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Gender-Related Differences in Presentation and Outcome of Acute Type a Aortic Dissection

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ABSTRACT

Background: Although acute type-A aortic dissection (AAOD) is more common in males, the course of the disease may differ in females.
Objectives: We aimed to investigate the gender-related differences in patients with AAOD with regard to clinical presentation, short-term and long-term mortality.
Patients and Methods: Medical records of 192 patients with a confirmed diagnosis of AAOD in a University Heart Center from March 2004 through October 2015 were evaluated. Clinical information, hospital mortality, and long-term survival were explored with regard to gender. Propensity matching was performed to adjust for baseline differences. Kaplan-Meier survival analysis was used to determine the impact of gender on long-term mortality.
Results: Among 192 patients, 71 (37.0%) were females. The women were older (65.7 ± 13.8 vs. 53.9 ± 15.1 years, P < 0.001). Hypertension (77.5% vs. 56.7%; P = 0.006) and diabetes mellitus (12.7% vs. 0.1%; P = 0.001) were more common among women than men, while active smoking was significantly more prevalent in men (46.7% vs. 9.9%; P < 0.001). The frequency of various clinical presentations was not different between the two groups. Among men, 71.7% were surgically managed compared to 67.6% among women. In-hospital mortality was 50.7% in women and 42.1% in men and remained statistically similar after matching. For long-term survival female to male hazard ratio (HR) was 1.24 with 95% CI: 0.85 - 1.81 (P = 0.257), which basically remained unchanged after propensity matching, HR was 1.13, 95%CI: 0.73 - 1.73 (P = 0.300).
Conclusions: In patients admitted with AAOD, there was no gender-related differences in clinical presentation and type of management. Similarly, hospital and long-term mortality did not differ with regard to gender.

1. Background

Acute type-A aortic dissection (AAOD) is considered as a serious disease, which needs immediate diagnosis and treatment (1). With increasing number of patients undergoing surgery for management of AAOD, considerable improvement has been made with regard to the mortality rate (2). Although higher mortality in females in comparison to males is reported in some recent studies, there are no conclusive reasons for the observed disparity (3-6).

Along with the fact that AAOD more commonly occurs in males than in females, demographic characteristics and co-morbidities may differ in male and female patients (2, 5, 7). In addition, there might be some differences in pathophysiology of the disease in males and females (8, 9). On the other hand, presentation delay, less aggressive treatment and non-typical clinical presentation in females might also influence the course of AAOD, which ultimately alters the prognosis in females (5). Furthermore, pregnancy-associated hormonal and hemodynamic alterations in females rarely lead to aortic dissection in predisposed females (10, 11). While important insight has been gained with regard to AAOD in recent years, gender related differences and the associated impact on short-term and

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long-term mortality rate of patients in our region have not been investigated.

To further examine the gender difference in this potentially lethal medical/surgical emergency, we investigated the gender related differences in short-term and long-term outcome of AAOD. We hypothesized that female patients with AAOD experienced longer delay in healthcare access and, therefore, carried a higher hospital mortality compared to men with similar pathology. We further hypothesized that there was no difference in long-term survival between men and women once they survived the initial hospital admission and surgical repair.

2. Objectives

In this study, we aimed to investigate the gender-related differences in patients with AAOD with regard to clinical presentation, short-term and long-term mortality.

3. Patients and Methods

In this retrospective cohort study, we reviewed medical records of patients admitted to the University Heart Center from March 2004 to October 2015 with a confirmed diagnosis of AAOD. Definition of AAOD was based on Stanford classification and referred to the dissection of the thoracic aorta proximal to the take off of the left subclavian artery. The study was waived from obtaining informed consent due to its chart review design; however, care was taken to assure the patients' privacy. Hospital mortality within 30 days was the primary endpoint for this study. Previously reported hospital mortality ranged from 30% to 35% among females and 15% to 25% among males (12, 13). In order to detect a difference of 15% in hospital mortality between the two genders, a total of 72 patients were required in each gender to yield a power of 80%. The study design was reviewed and approved by the institutional review board of Tabriz University of Medical Sciences for its scientific and ethical merit. The secondary endpoints included long-term all-cause mortality and hospital length of stay. Intra-operative mortality as well as hospital mortality and long-term mortality stratified by therapeutic approach were also investigated in this study. In order to examine the possible effect of androgens and sex hormones on possible differences in hospital mortality, we compared hospital mortality rate in males and females within two major age strata (² 50 years and those > 50 years old). Demographic variables, co-morbidities and medication history, presentation symptoms/signs and results of para-clinical studies were documented in an Excel-based data collection spreadsheet. The frequencies of co-morbidities, presentation symptoms/signs, the results of para-clinical studies, echo-cardiographic findings and therapeutic approaches were compared in both genders. Delay in diagnosis was also documented. Following confirmation of diagnosis, the patients were offered emergent surgical repair of the aorta unless they already suffered from irreversible brain death or refused the surgical treatment. The patients were followed up after they were discharged from the hospital through routine annual visits in the cardiothoracic surgery clinic or by a phone call from a member of the study team.

All patients with AAOD were included if they were admitted within two weeks from the onset of the symptoms. Patients in whom the diagnosis could not be confirmed by computed tomography angiography, transthoracic/transesophageal echocardiography or conventional aortography were excluded from the study. Additionally, all patients with traumatic dissection of the aorta were excluded.

3.1. Statistical Analysis

All data were transferred from the Microsoft Excel-based data collection tool to a SPSS® ver. 22 (IBM Inc. Chicago, IL) worksheet. Normal distribution was examined using Kolmogorov-Smirnov test. Mann–Whitney U test (non-parametric) was used to compare numerical variables if the normality was rejected and independent t-tests were used for comparison if they deemed to have a normal distribution. Binomial and polynomial variables were analyzed using Fishers exact test and chi-square analysis, respectively. Kaplan– Meier analysis with log-rank statistics were used for comparisons of the landmark event of hospital death and long-term mortality between the two genders. To adjust the data for the confounding variables, 64 female patients were matched to an equal number of male patients using propensity scores with a 0.5 caliber. Hypertension, diabetes, smoking, age, prior stroke, history of bicuspid aortic valve, and hemoglobin concentrations on admission (with P values < 0.1 in univariate analyses) were included in logistic regression model to calculate the propensity scores and probabilities. Cox proportional-hazards models were also constructed with in-hospital mortality and long-term mortality; however, the total number of the tested variables were limited to 3 factors at a time due to the limited number of the events. Null hypotheses were rejected if p values were < 0.05.

4. Results

A total of 192 patients with a confirmed diagnosis of AAOD were included in this study. Of these patients, 121 were male (63.0%) and 71 (37.0%) were female. Of whom two were pregnant within their third trimester. In 58 patients (30.2%), surgical repair was not performed. Eighty-seven patients (45.3%) died during hospitalization. Follow-up data were available for 101 out of 105 patients, who were discharged from the hospital. The median follow-up time was 28 months (interquartile range; 11 to 69), which was similar in males (median: 31 months, Interquartile range; 9 to 73 months) and females (median: 27 months, interquartile range: 11 to 46 months), P = 0.395. The other 31 patients (29.5%) expired during the follow-up period.

4.1. Baseline Characteristics and Comorbidities

Baseline characteristics and medication history of AAOD are tabulated in Table 1 before and after propensity matching. Prior to propensity matching, hypertension (77.5% vs. 56.7%; P = 0.006) and diabetes mellitus (12.7% vs. 0.1%; P = 0.001) were more common among women than men, while active smoking was significantly more prevalent in males than in females (46.7% vs. 9.9%; P < 0.001). After data were matched, the observed differences in hypertension and diabetes between men and women disappeared.

Table 1. Gender Differences in Demographics, Co-Morbidities, and Medication History

	Before Matching			After Matching		
	Male, N = 121	Female, N = 71	P value	Male, N = 67	Female, N = 67	P value
Age (years)	53.9 ± 15.1	65.7 ± 13.8	< 0.001 *	59.3 ± 12.6	65.3 ± 14.0	0.010
Body Mass Index (kg/m2)	25.1 ± 3.9	26.3 ± 4.3	0.113	32.6 ± 30.6	32.7 ± 27.1	0.980
Marfan/Bicuspid Aortic Valve	10 (8.3%)	1 (1.4%)	0.094 *	0 (0.0%)	0 (0.0%)	-
Hypertension	68 (56.7%)	55 (77.5%)	0.006 *	45 (67.2%)	51 (76.1%)	0.250
Diabetes mellitus	1 (0.8%)	9 (12.7%)	0.001 *	1 (1.5%)	6 (9.0%)	0.052
Hyperlipidemia	7 (5.8%)	5 (7.0%)	0.764	6 (9.0%)	5 (7.5%)	0.752
Smoking	56 (46.7%)	7 (9.9%)	< 0.001 *	21 (31.3%)	7 (10.4%)	0.002 *
Chronic kidney disease (eGFR < 60 mL/min)	6 (5.0%)	5 (7.1%)	0.537	4 (6.0%)	5 (7.5%)	0.730
Congestive heart failure	11 (9.1%)	4 (5.6%)	0.579	8 (11.9%)	4 (6.0%)	0.226
Coronary artery disease	14 (11.7%)	12 (16.9%)	0.423	10 (14.9%)	11 (16.4%)	0.812
Cerebrovascular Accident	3 (2.5%)	6 (8.5%)	0.080 *	2 (3.0%)	6 (9.0%)	0.145
Chronic obstructive pulmonary disease	3 (2.5%)	3 (4.2%)	0.672	2 (3.0%)	2 (3.0%)	1.000
Valvular heart disease	5 (4.1%)	4 (5.6%)	0.728	4 (6.0%)	3 (4.5%)	0.698
Beta blockers	23 (19.0%)	21 (30.0%)	0.119 *	14 (20.9%)	21 (31.3%)	0.169
Digoxin	3 (2.5%)	1 (1.4%)	0.614	3 (4.5%)	1 (1.5%)	0.310
Calcium channel blockers	9 (7.4%)	7 (10.0%)	0.592	7 (10.4%)	6 (9.0%)	0.770
Acetyl salicylic acid	21 (17.4%)	11 (15.7%)	0.927	13 (19.4%)	10 (14.9%)	0.492
Statins	4 (3.3%)	3 (4.3%)	0.708	3 (4.5%)	3 (4.5%)	1.000
ACE-inhibitor/angiotensin-receptor-blocker	10 (8.3%)	10 (14.3%)	0.223	8 (11.9%)	9 (13.4%)	0.795
Diuretics	19 (15.7%)	8 (11.4%)	0.520	12 (17.9%)	7 (10.4%)	0.216

* Variables marked with asterisks were used for calculation of propensity matching

4.2. Gender Differences in Clinical and Laboratory Manifestations of AAOD

Table 2 shows the clinical manifestations and laboratory findings of patients. Chest pain was the most common presenting symptoms (70.3%) of AAOD followed by tachycardia (37.5%). Ninety male patients (74.4%) and 45 female patients (63.4%) had chest pain on hospital presentation (P = 0.141). Hemoglobin level was significantly lower in women (11.6 ± 1.7 g/dL vs. 12.8 ± 2.0 g/dL, P < 0.001).

Table 3 summarizes echocardiographic findings of the patients. Aortic root diameter was also larger in males (44 ± 9 mm vs. 40 ± 10, P = 0.013). The frequencies of significant valvular insufficiency were similar between females and males; however, pericardial effusion was significantly more common in women than in men (42.6% vs. 24.3%; P = 0.016).

4.3. Mortality and Adverse Outcomes

Heart rate was significantly higher in females (79 ± 19 vs. 88 ± 19 beat per minute, P = 0.002). After propensity matching, the heart rate was observed to be still higher in women (P < 0.001). Frequency of elevated cardiac troponin-I and acute electrocardiographic changes was

Table 2. Gender Differences in Clinical and Laboratory Manifestations of Acute Type-A Aortic Dissection

Clinical/Laboratory Finding	Total, N = 192	Men, N = 121	Women, N = 71	P value
Time from admission to operation (Hours)	18 (3 - 58)	19 (3 - 58)	15 (3 - 52)	0.823
Chest pain	135 (70.3%)	90 (74.4%)	45(63.4%)	0.141
Tachycardia	72 (37.5%)	41 (33.9%)	31 (43.7%)	0.231
Dyspnea on exertion	61 (31.8%)	37 (30.6%)	24 (33.8%)	0.748
Pain other than chest pain	50 (26.0%)	30 (24.8%)	20 (28.2%)	0.731
Gastrointestinal symptoms	34 (17.7%)	23(19.0%)	11(15.5%)	0.674
Shock (systolic blood pressure < 90mmHg)	34 (17.7%)	24(21.1%)	10(15.2%)	0.430
Palpitation	16 (8.3%)	7(5.8%)	9(12.7%)	0.162
Malaise and fatigue	12 (6.3%)	8(6.6%)	4(5.6%)	0.787
Syncope	10 (5.2%)	7(5.8%)	3(4.2%)	0.894
Cough	2 (1.1%)	1(0.8%)	1(1.4%)	0.789
Hemoglobin g/dL	12.4 ± 2.1	12.8 ± 2.0	11.6 ± 1.7	< 0.001 *
White blood cells x 1000/ µL	11.7 ± 4.2	11.9 ± 4.4	11.3 ± 3.8	0.384
Platelets x 1000/ µL	181 ± 77	175 ± 77	195 ± 73	0.085
Sodium mmol/L	142 ± 14	141 ± 14	143 ± 14	0.379
Potassium mmol/L	4.4 ± 0.5	4.3 ± 0.4	4.8 ± 0.7	0.312
Blood urea nitrogen mg/dL	26 ± 16	26 ± 17	25 ± 13	0.564
Creatinine mg/dL	1.5 ± 1.3	1.6 ± 1.4	1.3 ± 0.7	0.108
Triglyceride mg/dL	105 ± 64	104 ± 42	107 ± 109	0.979
High density lipoprotein mg/dL	36 ± 13	38 ± 14	33 ± 12	0.632
Low density lipoprotein mg/dL	98 ± 25	102 ± 27	76 ± 18	0.223

* Variables marked with asterisks were used for calculation of propensity matching

Table 3. Echocardiographic Findings of Patients with Acute Type-A Aortic Dissection

Finding	Total, N = 192	Men, N = 121	Women, N = 71	P value
Right ventricular diameter (cm)	3.1 ± 0.6	3.3 ± 0.7	2.7 ± 0.4	0.004*
Aortic insufficiency	124 (64.6%)	79 (70.5%)	45 (66.2%)	0.655
Mitral regurgitation	20 (10.4%)	15 (13.2%)	5 (7.2%)	0.318
Tricuspid regurgitation	19 (9.9%)	9 (7.6%)	10 (14.3%)	0.217
Pericardial effusion	57 (29.7%)	28 (24.3%)	29 (42.6%)	0.016*
Left ventricular ejection fraction (%)	50 ± 10	49 ± 10	51 ± 8	0.129
Aortic valve annulus (mm)	23 ± 5	24 ± 6	21 ± 3	0.004*
Aortic root (mm)	43 ± 9	44 ± 9	40 ±10	0.013*
Sinutubular junction (mm)	29 ± 10	30 ± 13	28 ± 8	0.483
Ascending aorta (mm)	53 ±13	53 ± 12	53 ± 14	0.798
Aortic arch (mm)	32 ± 9	32 ± 9	33 ± 7	0.760
Maximum aortic size	50.4 ± 17.1	50.4 ± 17.3	50.5 ± 14.6	0.968

* Variables marked with asterisks were used for calculation of propensity matching

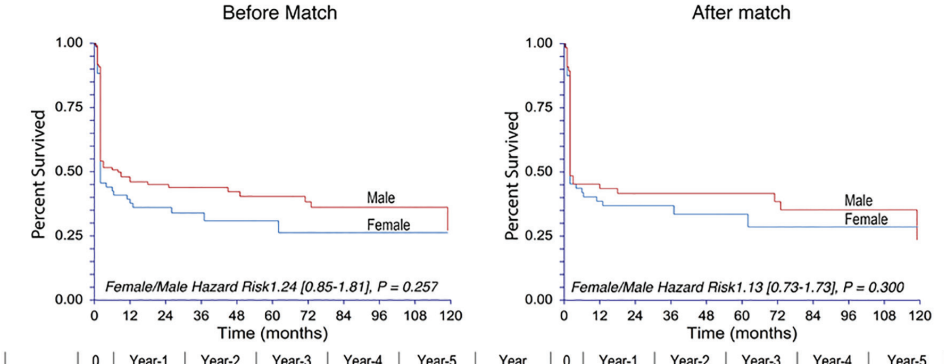
similar. Among men, 71.7% were surgically managed compared to 67.6% among women (P = 0.732). There was a strong trend in the operative mortality occurring in 3.4% of men versus 12.5% of female patients (P = 0.069). (See Table 4) Fifty-one men (42.1%) and 50.7% of women did not survive during hospitalization. Among surgically treated patients, in-hospital mortality was comparable between men and women (34.9% vs. 41.7%; P = 0.554). Likewise, in medically managed patients, in-hospital mortality was 60.0% in men and 69.6% in women (P = 0.644; Table 4).

During the follow-up period, 21.69 male patients (30.4%) and 10.32 female patients (31.3%) did not survive. There were no gender differences in long-term mortality before and after propensity matching. Although the survival plots included a 10-year follow-up period, the numbers of patients at risk was too few to draw reasonable conclusions beyond the initial period of 60 months and, therefore, at risk tables were confined to 5 years. For long-term survival, female to male hazard ratio (HR) was 1.24 with 95% CI: 0.85 - 1.81 (P = 0.257), which basically remained unchanged after propensity matching; HR was 1.13, 95% CI: 0.73 - 1.73 (P = 0.300) (Figure 1).

Table 4. Gender Differences in Mortality and Adverse Outcome of Patients with Acute Type-A Aortic Dissection

	Before Matching			After Matching		
	Male, N = 121	Female, N = 71	P value	Male, N = 67	Female, N = 67	P value
Heart Rate (bpm)	79 ± 19	88 ± 19	0.002	78 ± 17	88 ± 19	< 0.001*
Acute electrocardiographic changes	50 (41.7%)	22 (31.0%)	0.188	20 (29.8%)	21 (31.3%)	0.880
Positive cardiac troponin-I	13(13.5%)	6(12.2%)	0.827	5 (7.5%)	4 (6.0%)	0.730
Hospital length of stay in survived patients (days)	12 (9 - 17)	16 (12 - 21)	0.016*	15 (11-19)	16 (12-21)	0.650
Hospital mortality	51 (42.1%)	36 (50.7%)	0.294	30 (44.8%)	33 (49.3%)	0.603
Long-term mortality (after discharge)	21 (30.4%)	10 (31.3%)	0.555	12 (17.9%)	9 (13.4%)	0.751
Non surgical treatment	35 (28.9%)	23 (32.4%)	0.628	19 (28.4%)	22 (32.8%)	0.574
Aortic insufficiency	79 (70.5%)	45 (66.2%)	0.619	44 (68.8%)	42 (64.6%)	0.618
Mitral regurgitation	15 (13.2%)	5 (7.2%)	0.328	12 (18.5%)	4 (6.0%)	0.030*
Tricuspid regurgitation	9 (7.6%)	10 (14.3%)	0.209	7 (10.4%)	9 (13.4%)	0.594

* Variables marked with asterisks were used for calculation of propensity matching



		0	Year-1	Year-2	Year-3	Year-4	Year-5
Male	N	50	40	33	25	21	
Female		25	19	12	7	7	
Male	Hz	0.656	0.679	0.705	0.742	0.785	
Female		0.788	0.832	0.891	0.981	0.981	
Male	SE	0.086	0.089	0.092	0.099	0.109	
Female		0.129	0.137	0.149	0.174	0.174	

Year		0	Year-1	Year-2	Year-3	Year-4	Year-5
Male	N	26	20	16	15	14	
Female		23	18	12	7	7	
Male	Hz	0.671	0.715	0.715	0.715	0.715	
Female		0.766	0.811	0.811	0.902	0.902	
Male	SE	0.115	0.123	0.123	0.123	0.123	
Female		0.130	0.137	0.137	0.165	0.165	

Figure 1. Long-Term Survival Plot before (Left) and after (Right) Propensity Matching, Comparing Male and Female Patients

To examine the possible role of gender-specific hormones in the outcome of AAOD, a subgroup analysis was performed for comparing the patients younger and older than 50 years. As shown in Table 5, patients younger than 50 were different in terms of heart rate and hemoglobin concentrations (P = 0.002 and P < 0.001; respectively). For older patients, the only different variable was the heart rate (P < 0.001).

5. Discussion

According to the results of our study, male and female patients with AAOD carried comparable in-hospital and long-term mortality rates. Despite lack of gender difference in the outcome of these patients, we performed propensity matching because male and female patients differed from each other on several characteristics. For example, in our cohort women were older and more likely to have co-morbidities such as hypertension and diabetes mellitus at the time of their presentation to the hospital. On the contrary, active smoking was more common among men. Even after women with AAOD were matched to an equal number of men with the same pathology, still there was no difference in both short-term and long-term mortality between the two genders. Propensity matching satisfactorily eliminated the differences in co-morbidities; matched groups still differed from each other in age and active smoking. Since no significant outcome difference had been shown prior to propensity matching, more stringent matching for age and smoking status was not expected to change the results. Furthermore, this stringent matching did result in elimination of too many cases and left very few patients for comparison.

In line with the findings of this study, several investigators report no difference between the two genders in either the short-term or the long-term mortalities following the surgical repair of AAOD (14, 15). Tsai and his colleagues have identified old age, previous cardiac surgery and history of atherosclerotic disease as independent predictors of long-term mortality of the patients with AAOD following discharge from the hospital regardless of their gender (6). In a study by Conway et al., neither operative death (within 30 days) nor long-term mortality following surgical repair of AAOD has been influenced by gender (3). In contrast, in a report by Tsai et al., the female gender has been identified as an independent predictor of one-year mortality after surgery in patients with aortic dissection after adjusting for age and the type of dissection (6).

On the other hand, Nienaber et al. suggested that female gender adversely influences the short-term outcome of patients with aortic dissection (5). In contrast to our cohort, women were more likely to be treated non-surgically for AAOD. Moreover, among the patients who were surgically repaired, in-hospital mortality occurred more frequently in women. However, in medically treated patients both genders had comparable mortality rates. They attributed the higher surgical death rates in women to their relatively older age; however, there was no effort to match the patients according to their age (5). The only adjustment was to analyze the subgroup of patients with a higher risk, which included the presence of co-morbidities (not age), which is not as robust as propensity score matching. Considering the higher initial number of patients enrolled in this registry, more stringent propensity matching would have been more appropriate. Despite the fact that females were also older in our study sample before and after they were matched for comorbid conditions, we observed no gender-related difference in operative mortality or in-hospital mortality.

Due to the social structure, especially in the third world countries, access to health care may not be the same for men and women. Moreover, gender difference in pain perception or psychological coping with perceived pain is well known in acute pain settings (16, 17). All these factors may result in delays in seeking medical advice following the early signs of this ominous pathologic condition. One of the main explanations for the observed gender differences in in-hospital mortality in aortic dissection registry has been the delay in presenting to the emergency room among female patients (5). Our findings, however, fail to establish any connection between the gender and the delay in presenting to the emergency room following the onset of symptoms of aortic dissection. Additionally, the delay in treatment may be diagnostic in nature that is defined from the time of admission to the emergency room until the time that the patient undergoes surgical repair. In a

Table 5. Gender Differences in Mortality and Adverse Outcome of Patients with Acute Type-A Aortic Dissection with an Age Cutoff of 50 Years Old

	² 50 years old			> 50 years old		
	Male, N = 52	Female, N = 10	P value	Male, N = 69	Female, N = 61	P value
Heart rate (bpm)	79 ± 19	88 ± 19	0.002	78 ± 17	88 ± 19	< 0.001 *
Hemoglobin (gm/dL)	13.8 (12.7 - 14.5)	11.8 (7.6 - 12.6)	< 0.001 *	12.3 (11.7 - 12.8)	11.6 (11.2 - 12.5)	0.086
Positive cardiac troponin-I	14 (26.9%)	4 (40.0%)	0.404	18 (26.1%)	18 (29.6%)	0.664
Hospital length of stay in survived patients (days)	10 (9 - 13)	15 (2 - 45)	0.173	7 (3 - 12)	12 (4 - 15)	0.259
Hospital mortality	18 (30.8%)	6 (60.0%)	0.077	35 (50.7%)	30 (49.2%)	0.860
Long-term mortality (after discharge)	7 (13.5%)	0 (0.0%)	0.153	14 (20.3%)	10 (18.4%)	0.746
Non surgical treatment	11 (21.2%)	2 (20.0%)	0.828	24 (34.8%)	21 (34.4%)	0.966
Aortic insufficiency	36 (72.0%)	8 (80.0%)	0.602	43 (63.2%)	37 (62.7%)	0.951
Mitral regurgitation	3 (5.9%)	1 (10.0%)	0.328	12 (17.5%)	4 (6.7%)	0.060
Packed red blood cells (units)	47 (438 units)	9 (118 units)	0.366	53 (526 units)	52 (404 units)	0.282
Fresh frozen plasma (units)	14 (45 units)	1 (26 units)	0.003	20 (108 units)	26 (146 units)	0.946
Platelet Rich Plasma	47 (331 units)	10 (77 units)	0.823	54 (602 units)	52 (299 units)	0.095

* Variables marked with asterisks were used for calculation of propensity matching

good number of the symptoms of aortic dissection, it is difficult to be differentiated from those secondary to acute coronary syndromes, especially in those associated with acute electrocardiographic changes in high-risk patients. The direction of the early treatment with anticoagulants and antiplatelets for possible acute coronary syndrome may further complicate the surgical course of the major vascular repair for the aortic dissection. Although we did not separate the presentation and diagnostic delay in this study, it should be noted that the time from hospital presentation to operation room was not different in our study.

Atherosclerosis, hypertension and smoking are repeatedly reported as risk factors contributing to development of aortic dissection by increasing the shear stress forces against the vascular wall and wall weakness secondary to peri-vascular inflammation (18). Since most of the studies that have examined gender difference in AAOD report fundamental differences in hypertension, age and state of smoking between male and female patients, meticulous adjustments for these factors are crucial before attributing the observed differences to gender alone. This adjustment is not that crucial in studies that did not find any gender-related difference in outcome, such as ours. "Smoking paradox" has been reported in several outcome studies in cardiovascular diseases and it is our observation in univariate analysis herein. A recent large cross-country study has reported no association between the prevalence of smoking and mortality trends in aortic dissection (19).

In order to examine the potential role of gender-related hormones on post-operative outcome of patients with AAOD, we compared the clinical outcome and survival of patients younger than 50 years, who are more likely to have different gender-related endocrine profile. This age was selected retrospectively based on the National Health registry statistics on the age of menopause for the population of the region where the subjects were enrolled. We understand that the age of 50 is not uniformly associated with the age of menopause in all of our patients. This sub-classification reveals some interesting findings in terms of gender difference in outcome data. Although in-hospital mortality is similar in males and females, hospital length of stay in survived patients was longer in female patients younger than 50 years of age. Comparatively, younger women present with hemoglobin 2 gm/dL less than men which may have contributed to the observed tachycardia and higher heart rates among them.

Pregnancy may increase the risk of aortic dissection, particularly in predisposed patients such as those with Marfan syndrome (11, 20) Although hormonal and hemodynamic changes as well as increased aortic diameter during pregnancy are believed to increase the risk of aortic dissection (20-22), recent large registry–based studies found that dissection of aorta during pregnancy was a rare condition (10, 23). In the current study, only two pregnant patients with no underlying diseases were reported. Both patients were managed surgically and discharged; they are alive and well now.

The results of our study regarding the gender differences of aortic diameter in patients with AAOD are intriguing. Although maximum aortic diameter was similar in men and women, there were gender-related differences in regional aortic diameter. Expectedly, female patients had significantly smaller aortic valve annulus and aortic root diameter at the time of dissection. However, ascending aorta and aortic arch diameters were similar in males and females. Tsai et al. report similar maximum dimensions of ascending aorta in both sexes (6). Likewise, no association has been reported between in-hospital mortality and aortic diameters of 5.5 cm or greater (24). In a meta-analysis of eight studies on patients with hypertension, aortic root dilation has been reported more frequently in men than in women with hypertension (25).

5.1. Conclusion

In summary, we reported similar short-term death rate and long-term survival even after matching in men and women with a final diagnosis of AAOD. There were no gender related differences in the type of management and time delay from presentation to surgery. While hypertension is more common among women, active smoking, another major risk factor for aortic dissection, is more common in males. Varying results regarding the effect of gender on the outcome in AAOD may originate partly from different risk factor distributions among communities. We have observed a similar mortality rate among the patients under age of 50 years old. However, the number of patients in this age category is too small and underpowered to show any possible existing difference. Therefore, larger studies that include premenopausal women and age- matched men with AAOD are recommended to examine the true effects of gender-specific endocrine profile on the clinical outcome and survival of patients.

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Authors' Contribution

Leili Pourafkari: study design, literature review, data collection, data analysis, manuscript preparation; Samad Ghaffari: study design, literature review, data collection, manuscript preparation; Arezou Tajlil: study design, literature review, data analysis, manuscript preparation; Naser Safaei: study design, literature review, manuscript preparation; Razieh Parizad: literature review, data collection, manuscript preparation; Mohammadreza Chavoshi: literature review, data collection, manuscript preparation; Kasra Kolahdouzan: study design, literature review, data collection, data analysis, manuscript preparation; Nader D. Nader: study design, literature review, data analysis, data interpretation, critical revision of the manuscript

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