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Modifiable Risk Factors for Early Mortality in Low-Risk Penn Class Aa Acute Type A Aortic Dissection Patients – A Descriptive Study

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Abstract

Background: **Acute Type A aortic dissection (ATAAD) without end-organ or generalized ischemia is Penn class Aa and considered low-risk. Nevertheless, surgical mortality can be considerable in this subgroup and may be related to modifiable factors. The objective of this study was to analyze 30-day mortality among ATAAD Penn class Aa patients with special reference to modifiable perioperative factors.**

Methods: **Among all patients operated for ATAAD from 1990 to 2010, all Penn class Aa patients dying within 30 days were included in a retrospective descriptive study. Pre- and intraoperative variables related to 30-day mortality were retrieved from medical records and analyzed according to avoidable or modifiable errors such as initial misdiagnosis, preoperative delay, adverse events, and forced and unforced additional procedures.**

Results: **Overall 30-day mortality was 13% (31/235). Intraoperative death occurred in 32% (10/31) of patients. Among patients not dying intraoperatively, stroke was the most common complication (48%) and cause of death overall, followed by reoperation for bleeding (33%), respiratory failure (24%), and renal failure (14%). Preoperative errors were detected in 48% of patients; one-third had initial misdiagnosis and/or diagnostic delay ≥ 24 hours. Intraoperative error(s) was noted in 74% of patients, mainly involving adverse event(s), forced additional procedures, and assisted bleeding control, with each affecting approximately 45% of patients.**

Conclusion: **Modifiable errors in pre- and intraoperative management are not uncommon among Penn class Aa patients and may contribute to 30-day mortality. Efforts should be made to mitigate the effects of modifiable factors to reduce early mortality in low-risk ATAAD.**

Key Words

Aortic dissection • Risk factors • Mortality

Introduction

The Penn classification for acute Type A aortic dissection (ATAAD) is a simple, reproducible, and validated means of stratifying the risk of early (30-day) mortality due to ischemic complications [1-4]. In the original Philadelphia study, 30-day mortality was 3.1% in Penn class Aa (i.e., uncomplicated ATAAD) patients versus 17.6-40.0% in Penn class non-Aa patients [1]. This finding demonstrates that Penn class Aa patients can be considered relatively "low-risk", although 30-day mortality in this group is more often reported in the 10-15% range [2, 4]. However, why Penn class Aa patients die is unclear, as deranged preoperative physiology secondary to localized or generalized ischemia is, by definition, not present. Therefore, the objective of this study was to analyze the cause of early death

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of Penn class Aa ATAAD patients. More specifically, we investigated putatively influential pre- and intraoperative factors (e.g., modifiable errors) that could contribute to early mortality in the absence of increased risk for cardiac and multiorgan failure related to preoperative ischemia. Identifying modifiable factors could help improve early outcomes of both Penn class Aa and non-Aa ATAAD patients.

Material and Methods

Patient Population

The underlying patient cohort from which the present study population was obtained was previously described in detail [2] and consisted of 360 consecutive patients undergoing surgery for ATAAD from 1990 to 2009. This study was extended with operations performed in 2010 to include an additional 31 patients (n = 391). After re-examination of all case notes, 72 (18%) early (i.e., in-hospital) deaths were identified. To conform to the original Penn classification cohort definitions, nine patients were excluded (three surviving more than 30 days, six operated without hypothermic circulatory arrest) to form the final study population of 31 patients (Figure 1). Thus, the study population comprised only Penn class Aa patients dying within 30 days. Demographic and basic clinical characteristics of patients in the study group (died within 30 days, n = 31) and, for comparison, operative (>30 days) survivors in Penn class Aa (n = 189) are shown in Table 1.

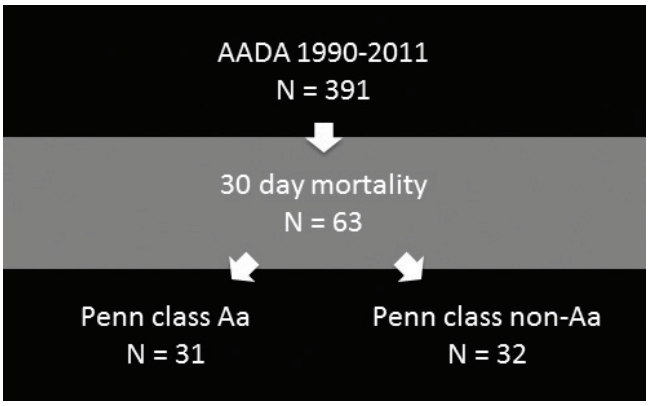

Figure 1. The study group consisted of all Penn class Aa patients dying within 30 days (n = 31) from a cohort of 391 consecutively operated patients with Acute Type A aortic dissection.

Table 1. Preoperative demographic and clinical characteristics in the study group (30-day mortality) and group of Penn class Aa 30-day survivors.

	30-day mortality (n = 31) n (%)	30-day survivor (n = 189) n (%)
Male	24 (77)	140 (74)
Age, median (IQR)	62 (56-72)	59 (51-68)
Smoking history	4 (13)	49 (26)
COPD	3 (10)	11 (5.8)
Diabetes	0	2 (1.1)
Hypertension	20 (65)	123 (65)
Obesity	6 (19)	13 (6.9)
Marfan	2 (6)	5 (2.6)
Stroke history	1 (3)	25 (13)
DeBakey Type I	22 (76)	104 (55)
Severe aortic regurgitation	8 (26)	28 (15)
Redo operation	2 (6)	7 (3.7)
Tamponade	12 (39)	45 (24)

COPD = chronic obstructive pulmonary disease; IQR = interquartile range.

Study Variables and Definitions

Age, gender, weight, height, date of operation, and date of death were collected for all patients. Family history was defined as a known occurrence of an aortic condition in a first-degree relative. Chronic obstructive pulmonary disease, diabetes, hypertension, previous cerebrovascular accident, Marfan syndrome, and shock were defined in accordance with the Society of Thoracic Surgeon's database criteria. The extent of dissection was categorized as DeBakey I (entire aorta) or II (ascending aorta, including but not distal to the arch) [5]. Penn class was defined as Aa with no clinical ischemic complications (localized or generalized), Ab with localized ischemia of one or more organ systems (brain, spinal cord, kidneys, abdominal viscera, or extremities), Ac with generalized ischemia (also including myocardial ischemia), and Abc with the combination of Ab and Ac [1]. Of note, radiological findings of malperfusion without clinical correlation were considered Penn class Aa (e.g., hemodynamically stable patients with tamponade).

Putatively modifiable pre- and intraoperative variables were examined in detail. Preoperative variables included initial misdiagnosis (explicitly affecting diagnostic or therapeutic procedures), time elapsed from symptoms to surgical treatment (any delay categorized as ≥ 24 or 48 hours); use of coronary angiography for suspicion of acute coronary syndrome (ACS) and not as part of a planned preoperative work-up, and medical treatment (thrombolysis and/or antithrombotic or antiplatelet regimens) for ACS. Intraoperative variables included errors related to adverse events, additional procedures, residual dissection, severe hemorrhage, and surgeon experience (Table 2). Assisted bleeding control was defined as pharmacological or surgical methods to achieve hemostasis that went beyond first-line management, such as mediastinal tamponade with delayed sternal closure, cabrol shunt, or NovoSeven®.

Table 2. Definitions of variables used to characterize intraoperative modifiable errors and problems.

Variable	Definition	Example(s)
Adverse event	Any sudden, unexpected intraoperative event deviating from anticipated normal course	- circulatory decompensation after anesthetic induction - aortic rupture after sternotomy - malperfusion on commencing extracorporeal circulation
Unforced additional procedure	Unplanned surgical procedure dictated by surgeon's preference	- Composite graft to manage aortic root dissection - closure of patent foramen ovale
Forced additional procedure	Unplanned surgical procedure dictated by intraoperative findings and/or events	- Coronary artery bypass grafting in response to myocardial ischemia - cabrol conduit in response to hostile coronary ostia - cabrol shunt in response to intractable bleeding
Assisted bleeding control	Intraoperative bleeding requiring any of Re-clamping, Restart CPB, forced additional procedure, use of recombinant factor VIIa, or explicit expression in case notes indicating severe bleeding problems	
Incomplete resection	Primary entry not completely resected, proximally or distally	
Re-clamping	Re-clamping of the aorta to address intraoperative problem	
Restart CPB	Re-start of cardiopulmonary bypass to address intraoperative problem	
High-volume surgeon	Surgeon belonging to the top quartile (6 out of 22 during the entire study period	

Surgical and Perioperative Procedures

All operations were performed through median sternotomy on cardiopulmonary bypass using hypothermic circulatory arrest. Utilization of ante- or retrograde cerebral perfusion for cerebral protection was at the discretion of the surgeon. Sites of arterial and venous cannulation varied but typically included the femoral artery or right axillary artery and the femoral vein or right atrium, respectively. Myocardial protection was typically provided by a combination of cold blood ante- (coronary osteal) and retrograde cardioplegic arrest. The most common surgical procedure was a supracoronary graft replacement with an open distal anastomosis often in the shape of a hemiarch replacement, with resuspension of the aortic valve and Teflon felt suture line reinforcement. Aortic root replacement and total arch replacement were used selectively, and additional surgical procedures, such as separate valve repair/replacement or coronary artery bypass grafting, were performed after individual assessment. Main intraoperative procedures are summarized in Table 3. BioGlue® was not used, and gelatin-resorcinol-formaldehyde glue was discontinued around 2004.

Table 3. Intraoperative procedures (surgical repair, cannulation, perfusion).

	n (%)
Supracoronary graft	18 (58)
Composite graft	12 (39)
Total arch replacement	4 (13)
Coronary artery bypass	6 (19)
Femoral artery cannulation	28 (90)
Mechanical assist (ECMO)	1 (3)
AXC, min, median (IQR)	138 (74-208)
CPB, min, median (IQR)	232 (173-327)
HCA, min, median (IQR)	33 (25-43)

AXC = Aortic cross-clamp; CPB = cardiopulmonary bypass; ECMO = extracorporeal membrane oxygenation; HCA = hypothermic circulatory arrest; IQR = interquartile range.

Table 4. Preoperative avoidable errors.

	n (%)
Initial misdiagnosis	11 (35)
Coronary angiography	0
ACS treatment	3 (10)
Delay ≥ 24 h	10 (32)
Delay ≥ 48 h	8 (26)
Any preoperative failure	15 (48)

ACS = Acute coronary syndrome.

Statistical Analysis

Data were summarized using descriptive statistics (i.e., frequency with percentage, median with interquartile range). Analyses were performed using Stata 13 (Stata Corp LP, College Station, TX).

Results

Overall 30-day mortality across 391 consecutive operations for ATAAD was 16.1% (n = 63). Thirty-day mortality among Penn class Aa patients was 13.2% (31/235) and among Penn class non-Aa patients was 20.6% (32/155; class Ab: 18.2% (10/55), class Ac: 15.9% (11/69), class Abc: 35.5% (11/31)). For the study patients, (i.e., died within 30 days, but not intraoperatively), major complications occurred as follows: permanent neurological damage (48%); reoperation for bleeding (33%); respiratory insufficiency requiring tracheostomy or reintubation (24%), and acute renal failure requiring hemodialysis (14%). Intraoperative death occurred in 32% of patients (10/31). Neurological damage was the most common cause of death (26%, 8/31), followed by hemorrhage alone or in combination with cardiac failure.

In the preoperative phase, initial misdiagnosis occurred in over one-third of patients. A suspicion of ACS was most common, followed by, in equal numbers, suspicion of pulmonary embolism, acute abdomen, and ruptured abdominal aortic aneurysm. The delay from first documented symptoms to surgical treatment was > 24 hours for 32% of patients and > 48 hours for 26% of patients (Table 4). Preoperative coronary angiography (for suspected ACS) was not performed, but inadvertent pharmacological treatment for ACS did occur.

Table 5. Intraoperative avoidable errors.

	n (%)
Adverse event	14 (45)
Incomplete resection	7 (23)
Forced additional procedure	14 (45)
Unforced additional procedure	6 (19)
Restart CPB	3 (10)
Re-clamping	12 (39)
Assisted bleeding control	15 (47)
Any intraoperative failure	23 (74)
Sum of intraoperative failures	
	0-7 (23)
	1-6 (19)
	2-5 (16)
	3-9 (29)
	4-2 (6)
	5-2 (6)
High-volume surgeon	13 (43)

CPB = Cardiopulmonary bypass.

Table 6. Adverse events and forced additional procedures.

Situation	Description
Adverse events	- Coronary artery destruction and disintegration (n = 4) - Aortic rupture (n = 3) - Sudden tamponade (n = 2) - Ventricular fibrillation prior to cardiopulmonary bypass - Venous air embolism from Cellsaver circuit - Compromised flow and arterial recannulation to contralateral femoral artery - Femoral venous cannula atrial septal perforation - Liver injury from rapid sternotomy
Forced additional procedures	- CABG to left coronary circulation due to LV failure or left main stem destruction (n = 4) - CABG to RCA due to RV failure (n = 3) - Cabrol patch with RA shunt (n = 3) - Supracoronary graft replaced by composite graft due to hemorrhage (n = 2) - Secondary AVR due to residual AR - Laparotomy

AR = Aortic regurgitation; AVR = Aortic valve replacement; CABG = Coronary artery bypass grafting; LV = Left ventricle; RCA = Right coronary artery; RV = Right ventricle.

Intraoperative modifiable errors occurred in 74% of cases (Table 5). Severe hemorrhage, adverse events, re-clamping of the aorta, and forced additional procedures were relatively common, with 41% of cases involving three or more such intraoperative errors. The frequency and nature of adverse events and forced additional procedures are shown in Table 6. High-volume surgeons performed approximately half of the operations in both groups.

Discussion

In Penn class Aa ATAAD patients, the absence of preoperative deranged physiology or end-organ ischemia entail lower risk of cardiac and multiorgan failure as well as lower risk of critical end-organ dysfunction, which are conditions associated with early mortality [6].

In the present study of 31 early ATAAD Penn class Aa deaths, the frequency of putatively modifiable factors in the pre- and intraoperative course was substantial. Preoperative misdiagnosis was relatively common and could include very potent pharmacotherapeutics such as thrombolysis for suspected ACS. Delay of surgical treatment ≥ 48 hours was noted in 26% of cases. Hemodynamic instability and ECG alterations are likely to occur more often in Penn class non-Aa patients, whereas Penn class Aa patients may be completely stable without presentation of alarming symptoms, contributing to broadened and/or delayed diagnostic work-up. Whether increasingly sensitive ACS diagnostics combined with earlier, often pre-hospital, initiation of ACS treatment will affect this scenario remains to be determined. In this study, management delay had no apparent effect on outcomes, although most physicians and surgeons would agree that such delays should always be avoided and that stable Penn class Aa patients can rapidly deteriorate.

Adverse intraoperative events occurred frequently, and, as a result, forced additional procedures such as coronary artery bypass grafting and graft exchange were also common. At least four adverse events appeared as surgical technical failures. Re-applying the aortic cross-clamp to address an intraoperative prob-

lem is likely a strong marker of significant technical problems that were not resolved by other means. Restarting cardiopulmonary bypass, on the other hand, may be forced by different conditions such as hemorrhage, respiratory failure, cardiac failure, volume overload, and protamine reaction.

Severe bleeding was also common, both in terms of assisted bleeding control and re-exploration. Blood product usage data were not available for analysis. Blood-conserving strategies vary, but a more liberal or even routine use of recombinant factor VIIa (NovoSeven®), for example, is becoming more popular. In this context, we used the term assisted bleeding control to describe when extraordinary measures were needed due to bleeding, a general situation applicable regardless of local treatment protocols. However, bleeding as cause of death was not dominating; rather, brain damage prevailed as the most common cause of death. The study design did not allow further analysis of whether strokes were predominantly of an embolic or hypoperfusion nature; as etiology varies, so does their potential modifiability.

Despite increased occurrence of delayed surgical treatment, adverse events, additional procedures, and intraoperative failures, intraoperative death was not excessively common. This could be related to the better preserved preoperative physiological status of Penn class Aa patients as compared with their class non-Aa counterparts. High-volume surgeons operated on patients in both groups in equal proportions, and surgeon experience was not statistically related to adverse events, additional procedures, or assisted bleeding control. In this retrospective study based on medical records, it was not possible to discern the degree to which individual deaths could have been avoided or should be regarded as unnecessary, but it must be argued that several variables related to early death in Penn class Aa ATAAD patients were modifiable and could be improved.

Recent reports suggest that the concept of "low-risk" ATAAD is reasonable. The operative risk of the typical (i.e., 62-year-old male without significant comorbidity) Penn class Aa patient according to EuroScore II is around 2.0%. In the original Philadelphia study, 30-day mortality was 3.1% in Penn class Aa [1] and equally low (3%) in a Japanese experience [3]. Some centers of excellence even report overall early mortality of 3.3-5.3% in smaller (n = 72-107) case series [7-9]. In comparison, larger single- or multicenter studies typically report 17-26% early mortality [2, 4, 10-13]. Notably, these estimates are more similar to those for high-risk groups corresponding to Penn class non-Aa, ranging from 15% to 45% [1-2, 4]. Thus, it is important to improve outcomes of Penn class Aa ATAAD and to further analyze such low-risk deaths. The seminal Cambridge FIASCO study [14] (n = 4294) analyzed early death in general low-risk cardiac operations and found that technical errors were probable in 7/16 instances of preventable death and concluded that quality improvement programs may further reduce such mortality, as evidenced by the subsequent FIASCO II study [15] showing similar crude mortality but a lower proportion of preventable deaths. The findings of the present study also indicate that pre- and intraoperative avoidable errors contribute to early mortality in the otherwise low-risk Penn class Aa group and that these factors are potentially modifiable by improved diagnostic procedures, improved primary surgical procedures including complete resection of the primary entry, and meticulous attention to surgical technical detail.

Recently, using a similar study design, Buonocore et al. investigated surgical factors related to their 23% 30-day mortality in 111 consecutive Penn class Aa patients [16]. They found an association between "non-aortic surgeon" and early mortality (odds ratio 6.40 in multivariable analysis) and noted that aortic surgeons used more extensive procedures. However, they did not investigate intraoperative details. Thus, the present study findings may point to the occurrence of intraoperative adverse events, rather than operator experience *per se*, as related to early outcome.

In summary, we found that death of Penn class Aa ATAAD patients was often related to intraoperative avoidable errors. This could explain why mortality for this subgroup is very low when reported from experienced centers in contrast to the more equivalent outcomes of Penn class Aa and non-Aa patients in other studies. Efforts should be made to analyze and explain early Penn class Aa mortality to identify modifiable factors amenable to improvement by structured programs. While not surprising, our study findings should be interpreted cautiously, acknowledging the small study sample, retrospective study design, omitted potentially influential variables, and

ambiguity between different Penn classes. In this descriptive study, no groupwise comparisons or attempts at causal inferences were made. Therefore, further investigation should be undertaken to more clearly evaluate the role of modifiable factors.

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

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