Management of complicated and uncomplicated acute type B dissection. A systematic review and meta-analysis

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Background: The management of acute type B dissection represents a clinical challenge. We undertook a systematic review of the available literature regarding medical, surgical and endovascular treatments of acute type B aortic dissection and combined the eligible studies into a meta-analysis.

Methods: An extensive electronic health database search was performed on all articles published from January 2006 up to November 2013 describing the management of acute type B aortic dissection. Studies including less than 15 patients were excluded.

Results: Acute complicated type B dissection: overall, 2,531 patients were treated with endovascular repair (TEVAR) and the pooled rate for 30-day/in-hospital mortality was 7.3%. The pooled estimates for cerebrovascular events, spinal cord ischemia (SCI) and total neurologic events were 3.9%, 3.1% and 7.3%, respectively. A total of 1,276 patients underwent open surgical repair and the pooled rate for 30-day/in-hospital mortality was 19.0%. The pooled rate for cerebrovascular events was 6.8%, for SCI 3.3% and for total neurologic complications 9.8%. Acute uncomplicated type B dissection: outcome of 2,347 patients who underwent conservative medical management were analyzed. The pooled 30-day/in-hospital mortality rate was 2.4%. The pooled rate for cerebrovascular events was 1%, for SCI 0.8% and for overall neurologic complications 2%.

Conclusions: Endovascular repair provides a superior 30-day/in-hospital survival for acute complicated type B aortic dissection compared to surgical aortic reconstruction. However, open repair still has a significant role as endovascular repair is not applicable in all patients and there remains concerns regarding the durability of this technique. TEVAR seems to have a more favorable outcome regarding aortic remodeling and the aortic-specific survival rate when compared with medical therapy alone. Randomized controlled trials focusing on the prognostic factors of early and late complications in uncomplicated type B dissections are needed.

Keywords: Type B aortic dissection; acute; medical treatment; endovascular

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Introduction

Aortic dissection is a potentially life-threatening condition that occurs when a tear is formed in the wall of the aorta. Stanford type B or DeBakey III aortic dissection originates in the descending thoracic aorta without retrograde extension into the ascending aorta (1). Acute type B dissections may be classified as uncomplicated or complicated. Approximately 25% of patients presenting with acute type B aortic dissection are complicated at admission by malperfusion syndrome or hemodynamic instability, resulting in a high risk of early death if untreated (1-3). Complicated type B aortic dissection refers to malperfusion...
syndrome involving visceral, renal, or extremity ischemia, rupture or impending rupture, uncontrolled hypertension, persistent abdominal or chest pain, or findings of rapid expansion on computed tomography (CT) imaging.

The management of acute complicated type B dissection represents a clinical challenge. Uncomplicated dissections have traditionally been managed non-operatively with aggressive blood pressure control. However, best medical treatment (BMT) is associated with a considerable risk of disease progression to complicated dissection or aneurysmal degeneration of the affected aortic segment, which is the most feared complication in the long term, involving about 30-40% of patients (4,5). The lower morbidity and mortality rates associated with endovascular procedures have generated interest in the treatment of uncomplicated dissections.

We undertook a systematic review of the available literature regarding medical, surgical and endovascular treatments of acute type B aortic dissection. We combined the eligible studies into a meta-analysis with the intention of studying the efficacy of these treatment strategies.

**Methods**

**Definitions**

**Acute type B aortic dissection**
Aortic dissection involving the descending thoracic aorta and distal sites only and the diagnosis has to be within 14 days of onset of symptoms.

**Complicated type B aortic dissection**
Complicated dissections refer to aortic rupture, visceral and renal ischemia, lower extremities ischemia, or spinal cord ischemia (SCI). Expansion to the aortic arch or proximal descending aorta with a total diameter of 4.5 cm or greater is also considered a complicated dissection. However, refractory hypertension, hypertension persisting despite three different classes of antihypertensive therapy at maximal recommended or maximal tolerated doses, if not present in the clinical history before the onset of dissection, is considered a sign of instability or of renal malperfusion.

Malperfusion syndrome is the most frequent complication of type B dissection. The clinical presentation includes paraparesis or paraplegia, lower limb ischemia, abdominal pain, nausea, or diarrhea. Visceral artery malperfusion may be associated with an increase in laboratory markers (bilirubin, amylases, hepatic and intestinal enzymes). The CT angiography or magnetic resonance angiography findings such as true lumen compression, or an intimal flap inside the renal, celiac, or mesenteric arteries, carry a high suspicion of visceral malperfusion. Delay or absence of nephrographic effect during the late phase of contrast-enhanced CT scan, often accompanied by an increase in serum creatinine and/or refractory hypertension, indicates renal malperfusion.

**Search strategy**

The present meta-analysis was conducted in accordance with the recommendations of the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) group (6). An extensive electronic health database search was performed on all articles published from January 2006 up to November 2013 describing the management of acute type B aortic dissection. The search was performed using exploded medical subject heading (MeSH) terms: “acute type B aortic dissection”, “complicated”, “uncomplicated”, “medical treatment”, “surgical treatment”, “open repair” and “endovascular treatment”. Publications were retrieved through electronic search engines (Medline, Embase, Scopus, Google Scholar, Ovid, and the Cochrane Library).

All studies were independently assessed, and full texts of potentially eligible studies were retrieved. In addition, the reference lists of all retrieved articles were examined for further relevant series.

**Study eligibility, and exclusion criteria**

Studies were included in the present review if (I) the index aortic pathology was acute type B aortic dissection; (II) BMT, open surgical repair or TEVAR were the applied treatment options; (III) stated the incidence of at least one of the basic outcome criteria; (IV) included ≥15 patients. Articles in languages other than English were eliminated from further analysis. Case reports and case series with less than 15 patients were excluded. Studies referring to chronic aortic dissection were excluded. Studies referring to type A aortic dissection or to combined hybrid endovascular and open thoracic aorta repairs were excluded as well. When multiple publications on the same patient population were identified or study populations overlapped, only the latest report was included, unless the reported outcomes were mutually exclusive. Furthermore, several studies included patients with acute type B dissection as a subset of the entire study cohort. These were included in the present review if separate data for this patient subgroup was provided.

The available data were independently extracted and
analyzed by two reviewers (S.M. and K.M.), and a consensus was reached if discrepancies were observed. Primary endpoints included peri-procedural (30-day/in-hospital) mortality, stroke, SCI and total neurologic complications rates. Data regarding long-term survival and aortic event freedom were also analyzed.

Statistical analysis
Separate meta-analyses was carried out on all eligible studies for peri-procedural (30-day/in-hospital) mortality, stroke, SCI and total neurologic complications. The pooled proportion was calculated as the back-transformation of the weighted mean of the transformed proportions. Statistical heterogeneity was measured using the Cochran Q statistic score (P<0.10 was considered indicative of statistically significant heterogeneity) and the I² test. A fixed-effects model was used when no heterogeneity existed among studies. Otherwise, the random effects model was used. The meta-analyses were conducted using StatsDirect statistical software (StatsDirect Ltd, UK). Frequency study-specific estimates were pooled and are reported as event rates with corresponding 95% confidence intervals (95% CI). Long-term data were reported with Kaplan-Meier rates by the study investigators. No pooled analyses of long-term results were performed as there were variable event definitions among studies.

Results
The literature search identified 141 potentially relevant citations. Fifteen were excluded at the title or abstract level as being irrelevant. Of the remaining 126, 27 included overlapping patient populations and were excluded, 28 reported on series of <15 patients and were also excluded, and a further 23 publications reported insufficient data on study outcomes. Eventually, 54 studies were considered eligible and included in the present meta-analysis. This included 30 studies with a total of 2,531 patients with acute type B aortic dissection treated with TEVAR, 15 studies with a total of 2,347 patients treated with best medical therapy and 9 studies with a total of 1,276 patients treated with open surgical repair (Figure 1).

Acute complicated type B dissection
Endovascular treatment for acute complicated type B dissection
Overall, 2,531 patients with acute type B aortic dissection were treated with TEVAR (Table 1). The pooled rate for 30-day/in-hospital mortality was 7.3% (95% CI, 5.3% to 9.6%). The pooled estimates for cerebrovascular events, SCI and total neurologic events were 3.9% (95% CI, 3.2% to 4.8%), 3.1% (95% CI, 2.0% to 4.4%) and 7.3% (95% CI, 5.2% to 9.7%), respectively (Figure 2). Survival rates ranged from 62% to 100% at 1-year and from 61% to 87% at 5-years, whereas freedom from aortic events ranged from 45% to 77%.

Open surgical repair
A total of 1,276 patients from nine studies who underwent open surgical repair for acute complicated type B aortic dissection were analyzed (Table 2). The pooled rate for
### Table 1
Endovascular treatment summary for acute complicated type B dissection

<table>
<thead>
<tr>
<th>Author</th>
<th>Period of study</th>
<th>N (pts)</th>
<th>Indication</th>
<th>30-day/in-hospital (n)</th>
<th>FU (Months)</th>
<th>Survival rate (%)</th>
<th>Aortic event freedom rate (%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CVE</td>
<td>SCI</td>
<td>Mortality</td>
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<tr>
<td>Di Tommaso</td>
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<td>26</td>
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<tr>
<td>Chen</td>
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<td>1</td>
<td>27.5</td>
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<td>Yang</td>
<td>2001-2005</td>
<td>36</td>
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<td>15</td>
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<tr>
<td>Jing</td>
<td>2002-2007</td>
<td>32</td>
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<td>0</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>Sayer</td>
<td>2000-2007</td>
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<td>Acute complicated</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>30</td>
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<tr>
<td>Rodríguez</td>
<td>2000-2006</td>
<td>59</td>
<td>Acute complicated</td>
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<td>3</td>
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<td>15.6</td>
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<tr>
<td>Böckler</td>
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<td>6</td>
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</tr>
<tr>
<td>Alves</td>
<td>1997-2004</td>
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<td>Acute complicated</td>
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<td>–</td>
<td>3</td>
<td>35.9</td>
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<td>Acute complicated</td>
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<td>4</td>
<td>12</td>
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<tr>
<td>Guangqi</td>
<td>2001-2006</td>
<td>72</td>
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<td>1</td>
<td>14.4</td>
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<td>Feezor</td>
<td>2005-2007</td>
<td>33</td>
<td>Acute complicated</td>
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<td>5</td>
<td>7</td>
<td>5</td>
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<tr>
<td>Manning</td>
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<td>4</td>
<td>5</td>
<td>30</td>
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<tr>
<td>Sze</td>
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<td>23</td>
<td>Acute complicated</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>22.3</td>
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<tr>
<td>Chemelli-Steingruber</td>
<td>1996-2008</td>
<td>38</td>
<td>Acute complicated</td>
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<td>0</td>
<td>5</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ND</td>
<td>1</td>
<td>3</td>
<td>32.1</td>
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<tr>
<td>Botsios</td>
<td>2001-2006</td>
<td>32</td>
<td>Acute complicated</td>
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<td>6</td>
<td>2</td>
<td>37</td>
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<tr>
<td>Zeeshan</td>
<td>2002-2010</td>
<td>45</td>
<td>Acute complicated</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>23.1</td>
</tr>
<tr>
<td>Torsello</td>
<td>2005-2008</td>
<td>32</td>
<td>Acute complicated</td>
<td>37</td>
<td>32</td>
<td>107</td>
<td>ND</td>
</tr>
<tr>
<td>Brunt</td>
<td>2005-2008</td>
<td>991</td>
<td>Acute complicated</td>
<td>ND</td>
<td>0</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Tang</td>
<td>2007-2008</td>
<td>30</td>
<td>Acute complicated</td>
<td>ND</td>
<td>0</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>O’Donnell</td>
<td>2005-2008</td>
<td>28</td>
<td>27 acute complicated</td>
<td>ND</td>
<td>0</td>
<td>1</td>
<td>21</td>
</tr>
</tbody>
</table>

Table 1 (continued)
30-day/in-hospital mortality was 19.0% (95% CI, 16.8% to 21.1%, Figure 3A). The pooled rate for cerebrovascular events was 6.8% (95% CI, 5.4% to 8.2%), for SCI 3.3% (95% CI, 2.4% to 4.4%) and for total neurologic complications 9.8% (95% CI, 8.2% to 11.5%) (Figure 3B-D). Survival rates ranged from 74.1% to 86.0% at 1-year and from 44.0% to 82.6% at 5-years, whereas freedom from aortic events could not be estimated as there were no available data.

Acute uncomplicated type B dissection

Best medical therapy
Outcome data of medical therapy were available for 2,347 patients from 15 studies who underwent conservative medical management for acute type B aortic dissection (Table 3). In the vast majority of the papers, indication for BMT was uncomplicated acute type B dissection. However, a percentage of patients with complications were treated with medical therapy only, either due to the lack of appropriate facilities or due to the presence of comorbidities or morphology that made open surgery or TEVAR not feasible. The 30-day/in-hospital mortality pooled rate was 2.4% (95% CI, 0.9% to 4.6%, Figure 4A). The pooled rate for cerebrovascular events was 1% (95% CI, 0.6% to 1.6%) for SCI 0.8% (95% CI, 0.5% to 1.3%) and for overall neurologic complications 2% (95% CI, 0.6% to 4.1%) (Figure 4B-D). Survival rates ranged from 86.2% to 100% at 1-year and from 59.0% to 97.2% at 5-years, whereas freedom from aortic events ranged from 34% to 83.9%.

Endovascular treatment for acute uncomplicated type B dissection
Preliminary results of the European study, Acute Dissection:...
Figure 2 (A) Proportion meta-analysis plot (random effects) of 30-day/in-hospital mortality in endovascular treatment for acute complicated type B dissection. [Pooled proportion, 0.073 (95% CI, 0.053 to 0.096), I², 69.3% (95% CI, 53.4% to 78.1%)]; (B) Forest plot of cerebrovascular events in endovascular treatment for acute complicated type B dissection. Data were available from 25 studies [pooled proportion, 0.039, (95% CI, 0.032 to 0.048), I², 30% (95% CI, 0% to 56.4%)]; (C) Proportion meta-analysis plot (random effects) of spinal cord ischemia in endovascular treatment for acute complicated type B dissection. Data were available from 27 studies [pooled proportion, 0.031, (95% CI, 0.02 to 0.049), I², 46.3% (95% CI, 6.1% to 64.9%)]; (D) Proportion meta-analysis plot (random effects) of total neurological events in endovascular treatment for acute complicated type B dissection. Data were available from 25 studies [pooled proportion, 0.073, (95% CI, 0.052 to 0.097), I², 65.8% (95% CI, 44.1% to 76.6%)].
Table 2 Eligible studies on open surgery for complicated acute type B dissection

<table>
<thead>
<tr>
<th>Author</th>
<th>Period of study</th>
<th>N (pts)</th>
<th>CVE (n)</th>
<th>SCI (n)</th>
<th>30-day/in-hospital mortality (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimarchi et al., 2006 (48)</td>
<td>1995-2005</td>
<td>82</td>
<td>8</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>Estera et al., 2007 (38)</td>
<td>2001-2006</td>
<td>21</td>
<td>ND</td>
<td>ND</td>
<td>4</td>
</tr>
<tr>
<td>Bozinoski et al., 2008 (49)</td>
<td>1989-2004</td>
<td>76</td>
<td>5</td>
<td>5</td>
<td>17</td>
</tr>
<tr>
<td>Shimokawa et al., 2008 (50)</td>
<td>2003-2008</td>
<td>24</td>
<td>ND</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Zeeshan et al., 2010 (22)</td>
<td>2002-2010</td>
<td>20</td>
<td>0</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Brunt et al., 2011 (24)</td>
<td>2005-2008</td>
<td>991</td>
<td>61</td>
<td>25</td>
<td>173</td>
</tr>
<tr>
<td>Murashita et al., 2012 (51)</td>
<td>2003-2010</td>
<td>31</td>
<td>2</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Minami et al., 2013 (52)</td>
<td>2000-2012</td>
<td>14</td>
<td>4</td>
<td>ND</td>
<td>2</td>
</tr>
<tr>
<td>Wilkinson et al., 2013 (35)</td>
<td>1995-2012</td>
<td>17</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

CVE, cerebrovascular event; SCI, spinal cord ischemia; ND, not determined.

Figure 3 (A) Proportion meta-analysis plot (fixed effects) of 30-day/in-hospital mortality after open surgery for complicated acute type B dissection. [Pooled proportion, 0.19 (95% CI, 0.168 to 0.211), I², 43.6% (95% CI, 0% to 72.4%)]; (B) Proportion meta-analysis plot (fixed effects) of cerebrovascular events after open surgery for complicated acute type B dissection. [Available data in nine studies, pooled proportion, 0.066 (95% CI, 0.047 to 0.085), I², 76.8% (95% CI, 0% to 77.7%)]; (C) Proportion meta-analysis plot (fixed effects) of spinal cord ischemia after open surgery for complicated acute type B dissection. [Available data in nine studies, pooled proportion, 0.033 (95% CI, 0.024 to 0.044), I², 39.7% (95% CI, 0% to 73.3%)]; (D) Proportion meta-analysis plot (fixed effects) of total neurologic events after open surgery for complicated acute type B dissection. [Available data in nine studies, pooled proportion, 0.098 (95% CI, 0.082 to 0.115), I², 39.4% (95% CI, 0% to 74.8%)].
Stent Graft or Best Medical Treatment (ADSORB) (46,53), which evaluates TEVAR + BMT vs. BMT alone in patients with acute uncomplicated type B aortic dissection showed zero mortality and neurological complication rates in both groups but aortic remodeling after one year was in favor of TEVAR. Another study from China (47) comparing TEVAR + BMT vs. BMT alone in patients with acute uncomplicated type B aortic dissection showed a better long-term survival rate in TEVAR group and confirmed the favorable aortic remodeling rate (true lumen diameter, false lumen thrombosis).

**Discussion**

Endovascular stent-graft repair of complicated type B acute dissection seems to be associated with favorable short-term and mid-term results. In our analysis, the 30-day/in-hospital mortality was 7.3% in patients treated endovascularly.
whereas the pooled rate for 30-day/in-hospital mortality was 19.0% in the operative group. Cerebrovascular events and SCI also occurred more frequently in the operative group. Interestingly, the survival rates for 1- and 5-years were comparable between the two groups. However, the absence of randomized trials comparing endovascular with open repair treatments in complicated type B acute dissection remains a limitation. In addition, it is doubtful whether any diseased anatomy of the dissected aorta can be totally treated by endovascular means. Longer follow-up is warranted to assess the durability of endovascular stent-graft repair for complicated type B acute dissection and potential progression of disease at the downstream aorta.

Uncertainty remains regarding the optimal management strategy for uncomplicated acute type B dissection. The basic medical treatment comprises beta-blockers, diuretics, calcium blockers, angiotensin-converting enzyme inhibitors and alpha-blockers, as well as nitroglycerin. The primary aim of this approach is to obtain a systolic blood pressure between 100 to 120 mmHg and thus reduce the shear stress
of the aortic wall while maintaining urinary output and visceral perfusion (38). However, BMT is associated with a considerable risk of disease progression to complicated dissection or aneurysmal degeneration of the affected aortic segment, which is the most feared complication, involving about 30-40% of patients (3,54). Long-term outcome of medical therapy has shown a complication rate over 30% and total death rate up to 10% (4).

In our analysis, including predominantly patients with uncomplicated acute type B dissection treated with optimal medical treatment, the pooled 30-day/in-hospital mortality rate was 2.4%. Survival rates ranged from 59.0% to 97.2% at 5-years, whereas freedom from aortic events ranged from 34% to 83.9%, underlining the risk of disease progression to complicated dissection or aneurysmal degeneration of the affected aortic segment in the follow-up and the need for additional surgical interventions. Taking into account the potential risk of disease progression, a crucial question is whether we can expand the indication of endovascular repair in uncomplicated type B aortic dissection and, if so, what are the prognostic factors of early or late complications? The 1-year results of the ADSORB trial showed more frequent false lumen thrombosis and aortic remodeling in those patients treated medically plus TEVAR compared to those managed only medically (53). Favorable aortic remodeling rate was also confirmed by the results of the Investigation of Stent-grafts in Aortic Dissection (INSTEAD-XL) randomized trial which showed that thoracic endovascular aortic repair of uncomplicated type B dissections in addition to medical therapy was associated with improved 5-year aorta-specific survival and delayed disease progression compared to medical therapy alone (5).

The predisposing factors of early and late complications in uncomplicated type B aortic dissection seem to be a critical point that may influence the treatment strategy. Can we identify a high-risk population with uncomplicated type B patients that will benefit from TEVAR? The ideal concept is to perform stent-grafting in the subgroup of patients prone to developing progression of the disease and future complications. A number of studies have suggested several prognostic factors of early or late adverse events such as the patency of the false lumen in the follow-up, an initial aortic diameter $\geq 4$ cm with a patent false lumen, an initial false lumen diameter $\geq 22$ mm in the proximal descending aorta, visceral involvement and recurrent or refractory pain or hypertension (37,42,55-57). Partial false lumen thrombosis, a proximal entry tear size $>10$ mm and a spiral configuration of the dissection have also been suggested to be associated with an increased rate of aortic growth. Spiral dissection is associated with a lower incidence of false lumen thrombosis and aorta-related adverse events are more likely to occur in spiral dissection patients. Randomized trials that will focus on these prognostic factors and the optimal timing of intervention are needed.

Our study has the inherent limitations associated with meta-analyses. The considerable heterogeneity amongst identified reports may reflect differing patient characteristics between studies. Hence, these pooled estimates without raw patient data prohibits subset analysis, and our results should be interpreted with caution.

Conclusions

Currently, the less invasive method of endovascular repair provides a better 30-day/in-hospital survival for complicated acute type B aortic dissection. Surgical aortic reconstruction, on the other hand, still has a significant role as endovascular repair is not applicable in all of the dissected aortas and there is concern regarding the durability of this technique.

Although the ideal treatment for uncomplicated acute type B aortic dissection is still unclear, the combination of TEVAR with antihypertensive therapy seems to have a more favorable outcome regarding aortic remodeling and aorta-specific survival rate when compared with medical therapy alone. Expansion of TEVAR, however, to treating uncomplicated type B aortic dissection requires further investigation and the proposed factors predicting the outcome of these patients may help in the identification of the appropriate treatment strategy. Until this issue is clarified, patients with uncomplicated acute type B dissection should be treated on a case-by-case basis. There is a need for randomized clinical trials that will focus on the prognostic factors of early and late complications in uncomplicated type B aortic dissection and the timing of intervention.

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