Perspective

IRAD experience on surgical type A acute dissection patients: results and predictors of mortality

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Type A acute aortic dissection (TAAD) is a disease that has a catastrophic impact on a patient's life and emergent surgery represents a key goal of early treatment. Despite continuous improvements in imaging techniques, medical therapy and surgical management, early mortality in patients undergoing TAAD repair still remains high, ranging from 17% to 26%. In this setting, the International Registry of Acute Aortic Dissection (IRAD), the largest worldwide registry for acute aortic dissection, was established to assess clinical characteristics, management and outcomes of TAAD patients. The present review aimed to evaluate and comment on outcomes of TAAD surgery as reported from IRAD series.

Keywords: Type A aortic dissection; aorta; international registry of acute aortic dissection (IRAD); aortic surgery

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Introduction

Type A acute aortic dissection (TAAD) is a catastrophic event with a high natural mortality and morbidity (1-3). In recent series, surgical mortality still ranges from 17% to 26% and TAAD continues to represent a great challenge for aortic surgeons (4-6). In this setting, the international registry of acute aortic dissection (IRAD), the largest worldwide registry for acute aortic dissection, was established to assess clinical characteristics, management and outcomes of TAAD patients, minimizing the inherent biases seen in small surgical registries or single center series. The present review aimed to evaluate and comment on the outcomes of TAAD surgery, as reported from IRAD analyses.

IRAD design

The rationale and methodology of the International Registry of Acute Dissection (IRAD) have been published previously (1,7). In brief, IRAD was founded by agreement of 12 aortic centers in 1996, with its main purpose being

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to assess the etiology, clinical features, imaging findings, treatment and outcomes of patients with acute aortic dissection (both type A and type B). Currently, 43 sites enroll patients. 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 of aortic dissection was based on history, imaging studies, direct visualization at surgery and/or post-mortem findings. Type A acute aortic dissection was defined as any dissection that involved the ascending aorta and/or aortic arch presenting within fourteen 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. In 2010, IRAD developed the IRAD Interventional Cohort (IRAD-IVC) in order to collect more detailed information (previously not captured in IRAD) on interventional procedures regarding extent of repair, extracorporeal circulation as well as methods of organ and brain protection etc. 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.

Demographics

In a recent IRAD study by Pape *et al*. assessing outcomes and trends in 4428 consecutive patients with acute aortic dissection enrolled between December 1995 and February 2013, 2,952 (67%) had type A dissection (8). The mean age of TAAD patients was 62±14.6 years. Although less frequently affected by TAAD, women enrolled in IRAD were significantly older than men (67.9 *vs*. 60.6 years) and had a higher mortality than males (33.5% *vs*. 24.1%) (9). A history of hypertension (74.4%) was the most common predisposing condition and there was also a relatively high proportion of patients who had a history of atherosclerosis (23.8%). Furthermore, in the total registry, 4.5% and 3% of TAAD were related to Marfan syndrome and iatrogenic causes respectively (8). Several race-related differences have also been described in IRAD patients (10). Among all dissections, TAAD was less frequent in the black population compared with whites (47.6% *vs*. 60.7%). Black patients were on average younger (54.6±12.8 *vs*. 64.2±15.2 years) and more likely to have a history of cocaine abuse (12% *vs*. 1.6%) and hypertension (89.7% *vs*. 73.9%). Conversely, a history of atherosclerosis, bicuspid aortic valve, existing aortic aneurysm, iatrogenic origin, or prior surgical repair of a dissection or aneurysm were more common in the Caucasian patient cohort.

Clinical presentation

In IRAD, the most common presenting symptom was the abrupt onset of pain described as 'severe' or the 'worst ever' (93%), sharp (64.4%) and frequently localized to the chest (83%) (8). One or more pulse deficits was documented in 31% of patients and hypotension was noted in 25% (1,8). The latter was often associated with neurologic deficits, myocardial ischemia, mesenteric ischemia or limb ischemia and death. Syncope was reported in 19% of patients and often indicated the presence of dangerous complications such as cardiac tamponade or obstruction of cerebral vessels (1,8). IRAD data suggest that classic symptoms and signs may be absent in TAAD patients, impeding a prompt establishment of diagnosis. Harris *et al*. (11) demonstrated that delay in acute aortic dissection diagnosis is more likely in female patients, patients without abrupt onset of pain or those presenting without pain, patients with an absence of pulse deficit or hypotension or patients who initially presented to a non-tertiary care hospital. The registry reported that 6.4% of patients presented with painless aortic dissection. In these patients hospital mortality was significantly higher than patients with painful dissection (33.3% *vs*. 23.2%) (12). Typical symptoms (abrupt onset of chest or back pain) and signs (aortic regurgitation murmur or pulse deficits) of dissection were less common among the elderly (13). In the 2010 Guidelines on Thoracic Aortic Disease, a risk assessment tool had been proposed in this setting to provide clinicians with a simple and systematic method for rapidly identify patients at high risk and to provide a framework for additional diagnostic testing based on a pretest probability of disease (14). Recently IRAD investigators validated the sensitivity of these risk markers, demonstrating that their application as part of an aortic dissection detection risk score comprise a highly sensitive (96–98%) clinical tool for the detection of acute aortic dissection (15).

Imaging studies

Given the frequency of atypical presentations and time dependent mortality, timely and accurate imaging is paramount to the prompt detection and treatment of TAAD. With similar sensitivity, computed tomography

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(CT) and trans-esophageal echocardiography (TEE) have become the standard of care for the diagnosis of this acute aortic syndrome. In IRAD, almost 70% of patients underwent multiple imaging studies. The first diagnostic modality of choice was CT in 63%, followed by TEE in 32%, aortography in 4% and MRI in 1% (16).

Surgical management

Type A acute aortic dissection is a disease that has a catastrophic impact on a patient's life and emergent surgery represents a key goal of early treatment The mortality of untreated patients with TAAD has been reported to be approximately 1% to 2% per hour after symptom onset, with up to 90% of patients succumbing within 30 days (1-3). The majority of IRAD patients presenting with TAAD were managed surgically (86% overall) with significantly more operative procedures undertaken in the more recent time periods (79% to 90%) (8). The primary aim of surgery is prevention of death from aortic rupture and is mainly accomplished by excision of the proximal intima tear, supracoronary ascending aortic replacement and re-establishment of dominant flow in the distal true lumen (17). Conservative repair of the dissected aortic root with commissural resuspension or prosthetic replacement of the pathologic aortic valve leaflets frequently completes the operation (18). Rampoldi *et al*. (19) reported on 682 IRAD patients undergoing surgical repair at 18 tertiary centers. A conservative aortic repair (supra-coronary ascending aorta replacement) was performed in 399 (58.5%) patients. More extensive aortic resections involving aortic root replacement were performed in 33.6% (n=190) of patients (aortic valve sparing procedure 5.8%, composite root replacement 16.2%) and the total arch replacement in 11.5% (n=72). An open procedure with hypothermic circulatory arrest was used in 597 patients (92%), with cerebral perfusion in 322 patients (51.4%). Evidence coming from this study showed that a standardized surgical approach is yet to be defined and that more extensive aortic resection continues to represent a matter of debate. In particular, how to manage the dissected aortic root is still an open question. Although some surgeons advocate a conservative repair of the dissected aortic root involving supracoronary ascending aorta replacement and commissural resuspension or aortic valve replacement to minimize post-operative mortality and morbidity (17), others propose more extensive interventions to replace the entire dissected aortic root tissue (20,21). Compared with conservative root replacement, a more radical root substitution is expected to improve long-term prognosis by minimizing late aortic dilatation, re-dissection and the occurrence of aortic insufficiency. However, this approach is also perceived to carry a higher immediate mortality. Recently IRAD investigators reported on 1995 patients undergoing TAAD surgery, stratifying outcomes according to type of root management: root replacement (RR) (n=699, 35%) versus more conservative root management (CR) (n=1,296, 65%). Results demonstrated that a full aortic root replacement did not increase hospital mortality (propensity score-adjusted odds ratio, 1.14) compared to more conservative root treatment. However, midterm survival (91.6% for CR and 92.5% for RR) and freedom from aortic reoperation were independent of root management type (22).

Therefore the authors concluded that the extension of aortic replacement should remain determined by each patient's clinical and anatomical characteristics as well as by the surgical experience of the operating surgeon. An aggressive approach with replacement of the aortic root seems appropriate in patients with well-acknowledged risk factors for late aortic complications or likely downstream need for re-interventions (young age, connective tissue disease and bicuspid aortic valve).

Results

In large multicenter surgical registries, in-hospital mortality for TAAD patients ranges from 17% to 26% (4-6). In a recent IRAD study assessing trends over a 17-year span, surgical mortality in patients with TAAD has significantly decreased from 25% to 18% (8). Consistent with data reported by others (5,6,23-25), IRAD results suggested that in patients undergoing TAAD surgery, early survival was affected more by preoperative complications and patients' comorbidities than by the type of surgical management (4,19). The principal independent pre-operative predictors of mortality identified in IRAD a were history of aortic valve replacement (OR, 3.12), migrating chest pain (OR, 2.77), pre-operative limb ischemia (OR, 2.10), hypotension during presentation (OR, 1.95) or shock/cardiac tamponade (OR, 2.69) (4).

Almost one-third of patients presenting with TAAD are over 70 years of age (26,27). In this setting, data from IRAD (26) demonstrated that, although surgical mortality significantly increased with increased age (38.2% for patients ≥70 years of age compared to 26.0% of younger patients), surgical management is still associated with

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significantly lower in-hospital mortality rates compared with optimal medical management (23.8% *vs.* 59.35% in patients ≤80 years of age). Therefore a surgical approach should be considered in all patients with TAAD and should not be denied on the basis of advanced age alone.

According to risk profile, more than 50% of IRAD patients who underwent TAAD surgery could be categorized as unstable at the time of surgery. In the registry patients were defined as unstable in the presence of cardiac tamponade, shock, congestive heart failure, cerebrovascular accident, stroke, coma, myocardial ischemia, infarction (or both), acute renal failure, or mesenteric ischemia/infarction at the time of the operation. As would be predicted, in-hospital mortality in this group was much higher compared to patients without unstable features (31.4% *vs.* 16.7%) regardless of the type of surgical procedure (4). A predictive factor of survival in this high-risk category of patients was time to operation. Not surprisingly, mean time interval from onset of symptoms to surgical intervention was shorter in unstable patients than in stable patients (3.4 *vs.* 5 hours) (4). Congestive heart failure on presentation was detected in 6.4% of IRAD patients and was not associated with increased risk mortality (28).

Contrariwise, malperfusion syndromes are associated with elevated mortality and dismal postoperative outcomes in TAAD patients (5,29-31). According to literature, the incidence of brain malperfusion ranges from 7% to 14% (29,30,32,33), and significantly affected the therapeutic management. IRAD data (33) showed that nearly 1 out of 10 TAAD patients are complicated by major brain injury at onset of dissection [cerebrovascular accident (CVA) 4.7%; coma 2.9%], carrying a two or threefold higher mortality depending on presence of CVA or coma respectively. Even in this cohort, surgery was found to be a protective factor against hospital mortality in patients with preoperative brain injury (OR, 0.058; P<0.001), although more than half of these patients do not still undergo TAAD repair. Nevertheless, medical therapy was associated with dismal outcomes: 100% mortality in patients with coma and 76.2% in those with CVA. Furthermore, return of brain function was frequent after surgery occurring in 84.3% of CVA patients and in 78.8% of those with coma. Therefore TAAD patients with brain injury should always be considered for intervention, especially if they do not present with signs of neurologic devastation.

Mesenteric ischemia is often an insidious end-organ malperfusion complication occurring in 3.7% of IRAD patients and is an important predictor for hospital mortality (OR, 2.5) (34). Although mesenteric ischemia is a fairly rare complication, it is very often associated with clinical or imaging signs of other organ injury or malperfusion making the prognosis really unfavorable (34,35). In such patients, when compared with medical therapy, surgery or hybrid management (central aortic operation with percutaneous treatment of mesenteric malperfusion) was associated with better outcomes. Hospital mortality of patients with mesenteric malperfusion receiving medical and surgical/hybrid therapy was 95.2% and 41.7% respectively (P<0.001). However, IRAD data showed that hybrid management was applied in a very few cases and that immediate surgical repair of the proximal dissected aorta still represents the most common therapeutic approach for patients with TAAD complicated by mesenteric malperfusion (34).

Pulse deficits are common signs in TAAD patients and were associated with higher risk of early mortality and post-operative complications (RR, 2.73) (36). Pre-operative limb ischemia was reported in 9.7% of IRAD cohort and emerged as independent predictor (OR, 2.1) of subsequent operative mortality (4)

As shown by IRAD data, the aforementioned TAAD-related complications increased operative mortality and morbidity in patients undergoing TAAD repair. Nevertheless, surgery was consistently associated with considerably lower in-hospital mortality rates compared with medical treatment. Therefore surgery should be considered in all TAAD patients, but the definitive management should be individualized for each case based on patient clinical and anatomical characteristics, institutional volume of TAAD operations, surgical experience of the operating surgeon and patient/family preferences (6,37).

Conclusions

Data from IRAD showed that mortality in TAAD patients remains high even though surgical outcomes have significantly improved over the past 20 years. Prognosis of TAAD patients was largely determined by patient's characteristics, comorbidities and dissection-related complications; in particular surgical mortality was mainly related to unstable patients with pre-operative organ malperfusion. Compared with other forms of therapy, surgery was associated with superior survival, even in high-risk patients, and thus should be considered in all patients with definitive management individualized for each case based on patients' characteristics and surgical experience of the operating surgeons.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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