COMPARISON of MID-TERM ANGIOGRAPHIC RESULTS in DIABETIC and NON-DIABETIC PATIENTS AFTER CORONARY ARTERY BYPASS GRAFTING

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Summary

Diabetes mellitus is an established independent risk factor for significant morbidity and mortality for coronary artery bypass grafting. The impact of diabetes on bypass graft patency, development of new lesions and the rates of re-operation, re-intervention were assessed angiographically in 101 diabetic and 309 non-diabetic patients who had been operated between 1992-2001. The mean period of control angiography was 53.4 ±21.±2 vs 54.0 ±22.6 months. Compared with nondiabetic patients, the group with diabetes was older (61.3 ±10.7 years versus 59.4 ±11.2 years), comprised more women (26.7% versus 11.7% p=0,001), had more common triple-vessel disease (55.4 % versus 41.7%, p=0,02) and had lower ejection fractions (54.5 ±8.9 versus 56.6 ±8.5, p=0.03). A total of 309 (3.0 ±1.1) vs 902 (2.9 ±1.1) anastomosis was performed in 101 diabetic and 309 non-diabetic patients. The patency of left internal mammary artery -left anterior descending artery anastomosis were 95.9% vs 94.6% and 79.6% vs 73.7% in saphenous vein graft anastomosis. Development of new lesions were 37 (36.6 %) vs 79 (25.6%), (p =0.041); reintervention rates were 33 (32.7%) vs 85 (27.5%)(p =0.3). The reoperation rate was 0 % vs 0.6% , in diabetic and non-diabetic patients, respectively. Freedom from reintervention and reoperation were 67.3% vs 72.7% (p=0.3) in group I and group II. Although diabetes appeared to be an independent risk factor for development of new lesions, no correlation was found on graft patency and in reinterventions between diabetics and non-diabetics. ***(Arch Turk Soc Cardiol 2003;31:498-503)***

Key words: *Diabetes mellitus, coronary artery by-pass surgery, coronary angiography*

Özet

Koroner Bypass Cerrahisi Uygulanan Diabetik ve Non-diabetik Hastalarda Orta Dönem Anjiyografik Sonuçların Karşılaştırılması

Diabetes mellitus koroner bypass cerrahisi (CABG) uygulanan olgularda erken ve geç dönem sonuçlarını etkileyen bir risk faktörüdür. 1992-2001 yılları arasında konvansiyonel metodla CABG uygulanan olgulardan 101 diabetik ve 309 non-diabetik hastada operasyondan ortalama 53 ve 54 ay sonra anjiyografik olarak greft açıklığı, yeni lezyon gelişimi ve reintervensiyon-reoperasyon oranları değerlendirildi. Ortalama yaş diabetik grupta 61.3 ±10.7

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Received: 20 June, accepted: 12 August 2003

yıl, non-diabetik grupta 59.4 ±11.2 yıl saptandı. İki grup arasında preoperatif parametreler incelendiğinde kadın hasta oranı %26.7'ye karşı %11.7 (p=0,001), 3 damar hastalığı %55.4'e karşı %41.7 (p=0.02), sol ventrikül ejeksiyon fraksiyon değeri %54.5 ±8.9'a karşı %56.6 ±8.5 (p=0,03) saptandı. Diabetik grupta toplam 309, non-diabetik grupta toplam 902 distal anastomoz değerlendirildi. Buna göre her iki grupta sol internal mamari arterde ve safen vende açıklık oranı sırasıyla; %95.9'a, %94.6 (p>0,05) %79.6'a, %73.7 (p>0,05) olarak saptandı. Diabetik grupta 37 olguda (%36.6), non-diabetik grupta 79 (%25.6) olguda yeni lezyon gelişimi saptandı (p=0.04). Buna göre yeni lezyondan muaf olma oranı diabetik grupta %66.3, (%95 CI 81.4 –109.1 ay), non-diabetik grupta %76.6 (%95 CI: 98.5-118.8 ay) olarak saptandı (p>0.05). Reintervasyon oranı %32.7'ye, %27.5, (p>0.05) reoperasyon oranı ise %0 ve %0.6 (p>0.05) olarak saptandı. Buna göre reintervensiyon – reoperasyondan bağımsız yaşam oranı %67.3 (%95 CI: 84.7 –112.6 ay), %72,7 (%95 CI: 96–117 ay) olarak saptandı (p>0,05). Bu çalışmada CABG sonrası yeni lezyon gelişiminde diabet bağımsız bir risk faktörü olarak saptanmasına karşın orta dönemde diabetik ve non diabetik hastalarda greft açıklığı ve reintervasyon oranlarında istatistiksel olarak bir fark bulunamamıştır. ***(Türk Kardiyol Dern Arş 2003;31:498-503)***

Anahtar kelimeler: *Diabetes mellitus, koroner anjiyografi, koroner arter by-pass cerrahisi*

Diabetics are predisposed to coronary artery disease (CAD) and as a consequence approximately one-fifth of those undergoing coronary artery bypass grafting (CABG)[1-3]. Diabetes mellitus is a major independent risk factor for cardiovascular disease even after adjusting for other confounding risk factors such as age, hypertension, hypercholesterolemia and smoking[4]. Compared with non-diabetics, diabetics have a greater tendency for adverse effects on the coronary circulation, an increased propensity for accelerated atherosclerosis and a higher incidence of two and three-vessel disease and a lower incidence of one-vessel disease than do nondiabetic patients[5]. Therefore, diabetic patients constitute an important and more challenging segment of the population undergoing surgical coronary revascularization. Diabetes has been associated with higher perioperative morbidity as well as decreased survival after CABG[2,3,6]. Diabetic patients represent a large and complex subgroup of bypass patients. As the effects of diabetes are known to progress over time, studies incorporating both short and long-term follow-up are necessary. The revascularization strategy in diabetics is either percutaneous coronary interventions (PCI) or CABG but randomized controlled trials have shown that diabetics benefit mostly from CABG [7]. The aim of this retrospective study was to compare the mid-term angiographic results, reintervention rate and disease progression in diabetic and non-diabetic patients and to determine the predictors effecting on graft patency.

PATIENTS and METHODS

Patients

4388 patients underwent CABG during the period from June 1992 to January 2001. Seven hundred seventy-four patients (18%) were diabetic and 3614 (82%) were non-diabetic. 101(13%) of diabetic (group I) and 309 (8.5%) of non-diabetic (group II) patients were re-evaluated angiographically (74 male, 27 female; mean age 61.3 ±10.7 for group I, and 273 male, 36 female; mean age 59.4 ±11.2 for group II, respectively). In group I; mean duration of diabetes was 7.52 ±6.11 years. Characteristics, risk factors and left ventricular function (LVF) parameters of the patients were presented in Table 1.

Definitions of individual risk factors were as follows: diabetes mellitus= insulin-dependent or non-insulin dependent; hypercholesterolemia= total cholesterol level greater than 220 mg/dL; hypertension= diastolic blood pressure of 95 mm Hg or greater; smoking= use of cigarette more than half pack per day; positive family

history= atherosclerotic coronary artery disease in a first-degree relative.

Ventricular performance score as seen in Table 1 is a scoring system of LVF due to wall motion of the seven segments (antero-basal, antero-lateral, apical, inferior, postero-basal, postero-lateral and septal segments) of the heart at left and right oblique ventriculography, and defined as; normal: 1, hypokinesia: 2, akinesia: 3, dyskinesia: 4, aneursym: 5.

Table 1: *Patient characteristics and risk factors*

	DM (n:101)	Non DM (n:309)	p
Age (year)	61.3 ±10.7	59.4 ±11.2	0.29
Sex (female %)	26.7	11.7	0.001
Smoking (%)	47.5	58.6	0.06
Hypercholesterolemia (%)	24.8	24.3	0.9
Total cholestrol level (mean mg/dL)	215.8 ±38.1	219.8 ±45.2	0.4
Hypertension (%)	49.5	39.2	0.08
Familial history (%)	30.7	33.3	0.7
Prior MI (%)	40.6	38.1	0.7
Ejection fraction %	54.5 ±8.9	56.6 ±8.5	0.03
VPS (mean)	9.2 ±2.1	8.7 ±2.0	0.02
Vessel disease (%)			
One vessel	15.8	15.2	p= 0.8
Two vessels	28.7	44.0	p= 0.007
Three vessels	55.4	41.7	p= 0.02

MI: Myocardial infarction, VPS: Ventricular performance score, DM: Diabetes mellitus

Operative technique

All operations were performed under cardiopulmonary bypass and moderate hypothermia (28°-32°C). Cardiac arrest was performed by initial crystalloid cardioplegia (Plegisol, 4C, 15cc/kg) and myocardial preservation was supported with 400 cc cold blood cardioplegia in every 20 minutes and topical cooling. A hot shut was performed just before removal of the cross clamp. Insitu left internal mammarian arter (LIMA) was used as a graft to left anterior descending artery (LAD) whereas saphenous vein grafts (SVGs) were used to remaining vessels.

Quality assessment of the each anastomosed native coronary artery had been defined during the operation according to the diameter and plaque formation of the vessel. The plaque formation was evaluated both visual and palpation of the vessel and the diameter was assessed using 1, 1.5 and 2 mm metal-tipped coronary probes.

Table 2: *Operative data*

	DM	Non DM	
Approach			
Median sternotomy	101	309	
Number of bypassed vessels			
One	10 (9.9%)	38 (12.2%)	
Two	18 (17.8%)	78 (25.2%)	
Three	42 (41.5%)	90 (29.1%)	
Four	20 (19.8%)	82 (26.5%)	
Five	9 (8.9%)	16 (5.1%)	
Six	2 (1.9%)	5 (1.6%)	
Revascularization			
Complete	94 (93.1%)	289 (93.5%)	
Incomplete	7 (6.9%)	20 (6.5%)	
Use of LIMA			
Individual	98 (97%)	300 (97%)	
Use of SVG			
LAD	3 (1.4%)	9 (1.4%)	
Diagonal	38 (18%)	102 (16.9%)	
Intermediate	11 (5.2%)	32 (5.3%)	
Cx branches	89 (42.1%)	254 (42.1%)	
RCA	31 (14.6%)	86 (14.2%)	
RPD	39 (18.4)	119 (19.2%)	
Total	211	602	
Vessel Quality (mean)			
LAD	1.7 ±0.6	1.7 ±0.7	p= 0.9
Cx	1.7 ±0.7	1.6 ±0.6	p= 0.6
RCA	1.7 ±0.6	1.9 ±0.7	p= 0.1
RPD	1.6 ±0.5	1.7 ±0.7	p= 0.2

LIMA: Left internal mammarian artery, SVG: Saphenous vein graft, LAD: Left anterior descending artery, Cx: Circumflex artery, RCA: Right coronary artery, RPD: Right coranary posterior descending artery, DM: Diabetes mellitus unless otherwise indicated, numbers in parentheses are percentages

The findings were noted as follows

Grade 1: Normal distal run off, coronary artery > 1.5 mm

Grade 2: Intimal proliferation + minimal plaque formation, coronary artery ≥ 1,5 mm.

Grade 3: Intimal proliferation + multiple plaque formation, coronary artery ≤ 1,5 mm.

Grade 4: Endarterectomy

Operative data and the scoring of the vessel quality were presented in Table 2.

Control angiograms

Patient symptoms leading to angiographic assessment was; angina pectoris 75.2% vs. 72.7%, myocardial infarction 6.9% vs. 7.7%, congestive heart failure 6.9% vs. 5.1%, non-specific/control 10.8% vs. 14.1% in diabetic and non-diabetic groups respectively. Angiograms were assessed by a council of staff surgeons and cardiologists. Patency rate of each graft and newly developed vessel lesion were noted as follows; patent:

Table 3: *Angioggraphic data*

	DM				Non-DM			
	Patent	Occluded	Stenotic	Total	Patent	Occluded	Stenotic	Total
Type of graft								
LİMA	92 (93.8%)	4 (4%)	2 (2%)	98	282 (94%)	16 (5.3%)	2 (0.6%)	300
SVG	162 (76.7%)	43 (20.3%)	6 (2.8%)	211	421 (69.9%)	158 (26.2%)	23 (3.8%)	602
Bypassed coronary artery							1 (0.3%)	309
LAD	95 (94%)	4 (3.9%)	2(1.9%)	101	291 (94.1%)	17 (5.5%)	2 (1.9%)	102
Diagonal	30 (78.9%)	7 (18.4%)	1 (2.6%)	38	80 (78.4%)	20 (19.6%)	1 (3.1%)	32
Intermediate	7 (63.6%)	4 (36.3%)	0 (0%)	11	21 (65.6%)	10 (31.2%)	9 (3.5%)	254
Cx branches	70 (78.6%)	17 (19.1%)	2 (2.2%)	89	188 (74.0%)	57 (22.4%)	4 (4.6%)	86
RCA	21 (67.7%)	8 (25.8%)	2 (6.4%)	31	48 (55.8%)	34 (39.5%)	6 (5.0%)	119
RPD	28 (71.7%)	10 (25.6%)	1 (2.5%)	39	76 (63.8%)	37 (31.0%)		
Ejection Fraction (%)								
Preoperative		54.5 ±8.9			56.6 ±8.5	p= 0.03		
Postoperative		56.9 ±9.5			57.6 ±9.0	p= 0.5		
VPS (Mean)								
Preoperative		9.2 ±2.1			8.7 ±2.0	p= 0.02		
Postoperative		8.9 ±1.9			8.6 ±1.9	p= 0.1		

LİMA: Left internal mamarian artery, SVG: Sapheneous vein graft, LAD: Left anterior descending coronary artery, Dia: Diagonal coronary artery, Cx: Circumflex coronary artery Rca: Right coronary artery, RPD: Right posterior descending coronary artery. Unless otherwise indicated, numbers in parenthesis are percentages

no stenosis, occluded: non-opacified graft, partially patent: important; when stenosis >60 % and negligible; when stenosis < 40%, lesions between 40-60 % were evaluated by the aid of treadmill test and/or Thallium myocard perfusion scintigraphy. Newly developed vessel lesion: stenosis more than 60% of vessel when compared the baseline angiogram. Also the parameters of the LVF patients were noted. The angiographic results were presented in Table 3.

Statistical analysis

Results were expressed as mean value standard deviation unless otherwise indicated. Statistical analysis comparing two groups was performed with students t test for the means or x^2 or Fischer's exact test for categorical variables. Freedom from reintervention and reoperation plots showed the estimated survival probability by the Kaplan-Meier method, with log-transformed 95% point-wise confidence intervals. Comparison of patency rates according to time intervals was made by Log-Rank analysis.

RESULTS

Table 1 summarizes the patient characteristics and risk factors of the study groups and Table 2 the operative data.

Angiographical findings

The mean interval from operation to angiography was 53.4 ±21.2 vs 54.0 ±22.6 months (2 to 103 months) in diabetic and non-diabetic patients, respectively.

Graft patency is demonstrated in Table 3. Among different predictors, there were no detectable independent risk factors as a whole and between the groups for graft patency. The overall patency was not affected from any of the presumed risk factors; hypercholesterolemia (p=0.1) and hypertension (p=0.5), for group I, hypercholesterolemia (p=0.09) and hypertension (p=0.2), for group II.

Ventricular function

Although there was an improvement in the values of LVF parameters in both groups, the results did not differ statistically when compared with the preoperative values (p= 0.06 for EF % and p= 0.3 for VPS in group 1, p=0.1 for EF % and p=0.5 for VPS in group 2).

Development of new lesions is shown in Table 4. Freedom from development of new lesions was 66.3% in a mean period of 95.2 ±7.15 months (%95 CI 81.4 –109.1) vs. 76.6 % in a mean period of 108.6 ±5.2 months (%95 CI: 98.5-118.8) in group and group II, respectively (p=0.07).

Reintervention-reoperation

The reoperation rate was 0 % vs. 0.6% and reintervention rate 32.7 % vs. 27.5% in group I and group II, respectively (p=0.3).

Reintervention-reoperation free survival was 67.3 % in a mean period of 98.7 ±7.1 months (%95 CI: 84.7 –112.6) vs. 72.7% in a mean period of 106.5 ±5.4 months (%95 CI: 96–117) in group I and group II, respectively (p= 0.3).

DISCUSSION

As, confirmed with the literature[7,8]; we found that diabetic patients were older, had more extensive coronary artery disease, lower - preoperative ejection fraction and higher incidence of hypertension, previous myocardial infarction, class III-IV angina, and heart failure at the time of presentation. Surprisingly, the major concern; the graft patency did not differ between the groups in a mean period of 53.4 ±21.2 vs 54.0 ±22.6 months (2 to 103 months). When compared with non-diabetic patients, diabetics had a significantly higher triple vessel disease, higher rate of development of new lesion and accordingly more reinterventions. But, among different predictors, there were no detectable independent risk factors as a whole and between the groups for graft patency. The overall patency was not affected from any of the presumed risk factors such as hypercholesterolemia and hypertension. But, considerable scientific evidence indicates that the presence of both hypertension and diabetes accelerates the development of atherosclerosis more than either co morbid factor alone[9,10]. In our study, a significantly greater percentage of diabetic patients (49.5%) compared with non-diabetic patients (39.2%) had a history of hypertension. Also, in this group of patients the extension of atherosclerosis and accelerated atherosclerosis was more common.

Although coronary artery bypass grafting is well tolerated by diabetic patients, long-term survival continues to be poorer for these patients compared with their non-diabetic counterparts as a result of the underlying pathophysiology of diabetic heart disease. Our data revealed that there were no difference in graft patencies neither for LIMA-LAD grafts with 95.9% vs. 94.6% patency rates in group I and group II respectively nor for the SVG where the patency rates was 79.6 % in group I and 73.7 % in group II. The development of new lesions and correspondingly the rate of reinterventions were more common in the existence of diabetes mellitus. Our study was performed in retrospective fashion and patient follow-up, morbidity and mortality were not examined. These were the limitations of our study. The poor outcome, extension and acceleration of the CAD in the presence of diabetes were explained by the abnormalities in the vascular endothelium, abnormal endothelium dependent vasodilatation (decrease in the synthesis or release of nitric oxide) in both conduit arteries and resistance vessels of diabetic animals[11, 12] and humans[13-15]. This has been associated with greater inflammatory like responses to stresses such as ischemia-reperfusion, thus resulting in greater post-ischemic injury. Other possible mechanisms that explain endothelial dysfunction in diabetic patients include accelerated inactivation of nitric oxide by high levels of free radicals and advanced glycosylation end products[13]. Release of potent vasoconstrictor prostanoids[11,16], increased activation of protein kinase C[17], and decreased expression of inhibitory C proteins[18] may also be responsible in pathophysiology of endothelial dysfunction. Endothelial cell dysfunction in diabetics may serve as a major initiating process for the development of vascular disease in resistance vascular conduits. Nitenberg[13] reported a reduction in coronary flow reserve in epicardial arteries in diabetic patients compared with nondiabetics, correspondingly. Nahser[14] demonstrated reduced maximal coronary microvascular vasodilatation and increased impairment in the regulation of coronary flow of the myocardial resistance vessels in response to submaximal increases of myocardial demand in diabetics compared to non-diabetic controls. The

detrimental effects of sustained elevated glucose levels on the vascular endothelial cell and in the small resistance myocardial microvessels in diabetic patients may contribute to the adverse cardiovascular events, severe and extensive coronary artery atherosclerosis and reduced survival in diabetic patients after coronary artery bypass procedures. Despite all of the above mentioned pathophysiologic findings; our data revealed that the quality of the native coronary arteries did not differ between the groups.

As a conclusion; diabetes appeared to be a major risk factor for development of new lesions, but did not reach to statistical significance for reinterventions. This risk was accelerated in the presence hypertension but our angiographic data revealed no correlation in graft patency between diabetics and non diabetics neither for LİMA-LAD anastomosis nor for the SVG

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