Original Article

The impact of age and sex on in-hospital outcomes in acute type A aortic dissection surgery

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Background: Older age and female sex are thought to be risk factors for adverse outcomes after repair of acute type A aortic dissection (AAAD). The aim of this study is to analyze age- and sex-related outcomes in patients undergoing AAAD repair.

Methods: Retrospective analysis of patients undergoing emergency AAAD repair. Patients were divided in Group A, patients aged ≥75 years and Group B <75. Intraoperative and postoperative data were compared between groups before and after propensity score matching. Sex differences were analyzed by age group.

Results: Between January 2006 and December 2018, 638 patients underwent emergency AAAD repair. Group A included 143 patients (22.4%), Group B 495 (77.6%). More patients in Group A presented with circulatory collapse (Penn C 26.6% *vs.* 9.7%, P=0.001) while Group B presented with circulatory collapse-branch malperfusion (Penn BC 29.3% *vs.* 15.4% P=0.001). After propensity score matching, Group B patients received more complex aortic root (33.6% *vs.* 23.2%, P=0.019) and concomitant bypass surgery (12.3% *vs.* 6.3%, P=0.042). There was no significant difference in in-hospital mortality between age groups (18% *vs.* 12% P=0.12). In Group B, in-hospital mortality was significantly higher in females (22.2% *vs.* 8.2%, P=0.028). Differences in mortality disappeared after the age of 75 (18.3% *vs.* 19.4% P=0.87).

Conclusions: Morbidity and mortality are comparable between patients under and over 75 years after AAAD repair. Female patients <75 had higher in-hospital mortality than their male counterparts.

Keywords: Acute type A aortic dissection (AAAD); age; gender

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Introduction

Acute type A aortic dissection (AAAD) is a life-threatening emergency associated with high mortality reaching 1% per hour if not treated (1). Surgical repair is the gold standard as it increases survival and reduces mortality (1). Age, clinical presentation, compromised neurological status, organ malperfusion, pre-operative shock and renal dysfunction have been described as risk factors for death (1,2).

Age remains a determining factor in the outcomes of cardiovascular surgery. Patients aged 75 years or more must be evaluated critically before elective cardiovascular surgery, since outcome and postoperative quality of life may be unsatisfactory. In the setting of AAAD, deep hypothermia, long cardiopulmonary bypass and aortic cross-clamping times, need for circulatory arrest, and selective brain perfusion further increase the risk of adverse outcome

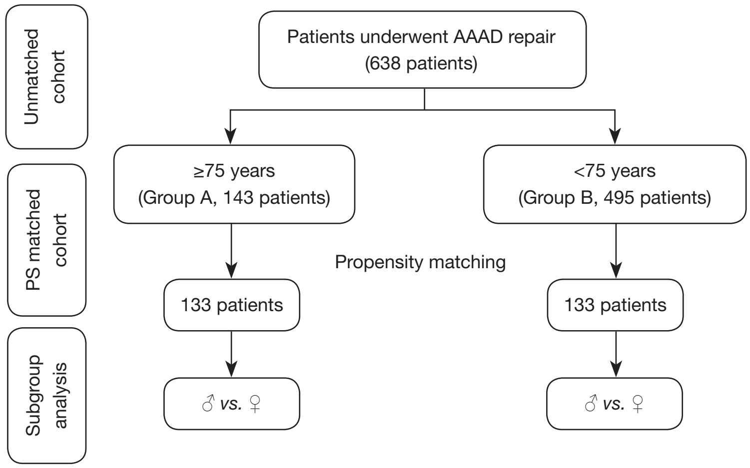

Figure 1 Patients selection and study design. AAAD, acute type A aortic dissection.

in elderly patients (2). However, on-going progress in technology, surgical technique and anesthesiological management resulted in progressively better outcomes of elective and emergency cardiac surgery, leading to an increased number of elderly patients accepted for AAAD repair in the past decades.

Several retrospective studies have tried to shed light on the results of AAAD surgery in the elderly population, reporting quite encouraging outcomes (3). In addition, given the tendency to consider female sex as an important risk factor for morbidity and mortality in AAAD, the aim of the present study was to analyze age- and sex-related differences in outcome in patients undergoing surgery for AAAD. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1863/rc).

Methods

Study design

This is a departmental retrospective study of all consecutive patients who underwent emergency surgery for AAAD between January 1st, 2006 and December 31st, 2018.

Patient selection, data collection and study outcomes

All consecutive patients undergoing surgery for AAAD in the above mentioned period were included and non were excluded. Data on demographics, surgical indications, operative notes were collected. Based on age, patients were divided into two groups; Group A includes patients aged 75 years or older and Group B those younger than 75. In-hospital mortality was the primary study outcome. In addition, Intra operative and post-operative data were compared between the two groups before and after propensity score matching. In each matched group, outcomes were compared based on sex (*Figure 1*).

Definitions of variables and outcomes

There are some definitions of "elderly" and the World Health Organisation has elaborated on the topic based on the expected projection until 2050 of the worldwide proportion of persons above the age of 65 years. On the other hand, as also stated by the WHO, categorical definitions of the old, elderly, aged and ageing are neither straightforward nor universally applicable (4). Furthermore, ageing and health cannot be understood without a sex perspective. Based on all this, with regard to our European area of influence and surgical literature, we arbitrarily choose the cutoff value of 75 years aiming at identifying a subgroup of individuals in whom frailty and comorbidities would be of impact on surgical outcomes (5).

The Penn classification defines the presence or absence of branch-vessel malperfusion, circulatory collapse, or both (6).

In hospital mortality was defined as procedural mortality which consists of all-cause mortality within 30 days or index procedure hospitalization if the postoperative stay is longer than 30 days (7). Myocardial Infarction (MI) was defined according to the Fourth Universal Definition of Myocardial Infarction (8). Stroke was defined as an acute episode of focal or global neurological dysfunction confirmed by specialized clinical and neurological examination and/or computed tomography (9). Renal impairment was defined as serum creatinine value >200 µmol/L (10). Familiality was defined as a positive family history for aortic pathology, based on collected information about disorders from which the direct blood relatives of the patient have suffered (11).

Replacement of the ascending aorta (RAA) was intended as ascending aorta replacement proximally to the innominate artery with or without open distal anastomosis. Hemiarch replacement (HAR) was defined as resection of the concavity of the aortic arch down to the proximal descending thoracic aorta without arch vessel re-implantation. Total arch replacement (TAR) was intended as replacing the entire aortic arch from the offspring of the Innominate artery to a point beyond the offspring of the left subclavian artery (LSA) (12).

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Cantonal Ethics Committee in Zurich (No. 2017-00824) and informed consent was waived for all patients included until December 31st, 2015. From January 1st 2016, all patients signed an informed consent according to the new national data privacy protection.

Statistical analysis

Continuous variables were reported as mean ± standard deviation and compared with analysis of variance (paired Student's t-test). Categorical variables were expressed as frequencies and compared with fisher exact test or chi quadrat (χ^2) test. Normality of data was verified using Quantil-Quantil-Diagramm (Q-Q-plots). A two-sided P value of 0.05 was considered significant. Since the patient cohort was chosen in a non-randomized fashion, we used 1:1 propensity score (PS) matching to reduce the confounding impact of variables in this non-randomized study. To estimate the PS, a logistic regression model including all baseline covariates reported in *Table 1* (except sex) as main effects was utilized. Matching was performed with the PS matching plug-in for Statistical Product and Service Solutions software (SPSS) using the Nearest-Neighbour Matching algorithm without replacement, as recommended by Austin (13). Good covariate balance and a fair number of matched pairs were achieved with a caliper width of 0.2 standard deviations of the linear predictor. Balance of baseline covariates was assessed by computing the P value by χ^2-, fisher exact- and *t*-test (balance achieved, if P<0.5) and by computing the standardized mean difference (SMD) (balance achieved, if SMD <0.2). All statistical analyses were conducted using SPSS version 26 (SPSS, Chicago, IL, USA).

Results

Between January 1st, 2006 and December 31st, 2018, a total of 638 patients underwent emergency surgery for AAAD, 143 patients (22.4%) were aged 75 years or older (Group A) and 495 patients (77.6%) were younger than 75 (Group B). The propensity score matching yielded 133 patients in each group.

Elderly (Group A) vs. young (Group B)

Patient characteristics and clinical presentation (*Table 1*)

In the non-matched groups, the rate of female sex was significantly higher in the elderly group (47.6% *vs.* 25.5%, P=0.001). More patients in Group A presented with circulatory collapse (Penn C, 26.6% *vs.* 9.7%, P=0.001) while more patients in Group B presented with both circulatory collapse and branch malperfusion (Penn BC, 29.3% *vs.* 15.4%, P=0.001). After matching, there were no more significant differences between the groups.

Intraoperative characteristics (*Table 2*)

In the non-matched groups, Group B patients received more TAR in combination with RAA (8.5% *vs.* 2.8%, P=0.021), this difference disappeared after matching (3% *vs.* 6.8%, P=0.15). In Group A the combination of RAA und hemiarch replacement (HAR) was higher (42% *vs.* 29.1%, P=0.004) and persisted after matching (41.4% *vs.* 28.6%, P=0.029). More Group B patients received aortic root replacement (ARR) (33.6% *vs.* 23.2%, P=0.019) and needed concomitant bypass surgery (CABG) (12.3% *vs.* 6.3%, P=0.042) which stayed significant after matching (37.6% *vs.* 23.3%, P=0.01, 15% *vs.* 6%, P=0.017, respectively). Cross clamping time and cardiopulmonary bypass (CPB) time were similar.

Morbidity and mortality (*Table 2*)

Group A showed a higher incidence of pneumonia (31.6% *vs.* 20.4%, P=0.006), which became comparable after matching. In-hospital mortality was comparable between the groups.

Table 1 Baseline characteristics before and after propensity matching

Variable	Unmatched				PS matched			
	Age ≥75 years, Group A?		P value	SMD	Age ≥75 years, Group A?		P value	SMD
	Yes (n=143)	No (n=495)			Yes (n=133)	No (n=133)		
Baseline characteristics used for matching								
Age	80.6±5.5	58.7±10.8	0.001		80.4±5.6	58.26±12	0.001	
Female sex, n (%)	68 (47.6)	131 (26.5)	0.001		62 (46.6)	36 (27.1)	0.001	
Used for propensity score matching, n (%)								
Penn A	56 (39.2)	209 (42.2)	0.51	−0.062	56 (42.1)	53 (39.8)	0.7	0.046
Penn B	26 (17.8)	88 (17.8)	0.9	0.010	26 (19.5)	21 (15.8)	0.4	0.097
Penn C	38 (26.6)	48 (9.7)	0.001	0.381	28 (21.1)	33 (24.8)	0.46	−0.085
Penn BC	22 (15.4)	145 (29.3)	0.001	−0.384	22 (16.4)	24 (18.0)	0.75	−0.042
Arterial hypertension	101 (70.6)	328 (67.4)	0.46	0.096	95 (71.4)	87 (65.4)	0.29	0.132
Preoperative CPR	3 (2.1)	23 (4.6)	0.17	−0.177	3 (2.3)	5 (3.8)	0.47	−0.105
Diabetes Mellitus	10 (7.0)	18 (3.6)	0.08	0.131	10 (7.5)	10 (7.5)	1.0	0.000
Hypercholesterolemia	40 (28.0)	127 (25.7)	0.58	0.051	37 (27.8)	34 (25.6)	0.68	0.050
Nicotine abuse	17 (11.9)	123 (24.9)	0.001	−0.399	17 (12.8)	18 (13.5)	0.86	−0.023
Familiality	8 (5.8)	59 (12.4)	0.028	−0.274	8 (6.0)	7 (5.3)	0.8	0.033
COPD	13 (9.1)	31 (6.3)	0,79	0.098	11 (8.3)	6 (4.5)	0,21	0.130
Renal dysfunction	9 (7.8)	25 (6.3)	0,58	0.051	8 (6.0)	5 (3.8)	0,4	0.093

PS, propensity score; Penn, Penn classification; COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; SMD, standardized mean difference.

Gender differences

Patient characteristics and clinical presentation (*Table 3*)

In the matched cohorts, females in group B presented a higher rate of circulatory collapse and branch malperfusion when compared to male patients in the same group of age (Penn BC, 30.6% *vs.* 13.4%, P=0.022).

Intraoperative characteristics and outcomes

Group A (Table 4)

Although significantly longer operation time was noted in male both unmatched (340±160 *vs.* 276±136, P=0.028) and matched (348.85±163 *vs.* 274.85±126.9, P=0.024), no differences were noted in proximal and distal repair complexity. A higher rate of pneumonia (35.2% *vs.* 19.4%, P=0.042) and renal dysfunction (36.6% *vs.* 21%, P=0.048) were noted. However, mortality was comparable between groups.

Group B (Table 5)

When comparing the two genders, there were significant differences in the distal repair technique: the rate of RAA was higher in female (26.7% *vs.* 18.1%, P=0.037), while HAR was higher in men (9.2% *vs.* 24.7%, P=0.001) which was still present after matching (P=0.015 and 0.006, respectively). Further significant differences such as TAR or combination of RAA and HAR were eliminated after matching (P=0.076 and 0.1, respectively). Regarding proximal repair, men received more frequently ARR before (40.4% *vs.* 14.5%, P=0.001), and after matching (47.4% *vs.* 11.1%, P=0.001). CPB time (211.2±94 *vs.* 176.8±82, P<0.001), cross clamping time (111.2±62 *vs.* 83.6±46, P<0.001), and operation time (338.5±168 *vs.* 279.4±168, P=0.003) were significantly shorter in young women in the unmatched group. The in-hospital mortality was significantly higher in females before (19.8% *vs.* 12.6%, P=0.045) and after matching (22.2% *vs.* 8.2%, P=0.028).

Table 2 Intra- and postoperative characteristics before and after propensity matching

Variable	Unmatched			PS Matched		
	Age ≥75 years, Group A?		P value	Age ≥75 years, Group A?		P value
	Yes (n=143)	No (n=495)		Yes (n=133)	No (n=133)	
Intraoperative data						
CPB time (min)	191.9±81	202.1±92	0.21	191.7±80	202.8±93	0.30
Cross-Clamping time (min)	96.6±58	104±60	0.20	97.1±57	102.8±65	0.45
Circulatory arrest time (min)	29.7±81	33.1±91	0.70	28.3±79	41.9+103	0.26
Hypothermia (℃)	26.4±7	26.5±6	0.78	26.4±7	26.1±8	0.76
Operation time (min)	309.2±152	322.7±172	0.43	310.9±151	303.6±186	0.76
Isolated ascending aorta, n (%)	32 (22.4)	101 (20.4)	0.61	30 (22.6)	26 (19.5)	0.55
Ascending aorta + hemiarch, n (%)	60 (42.0)	144 (29.1)	0.004	55 (41.4)	38 (28.6)	0.029
Isolated hemiarch, n (%)	25 (17.5)	102 (20.6)	0.41	23 (17.3)	29 (21.8)	0.35
Isolated aortic arch, n (%)	7 (4.9)	46 (9.3)	0.09	7 (5.3)	14 (10.5)	0.11
Ascending aorta + arch, n (%)	4 (2.8)	42 (8.5)	0.02	4 (3.0)	9 (6.8)	0.16
Root repair (Glue), n (%)	22 (15.4)	88 (18.0)	0.47	21 (15.8)	24 (18.0)	0.62
Root replacement, n (%)	33 (23.1)	166 (33.5)	0.0179	31 (23.3)	50 (37.6)	0.011
Mechanical prosthesis, n (%)	3 (2.1)	93 (18.8)	<0.001	3 (2.3)	26 (19.5)	<0.001
Biological prosthesis, n (%)	30 (21.0)	69 (13.9)	0.041	28 (21.1)	21 (15.8)	0.27
David procedure, n (%)	2 (1.4)	13 (2.6)	0.39	1 (0.8)	6 (4.5)	0.055
Yacoub procedure, n (%)	5 (3.5)	31 (6.3)	0.21	4 (3.0)	8 (6.0)	0.24
Coronary bypass grafting, n (%)	9 (6.3)	61 (12.3)	0.042	8 (6.0)	20 (15.0)	0.017
Postoperative outcome						
Pneumonia, n (%)	43 (30.1)	100 (20.2)	0.013	37 (27.8)	26 (19.5)	0.11
Postoperative MI, n (%)	6 (4.2)	28 (5.7)	0.49	6 (4.5)	8 (6.0)	0.58
ECMO, n (%)	9 (6.3)	21 (4.2)	0.31	8 (6.0)	7 (5.3)	0.79
Stroke, n (%)	23 (16.1)	74 (14.9)	0.74	21 (15.8)	21 (15.8)	1
Renal dysfunction, n (%)	44 (30.8)	146 (29.5)	0.77	39 (29.3)	37 (27.8)	0.79
Intraoperative mortality, n (%)	7 (4.9)	12 (2.4)	0.13	7 (5.3)	5 (3.8)	0.56
In-hospital mortality, n (%)	26 (18.2)	72 (14.5)	0.29	25 (18.8)	16 (12.0)	0.13
Ventilation time (h)	99.9±202	94.1±168	0.74	97.9±201	86.1±151	0.60
Days on ICU (days)	10.7±12	11.6±17	0.57	10..8±13	11.3±13	0.77

PS, propensity score; CPB, cardiopulmonary bypass; MI, myocardial infarction; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

Discussion

As a main finding of this study, we could show that morbidity and mortality are comparable between young and old patients undergoing surgical repair for AAAD. Certainly, this result must be interpreted with great caution and may appear in contrast to previous studies reporting age as an independent factor for mortality in AAAD (2,3). However, in contrary to our study, they did not take into account the preoperative characteristics of young and old

Table 3 Gender differences before and after matching (baseline characteristics)

Variable	Unmatched						PS matched					
	Age ≥75 years, Group A			Age <75 years, Group B			Age ≥75 years, Group A			Age <75 years Group B		
	Female (n=68)	Male (n=75)	P value	Female (n=131)	Male (n=364)	P value	Female (n=62)	Male (n=71)	P value	Female (n=36)	Male (n=97)	P value
Penn A	27 (39.7)	29 (38.7)	0.899	49 (37.4)	160 (44.0)	0.193	27 (43.5)	29 (40.8)	0.753	12 (33.3)	41 (42.3)	0.350
Penn B	8 (11.8)	18 (24.0)	0.058	27 (20.6)	61 (16.8)	0.323	8 (12.9)	18 (25.4)	0.071	4 (11.1)	17 (17.5)	0.367
Penn C	22 (32.4)	16 (21.3)	0.136	14 (10.7)	34 (9.3)	0.655	16 (25.8)	12 (16.9)	0.209	8 (22.2)	25 (25.8)	0.674
Penn BC	11 (16.2)	11 (14.7)	0.803	39 (29.8)	106 (29.1)	0.888	11 (17.7)	11 (15.5)	0.728	11 (30.6)	13 (13.4)	0.022
Arterial hypertension	54 (79.4)	47 (62.7)	0.028	94 (71.8)	234 (64.3)	0.121	49 (79.0)	46 (64.8)	0.070	25 (69.4)	62 (63.9)	0.552
Preoperative CPR	2 (2.9)	1 (1.3)	0.503	5 (3.8)	18 (4.9)	0.599	2 (3.2)	1 (1.4)	0.481	2 (5.6)	3 (3.1)	0.507
Diabetes mellitus	5 (7.4)	5 (6.7)	0.872	5 (3.8)	13 (3.6)	0.898	5 (8.1)	5 (7.0)	0.824	2 (5.6)	8 (8.2)	0.601
Hypercholesterolemia	22 (32.4)	18 (24.0)	0.266	28 (21.4)	99 (27.2)	0.191	20 (32.3)	17 (23.9)	0.286	10 (27.8)	24 (24.7)	0.721
Nicotine abuse	6 (8.8)	11 (14.7)	0.281	28 (21.4)	95 (26.1)	0.283	6 (9.7)	11 (15.5)	0.316	4 (11.1)	14 (14.4)	0.619
Familiarity	2 (2.9)	6 (8.0)	0.189	15 (11.5)	44 (12.1)	0.847	2 (3.2)	6 (8.5)	0.206	1 (2.8)	6 (6.2)	0.434
COPD	7 (10.3)	6 (8.0)	0.634	6 (4.6)	25 (6.9)	0.354	5 (8.1)	6 (8.5)	0.936	1 (2.8)	5 (5.2)	0.557
Renal dysfunction	5 (7.4)	4 (5.3)	0.619	7 (5.3)	18 (4.9)	0.858	4 (6.5)	4 (5.6)	0.843	2 (5.6)	3 (3.1)	0.507

PS, propensity score; Data are shown as number (percentage). Penn, Penn classification; CPR, cardiopulmonary resuscitation; COPD, chronic obstructive pulmonary disease.

patients undergoing surgery for AAAD.

Several factors may have contributed to this relatively low mortality in elderly patients: there is no data available about the number of patients who died before reaching a hospital or were denied surgery. And it is also a practice choosing conservative therapy in older patients due to high surgical risk and expected adverse outcomes (14). This results in a selection bias in patients who receive surgery, and therefore may underestimate the true surgical mortality rate if the number accepted for surgery was comparable to that of younger patients. Furthermore, in elderly patients, surgery tends to be less complex in order to decrease CPB time and ischemia time, as noted in our study, by the lower frequency of aortic replacement surgery, which presumably reduces the postoperative mortality.

Similar to the findings of Kreibich *et al.* we confirmed that Group A patients with AAAD had more frequently cardiovascular collapse classified as Penn class C (15). This tendency to develop shock in elderly patients was interpreted as a lower compensatory capacity with increasing age. On the other hand, Group B patients had a higher frequency of Penn Class BC presentation with greater extent of dissection with organ malperfusion in association with cardiovascular collapse. This observation concurs with the observations of other groups, Malvindi *et al.* reported that the extension to the coronary sinus, descending thoracic aorta and abdominal aorta and the presence of an intimal tear at the level of the aortic root correlated inversely with age (16). The reason for this finding might be that younger patients are more likely to have connective tissue diseases or bicuspid aortic valve, which facilitate extension of the dissection proximally and distally. However, information regarding these disorders is not available in our database, one of the limitations of this study.

Despite our results confirm a tendency to conduct more complex surgery at the distal level, intended as TAR in Group B, this tendency was not confirmed after matching. This finding can be interpreted as follows: first, in younger patients the site of intimal tear tends to be more proximal to the aortic root as reported in the International Registry of Aortic Dissection (IRAD), which often results in complex root replacement surgery rather than reparative surgery as will be discussed later (17). Second, the development of interventional techniques to treat the aortic arch in recent years may have contributed to reduce surgical aggressiveness at the level of the aortic arch, even in younger patients. Interestingly, the combination of RAA and HAR was

Table 4 Gender differences before and after matching (age ≥75 years)

Variable	Unmatched cohorts (≥75 years), Group A			PS matched cohorts (≥75 years), Group A		
	Male (n=75)	Female (n=68)	P value	Male (n=71)	Female (n=62)	P value
Intraoperative data						
CPB time (min)	202.5±78	180.1±84	0.1	203.4±80	178.1±80	0.074
Cross-Clamping time (min)	101.6±57	91.0±59	0.28	102.9±58	90.2±55	0.21
Circulatory arrest time (min)	25.9±66	33.7±96	0.60	26.2±67	30.8±90	0.76
Hypothermia (℃)	26.4±4	26.3±9	0,95	26.5±4	26.4±9	0.94
Operation time (min)	340.0±160	276.1±136	0.028	342.9±164	274.9±127	0.024
Isolated ascending aorta, n (%)	12 (16.0)	20 (29.4)	0.06	12 (16.9)	18 (29.0)	0.10
Ascending aorta + hemiarch, n (%)	35 (46.7)	25 (35.8)	0.23	32 (45.1)	23 (37.1)	0.35
Isolated hemiarch, n (%)	14 (18.7)	11 (16.2)	0.70	13 (18.3)	10 (16.1)	0.74
Isolated aortic arch, n (%)	4 (5.3)	3 (4.4)	0.80	4 (5.6)	3 (4.8)	0.83
Ascending aorta + arch, n (%)	3 (4.0)	1 (1.5)	0.36	3 (4.2)	1 (1.6)	0.38
Root repair (Glue), n (%)	12 (16.0)	10 (14.7)	0.83	11 (15.5)	10 (16.1)	0.92
Root replacement, n (%)	18 (24.0)	15 (22.1)	0.78	17 (23.9)	14 (22.6)	0.85
Mechanical prosthesis, n (%)	2 (2.7)	1 (1.5)	0.62	2 (2.8)	1 (1.6)	0.64
Biological prosthesis, n (%)	16 (21.3)	14 (20.6)	0.91	15 (21.1)	13 (21.0)	0.98
David procedure, n (%)	0 (0)	2 (2.9)	0.13	0 (0.0)	1 (1.6)	0.28
Yacoub procedure, n (%)	2 (2.7)	3 (4.4)	0.57	2 (3.2)	2 (2.8)	0.89
Coronary bypass grafting, n (%)	6 (8.0)	3 (4.4)	0.38	6 (8.5)	2 (3.2)	0.21
Postoperative outcome						
Pneumonia, n (%)	27 (36.0)	16 (23.5)	0.10	25 (35.2)	12 (19.4)	0.042
Postoperative MI, n (%)	2 (2.7)	4 (5.9)	0.34	2 (2.8)	4 (6.5)	0.31
ECMO, n (%)	5 (6.7)	4 (5.9)	0.85	5 (7.0)	3 (4.8)	0.59
Stroke, n (%)	15 (20.0)	8 (11.8)	0.18	14 (19.7)	7 (11.3)	0.18
Renal dysfunction, n (%)	28 (37.3)	16 (23.5)	0.07	26 (36.6)	13 (21.0)	0.048
Intraoperative mortality, n (%)	6 (8.0)	1 (1.5)	0.07	1 (1.0)	4 (11.1)	0.007
In-hospital mortality, n (%)	13 (17.3)	13 (19.1)	0.78	13 (18.3)	12 (19.4)	0.88
Ventilation time (h)	123.3±255	75±119	0.17	125.5±262	67.6±88	0.10
Days on ICU (days)	11.4±15	10.1±9	0.54	11.9±16	9.6±8	0.29

CPB, cardiopulmonary bypass; MI, myocardial infarction; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

frequent in older patients and this may be attributed to a higher frequency of distal localization of intimal tear in the older population as reported by the IRAD analysis.

Furthermore, our results show that Group B patients had a higher rate of complex proximal surgery intended as ARR and need of concomitant CABG surgery. This is our experience when specifically looking at patients requiring concomitant CABG in the setting of AAAD (18). As above mentioned, the site of intimal tear tends to be more proximal to the aortic root in young patients, which requires more aggressive and durable surgery at the level of the aortic root rather than conservative approaches

Table 5 Gender differences before and after matching (intra- and postoperative characteristics, age <75 years)

Variable	Unmatched cohorts (<75 years), Group B			PS matched cohorts (<75 years), Group B		
	Male (n=364)	Female (n=131)	P value	Male (n=97)	Female (n=36)	P value
Intraoperative data						
CPB time (min)	211.2±94	176.8±82	<0.001	208.8±94	186.5±88	0.22
Cross-Clamping time (min)	111.2±62	83.6±46	<0.001	107.5±69	90.0±49	0.17
Circulatory arrest time (min)	31.2±87	38.8±100	0.45	45.4±105	31.3±97	0.52
Hypothermia (℃)	26.7±6	26.1±6	0.33	26.9±8	24.1±8	0.09
Operation time (min)	338.5±168	279.4±168	0.003	304±182	299±200	0.9
Isolated ascending aorta, n (%)	66 (18.1)	35 (26.7)	0.037	14 (14.4)	12 (33.3)	0.015
Ascending aorta + hemiarch, n (%)	97 (26.6)	47 (35.9)	0.046	24 (24.7)	14 (38.9)	0.11
Isolated hemiarch, n (%)	90 (24.7)	12 (9.2)	<0.001	27 (27.8)	2 (5.6)	0.006
Isolated aortic arch, n (%)	40 (11.0)	6 (4.6)	0.030	13 (13.4)	1 (2.8)	0.08
Ascending aorta + arch, n (%)	27 (7.4)	15 (11.5)	0.16	5 (5.2)	4 (11.1)	0.22
Root repair (Glue), n (%)	66 (18.1)	23 (17.6)	0.88	18 (18.6)	6 (16.7)	0.80
Root replacement, n (%)	147 (40.4)	19 (14.5)	<0.001	46 (47.4)	4 (11.1)	<0.001
Mechanical prosthesis, n (%)	86 (23.6)	7 (5.3)	<0.001	25 (25.8)	1 (2.8)	0.003
Biological prosthesis, n (%)	59 (16.2)	10 (7.6)	0.015	19 (19.6)	2 (5.6)	0.049
David procedure, n (%)	11 (3.0)	2 (1.5)	0.36	6 (6.2)	0 (0)	0.13
Yacoub procedure, n (%)	19 (5.2)	12 (9.2)	0.11	6 (6.2)	2 (5.6)	0.89
Coronary bypass grafting, n (%)	43 (11.8)	18 (13.7)	0.57	15 (15.5)	5 (13.9)	0.82
Postoperative outcome						
Pneumonia, n (%)	82 (22.5)	18 (13.7)	0.032	20 (20.6)	6 (16.7)	0.61
Postoperative MI, n (%)	23 (6.3)	5 (3.8)	0.29	5 (5.2)	3 (8.3)	0.49
ECMO, n (%)	14 (3.8)	7 (5.3)	0.47	5 (5.2)	2 (5.6)	0.93
Stroke, n (%)	52 (14.3)	22 (16.8)	0.49	14 (14.4)	7 (19.4)	0.48
Renal dysfunction, n (%)	106 (29.1)	40 (30.5)	0.76	27 (27.8)	10 (27.8)	1.00
Intraoperative mortality, n (%)	7 (1.9)	5 (3.8)	0.23	1 (1.0)	4 (11.1)	0.007
In-hospital mortality, n (%)	46 (12.6)	26 (19.8)	0.045	8 (8.2)	8 (22.2)	0.028
Ventilation time (h)	88.0±146	111.8±218	0.17	71.5±114	128.1±223	0.17
Days on ICU (days)	11.2±17	12.6±16	0.42	11.0±12	12.1±16	0.67

CPB, cardiopulmonary bypass; MI, myocardial infarction; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

as recommended by Castrovinci *et al.* (19), who found that a more extensive root intervention appeared to be protective against aortic reintervention. In addition, Group B patients presented often with Penn class BC. Myocardial malperfusion could not be excluded in these patients and could explain the higher rate of concomitant CABG surgery.

The data reported in the literature regarding gender and sex difference in AAAD are controversial. In a sub-analysis of the IRAD study (20), the surgical mortality rate for acute Type A dissection was 31.9% in women and 21.9% in men (P=0.013). Older age at onset, delayed transfer to hospital and more complications including tamponade, shock, heart failure and coma are cited as potential reasons for higher surgical mortality. Fukui *et al.* (21) analyzed the impact of sex on preoperative characteristics and outcomes in patients undergoing surgery for AAAD. The operative mortality was found to be similar in Japanese male and female patients (4.5% *vs.* 5.8%; P=0.6463) and no difference in pre-operative conditions was found.

In a recent analysis from the German Registry for Acute Aortic Dissection Type A (GERAADA), Rylski *et al.* (22) reported a comparable operative mortality in both sexes, despite a more complicated clinical presentation in males. Compared to the IRAD data, the authors of this analysis believed that a better understanding of aortic pathology, together with advances in surgical therapy underlie a decrease in surgical mortality in AAAD and consequently an improvement in survival in females as well. The three previous studies agreed on 2 elements: an older age by presentation, and a less complex surgery in female patients. The last point was precisely attributed to the older age of the female patients.

In the present study, we observed no sex related difference in the older group (Group A). In the younger group (Group B), female patients underwent less complex surgery with shorter cross clamp time and duration when compared to their male counterpart, perhaps because of smaller aortic diameters, which facilitate the surgeon's choice of more conservative reparative approaches of the aortic root. However, the mortality in female patients in group B was higher.

The tendency to have a high mortality in young women has been noted after other cardiac surgery procedures. In a landmark study, Vaccarino *et al.* (23) analyzed the outcomes of 51,187 patients undergoing CABG. Younger women undergoing CABG surgery were at higher risk of in-hospital death than men, but this difference in risk decreased with advancing age. Similar results were reported from Enger *et al.* (24) in patients undergoing combined valve and CABG surgery. Genetic and hormonal mechanisms have been cited in both studies to explain these findings.

This paradox between complexity of surgery and mortality in young female patients in our study may be attributed in part to a more complex clinical presentation, similar to that reported in the IRAD analysis, since the incidence of a Penn BC class was more significant in female patients in Group B. However, other genetic and pathological factors cannot be ruled out and more in-depth studies are needed to shed light on the histological and genetic features of young females with AAAD.

Limitations

The limitations of our study are the following: it is single-center, retrospective and observational. Furthermore, data regarding connective tissue disorder and aortic morphology are missing. In addition, patients with AAAD who died before reaching the hospital or were denied for surgery are not reported, which could result in an underestimation of the real mortality in old patients.

Conclusions

After propensity matching of our large cohort of AAAD patients, we were unable to show a significant difference in mortality and morbidity comparing patients under and over 75 years of age. When comparing both sexes after matching, female patients younger than 75 seem to have experienced a higher rate of in-hospital mortality than their male counterparts.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Cantonal

Ethics Committee in Zurich (No. 2017-00824) and informed consent was waived for all patients included until December 31st, 2015. From January 1st, 2016, all patients signed an informed consent according to the new national data privacy protection act.

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