (%)	514 (%52.8)	
Prior percutaneous coronary intervention, n (%)	174 (%17.9)	
Prior cerebrovascular events, n (%)	42 (%43)	
Carotid artery disease, n (%)		
Mild (< %50)	162 (%16.6)	
Moderate (%50-69)	34 (%3.5)	
Severe (> %70)	32 (%3.3)	
EF (%)		
> %50	538 (%55.2)	
< %30	14 (%1.4)	

BMI: Body mass index, EF: Ejection fraction, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.

Table 2. Regression analysis giving information about independent predictors of all graft occlusions

	Beta	p value
Age	0.006	< 0.001
Smoking	0.101	0.003
Family History	0.063	0.03
Prior MI	0.097	0.02
Prior PCI	0.078	0.02

MI: Myocardial infarction, PCI: Percutaneous coronary intervention.

Table 3. Regression analysis giving information about independent predictors of LIMA graft occlusion

	Beta	p value
Type 2 DM	0.039	0.02
Prior MI	0.036	0.04
Gensini score	0.001	0.03

LIMA: Left internal mammary artery, DM: Diabetes mellitus, MI: Myocardial infarction.

Table 4. Regression analysis giving information about independent predictors of SVG occlusion

	Beta	p value
Age	0.005	0.002
Prior PCI	0.080	0.02
Smoking	0.073	0.012
EF	0.101	0.004
Gensini Score	0.001	0.002

SVG: Saphenous vein graft, PCI: Percutaneous coronary intervention, EF: Ejection fraction.

Table 5. Regression analysis giving information about independent predictors of RIMA graft occlusion

	Beta	p value
Smoking	0.047	0.001
Family history	0.033	0.013
PAD	0.059	0.002
Gensini score	0.001	0.001

RIMA: Right internal mammary artery, PAD: Peripheral artery disease.

DISCUSSION

In our study, long-term overall graft patency rates were 52.6%, 64.6%, 38.4% in the 1st, 5th, and 10th years after CABG surgery, respectively. Patency rates of arterial grafts were higher than those of venous grafts both in short (1st year) and long (5th and 10th years) terms. Detailed examination revealed that DM and GSI were independent risk factors for LIMA graft occlusion. Age, smoking, and GSI were independent risk factors for SVG occlusion.

Nearly 15% to 20% of all the grafts are occluded in the 1st year after CABG surgery[7,8]. Many occlusion occurs in the first month[9]. Vessel-specific factors (the diameter of the vein, perioperative trauma) have an impact on the graft occlusion that occurs within the 1st postoperative month, and atherosclerosis and intimal hyperplasia have an effect on the late graft occlusion (that occurs 1 year after surgery)[10].

In our study, age, family history, smoking, PAD, and prior MI were found to be independent risk factors for all occluded grafts. However, preoperative hypertension, DM, and high-low levels of lipids were found to have no effect on all occluded grafts. Previous studies also suggest various results. In a study by Kaya et al., age, sex, the existence of LMCA disease, DM, hyperlipidemia, and low EF were reported to have no effect on long-term graft patency rate[4]. In a study by Ulus et al., serum low-density lipoproteins (LDL) cholesterol level, and triglyceride level were reported to have an effect on graft occlusion[11]. Another study indicated that high serum lipid levels might be associated with delayed postoperative clinical events such as MI and PCI by causing atherosclerosis progression in the graft[12]. These various results show that the development and the progression rate of atherosclerosis are affected by multifactorial risk factors. Moise et al. reported that patients with high preoperative coronary angiography scores more commonly presented with atherosclerosis progression[2]. However, there are also studies indicating that coronary scoring is not predictive of the disease course because insignificant occlusions are also taken into account in scoring[13,14]. In our study, subgroup analysis results also reported a relation between LIMA, SVG, and RIMA occlusions and GSI.

The attrition rates of the internal mammary arteries are exceptionally lower than those of other veins; moreover, their patency rates (96.4% > 15 years) are great in the long-term[15,16]. Early occlusion and progressive atherosclerosis are rather rare in arterial grafts. Internal mammary artery (IMA) is commonly preferred in CABG surgery due to its different molecular and cellular structure and resistance to atherosclerosis[17,18]. In a study by Goldman et al., IMA graft patency was reported to be 95%, 87%, and 85% in the 1st, 5th, and 10th years, respectively[10]. In our study, LIMA graft patency was also found similar to other studies as we reported a 90%, 94.6%, and 95.3% patency rate in the 1st, 5th, and 10th years, respectively. DM, prior MI, and GSI were found to be independent risk factors for LIMA occlusion. Serum lipid level, hypertension, and other comorbid diseases were found to have no effect on LIMA occlusion. In studies, DM was reported to be a significant risk factor that affected mortality and morbidity in CABG surgeries[19,20]. In the literature, five-year patency rates for RIMA ranged from 52% to 95%[21,22]. In our study, the patency rate for RIMA was 92.9% and 93.8% in the 1st and 10th years, respectively.

Long-term patency rates are lower in vein grafts compared to arterial grafts as the atherothrombotic disease progression is faster in vein grafts[23]. The SVG has the potential to malfunction due to thrombosis in the first month because of the focal damage of venous endothelium during harvesting. Thus, intimal hyperplasia occurs from the 1st month to 12 months, and atherosclerotic lesions are observed after 1 year[24]. In a study by Barner et al., the patency rates of vein grafts were 95% and 74% in the 1st and 5th years, respectively[25]. In another study by Goldman et al., patency rates of SVGs were 84% and 61% in the 1st and 10th years, respectively[10]. The PREVENT IV (PRoject of Ex-vivo Vein graft ENgineering via Transfection IV) was a multi-center study which was conducted in 2014 in 1828 patients who underwent CABG, the study retrospectively examined the results of the control coronary angiography of these patients between the 12th and 18th months of the

operations[24]. As a result, SVG failure was defined as a ≥ 75% stenosis or occlusion. SVG failure occurred in almost 43% of the patients included in the study, and about 25 percent of vein grafts had failed.

In our study, patency rates of SVGs were found to be 73.6% and 61.5% in the 1st and 10th years, respectively. SVG occlusion has many factors associated with patient, graft, and surgery. The patient-related factors are age, female gender, malfunction of the left ventricle, renal failure, diabetes, and also risk factors for atherosclerosis[26]. In other studies, hyperlipidemia, hypertension, and low EF were primarily found to have an effect on the atherosclerosis progression of the vein graft[27,28]. In our study, smoking, age, GSI, prior PCI, and EF were reported to be independent risk factors for SVG occlusion.

LIMITATIONS

Our study was a retrospective study, so we only evaluated the effect of preoperative risk factors on graft patency and occlusion rates. We did not evaluate the effect of pre-and postoperative medical treatment on atherosclerosis progression. Technical differences among operations were also disregarded. We also did not evaluate the impact of graft occlusion rates which were obtained during long-term patient follow-up on clinical outcomes.

CONCLUSION

In conclusion, CAD risk factors alone have a limited effect on grafts. This might be due to the multifactorial development and progression of atherosclerosis. However, the struggle against risk factors should be handled individually as coronary atherosclerosis progression is known to continue in both native coronary arteries and bypass grafts.

Ethics Committee Approval: This study was approved by the Scientific Research and Evaluation Committee of Istanbul Bilim University Faculty of Medicine (Decision No: 24.12.2010/1).

Informed Consent: Informed consent was obtained.

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Author Contributions: Concept/Design - KS; Analysis/Interpretation - YT; Data Collection - KS, BD; Writing - KS; Critical Revision - ÇÇ, NY; Statistical Analysis - YT, SY; Overall Responsibility - KS; Final Approval - All of authors.

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