Distinction between Acute and Chronic Type B Aortic Dissection: Is there a Sub-acute Phase?

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WHAT THIS PAPER ADDS
Aortic dissection is defined as acute within 14 days after onset of symptoms. This definition is used in trials and in clinical practice. In contrast to patients with acute complications, such as rupture, rapid enlargement and malperfusion, patients with chronic dissection are treated for aneurysm formation. In this study, a significant proportion of patients presented with acute complications requiring TEVAR 15-85 days after onset of aortic dissection. This indicates that there is a sub-acute, unstable phase in the transition between acute and chronic dissection during which acute and life-threatening complications might occur, which questions the relevance of the current definition.

Objectives: This study aims to assess the relevance of the definition of acute dissection, to analyse whether there is a sub-acute phase and to determine early outcome of thoracic endovascular aortic repair (TEVAR) in acute complicated type B aortic dissection.

Design: Dual-centre consecutive case series.

Materials: Between 1999 and 2011, 102 patients underwent TEVAR for non-traumatic acute complicated type B dissection in Zurich, Switzerland, and Uppsala, Sweden. In addition, 22 patients treated for an acute dissection-related complication occurring >14 days after onset of symptoms were included. Median age was 68 years, 35% were women.

Methods: Demographic, procedural and outcome data were collected prospectively. The patients were followed up on 1 January 2012.

Results: In the 22 sub-acute patients (18%), there were no early deaths or neurological complications. The predominant complication in these patients was rapid aortic enlargement, whereas rupture was more prevalent in patients treated within 14 days. In total, there were nine (7%) early deaths, three (2%) post-intervention paraplegias and six cases of stroke (5%).

Conclusions: TEVAR was performed with low early mortality and few neurological complications. A significant proportion of patients presented with acute complications >14 days after onset of symptoms, indicative of a sub-acute phase in the transition between acute and chronic dissection, questioning the relevance of the current definition.

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Acute complicated type B aortic dissection is a potentially life-threatening emergency. During the last decade, thoracic endovascular aortic repair (TEVAR) has revolutionised management, by allowing redistribution of blood flow to the true lumen and stabilisation of the dissected aorta.1,2,3 According to the current definition, the dissection is acute ≤14 days from onset of symptoms, and treatment within this time period is regarded as acute.4 The definition of acute dissection was based on autopsy studies of patients with aortic dissection of any type, showing that 74% of the deaths from complications of dissection occurred within 2 weeks. This definition is used in trials and in everyday clinical practice. In contrast to patients with acute complications, such as end-organ malperfusion, rupture or rapid aortic enlargement, patients with chronic dissection are commonly treated for progressive dilatation and aneurysm formation. We have previously questioned the 2-week definition, which was based...
on a mixed type A and type B cohort, with many patients left untreated, as clinical data indicated that it may take longer than 2 weeks for a dissection to stabilise. In recent reports, a subdivision of patients with acute complicated type B dissection into acute (≤14 days), sub-acute (15–30 days) and chronic (31–90 days) has been suggested, relating to the time of onset of complications requiring intervention.

The aims of this study were to determine early outcome of TEVAR in patients with acute complicated type B dissection, and to assess the relevance of the current definition of acute dissection by merging data from two European tertiary referral centres. Outcome of TEVAR in a subgroup of the present patients has been published previously. That cohort of patients has now been followed up for another 2 years, and a large number of patients were added.

MATERIALS AND METHODS

The TEVAR programme for acute aortic dissection was initiated in 1999 at both participating tertiary referral centres, the Zurich University Hospital, Switzerland, and the Uppsala University Hospital, Sweden, respectively. During a 12-year-period from the first patient in 1999 until 31 December 2011, a total of 188 patients underwent TEVAR for aortic dissection at the two centres. In all, 102 patients were treated for non-traumatic acute complicated type B dissection. In addition, 22 patients undergoing TEVAR for an acute dissection-related complication occurring >14 days after onset of symptoms were included in the study group, which thus consisted of 124 patients. In the remaining 64 patients, who underwent TEVAR for aortic dissection but who were not included in the present report, chronic type B dissection with aneurysm formation was the indication for TEVAR in 53 patients, acute type A dissection with distal malperfusion in eight and chronic type A dissection in three.

Among the 124 included patients, 44 had a DeBakey type IIIa dissection and 80 had type IIIb. Median age was 68 years, 35% were women. A total of 43 patients underwent TEVAR within the first 24 h. In the whole study group, median time to TEVAR from the first symptoms of aortic dissection was 4 days, whereas among those who had a complication within 2 weeks, median time was 2 days (25–48 h after onset). In the 22 patients requiring treatment after more than 14 days, median time to TEVAR was 23 days (range, 15–85 days) after the first symptoms of aortic dissection. All of these 22 patients underwent TEVAR for an acute complication, that is, end-organ malperfusion, rupture or rapid aortic enlargement, associated with a deterioration of the clinical condition. The distribution of time of TEVAR is depicted in Fig. 1(a) and (b).

On admission, the patients were assessed by a team of vascular surgeons, radiologists, anaesthesiologists and angiologists. Absence of signs of rupture or end-organ malperfusion resulted in non-surgical management based on alleviation of the pain and aggressive anti-hypertensive management. The target upper limit of the systolic blood pressure was 120 mmHg, aiming at 100–110 mmHg. The purpose was to decrease aortic wall stress, but at the same time maintaining adequate end-organ perfusion. First-line treatment was beta-blocking agents. In the case of contra-indication to beta-blockers or insufficient effect, other anti-hypertensive drugs were used. If no additional complications occurred, such patients could be discharged at the discretion of the physician in charge after a hospital stay of ≥14 days, and after having undergone a pre-discharge contrast-enhanced computed tomography (CT) of the aorta. Patients who were still hospitalised and sustained complications after >14 days after onset of symptoms and patients who were re-admitted for acute complications requiring TEVAR were categorised as sub-acute. There was no pre-defined upper time limit for categorisation as sub-acute, as this was determined by the occurrence of acute complications. The TEVAR and patient management routines at the two centres are virtually identical and follow the principles of the Uppsala protocol which has been described previously.

Rupture and malperfusion in the setting of aortic dissection, respectively, were defined in accordance with a recent report of the Society for Vascular Surgery (SVS). Demographic, peri- and postoperative data on the 124 patients undergoing TEVAR for non-traumatic acute or sub-acute complicated type B aortic dissection were collected prospectively. Early and long-term survival, as well as complications, were registered until 31 December 2011. The study was ethically approved by the Swedish Vascular Registry (Swedvasc) steering committee and by the Institutional Review Board of the Zurich University Hospital.

Statistical methods

Continuous variables were summarised with medians and ranges and categorical variables with frequencies. Categorical data were analysed by the Fischer exact test; for age comparisons, the Mann–Whitney U test was used. Statistical Package for the Social Sciences (SPSS) for Windows 20.0 was used for data processing and statistical analyses.

RESULTS

Baseline characteristics are given in Table 1, comparing the acute and the sub-acute patient cohorts, respectively. Patients with sub-acute onset of complications were younger than those requiring TEVAR ≤14 days after the initial symptoms of aortic dissection. A high prevalence of hypertension and proportion of smokers was observed in both groups.

In the entire cohort of 124 patients undergoing TEVAR for acute non-traumatic type B aortic dissection, additional stenting of one or more renal, visceral or lower-extremity arteries was carried out in 31 patients (25%), and six patients (5%) underwent endovascular fenestration, three of whom also got one or more stents. One patient underwent open membrane fenestration through a laparotomy. A total of 89 patients (72%) were treated with TEVAR alone, and no adjunctive procedures. The predominant indication for TEVAR was rupture or contained rupture in 56 patients (45%), severe malperfusion in 42 (34%), rapid enlargement in 22 (18%) and intractable pain in four patients. Data on the
distribution of dissection-related complications are given in Table 2. There were nine (7%) early deaths, three patients (2%) had post-intervention paraplegia and six (5%) had a stroke. In a total of 47 patients (38%) the left subclavian artery was covered without prior revascularisation. Among the 22 patients (18%) who had an acute complication necessitating TEVAR more than 14 days after onset of symptoms, rapid aortic enlargement was the precipitating, predominant complication in 10 and end-organ ischaemia in eight; there were two ruptures and two cases of intractable pain. The eight patients with subacute malperfusion underwent TEVAR after a median of 22 days (range, 15–38) after the onset of the acute

Figure 1. a. Distribution of patients undergoing TEVAR for acute (≤14 days) complicated type B aortic dissection in relation to day of treatment. b. Distribution of patients undergoing TEVAR for subacute (15–90 days) complicated type B aortic dissection in relation to day of treatment.

Table 1. Baseline characteristics of patients treated with TEVAR for complicated type B dissection by time to onset of complication requiring treatment.

<table>
<thead>
<tr>
<th></th>
<th>Acute (n = 102)</th>
<th>Sub-acute (n = 22)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>35 (34%)</td>
<td>8 (36%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>69 (36–86)</td>
<td>58 (34–81)</td>
<td>0.012</td>
</tr>
<tr>
<td>Hypertension</td>
<td>70 (69%)</td>
<td>18 (82%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4 (4%)</td>
<td>1 (5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>27 (26%)</td>
<td>4 (18%)</td>
<td>0.59</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>18 (18%)</td>
<td>6 (27%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Smoking</td>
<td>39 (38%)</td>
<td>13 (59%)</td>
<td>0.10</td>
</tr>
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Until recently, there has been little debate regarding the sustaining type B aortic dissection needs particular attention even though the first 14 days might be uneventful. Until recently, there has been little debate regarding the definition of acute dissection and the distinction between acute and chronic. We questioned the relevance of the 14-day cut-off in a prior report, owing to the finding that one in six patients treated for rupture, rapid aortic expansion or aortic branch malperfusion in association with type B dissection had onset of one or more of these life-threatening complications >14 days after the initial symptoms of aortic dissection.

In the subset of sub-acute patients, the predominant complication was rapid aortic enlargement, whereas rupture was more prevalent in patients treated during the first 2 weeks. Leg ischaemia, that is lower-extremity malperfusion threatening the limb, requiring revascularisation for salvage, did not occur in any of the sub-acute patients, whereas it was seen in nearly one in five patients treated during the early acute phase. The distal extension of the dissection with regard to the DeBakey classification did not differ between the groups, however. Plausibly, this could indicate distal stabilisation of the membrane in the sub-acute group. The occurrence of acute limb ischaemia in acute type B dissection has been shown to be associated with worse outcome, both in the pre-TEVAR and current eras.3,10

The 14-day definition was applied in two recent randomised trials of patients with type B aortic dissection: the ADSORB11 study comparing best medical treatment (BMT) with BMT and stent-grafting of the entry tear in patients with uncomplicated acute type B dissection, randomising patients within 14 days of onset of symptoms, and the INSTEAD (Investigation Of Stent Grafts in Patients with type B Aortic Dissection)12,13 study including patients considered to have sustained an uncomplicated chronic dissection >14 days after onset, randomising the patients to BMT alone or BMT and TEVAR with a median time of 6 weeks to randomisation. The former study has been re-designed and is still ongoing. At 1-year follow-up of the latter, seven (11%) patients had crossed over from BMT alone to TEVAR, the majority for aortic expansion to >60 mm, in one case for late malperfusion. In the group of patients categorised as having stable chronic dissection, there could thus have been patients who, in fact, had unstable, sub-acute dissection.

In our series, there were no deaths or neurological complications in the sub-acute cohort, which would indicate that the current definition does have relevance. However, there seems to be a transition between acute and chronic, a period during which the flap matures and stabilises. The terms stable and unstable acute dissection, respectively, have been suggested,14 and, as discussed by Tang and Dake,15 increased flap stability would make TEVAR safer, but also decrease the success rate. Moreover, two recent papers have sub-divided patients undergoing TEVAR >14 days after onset of an acute type B dissection into sub-acute (15–30 days) and chronic (31–90 days).1,6 No group comparisons were made with respect to complications, but there was a tendency towards more rupture cases in the acute group and more cases of expansion among the sub-acute patients.1

Our study is limited by lack of data on patients admitted to the two participating tertiary referral centres allocated to non-surgical therapy. At our two centres, those patients are mostly followed up by cardiologists or angiologists, whereas patients having undergone TEVAR are under surveillance by vascular surgeons. Our results support meticulous early...
monitoring of these patients and are suggestive of the need to define a subset of patients that might benefit from TEVAR in uncomplicated dissection to prevent later complications. Even though we did not experience any lethal complications in the small cohort of patients with sub-acute dissection it is likely that in a larger group of patients both death and major morbidity would occur.

We conclude that a significant proportion of patients with acute type B dissection presented with complications necessitating TEVAR more than 14 days after onset of symptoms. Patients presenting with acute complications after >14 days were younger and more often were treated for rapid enlargement of the aorta, whereas rupture was much more frequent in those undergoing TEVAR ≤14 days.

This indicates that there is a sub-acute, dynamic and/or unstable phase in the transition between acute and chronic dissection during which acute and life-threatening complications might occur and that the relevance of the old, and commonly used, distinction between acute and chronic dissection could be questioned. We suggest that future trials and clinical surveillance and follow-up protocols document patients treated during the sub-acute phase separately and that this phase is defined as 15—90 days after onset of symptoms.

CONFLICT OF INTEREST
None.

FUNDING
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REFERENCES