The Effect of Type II Diabetes Mellitus on Early Morbidity after Mitral Valve Replacement for Mitral Valve Disease

Mitral Kapak Hastalığı Nedeniyle Mitral Kapak Replasmanı Yapılan Hastalarda Diyabetes Mellitusun Erken Morbiditeye Etkisi

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ABSTRACT

Objective: The impact of DM on post-operative morbidity and mortality after valve surgery is less well defined and the results of the studies are controversial. This study evaluated the effects of DM on post-operative short-term morbidity after isolated mitral valve replacement.
Methods: The study population included 214 consecutive patients undergoing isolated mitral valve replacement (MVR) with mechanical valves under cardiopulmonary bypass (CPB). Patients were divided into two groups; diabetics (group I, n=36) and non-diabetics (group II, n=178). The groups were compared with respect to pre- and post-operative creatinine and blood urea nitrogen (BUN) levels, post-operative cerebrovascular disorders, arrhythmia, post-operative revision due to blood loss, surgical site infection, post-opertive extubation time, intensive care unit (ICU) and in-hospital stay time, CPB and aortic cross-clamp time.
Results: In the diabetic group, post-operative rate of cerebrovascular disorders (13.9% vs. 2.8%; p=0.015), intubation time (11.5±7.6 h vs. 10.4±15.9 h; p=0.001), length of ICU stay (3.5±2.9 d vs. 2.7±2.1 d; p=0.001) and in-hospital stay (14.4±8.9 d vs. 11.1±6.9 d; p=0.023), rate of surgical site infection (19.4% vs. 3.9%; p=0.003), revision requirement rate (16.7% vs. 6.2%; p=0.045) were significantly higher. DM was also identified as an independent risk factor for surgical site infection, cerebrovascular disorder, arrhythmia and requirement of revision.
Conclusion: This study showed that DM not only increases short-term morbidity due to its multiple effects but is also an independent risk factor for surgical site infection, cerebrovascular disorder, arrhythmia and requirement of revision after isolated mitral valve replacement procedures. *(Gazi Med J 2011; 22: 105-9)*

Key Words: Diabetes mellitus, mitral valve replacement, morbidity

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ÖZET

Amaç: Diyabetes mellitus'un izole kalp kapağı operasyonları sonrası morbidite ve mortaliteye etkisi halen tam anlamıyla tanımlanamamıştır. Bizim çalışmamızın amacı da mitral kapak hastalığına bağlı izole mitral kapak replasmanı yapılan hastalarda diabetes mellitusun postoperatif erken morbidite üzerine olan etkisinin incelenmesidir.
Yöntemler: 2000-2010 yılları arasında Hacettepe Üniversitesi Tıp Fakültesi Kalp ve Damar Cerrahisi Kliniğinde mitral kapak replasmanı yapılan 214 erişkin hasta retrospektif olarak incelenmiştir. DM tanısı olan 36 hasta grup I'i, DM tanısı olmayan 178 hasta da grup II'yi oluşturmuştur.
Bulgular: Hastaların preoperatif özellikleri karşılaştırıldığında, serebrovasküler bozukluk, KOAH, aritmi ve renal fonksiyon bozukluğu açısından gruplar arasında farklılık saptanmadı. Ancak, preoperatif hipertansiyon öyküsü diabetik grupta istatistiksel olarak anlamlı olacak şekilde daha sık olarak görüldü. Preoperatif Ejeksiyon fraksiyon (EF) değeri de grup I'de grup II'ye göre anlamlı biçimde düşük bulundu. Grup I'de postoperatif serebrovasküler bozukluk oranı, postoperatif entübasyon süresi, postoperatif yoğun bakımda ve hastanede kalış süresi, yara yeri enfeksiyonu oranı ve revizyon oranı istatistiksel olarak anlamlı düzeyde yüksek saptandı (sırasıyla p=0.015, p=0.01, p=0.01, p=0.023, p=0.003 ve p=0.045). Postoperatif aritmi oranı, postoperatif renal fonksiyon bozukluğu, KPB süresi, aort klemp süresi ve erken mortalite açısından gruplar arasında anlamlı farklılık görülmedi. Diabet'in yara yeri enfeksiyonu oranını 5.9 kat (p=0.002), SVB oranını 5.6 kat (p=0.009), aritmi oranını 1.3 kat (p=0.497) ve revizyon oranını 3 kat (p=0.042) arttırdığı hesaplandı.

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Sonuç: Mitral kapak hastalığı nedeniyle MVR yapılan hastalarda DM birçok yönden risk faktörü oluşturarak erken dönem morbiditeyi olumsuz etkilemektedir. Kapak replasmanı planlanan ileri yaşlı ve ciddi risk profili içeren hastaların sayısının giderek arttığı da düşünüldüğünde DM'nin bu etkisi cerrahi planlamada değerlendirmeye alınmalıdır. *(Gazi Med J 2011; 22: 105-9)*

Anahtar Sözcükler: Diyabetes mellitus, mitral kapak replasmanı, morbidite

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INTRODUCTION

The number of patients of advanced age and high-risk profile requiring cardiac operations are increasing gradually. Despite this compilation, due to advances in cardiac surgical techniques and cardiac anesthesia management, cardiac surgical operations have become applicable for most patients with acceptable morbidity and mortality in recent years (1).

Diabetes mellitus (DM) is a multi-systemic disease and has a potential of increasing morbidity due to its effects on target organs including autonomic, immune, cardiovascular, renal, gastrointestinal and ophthalmic systems (2). The role of DM as a potential risk factor in cardiovascular diseases is well known. According to the data of the Department of Health and Human Services and Centers for Disease Control and Prevention in the United States, cardiovascular diseases arise in 38.1% of diabetic patients. Cardiovascular diseases are 3-5 times more common in diabetics. Post-operative complications are also more frequent than in non-diabetics (3-6).

DM is an important risk factor in coronary artery disease. Coronary lesions are widely distributed and progress of the disease is worse in diabetics (1, 7). Influences of DM after coronary artery bypass surgery (CABG) are well documented. Various studies showed that DM increases in-hospital morbidity and decreases long-term survival, particularly when peri-operative blood sugar management is poor (8-12).

The impact of DM on post-operative morbidity and mortality after valve surgery is less well defined and the results of the studies are controversial. Although some studies showed increased mortality in diabetics, others reported no difference between the groups. Whatever the case, in the Society of Thoracic Surgeons Quality Measurement Task Force study, which was published recently, DM is accepted as an important factor associated with in-hospital mortality and morbidity (13, 14).

The effects of DM on long term morbidity and mortality after isolated valve operations have not yet been described. Since determination of short and long-term survival in this particular group of patients may have influences on important steps such as operative strategy and selection of valve type, which are associated with progression of the valve disease, this topic should be evaluated and clarified with further studies. In this study, we aimed to evaluate the effects of DM on post-operative short-term morbidity after isolated mitral valve replacement.

PATIENTS AND METHODS

Patients

The study population included 214 consecutive patients undergoing isolated mitral valve replacement (MVR) with mechanical valves under cardiopulmonary bypass (CPB) for treatment of mitral valve disease between January 2000 and September 2010. After approval from the institutional review board, the medical records of the patients were retrospectively reviewed. Patients were divided into two groups; diabetics (group I, n=36) and non-diabetics (group II, n=178). Patients who underwent mitral valve repair or bioprosthesis replacement, tricuspid/aorta replacement or reconstruction and radio frequency ablation for atrial fibrillation were not included in this study. We excluded the patients undergoing concomitant CABG because they represent a different profile of patients from those presenting for isolated valve operations.

Definition of Peri-operative Variables

Cardiac and valvular function was assessed by transthoracic echocardiography (TTE). Cardiac catheterization was performed for further investigation on selected patients. DM was defined as preoperative glucose intolerance either treated by diet only, with oral hypoglycemic drugs or with insulin. Peri-operative treatment of constantly high glucose levels (>120 mg/dl) in patients with diabetic disease was carried out by subcutaneous or intravenous application of insulin during the ICU-stay and establishment of pre-operative treatment either by diet, with oral hypoglycemic drugs or with insulin on the normal ward. Post-operative cerebrovascular accident (CVA), transient ischemic attack (TIA) and confusion/delirium were all accepted as cerebrovascular disorders. Cardiac rhythm disturbances including atrial and ventricular extra beats, supraventricular/ventricular tachycardia, heart blocks and need of pacemaker implantation were all grouped as arrhythmias. Renal dysfunction was defined as increased serum creatinine (≥2.0 mg/dl). Surgical site infections were separated into superficial and deep infections. Non-invasive (up to subcutaneous tissue) infections which heal only with antibiotherapy and local wound care were accepted as superficial. In contrast, invasive infections (muscle, bone and mediastinal involvement) which require debridement and drainage were accepted as deep infections. Revision was defined as chest reopening in almost all cases due to bleeding.

The groups were compared with respect to pre- and post-operative creatinine and blood urea nitrogen (BUN) levels, post-operative cerebrovascular disorders, arrhythmia, post-operative revision due to blood loss, surgical site infection, post-operative extubation time, intensive care unit (ICU) and in-hospital stay time, CPB and aortic cross-clamp time.

Surgical Technique

Standard CPB techniques for valve operations were used in all patients. Conventional CPB was typically performed using roller head pumps, membrane oxygenators, cardiotomy suction, arterial filters, cold antegrade cardioplegia and moderate systemic hypothermia (32° to 34°C). MVR was performed with mechanical mitral valve prostheses in the routine manner. Air removal maneuvers were performed before the cross clamp was released.

Statistical Analysis

Statistical analyses were calculated with SPSS 15.0 software (SPSS Inc, Chicago, IL, USA). Continuous variables are expressed as mean±standard deviation, categorical data as proportions. For continuous variables comparisons between patients with and without diabetes mellitus were carried out using the student's t-test for continuous variables with normal distribution or with the Mann-Whitney U test for those which were not normally distributed. Categorical variables were compared by χ^2 analysis. Adjusted odds ratios and 95% confidence intervals (CI) were computed for diabetes and each covariate. All tests were evaluated at the p=0.05 level.

RESULTS

Two hundred and fourteen consecutive patients were enrolled into the study and analyzed. Demographic and peri-operative characteristics are summarized in Tables 1 and 2. Etiology for MVR was shown in Figure 1.

The groups were similar with respect to age, history of cerebrovascular disorder and chronic obstructive pulmonary disease (COPD), pre- and post-operative arrhythmia and renal function and CPB and aortic cross-clamp time. In-hospital mortality was also similar between the groups.

However, history of hypertension was significantly higher in the diabetic group (group I: 47.2%, group II: 28.2%; p=0.03). Pre-operative ejection fraction (EF) was significantly lower in the diabetic group (group I: 48.7%, group II: 62.2%; p=0.03). Besides, in group I, post-operative rate of cerebrovascular disorders (13.9% vs. 2.8%; p=0.015), intubation time (11.5±7.6 h vs. 10.4±15.9 h; p=0.001), length of ICU stay (3.5±2.9 d vs. 2.7±2.1 d; p=0.001) and in-hospital stay (14.4±8.9 d vs. 11.1±6.9 d; p=0.023), rate of surgical site infection (19.4% vs. 3.9%; p=0.003), revision requirement rate (16.7% vs. 6.2%; p=0.045) were significantly higher. Comparison of peri-operative parameters between the groups was shown in Table 3. DM was also identified as an independent risk factor for surgical site infection, cerebrovascular disorder, arrhythmia and requirement of revision, as shown in Table 4.

DISCUSSION

An increasing number of patients with a history of DM are presenting for valve operations; thus, the effect of this disease on outcomes becomes important when discussing surgical options. DM continues to be a leading cause of cardiovascular disease and death, with a steadily increasing prevalence (15). Valve replacement procedures constitute nearly 20% of all open-heart surgical procedures and are responsible for 30% of overall mortality due to risk factors in this population (16). Therefore, before deciding surgical options, the effects of DM should be evaluated in this subgroup of patients.

The surgical risk of heart valve procedures is decreasing due to the progression of diagnostic methods, surgical techniques and anesthesia management. High-risk patients of the past have been operated with acceptable morbidity and mortality in recent years. Along with these advancements, increasing life expectation demonstrates to us the rearrangement of risk factors (17). Nowicki et al. (18) demonstrated the risk factors of MVR as female gender, advanced age, DM, concomitant CABG, history of stroke, high serum creatinine, NYHA class IV symptoms, urgent operation and chronic

Table 1. Patient demographics

Variable		n	(%)
Gender	Male	136	63.6
	Female	78	36.4
DM	Yes	178	83.2
	No	36	16.8
Medical treatment for DM	No	16	7.5
	Insulin	11	5.1
	OAD	2	0.9
Pre-operative HT	No	147	68.7
	Yes	67	31.3
Pre-operative COPD	No	197	92.1
	Yes	17	7.9
Pre-operative cerebrovascular disorder	No	198	92.5
	Yes	16	7.5
Pre-operative arrhythmia	No	144	67.3
	Yes	70	32.7
History of open-heart surgery	No	170	79.4
	Yes	44	20.6
Post-operative cerebrovascular disorder	No	204	95.3
	Yes	10	4.7
Post-operative arrhythmia	No	118	55.1
	Yes	96	44.9
Surgical site infection	No	200	93.4
	Superficial	13	6.1
	Deep	1	0.5
Revision requirement	No	197	92.1
	Yes	17	7.9

DM: Diabetes mellitus, HT: Hypertension, OAD: Oral anti-diabetic, COPD: Chronic obstructive pulmonary disease

Table 2. Patient characteristics

	Mean±SD	Median	Min-Max
Age	51.7±12.9	53	18-86
EF (%)	61.6±8.7	62	32-87
Intubation time (hour)	10.6±14.8	8	3-168
Pre-operative BUN (mg/dl)	17.7±9.4	15.7	3.4-83
Post-operative BUN (mg/dl)	18.7±13.3	15.4	7-107
Pre-operative creatinine (mg/dl)	0.87±0.43	0.8	0.3-4.0
Post-operative creatinine (mg/dl)	0.97±0.85	0.8	0.2-7.0
ICU stay (day)	2.9±2.3	2	1-24
In-hospital stay (day)	11.7±7.4	10	5-65
CPB time (minute)	73.1±29.5	65	33-197
Aortic cross-clamp time (minute)	50.1±20.5	45	15-146

EF: Ejection fraction, BUN: Blood urea nitrogen, ICU: Intensive care unit, CPB: Cardiopulmonary by-pass

Table 3. Comparison of peri-operative parameters

	Group I (n=36)	Group II (n=178)	P value
History of HT	17 (47.2%)	50 (28.1%)	0.030
History of cerebrovascular disorder	2 (5.6%)	14 (7.9%)	1.000
History of COPD	4 (11.1%)	13 (7.3%)	0.496
EF %	58.7±9.3	62.2±8.5	0.030
Pre-operative arrhythmia	17 (47.2%)	53 (29.8%)	0.066
Pre-operative renal function disorder	7 (19.4%)	13 (7.3%)	0.052
Post-operative cerebrovascular disorder	5 (13.9%)	5 (2.8%)	0.015
Post-operative arrhythmia	18 (50%)	78 (43.8%)	0.620
Post-operative renal function disorder	7.1 (19%)	29 (13.5%)	0.505
Intubation time (hour)	11.5±7.6	10.4±15.9	0.001
ICU stay (day)	3.5±2.9	2.7±2.1	0.001
In-hospital stay (day)	14.4±8.9	11.1±6.9	0.023
Surgical site infection	7 (19.4%)	7 (3.9%)	0.003
Revision requirement	6 (16.7%)	11 (6.2%)	0.045
CPB time (minute)	83.4±39.5	70.3±25.6	0.062
Aortic cross-clamp time (minute)	54.2±25.6	48.9±18.8	0.288
Death	1 (2.8%)	3 (1.7%)	0.524

EF: Ejection fraction, BUN: Blood urea nitrogen, ICU: Intensive care unit, CPB: Cardiopulmonary by-pass, HT: Hypertension, COPD: Chronic obstructive pulmonary disease

Table 4. Outcome variables significantly associated with DM

Outcome variables	Odds ratio (95% Confidence interval)	p value
Surgical site infection	5.9 (1.9-18.1)	0.002
Cerebrovascular disorder	5.6 (1.5-20.4)	0.009
Arrhythmia	1.3 (0.6-2.6)	0.497
Revision requirement	3.0 (1.0-8.8)	0.042

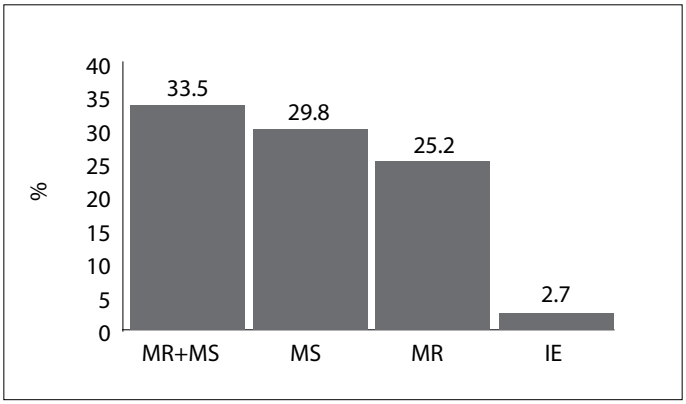

Figure 1. Etiology of MVR
MS: Mitral Stenosis, MR: Mitral Regurgitation, IE: Infective Endocarditis

renal failure. Roques et al. (19) pointed out EF, pulmonary hypertension, multiple valve replacement and concomitant tricuspid valve repair as additional risk factors. Concomitant CABG, tricuspid valve repair and arrhythmia surgery and multiple valve replacements are well-documented risk factors of mitral valve surgery. Therefore, we excluded these patients and evaluated the effects of DM on isolated mitral valve replacements.

The effect of DM on short-term and long-term outcomes after CABG has been well documented. Most studies have reported increased in-hospital mortality among patients with DM. Similarly, long-term survival is reduced after CABG in diabetic patients (8-12).

Several studies have evaluated diabetes as a risk factor for hospital morbidity and mortality after valve operations. In general, conclusions have been less consistent. Some studies have documented increased mortality whereas others showed no significant difference (9, 13-17). In conclusion, the effect of diabetes on long-term mortality after isolated heart valve operations is not well defined. In this study we investigated the effects of DM on post-operative short-term morbidity after isolated MVR.

Morricone and associates found a significant association between DM and postoperative renal insufficiency, a finding that emphasizes the systemic character of diabetic disease. Atherosclerosis, as one of the most reported diseases caused by diabetes mellitus, may affect several organ systems. As such, renal insufficiency due to atherosclerotic alterations of the renal arteries is not surprising (20-23). However in our study, renal function was similar between the groups. Creatinine level was slightly higher in both pre- and post-operative periods in the diabetic group but it was statistically insignificant.

DM is a well-known risk factor of atherosclerotic disease due to medial arterial calcification. As such, diabetics are at an increased risk of cerebral embolization. Due to the systemic character of atherosclerotic disease, involvement of the cerebral and carotid arteries leading to an impaired cerebral blood flow is not an uncommon finding. Additionally, auto-regulation of cerebral blood flow seems to be impaired by DM, potentially exacerbated intra-operatively during CPB (24-27). In this study, although the rate of cerebrovascular disorders were similar during the pre-operative period, cerebrovascular disorders were significantly higher in diabetics during the post-operative period.

In diabetic patients, hyperglycemia diminishes the bactericidal activity of leucocytes and impairs neutrophil function, which eventually increases surgical site infections (28, 29). Many studies demonstrated the increased risk of surgical site infection, sternal instability, mediastinitis and post-operative revision requirement after open-heart surgical procedures (30-33). We also reported a higher incidence of surgical site infection and post-operative revision requirement which are compatible with the literature.

Most of the reported postoperative complications associated with diabetic disease are followed by an impaired respiratory function. The impact of DM on post-operative respiratory insufficiency arises most probably both from the direct influence of DM on respiratory function and the indirect systemic pathway (21). Lauruschat et al. also reported a higher incidence of pulmonary complications in diabetic patients after CABG (34). In our study, the prolonged need for mechanical ventilation due to respiratory insufficiency in diabetics may be one reason for prolonged ICU-stay.

As expected and reported by other series, diabetic patients have longer ICU and in-hospital stay after open-heart surgical procedures, which may be explained by the overall negative impacts of DM on cardiovascular diseases (15, 21, 22, 32-35).

In conclusion, from these results it is apparent that the metabolic ramifications of this disease on survival are even apparent in valve patients without overt coronary disease. Our study showed that DM increases short-term morbidity due to its multiple effects after an isolated mitral valve replacement procedure. It is also an independent risk factor for surgical site infection, cerebrovascular disorder, arrhythmia and requirement of revision. Therefore, these data suggest that careful consideration should be given to the diabetic status when considering valve procedures.

Conflict of Interest

No conflict of interest was declared by the authors.

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