Type A Acute Aortic Dissection Presenting With Cerebrovascular Accident at Advanced Age

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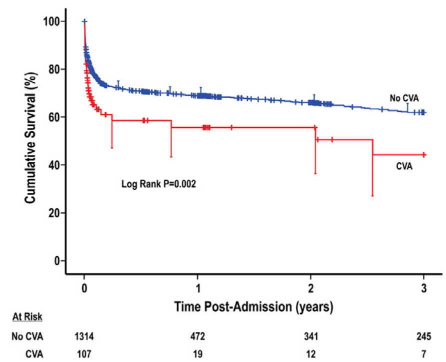
Our aim was to analyze outcomes of patients aged 70 years or above presenting with type A acute aortic dissection (TAAAD) and cerebrovascular accident (CVA). A retrospective analysis of the International Registry of Acute Aortic Dissection (IRAD) was conducted. Patients aged 70 years or above (n = 1449) were stratified according to presence or absence of CVA before surgery (CVA: n = 110, 7.6%). In-hospital outcomes and mortality up to 5 years were analyzed. Additionally, in-hospital outcomes of patients who received medical management were described. No patient presenting with CVA over the age of 87 years underwent surgery. The rates of in-hospital mortality and post-operative CVA were significantly higher in patients presenting with CVA (in-hospital mortality: 32.7% vs 21.7%, *P* = 0.008; post-operative CVA: 23.4% vs 8.3%, *P* < 0.001). Presence of CVA was independently associated with significantly increased in-hospital mortality (odds ratio 2.99, 95% confidence interval 1.35 – 6.60, *P* = 0.007). In survivors of the hospital stay, presenting CVA had no independent influence on mortality



Survival curves of patients presenting with and without cerebrovascular accident (CVA).

Abbreviations: ACP, antegrade cerebral perfusion; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; CVA, cerebrovascular accident; GERAADA, German Registry for Acute Aortic Dissection Type A; HCA, hypothermic circulatory arrest; HR, hazard ratio; IRAD, International Registry of Acute Aortic Dissection; OR, odds ratio; PAD, peripheral arterial disease; RCP, retrograde cerebral perfusion; SCI, spinal cord ischemia; TAAAD, type A acute aortic dissection

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up to 5 years (hazard ratio 1.52, 95% confidence interval 0.99 – 2.31, $P = 0.54$). In medically managed patients, exceedingly high rates of in-hospital mortality (71.4%) and CVA (90.9%) were noted. Patients presenting with TAAAD and CVA at ≥ 70 years of age are at significantly increased risk of in-hospital mortality, although long-term mortality is not affected in hospital survivors. Medical management is associated with poor outcomes. We believe that surgical management should be offered after critical assessment of comorbidities.

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Central Message

Timely surgical management should be offered to selected patients presenting with TAAAD and CVA at 70 years of age after critical assessment of comorbidities.

Perspective Statement

Patients aged 70 years or above presenting with TAAAD and CVA are at increased risk of in-hospital mortality, although late mortality is not affected in hospital survivors. No patient presenting with CVA over the age of 87 years was operated in IRAD centers. Medical management is associated with poor outcomes. We believe that surgery should be offered after critical assessment of comorbidities.

INTRODUCTION

Surgical management of type A acute aortic dissection (TAAAD) is currently associated with operative mortality rates between 2.8% and 28.6%.[1] In comparison, in-hospital mortality rates of patients receiving medical management have been reported between 54.7% and 100%.[2,3] Thus, surgery is recommended as a Class 1 indication for essentially all patients presenting with TAAAD.[4] However, patients with cerebrovascular accident (CVA) in the presence of TAAAD constitute a therapeutically challenging group. Reported incidence rates of preoperative CVA or cerebral malperfusion range between 4.7% and 23.6%.[5–10] Major neurological dysfunction at presentation has been shown to be associated with significantly increased post-operative morbidity and mortality.[5,6,8,11] Our hypothesis was that presence of CVA might exert more detrimental effects on post-operative outcomes in patients aged 70 years or above. To the best of our knowledge, no studies exist that have specifically investigated this question so far. The International Registry of Acute Aortic Dissection (IRAD) offers a unique opportunity for meaningful statistical analysis of this comparatively small sub-group of TAAAD.

METHODS

A retrospective analysis of the IRAD was performed. The registry currently holds clinical data of almost 10,000 patients from over 50 sites in North America, Europe, Asia, and Australia.[2] All IRAD centers received ethics board approval to participate in the registry. Individual informed written consent was waived for the retrospective use of anonymized patient data.

Patients presenting with TAAAD aged 70 years or above (n = 1449) were stratified according to presence or absence of CVA before surgery (CVA: n = 110, 7.6%). Additionally, we analyzed patients presenting with CVA in whom a strategy of medical management was followed (n = 35).

Variable Definitions

In the IRAD, preoperative CVA is defined as a loss of neurological function caused by a disturbance in cerebral blood supply with residual symptoms 24 hours after onset. Among baseline characteristics, aortic valve disease is defined as presence of either severe aortic valve stenosis or regurgitation. Among variables characterizing patients' clinical presentation, coma is defined as complete or partial mental unresponsiveness beyond that expected from anesthesia or no evidence of psychological or physiologically appropriate responses to stimulation. Presenting hypertension indicates blood pressure values > 150 of 90 mm Hg on admission. Shock indicates a maximum systolic blood pressure < 80 mm Hg for at least 30 minutes, pump failure, or signs of hypoperfusion. Signs of congestive heart failure include paroxysmal nocturnal failure, dyspnea on exertion or at rest, and pulmonary congestion on x-ray. Ischemic lower extremity indicates pain, pulselessness, pallor of the foot on elevation, rubor on dependency, necrosis, paralysis, paresthesia, intermittent claudication, or rest pain. Among preoperative imaging results, arch vessel involvement is present if the aortic pathology includes the level of the left subclavian artery or any more proximally originating arch vessels. Among in-hospital outcomes, post-operative CVA is defined as loss of neurological function (loss or slurring of speech, altered state of consciousness) caused by an ischemic event that is confirmed by either computed tomography or magnetic resonance imaging. Spinal cord ischemia is defined as evidence of occlusion of the radicular arteries of the spinal cord with loss of function to the lower extremities with or without bowel/bladder involvement. Post-operative hypotension indicates a systolic blood pressure that has decreased below 90 mmHg from an earlier higher recording.

Statistical Analysis

Continuous variables with non-normal distributions are reported using medians and interquartile ranges. Categorical variables are presented using absolute frequencies and percentages. The Kruskal-Wallis test was used for group-wise comparison of non-normally distributed continuous variables. Categorical variables were compared using the chi-square test or Fisher's exact test where appropriate.

Because the CVA and non-CVA groups presented with marked differences in underlying comorbidities that could have had a confounding influence on postoperative outcomes, a binary logistic regression was generated to identify the independent association of particular comorbidities associated with CVA at presentation. To avoid the confounding influence of missing data, multiple imputation was utilized to first generate missing data for the variables in the model. After considering clinical relevance, variables exhibiting significant differences between the 2 groups during univariate analysis were used to generate the conditional probability of CVA calculated for each case, adjusting for the covariates in the model. This conditional probability generated was utilized to create both a balancing score as well as a propensity score for use in analysis of outcomes. The variables used to generate the balancing score were 4 baseline characteristics (chronic obstructive pulmonary disease, peripheral arterial disease, atherosclerosis, aortic valve disease) and 9 clinical characteristics (chest pain, head/neck pain, radiating pain, coma, syncope, hypertension, shock, signs of congestive heart failure, and ischemic lower extremity).

Primary outcome variables were defined as in-hospital mortality and the rates of postoperative complications (neurological deficit [CVA, coma, spinal cord ischemia], mesenteric ischemia, acute renal failure, extension of dissection, hypotension, cardiac tamponade, limb ischemia, and discharge to tertiary hospital). To investigate the independent influence of CVA on in-hospital mortality, a multivariable logistic regression model was created based on a matched dataset. Propensity matching using a nearest neighbor technique without replacement was used to compare groups for in-hospital mortality. A caliper of 0.2 was specified for the maximum difference between propensity scores for the matched pairs. The following variables were considered for introduction into the multivariable model: CVA (forced), gender, atherosclerosis, prior cardiac surgery, head/neck pain, coma, syncope, preoperative hypotension, cardiac tamponade, mesenteric ischemia, limb ischemia, proximal extension of dissection to aortic root, proximal extension of dissection to ascending aorta, post-operative hypotension, and acute renal failure.

The secondary outcome variable was mortality up to 5 years after discharge. A multivariable Cox proportional hazards regression model was generated to analyze independent associations between CVA and the secondary outcome. Because groups had fewer numbers at follow-up, instead of propensity matching the balancing score for CVA was used to maximize the number of cases included in this analysis. The balancing score was forced into the model to balance for group differences in comorbidities at presentation. After evaluating clinical relevance, variables with p-values of less than 0.15 were considered for introduction into the multivariable model. These variables included age, diabetes mellitus, atherosclerosis, aortic valve disease, prior cardiac surgery, family history of aortic disease, preoperative spinal cord ischemia, distal extension of dissection to descending aorta, time between initial admission and surgery, post-operative acute renal failure, chronic beta blocker therapy at discharge, and angiotensin converting enzyme inhibitor therapy at discharge. A backward stew-wise method was utilized as a tool leading to the creation of the final model.

Simple survival probabilities were also compared by the Kaplan-Meier method using the log-rank test to evaluate statistically significant differences between survival curves. Date of admission was defined as starting point for Kaplan-Meier survival curves.

Additionally, in-hospital outcomes of patients presenting with CVA who received medical management were described (in-hospital mortality, and the rates of in-hospital complications). Moreover, reasons for medical management were reported.

Two-sided *P*-values < 0.05 were defined as statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) for Windows, version 25.0 (IBM Corporation, Armonk, NY).

RESULTS

Preoperative Baseline Characteristics

Baseline characteristics of the study groups are shown in Table 1. Median age of patients presenting with and without CVA was similar (75.5 years vs 76.3 years, *P*= 0.101). The CVA group showed a lower rate of patients aged 80 years or above, although not statistically significant (*P* = 0.088). In the CVA group, the oldest patient was 87 years of age, while the maximum age in the non-CVA group amounted to 100 years. No significant sex differences were found between the CVA and non-CVA groups (female patients: 45.5% vs 50.0%, *P* = 0.355). Patients with CVA were more commonly of Asian origin (10.3% vs 2.4%, *P* < 0.001) and had a history of chronic obstructive pulmonary disease (COPD) (23.0% vs 13.8%, *P* = 0.049), peripheral arterial disease (PAD) (12.3% vs 4.9%, *P* = 0.016), and aortic valve disease (24.4% vs 13.8%, *P* = 0.010).

Preoperative Clinical Presentation

Table 2 shows between-group differences in clinical presentation. In the CVA group, chest pain (70.4% vs 81.8%, *P* = 0.006) and radiating pain (9.4% vs 40.3%, *P* < 0.001) were less commonly reported at presentation. Patients with CVA more frequently presented with coma (38.4% vs 8.1%, *P* < 0.001) and syncope (36.8% vs 19.4%, *P* < 0.001). These patients less commonly presented with hypertension (12.4% vs 25.7%, *P* = 0.002) or normotension (34.3% vs 45.1%, *P* = 0.033) but were more commonly in shock (32.4% vs 8.0%, *P* < 0.001). Also, the CVA group more frequently presented with signs of congestive heart failure (19.2% vs 5.8%, *P*

Table 1. Preoperative Baseline Characteristics

Variables	Missing Data n (%)	All Patients n = 1449 (100%)	CVA n = 110 (7.6%)	No CVA n = 1339 (92.4%)	*P*-Value	Effect Size
Age (y)	0 (0%)	76.3 (73.2-80.0)	75.5 (72.5-78.8)	76.3 (73.2-79.7)	0.101	-0.043
Age (%)	0 (0%)					
≥ 80 y		376/1449 (25.9%)	21/110 (19.1%)	355/1339 (26.5%)	0.088	-0.045
≥ 90 y		13/1449 (0.9%)	0/110 (0%)	13/1339 (1.0%)	0.616	-0.027
≥ 100 y		1/1449 (0.1%)	0/110 (0%)	1/1339 (0.1%)	1.000	-0.008
Female (%)	0 (0%)	720/1449 (49.7%)	50/110 (45.5%)	670/1339 (50.0%)	0.355	-0.024
Ethnicity (%)	141 (9.7%)					
White		1157/1308 (88.5%)	94/107 (87.9%)	1063/1201 (88.5%)	0.838	-0.006
Black		61/1308 (4.7%)	1/107 (0.9%)	60/1201 (5.0%)	0.055	0.056
Asian		40/1308 (3.1%)	11/107 (10.3%)	29/1201 (2.4%)	**<0.001**	0.125
Hispanic		31/1308 (2.4%)	0/107 (0%)	31/1201 (2.6%)	0.171	-0.047
Other		19/1308 (1.5%)	1/107 (0.9%)	18/1201 (1.5%)	1.000	-0.013
Body mass index (kg/m^2)	537 (37.1%)	26.9 (24.0-30.1)	26.4 (23.4-29.6)	26.9 (24.0-30.1)	0.578	-0.018
Hypertension (%)	87 (6%)	1151/1362 (84.5%)	88/98 (89.8%)	1063/1264 (84.1%)	0.133	0.041
Diabetes mellitus (%)	161 (11.1%)	173/1288 (13.4%)	16/83 (19.3%)	157/1205 (13.0%)	0.106	0.045
Chronic renal failure (%)	538 (37.1%)	84/911 (9.2%)	6/60 (10.0%)	78/851 (9.2%)	0.829	0.007
COPD (%)	525 (36.2%)	133/924 (14.4%)	14/61 (23.0%)	119/863 (13.8%)	**0.049**	0.065
PAD (%)	569 (39.3%)	47/880 (5.3%)	7/57 (12.3%)	40/823 (4.9%)	**0.016**	0.081
Smoker, ever (%)	681 (47%)	366/768 (47.7%)	19/51 (37.3%)	347/717 (48.4%)	0.124	-0.056
Marfan syndrome (%)	191 (13.2%)	4/1258 (0.3%)	0/75 (0%)	4/1183 (0.3%)	1.000	-0.014
Atherosclerosis (%)	180 (12.4%)	366/1269 (28.8%)	40/86 (46.5%)	326/1183 (27.6%)	**<0.001**	0.105
Aortic valve disease (%)	181 (12.5%)	183/1268 (14.4%)	19/78 (24.4%)	164/1190 (13.8%)	**0.010**	0.072
Bicuspid aortic valve (%)	230 (15.9%)	24/1219 (2.0%)	2/70 (2.9%)	22/1149 (1.9%)	0.644	0.016
Known aortic aneurysm (%)	162 (11.2%)	272/1287 (21.1%)	14/73 (19.2%)	258/1214 (21.3%)	0.673	-0.012
Prior aortic dissection (%)	177 (12.2%)	59/1272 (4.6%)	3/72 (4.2%)	56/1200 (4.7%)	1.000	-0.005
Iatrogenic dissection (%)	35 (2.4%)	60/1414 (4.2%)	2/109 (1.8%)	58/1305 (4.4%)	0.317	-0.035
Prior cardiac surgery (%)	176 (12.1%)	225/1273 (17.7%)	12/82 (14.6%)	213/1191 (17.9%)	0.456	-0.021
Prior cardiac catheterization (%)	269 (18.6%)	210/1180 (17.8%)	15/76 (19.7%)	195/1104 (17.7%)	0.648	0.013

Bold indicates statistical significance ($P < 0.05$).
COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; PAD, peripheral arterial disease

Table 2. Preoperative Clinical Presentation

Variables	Missing Data n (%)	All Patients n = 1449 (100%)	CVA n = 110 (7.6%)	No CVA n = 1339 (92.4%)	*P*-Value	Effect Size
Chest Pain (%)	107 (7.4%)	1086/1342 (80.9%)	69/98 (70.4%)	1017/1244 (81.8%)	**0.006**	-0.075
Head/Neck pain (%)	307 (21.2%)	317/1142 (27.8%)	10/59 (16.9%)	307/1083 (28.3%)	0.057	-0.056
Radiating pain (%)	331 (22.8%)	434/1118 (38.8%)	5/53 (9.4%)	429/1065 (40.3%)	**<0.001**	-0.135
Coma (%)	202 (13.9%)	123/1247 (9.9%)	28/73 (38.4%)	95/1174 (8.1%)	**<0.001**	0.238
Syncope (%)	242 (16.7%)	247/1207 (20.5%)	28/76 (36.8%)	219/1131 (19.4%)	**<0.001**	0.105
Hypertension (%)	111 (7.7%)	330/1338 (24.7%)	13/105 (12.4%)	317/1233 (25.7%)	**0.002**	-0.083
Normotension (%)	110 (7.6%)	592/1339 (44.2%)	36/105 (34.3%)	556/1234 (45.1%)	**0.033**	-0.058
Hypotension (%)	110 (7.6%)	237/1339 (17.7%)	16/105 (15.2%)	221/1234 (17.9%)	0.491	-0.019
Shock (%)	110 (7.6%)	133/1339 (9.9%)	34/105 (32.4%)	99/1234 (8.0%)	**<0.001**	0.219
Cardiac Tamponade (%)	233 (16.1%)	50/1216 (4.1%)	6/92 (6.5%)	44/1124 (3.9%)	0.226	0.035
Signs of congestive heart failure (%)	206 (14.2%)	83/1243 (6.7%)	15/78 (19.2%)	68/1165 (5.8%)	**<0.001**	0.130
Limb Ischemia (%)	133 (9.2%)	80/1316 (6.1%)	5/75 (6.7%)	75/1241 (6.0%)	0.826	0.006
Ischemic lower extremity (%)	248 (17.1%)	81/1201 (6.7%)	12/67 (17.9%)	69/1134 (6.1%)	**<0.001**	0.108

Bold indicates statistical significance ($P < 0.05$).
CVA, cerebrovascular accident.

< 0.001) and ischemia in the lower extremities (17.9% vs 6.1%, $P < 0.001$).

Preoperative Imaging Results

Preoperative imaging results are shown in Supplementary Table 1. Figure QR Code An intimal flap was more commonly demonstrated in the CVA group (61.8% vs 43.2%, $P < 0.001$). In patients with CVA, the proximal extension of dissection was less frequently located in the aortic root (35.3% vs 55.0%, $P < 0.001$) but more frequently in the ascending aorta (51.8% vs 29.4%, $P < 0.001$). In this group, the most distal extension of dissection more commonly reached the abdominal aorta (30.2% vs 17.6%, $P = 0.022$). Arch vessel involvement was more prevalent in the CVA group (56.9% vs 37.9%, $P = 0.007$).

Operative Characteristics

Supplementary Table 2 shows operative characteristics of both groups. Time between initial admission and surgery was significantly shorter in patients presenting with CVA (6.0 hours vs 7.0 hours, $P = 0.024$). Surgical techniques to repair the aortic arch were similar between both groups. During hypothermic circulatory arrest (HCA), cerebral perfusion was more commonly applied in the CVA group (94.9% vs 81.8%, $P = 0.036$).

Primary Outcome Variables: In-Hospital Mortality and Complications

Table 3 shows a comparison of primary outcome variables. The CVA group had significantly higher rates of in-hospital mortality (32.7% vs 21.7%, $P = 0.008$) and postoperative CVA (23.4% vs 8.3%, $P < 0.001$). A significantly lower rate of post-operative hypotension (9.5% vs 18.8%, $P = 0.044$) was noted in the CVA group. No statistically significant differences were found among all other primary outcome variables.

Table 4. Primary Outcome Variable: In-Hospital Mortality (Multivariable Logistic Regression Analysis, Matched Dataset)

Variables	Odds Ratio	95% Confidence Interval	*P*-Value
CVA	2.99	1.35 – 6.60	**0.007**
Preoperative hypotension	2.35	1.06 – 5.21	**0.036**
Preoperative limb ischemia	8.72	2.03 – 37.48	**0.004**

Bold indicates statistical significance ($P < 0.05$).
CVA, cerebrovascular accident.

Table 4 shows results of a multivariable logistic regression analysis based on a matched dataset, confirming that presenting CVA was independently associated with significantly increased risk of in-hospital mortality (odds ratio 2.99, 95% confidence interval [CI] 1.35−6.60, $P = 0.007$). The c-statistic for this model amounted to 0.701 (Hosmer-Lemeshow test: 0.789).

Secondary Outcome Variable: Mortality up to 5 Years After Discharge

Median follow-up time amounted to 2.0 years (interquartile range, 1.0−4.0 years). Multivariable Cox proportional hazards regression analysis demonstrated that CVA at presentation was not independently associated with mortality up to 5 years after discharge in survivors of the post-operative hospital stay (hazard ratio 1.52, 95% confidence interval 0.99−2.31, $P = 0.54$) (Table 5). Covariables used in this model included the balancing score for CVA, age, chronic beta blocker therapy, prior cardiac surgery, distal extension of dissection to the descending aorta, and post-operative acute renal failure.

Figure 1 shows Kaplan-Meier survival curves of patients presenting with CVA vs without CVA. As shown by the log-rank

Table 3. Primary Outcome Variables: In-Hospital Mortality and Post-Operative Complications (Chi-Square Test or Fisher's Exact Test)

Outcome Variables	Missing Data n (%)	All Patients n = 1449 (100%)	CVA n = 110 (7.6%)	No CVA n = 1339 (92.4%)	*P*-Value	Effect Size
In-hospital mortality (%)	0 (0%)	326/1449 (22.5%)	36/110 (32.7%)	290/1339 (21.7%)	**0.008**	0.070
Neurological deficit (%)						
CVA	262 (18.1%)	108/1187 (9.1%)	15/64 (23.4%)	93/1123 (8.3%)	**<0.001**	0.119
Coma	271 (18.7%)	42/1178 (3.6%)	4/64 (6.3%)	38/1114 (3.4%)	0.282	0.035
SCI	273 (18.8%)	13/1176 (1.1%)	0/63 (0.0%)	13 /1113(1.2%)	1.000	-0.025
Mesenteric ischemia (%)	100 (6.9%)	39/1349 (2.9%)	1/78 (1.3%)	38/1271 (3.0%)	0.723	-0.024
Acute renal failure (%)	91 (6.3%)	295/1358 (21.7%)	22/84 (26.2%)	273/1274 (21.4%)	0.305	0.028
Extension of dissection (%)	114 (7.9%)	29/1335 (2.2%)	3/77 (3.9%)	26/1258 (2.1%)	0.232	0.029
Hypotension (%)	140 (10.3%)	237/1300 (18.2%)	7/74 (9.5%)	230/1226 (18.8%)	**0.044**	-0.056
Cardiac tamponade (%)	132 (9.1%)	86/1317 (6.5%)	7/76 (9.2%)	79/1241 (6.4%)	0.330	0.027
Limb ischemia (%)	114 (7.9%)	49/1335 (3.7%)	5/77 (6.5%)	44/1258 (3.5%)	0.175	0.037
Discharge to tertiary hospital (%)	386 (26.6%)	507/1063 (47.7%)	36/71 (50.7%)	471/992 (47.5%)	0.599	0.013

Bold indicates statistical significance ($P < 0.05$).
CVA, cerebrovascular accident; SCI, spinal cord ischemia.

Table 5. Secondary Outcome Variable: Mortality up to 5 Years After Discharge (Multivariable Cox Proportional Hazards Regression Analysis)

Variables	Hazard Ratio	95% Confidence Interval	*P*-Value
CVA	1.52	0.99 – 2.31	0.54
Balancing score for CVA	5.82	1.81 – 18.74	**0.003**
Age (y)	1.06	1.04 – 1.08	**<0.001**
Chronic beta blocker therapy	0.50	0.40 – 0.61	**<0.001**
Prior cardiac surgery	1.99	1.58 – 2.51	**<0.001**
Distal extension of dissection to descending aorta	1.43	1.14 – 1.79	**0.002**
Post-operative acute renal failure	1.60	1.29 – 1.97	**<0.001**

Bold indicates statistical significance ($P < 0.05$).
CVA, cerebrovascular accident.

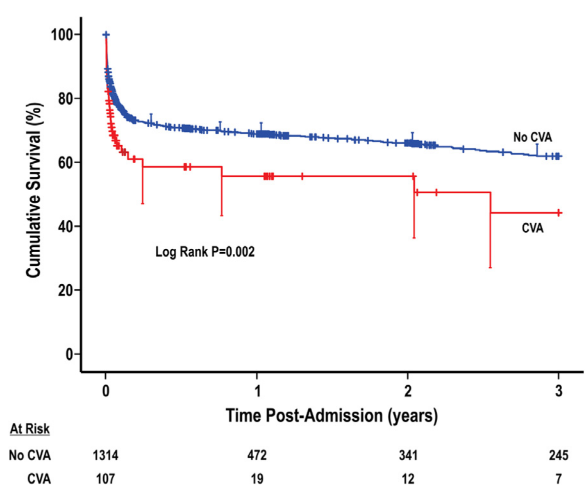

Figure 1. Survival up to 3 years after admission in patients with CVA vs without CVA (Kaplan-Meier Survival Curves). Kaplan-Meier survival curves indicate that patients presenting with cerebrovascular accident (CVA) are at significantly increased risk of mortality mainly in the early postoperative phase, in accordance with our analysis of in-hospital mortality (log-rank test, P = 0.002). Importantly, our multivariable Cox proportional hazards regression model shows that presenting CVA is not independently associated with long-term survival in survivors of the postoperative hospital stay (P = 0.54). Vertical bars indicate 95% confidence intervals. (Color version of figure is available online.)

test, the CVA group was at risk of significantly impaired unadjusted survival up to 3 years after admission (log-rank test, P = 0.002).

Table 6. In-Hospital Outcomes of Patients receiving Medical Management

Outcome Variables	Medical Management n = 35 (100%)
In-hospital mortality (%)	25/35 (71.4%)
Neurological feficit (%)	
CVA	30/33 (90.9%)
Coma	6/30 (20.0%)
SCI	0/31 (0.0%)
Mesenteric ischemia (%)	1/32 (3.1%)
Acute renal failure (%)	6/32 (18.8%)
Extension of dissection (%)	1/32 (3.2%)
Hypotension (%)	15/33 (45.5%)
Cardiac tamponade (%)	2/31 (6.5%)
Limb ischemia (%)	1/30 (3.3%)
Discharge to tertiary hospital (%)	3/10 (30.0%)

CVA, cerebrovascular accident; SCI, spinal cord ischemia.

In-Hospital Outcomes of Patients Receiving Medical Management

Table 6 shows in-hospital outcomes of patients presenting with CVA who received medical management. This group of patients was at exceedingly high risk of in-hospital mortality (71.4%), CVA (90.9%), and coma (20.0%) during the hospital stay. Also, the rates of acute renal failure (18.8%) and hypotension (45.5%) were substantial in this patient group.

Supplementary Table 3 shows the reasons for medical management in patients presenting with CVA. Most patients received medical management due to comorbidities (96.9%), followed by age (75.0%), and patient refusal (20.0%).

DISCUSSION

Our analysis was based on the clinical notion that CVA in the presence of TAAAD might exert more deleterious effects on post-operative outcomes in patients of advanced age. Surgery for TAAAD commonly necessitates prolonged durations of CPB, HCA and cerebral perfusion. Patients are at risk of severe peri-operative complications, including the requirement of postcardiotomy extra-corporeal membrane oxygenation support, re-exploration for bleeding, renal replacement therapy, or permanent neurological deficit necessitating prolonged rehabilitation.[2]

Thus, judicious patient selection for surgery is critically important when a diagnosis of TAAAD has been established. Over the last 2 decades, clinical research has been conducted to evaluate whether surgical management remains the preferential treatment strategy in septuagenarians and octogenarians presenting with TAAAD. Evidence from the IRAD published in 2010 indicates that patients aged 70 years or above are at significantly increased risk of in-hospital mortality after surgical repair (30.8% vs 21.2%, P = 0.005).[3] The present analysis of a more contemporary IRAD cohort shows improved but comparable results, with an in-hospital mortality rate of 22.5% in the

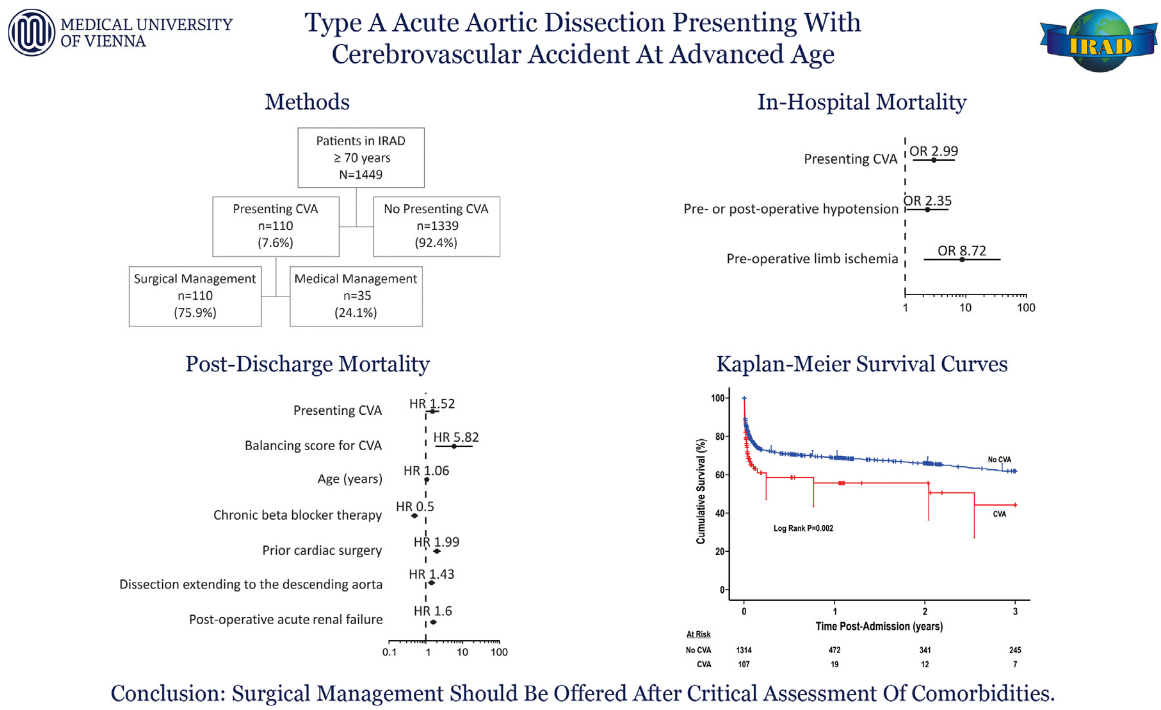

Figure 2. Type A acute aortic dissection presenting with cerebrovascular accident at advanced age (Graphical Abstract). Patients aged 70 years or above presenting with type A acute aortic dissection and cerebrovascular accident (CVA) are at significantly increased risk of in-hospital mortality (odds ratio 2.99, 95% confidence interval 1.35−6.60, $P = 0.007$). However, late mortality is not influenced by pre-operative CVA in hospital survivors (hazard ratio 1.52, 95% confidence interval 0.99−2.31, $P = 0.54$). Based on our results, we believe that surgical management should be offered after critical assessment of comorbidities (Abbreviations: CVA, cerebrovascular accident; HR, hazard ratio; IRAD, International Registry of Acute Aortic Dissection; OR, odds ratio). (Color version of figure is available online).

entire surgical cohort of patients aged 70 years or above (Table 3). Similar findings have been reported from the German Registry for Acute Aortic Dissection Type A (GERAADA), with postoperative mortality rates of 16% in septuagenarians and 35% in octogenarians.[12] Other groups have reported acceptable rates of surgical mortality between 0% and 15.6% in octogenarians.[13−15]

A number of studies have investigated outcomes of patients presenting with neurological deficit as a complication of TAAAD. Several analyses have shown that patients who present with CVA in the presence of TAAAD are at risk of significantly increased rates of postoperative mortality between 25.7% and 40.2%.[5,6,8,11] A recently published analysis from the IRAD including all age groups has shown an in-hospital mortality rate of 25.7% and a postoperative CVA rate of 17.5% in patients presenting with CVA.[11] In line with these results, our analysis reveals an in-hospital mortality rate of 32.7% in the CVA group, compared with 21.7% in patients presenting without CVA (P = 0.008) (Table 3). Moreover, our analysis confirms presenting CVA as an independent risk factor for in-hospital mortality after surgery (Table 4). Importantly, multivariable analysis shows that long-term mortality is not affected by CVA at presentation in hospital survivors (Table 5).

Considering these results, we believe that a strategy of timely surgical management should be initiated in selected patients aged 70 years or above presenting with CVA Figure 2. Notably, our conclusions cannot be extended to patients aged 90 years or above. Our data show that no patient presenting with CVA over the age of 87 years underwent surgical management in IRAD centers, suggesting that this was considered the upper age limit by aortic surgeons (Table 1). Additionally, comorbidities were commonly reported as a reason for medical management (96.9%) (Supplementary Table 3). Unfortunately, the IRAD does not provide specific diagnoses of comorbidities. Based on the literature, we believe that the following comorbidities might render patients presenting with CVA unsuitable for surgery: presence of mesenteric malperfusion with severe acidosis (base deficit ≤ 10); cardiopulmonary resuscitation over 15 min; chronic comorbidities that limit life expectancy below 12 months.[16,17] Importantly, we believe that a highly individualized decision needs to be made in each case after critical risk-benefit assessment. Patients and their families need to be centrally involved in these decision processes, given that a considerable rate of patients refused to undergo surgery (20.0%) (Supplementary Table 3).

Our analysis of patients who received medical management demonstrated that this treatment group was at substantial risk of in-hospital mortality, CVA, coma, acute renal failure, and hypotension (Table 6). These findings are in line with a meta-analysis of 6,894 medically managed patients showing substantial in-hospital mortality of 39.1% in patients presenting with TAAAD.[18] An IRAD analysis published in 2010 demonstrated that in-hospital mortality rates of patients receiving medical management were significantly higher when compared with patients receiving surgical management (septuagenarians: 54.7% vs 29.7%, P = 0.001; octogenarians: 55.2% vs 37.9%, P = 0.188).[3] In patients aged 90 years or above, survival at 5 years was reported to be at 25% following medical management, compared with 49.2% in patients undergoing surgery (P = 0.011).[19]

If a decision for surgical management has been made, rapid restitution of cerebral perfusion is of utmost importance. Time between symptom onset and the beginning of surgery is significantly associated with the risk of postoperative permanent neurological deficit.[7,20] Early surgical repair within 5 hours of presentation has been associated with neurological improvement even in patients who present in a comatose state.[21,22] On the other hand, a duration of more than 9.1 hours between symptom onset and skin incision is associated with a lack of postoperative neurological improvement.[20] Our findings suggest that IRAD centers were following a strategy of rapid diagnosis and early initiation of surgery in more critically ill patients, given that the median time between initial admission and surgery was significantly shorter in the CVA group (6.0 hours vs 7.0 hours, P = 0.024) (Supplementary Table 2).

During surgical repair of the ascending aorta, various techniques have been proposed to ascertain timely cerebral re-perfusion. A recent paper has shown that echocardiography-guided ascending aortic cannulation using Seldinger's technique enables a median time of 5.5 hours between symptom onset and the beginning of CPB in patients presenting with CVA.[23] Although reporting on a small cohort of only 16 patients, this paper demonstrates an excellent postoperative mortality rate of 6.3% and significantly improved Modified Rankin Scale scores in all patients.[24] Also, a surgical protocol has been proposed that includes standardized total arch replacement and common carotid artery replacement in patients presenting with dissection of the carotid artery.[25] Despite a cerebral malperfusion rate of 33.7% at presentation, this group reports excellent postoperative rates of stroke (3.3%) and in-hospital mortality (14.1%) in patients undergoing total arch replacement. Other groups have reported direct surgical fenestration of the carotid artery, intra-operative carotid stenting, and percutaneous carotid stenting before the initiation of surgical repair, with favorable neurological outcomes.[26−30]

The role of cerebral perfusion during HCA has been extensively discussed. In the present analysis, cerebral perfusion was utilized more commonly in patients presenting with CVA (94.9% vs 81.8%, P= 0.036) (Supplementary Table 2). A recent meta-analysis of 68 studies including 26,968 patients showed that both antegrade and retrograde cerebral perfusion (ACP, RCP) were associated with significantly improved postoperative neurological outcomes and survival when compared with deep HCA alone.[31] Moreover, bilateral ACP is associated with significantly improved survival in patients who require prolonged durations of ACP.[32] More detailed subgroup analyses are necessary to determine the optimal strategy of cerebral perfusion in patients with pre-operative CVA or carotid dissection in the presence of TAAAD.

Limitations

The present study is subject to typical limitations of retrospective registry analyses. Among these, the IRAD doesn't provide standardized insights into the extent of pre- or postoperative clinical neurological impairment (eg, National Institutes of Health Stroke Scale, Modified Rankin Scale, Glasgow Coma Scale).[24] Comparative statistical analysis of patients who received surgical vs medical management could not be performed due to selection bias.

CONCLUSIONS

Our results demonstrate that patients presenting with TAAAD and CVA at the age of 70 years or above are at significantly increased risk of in-hospital mortality and postoperative rates of CVA. However, long-term mortality is not affected in hospital survivors. Medical management is associated with poor outcomes. Based on our results, we believe that surgical management should be offered after critical assessment of comorbidities.

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SUPPLEMENTARY MATERIAL

Scanning this Supplementary QR Code will take you to the article title page to access supplementary material.

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