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The Differences Between Gender in Intra- and Postoperative Results After Surgical Repair of Acute Type A Aortic Dissection

Akut Tip A Aort Diseksiyonunda Cerrahi Onarım Sonrası İntra- ve Postoperatif Sonuçlar Açısından Cinsiyetler Arasındaki Farklar

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ABSTRACT Objective: Acute aortic dissection is a severe disease that can be fatal and requires rapid treatment. Multiple clinical factors have been researched for the risk of acute dissection, but gender-related differences in this disease are still not clear. Female gender is related with worsened effects. The aim of this study is to compare gender differences in intra- and postoperative outcomes after surgical repair of acute type A aortic dissection. **Material and Methods:** We studied the records of 50 patients operated for acute type A aortic dissection between January 2011 and January 2015 in our hospital. We crosschecked the preoperative and postoperative results of patients. The primary endpoints of this study were in hospital mortality and discharging from the hospital and the secondary end points were long lasting entubation, long staying time in intensive care unit and in hospital. **Results:** The women were older than the men (64.67 vs. 63.73 years). The mean diameter of the ascending aorta was larger in men (56.15 mm vs. 53.83 mm). The cross-clamp time and total circulatory arrest time were longer in men, but the total time for cardiopulmonary bypass was longer in women (175.4 min. vs. 177.5 min.). Extubation time and intensive care unit stay were longer in women, but discharging from the hospital was longer in men. The mortality rate was 23,07% in men and 29,1 % in women. The differences between genders were not statistically significant. **Conclusion:** There was no significant difference in intraoperative data. When the time of extubation, period in intensive care unit, also time of hospital discharge and mortality were examined there were no significant difference in male and female gender. Postoperative inotrope use and the use of blood products were not affected by gender. Postoperative complications were similar between genders.

Keywords: Aortic dissection; gender; mortality

ÖZET Amaç: Akut aort diseksiyonu ölümcül olabilen ve hızlı tedaviye ihtiyaç duyan ciddi bir hastalıktır. Akut diseksiyon için risk olabilen birçok klinik faktör incelenmiştir ancak bu hastalıkta cinsiyet ilişkili farklar hala daha tam açık değildir. Kadın cinsiyet kötü sonuçlarla ilişkilendirilmiştir. Bu çalışmanın amacı, akut tip A aort diseksiyonunun cerrahi onarımından sonra intra- ve postoperatif sonuçlardaki cinsiyet farklılıklarını karşılaştırmaktır. **Gereç ve Yöntemler:** Hastanemizde Ocak 2011-Ocak 2015 yılları arasında tip A aort cerrahisi uygulanan 50 hastanın kayıtlarını inceledik. Hastaları preoperatif ve postoperatif verilerine göre karşılaştırdık. Bu çalışmanın birincil sonlanım noktaları hastane mortalitesi ve taburculuk zamanı ve ikincil sonlanım noktaları uzun süreli entübasyon, yoğun bakımda ve hastanede uzun süre yatış idi. **Bulgular:** Kadınlar erkeklerden daha yaşlıydı (64,67-63,73 yıl). Çıkan aortun ortalama çapı erkeklerde daha genişti (56,15 mm-53,83 mm). Kros klemp süresi ve total sirkülatuvar arrest süresi erkeklerde daha uzundu, ancak kardiyopulmoner baypas için toplam süre kadınlarda daha uzundu (175,4 dk-177,5 dk). Ekstübasyon süresi ve yoğun bakımda kalış süresi kadınlarda daha uzundu, ancak hastanede yatış süresi erkeklerde daha uzundu. Mortalite oranı erkeklerde %23,07, kadınlarda %29,1 idi. Cinsiyetler arasındaki farklar istatistiksel olarak anlamlı değildi. **Sonuç:** Cinsiyetler arasında intraoperatif veriler açısından istatistiksel olarak anlamlı farklar yoktu. Ekstübasyon süresi, yoğun bakımda kalış süresi, hastaneden taburcu olma süresi ve mortalite incelendiğinde de kadın ve erkek cinsiyet açısından anlamlı farklar yoktu. Ameliyat sonrası inotrop kullanımı ve kan ürünlerinin kullanımı da cinsiyetten etkilenmiyordu, postoperatif komplikasyonlar açısından da cinsiyetler arası anlamlı farklılık yoktu.

Anahtar Kelimeler: Aort diseksiyonu; cinsiyet; mortalite

Aortic dissections occur 2.6 to 3.5 times per 100.000 person-years in the general population.[1] Acute aortic dissection (AAD) involves a tear in the intimal aortic layer. Those with degeneration of the medial aortic layer are predisposed to this condition. Aortic wall tears can cause aortic dilatation, aneurysm formation, intramural hemorrhage, aortic dissection, or rupture. Aortic aneurysm, chronic hypertension, smoking, dyslipidemia, and cocaine use are risk factors for aortic dissection. Trauma and iatrogenesis are the other causes.

AAD can cause death in both sexes. Studies on sex-related differences in the outcome of cardiac surgery procedures reported high risk for women.[2] Several reasons have been explained for the worse outcome in female patients.[3] Older age and more preoperative comorbidities are common reasons. The incidence, age at admission, and the extent of dissected aorta are influenced by gender. On the other hand, it is unclear whether gender affects post-surgical clinical outcomes and survival.

MATERIAL AND METHODS

PATIENTS

Records of 50 patients (24 females and 26 males) who underwent surgery for acute type aortic dissection between January 2011 and January 2015 were reviewed at Ordu State Hospital.

Patients were divided into two groups according to sex. We compared the preoperative datas and postoperative outcomes between men and women. Acute type A dissection was defined as any dissection that involved the ascending aorta and/or aortic arch. Computed tomography angiography (CTA) and transthoracic echocardiography were used for diagnosis.

The primary endpoints of this study were in hospital mortality and discharging from the hospital and the secondary end points were long lasting entubation, long staying time in intensive care unit (ICU) and in hospital. Because of the retrospective structure of this study, permission from the ethics committee was not needed. All patients signed written informed consent and the study complied with the Declaration of Helsinki.

SURGERY

There were no significant differences in techniques between genders. Cardiopulmonary bypass was started with right atrial venous cannulation and right axillary arterial cannulation after median sternotomy. In some cases antegrade and/or retrograde cold blood cardioplegia was performed along the coronary sinus for myocardial protection.

A vent was placed through the right ventricle. After the average cooling temperature reaches 17 to 19 °C, the aortic clamp was taken out, total circulatory arrest (TCA) was started, and the aortic arch was inspected.

Intimal tear was resected, then aortic replacement and, if necessary, the aortic valve repair were done. The distal anastomosis was then completed under selective antegrade cerebral perfusion. Teflon (polytetrafluoroethylene) strips were used to strength both the proximal and distal suture lines. A Bentall procedure was performed if necessary. Postoperatively, patients were admitted to the ICU. If patients were hemodynamically stable, they were discharged from the ICU to the general cardiothoracic ward, usually on the second postoperative day. Patients were generally discharged from the hospital on postoperative day 7. Age, the mean diameter of the ascending aorta, the cross-clamp time, total circulatory arrest time and total cardiopulmonary bypass time, inotrope and blood product support, extubation time and ICU and hospital stay time were collected. Postoperative complications (pulmonary, renal, stroke, bleeding revision, stroke and mortality) were documented.

STATISTICAL ANALYSIS

The normal distribution of continuous data was examined with the Kolmogorov-Smirnov test, and the Levene test was performed for the homogeneity control of group variance. For descriptive statistics value, the mean value for continuous variables and standard error were calculated. For categorical variables the standard error frequency % and frequency were calculated. In the analysis of continuous data, the groups were compared using a student's t-test. Categorical variables were

analyzed by a chi-square test. If the expected frequency was smaller than 5, then Fisher's Exact test was used. A significance level of 5% was used in the calculations and explication of results. All calculations were performed with the statistical software package SPSS 23. The statistical power of the test is calculated by G * Power 3.1 program. In the study 51 people are needed to reach, to exceed 80% of the value of the work force; 5% level of significance and impact at the level of 0.5.

RESULTS

Table 1 shows the descriptive statistics for the characteristics and the results of the t-test. The women were older than the men on average (64.67±2.57 vs. 63.73±3.09 years). The minimum age was 35 years for men and 40 years for women, while the respective maximum ages were 86 and 94 years. The mean diameter of the ascending aorta was larger in men (56.15±1.63 mm vs. 53.83±1.71 mm). All patients had hypertension. The cross-clamp time and total circulatory arrest time were longer in men, but the total time for cardiopulmonary bypass was longer in women (175.4±13.70 vs. 177.5±15.10 min.). Extubation time and ICU stay were longer in women, as expected, but discharging from the hospital was longer in men (Extubation time: 24.8±5.88 vs. 29.2±5.77 hours; ICU stay: 3.9±0.88 vs. 5±1.31 days; discharge from hospital: 7.3±1.04 vs. 5.8±1.15 days). The differences between genders according to the t-test results were not statistically significant ($p>0.05$). Thus, there was no difference between men and women in terms of the features considered in this study.

Table 2 shows the postoperative characteristics for gender. The mortality rate was 26% over all, 23.07% in men (6 patients), and 29.1% in women (7 patients). Inotropic agents were used more often in females (16 patients vs. 14 patients), while blood products were unexpectedly used more often in males. Intra- and postoperatively total blood product requirement was a median of 3 units of packed red blood cells, 4 units of fresh frozen plasma, 3 units of platelets .

TABLE 1: Descriptive parameters.

Characteristics	Gender	n	Mean	Std. Error	Std. Deviation	Minimum	Maximum	P-Value
Age, year	Male	26	63.73	2.57	13.09	35.0	86.0	0.816[NI]
	Female	24	64.67	3.09	15.12	40.0	94.0	
Aortic Diameter, mm	Male	26	56.15	1.63	8.33	41.0	71.0	0.331[NI]
	Female	24	53.83	1.71	8.39	33.0	70.0	
TCA, minute	Male	26	37.81	2.60	13.26	20.0	78.0	0.518[NI]
	Female	24	35.42	2.58	12.64	17.0	64.0	
XCT, minute	Male	26	92.15	9.84	50.18	38.0	212.0	0.705[NI]
	Female	24	87.00	9.22	45.15	30.0	230.0	
CPB, minute	Male	26	175.4	13.70	70.00	103.0	310.0	0.919[NI]
	Female	24	177.5	15.10	74.00	98.0	350.0	
Diameter of Grafts, mm	Male	26	27.00	0.63	3.21	21.0	34.0	0.766[NI]
	Female	24	27.25	0.54	2.64	19.0	30.0	
Extubation time, hour	Male	25	24.84	5.88	29.38	0.0	144.0	0.595[NI]
	Female	24	29.25	5.77	28.28	0.0	120.0	
Bleeding, cc	Male	26	669.20	88.3	450.10	0.0	1700.0	0.945[NI]
	Female	24	660.40	91.20	447.00	0.0	1850.0	
ICU stay, day	Male	25	3.920	0.88	4.42	0.0	21.00	0.478[NI]
	Female	24	5.04	1.31	6.42	0.0	25.0	
Discharge from hospital, day	Male	26	7.35	1.04	5.29	0.0	20.0	0.333[NI]
	Female	24	5.83	1.15	5.65	0.0	23.0	

[NI]: not important for statically ($p>0.05$).

CPB:Cardiopulmonary bypass time; ICU: Intensive care unit; XCT: Crossclemp time TCA: Total circulatory arrest time.

TABLE 2: Postoperative characteristics for gender.

		Male		Female		
Characteristics	**Category**	**n**	**%**	**n**	**%**	**P-Value**
Blood Products Used (unit)	None	2	4.0	4	8.0	0.749[NI]
	<5	5	10.0	3	6.0	
	5-10	9	18.0	8	16.0	
	≥10	10	20.0	9	18.0	
Mortality	No	20	76.92	17	70.8	0.624[NI]
	Yes	6	23.07	7	29.1	
Concamitant Surgery	No	18	36.00	15	30.00	0.164[NI]
	CABG	0	0.00	3	6.00	
	AVR	4	8.00	5	10.00	
	Bentall	4	8.00	1	2.00	
Inotrope Use	No	12	24.00	8	16.00	0.263[NI]I
	Yes	14	28.00	16	32.00	

[NI]: not important for statically (p>0.05).

AVR: Aortic valve replacament; CABG: coronary artery bypass surgery.

When the test results in Table 2 are examined; it was seen that the use of blood products, mortality, concomitant surgery and the use of inotropic agents were not dependent to the gender (p>0.05).

Table 3 shows the postoperative complications in both groups. All complications were seen in similar number of patients and had similar rates. There were no statistically differences between genders.

TABLE 3: Postoperative complications.

Complications	**Men (n:26)**	**Women (n:24)**	**P-value**
Pulmonary (prolonged ventilation)	5 (19.2%)	6 (25%)	0.162 NI
Renal (ARF)	4 (15.3%)	3(12.5%)	0.64 NI
Stroke	1 (3.8%)	1(4.1%)	0.89 NI
Bleeding revision	3 (11.5%)	3 (12.5%)	0.105 NI
Mortality	6 (23.07%)	7 (29.1%)	0.624 NI

[NI]: not important for statically (p>0.05)

ARF: Acute renal failure; Prolonged ventilation: ventilation >72 hours.

DISCUSSION

Treatment of AAD depends on the location and extension of the tear. The Stanford system defines dissections as type A if they originate in the ascending aorta and as type B if they originate in the descending aorta.[4] Type A dissections require emergency surgery to prevent aortic rupture and death. Medical management is the preferred way to treat type B dissections. For untreated patients, AAD has a mortality of 33% in the first 24 h, which increases to 50% within the first week and 90% within 3 months.[4] Continued dilation that results rupture is the most common cause of death after operation for dissection. Factors associated with aortic enlargement are the location and size of the intimal tear, age <60 years at time of dissection, type B aortic dissection undergoing surgery at presentation, male gender, a large false lumen, the presence of blood in the dissection false lumen, partially or completely patent false lumen, elevated pulse pressure or systolic blood pressure and an initial aortic diameter of >4 cm postoperatively.[5,6]

Gender differences in cardiovascular disease are an area of interest and importance. In cardiac surgery, female sex has been thought to be a risk factor in the risk models of both the Society of Thoracic Surgeons and the European System for Cardiac Operative Risk Evaluation.[7,8] The differences are based on the neurohormonal situation. Estrogen affects the aorta and reduces the risk for dissection in younger women. Post-menopause, women lose this protection and face increased risk.

Numerous studies report the effect of female gender after isolated coronary artery bypass grafting (CABG). Alam et al. Goksedef et al. and Bagheri et al. reported worse results for women than men.[9-11]

However, Aldea et al. reported that the gender was not an independent indicator of death or post-operative complications, predicted hospitalization, arterial graft use, and size of revascularization.[12] And Uncu et al. reported the differences of gender in patients aged above 75 years undergoing CABG.[13] And they reported similar mortality rates. Symptom difference at the time of admission, different preoperative risks, and surgical factors are the causes of increased mortality and morbidity for women when compared to men who undergo CABG.

Other studies compare the differences by gender for other cardiovascular diseases, such as acute coronary syndromes (ACS) and abdominal aortic aneurysms (AAAs).[14] AAAs are more common in men than in women, for which estrogen may also play a protective role in premenopausal women. However, outcomes in women are worse than in men.[15] It is unclear what the specific reasons are for this situation.

Very few studies have researched diseases of the thoracic aorta. Mehta et al. reported that male gender conferred a survival benefit, while female gender was associated with increased mortality even after adjusting for age and various comorbidities in type A AAD.[16] In our study, women were older, but there was no significant difference (64.67±2.57 vs. 63.73±3.09 years). Nienaber et al. reported the largest study to date to examine the role of gender in AAD and its outcomes (346 women and 732 men).[17] Women were significantly older than men (67 vs. 60 years). In that study, nearly 50% of women were >70 years old, while only 29% of men were in this age group. There was a 4.7-hour delay in the female group compared to the males for the interval from symptom onset to diagnosis. Men applied within 6 hours of symptom onset, and 40% of women waited more than 24 hours before the initial diagnosis, perhaps because the symptoms were less typical: congestive heart failure and coma were more common presentations in women, but men had typical acute onset of chest pain. Similarly, the classical findings of pulse deficit and widened mediastinum in chest X-ray were less likely in women than in men. Hypotension or cardiac tamponade was elevated in women, and while risk of limb ischemia was higher in men. Mortality was higher in women.

Shih and colleagues reported worse outcomes in their female patients compared with their male patients.[18] Brar et al. reported higher 12-month mortality rates in women following diagnosis of aortic dissection in 714 patients.[19]

In our study there was no significant difference in age between men and women unlike these studies. Liu et al. studied 884 chinese patients and found that sex was not associated with long-term clinical outcomes.[20] Our study showed similar outcomes in both sexes.

Our results showed that complications with aortic dissection were similar between men and women. We found the mortality rate 23.07% in men (6 patients), and 29.1 % in women (7 patients). The difference between genders was not statistically significant (p=0.624).

In this disease population the use of blood products was very important. Although preoperative hemoglobin levels of women were generally lower than men as known , no significant difference was found in the use of postoperative blood products. On the other hand, there was more in men.

In another study, there were no significant differences between early and long-term outcomes between male and female patients operated for AAAD when they reviewed the records of 504 patients (245 women and 259 men) in spite of women were older.[21]

Conway and colleagues compared 251 patients (79 women and 172 men) for major morbidity, operative mortality, and 10-year survival.[22] They reported no significant differences between gender, too. Operative mortality rates were alike between women and men.

Our study showed there are no differences in early outcomes between male and female patients undergoing surgery for acute type A aortic dissection.

CONCLUSION

Women at risk for dissection (aortic aneurysm, severe hypertension and/or known connective tissue disease) should be evaluated carefully despite non-typical symptoms. Variable presentations and gender-related differences in treatment and outcomes must be examined by larger studies, and early diagnosis and successful surgery must be achieved in the future. Early recognition, and careful management (through improvement of surgical technique and postoperative management) are essential for optimizing patient outcomes.

Study Limitation

The operations in this study were performed in one center and despite the involvement of 6 surgeons, the surgical procedure was uniform. The retrospective nature of the study and the small study sample are the main limitations.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Mihriban Yalçın, Melih Ürkmez;* ***Design:*** *Melih Ürkmez, Serkan Yazman;* ***Control/Supervision:*** *Serkan Yazman, Melih Ürkmez;* ***Data Collection and/or Processing:*** *Mihriban Yalçın, Eda Gödekmerdan Katırcıoğlu;* ***Analysis and/or Interpretation:*** *Mihriban Yalçın, Serkan Yazman;* ***Literature Review:*** *Mihriban Yalçın, Eda Gödekmerdan Katırcıoğlu;* ***Writing the Article:*** *Mihriban Yalçın;* ***Critical Review:*** *Eda Gödekmerdan Katırcıoğlu.*

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