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Investigating of Aortic Diameter Effect on Mortality in Type 2 Diabetic Patients After Coronary Surgery: In Our Clinic Experience

Tip 2 Diyabetik Hastalarda Koroner Cerrahi Sonrası, Aortik Çapın Mortalite Üzerine Etkisinin Araştırılması: Klinik Deneyimimiz

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Özet

Amaç: Valvüler patolojisi olmayan normal sınırlarda kabul edilen aortik sinotubular junctional çap(SJD)' a sahip Tip 2 diyabetik hastalarda, SJD' si üst elli persentilde kalanlar ile alt elli persentilde kalanların, Koroner arter bypas greft operasyonu (KABGO) sonrasında görülen mortalitelerindeki farkın istatiksel anlamlığı araştırıldı.

Yöntem: : Ocak 2008 – Ağustos 2011 tarihleri arasında, Kalp ve Damar Cerrahisi(KVC) Kliniğinde, Assending aorta çapı cerrahi sınırın altında olan(<50 mm) konnektif doku hastalığı içermeyen, SJD' si normal sınırlarda olan Tip 2 diyabetik hastalara, izole on-pump CABG operasyonu yapılmış, 155 hasta çalışmaya alınmıştır. Hastalar operasyon için KVC kliniğine yatırıldıktan sonra, normotansif olacak şekilde medikasyonları düzenlenmiştir. M mode transtorasik echocardiography ile SJD minimum= 2.20 santimetre(cm), maksimum= 4.32 cm (median ± standart sapma 3.1 ± 0.41 cm) olarak ölçülmüştür. Median değer olan 3.1 cm sınır olarak alınmış; SJD' si 3.1 cm ve altında olanlar grup 1, SJD' si 3.1 cm' nin üstünde olanlar grup 2 olarak adlandırılmıştır. Bütün hastalara izole KABGO operasyonu standart cardiopulmonary baypass(CPB) ile uygulanmıştır. Operasyondan sonraki 30 gün içinde görülen ölüm vakaları çalışmaya dahil edilmiştir.

Bulgular: Grup 1' de 2, grup 2' de 4 exitus olmuştur. Masif iskemik ensefalopati 1 hastada, multiorgan yetmezliği 3 hastada, Low Cardiac Output Sendromu(LCOS) 2 hastada, mortalite sebebi olarak gözlenmiştir.

Sonuç: Grup 1 ve Grup 2 arasında KABGO sonrası ölüm oranlarında anlamlı bir fark bulunmamıştır. (2/72 versus 4/83, p=0.686).

Anahtar Kelimeler: Tip 2 Diyabet, Koroner Arter Bypas Greftleme, Torasik Aorta, Mortalite oranı.

Abstract

Objective: To compare the patients with a sinotubular junction diameter (SJD) in the upper percentile and those with a SJD in the lower percentile in terms of the mortality rates following coronary artery bypass grafting (CABG) among type 2 diabetic patients with a SJD within the normal limits who had no valvular pathology.

Method: One hundred and fifty-five type 2 diabetic patients with an ascending aorta diameter below the surgical limit (<50 mm), without any connective tissue disease, and with a SJD within the normal limits in whom isolated on-pump CABG surgery was performed in the Cardiovascular Surgery (CVS) Clinic between January 2008 and August 2011 were included. On M-mode transthoracic echocardiography, the minimum and maximum SJDs were found to be 2.20 cm and 4.32 cm (mean±standard deviation 3.1±0.41 cm). The mean value of 3.1 cm was accepted as the cut off value; patients with a SJD of ≤3.1 cm were constituted Group 1, whereas patients with a SJD of >3.1 cm constituted Group 2. Deaths within 30 days following the surgery were included in the study.

Results: Two patients in Group 1, four patients in Group 2 died. The causes of death were massive ischemic encephalopathy in one patient, multi-organ failure in three patients, and low cardiac output syndrome in two patients.

Conclusion: There was no significant difference between Group 1 and Group 2 patients in terms of mortality rates after CABG (2/72 vs. 4/83, p=0.686).

Keywords: Type 2 Diabet, Coronary Artery Bypass Grafting, Thoracic Aorta, Mortality Rate

Introduction

Atherosclerosis is a process involving the aorta as well as the coronary arteries. Advanced age leads to dilatation of the central aorta (1). Structural changes occur in the aorta with age. Such changes occur due to the weakening, fragmentation, and breakdown of elastin fibers in the media layer of the aorta, which are secondary to the repetitive tension cycles (2). Exposure to chronic, high intra-arterial pressure also leads to proximal aortic dilatation through a similar mechanism (3,4).

Diabetes itself is a problem for vascular structure. Moreover, diabetic patients have been found to be more prone to coronary artery disease, stroke, left ventricular hypertrophy, atrial fibrillation, and peripheral artery disease as compared to healthy individuals (5).

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Coronary artery bypass grafting (CABG) surgery is one of the most common procedures performed worldwide. Although surgical mortality is an unwanted complication, it is an inevitable result for certain types of patients. A risk scoring method, which is performed by scoring various data of the patients such as age, gender etc., was developed by the American College of Cardiology/American Heart Association (ACC/AHA) to estimate the percentage of mortality risk prior to CABG.

The fact that aortic root structure and sinotubular junction are affected by the factors having systemic reflections such as aging, hypertension, and atherosclerosis, has raised the thought that aortic sinotubular junction diameter (SJD) might be a risk factor for the mortality following CABG and formed a basis for the present study. The diameter of the aortic root changes with age, gender, height, body weight, and body surface area. In the present study, the size of the diameter was not evaluated, but it was aimed to compare the patients with a SJD in the upper percentile (3.1 cm < SJD < 4.32 cm) and those with a SJD in the lower percentile (2.20 cm < SJD ≤ 3.1 cm) in terms of the mortality rates following on-pump CABG among type 2 diabetic patients with a SJD within the normal limits who had no connective tissue disease and valvular pathology.

Materials and Methods

Clinical Characteristics of Patients

One hundred and fifty-five type 2 diabetic patients who underwent isolated on-pump CABG surgery in the Cardiovascular Surgery (CVS) Clinic between January 2008 and August 2011 were included in the present study. The patients had no valvular pathology and connective tissue disease (Marfan's syndrome, etc.) and their ascending aorta diameter was below the surgical limit (<50 mm). All patients were on antidiabetic agents. Data were collected retrospectively, and the study was approved by the Ethical Committee.

All patients were questioned in terms of personal medical history, and a detailed physical examination was performed on all patients. Standard laboratory analyses, respiratory function test (Spirobank Spirometry, MIR-Medical International Research Product), transthoracic echocardiography (TTE) (General Electric, Vivid S3 - Vivid S5), and bilateral carotid artery Doppler ultrasonography (Toshiba XARIO Prime Ultrasound) were performed in the CVS Clinic in the preoperative period.

Mortality risk was estimated preoperatively for all patients in accordance with the ACC/AHA guideline, which was updated in 2004 (6). and the mortality risk was calculated in percentages. According to this preoperative estimation of mortality risk, the following patient or disease characteristics are scored: age, female sex, diabetes(oral and parenteral antidiabetic agents using), chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), dialysis, a creatinine level of ≥2 mg/dL, a history of myocardial infarction (MI) within seven days prior to the surgery, previous CABG surgery, an ejection fraction (EF) of less than 40% (according to TTE), three vessel disease, a left main lesion between 50% and 89% or over 90%, a white blood cell (WBC) count of >12000/mm³, and emergency or urgent surgery (Table 1).

Echocardiographic Measurements

After hospitalization of the patients in the CVS clinic for surgical procedure, patients were medicated to maintain their blood pressure at normotensive levels, and standard TTE was performed. SJD was measured at maximum distention via M-mode TTE using Vivid S3 - Vivid S5 ultrasound device (General Electric) with a 3.5 mHz Linear probe. Internal diameters between the anterior and posterior walls were measured at end-systole. The minimum and maximum SJDs were found to be 2.20 cm and 4.32 cm (mean ± standard deviation 3.1±0.41 cm). The mean value of 3.1 cm was considered the cut-off value; patients with a SJD of ≤ 3.1 cm were constituted Group 1 and patients with a SJD of >3.1 were constituted Group 2.

Surgical Method

All patients underwent the first isolated CABG surgery with a standard cardiopulmonary bypass (CPB). Anesthesia induction was performed by fentanyl, midazolam, and pancu-

ronium bromide. After performing standard median sternotomy, the left internal mammary artery (LIMA) and other vascular conduits were prepared prior to the CPB. After administration of 300 IU/kg heparin, CPB was initiated with a roller pump using standard aortic and two-stage venous cannulas. During the surgical procedure, all patients were administered crystalloid, which was followed by cold blood cardioplegia, and terminal hotshot cardioplegia. CPB duration and cross clamp (X-clamp) time of all patients are presented in Table 2. While LIMA was used in all patients, the right internal mammary artery (RIMA) was not used. Meticulous aseptic technique was used was performed during the surgery. Unnecessary use of electrocautery and unnecessary perfusion during CPB were avoided.

Postoperative Care

Under normal conditions, all patients were given 100 mg/day asetyl salislycacid together with enteral nutrition postoperatively, as acetylsalicylic acid reduces the complication risk following CABG. Blood glucose level was strictly regulated with Lantus® flacon (Insulin glargine 100 IU/mL; Sanofi Aventis) and Humulin-R® flacon (Human soluble regular insulin 100 IU/mL; Lilly) both before and after the surgery. Three times per day Humulin-R® flacon and one per day Lantus® flacon (bed time) were performed according to blood glucose level of all patients. Oral antidiabetic agents were not performed. Insulin infusion was performed when necessary. Blood glucose levels of all patients were maintained below 200 mg/dL. Cefamezine IM/IV® (cefazolin sodium), which is used in our clinic as the standard prophylactic antibiotic, was administered at a dose of 1 g 30 min before the surgery and at a dose of 1 g at 8-h intervals for 48 h after the surgery.

Study patients stayed at the intensive care unit of CVS for 24 hours after the surgery; their drains and arterial catheters were removed within the next 24 hours and they were transferred to the CVS clinic. Central venous catheters were removed on the postoperative 2nd day. The patients were discharged from the hospital between the postoperative 4th and 11th days. Deaths within 30 days following the surgery were evaluated in the study.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS 14 Inc., Chicago, IL, USA). Parametric data were expressed as minimum, maximum, and mean ± standard deviation, whereas nonparametric data were expressed as frequency and percentage. While Student's t-test was used for independent variables, the Fisher's exact test (if assumed values were less than 5) and the Yates-corrected chi-Square test were used to compare categorical variables. The results were considered statistically significant if the two-tailed p value was 0.05 or lower ($p \leq 0.05$).

Results

Of the patients participated in the study, 63.9% (n=99) were males and 36.1% (n=56) were females. The mean age was 61±8.5 years in males and 62.1±7.9 years in females. The patients were dichotomized as Group 1 and Group 2 according to their SJD measurements.

Demographical, clinical and surgical data of the groups are presented in Tables 1 and 2. No significant difference was found between the groups in terms of the following parameters: presence of diabetes, COPD, PVD, or dialysis, having a creatinine level higher than 2 mg/dL, a history of MI within seven days prior to the surgery, previous CABG surgery, EF of less lower than 40%, three vessel disease, left main lesion between 50% and 89% or higher than 90%, and a WBC count of >12000 /mm^3, and need for urgent or emergency surgery, as well as age, body mass index, CPB duration, X-clamp duration, and the percentage of preoperative mortality risk. However, the rate of male patients in Group 1 and in Group 2 was significantly different (41.7% vs. 83.1%, $p<0.001$).

Coronary artery bypass graft with CPB was performed on all patients. The mean number of the grafts was 3±1, the mean volume of postoperative 24-hour drainage was 521±263 mL, the mean X-clamp time was 71±20 min, and the mean CPB duration was 104±28 min. Detailed descriptive data of the groups are presented in Table 2.

Table 1. Demographical characteristic of patients

	Group 1 (n=72)	Group2 (n=83)	P values
Gender (male)	30 (41.7%)	69 (83.1%)	<0.001**
Age(years)(mean±st. deviation)	60.9±9.1	61.9±7.5	0.482
Body Mass Index (kg/m²)(mean±st. deviation)	29.6±5.1	28.7±3.6	0.214
SJD(cm)(mean±st. deviation)	2.79±0.3	3.44±0.22	0.000
Diabet oral a/d parenteral a/d	43 (59.7%) 29 (40.3%)	60 (72.3%) 23 (27.7%)	0.138**
COPD	3 (4.2%)	8 (9.6%)	0.312**
PVD	0 (0%)	0 (0%)	1*
Dialysis	3 (4.2%)	3 (3.6%)	1*
Creatinine level ≥ 2mg/dl	5 (6.9%)	7 (8.4%)	0.964**
MI less than 7 days	2 (2.8%)	6 (7.2%)	0.286*
Prior CABG	1 (1.4%)	0 (0%)	0.464*
Ejection fraction EF< % 40	12 (16.7%)	15 (18.1%)	0.985**
3 vessel disease	43 (59.7%)	53 (63.9%)	0.716**
Left main disease (% 50-%89)	0 (0%)	3 (3.6%)	0.248*
Left main disease (≥% 90)	2 (2.8%)	3 (3.6%)	1*
Leukocytes >12000/ mm³	8 (11.1%)	3 (3.6%)	0.133**
Urgent surgery	2 (2.8%)	4 (4.8%)	0.686*
Emergency surgery	0 (0%)	0 (0%)	1*
Risk of mortality■ (mean±st. deviation)	1.01± 0.84	0.88± 0.91	349
Mortality	2 (2.8%)	4 (4.8%)	0.686*

SJD : Sinotubular Junction Diameter

■ : It was estimated at preoperative period and given percentage

* An expected cell value is less than 5. Fisher exact result was given.

**Chi-Squares with Yates corrected result was given

a/d : antidiabetic agent

Tablo 2. Operative data of patients

	Group 1 (n=72) (mean±st. deviation)	Group 2 (n=83) (mean±st. deviation)	P values
CPB time(minute)	107.6±30.2	102±27.4	0.225
X-clamp time(minute)	73.4±21.8	69±19.9	0.192
Number of grafts	3.35±1.05	3.22±1	0.430
24th hour drainage(mL)	477.3±262	559.3±259.5	0.053

CPB : Cardiopulmonary Bypass

The patients were monitored for mortality until the postoperative 30th day. Two patients from Group 1 and four patients from Group 2 died (2/72 vs. 4/83, p=0.686). The causes of death were massive ischemic encephalopathy, multi-organ failure, and low cardiac output syndrome (LCOS) in in one, three, and two of the six patients (Table 3).

Discussion

Normal aortic root, which is approximately 25 mm in length and has functional anatomical structure, is a transition zone between the left ventricle and the aorta. While the aortic annulus fibrosus, named as sinoventricular junction that is approximately 23 mm in diameter, forms its caudal border, the aortic ridge, named as sinotubular junction that is approximately 22 mm in diameter, forms its distal border. The sinotubular junction is definitely

Tablo 3 Demographical characteristics of death cases

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age(year)/gender	77/female	75/male	62/male	76/female	66/female	74/male
Antidiabetic agents	parenteral	oral	oral	oral	parenteral	oral
COPD/PVD	- / -	- / -	+ / -	- / -	- / -	- / -
Dialysis	-	-	-	-	-	+
Creatinine level ≥ 2 mg/dl	+	-	-	-	-	+
MI less than 7 days	-	-	-	-	-	-
Prior CABG	-	-	-	-	+	-
Ejection farction	%40>	≥%40	%40>	≥%40	%40>	≥%40
3 vessel disease	+	+	+	-	+	-
Left main disease	-	-	-	-	-	-
WBC > 12000/mm³	-	-	-	-	-	-
Urgent / emergency surgery	- / -	- / -	- / -	- / -	- / -	- / -
Body Mass Index	33.7	27.1	27.6	32.9	30	34.2
SJD (cm)	3.2	3.2	3.9	3.5	3.1	3
CPB time(minute)	121	148	120	62	170	100
X-clamp time(minute)	60	96	104	42	120	62
Preoperative risk of mortality(%)	6.9	1.3	1.8	1	4	3
Number of grafts	3	5	3	2	3	3
24th hour dranaige (mL)	300	350	300	500	150	250
Cause of death	MIE	MOF	LCOS	MOF	LCOS	MOF

COPD : Chronic Obstructive Pulmonary Disease
PVD : Peripheral Vascular Disease
SJD : Sinotubular Junction Diameter
MI : Myocardial Infarction
CPB : Cardiopulmonary Bypass
MIE : Massive Ischemic Encephalopathy
MOF : Multiple organ Failure
LCOS : Low Cardiac Output Syndrome

bordered between the sinuses of Valsalva and the ascending aorta. The ascending aorta is a structure that is approximately 55 mm in length and has a wall thickness of 2.5 mm; its diameter varies 22 mm to 47 mm according to age and gender (7).

Atherosclerosis is a process involving the aorta as well as the coronary arteries. Many studies have demonstrated the coexistence of aortic atherosclerosis with coronary artery disease or increased risk of stroke (7-9). There are studies showing that aortic root changes result from aging and aortic regurgitation (9, 10). In our study, there is no different mortality between patients who have wide aortic diameters and patients who have small aortic diameters after coronary surgery.

Advanced age is characterized by central arterial stiffness leading to increased pulse pressure and increased prevalence of systolic hypertension in the elderly (10-12). Proximal aorta stores the pressure and flow during systole and releases them during diastole due to the elastic elements in its wall (12, 13). Pulse pressure is affected by both structural and functional characters of the left ventricle and proximal aorta (13, 14).

Dilatation of the central aorta occurs with aging (14, 15). Structural changes occur in the aorta with age; such changes occur due to the

weakening, fragmentation and breakdown of elastin fibers in the media layer, which are secondary to the repetitive tension cycles (2). Exposure to chronic, high intra-arterial pressure also causes proximal aortic dilatation with a similar mechanism (3-4).

It is well known that the aorta does not act as a simple conduit in the cardiovascular system, but has a functional role (15, 16). Its functions may vary due to its elasticity; it may affect left ventricle work, coronary blood flow, and cerebral and peripheral circulation (16, 17). Such anatomical and functional changes can be seen on echocardiogram (17, 18). With advanced age, thickening of the aorta, atherosclerosis of the intima, cystic necrosis, elastin fragmentation, fibrosis of the media layer and medionecrosis, and fibrosis of the adventitia serve as histological indicators. Such aortic changes with aging cause a reduction in aortic elasticity (distensibility) and appear as pulse pressure widening (18, 19). Aging process of the aorta leads to a cycle of events in which increased pulse pressure causes greater aortic damage, which in turn results in greater increase in pulse pressure (19, 20). Measurement of the aortic diameter is an important method to estimate anatomical changes.

There is a significant association between wall thickening in the sinotubular junction and age. Age-related atherosclerotic changes and plaque formation were detected in the sinotubular junction. Local calcification and hemorrhages have been determined in the aged subjects (20, 21).. As a result of our study, there is no different mortality between patients who have wide aortic diameters and patients who have small aortic diameters after coronary surgery.

Cardiovascular diseases are the major causes of death among patients with diabetes (22). (21). Increased tendency to atherosclerosis in diabetic patients has been definitely specified (22, 23). Although the underlying mechanism has not been clarified in detail, there are evidences indicating that advanced glycation end-products (AGEs) play an important role in the pathogenesis (23, 24). Vascular diseases in diabetic patients are associated with impaired interaction between extracellular matrix and endothelial cells, cell separation, and premature cell death (24, 25). It has been determined that diabetic patients are more prone to coronary artery disease, stroke, left ventricular hypertrophy, atrial fibrillation, and peripheral artery disease as compared to the normal subjects (5).

In conclusion, in type 2 diabetic patients with normal aorta and no valvular pathology that underwent isolated CABG surgery with similar preoperative mortality risk, no statistically significant difference was found between the postoperative mortality rates of those with a SJD in the upper percentile and that of those with a SJD in the lower percentile according to mean value. In the light of these data, it can be suggested that a SJD within the normal ranges, either in the upper or in the lower percentile, does not statistically significantly influence the postoperative mortality. We believe that this issue should be investigated in further large-scale studies.

Study Limitations

In the present study, the rate of male patients was significantly higher in Group 2. The groups could not be matched for gender in the study population that has many characteristics.

Abbreviations

ACC/AHA : American College of Cardiology/American Heart Association
CABG : Coronary artery bypass grafting
COPD : Chronic obstructive pulmonary disease
PVD : Peripheral vascular disease
mL : Milliliter
cm : Centimeter
mm : Millimeter

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