Patients with type A acute aortic dissection presenting with major brain injury: Should we operate on them?

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Objectives: The management strategy remains controversial for patients presenting with type A acute aortic dissection with cerebrovascular accident or coma. The present study aimed to help guide surgeons treating these high-risk patients.

Methods: Of 1873 patients with type A acute aortic dissection enrolled in the International Registry for Acute Dissection, 87 (4.7%) presented with cerebrovascular accident and 54 (2.9%) with coma. The hospital and 5-year results were stratified by the presence and type of brain injury (no injury vs stroke vs coma) and management type (medical vs surgical). Independent predictors of short- and mid-term survival were identified.

Results: Presentation with shock, hypotension, or tamponade (46.8% vs 25.2%; $P < .001$) and arch vessel involvement (55.0% vs 36.1%; $P < .001$) was more likely in patients with brain injury. Surgical management was avoided more often in patients with coma (33.3%) or cerebrovascular accident (24.1%) than in those without brain injury (11.1%; $P < .001$). The overall hospital mortality was 22.7% without brain injury, 40.2% with cerebrovascular accident, and 63.0% with coma ($P < .001$). Mortality varied among the management types for both cerebrovascular accident (76.2% medical vs 27.0% surgical; $P < .001$) and coma (100% medical vs 44.4% surgical; $P < .001$). Postoperatively, cerebrovascular accident and coma resolved in 84.3% and 78.8% of cases, respectively. On logistic regression analysis, surgery was protective against mortality in patients presenting with brain injury (odds ratio 0.058; $P < .001$). The 5-year survival of patients presenting with cerebrovascular accident and coma was 23.8% and 0% after medical management versus 67.1% and 57.1% after surgery (log rank, $P < .001$), respectively.

Conclusions: Brain injury at presentation adversely affects hospital survival of patients with type A acute aortic dissection. In the present observational study, the patients selected to undergo surgery demonstrated improved late survival and frequent reversal of neurologic deficits. (J Thorac Cardiovasc Surg 2013;145:S213-21)

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Type A acute aortic dissection (TA-AAD) is a lethal condition requiring emergency surgery.[1,2] However, in patients with TA-AAD presenting with major brain injury, surgical management remains controversial because of the likely persistence (or progression) of neurologic deficit and considerable mortality and morbidity after surgery.[3] Given the rare occurrence of brain complications at the onset of dissection, few (and conflicting) data exist, mostly derived from limited study populations.[3-8] The International Registry for Acute Dissection (IRAD) was designed to enroll consecutive

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Abbreviations and Acronyms

CI = confidence interval
CVA = cerebrovascular accident
IRAD = International Registry for Acute Dissection
OR = odds ratio
TA-AAD = type A acute aortic dissection

patients from a broad geographic region to minimize the inherent biases seen in small surgical registries or single-center series. The aims of the present study were to compare the clinical and imaging characteristics, management, and short- and mid-term outcomes of a large group of patients with TA-AAD presenting with and without preoperative cerebrovascular accident (CVA) and coma and to assess the outcomes of patients with major brain injury according to different therapeutic strategies (surgical vs medical).

METHODS

IRAD Registry and Data Collection

The rationale and method of IRAD have been previously published.[9] In brief, IRAD was founded by agreement of 18 large referral centers in 1996, with its main purpose being to assess the etiology, clinical features, imaging findings, treatment, and outcomes of patients with acute aortic dissection (both type A and type B). Patients with acute aortic dissection were identified either prospectively at presentation or retrospectively by searching hospital discharge diagnosis records and/or the surgery, pathology, and imaging databases. The diagnosis was determined from the imaging, surgical visualization, or autopsy findings. TA-AAD was defined as any dissection that involved the ascending aorta and/or aortic arch presenting within 14 days of symptom onset. Patient data were collected using standardized forms, including 290 variables for patient demographics, history, clinical presentation, physical findings, imaging studies, therapeutic management, in-hospital mortality, and adverse events. The completed data forms were forwarded by the participating IRAD sites to the coordinating center at the University of Michigan and reviewed for face validity and completeness. Annual follow-up data were obtained for up to 5 years after discharge using standardized data forms. The collected follow-up data included variables on clinical, imaging, and vital information. When applicable, missing data on mortality were obtained by searching the Social Security Death Index. At each enrolling hospital, the study investigators obtained approval from their ethics and/or institutional review board to participate in the IRAD studies.

Patient Selection and Data Analysis

We examined 1873 consecutive patients with TA-AAD enrolled from January 1996 to February 2011. The patients were categorized according to presence and type of preoperative major brain injury (no brain injury vs CVA vs coma). The preoperative clinical characteristics, imaging data, management, and mid-term outcomes were compared among the 3 subcohorts. CVA was defined as the persistent loss of neurologic function caused by an ischemic event, with or without confirmation by either computed tomography or magnetic resonance imaging. Coma was indicated if the patient experienced complete mental unresponsiveness (beyond that expected from anesthesia), with no evidence of psychological or physiologically appropriate responses to stimulation. A composite variable of adverse outcomes was created to report the incidence of the most severe and incapacitating complications after surgical repair: death and/or CVA and/or coma.

In patients with preoperative brain injury, the in-hospital outcomes were assessed according to type of management used (medical vs surgical), and the independent risk factors for hospital death were identified in all and in surgically treated patients with preoperative brain injury.

The estimates of 5-year survival were stratified by the presence and type of brain injury at admission (no brain injury vs CVA vs coma) in the overall population and in the subgroups of patients undergoing medical or surgical therapy. The independent predictors of follow-up mortality were identified in patients presenting with brain injury.

Statistical Analysis

Continuous variables are presented as the mean ± standard deviation or median and quartile 1 to quartile 3 and categorical variables as percentages. In all cases, the missing data were not defaulted to negative, and the denominators reflected only the cases reported. Univariate analyses between groups were done using chi-square tests (or Fisher's exact tests) and Student's *t* tests, as appropriate. Univariate analysis was first performed using preoperative and intraoperative variables to determine their individual relationship to in-hospital mortality in all patients and in surgically treated patients with preoperative brain injury. The variables that achieved $P < .15$ on univariate analysis and the variables from the previously published IRAD type A aortic dissection mortality model[10] were introduced to a gender-adjusted multivariate analysis by backward stepwise logistic regression to estimate the independent adjusted odds ratios (ORs) of factors related to hospital mortality. Long-term survival analysis was performed using Kaplan-Meier curves, and differences in survival between groups were examined with the log-rank test. Statistical analysis was performed using SPSS, version 18.0 (SPSS, Chicago, Ill).

RESULTS

Characteristics of Patients With and Without Brain Injury

Of 1873 patients with TA-AAD enrolled in IRAD, 87 (4.7%) presented with CVA and 54 (2.9%) with coma. Compared with the patients without brain injury, those with CVA and coma presented more rapidly to a referring or tertiary hospital (no brain injury, 2.1 hours; CVA, 1.1 hours; coma, 1.0 hour; $P < .001$) and less frequently complained of chest pain (no brain injury, 81.7%; CVA, 73.8%; coma, 52.3%; $P < .001$) or abdominal pain (no brain injury, 43.4%; CVA, 32.5%; coma, 34.1%; $P = .077$) at the onset of dissection. Hypotension/shock/tamponade (no brain injury, 25.2%; CVA, 40.2%; coma, 59.3%; $P < .001$) and syncope (no brain injury, 15.3%; CVA, 43.2%; coma, 56.5%; $P < .001$) were more likely to occur in patients with brain complications. Moreover, the risk profile of patients with CVA and coma was more often aggravated by renal failure (no brain injury, 7.9%; CVA, 13.4%; coma, 21.2%; $P = .002$), myocardial ischemia or infarction (no brain injury, 10.2%; CVA, 13.4%; coma, 25.0%; $P = .002$), and limb ischemia (no brain injury, 9.7%; CVA, 18.3%; coma, 15.4%; $P = .019$; Tables 1 and 2).

On the imaging studies, the characteristics of dissection were similar in the patients with and without brain injury, except for arch vessel involvement by the dissection, which was documented in 61.8% of patients with CVA, 43.6% of patients with coma, and 36.1% of uncomplicated patients ($P < .001$; Table 3).

TABLE 1. Demographics and history of patients with and without major brain injury (CVA and coma)

Variable	No brain injury	CVA	Coma	P value
Age (y)	61.5 ± 14.6	63.1 ± 13.7	62.8 ± 12.2	.506
Men	1177 (67.9%)	54 (62.1%)	31 (57.4%)	.151
White race	1449 (89.7%)	78 (95.1%)	47 (90.4%)	.281
Interval from symptoms to presentation (h)	2.1 (1.0-11.9)	1.1 (0.7-2.9)	1.0 (0.5-1.9)	<.001
Interval from presentation to surgery (h)	12.8 (5.7-30.7)	9.8 (4.4-54.6)	9.7 (5.1-20.0)	.494
Interval from symptoms to surgery (h)	15.9 (7.5-42.7)	12.3 (6.6-56.1)	13.8 (6.3-24.0)	.310
Etiology and history				
Atherosclerosis	369 (22.1%)	28 (32.6%)	13 (25.5%)	.072
Diabetes	103 (6.2%)	4 (4.7%)	4 (7.8%)	.737
Hypertension	1192 (70.6%)	68 (80.0%)	33 (66.0%)	.131
Aortic valve disease	205 (12.3%)	10 (11.9%)	5 (10.0%)	.882
Bicuspid aortic valve	65 (4.5%)	4 (5.6%)	2 (4.8%)	.701
Marfan	78 (4.7%)	3 (3.5%)	0 (0.0%)	.358
Peripartum	4 (0.2%)	1 (1.2%)	0 (0.0%)	.329
Cocaine abuse	23 (1.4%)	1 (1.2%)	0 (0.0%)	1.000
Known aortic aneurysm	219 (13.1%)	9 (10.6%)	4 (8.0%)	.466
Previous aortic dissection	69 (4.1%)	2 (2.4%)	0 (0.0%)	.355
Previous cardiac surgery	236 (14.3%)	12 (14.5%)	6 (11.8%)	.879
History of catheterization/ angiography	162 (11.5%)	6 (9.1%)	3 (7.3%)	.752

Data presented as n (%) or median (quartile 1 to quartile 3). *CVA*, Cerebrovascular accident.

TABLE 2. Clinical presentation of patients with and without major brain injury (CVA and coma)

Variable	No brain injury	CVA	Coma	P value
Chest pain	1368 (81.7%)	62 (73.8%)	23 (52.3%)	<.001
Anterior	1105 (80.0%)	55 (78.6%)	19 (52.8%)	<.001
Posterior	499 (39.4%)	26 (40.0%)	8 (24.2%)	.209
Back pain	702 (43.4%)	27 (32.5%)	15 (34.1%)	.077
Abdominal pain	426 (26.5%)	15 (18.5%)	12 (26.7%)	.282
Leg pain	189 (11.9%)	13 (16.3%)	6 (14.0%)	.474
Quality of pain				
Migrating	194 (12.4%)	16 (20.3%)	4 (9.5%)	.102
Radiating	602 (38.1%)	16 (20.3%)	12 (28.6%)	.003
Pain severity				
Mild	110 (8.0%)	6 (9.0%)	2 (6.7%)	.950
Severe	1044 (76.3%)	52 (77.6%)	19 (63.3%)	.246
Worst ever	214 (15.6%)	9 (13.4%)	9 (30.0%)	.104
Abrupt onset of pain	1340 (82.7%)	67 (83.8%)	34 (81.0%)	.927
Febrile	33 (2.4%)	2 (3.2%)	2 (5.9%)	.219
Hypotension/ shock/tamponade	403 (25.2%)	33 (40.2%)	32 (59.3%)	<.001
Hypertension	501 (31.4%)	21 (25.6%)	10 (18.5%)	.079
Syncope	252 (15.3%)	35 (43.2%)	26 (56.5%)	<.001
Ischemic spinal cord damage	25 (1.6%)	2 (2.4%)	2 (4.3%)	.131
Myocardial ischemia/ infarction	172 (10.2%)	11 (13.4%)	13 (25.0%)	.002
Cardiac heart failure	112 (6.7%)	7 (8.3%)	7 (14.0%)	.127
Acute renal failure	134 (7.9%)	11 (13.4%)	11 (21.2%)	.002
Limb ischemia	163 (9.7%)	15 (18.3%)	8 (15.4%)	.019
Any pulse deficit	363 (28.1%)	40 (52.6%)	18 (43.9%)	<.001

Data presented as n (%). *CVA*, Cerebrovascular accident.

Therapeutic Strategies for Patients With and Without Brain Injury

Surgical management was avoided more often in patients with coma (33.3%) or stroke (24.1%) than in those without brain injury (11.1%; $P < .001$). The reasons given for medical management included 1 or more of the following: comorbid illness, advanced age, and patient or family refusal. In surgically treated patients, the extent of aortic replacement, rate of associated cardiac procedures, and rate of open aortic anastomosis were equally distributed in patients with and without a brain deficit (Table 4).

Hospital Outcomes: Preoperative Brain Injury Versus No Brain Injury

Overall, hospital mortality was 22.7% in patients without a preoperative brain deficit, 40.2% in patients with CVA, and 63.0% in those with coma ($P < .001$). After treatment (either medical or surgical), CVA and coma were noted in 8.1% and 3.0% of patients presenting without brain injury, 26.7% and 5.0% of patients presenting with CVA, and 9.4% and 21.9% of patients presenting with coma, respectively ($P < .001$). Myocardial infarction or ischemia (no brain injury, 13.9%; CVA, 17.7%; coma, 32.1%; $P = .001$) and limb ischemia (no brain injury, 10.1%; CVA, 19.0%; coma, 19.2%; $P = .006$) were more likely to occur in patients with preoperative brain injury than in those without (Table 5).

Hospital Outcomes in Patients With Preoperative Brain Injury: Medical Versus Surgical Management

All patients (100%) presenting with coma and 76.2% of those with CVA died when medical management was undertaken. Only 5 (12.8%) of the 39 medically managed patients with preoperative brain injury survived to discharge. Alternatively, after surgery, mortality was 27.0% for the patients with CVA and 44.0% for those with preoperative coma ($P < .001$). Of these 99 patients with

TABLE 3. Characteristics of dissection in patients with and without mesenteric ischemia

Variable	No brain injury	CVA	Coma	P value
Origin of dissection flap				
Sinotubular junction	197 (12.1%)	7 (8.2%)	5 (10.0%)	.512
Aortic root	786 (48.4%)	42 (49.4%)	25 (50.0%)	.959
Ascending	540 (33.2%)	31 (36.5%)	17 (34.0%)	.823
Arch	64 (3.9%)	5 (5.9%)	0 (0.0%)	.210
Site of intimal tear				
Multiple	44 (3.6%)	1 (1.4%)	2 (5.4%)	.507
Not identified	481 (39.8%)	32 (46.4%)	16 (43.2%)	.546
Descending	25 (2.1%)	0 (0.0%)	0 (0.0%)	.695
Ascending	569 (47.0%)	30 (43.5%)	19 (51.4%)	.732
Arch	91 (7.5%)	6 (8.7%)	0 (0.0%)	.187
False lumen patency				
Patent	768 (71.2%)	46 (68.7%)	26 (81.3%)	.411
Partial thrombosis	214 (19.9%)	15 (22.4%)	4 (12.5%)	.507
Complete thrombosis	96 (8.9%)	6 (9.0%)	2 (6.3%)	1.000
Arch vessels involvement	449 (36.1%)	42 (61.8%)	17 (43.6%)	<.001
Any abdominal artery involvement	341 (19.9%)	29 (33.7%)	18 (34.0%)	.001
Coronary arteries compromised	161 (12.8%)	7 (10.1%)	7 (17.5%)	.542
Aortic regurgitation	794 (55.3%)	39 (53.4%)	15 (31.9%)	.006
Aortic measurement (cm)				
Aortic annulus	2.5 (2.3-2.9)	2.6 (2.3-2.9)	2.4 (2.2-2.6)	.215
Aortic root	4.2 (3.7-5.0)	4.2 (3.6-4.7)	4.2 (3.8-5.0)	.905
Ascending aorta (widest)	5.0 (4.5-5.8)	4.8 (4.0-5.5)	4.9 (4.5-5.4)	.379
Aortic arch	3.7 (3.2-4.1)	3.5 (3.1-4.3)	3.8 (3.5-4.0)	.481
Descending aorta (widest)	3.4 (3.0-3.9)	3.4 (3.0-3.9)	3.1 (2.8-3.5)	.950

Data presented as n (%) or median (quartile 1 to quartile 3). *CVA*, Cerebrovascular accident.

preoperative brain injury, 66 (66.7%) survived to discharge. Postoperatively, brain injury reversal occurred in 80.4% and 74.2% of those with CVA and coma, respectively. Thus, the composite adverse outcome occurred in 36.5% and 50.0% of those with CVA and coma, respectively (Table 6).

Independent Predictors of Hospital Mortality in Patients With Preoperative Brain Injury

On binary logistic regression analysis, surgery was protective against mortality in patients with preoperative brain injury (CVA or coma; OR, 0.058; 95% confidence interval [CI], 0.018-0.192; $P < .001$). In contrast, hypotension/shock/tamponade (OR, 3.4; 95% CI, 1.365-8.415; $P = .009$) and renal failure (OR, 3.4; 95% CI, 1.292-9.159; $P = .013$) were independent risk factors for reduced hospital survival (Figure 1).

TABLE 4. Therapeutic management and surgical procedures for patients with type A acute dissection with and without major brain injury

Variable	No brain injury	CVA	Coma	P value
Therapeutic management				
Surgical	1496 (86.3%)	63 (72.4%)	36 (66.7%)	<.001
Medical	192 (11.1%)	21 (24.1%)	18 (33.3%)	<.001
Extent of aortic replacement				
Ascending aorta replacement	1361 (93.2%)	59 (92.2%)	33 (94.3%)	.897
Root replacement	488 (36.7%)	17 (30.9%)	8 (25.8%)	.352
Complete arch replacement	229 (16.0%)	8 (13.3%)	4 (11.8%)	.783
Partial arch replacement	560 (39.5%)	30 (50.0%)	12 (36.4%)	.247
Open procedure	773 (90.0%)	36 (90.0%)	19 (86.4%)	.739
Reoperation	180 (12.9%)	7 (11.9%)	2 (6.1%)	.625
Associated procedures				
CABG	166 (11.7%)	3 (4.8%)	6 (17.1%)	.128
MVR	8 (0.6%)	0 (0.0%)	0 (0.0%)	1.000
AVR	397 (27.8%)	12 (19.7%)	9 (25.7%)	.367
Peripheral vessels replaced	71 (5.0%)	4 (6.6%)	0 (0.0%)	.360

Data presented as n (%). *CVA*, Cerebrovascular accident; *CABG*, coronary artery bypass grafting; *MVR*, mitral valve replacement; *AVR*, aortic valve replacement.

Independent Predictors of Hospital Mortality in Surgical Patients With Preoperative Brain Injury

In surgically treated patients, the only independent predictor of hospital death was hypotension/shock/tamponade (OR, 5.4; 95% CI, 0.018-0.192; $P = .009$); however, brain injury reversal was protective against hospital mortality (OR, 0.014; 95% CI, 0.069-0.742; $P = .226$; Figure 2). The delay from the onset of dissection and surgery did not correlate with mortality and brain injury reversal.

Follow-up Mortality

Of 1411 patients, 705 (50.0%) had follow-up death data available. The median follow-up duration was 36 months (quartile 1 to quartile 3, 1.02-60.0 months). The Kaplan-Meier estimate of 1-, 3-, and 5-year survival was 76.5%, 74.1%, and 72.9% for patients presenting without brain injury, 57.0%, 55.4%, and 55.4% for those with preoperative CVA, and 37.7%, 37.7%, and 37.7% for those with preoperative coma, respectively (log-rank, $P < .001$; Figure 3, *A*). The mid-term estimates of postadmission survival for patients receiving medical and surgical management are depicted in Figure 3, *B,C*: the 5-year survival of patients presenting with CVA and coma was 23.8% and 0% after medical management and 67.1% and 57.1% after surgery.

Independent Predictors of Follow-up Mortality in Patients With Preoperative Brain Injury

In patients with TA-AAD complicated by preoperative brain injury, Cox proportional hazards regression analysis

TABLE 5. Overall in-hospital mortality and complications for patients with type A acute dissection patients with and without major brain injury

Result	No brain injury	CVA	Coma	*P* value
Discharged home	1141 (74.8%)	38 (54.3%)	17 (39.5%)	<.001
Mortality	394 (22.7%)	35 (40.2%)	34 (63.0%)	<.001
CVA	177 (8.1%)	16 (26.7%)	3 (9.4%)	<.001
Coma	44 (3.0%)	3 (5.0%)	7 (21.9%)	<.001
Spinal cord injury	55 (3.4%)	4 (5.4%)	2 (4.1%)	.479
Myocardial infarction/ ischemia	231 (13.9%)	14 (17.7%)	17 (32.1%)	.001
Acute renal failure	362 (21.9%)	19 (24.1%)	17 (32.7%)	.168
Limb ischemia	166 (10.1%)	15 (19.0%)	10 (19.2%)	.006
Cardiac tamponade	289 (17.5%)	16 (20.3%)	14 (26.9%)	.189

Data presented as n (%). *CVA*, Cerebrovascular accident.

indicated hypotension/shock/tamponade (hazard ratio, 6.2; 95% CI, 2.710-14.348; $P < .001$) and renal failure (hazard ratio, 1.9; 95% CI, 1.029-3.768; $P = .041$) as significant independent predictors of reduced 5-year postadmission survival. In contrast, surgical management (hazard ratio, 0.084; 95% CI, 0.035-0.202; $P < .001$) was protective against follow-up mortality (Table E1).

DISCUSSION

Risk Profile and Outcomes of Patients With TA-AAD Presenting With Brain Injury

Different pathogenetic mechanisms could determine CVA and coma in patients with TA-AAD. These include brain malperfusion from occlusion of the arch vessels by the intimal-medial flap, hypoxic encephalopathy secondary to shock/tamponade, brain embolism from thrombus in the false lumen, and/or a combination of several of these. The IRAD data from 1873 patients with TA-AAD indicated preoperative major brain injury occurred in approximately 8% of patients (CVA, 4.7%; coma, 2.9%), and hypotension/shock/tamponade and arch vessel involvement were strongly associated with CVA and coma at presentation. Although thromboembolic and composite etiologies of brain injury could not be assessed in our study, univariate analysis showed a significantly greater incidence of hypotension/shock/tamponade (59.3% vs 25.2%) and arch vessel involvement (61% vs 36.1%) in patients with coma and CVA, respectively, than in patients without any brain injury. Furthermore, renal failure, myocardial infarction/ischemia, limb ischemia, any pulse deficit, and any abdominal artery involvement were significantly more prevalent in patients with CVA and coma, confirming the predominant and detrimental role that hypotension/shock/tamponade and malperfusion have in the clinical presentation (and prognosis) of

TABLE 6. Hospital outcomes of patients with brain injury stratified by treatment strategy

	CVA			Coma		
Outcome	Medical	Surgical	*P* value	Medical	Surgical	*P* value
Mortality	16 (76.2)	17 (27.0)	<.001	18 (100.0)	16 (44.4)	<.001
Discharged home	3 (21.4)	34 (61.8)	.007	0 (0.0)	17 (58.6)	<.001
CVA	NA	8 (15.7)		NA	3/31 (9.7)	
Coma	NA	2 (3.9)		NA	7/31 (22.6)	
Brain injury reversal	NA	4 (80.4)		NA	23/31 (74.2)	
Spinal cord injury	1 (4.8)	3 (5.7)	1.000	2 (11.1)	0 (0.0)	.130
Myocardial infarction/ ischemia	5 (26.3)	9 (15.0)	.306	4 (23.5)	13 (36.1)	.530
Acute renal failure	6 (31.6)	13 (21.7)	.374	5 (29.4)	12 (34.3)	.725
Limb ischemia	2 (10.5)	13 (21.7)	.502	5 (29.4)	5 (14.3)	.264
Cardiac tamponade	2 (10.5)	14 (23.3)	.332	4 (23.5)	10 (28.6)	1.000

Data presented as n (%). *CVA*, Cerebrovascular accident; *NA*, not applicable.

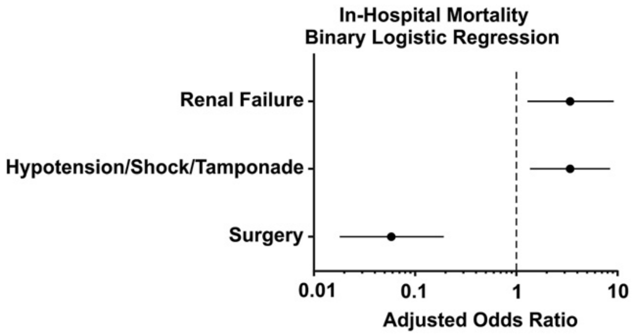


FIGURE 1. On binary logistic regression analysis, surgery was protective against mortality in patients with preoperative brain injury (cerebrovascular accident or coma; odds ratio, 0.058; 95% confidence interval, 0.018-0.192; $P < .001$), but hypotension/shock/tamponade (odds ratio, 3.4; 95% confidence interval, 1.365-8.415; $P = .009$) and renal failure (odds ratio, 3.4; 95% confidence interval, 1.292-9.159; $P = .013$) were independent risk factors for reduced hospital survival.

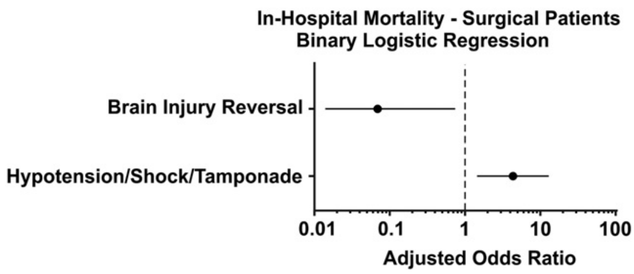
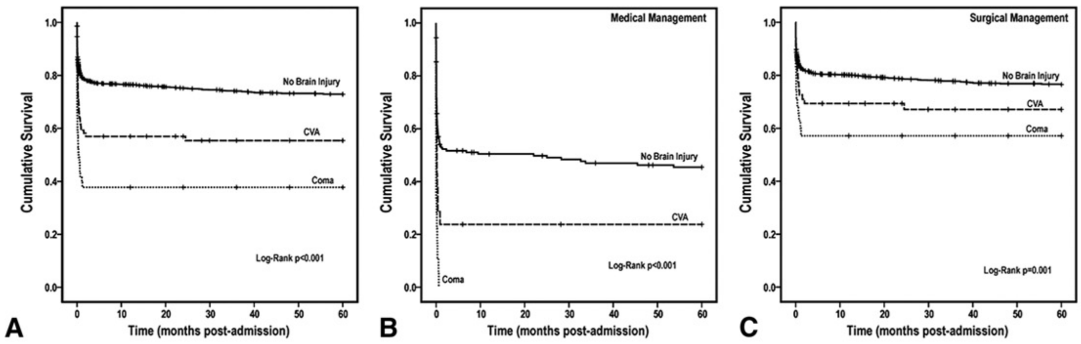


FIGURE 2. In surgically treated patients, the only independent predictor of hospital death was hypotension/shock/tamponade (odds ratio, 5.4; 95% confidence interval, 0.018-0.192; $P = .009$); however, brain injury reversal was protective against hospital mortality (odds ratio, 0.014; 95% confidence interval, 0.069-0.742; $P = .226$).



A. All Patients: 5-Year Post-Admission Survival.

Survival Estimate	1-Year	2-Year	3-Year	4-Year	5-Year
No Brain Injury	76.5 ± 1.0%	75.2 ± 1.1%	74.1 ± 1.1%	73.2 ± 1.1%	72.9 ± 1.1%
Total Events	393	411	420	435	439
At Risk	1200	1017	937	838	770
Preop CVA	57.0 ±5.3%	57.0 ± 5.3%	55.4 ± 5.4%	55.4 ± 5.4%	55.4 ± 5.4%
Total Events	37	37	38	38	38
At Risk	46	39	32	28	26
Preop Coma	37.7 ± 6.7%	37.7 ± 6.7%	37.7 ± 6.7%	37.7 ± 6.7%	37.7 ± 6.7%
Total Events	33	33	33	33	33
At Risk	20	17	16	13	11

B. Medical Management Patients Only: 5-Year Post-Admission Survival.

Survival Estimate	1-Year	2-Year	3-Year	4-Year	5-Year
No Brain Injury	50.4 ± 3.8%	49.7 ± 3.8%	47.0 ± 3.8%	46.2 ± 3.9%	45.4 ± 3.9%
Total Events	86	87	91	92	93
At Risk	80	72	67	60	55
Preop CVA	23.8 ± 9.3%	23.8 ± 9.3%	23.8 ± 9.3%	23.8 ± 9.3%	23.8 ± 9.3%
Total Events	16	16	16	16	16
At Risk	4	4	3	3	2
Preop Coma	0.0%	0.0%	0.0%	0.0%	0.0%
Total Events	18	18	18	18	18
At Risk	0	0	0	0	0

C. Surgical Management Patients Only: 5-Year Post-Admission Survival.

Survival Estimate	1-Year	2-Year	3-Year	4-Year	5-Year
No Brain Injury	80.1 ± 1.0%	78.7 ± 1.1%	77.8 ± 1.1%	76.9 ± 1.1%	76.5 ± 1.1%
Total Events	289	306	316	325	328
At Risk	1091	919	836	754	691
Preop CVA	69.4 ± 5.9%	69.4 ± 5.9%	67.1 ± 6.1%	67.1 ± 6.1%	67.1 ± 6.1%
Total Events	19	19	20	20	20
At Risk	41	34	28	24	22
Preop Coma	57.1 ± 8.4%	57.1 ± 8.4%	57.1 ± 8.4%	57.1 ± 8.4%	57.1 ± 8.4%
Total Events	15	15	15	15	15
At Risk	19	17	14	13	11

FIGURE 3. Kaplan-Meier survival *curves* stratified by presence and type of brain injury in A, overall population of patients with type A acute dissection, B, patients receiving medical management, and C, patients undergoing surgical repair. *CVA*, Cerebrovascular accident.

patients with brain injury.[11] Hence, hospital mortality was twofold (40.2%) and threefold (63.0%) greater in patients presenting with CVA and coma, respectively, than in those without any brain injury (22.7%). Hypotension/shock/tamponade and renal failure, with a similar OR of 3.4, were strong predictors of reduced hospital survival in patients presenting with major brain injury.[10]

Therapeutic Management and Outcomes of Patients With TA-AAD Presenting With Brain Injury

TA-AAD is a lethal condition, and, although no randomized studies of medical versus surgical management have been performed, it represents an accepted indication for emergent surgery, which can convert a 90% mortality risk to at least a 70% chance of survival.[12] However, because cerebral reperfusion and hemorrhagic conversion of the ischemic region might worsen neurologic outcomes and lead to prohibitive postoperative mortality and morbidity rates, the pivotal role of surgery is questioned when serious preoperative brain injuries are present and remains controversial.[3-5,12,13] In the IRAD centers, the presence and type of brain injury significantly affected the therapeutic management. Surgery was not performed in 11% of patients without brain injury, 24.1% of patients with CVA, and 33.3% of patients with coma, echoing a surgical preference to sidestep surgery for these high-risk patients.

When assessing hospital outcomes according to therapeutic management, however, our data showed that medical therapy was associated with dismal outcomes: 100% mortality in patients with coma and 76.2% in those with CVA. Thus, surgery led to a hospital survival benefit of 49.6% in patients with preoperative CVA and 55.6% of those with coma. Only 12.8% of the medically treated patients with preoperative brain injury survived to discharge compared with 66.7% of those undergoing surgical repair. Hospital mortality after surgical treatment was particularly satisfactory in those with CVA (27.0%), not deviating markedly from that observed in patients without brain injury in the present series (22.7%) or from those previously reported by IRAD and other registries of aortic dissection.[14,15] Moreover, surgical survival benefits were maintained at 5 years, with curves parallel during follow-up (Figure 4). Such observations were also supported by multivariate and Cox analyses, suggesting surgery as a protective factor against both hospital and follow-up mortality in patients with preoperative brain injury.

We are well aware that our study had all the limitations inherent to registry data analysis and that patients deemed operable at the IRAD sites likely presented with a more favorable risk profile than those who were treated medically and, therefore, associated with the best hospital and mid-term outcomes. Nevertheless, the hospital and 5-year survival benefits of surgery compared with medical therapy were dramatic and, therefore, important to consider.

Brain Injury Reversal

Urgent repair in patients with TA-AAD presenting with major brain injury might be tempered by the concern that immediate cerebral reperfusion could worsen neurologic outcomes. Cambria and colleagues[3] reported that 6 of 7 patients with preoperative brain infarction died of brain damage after aortic dissection repair. However, in a series of 14 patients with preoperative stroke and aortic dissection, Estrera and colleagues[4] recently reported hospital mortality of 7.0%, with neurologic status completely recovered in 14%, improved in 43%, unvaried in 43%, and worsened in 0% after surgery. Early surgical repair (within 10 hours) correlated with improvement in neurologic status. Similarly, Tsukube and colleagues,[6] in 27 patients with TA-AAD presenting with coma, reported hospital mortality of 14% after early surgery, with full recovery of consciousness achieved in 86% of patients and complete independence in daily activities reached in 52% of survivors at 3 years. Our data from 141 patients with TA-AAD presenting with CVA or coma strongly support those reported by Estrera and colleagues[4] and Tsukube and colleagues,[6] showing that brain injury reversal is likely after surgery in selected patients, occurring in 80.4% and 74.2% of our patients with CVA and coma, respectively.

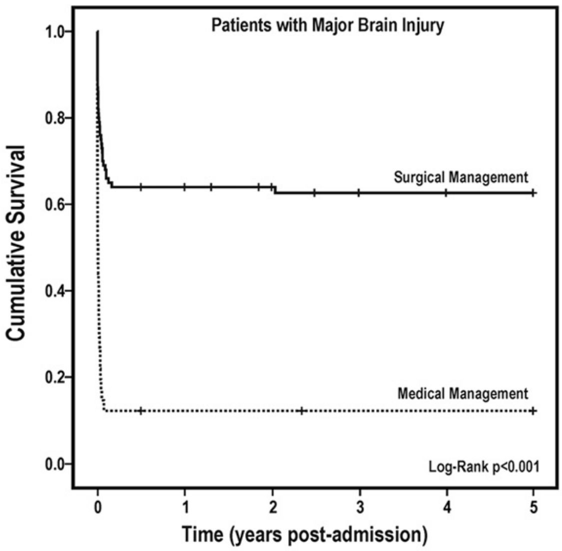
Study Limitations and Strengths

Our definitions of stroke and coma were based on a general clinical assessment and not specific quantitative or qualitative clinical criteria, such as the Glasgow Coma Scale, National Institutes of Health Stroke Scale, Rankin Score, or radiologic tests. We were not able to distinguish between patients with different cerebral lesions by location, size, or clinical relevance. Thus, the comparison of the short- and mid-term outcomes between surgical and medical management might have been influenced by a selection bias in the therapeutic referral process.

Only recently, IRAD has developed an ‘‘invasive treatment data form,’’ aiming to collect detailed information about the surgical techniques and strategies used by IRAD surgeons. Thus, data on cannulation techniques, methods of brain protection, and techniques for arch (and arch vessel) repair were sparse and not sufficient to indicate their potential effect on surgical outcomes.

Only 50% of our patients had follow-up data available, an additional limitation of our study. Nevertheless, our estimate of follow-up survival was in line with that previously reported by our registry.[16] Our follow-up did not address the quality of life of the discharged patients with preoperative brain injury.

The current knowledge of patients with TA-AAD complicated by brain injury is limited and mostly from small surgical case studies. Our study assessed the largest series of



Survival Estimate	1-Year	2-Year	3-Year	4-Year	5-Year
Medical Management	12.2 ± 5.1%	12.2 ± 5.1%	12.2 ± 5.1%	12.2 ± 5.1%	12.2 ± 5.1%
Total Events	36	36	36	36	36
At Risk	4	4	3	3	2
Surgical Management	64.0 ± 4.8%	64.0 ± 4.8%	62.6 ± 4.9%	62.6 ± 4.9%	62.6 ± 4.9%
Total Events	36	36	37	37	37
At Risk	62	47	44	39	35

FIGURE 4. Kaplan-Meier survival *curves* of patients with type A acute aortic dissection presenting with major brain injury stratified by therapeutic management.

unselected patients with TA-AAD presenting with brain injury, irrespective of therapeutic management, with the short- and mid-term outcomes stratified by the presence and type of cerebral damage, in contrast to most previous studies, which assessed only surgical cohorts.

CONCLUSIONS

Our data have shown that nearly 1 of 10 TA-AAD cases are complicated by major brain injury at the onset of dissection, resulting in a two- or threefold greater risk of mortality, depending on the presence of CVA or coma. The observation that, compared with medical therapy, surgery appeared to be associated with better early and late outcomes and that brain injury reversal occurred in 84.3% of patients with CVA and 78.8% of those with coma, suggests that brain injury, per se, should not contraindicate surgery, especially if patients do not present with signs of neurologic devastation. In the present high-risk subcohort of patients with TA-AAD, hypotension/shock/tamponade and renal failure were also confirmed as strong predictors of short- and long-term mortality. Our data suggest that in patients with TA-AAD and neurologic injury, intervention should always be considered.

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TABLE E1. Independent predictors of follow-up mortality in all patients with type A acute dissection with preoperative brain injury (CVA or coma)

Variable	HR	95% CI	*P* value
Hypotension/shock/tamponade	6.24	2.71-14.35	<.001
Renal failure	1.97	1.03-3.77	.041
Surgical management	0.08	0.04-0.20	<.001
Female gender	0.69	0.36-1.31	.253
Age ≥70 y	1.43	0.64-3.17	.386
Abnormal ECG findings	1.63	0.80-3.35	.180
Abrupt onset of pain	1.65	0.66-4.16	.286
History of atherosclerosis	1.31	0.68-2.54	.425
Previous cardiac surgery	0.42	0.13-1.33	.138

CVA, Cerebrovascular accident; *HR*, hazard ratio; *CI*, confidence interval; *ECG*, electrocardiographic.