Faculty of Health Sciences
Department of Clinical Medicine

Prognosis in acute aortic dissection

Insights from the International Registry of Acute Aortic Dissection (IRAD)

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“The tragedies of life are largely arterial.”

Sir William Osler
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3. List of papers

**Paper I**

**Paper II**

**Paper III**

**Paper IV**

**Appendix**
4. Abstract

Background/aims
Acute aortic dissection (AAD) is a rare life-threatening disease that does not easily lend itself to randomized controlled trials. Data regarding the effect of treatment advances in the recent decades is limited. Determinants of follow-up mortality are poorly understood. To include many patients and evaluate contemporary management of AAD, the International Registry of Acute Aortic Dissection (IRAD) was established in 1996. This work was undertaken to examine factors associated with morbidity and mortality after an AAD – specifically whether a partial thrombosis of the false lumen is a negative prognostic marker in type A AAD (AAAD), whether an open distal anastomosis confer prognostic benefit in AAAD surgery and finally whether the aortic arch should be resected at initial surgery for AAAD. Furthermore, we assessed the changes in management and outcomes of patients with AAD over time.

Methods
Data collected in the IRAD since 1996 was used for analyzes. A literature search was done to evaluate the existing evidence for an open distal anastomosis in AAAD surgery.

Results/conclusions
A partial thrombosis of the false lumen was not associated with increased mortality, aortic growth or re-intervention in the follow-up period after an AAAD. Patients with an AAAD who survive the acute event have a favorable mid-term prognosis. Over time, a decrease in in-hospital mortality was seen in AAAD, but not in type B AAD. More patients with AAD are managed with interventional procedures in the current era. An extended arch resection in AAAD has no discernable acute downside compared with less extensive surgery. Finally, based on the available literature, the data to support either an open or a closed distal anastomosis in AAAD is insufficient, and the surgical management of AAAD should be based on individual and aortic-specific assessment and take the patient’s age, comorbidities and preoperative clinical condition into account.
### 5. Selected abbreviations

<table>
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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AAAD</td>
<td>Acute type A aortic dissection (Stanford)</td>
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<td>AAD</td>
<td>Acute aortic dissection</td>
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<td>AAS</td>
<td>Acute aortic syndrome</td>
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<td>ABAD</td>
<td>Acute type B aortic dissection (Stanford)</td>
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<td>ADSORB</td>
<td>Acute Dissection Stentgraft or Best Medical Treatment</td>
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<tr>
<td>CABG</td>
<td>Coronary artery bypass grafting</td>
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<td>CI</td>
<td>Confidence interval</td>
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<td>CPB</td>
<td>Cardiopulmonary bypass</td>
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<td>CT</td>
<td>Computed tomography</td>
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<td>ECG</td>
<td>Electrocardiography</td>
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<td>ET</td>
<td>Elephant trunk</td>
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<tr>
<td>EVAR</td>
<td>Endovascular aneurysm repair</td>
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<tr>
<td>FET</td>
<td>Frozen elephant trunk</td>
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<tr>
<td>GERAADA</td>
<td>German Registry for Acute Aortic Dissection Type A</td>
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<tr>
<td>HCA</td>
<td>Hypothermic circulatory arrest</td>
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<td>HR</td>
<td>Hazard ratio</td>
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<tr>
<td>IMH</td>
<td>Intramural hematoma</td>
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<tr>
<td>INSTEAD</td>
<td>Investigation of Stent Grafts in Aortic Dissection</td>
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<tr>
<td>IRAD</td>
<td>International Registry of Acute Aortic Dissection</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<td>OR</td>
<td>Odds ratio</td>
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<td>PAU</td>
<td>Penetrating atherosclerotic ulcer</td>
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<td>PET</td>
<td>Positron emission tomography</td>
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<td>RCT</td>
<td>Randomized controlled trial</td>
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<td>SD</td>
<td>Standard deviation</td>
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<td>TAR</td>
<td>Total (aortic) arch replacement</td>
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6. Introduction

Acute aortic dissection (AAD; the splitting of the aortic wall with the creation of two separate lumens in which blood can flow) is one of the most dreaded conditions faced by cardiac surgeons due to its rapid presentation, dismal prognosis if left untreated and complexity of surgical repair. In 1958, Hirst et al published a review of 505 cases of aortic dissection reported in the English literature over a 21 year period. The mortality rate was 50% at four days, 75% at two weeks and 90% after three months. In their seminal series, mortality during the acute phase was due to aortic rupture in almost 90% of cases. The dismal prognosis of untreated aortic dissection had already been recognized nearly 200 years earlier, when Morgagni described in detail three fatal cases of aortic dissection.

The first major breakthrough in the surgical treatment of aortic dissection took place on 7 July 1954, when DeBakey, Cooley and Creech performed the first successful surgical resection of a descending thoracic aortic dissection. In the more than six decades passed since, surgical treatment of aortic dissection has developed tremendously in conjunction with cardiac and vascular surgery as a whole. Bigelow’s experiments on hypothermia in 1950 and the first simultaneous application of deep hypothermic circulatory arrest (HCA) and cardiopulmonary bypass (CPB) by Barnard and Schrire in 1963 predated Griepp’s work on surface cooling in conjunction with CPB in aortic arch replacement. As aortic arch pathology could be addressed at acceptable risk, finally all aortic segments were available for successful repair, which almost invariably involves replacement of the aorta with a prosthetic graft. In 1983, Borst et al described the elephant trunk (ET) technique in which a segment of a prosthetic graft is left in the descending aorta during a first stage procedure to facilitate a second stage completion. In 1991, Parodi et al introduced the concept of endovascular aneurysm repair (EVAR), which in turn paved the way for the frozen elephant trunk (FET; the descending aortic graft is replaced by a stent graft implanted from the aortic arch in a single-stage procedure), the original indication being thoracic aortic aneurysms. In the present era, extensive procedures such as total arch replacement (TAR) and FET are gaining popularity, and can be carried out in the acute phase of an acute type A aortic dissection (AAAD) with excellent results.

Parallel to the progress in cardiac and vascular surgery, medical management directed at lowering blood pressure and heart rate was introduced, and is still considered first line...
management in uncomplicated acute type B aortic dissections (ABAD). However, evidence is emerging that might come to challenge this paradigm. Data from the INSTEAD and ADSORB trials have shown that endovascular treatment in the form of stent grafting of the descending thoracic aorta is safe, promotes favorable aortic remodeling and might improve long-term survival in patients presenting with uncomplicated ABAD.

Despite major advances in medical, surgical and endovascular treatment of aortic dissection, survivors of the acute event still face a sobering prognosis primarily related to aneurysmal degeneration of the dissected aorta. This work was undertaken to explore some of the clinical, surgical and radiologic factors associated with morbidity and mortality both in the short and long term after an acute aortic dissection. Furthermore, we aimed to assess whether there has been a change in management and outcomes of patients with AAD over the last two decades.
7. Background

7.1 Aortic wall anatomy
The aortic wall consists of three layers; the tunica intima, tunica media and tunica adventitia. The intima is the inner layer and is formed by a single layer of endothelial cells on the basement membrane, separated from the media by the internal elastic lamina. The media is the middle layer, and the thickest part of the aortic wall. It is made up of smooth muscle cells that secrete elastic tissue. In the largest arteries, such as the aorta, the amount of elastic tissue is considerable. The external elastic lamina separates the media from the adventitia, which is the outermost layer. This thin connective tissue contains collagen fibers that provide strength to the aortic wall and serves to anchor it to nearby tissues. Running along and within the vessel wall is a network of small blood vessels, the vasa vasorum, that supply the aortic tissue.

7.2 Acute aortic syndrome
Acute aortic dissection is part of the acute aortic syndrome (AAS) spectrum, first coined by Vilacosta et al in 1998.\textsuperscript{16, 17} It refers to a group of conditions with similar presentation, the most prominent feature being aortic pain, which in its classic form is acute and severely intense. Various conditions such as pseudoaneurysms and aortic aneurysm leak or rupture can cause this presentation, but the term AAS has come to include three distinct entities: Penetrating atherosclerotic (aortic) ulcer (PAU), intramural hematoma (IMH) and “classic” aortic dissection (Figure 1).

PAU was initially described by Shennan in 1934 and is a focal atherosclerotic plaque that erodes a variable length into the media.\textsuperscript{18} It can cause a pseudoaneurysm or frank aortic rupture, or rupture into the media, causing an IMH.\textsuperscript{19, 20} The hematoma may rarely develop to a “classic” aortic dissection. The natural history of a PAU however, is that of progressive aortic enlargement with saccular and fusiform aneurysm formation.\textsuperscript{21}

IMH was first described by Krukenberg in 1920.23 It may be the primary event, typically in hypertensive patients, in whom there is spontaneous bleeding from the vasa vasorum into the media, or it may be caused by a PAU.19 The hematoma extends within the media layer of the aorta.16 Consequently, the aortic wall is weakened and the hematoma may progress into outward rupture through the adventitia or inward through the inner media and the intima, causing a “classic” aortic dissection.24

Aortic dissection can be defined as a “disruption of the media layer of the aorta with bleeding within and along the wall leading to separation of the aortic layers”.13 It begins with a
laceration of the aortic intima and inner layers of the media, with creation of a (primary) entry tear that allows blood to enter the aortic wall. It is believed that the first intimal laceration occurs from the aortic lumen in most cases, but it can also occur because of inward rupture from a primary IMH as explained above. The separation within the media creates two channels, the true and false lumen, separated by an intimal flap which is composed of the intima and inner layers of the media. The outer wall of the false lumen is formed by the remaining outer layers of the media and the adventitia. There are often secondary tears in the intimal flap (re-entry tears) with additional communication between the true and false lumens.

7.3 Classification of aortic dissection
The anatomical classification schemes of aortic dissection are based on location of the intimal tear and extent of the intimal flap (Figure 2). The systems still used today were originally developed during the 1950s and 1960s to facilitate triage of patients with acute dissection, as it became evident that patients with dissection of the ascending aorta could benefit from surgery. One scheme is the Stanford classification from 1970, and it divides aortic dissection into two categories: In Stanford type A aortic dissection, the ascending aorta is involved, whereas in type B dissection it is not. Five years earlier, DeBakey and co-workers proposed their classification, dividing aortic dissection into three subtypes: DeBakey type I arises in the ascending aorta and extends into the descending or abdominal aorta, type II is limited to the ascending aorta and type III originates in the descending aorta.

Today, the most widely used classification is the Stanford system, due to its simplicity in the lettering system and close relationship to management; surgical for type A and medical for type B.

There is still debate on how to classify dissections that involve the aortic arch. Neither the Stanford or the DeBakey system addresses specifically dissections that extend proximally into the aortic arch without involving the ascending aorta. With the advent of endovascular therapy, especially in ABAD, new classification systems have been proposed to take into account anatomical involvement and risk factors for complications with relevance for endovascular management. Examples are the PENN ABC and the DISSECT systems.
In terms of temporal classification, the dissection is labeled acute within 2 weeks from onset of initial symptoms; subacute between 2 and 6 weeks, and chronic if the debut occurred more than 6 weeks ago. In an attempt to better characterize survival in patients presenting with aortic dissection, Booher et al, based on data from the International Registry of Acute Aortic Dissection.
Dissection (IRAD), have proposed a new temporal classification with four time domains: hyperacute (< 24 hours), acute (2-7 days), subacute (8-30 days) and chronic (> 30 days).  

7.4 Epidemiology of aortic dissection
The true incidence of acute aortic dissection is unknown, and difficult to estimate for various reasons: Older epidemiological studies of aortic dissection were potentially hampered by questionable diagnostic accuracy, as they were performed before widespread use of modern diagnostic technology (e.g. computed tomography [CT] angiography). Furthermore, hospital-based studies, which often originate from tertiary referral centers or registry data such as IRAD and the German Registry for Acute Aortic Dissection Type A (GERAADA), will probably underestimate both incidence and mortality due to incomplete inclusion of deaths prior to admission. For the same reason, analyses on risk factors and predictors of outcome might be biased.

In population-based studies commenced after the introduction of CT, the incidence of AAD has been estimated to about 3 cases per 100 000 people per year, and as high as 10 cases per 100 000 people per year in the elderly. In this first-ever prospective epidemiological study of acute aortic dissection, the incidence was 6 cases per 100 000 people per year (95% CI, 4-7). Of note, approximately 50% (18 out of 37) of patients with an AAAD died prior to admission. The prevalence of aortic dissection seems to be rising, independent of the aging population. 

Acute aortic dissection is most common between the ages of 50 and 70, and it affects men more often than women, with a male to female ratio of approximately two to one.

7.5 Risk factors for aortic dissection
Risk factors for aortic dissection are related to either weakening of the aortic media and intima (inherited or acquired) and to conditions that place increased stress on the aortic wall. Arterial hypertension is present in two thirds to three quarters of patients. Genetic predisposition is related to certain syndromes, such as Marfan syndrome, the vascular form of Ehler-Danlos syndrome, Turner syndrome and Loeys-Dietz syndrome, or it can be inherited in the form of “familial thoracic aortic aneurysm and dissection” without syndromic
features. Januzzi et al showed that in the IRAD, 50% of patients under 40 years with an AAD had Marfan syndrome, compared to only 2% among patients older than 40 years. Other congenital and inflammatory conditions associated with aortic dissection are bicuspid aortic valve, coarctation of the aorta and vasculitides (Takayasu arteritis, giant cell arteritis and Behçet arteritis).

**7.6 Histopathology of aortic dissection**

The main histological finding in aortic specimens from patients with an AAD is medial degeneration. This consists of degradation of the extracellular matrix (ECM) related to smooth muscle cell depletion, elastic fiber fragmentation, and collagen degradation. It has been shown that an imbalance between the production of matrix metalloproteinases (MMPs) and their inhibitors is central to the degenerative process that leads to an aortic dissection in any aortic segment, both in inherited and acquired conditions. In addition, immunological pathways are involved in the pathogenesis of aortic dissection through macrophages and cytotoxic cells.

**7.7 Presentation and diagnosis of aortic dissection**

Intense pain with acute onset is the most commonly reported presenting symptom of AAD. The location of pain may reflect the site of the initial intimal disruption, as patients with AAAD most frequently present with chest pain and ABAD patients are most likely to present with back pain. On the other hand, it has been estimated that only 0.3% of patients presenting to the emergency department with acute chest, back or abdominal pain will ultimately be diagnosed with an aortic dissection. The American Heart Association (AHA), American College of Cardiology Foundation (ACCF), American Association for Thoracic Surgery (AATS) and a number of other professional societies have published guidelines for the diagnosis and management of patients with thoracic aortic disease. In these, certain high-risk markers (conditions, pain features and exam findings) of aortic dissection are identified. Other symptoms and signs of aortic dissection are related to end-organ complications, such as aortic insufficiency, cardiac tamponade, myocardial ischemia, cerebrovascular or spinal ischemia, pleural effusion, mesenteric ischemia, renal failure and limb ischemia.

Due to the high mortality and rapid evolution of the disease, early and accurate diagnosis is paramount among patients with clinically suspected acute aortic dissection. The test of choice is contrast enhanced CT, which shows sensitivity and specificity close to 100%.
artifacts in the ascending aorta can mimic imaging findings suggestive of an AAAD, a problem that can be overcome by electrocardiography (ECG) gating. Transesophageal echocardiography (TEE) and magnetic resonance imaging (MRI) have comparable diagnostic capabilities in suspected thoracic aortic dissection, but TEE does not allow for an adequate evaluation of the distal ascending aorta and aortic arch, and MRI is time-consuming. However, TEE does allow for assessment of the entry tear, re-entry tears and true lumen compression and is particularly useful in an intraoperative setting, e.g. in the assessment of aortic valve patency.

A variety of biomarkers has been evaluated for their utility in the evaluation of AAS specially to identify patients who do not need definitive imaging studies. D-dimer is most widely studied. A pooled meta-analysis showed that D-dimer can be useful in ruling out AAD in the emergency department, with a sensitivity of 97% and a negative predictive value of 96% with a cutoff at 0.5 µg/mL. Similar diagnostic capabilities are found in patients with IMH, but the test is not reliable in patients with PAU. Currently, no biomarkers are recommended for screening in patients with suspected AAS.

### 7.8 Long-term outcome of the distal aorta in acute aortic dissection

Aortic dissection must be regarded a chronic, life-long disease that requires regular follow-up including imaging and medical treatment (i.e. blood pressure management). This is also the case after successful surgery or endovascular therapy regardless of false lumen patency, as the remaining aorta is at risk of re-dissection and aneurysm development.

However, most patients with an aortic dissection, who survive the acute event, will have a residually dissected aorta. This is the case both for patients with a medically treated ABAD and for most surgically treated AAAD patients; in more than 70% of patients with AAAD, the dissection extends beyond the ascending aorta (DeBakey type I). As many as 79% of these patients will have a dissected downstream thoracic aorta with a patent false lumen after ascending aortic replacement. These untreated, dissected aortic segments are at risk of aneurysmal degeneration and rupture. It is therefore not surprising that patients that are discharged alive after AAAD surgery have a higher aorta-related mortality rate than the normal population. In a recent large series from Sweden, the impaired survival outlook of AAAD patients compared to a healthy population was re-emphasized; 291 patients discharged alive after successful surgery were followed for a median of 5.5 years and survival was 82%
at 5, 64% at 10, and 48% at 15 years. Importantly, the cause of late death was aortic events in at least 27% of patients, possibly as many as 42%, when those with an unknown cause of death were included. Furthermore, the cumulative risk of aortic re-intervention is 2% to 26% in AAAD survivors 10 years after the index event. The risk of mortality with late distal aortic reoperation varies considerably, but has been reported to be as high as 31%. IRAD data have shown that the long-term prognosis in ABAD might be even more sobering. The three-year survival of 189 medically treated ABAD patients enrolled in IRAD between 1996 and 2003 was only 77.6%. Even under optimal circumstances with regular follow-up and best medical treatment, the 5-year aortic-specific mortality rate is as high as 19.3%, as demonstrated in the INSTEAD trial (patients with stable ABAD randomized to optimal medical treatment, intention to treat analysis).

It follows that there is considerable interest in the identification of robust markers of future complications in acute aortic dissection, to tailor individual surgical or endovascular treatment and controls. Several demographic, clinical and radiological risk factors for distal aortic growth, aortic re-intervention and mortality have been explored. Intuitively, these are to a certain degree overlapping, as aneurysmal degeneration detected at follow-up necessitates re-intervention, and death during follow-up is due to aortic events in a significant number of patients. The principal risk factors are accounted for in the following paragraphs.

### 7.8.1 Partial thrombosis and patency of the false lumen

Traditionally, complete thrombosis of the false lumen has been regarded as a prerequisite for healing of the aorta post dissection, as flow and pressurization of the false lumen are thought to contribute to late dilation and rupture. Several reports have indicated that patients with a patent false lumen after AAAD repair have an increased risk of distal aortic enlargement and death.

In 2007, based on the IRAD data, Tsai et al showed that in patients with ABAD, partial thrombosis, more than a completely patent false lumen, predicted a higher follow-up mortality with a hazard ratio of 2.7 (95% CI, 1.5–5.0, patent false lumen as the reference group). They suggested two potential mechanisms by which partial thrombosis of the false lumen can predict a poor outcome. One is related to the pressure within the false lumen, which may be
perfused by a proximal entry tear and decompressed through one or more distal re-entry tears. If such a distal re-entry tear is occluded by a thrombus, the false lumen may transform into a “blind sac”, resulting in increased mean and diastolic pressures with increased wall tension, which in turn may increase the risk of aortic expansion and rupture. Tsai et al have later confirmed that in an ex vivo model of ABAD, the diastolic false lumen pressure is highest in the setting of smaller proximal tear size and the lack of a distal tear.82 This observation has later been confirmed in a biologic (porcine) model of ABAD.83 The other proposed mechanism was that a thrombus in the false lumen might exert a negative effect similar to that of an intraluminal thrombus in abdominal aortic aneurysms, where hypoxia in the arterial wall adjacent to thrombi leads to inflammation, neovascularization and localized wall weakening.84-86

The relationship between partial thrombosis of the false lumen and long-term outcome in patients with aortic dissection, either ABAD or postoperative AAAD, has been examined in several studies. The results have been divergent. Fattori et al studied the evolution of aortic dissection in 58 patients after AAAD repair, conducting MRI for 12 to 90 months after surgery.87 In their material, thrombosis of the false lumen in the residual dissected aorta, whether partial or complete, seemed to be protective against aortic dilation compared to a residual false lumen and no thrombus. In addition, the rate of reoperation or sudden death was higher in patients without thrombus in the false lumen. In a similar study by Kim et al, 129 patients who underwent surgery for DeBakey type I dissection were evaluated with CT and followed for a median of 29.5 months.88 The thrombosis status of the false lumen at postoperative CT did not influence aortic aneurysm development, late survival or aortic reoperation. However, Song et al showed that partial thrombosis of the residual false lumen after repair of acute DeBakey type I dissection, compared to complete patency or complete thrombosis, was a significant predictor for both aortic growth, aorta-related reoperations and poor long-term survival.89 Their findings are supported in a recent report by Tsai et al90 in which the effect of false lumen partial thrombosis in repaired AAAD was examined. They found that partial false lumen thrombosis correlated with faster regional aortic growth rate and predicted a greater reoperation rate but did not affect long-term survival. Interestingly, in this study, a segmental analysis was used to assess the false lumen status independently at 3 different levels in the descending thoracic aorta, in contrast to the definition adopted by previous studies, where the entire false lumen has been categorized as one entity. The
negative effect of partial thrombosis was attenuated when data were re-analyzed using the definition of the entire false lumen status.

In case of ABAD, most studies have failed to identify partial thrombosis of the false lumen as a predictor of worse outcome or faster aortic growth or aneurysm formation.\textsuperscript{91-94} However, in the study by Sueyoshi et al\textsuperscript{92}, who compared aortic enlargement across different degrees of false lumen thrombosis in ABAD, a subset within the partial thrombosis group with a blind pouch in the false lumen (i.e., thrombosis covering the potential distal re-entry site) had considerably faster growth rates. This group was small and only accounting for 15\% of the patients with partial thrombosis of the false lumen. Nevertheless, Trimarchi et al showed that among 84 exclusively medically treated patients with ABAD, aortic segments with a partially thrombosed false lumen had a significantly higher annual growth rate compared to those presenting with patent or complete thrombosis of the false lumen.\textsuperscript{95} Their findings have recently been supported in another study by Tolenaar et al.\textsuperscript{96}

A recently published paper shed new light on the pathophysiologic processes involved in chronic aortic dissection and thrombosis in the false channel. Sakaliasan et al used \textsuperscript{18}F-fluorodeoxyglucose (\textsuperscript{18}F-FDG) positron emission tomography/computed tomography (PET/CT) in a series of 23 patients with ABAD to predict complications and aneurysmal expansion during follow-up.\textsuperscript{97} They found that both partial thrombosis of the false lumen and \textsuperscript{18}F-FDG uptake were associated with complications as well as aneurysmal expansion, along with biomarkers of thrombus renewal and lysis.

### 7.8.2 Entry tear exclusion

There is general agreement that the entry tear, if possible, should be excised during surgery for AAAD. This is based on the notion that a persistent entry tear will maintain inward flow and pressurize the false lumen (i.e. maintaining a patent false lumen), thereby augmenting the risk of dilation and rupture of the residually dissected aorta. The primary entry tear is located in the ascending aorta in most cases\textsuperscript{98} and is thus removed by simple ascending or hemiarch aortic replacement – in the latter the ascending aorta and the inferior part of the aortic arch is replaced. However, when the entry tear is in the convexity of the aortic arch, the descending thoracic aorta, or not found on imaging or intraoperative, should it still be managed during initial surgery? The procedures required to do so involve TAR or even TAR+FET, and the potential improvement in the long-term prognosis can be offset by an increase in operative
complexity and short-term morbidity and mortality. As the primary entry tear is located in the aortic arch in 10-30% of patients\textsuperscript{99}, it follows that this is a relevant question in many cases.

Unosawa et al studied 102 patients operated for AAAD, out of whom 45 underwent surgery without tear resection (group I) and 57 underwent resection that included the intimal tear (group II).\textsuperscript{100} In-hospital mortality was similar between groups. No difference was found in the freedom of aorta-related clinical events (aneurysmal change, reoperation and death) or actuarial survival at follow-up. In their multivariate logistic regression model, a patent false lumen and non-exclusion of the entry site were independent predictors for aortic dilation. Important limitations were only 4 years of follow-up and the fact that out of 89 patients discharged from the hospital alive, only 69 (77.5\%) underwent follow-up CT scanning.

Other retrospective, single-centre studies have found a non-resected primary tear to be an independent predictor of late reoperation after AAAD surgery, but without impact on long-term survival.\textsuperscript{68, 76, 79, 101}

### 7.8.3 Marfan syndrome

Marfan syndrome (MFS) is a heritable autosomal dominant connective tissue disease caused by mutations in the FBN1 gene. This gene encodes fibrillin-1, a large glycoprotein that is a major component of the extracellular matrix. Patients with MFS are prone to aortic aneurysm development and aortic dissections. Patients with MFS are on average younger at the time of AAAD\textsuperscript{42} and have a markedly increased risk of distal aortic growth and reoperations after initial AAAD repair.\textsuperscript{62, 68, 69, 71, 76, 79, 102, 103}

### 7.8.4 DeBakey subtype I

Even after successful initial surgery in AAAD with obliteration of the distal false lumen, the distal aorta is at risk of future dilation and re-dissection. Nevertheless, the extent of the initial dissection process affects long-term outcome. Specifically, a DeBakey type I aortic dissection has been identified as a negative prognostic marker, with increased risk of distal aortic reoperation after AAAD repair.\textsuperscript{67, 71, 102}

### 7.8.5 Age

Younger age at presentation predisposes to late distal reintervention in AAAD.\textsuperscript{71, 73, 79} This is perhaps not surprising, for two reasons; firstly, younger age means that the residually
dissected downstream aorta has more time to dilate. Secondly, a higher proportion of patients that present with AAAD at a younger age will have inheritable disorders (e.g. Marfan syndrome, Ehler-Danlos syndrome), and are at increased risk of aortic expansion and re-dissection irrespective of their previous aortic dissection.

7.8.6 Aortic diameter

7.8.6.1 AAAD

The primary diameter of the descending thoracic aorta also affects the reintervention frequency in AAAD. Fattouch et al followed 189 survivors of AAAD repair for a mean of 88 ± 44 months. A descending aortic diameter 45 mm or larger was an independent predictor of late retreatment with a hazard ratio of 5.8 (95% CI, 3.5-22.5). Similarly, Halstead et al calculated growth rates in 89 patients that were followed with serial CT scans after AAAD repair. Initial descending aortic size greater than 40 mm was associated with more rapid growth (median, 1.3 vs. 0.9 mm/year). Recently, Kimura et al reported on their experience with 534 AAAD patients, focusing on reoperation for enlargement of the distal aorta. They found that an initial descending aortic diameter of > 45 mm was an independent predictor of distal aortic events (sudden death, aortic rupture, re-dissection and reoperation in the downstream aorta) with a hazard ratio of 4.4 (95% CI, 2.5-7.6).

7.8.6.2 ABAD

Similar results are found in patients with ABAD. Schwarts et al followed 254 patients with initially medically treated ABAD for a mean of 6.8 years. There was a total of 97 (38%) patients who required an aortic intervention during follow-up. A total aortic diameter larger than 40 mm at time of presentation was predictive of late aortic intervention with an odds ratio of 2.2 (95% CI, 1.8-4.3). This “threshold” value of 40 mm seems to be consistent and has been reported repeatedly as an independent predictor of late aortic events in ABAD. The study by Marui et al is particularly interesting in this respect. They followed 141 patients with ABAD for a mean of 64.4 months and follow-up data were 98% complete. Of the 141 patients, 59 (42%) met the criteria for the development of late aortic events during the chronic phase. Late aortic events were defined as aortic diameter ≥ 60 mm, aortic rupture, refractory pain, visceral organ ischemia, rapid enlargement of the aorta by ≥ 10 mm/year or rapid enlargement of ulcer like projections by ≥ 5 mm/year. In their multivariate analysis, a maximum aortic diameter > 40 mm, a patent false lumen, and a “fusiform index” (an
expression of the degree of fusiform dilation in the proximal descending aorta calculated by
the diameter in this segment divided by [diameter of the distal arch+diameter of descending
aorta at the pulmonary artery level]) were independent predictors of late aortic events (hazard
ratios, 3.2, 2.6 and 2.7, respectively). In patients with all three aortic findings, the actuarial
freedom of aortic events was 22%, 17% and 8% at 1, 5 and 10 years. Conversely, in patients
with none of these predictors present, the corresponding values were 97%, 94% and 90%,
respectively.

7.8.7 Size of the intimal tear
Although not extensively studied, the size of the (primary) intimal tear in aortic dissection
seems to influence long-term outcome in at least ABAD. Schwarts et al found that an entry
tear of more than 10 mm in size predicted late aortic intervention in initially medically treated
ABAD patients (OR, 2.1, 95% CI, 1.5-3.8). Evangelista et al treated the entry size as a
continuous (not dichotomized) variable in their analyses of patients with ABAD and
surgically treated AAAD. They found that a larger size of the intimal entry at the index event
was an independent predictor for both mortality and dissection-related events during follow
up (HR, 1.1 and 1.13 respectively, per 1 mm increment in size). However, in a receiver
operator characteristics analysis, the optimal threshold value to predict aortic complications
during follow-up was ≥ 10 mm with 85% sensitivity and 87% specificity.

7.9 The objectives of surgery in acute type A aortic dissection
Acute type A aortic dissection is generally regarded as a surgical emergency. To clarify the
objectives of surgery one must consider the immediate risk of the disease. Mortality in the
acute phase is in most cases due to intra-pericardial rupture and cardiac tamponade, coronary
artery involvement causing myocardial ischemia or acute heart failure through major aortic
valve regurgitation in the setting of aortic root involvement. Thus, the main goal of surgery is
to eliminate these three consequences of ascending aortic dissection.

“We have to remember that acute type A aortic dissection is an inherently lethal condition.
Our first job is to produce a live patient. If the patient survives the acute episode, this
constitutes a success, regardless of later onset of further aortic problems.”

Accordingly, replacement of the ascending aorta and, in selected cases, replacement of the
aortic valve accomplishes the main objective of surgery - to save the patient’s life. Secondary
objectives are excision of the proximal entry tear, restoration of dominant true lumen flow in
the distal aorta, correction of distal malperfusion and, if feasible, permanent obliteration of the
false lumen.\textsuperscript{111}
8. Aims of the studies

8.1 Paper I
At the inception of this study, the concept of partial thrombosis of the false lumen as a potential negative prognostic marker in AAD was already well known. Based on IRAD data, Tsai et al found that in patients with ABAD, partial thrombosis, more than a completely patent false lumen, predicts a higher follow-up mortality. We identified another six studies that examined the relationship between partial thrombosis of the false lumen and long-term outcome in AAD – all of these included patients with either ABAD, postoperative AAAD, or a combination of both. No studies had evaluated whether the degree of false lumen thrombosis preoperatively in AAAD had an impact on outcome. Furthermore, the factors that accounted for the potential negative influence exerted by partial false lumen thrombosis were unknown. As such, we sought to examine whether a partial thrombosis of the false lumen observed at the first hospitalization would negatively affect the remodeling of the distal aorta, increase the need for re-intervention, or negatively influence the long-term survival of surgically treated AAAD patients.

8.2 Paper II
In an era of increasing focus on evidence-based treatment, there is an ongoing concern on how to document and investigate the merits of different surgical treatments for AAD. The use of an open distal anastomosis during reconstruction of the ascending aorta is one of the technical concepts that seems logical and potentially can improve the prognosis for patients with AAAD. The open distal anastomosis (i.e., construction of the anastomosis in hypothermic circulatory arrest without a cross-clamp on the distal ascending aorta) is appealing in several ways. Visualization is superior and allows for a better and hemostatic secure anastomosis. Additional intimal tears in the aortic arch can be detected and addressed. The repair can be extended to a hemiarch or total arch replacement. Finally, the friable, dissected aortic tissues are not subjected to further trauma by the cross-clamp. On the other hand, the closed technique with clamping of the distal ascending aorta has its advantages too. It is quicker because profound cooling is unnecessary, it avoids the introduction of additional air and debris into the aortic arch and cerebral perfusion is secured throughout the procedure. We did an updated systematic review of the literature to examine whether there is evidence to support the notion that the distal anastomosis in ascending aortic replacement should be performed in an open fashion in AAAD surgery.
8.3 Paper III
Since the IRAD was established in 1996, diagnostic pathways and treatment of AAD have changed parallel to other advancements in cardiovascular surgery. We wanted to examine in which way the presentation, diagnostic work-up, management and hospital outcomes of patients with an AAD have changed during 17 years of registration in the IRAD.

8.4 Paper IV
In most patients with AAAD, the dissection extends beyond the ascending aorta. An ascending aortic replacement alone will leave a residual dissected aorta with a patent false lumen in most of these patients. Replacement of the aortic arch and even simultaneous stent grafting of the proximal descending aorta ([frozen] elephant trunk) in AAAD has gained popularity as it can contribute to favorable aortic remodeling and reduce the incidence of aortic dilation and catastrophic events. However, the risks of such extensive surgery in the acute setting may outweigh potential long-term benefits. We used the IRAD data to compare the short- and mid-term outcomes of limited repairs versus complete arch surgery in patients with AAAD.
9. Materials and methods

9.1 Clinical registries

9.1.1 General considerations and rationale

The surgical treatment of aortic dissection does not easily lend itself to randomized controlled trials (RCTs) or other comparative studies. AAD is an extremely versatile disease and establishing the diagnosis is sometimes challenging. Presentation is highly variable as the dissection is a dynamic process and can originate anywhere in the aorta; symptoms caused by the disease process can mimic disease in almost any organ system primarily due to malperfusion phenomena. Even within groups of patients with either AAAD or ABAD, the pathological anatomy varies considerably in respect to dissection extent, aortic diameters and branch vessel involvement. Preoperative condition ranges from hemodynamic stability without symptoms to severe shock and cardiac tamponade, or neurologic deficits and even coma. All of this makes comparison between patients difficult. The treatment of AAD is perhaps as diverse as its presentation. Surgical technique, medical devices used, cannulation, perfusion and cerebral protective strategies varies between surgeons and hospitals. Therefore, the impact of a certain treatment or technique on outcome is problematic to assess. In addition, AAD is a relatively rare disease and acquisition of an adequate number of patients to conduct meaningful research is difficult. The vast amount of studies on AAD report single-center experiences, and in cases of outcomes of surgical techniques or strategies, they lack a contemporary control group. Consequently, most of the therapy principles in AAD are based on expert opinions and the evidence level is low. In fact, in the guidelines on the diagnosis and treatment of aortic diseases published by the European Society of Cardiology in 2014, none of the recommendations for the treatment of aortic dissection is based on level A evidence. Other known limitations to the RCT methodology are relevant to AAD as well. For most surgical or endovascular interventions there is a learning curve, thus early results may be inferior. Timing of a study is therefore an issue. However, if the study is started too late, the therapy in question may already be in widespread use and its merits obvious, rendering an RCT pointless. Other problems are rapid developments in equipment and technique, informed consent in the case of very different therapies, and blinding. Apart from the drawbacks in conducting RCTs in AAD, observational studies can also fulfil other objects complementary to RCTs:
- Apply findings from an RCT to a more representative population to evaluate their external validity.\textsuperscript{113}
- Generate hypotheses to be tested in an RCT.\textsuperscript{113}
- Identify outcomes that should be examined further.\textsuperscript{114}
- Aid in the estimation of appropriate sample sizes in RCTs.\textsuperscript{114}

The recognition of the difficulties concerning documentation of the efficacy of specialized, skill-dependent care in a rare and acute condition such as AAD, has led to the development of clinical aortic dissection registries, in which a large number of patients can be included within a reasonable amount of time and with (external) validity exceeding that of single-center reports.

9.1.2 The International Registry of Acute Aortic Dissection (IRAD)
To overcome the difficulties in collecting sufficient data on aortic dissection, the IRAD was established in 1996, initially as a collaborative effort between 12 aortic centers in six countries. The University Hospital of North Norway (UNN) joined IRAD in 1998. The number of collaborating centers has gradually increased, and today IRAD receives data from more than 40 centers worldwide (Figure 3), and the database contains core data from more than 6500 patients. IRAD is led by Professor Kim A. Eagle (University of Michigan), supported by Professor Christoph A. Nienaber (The Royal Brompton & Harefield, London) and Eric Isselbacher (Massachusetts General Hospital), the “founding fathers” of the database.

The stated intention of IRAD was “to assess the current presentation, management and outcomes of acute aortic dissection.”\textsuperscript{40} From 2010, a dedicated section of the IRAD, the Invasive Treatment Group, has established a more extensive data form with attention to the details of invasive treatment and its outcomes.
The IRAD was from its inception, and still is, primarily investigator driven with relatively few permanent supportive resources except for an established dedicated staff and facilities at Michigan Cardiovascular Outcomes Research and Reporting Program (MCORRP). IRAD has been built as a “pragmatic” investigators database. This means that each center is responsible for providing their data and do the follow up. The data is not reviewed by a “core laboratory” for detailed assessment of the information provided. Hence, the quality of the data that is added is exclusively each investigator’s responsibility.

9.1.2.1 Inclusion in the registry

All patients with a non-traumatic acute aortic dissection are eligible for inclusion in IRAD. Iatrogenic AADs are also included. For the purpose of the registry, an AAD is defined as either a “classic” double-barrel aortic dissection or as an IMH. Presentation must be within 14 days of symptom onset. Patients are identified either prospectively at presentation or retrospectively from discharge diagnoses. Patients that present to other hospitals in our region
but die before or during transfer to our tertiary care center, are also included. The diagnosis of AAD is based on symptoms, imaging, intraoperative findings and/or autopsy.

Inclusion in the registry requires written consent and does not imply treatment standardization per se, nor any changes in follow-up or treatment. Consent can be withdrawn at any time. Information that is used in the registry is gathered from the electronic patient records and imaging archives, rarely by communication with primary care physicians or patients directly.

**9.1.2.2 Data collection and storage**

A standardized form is used to record information on the index hospital stay for all patients. The form contains information on patient demographics, past medical histories, presenting symptoms, physical findings, imaging results, treatments and outcomes (including complications and mortality). Data are anonymized, and all patients are assigned a unique IRAD ID number. The form has been revised regularly since the first version in 1996 to account for developments in imaging and treatment over the years. The current version (v7.0) contains approximately 350 different variables. In the first years, the form was completed by investigators at each site and forwarded to the IRAD Coordinating Center at The University of Michigan by fax or mail where they were entered into the central database. This rather tedious process is replaced by electronic versions of the forms that are completed at a password-protected website (https://www.iradonline.org/) and stored in the database continuously. Each investigator has a separate user account at the website. The participating centers have access only to their own data through the online database, while the IRAD Coordinating Center have access to the complete dataset.

**9.1.2.3 Follow-up**

Follow-up is obtained in IRAD at 6 months, and then annually for a total of 5 years of follow-up in the registry. Like the index form, a standardized questionnaire is used which contains information on the date of last clinical follow-up or, when applicable, the date the patient was lost to follow-up. Recorded information include symptoms since last follow-up, medication, blood pressure and heart rate, imaging results and whether there have been adverse events in the form of death, re-intervention etc.
9.2 Limitations in the use of IRAD data

Results from observational studies in general, and IRAD specifically, must be interpreted considering certain common limitations. Quality of the information provided to the central database can be questioned. The datasets for each patient in the registry are in many cases not complete, and follow-up is lacking in a significant amount of cases. Some of the limitations in the use of IRAD as a source of knowledge are listed below.

9.2.1 Precision

Also referred to as reliability, precision is the lack of random error or random variation on a study’s estimates. Random variation may arise in several ways, but an important contributor is sampling, i.e. the process of selecting study subjects. The study subjects are considered a sample of possible people who could have been included in the study, thus the selection gives rise to sampling error and attendant random variation. Random variation not only arises from the sampling, but also from the way in which variables are measured and from variation in occurrence measures. Random error is reduced, i.e. precision is increased, by enlarging the size of the study. When estimates from observational studies are evaluated, a wide confidence interval for estimates of association may indicate low precision.

9.2.2 Validity

External validity (generalizability) is to which extent research findings based on a sample of individuals can be extrapolated to the entire population (or to other populations, times, and settings). RCTs often have narrow inclusion and exclusion criteria, and the study participants may not adequately reflect the population in which the treatment that was tested is to be applied. For instance, it was estimated that in the 1980s, only 5-10% of patients in the Duke Cardiovascular Disease Databank would have been eligible for inclusion in the early RCTs comparing CABG to medical treatment in stable angina pectoris. Consequently, one can assume that a potential RCT on treatment in AAD, in which presentation and treatment is expected to be much more diverse than stable angina pectoris, would potentially have a low external validity. Observational research such as the IRAD have advantages to this regard, in that all cases are ideally included consecutively and unselected in the registry. Still, there are elements that might limit the external validity.

First, the health care providers at institutions that participate in the IRAD may be unrepresentative. IRAD centers are tertiary, high-volume hospitals with an interest in aortic
disease. Thus, the awareness of aortic dissection can be higher in these institutions, and algorithms for the diagnosis and care of AAD patients might differ from others. Novel treatment and procedures may also find their way into standard care faster than at other centers. This effect may even be amplified when data from the Invasive Treatment cohort of IRAD patients are used in analyses of outcome, as these results are limited to centers with a particular interest in AAD surgery, and as such not representative even of the entire IRAD population. Such a limitation in the generalizability of data certainly apply to all highly skill-dependent therapies, as often is the case in surgical research.

Secondly, even though the intention is to recruit all patients in an unselected and consecutive manner, the patients that are included in the IRAD database may be atypical. Some patients do not agree to participate in the study. These patients might share certain characteristics in terms of age or past medical histories that differ from patient that consent to inclusion. Moreover, the participating IRAD centers are tertiary referral centers. Currently, 71% of patients with an AAAD in IRAD are transferred from a primary center. Thus, these patients are a selected group with better prognosis, since they have survived to arrive at the tertiary center. Consequently, the results drawn from IRAD with respect to outcome might not be valid in settings outside the registry.

Thirdly, even though inclusion in the IRAD requires written consent, the regional committee for medical and health research ethics have approved that patients who die before there has been an opportunity to gain written consent, can be included in the registry by default. This practice contributes to potential overestimation of mortality. Our aim is therefore that all cases of AAD in our region of care (North-Norway) are included.

Internal validity, on the other hand, refers to whether the results of a study are correct for the subjects being studied; i.e. high internal validity implies lack of bias (systematic error). Violations of internal validity can broadly be classified in three categories: selection bias, information bias and confounding.\textsuperscript{116} Their relationship to the IRAD and the papers in this thesis are discussed here.
9.2.2.1 Selection bias

The main difference between observational research and randomized trials is the elimination of selection bias by randomization. In any observational study, there may be large and unobserved differences between the treatment and control group. An observed difference in outcome can be due to these differences, rather than the treatment itself. Different statistical methods can be applied to control for and reduce selection bias, but it can never be eliminated. In addition, to control for selection bias, the characteristics must be observed and recorded in the data. If an unobserved characteristic is a significant predictor of outcome and unbalanced between groups that are being compared, the potential for significant selection bias exists. The number of unobserved characteristics that may influence analyses in a registry can be reduced by including all variables that might affect outcome. However, adjustment for such variables depend on their inclusion in analyses.

The index data form in the IRAD have many variables to ensure that patient information is recorded as detailed as possible. However, certain characteristics that might have a large impact on outcome are almost impossible to characterize in this manner, especially in the case of surgical management. In paper IV, the severity and extent of the dissection is described in terms of preoperative condition and imaging results, but intraoperative findings in each case that could have influenced management and outcome are not accounted for in any way. Furthermore, the acute and dynamic nature of AAD can give rise to major changes between admission and imaging, and subsequent surgical management. This can be regarded as a form of selection bias, as patients that are categorized in a certain way based on admission data, may in fact belong to a different category a few hours or days later.

In IRAD, as in other registries, there is a potential for a “selective” reporting bias, in that cases with poor outcome may be underreported for various reasons, one of them being reluctance by the investigators themselves to report unfavorable results. This will cause a systematic underestimation of mortality and morbidity. Efforts have been made to reduce risk of “selective” reporting: IRAD encourages consecutive and unselected inclusion of all AAD patients. Each participating center has access only to their own data, and the origin of patients are not disclosed in any publications.
9.2.2.2 Information bias

Information bias results from wrong or incorrect recording of individual factors. Information bias occurs in every type or research, but an “investigator driven” registry such as IRAD is particularly prone to errors of recording. The sheer number of variables themselves will inevitably lead to bias via different mechanisms. The investigators of GERAADA have described some of these\(^\text{124}\), and they are applicable to IRAD as well:

“Definition bias”: Whenever an item is recorded in the registry, the investigators definition of these can influence the information. This is not a problem in the case of clear, objective measures such as age or gender, but for many other variables there is a degree of subjective interpretation. When information is collected from the patient records through chart review, another layer of subjectivity is added. To eliminate “definition bias” as much as possible, the IRAD provides lexicons for each data form with clear definitions for each parameter. However, even these can be misunderstood, and if definitions of items systematically differ between centers, this will hamper the internal validity of the registry.

“Motivation bias”: The person that is doing the documentation may for any reason be inattentive and make mistakes. Especially variables that require chart review and/or calculation (e.g. finding cross clamp or selective cerebral perfusion times in the anesthesiology charts) are prone to omission or inaccuracies, which can lead to error of central tendency for continuous variables and missing documentation for categorical variables.

“Knowledge bias”: The person that is doing the documentation is rarely the treating physician and often documentation takes place a long time after the index hospitalization. Information may get lost on the way. Furthermore, interpretation of ECG and imaging requires a degree of training and experience.

The lack of a core laboratory to evaluate the information provided in the IRAD is problematic. The data forms contain detailed questions on imaging findings, beyond what is provided in the description by radiologists in every-day practice. Ideally, all images should be reviewed by an expert at least at each IRAD site if not a core laboratory, but this is not possible at the present time. Consequently, there is the potential for systematic and serious bias in the imaging data. Systematic validation of the data by chart review is not possible from
the IRAD Coordinating Center. With each IRAD project, the “master file” goes through a cleaning phase at the start of analyses in which unlikely values and duplicates are identified. In that respect, a validation and consistency check is at least in part performed regularly for the entire database.

9.2.2.3 Confounding

Confounding arises when a factor is associated both with the exposure (or treatment) and the outcome, and is not a part of the causal pathway from exposure to outcome.\(^{125}\) It raises issues with (lack of) comparability in observational studies, which hampers causal inference. Once a problem with confounding has been identified, it can be dealt with in different ways during the design or analysis of a study.\(^ {126}\) Measures during the design phase (randomization, restriction or matching) are not applicable to the IRAD database. In the analysis phase, there are a number of methods available to control for and reduce confounding. Multivariable regression analysis is perhaps the most used method. However, this method does not directly determine whether a factor is a confounder, and whether residual confounding remains in the final model cannot be determined.\(^ {127}\) In the recent years, propensity score methods have gained popularity as a mean of controlling for confounding in observational research. The intention is to match patients as well as possible with regard to characteristics that are associated with the choice of treatment.\(^ {123}\) There are different ways of applying a propensity analysis to a dataset, but the basic concepts most often involve the development of a logistic regression model with the choice of treatment as the dependent variable and the potential confounders as the non-dependent variables. The probability of receiving the treatment (propensity score) in question can be calculated from the model. From the propensity score, matching pairs of patients receiving different treatments, but having identical or similar probabilities of receiving the treatment in question can be identified. A different way of application of the propensity score, which we have used in paper IV, is to include the propensity score as an additional, independent variable in a regression model.

As one can attempt to control for confounding with different statistical methods, the main objection to such analyses remains. To control for a confounder, it must be identified and measured in the dataset. Selection of potential confounders in the analyses is based on prior knowledge. In addition, and especially true for the treatment choices in life-threatening conditions and acute conditions such as AAD, there are unknown variables that influence
treatment choices that remain unmeasurable. In paper IV, we have tried to control for known factors that we have measured that make the choice of extended arch replacement more likely. However, intraoperative circumstances that influenced treatment choice were not recorded. There is certainly a possibility that patients that received arch repair, on average, had a more malignant aortic pathology, which is not accounted for in the IRAD registry forms at the present state. Surgeon’s experience and hospital volume might also influence treatment choice; these factors are neither recorded in the registry.

9.2.4 Quality and quality control
A perfect large-scale database is an illusion. To consider the quality of the information in a registry, Skeet has identified five main areas of consideration:\textsuperscript{128}

- \textit{Completeness of cover}. Ideally, all cases of the condition under interest that occur within the population should be included. Failure to achieve this goal in the IRAD mainly involves lack of consent. Equally important is to avoid duplication of patients and registration of patients that are ineligible for registration (e.g. chronic as opposed to acute aortic dissection).

- \textit{Completeness of detail}. It is not possible nor desirable to ascertain every possible data item for each patient. However, some variables should be considered essential, and failure to register these should not be possible. In the IRAD, examples of such essential variables are dissection type and management, and during the electronic registration process, it is not possible to proceed before these data items are provided. For non-essential variables, the preset value in drop-down menus should be set to “unknown” instead of “not present”, as the latter might contaminate data.

- \textit{Accuracy of detail}. Inaccuracy can occur in many ways: abstraction, transcription, coding and punching errors. Even after consistency checks, such an item can appear satisfactory. Errors of such a kind will produce random error and not systematic bias.

- \textit{Accuracy of reporting}. Enquires in the database may be carried out by staff without first-hand knowledge of the data, on request by staff without first-hand knowledge of the computer file or statistical software used. This can yield results in which reporting errors are likely.
- Accuracy of interpretation. The proper interpretation of the information from a registry requires an understanding of the data sources and how the data are collected and processed. To aid in interpretation, a close collaboration between investigators, supportive staff and statisticians is necessary.

9.3 Statistical methods

Paper I, III and IV in this thesis contain statistical analyses, and the methods that were used are common for certain parts of these, but with special analyses carried out in paper IV in particular.

All data analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk NY, USA).

Missing values were not defaulted to negative or handled by imputation. Presented values represent only those cases reported. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as means and standard deviations (SD) or as medians and first and third quartiles (25th and the 75th percentiles, respectively) in cases of skewed data distributions. For categorical variables, differences between groups were analyzed using the chi-squared or Fisher’s exact test, as appropriate. Continuous variables were compared with the t-test or Mann-Whitney U-test in the case of two groups, and with an analysis of variance or Kruskal-Wallis test in the case of three or more groups under comparison. In paper III, patients were divided into 6 groups based on 6 roughly equal time spans in chronological order over a 17-year period. These groups were considered to be ordered, and linear-by-linear association was used to evaluate linear trends across time groups.

Regression analyses were done in a backwards stepwise fashion in which variables were evaluated for clinical significance and candidate variables from univariate testing (P < 0.20 or P < 0.15) introduced into a multivariate model.

In paper IV, we used propensity-adjusted multivariable analysis to assess risk factors for operative mortality as well as follow-up mortality in patients who survived the index hospitalization.
9.4 Ethics

Inclusion in the IRAD requires informed, written consent, except in cases where the patient dies before there has been an opportunity to gain such consent. At our institution, consent is usually obtained by the physicians who participate in the IRAD as well as being part of clinical practice with treatment of AAD patients. The dual role of scientist and clinician can be problematic. This is particularly the case in RCTs and other intervention studies, but apply to observational research as well. Patients might feel obligated to accept inclusion in the registry, even though they are well informed about the fact that inclusion does not change management or follow-up in any way. Consent can be withdrawn at any time, upon which all recorded data will be deleted. Patient anonymity is ensured by de-identification of information in the IRAD database. Participation in the registry does not grant the patient any benefits.
10. Summary of results and discussion

10.1 Results paper I

Our hypothesis was that a partial thrombosis of the false lumen observed at the first hospitalization in surgically treated AAAD patients would negatively affect the distal aortic remodeling, increase the need for re-intervention and negatively influence long-term survival.

The final study population included 522 patients with AAAD who were discharged alive from the index hospitalization. Of these patients, 414 (79.3%) had a patent, 84 (16.1%) a partially thrombosed and 24 (4.6%) a completely thrombosed false lumen on preoperative imaging. The mean age ± standard deviation (SD) was 57.9 ± 13.6 years. Most patients (74.9%) were male and had a history of hypertension (70.9%). Almost a quarter of patients presented in hypotension or shock, or with cardiac tamponade. Neurologic deficits were present in 15.0% and almost one-third had at least one pulse deficit. Arch vessel involvement occurred in 40.3% of the patients, and about one-third of the dissections were confined to the ascending aorta and aortic arch. CT was performed in 81.0% of patients, and more frequently in the partial thrombosis group (90.5% vs. 79.4% and 75.0%, P=0.034).

Patients with a patent false lumen were on average 3 years younger than those with a partially thrombosed false lumen and 6 years younger than those with complete false lumen thrombosis. Patients with a patent false lumen had fewer imaging studies per patient, while CT was performed more frequently in patients with partial thrombosis of the false lumen. Distal extension of the dissection merely to the aortic arch occurred more frequently in the partial thrombosis and complete thrombosis group than in the patent false lumen group (31.8%, 37.5% and 17.1%, respectively, P=0.005). Surgical strategy with respect to extent of aortic replacement and use of HCA and in-hospital complications did not differ between groups.

The median aortic growth rate was 0.5 (-0.3 to 2.0) mm/year in the aortic arch and 2.0 (0.2 to 4.0) mm/year in the descending thoracic aorta and similar regardless of the degree of preoperative false lumen thrombosis.

The Kaplan-Meier curves showed an overall 5-year survival of 84.7%. The extent of preoperative false lumen thrombosis did not affect the 5-year survival rates nor freedom of
major adverse events (all-cause mortality, aortic rupture, and reoperation [including endovascular repair]).

In the multiple regression models, age and the composite endpoint of postoperative cerebrovascular accident, coma or renal failure were significantly associated with death during follow up.

10.2 Discussion paper I

The hypothesis that a partial false lumen thrombosis, observed at the index hospitalization in surgically treated AAAD patients, predicts an ominous clinical course was rejected. Other studies that have examined the relationship between partial thrombosis of the false lumen and prognosis in AAAD have shown divergent results. The same is true for ABAD.

Recently, Li et al published a systematic review and meta-analysis that examined the long-term association (> 1 year) between the status of the false lumen and patient outcomes in AAD. A total of 11 cohort studies with 2924 participants were included. They concluded that a residual patent false lumen is independently associated with poor long-term survival in both AAAD and ABAD (HR, 1.71, 95% CI, 1.16-2.52 and HR, 2.79, 95% CI, 1.80-4.32, respectively) whereas a partial thrombosis of the false lumen increases late mortality risk in ABAD patients only (HR, 2.24, 95% CI, 1.37-3.65). However, direct comparison from other studies with our data is not necessarily valid, as we examined the influence of preoperative false lumen thrombosis in AAAD. Furthermore, the assumption that a partial thrombosis of the false lumen in an “untouched” (i.e. medically treated) ABAD is unfavorable, does not automatically imply that this is the case in postoperative AAAD. The notion that an operated AAAD with a persistent false lumen in the descending thoracic aorta mirrors a primary ABAD with identical anatomical extension is an oversimplification, at best. The location of the (primary) intimal tear is different in AAAD and ABAD. The size and location of the tear has been shown to play a role in the development of aneurisms and late aortic events. Therefore, the surgical management of an AAAD, in which one of the objectives is identification and excision of the intimal tear, might change the pathological process of the dissection fundamentally, even in the case of a postoperative patent false lumen downstream to the repair. If the primary intimal tear in the ascending aorta or the aortic arch is removed, a perfused false lumen after AAAD repair must be caused by either residual intimal tears (re-entries), or an insufficient connection between the prosthetic aortic graft and
the true lumen at the level of the distal anastomosis (or the distal anchoring zone of the stent-graft in the case of FET). These remaining communicating channels between the true and false lumen might influence flow and pressure of the false lumen differently than that associated with the primary entry tear in ABAD. This was illustrated in a study by Krähenbühl et al, in which the outcomes of 247 patients with “remaining type B after type A” and 112 patients with primary type B aortic dissections were compared.94 They concluded, “a remaining type B dissection after type A repair and a primary type B dissection represent two distinct pathophysiological entities with regard to late outcome”. The rate of intervention in the thoracoabdominal aorta was significantly higher in ABAD. Furthermore, a residual primary entry tear independently predicted the need for intervention during follow up in AAAD with an odds ratio of 6.4 (95% CI, 1.39-29.81), but not in ABAD. The observation that patients with a patent false lumen distal to AAAD repair have better outcomes than ABAD is supported by other studies.109

A potential source of bias in our study is misclassification of the false lumen status with respect to thrombosis. Firstly, participation in IRAD does not per se imply standardization of management, and this applies to imaging protocols as well. Hence, the imaging studies that form the basis of stratification might differ between patients and institutions. However, in CT imaging performed on suspicion of aortic pathology, first pass imaging (arterial phase, images are obtained during the first pass of the contrast material in the aorta and its branches) is routinely used, and delayed images are recommended only after stent-graft repair of aneurysms to detect endo-leaks.112 Flow patterns in the false lumen in AAD are highly variable, often with slow flow rates.131, 132 Under such circumstances, the contrast may not have time to distribute evenly throughout the false lumen before acquisition of serial images through the aorta. Lack of contrast in the false lumen may falsely be interpreted as thrombus. Clough et al found that first pass techniques to assess false lumen thrombosis in AAD consistently overestimate the apparent thrombus volume by five to six times.133 They compared first pass CT and MRI with delayed phase MRI with a blood pool agent in 12 patients with medically treated ABAD and evidence of false lumen thrombosis on previous CT imaging. The difference in thrombus volume between first pass imaging and delayed MRI imaging also correlated significantly with the mean velocity of flow in the false lumen – lower flow was related to a greater difference. In our material, the patients with thrombosis (partial or complete) underwent more imaging studies, and the partial thrombosis group in particular had more CT investigations. Detection of thrombi in the false lumen on (trans-
esophageal) echocardiography is difficult. As such, it could be argued that a certain number of patients that were classified as having completely patent false lumen, in fact might have had some degree of thrombosis.

A significant number of AAAD patients have aortic valve replacement (30% in our material). This necessitates life-long use of anticoagulants in the case of mechanical valve implantation, which might influence the degree of false lumen thrombosis and even dissolve thrombi that are present initially. This association might in part account for differences in the impact of false lumen thrombosis in AAAD and ABAD. The association between anticoagulant therapy and false lumen thrombosis after repair of DeBakey type I aortic dissection has been reported by Song et al.\textsuperscript{134} Although retrospective in nature and with wide indications for anticoagulant therapy, their study indicates that anticoagulants might promote positive aortic remodeling postoperatively. Patients with early anticoagulation after surgery had lower proportion of partial false lumen thrombosis and, interestingly, significantly lower segmental aortic growth rates compared to patients with no anticoagulation. Moreover, no anticoagulation was identified as an independent predictor for poor survival in their Cox proportional hazard analysis with an odds ratio of 12.8 (95% CI, 1.8-29.9, P=0.016). More recently, von Kodolitsch et al reported that long-term warfarin therapy was not associated with aortic growth, late mortality or late aortic events in their study of 243 postsurgical AAAD patients, out of whom 88 (36%) were on long-term anticoagulation therapy.\textsuperscript{135}

Another important aspect unique to our study is that patients were stratified according to their false lumen status at presentation (i.e. before surgery). Resection of the entry tear and restoration of true lumen flow will alter flow in the false lumen and might promote thrombosis. Thus, the classification may be altered postoperatively. However, 85% of the patients had a dissection that extended distal to the ascending aorta, and a distal false lumen remains patent in as many as 79% of patients after initial AAAD repair.\textsuperscript{61-64, 66, 136}

In conclusion, the significance of a partial false lumen thrombosis in AAD remains to be settled. Registry data with uniform imaging protocols can hopefully help with clarification on the matter in the future. New imaging techniques, for example, based on flow-dynamics\textsuperscript{137, 138} and/or bioimaging\textsuperscript{139, 140} can hopefully improve our ability to predict an ominous outcome in patients with AAD.
10.3 Results paper II

The intention of this study was to examine whether there is evidence in the literature to support the notion that the distal anastomosis in ascending aortic replacement should be performed in an open fashion in AAAD surgery.

After an updated systematic literature review using the PubMed database, nine studies matched the inclusion criteria (more than 20 patients, performed after 1980, follow-up period of more than 1 year and allow a two-group comparison between an open distal and clamped anastomosis). 76, 141-148 No randomized trials exist. All studies were either retrospective patient series or case-control studies with historical controls. No study had an observational period exceeding 5 years. A lower 60-day mortality was observed in the open distal anastomosis group in one study. Overall, there were no short or long-term survival benefit to an open distal anastomosis.

10.4 Discussion paper II

Apart from the limited number of dissections that are confined to the ascending aorta alone (DeBakey type II), most type A dissections affect the aorta from the ascending through the arch and well into the descending portion. As such, the most prevalent distal landing zone for the implanted graft, namely the upper part the ascending aorta, does not mark a logic natural site to truncate the reconstruction. However, reconstruction of the intra-pericardial portion of the aorta accomplishes the critical objectives of AAAD surgery – elimination of cardiac tamponade, myocardial ischemia through coronary artery involvement and acute heart failure through involvement of the aortic valve with aortic regurgitation. At the same time, the limited invasiveness of such a procedure might be desirable in acutely ill patients. From an anatomical point of view, a more extensive approach with reconstruction of the aortic arch (TAR) and even the proximal descending aorta (FET) is logical. Such a large reconstruction adds time to the procedure and inclusion of the neck vessels and placing the distal anastomosis in the descending aorta, puts increasing demand on brain protection and meticulous surgical technique to avoid neurological complications and bleeding from multiple anastomoses in friable tissue. Arch replacement is only possible with an open anastomosis technique under circulatory arrest, but an open anastomosis has theoretical benefits even in simple ascending aortic replacement: It allows for a diagnostic inspection of the arch, branch vessels and proximal descending aorta. If an intimal tear is identified in the arch, the operative strategy can be modified to an arch replacement. In addition, construction of the distal
anastomosis without a clamp crowding the site of the anastomosis, should make for a more secure and precise anastomosis with less risk of uncontrollable bleeding from the friable aortic tissue.

The challenges concerning best-evidence treatment in aortic dissection are illustrated in the case of open vs. closed distal anastomosis in AAAD surgery. The issue should be highly appropriate for comparative studies; still no randomized controlled trial has been done. The nine studies identified in our literature search all had obvious shortcomings. They are all retrospective either patient series or case-control studies with historical controls. They were single-center studies with relatively few patients. The observation periods were short. The control groups were overall the eldest and open anastomoses were mostly done in the contemporary era. As there was no overall survival benefit to an open distal anastomosis, this fact may actually put forward the hypothesis that an open anastomosis is inferior but masked by general improvements of treatment in the recent era.

Because of the low number of patients in the included studies, the lack of statistical superiority from an open distal technique could be due to a statistical type II error. Furthermore, as the follow-up period was limited, a potential long-term benefit due to favorable aortic remodeling after an open distal anastomosis may not be evident in the present studies.

In a study published after our literature search, Malvindi et al reported on their experience with open and closed distal anastomosis in AAAD repair. They reviewed 204 patients who underwent AAAD repair between 2000 and 2013. They also conducted a separate sub-group analysis of 100 patients with a De Bakey type I dissection and a proximal intimal tear, out of which 39 underwent an open and 61 a closed distal anastomosis. Their results were in concordance with previous findings as mortality, morbidity and survival rates were similar between the two groups of patients. On follow-up imaging, patients who underwent an open distal anastomosis showed a significant higher rate of complete thrombosis of the false lumen at the level of the thoracic descending aorta (50% vs. 27%, P=0.036). However, this did not translate into a lower rate of distal aortic reoperation during follow-up.

Recently, the Nordic Consortium for Acute Type A Aortic Dissection (NORCAAD) reported on long-term survival and predictors of mortality in 1159 patients operated between 2005 and
In their multivariable analysis of mid-term survival in 947 patients, who survived the index hospitalization, a strategy of open distal anastomosis (compared with distal anastomosis with the aorta cross-clamped) was independently associated with better outcomes (HR, 0.54, 95% CI, 0.34–0.85, P=0.008). As pointed out by the authors, there are several limitations to the study as it is based on retrospectively collected data and the findings might reflect selection bias, where a closed distal anastomosis may be preferred in a particularly old or severely ill subset of patients.

Based on the existing documentation, there is insufficient evidence to state that the distal anastomosis should be done in an open or closed fashion. Based on survival data, a closed anastomosis is a safe alternative in selected patients and should remain in the armamentarium as a safe and quick option, especially in elderly or frail patients.

10.5 Results paper III
The aim was to study trends in presentation, management and outcomes of patients with AAD during 17 years of registration in the IRAD.

Data from 4428 IRAD patients (2952 with AAAD and 1476 with ABAD) were analyzed. Based on enrollment date, patients were divided into 6 equal groups. Overall, an increase was seen in the proportion of patients referred from a primary site to an IRAD center for AAAD (from 62% to 71%), but this trend was not significant for patients with ABAD (from 62% to 68%). The frequency in the use of CT as the initial diagnostic imaging increased over time in AAAD patients, from 46% to 73% over the 17-year period. The frequency did not change in ABAD patients.

Surgical management for AAAD increased from 79% to 90%. Over time, the in-hospital mortality rate of patients presenting with AAAD decreased significantly from 31% to 22%, primarily due to a decline the surgical mortality rate from 25% to 18%. The in-hospital mortality rate among those managed medically remained high (57%) and did not change. The overall in-hospital mortality rate of patients presenting with ABAD was 10.7% and did not change over time. Most patients with ABAD were treated medically (63% of the entire cohort). This percentage decreased (75% to 57%) as endovascular management increased from 7% to 31%. Traditional surgical management of ABAD also decreased (17% to 8%),
although there was an increase in hybrid procedures that used surgical debranching techniques to facilitate endovascular intervention (0% to 5%).

Medications prescribed at discharge changed significantly over time as the use of beta-blockers, diuretics and statins increased for AAAD patients and the use of angiotensin receptor blockers, beta-blockers and statins increased for ABAD patients.

10.6 Discussion paper III
Several interesting trends in management and outcome appeared from the analysis. Patients with AAAD were increasingly transferred from outside institutions to IRAD tertiary care centers, and in the latest period, more than two thirds of the AAAD cohort in IRAD were initially admitted to another hospital. The exact reason for this increase is unknown. There can be an increased awareness about need for imminent surgical management, and earlier diagnosis due to more CT as the preferred initial imaging modality in suspected AAAD. The findings on diagnostic testing requires further attention. In historical materials, 85% of patients had a chest x-ray with abnormalities suggestive of AAD (abnormal aortic contour, wide superior mediastinum, or separation of an aortic wall intimal calcification from the outer margin of the aorta). In our material, the reported incidence of normal chest x-rays increased over time, to 29% and 35% in the latest period for AAAD and ABAD, respectively. Again, the reason is unclear. In the modern era with CT as the preferred method of diagnosis, there is probably less emphasis on conventional chest x-ray in the workup. Still, many patients will present without symptoms that immediately raise suspicion of AAD. These will not necessarily undergo CT or echocardiography, and recognition of subtle signs on x-ray can be of great importance in this subset of patients.

Advances and developments in the treatment of AAD are clearly reflected in the IRAD material. Firstly, the proportion of AAAD patients who underwent surgery increased significantly over time with an equivalent decline in medical management. It is likely that more rapid diagnosis and improved per- and postoperative care all contribute to this observation. Patients previously deemed inoperable, or where one considered intervention futile, e.g. due to advanced age or neurologic injury, are to a higher extent offered surgery in the present era. At the same time, for AAAD patients, both the overall mortality and surgical mortality declined. The same factors that contribute to increased incidence of surgical management, also contribute to lower surgical mortality – improved safety in aortic
replacement procedures and advances in cerebral protective strategies probably play a major role. However, the observed reduction in surgical mortality must be interpreted with caution without adjusted analyses. A higher percentage of patients were transferred in the latest period, and there may be selection bias as these might have better prognosis by default because they reach a tertiary center alive. Furthermore, demographics slightly changed – there was a significant trend towards less comorbidities with fewer patients having manifest atherosclerosis or previous cardiac surgery over time, both of which may contribute to lower risk of mortality.

The changes in management of ABAD are also apparent. In later time, just above 50% of patients were managed exclusively medically, which is the recommended treatment in uncomplicated ABAD. A marked increase in endovascular management was observed - in the current era in the IRAD registry, nearly one third of patients with an ABAD receive endovascular management. Surgical management (open repair) declined in use over time. The overall mortality as well as mortality for patients that were managed with medical or endovascular treatment did not change, but surgical mortality declined. The data in the present analysis does not allow for a detailed analysis on the cause of these patterns, but other studies show similar results and offer some explanation. Data from Medicare from 2000 to 2010 showed an overall increase in invasive treatment for ABAD, due to a marked increase in the use of TEVAR and despite a reduction in open surgical repair.\(^{157}\) At the same time, both endovascular and open repairs were done with lower mortality risk in patients with more comorbidities. Both the present study and the Medicare data referred to by Jones et al, coincides with the widespread adoption of endovascular repair of pathology in the thoracic aorta (TEVAR), first reported by Dake et al in 1994.\(^{158}\) The trend towards a higher total volume of interventions, despite less open surgery and due to more endovascular treatment, is also found in other diseases of the descending thoracic aorta.\(^{159}\) These data suggest at least two explanations. First, improved selection of patients for intervention, and second, a shift towards a lower threshold for operative intervention in ABAD. Traditionally, open surgical repair have been the standard of treatment for complicated ABAD, i.e. ABAD with malperfusion, intractable pain, uncontrollable hypertension, (impending) rupture, or rapid growth.\(^{160}\) In the present era, TEVAR adds a treatment option for patients that for different reasons were considered unsuitable for open repair. In our data, endovascular mortality did not change over time. The present data is insufficient to give a plausible explanation, but there
is reason to believe that as experience with TEVAR has increased, patients with more comorbidities and in direr clinical conditions, are being treated.

Medications prescribed at discharge also changed during the study. Use of beta-blockers and statins increased for both AAAD and ABAD patients and angiotensin II receptor blockers for ABAD patients. Guidelines for the management of aortic diseases have been published during the later years.\textsuperscript{13, 112} Awareness of these and adherence to the blood pressure limits suggested, may have caused physicians to pursue antihypertensive treatment more diligently. Small, observational studies have suggested that statins may inhibit the expansion of aneurysms.\textsuperscript{161, 162} This, combined with the fact that many AAD patients have atherosclerotic disease and there is more focus in secondary preventive measures, may have influenced the observed increase in statin use.

\textbf{10.7 Results paper IV}

The intention of this study was to compare outcomes of limited repairs (ascending and hemiarch replacement) versus complete arch surgery in patients with AAAD.

A total of 1241 patients were included in the analysis. Of these, 907 (73\%) underwent ascending aortic or hemiarch replacement (Group A) and 334 (27\%) had extended arch replacement (Group B). The mean age ± SD was 60.3 ± 14.0 years and 32.6\% were female. There were relatively more women in Group A than in Group B (35.6\% versus 24.3\%, P<0.001). More patients presented with syncope in Group A, whereas pulse deficits were more frequent in Group B. Arch vessel involvement occurred in 57.4\% of patients in Group B versus 41.9\% in group A (P<0.001). In addition, in Group B the maximal dimension of the descending aorta was marginally larger, and the dissections were more extensive compared to group A.

The frequency of concomitant coronary artery bypass grafting (CABG) was higher in Group A, and aortic valve procedures (although not aortic valve replacement) were more dominant in Group B. Furthermore, biological valves were used more frequently in group B and mechanical valves in group A. Elephant trunks were constructed in 9.6\% of patients in group B. Circulatory arrest times and total cardiopulmonary bypass times were longer in Group B. Cannulation strategy differed slightly between groups, as the axillary artery was more frequently selected as arterial cannulation site in Group B. This was also reflected in cerebral
perfusion strategy, where a higher proportion of patients in Group B had cerebral perfusion strategy during systemic circulatory arrest and more often than in Group A, the cerebral perfusion was antegrade.

The in-hospital mortality was 14.2% and similar between groups (Group A, 13.1% vs. Group B, 17.1%, \( P=0.077 \)). In a propensity-adjusted multivariable logistic regression model, coma at presentation (odds ratio [OR], 3.16, 95% CI, 1.60-6.25, \( P=0.001 \)), hypotension, shock or tamponade at presentation (OR, 2.03, 95% CI, 1.11-3.73, \( P=0.022 \)) and any pulse deficit (OR, 1.92, 95% CI, 1.04-3.54, \( P=0.038 \)) were significantly associated with in-hospital mortality.

Follow-up data was only available for about half of the patients who survived their index hospitalization. Kaplan-Meier curves on post-admission survival and post-discharge freedom of major adverse events showed no difference between groups. In a propensity-adjusted Cox proportional hazards model for 5-year post-discharge survival, age \( \geq 70 \) years (HR, 3.62, 95% CI, 1.22-10.80, \( P=0.021 \)), any pulse deficit (HR, 4.26, 95% CI, 1.30-13.40, \( P=0.017 \)), intimal tear located in the arch (HR, 8.41, 95% CI, 2.21-31.94, \( P=0.002 \)) and post-operative coma (HR, 11.03, 95% CI, 1.15-105.75, \( P=0.037 \)) were independently associated with poor long-term outcome.

10.8 Discussion paper IV

In the present study, short and mid-term mortality rates as well as freedom from aortic-related events were similar regardless the extent of aortic replacement.

Since the seminal paper from the Stanford group in 1970\(^{25} \), replacement of the ascending aorta with graft interposition has been the mainstay of surgical treatment in AAAD. However, the extent of the operation proximal and distal to the ascending aorta became, and still is, controversial. Initially, efforts to address the aortic arch in AAAD surgery was limited by the fact that, without adequate cerebral protection, arch procedures had excessive mortality.\(^{163, 164} \)

In the years following the application of hypothermic circulatory arrest by Grieppe et al in 1975\(^{7} \), several groups reported on their results with replacement of the transverse arch in AAAD.\(^{141, 165, 166} \)

In 2000, Kazui et al reported on their experience with TAR for AAAD in 70 patients.\(^{167} \) Although this was a highly selected group of patients (and all were operated by the first
author), a 16% early mortality demonstrated that TAR for AAAD could be justified in selected patients. Certainly, TAR adds complexity to an already challenging, high-risk procedure. The question is whether the increased risk of short-term complications is outweighed by the potential long-term benefits. As stated by Crawford 25 years ago, a randomized trial to clarify the indications for TAR in AAAD is not likely to be conducted. Some previous studies have used propensity score analyses in an attempt to eliminate treatment-selection bias, and these provide some insight in the long-term advantages and disadvantages of TAR in AAAD. Kim et al reported on 188 consecutive patients with DeBakey type I AAD, out of whom 144 underwent hemiarch and 44 total arch replacement. The early mortality was similar (13.4% and 9.7%, respectively), but there were more cases of low cardiac output syndrome and new neurological deficits in the TAR group. Their propensity-score adjusted model showed that TAR patients had poorer long-term survival (HR, 2.38, 95% CI, 1.22-4.67) and neurologic outcomes (HR, 3.25, 95% CI, 1.31-8.04) than those who underwent hemiarch replacement. The extent of initial surgery did not affect the rate of re-operation. Similarly, De Eusanio et al evaluated outcomes of 240 patients, 53 in the TAR group and 187 in the “conservative arch management” group. Hospital mortality (24.1% and 22.6%, respectively) and major complications were similar in the groups. Their propensity-score Cox regression analysis showed no relationship between type of arch management and follow-up survival or the need for re-intervention. Most investigations into the merit of including the arch in AAAD surgery are limited due by relatively few patients, and as such prone to type II statistical error as they might be underpowered to detect a real long-term benefit from aggressive aortic replacement. Yan et al recently performed a meta-analysis, in which nine studies with a total of 1872 patients with AAAD were included. They compared proximal aortic repair (ascending aortic with or without hemiarch replacement) to extensive aortic repair (ascending and total arch replacement, with or without elephant trunk placement). Proximal repair was associated with a lower early mortality risk (RR, 0.69, 95% CI, 0.54-0.90), but higher incidence of postoperative aortic events (RR, 3.14, 95% CI, 1.74-5.67). The long-term mortality was not influenced by initial surgical strategy (HR, 1.02, 95% CI, 0.51-2.06).

The overall in-hospital mortality in our material was 14.2%, within the range reported by others. Determinants of in-hospital mortality were related to preoperative complications and can be considered markers of severity of the AAD. Specifically, malperfusion either
manifested as coma or as pulse deficits and signs of hemodynamic compromise manifested as hypotension, shock or tamponade, independently predicted in-hospital mortality in the propensity-adjusted logistic regression analysis. This is consistent with previous findings, as cerebral malperfusion with fixed deficits or coma carries poor postoperative prognosis, particularly if surgery is delayed.\textsuperscript{171-173} Extended arch replacement did not influence early outcomes in this model. It seems that early outcome largely is determined by the patients presenting symptoms (i.e. the severity of the dissection and its complications), and to a lesser extent the surgical strategy that is chosen.

The propensity-adjusted Cox proportional hazards model for 5-year post-discharge survival in the supplemental material warrants special attention. In this model, patients that were discharged alive after AAAD repair were included. Independent propensity-adjusted predictors of poor survival were age \( \geq 70 \) years (HR, 3.62, 95% CI, 1.22-10.80), pulse deficit on presentation (HR, 4.26, 95% CI, 1.30-13.99), intimal tear located in the aortic arch (HR, 8.41, 95% CI, 2.21-31.93), and post-operative coma (HR, 11.03, 95% CI, 1.15-105.75). The fact that age and post-operative coma emerged as predictors of a poor mid-term outcome is not surprising. Pulse deficits may be regarded a marker of severity in AAD, and as such associated with poor outcome, even after successful initial surgery. Of importance, in this model, an extended arch replacement seemed protective against follow-up mortality, but did not reach statistical significance (HR, 0.17, 95% CI, 0.03-1.06, \( P=0.058 \)). With longer follow-up and more events, this may have changed. The crude Kaplan-Meier curves must be seen in conjunction with this model. However, it is crucial to point out again that this model included only patients that survived to discharge and does not take into account any increased in-hospital risk of mortality in extended arch replacement.

Of importance, and essential to evaluate the present study, 5-year follow-up does not give the complete overview of a potential prophylactic benefit of TAR, as aneurysms in the downstream aorta can develop slowly. In various series of reoperation after AAAD repair, the mean time from initial surgery to re-intervention has been approximately 5 years.\textsuperscript{64, 76, 174, 175}

Follow-up data were available only for half of the patients included in the study. This is partly because the majority if patients were operated in the last few years. Either way, it is a serious drawback to the study and conclusions must take the lack of follow-up into account.
In high-volume centers and in young, highly selected patients, complex procedures such as TAR with FET for AAAD, even when the entry tear is located in the arch, can be safely accomplished with excellent results. However, one must bear in mind that most patients with AAAD are not carefully selected and they do not necessarily present themselves at a high volume center. An inverse relationship between provider volume and outcome has been described for various conditions, and it also applies to AAAD. On average, patients that are treated at low-volume centers (less than 3 annual cases of AAD surgery) have approximately double the risk-adjusted mortality of patients treated at the highest volume institutions (more than 13 annual cases of AAD surgery).

In conclusion, based on the present study and the data available from other studies, it does not seem justified to routinely add additional complexity to an already challenging procedure (TAR with or without FET), with the intent to reduce the risk of future complications. However, a strategy of individual and aortic-specific assessment as a basis for extended procedures still remains crucial in decision-making processes to select the optimal surgical strategy for patients with AAAD. In the current hierarchy of evidence-based medicine and in the void of a proper RCT on the matter, identification of patient subgroups that will benefit from extensive aortic replacement requires high-quality registry data with diligent and sufficiently long follow-up. Future data from both IRAD, GERAADA, NORCAAD and other aortic dissection registries will hopefully enlighten us on the patient selection and long-term benefit of TAR in AAD.
11. Main conclusions

Paper I

- Patients with an AAAD who survive to discharge have a favorable prognosis.
- Preoperative partial thrombosis of the false lumen in surgically treated AAAD patients was not associated with aortic enlargement, intervention or death in the follow-up period.
- Factors that influence aortic dilation and rupture following an AAD are still incompletely understood.

Paper II

- Based on the literature review, the data available to support either an open or a closed distal anastomosis in AAAD surgery is insufficient.
- From the existing evidence, the surgeon can for him or herself decide whether to clamp the aorta during construction of the distal anastomosis.
- Both techniques should remain as a part of the armamentarium in AAAD surgery for use in different circumstances.

Paper III

- Presenting symptoms and physical findings of AAD have not changed over time in the IRAD registry.
- Use of CT as the first imaging modality for the diagnosis of AAAD has increased.
- More patients with AAD are managed with interventional procedures over time; surgery for AAAD and endovascular therapy for ABAD.
- A significant decrease in in-hospital mortality was seen for patients with type A but not type B AAD.

Paper IV

- In-hospital mortality was similar in AAAD patients whether they underwent ascending/hemiarch replacement or extended arch replacement.
- The patient’s preoperative condition determines in-hospital mortality.
- It does not seem justified to routinely perform TAR in AAAD with the intent to reduce the risk of future complications.
- The best surgical strategy for patients with AAAD should be based on individual and aortic-specific assessments.
12. References


(51) Fann JI, Smith JA, Miller DC et al. Surgical management of aortic dissection during a 30-year period. Circulation 1995 November 1;92(9 Suppl):II113-II121.


(113) Stables RH. Observational research in the evidence based environment: eclipsed by the randomised controlled trial? Heart 2002 February;87(2):101-2.


13. Paper I-IV
Paper I


Extent of Preoperative False Lumen Thrombosis Does Not Influence Long-Term Survival in Patients With Acute Type A Aortic Dissection.

*J Am Heart Assoc* 2013 July 1;2(4):e000112.
Paper II

Myrmel T, Larsen M, Bartnes K.

Does an Open Distal Anastomosis Confer Prognostic Benefit in Acute Dissection Surgery?

Paper III


Presentation, Diagnosis, and Outcomes of Acute Aortic Dissection: 17-Year Trends From the International Registry of Acute Aortic Dissection.

Paper IV


Extended versus limited arch replacement in acute Type A aortic dissection.

14. Appendices
Appendix 1

Myrmel T, Larsen M, Bartnes K.

The International Registry of Acute Aortic Dissections (IRAD) – experiences from the first 20 years.

Appendix 2

Supplemental material paper IV
Supplemental material to manuscript EJCTS – 2017 – 600223

Supplemental figure 1:

The figure shows how many of the patients in the complete IRAD database that have had an “Interventional Data Form” submitted to the database at the time of analysis. These 1241 patients are included in the present paper.
Statistical calculations done for revised manuscript

Variables Introduced to In-Hospital Mortality Model (Binary Logistic Regression):

(From univariate analysis, variables with p<0.20 selected for introduction to the model after evaluation for clinical relevance.)

Gender
Age
History of known aortic aneurism
History of catheterization or PTCI
Prior cardiac surgery
Chest pain
Radiating pain
Syncope
Pulse deficit
Coma or altered consciousness
Stroke or TIA
Hypotension/Shock/Tamponade

Forced into the model:

Partial/Complete Arch Repair (Simple Ascending or Hemi-Arch Repair as Reference)
Conditional Probability of Partial/Complete Arch Repair (Propensity)
Gender (female)

Final Propensity-Adjusted Model for In-Hospital Death:

<table>
<thead>
<tr>
<th></th>
<th>Beta Coef</th>
<th>P-value</th>
<th>Odds Ratio</th>
<th>95% C.I.for Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial/Complete Arch Procedure</td>
<td>0.146</td>
<td>0.665</td>
<td>1.157</td>
<td>0.598 - 2.242</td>
</tr>
<tr>
<td>Partial/Complete Arch Probability (Propensity)</td>
<td>1.434</td>
<td>0.245</td>
<td>4.194</td>
<td>0.375 - 46.916</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>0.087</td>
<td>0.796</td>
<td>1.091</td>
<td>0.565 - 2.105</td>
</tr>
<tr>
<td>Age &gt; 65 Years</td>
<td>0.793</td>
<td>0.011</td>
<td>2.210</td>
<td>1.203 - 4.060</td>
</tr>
<tr>
<td>Pulse Deficit</td>
<td>0.655</td>
<td>0.037</td>
<td>1.926</td>
<td>1.039 - 3.568</td>
</tr>
<tr>
<td>Presenting with Coma or Altered Consciousness</td>
<td>1.151</td>
<td>0.001</td>
<td>3.162</td>
<td>1.591 - 6.282</td>
</tr>
<tr>
<td>Hypotension/Shock/Tamponade</td>
<td>0.701</td>
<td>0.024</td>
<td>2.016</td>
<td>1.098 - 3.704</td>
</tr>
<tr>
<td>Constant</td>
<td>-3.340</td>
<td>&lt;0.001</td>
<td>0.035</td>
<td></td>
</tr>
</tbody>
</table>

C=0.730; Hosmer-Lemeshow p=0.300
Variables Introduced to Propensity Model for Partial or Complete Arch Procedure Performed:
(From univariate analysis, variables with p<0.20 selected for introduction to the model after evaluation for clinical relevance.)

Gender female
Age at initial admission (years)
History of iatrogenic dissection
History of Hypertension
History of diabetes
History of prior aortic dissection
History of COPD
History of chronic renal insufficiency
History of PTCI
Syncope
Pulse deficit
Arch vessel involvement
Distal extent of dissection arch
Distal extent of dissection left subclavian

Final Propensity Model:

|                                     | Beta Coeff. | P-value | Odds Ratio | 95% C.I. for Odds Ratio |
|                                     |            |        |            | Lower | Upper   |
| Gender (female)                     | -0.326     | 0.080  | 0.722      | 0.501 | 1.039   |
| Surgery Performed 2001-2006         | 1.094      | <0.001 | 2.987      | 1.998 | 4.466   |
| Arch Vessel Involvement             | 0.600      | <0.001 | 1.822      | 1.311 | 2.530   |
| Distal Extent of Dissection Left    | 0.760      | 0.051  | 2.139      | 0.996 | 4.595   |
| Subclavian                          |            |        |            |       |         |
| Constant                            | -1.396     | <0.001 | 0.248      |       |         |

C=0.651; Hosmer-Lemeshow p=0.904
Variables Introduced to Propensity-Adjusted Cox Proportional Hazards Model for 5-Year Post-Discharge Survival (From univariate analysis, variables with p<0.20 selected for introduction to the model after evaluation for clinical relevance.)

History of Aortic Valve Disease
History of Iatrogenic dissection
History of Surgery for Aortic Aneurism or Dissection
Renal Failure at Admission
Beta-Blocker Prescribed at Discharge
Age ≥ 70 Years
Pre-Operative Spinal Cord Ischemia
Post-Operative Coma
Limb Ischemia
Presenting Hypotensive
Presenting Normotensive
Evidence of Intramural Hematoma on Imaging Test
Most Proximal Extent of Dissection Arch
Most Proximal Extent of Dissection Left Subclavian Artery
Intimal Tear in Arch
Peri-aortic Hematoma
Current Smoker
Pulse Deficit
Diastolic BP at Discharge

Forced into the Model:
Partial/Complete Arch Procedure
Partial/Complete Arch Probability (Propensity)

Final Propensity-Adjusted Cox Proportional Hazards Model for 5-Year Post-Discharge Survival:

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>P-value</th>
<th>Hazard Ratio</th>
<th>95.0% CI for Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial/Complete Arch Procedure</td>
<td>- 1.760</td>
<td>0.058</td>
<td>0.172</td>
<td>0.028 - 1.063</td>
</tr>
<tr>
<td>Partial/Complete Arch Probability (Propensity)</td>
<td>- 0.236</td>
<td>0.919</td>
<td>0.790</td>
<td>0.008 - 75.123</td>
</tr>
<tr>
<td>Age ≥ 70 years</td>
<td>1.287</td>
<td>0.021</td>
<td>3.623</td>
<td>1.216 - 10.796</td>
</tr>
<tr>
<td>Pulse Deficit</td>
<td>1.449</td>
<td>0.017</td>
<td>4.259</td>
<td>1.296 - 13.992</td>
</tr>
<tr>
<td>Intimal Tear in Arch</td>
<td>2.129</td>
<td>0.002</td>
<td>8.405</td>
<td>2.212 - 31.938</td>
</tr>
<tr>
<td>Post-operative Coma</td>
<td>2.400</td>
<td>0.037</td>
<td>11.028</td>
<td>1.150 - 105.754</td>
</tr>
</tbody>
</table>
Appendix 3

IRAD registration form index hospitalization
**PATIENT IDENTIFICATION**

*DISSECTION TYPE:*
- Type A
- Type B

*MANAGEMENT:*
- Medical
- Surgical
- Endovascular Procedure
- Hybrid
- Surgical & Endovascular

**PATIENT IDENTIFIED BY:**
- Y
- N
- N/A

- ○ ○ ○ Symptom onset
- ○ ○ ○ Surgery
- ○ ○ ○ Post Mortem
- ○ ○ ○ Image

*Required fields*

**DATE OF SYMPTOM ONSET:**

Date initial hospital arrival:
(Referring or tertiary hospital)

*Date of symptom onset:*

Date dissection first suspected:

Date diagnosis confirmed:

**DATA COLLECTION:**

- ○ Prospective
- ○ Retrospective
- ○ Both

**MANAGEMENT:**

- Medical
- Surgical
- Endovascular Procedure
- Hybrid
- Surgical & Endovascular

**DEMOGRAPHICS**

*Date of Birth:*

*Gender:*  
- ○ Male
- ○ Female

*Race:*  
- ○ N/A
- ○ White
- ○ Black
- ○ Asian
- ○ Hispanic
- ○ Other

**Weight:**  
- ○ pounds
- ○ kilograms

**Height:**  
- ○ inches
- ○ centimeters
# 2 - SYMPTOMS AND HISTORY

## A: PRESENTING SYMPTOMS

- Chest Pain: 
  - Anterior
  - Posterior
- Pain severity (choose one):
  - N/A
  - Mild
  - Severe
  - Worst ever
- Pain in the head or neck
- Back Pain
- Abdominal Pain
- Radiating
- Migrating
- Leg Pain
- Quality of Pain:
  - Tearing/Ripping
  - Sharp
  - Pressure
  - Burning
- Abrupt onset of pain
- *Syncope
- Febrile
- Abnormal CXR w/o associated pain

## C: SIGNS OF AORTIC DISSECTION

**Presenting Hemodynamics (Choose one only)**
- N/A
- Hypertensive (BP>=150/90 mmHg)
- Normotensive (SBP 100-149 mmHg)
- Hypotensive (SBP <100 mmHg)
- Shock (SBP<=80 mmHg)
- Cardiac Tamponade

**First Blood Pressure:**

- **Systolic**
- **Diastolic**

  - N/A
  - YES
  - NO

- Murmur of aortic insufficiency:
  - (if yes...) Grade: 1, 2, 3, 4

- **Pulse deficits**
  - N/A
  - YES
  - NO

  - Were deficits checked?
    - (if yes...)
      - Right carotid
      - Left carotid
      - Right brachial
      - Left brachial
      - Right femoral
      - Left femoral

- Pericardial friction rub
- Ischemic peripheral neuropathy
- Ischemic spinal cord damage
- Cerebral vascular accident/Stroke
- Ischemic lower extremity
- Coma/ altered consciousness
- Congestive heart failure

## B: HEALTH HISTORY

- *Was health history information available?*
  - N/A
  - YES
  - NO

- Hypertension
- Diabetes
- Marfan Syndrome
- Ehlers-Danlos Syndrome
- Turner Syndrome
- Loeys-Dietz Syndrome
- Atherosclerosis
- Known aortic aneurysm
- Prior aortic dissection
- Mitral Valve Disease
- Bicuspid Aortic Valve
- Aortic Valve Disease
- (aortic stenosis/aortic insufficiency)
- Tricuspid Valve Disease
- Peripartum State
- Other aortic disease
- Cocaine Abuse
- Smoking
  - N/A
  - Current
  - Former smoker
  - Non-smoker
- Family history of aortic disease
- Peripheral arterial disease
- Chronic Obstructive Pulmonary Disease
- Chronic Renal Insufficiency
- Iatrogenic Aortic Dissection

**Specify cause:**
- N/A
- Cath/PTCA
- Cardiac Surgery
- Other

- Prior Cardiac Surgery/Procedures
  - Cath/angiography
  - PTCA
  - CABG
  - Aortic Aneurysm/Dissection
  - AVR
  - MVR
  - Other cardiac surgery

Please specify:

## D: CXR FINDINGS

- Chest X-ray done?
  - N/A
  - YES
  - NO

- Site of study:
  - N/A
  - Tertiary hospital
  - Referring hospital

- Normal
- Widening mediastinum
- Abnormal aortic contour
- Abnormal cardiac contour
- Displacement/calciﬁcation of aorta
- Pleural effusion (> minor)

## E: ECG FINDINGS

- ECG done?
  - N/A
  - YES
  - NO

- Site of study:
  - N/A
  - Tertiary hospital
  - Referring hospital

- Normal
- Ischemia
- Infarction, new Q’s or ST elevation
- Infarction, old Q’s
- Non-speciﬁc ST-T changes
- Left ventricular hypertrophy
- Low voltage

---

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08/15/2013
#3 - MEDICAL THERAPY

**MEDICAL THERAPY**

<table>
<thead>
<tr>
<th></th>
<th>INITIAL (AT YOUR CENTER)</th>
<th>CHRONIC AT DISCHARGE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>ACE Inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-Blocker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium Channel Blocker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitroprusside</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Vasodilator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specify:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**AT TIME OF DISCHARGE:**

<table>
<thead>
<tr>
<th></th>
<th>SYSTOLIC</th>
<th>DIASTOLIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td></td>
<td>/</td>
</tr>
<tr>
<td>Heart Rate</td>
<td></td>
<td>beats/min.</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>TEE</th>
<th>CT or MRI</th>
<th>Imaging Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Was test done?</strong></td>
<td>N/A</td>
<td>Gated study?</td>
</tr>
<tr>
<td><strong>Order of study</strong></td>
<td>1st</td>
<td>2nd</td>
</tr>
<tr>
<td><strong>Site of study</strong></td>
<td>Tertiary</td>
<td>Referring</td>
</tr>
<tr>
<td><strong>Date of study</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Modality used:</strong></td>
<td>Gated CT</td>
<td>Ungated CT</td>
</tr>
<tr>
<td><strong>(Order preferred: CT&gt;MRI&gt;TEE; when available)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maximum Diameter:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Includes TTE?</strong></td>
<td>N/A</td>
<td>Gated study?</td>
</tr>
<tr>
<td><strong>Site of most proximal extension of dissection or hematoma. One selection from each column only.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site of most distal extension of dissection or hematoma. One selection from each column only.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>False lumen patency. One selection from each column only.</strong></td>
<td>Not available</td>
<td>Patent</td>
</tr>
<tr>
<td><strong>Sites of intimal tear:</strong></td>
<td>N/A</td>
<td>Root</td>
</tr>
<tr>
<td><strong>Abdominal vessel involvement</strong></td>
<td>Right Renal</td>
<td>Left Renal</td>
</tr>
<tr>
<td><strong>Arch vessel involvement</strong></td>
<td>L. subclavian</td>
<td>L. common carotid</td>
</tr>
<tr>
<td><strong>Distal communication</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pericardial effusion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Periaortic hematoma</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Right coronary involvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Left coronary involvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aortic regurgitation</strong></td>
<td>Mild</td>
<td>&gt;Mild</td>
</tr>
</tbody>
</table>

*Includes TTE? N/A YES NO Gated study? N/A YES NO*
### Surgical

**Date and time of surgery:**

<table>
<thead>
<tr>
<th>Month</th>
<th>Day</th>
<th>Year</th>
<th>Hour</th>
<th>Minute</th>
</tr>
</thead>
</table>

Was surgery delayed beyond date of presentation?
- Yes
- No

Reason:
- Type A
  - Intramural hematoma - ascending
- Type B
  - Recurrent pain
  - Refractory pain
  - Limb ischemia
  - Visceral ischemia
  - Extension of dissection
  - Refractory hypertension
  - Aortic rupture
  - Acute renal failure

**Surgical Methods:**

- Cerebral Perfusion: n/a
- Hypothermic Circulatory Arrest: n/a
- Hypothermic Circulatory Arrest Time: ___ ___ Minutes
- Hemodynamics at surgery (echo or visual):
  - Hypotensive/shock
  - Normotensive
  - LV dysfunction
  - RV dysfunction
  - Lower extremity ischemia
  - Other complication

Replacement of:
- Ascending: n/a
- Root: n/a
- Interposition graft
- Homograft
- Composite

Arch Repair/Replacement:
- Partial Arch: n/a
- Complete Arch: n/a
- Descending: n/a

Open placement of stent graft in descending thoracic aorta
- Open visceral segment fenestration
- Open AAA repair
- Peripheral vessels
- CABG:
- Number of grafts: 1 2 3 4 >4
- MVR
- AVR
- Re-op
- Details of surgery unknown

**Endovascular**

**Date and time of endovascular procedure:**

<table>
<thead>
<tr>
<th>Month</th>
<th>Day</th>
<th>Year</th>
<th>Hour</th>
<th>Minute</th>
</tr>
</thead>
</table>

**Type B**
- Malperfusion
  - Limb ischemia
  - Visceral ischemia
  - Renal ischemia
- Refractory pain
- Refractory hypertension
- Rupture
- Contained rupture
- Free rupture
- Extension of dissection
- Type B dissection with aneurysm > 5.0 cm

Procedures done:
- Dissection flap fenestration
- Root aortic stent graft
- Ascending aortic stent graft
- Arch aortic stent graft
- Descending thoracic aortic stent graft
- Thoracoabdominal aortic stent graft
- Infrarenal stent graft
- Celiac artery stent
- SMA stent
- Renal artery stent
- Iliac artery stent

**Medical**

Reason:
- Type B
- Patient refusal
- Age
- Intramural hematoma - arch
- Comorbid illness
- Intramural hematoma - descending

---

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#6 - COMPLICATIONS AND OUTCOME

**A: IN-HOSPITAL COMPLICATIONS**

<table>
<thead>
<tr>
<th>Pre-procedure or Medical</th>
<th>Post-procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurological deficit:</strong></td>
<td>YES □ NO □ If yes: □ Transient □ Permanent</td>
</tr>
<tr>
<td>Cerebral vascular accident</td>
<td>□ □</td>
</tr>
<tr>
<td>Coma</td>
<td>□ □</td>
</tr>
<tr>
<td>Spinal cord ischemia</td>
<td>□ □</td>
</tr>
<tr>
<td>Transient neurological deficit</td>
<td>□ □</td>
</tr>
<tr>
<td><strong>Myocardial complications:</strong></td>
<td>□ □</td>
</tr>
<tr>
<td>Myocardial ischemia</td>
<td>□ □</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>□ □</td>
</tr>
<tr>
<td>Low output syndrome</td>
<td>□ □</td>
</tr>
<tr>
<td>Mesenteric ischemia/infarction</td>
<td>□ □</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>□ □</td>
</tr>
<tr>
<td>Requiring dialysis?</td>
<td>□ □ If yes: □ Temporary □ Permanent</td>
</tr>
<tr>
<td><strong>Extension of dissection</strong></td>
<td>□ □</td>
</tr>
<tr>
<td>Hypotension</td>
<td>□ □</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>□ □</td>
</tr>
<tr>
<td>Limb ischemia</td>
<td>□ □</td>
</tr>
<tr>
<td>Respiratory insufficiency</td>
<td>□ □</td>
</tr>
<tr>
<td>Bleeding requiring re-thoracotomy</td>
<td>□ □</td>
</tr>
<tr>
<td>Transfusion required</td>
<td>□ □</td>
</tr>
</tbody>
</table>

If yes, number of units: □ □

If yes, total post-operative transfusions: □ □

**B: OUTCOME**

- O Patient discharged to home
- O Patient discharged to tertiary hospital or care facility
- O Patient died while awaiting anticipated surgery or endovascular procedure

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month / Day / Year</td>
<td>Hour : Minute</td>
</tr>
</tbody>
</table>

- O Patient died Date

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month / Day / Year</td>
<td>Hour : Minute</td>
</tr>
</tbody>
</table>

**Cause of death:**

- O Neurologic
- O Bleeding
- O Rupture
- O Tamponade
- O Multi-organ Failure
- O Unknown
- O Visceral Ischemia
- O Cardiac
- O Other Specify: ____________________________
Appendix 4

Data definitions for IRAD registration form index hospitalization
Patient Report Form Data Definitions

*Denotes required fields

§ Patient Identification

Form ID: form version number generated by the software.
Hospital Code: a unique number assigned to each participating hospital by the IRAD coordinating center.
IRAD ID No.: a unique number generated by the online software upon form entry for each acute case. Once assigned to a record, this number can never be reused. IRAD will use this number to communicate issues about individual records with each center. This field is the primary key that links this record with the associated records in the follow-up tables.

*Definitive Management:

- Medical: non-invasive treatment
- Surgical: operative treatment
- Endovascular procedure: based on catheter techniques and radiological technology
- Hybrid: a staged procedure involving both surgical and endovascular techniques to facilitate treatment of the dissection
- Surgical and Endovascular: both surgical and endovascular procedures are employed separately to treat the dissection

Data Collection: Indicate whether data abstraction was performed:

- Prospectively: the risk factor groups were identified at the start of the study and followed into the future to determine the outcome status of each subject
- Retrospectively: past records were used to determine the past risk factor status of subjects and subsequent outcome status of each subject
- Both prospective and retrospective

*Dissection type: Indicate Stanford dissection type:

- Stanford Type A: all dissections or intramural hematomas involving the portion of the aorta proximal to the left subclavian artery, regardless of the site of origin.
- Stanford Type B: all dissections or intramural hematomas involving the area of the aorta distal to the left subclavian artery.

*Date of symptom onset mm/dd/yy: Indicate the month, date and year of onset of symptoms of acute aortic dissection for current hospitalization.

- Time hr:min: Indicate the time of onset of symptoms in hours and minutes on a 24 hour time scale.
- If the dissection was iatrogenic and no symptoms occurred, this may be left blank. In addition, the Presenting Symptoms section may also be left blank.

Date initial hospital arrival mm/dd/yy (Primary/referring or IRAD/tertiary hospital): Indicate the month, date and year of initial presentation to a hospital for current hospitalization.

- Time hr:min: Indicate the time in hours and minutes on a 24 hour time scale for this initial presentation.

*Patient transferred from another hospital?: Was patient transferred from a referring hospital?

- Y= yes, if patient was transferred from a referring hospital, or
• N= no, if patient was not a transfer and was directly admitted to this hospital for the current hospitalization.

If transferred, date of tertiary hospital arrival mm/dd/yy: Indicate the month, date and year and time (24 hour scale) when first seen at the hospital where advanced care was given for the current hospitalization.

Date dissection first suspected mm/dd/yy: Indicate month, date and year when the diagnosis of aortic dissection was first considered.
• Time hr:min: Indicate the time in hours and minutes on a 24 hour time scale when the diagnosis of aortic dissection was first considered.

Date diagnosis confirmed mm/dd/yy: Indicate the month, date and year when the diagnosis of aortic dissection was established.
• Time hr:min: Indicate the time in hours and minutes on a 24 hour time scale when this diagnosis was established.

Patient Identified by: Indicate the method(s) which was (were) used to identify and confirm the acute aortic dissection.
Select any / all options that apply:
• Sx onset
• Image
• Surgery
• Post mortem

§ Demographics

*Date of Birth mm/dd/yyyy: Indicate the month, date and year of patient’s birth.
*Gender: Indicate the gender at birth as either female or male.
Race:
White: Indicate if patient is Caucasian.
Black: Indicate if patient is of African descent.
Asian: Indicate if patient is of Asian descent.
Hispanic: Indicate if patient is of Latin American origin.
Other: Indicate if the patient’s race cannot be assigned to any one of the above groups.
*Weight (kg): Indicate the weight of the patient in kilograms or pounds (be sure to specify units).
*Height (cm): Indicate the height of the patient in centimeters or inches (be sure to specify units).

§ History

*Was health history information available?: Indicate if pertinent health information is available for this patient. If yes is marked, at least one of the following variables must have “yes” or “no” (not “n/a”) selected.
Hypertension: Indicate if the patient has documented history of hypertension diagnosed and treated with medication, diet and/or exercise by a physician; diagnosed by BP >140 systolic or >90 diastolic on two occasions or currently on antihypertensive meds.
Diabetes: Indicate if the patient has blood glucose values FBS ≥ 140 mg / dl or SI units ≥ 7.7 mmol/L on two occasions or by being treated with oral hypoglycemic agents, insulin or diet in the past.
Marfan syndrome: Indicate if the patient has a hereditary disorder characterized by disproportionately tall stature, thoracic deformity, joint laxity or contractures, ectopia lentis, myopia, aortic dilatation/dissection or mitral valve prolapse.

Atherosclerosis: Any history of PCI, CABG or cath demonstrating > 70% stenosis in coronary, peripheral, or cerebral vasculature.

Known aortic aneurysm: Indicate if the patient had been diagnosed to have an aortic aneurysm.

Prior aortic dissection: Indicate if the patient was known to have a linear tear in the intima of the aorta.

Mitral valve disease: Indicate if mitral valve regurgitation of at least grade 2 or greater or mitral valve area < 1.5 cm².

Bicuspid aortic valve: Indicate if the patient was known to have a bicuspid aortic valve at presentation, or whether one was initially identified during this event during care.

Aortic valve disease: Indicate if the patient was known to have aortic valve narrowing (aortic stenosis) or incompetence (aortic insufficiency). Aortic valve regurgitation of at least grade 2 or greater, aortic valve area ≤ 1.0 cm².

Tricuspid valve disease: Indicate if the patient has any disease of the tricuspid valve, including stenosis, regurgitation, etc.

Peripartum State: Indicate if the current hospitalization was associated with a pregnancy.

Other Aortic Disease: Indicate if the patient was known to suffer from any disease affecting the aorta excluding aortic dissection, aneurysm, or valvular heart disease.

Cocaine abuse: Indicate if the patient has taken cocaine to the detriment of his health and social functioning.

Smoking: N/A: Smoking status not recorded i.e. no information in case notes available on the patient’s smoking status.

Current smoker: indicate if the patient has used any form of tobacco in the past one month. This includes cigarette, cigar, tobacco chew, pipe, etc. (this does not include marijuana) if current smoker, do not mark former.

Former smoker: use of tobacco greater than one month prior to this admission. Only mark former smoker if not currently smoking.

Non-smoker: never smoked.

Family History of Aortic Disease: Indicate if the patient was known to have any direct blood relatives (parents, siblings, children) having any disease diagnosed affecting the aorta including aortic dissection, aneurysm, aortic valve disease, or other.

Peripheral Arterial Disease: Indicate whether the patient has a history of peripheral arterial disease (includes upper and lower extremity, renal, mesenteric, and abdominal aortic systems). This can include:

1. Claudication, either with exertion or at rest,
2. Amputation for arterial vascular insufficiency,
3. Vascular reconstruction, bypass surgery, or percutaneous intervention to the extremities (excluding dialysis fistulas and vein stripping),
4. Documented aortic aneurysm with or without repair,
5. Positive noninvasive test (e.g., ankle brachial index <= 0.9, ultrasound, magnetic resonance or computed tomography imaging of > 50% diameter stenosis in any peripheral artery, i.e., renal, subclavian, femoral, iliac).

Peripheral arterial disease excludes disease in the carotid or cerebrovascular arteries.

Chronic Obstructive Pulmonary Disease (COPD): Indicate if a diagnosis of Chronic Obstructive Pulmonary Disease has been made by a physician. Patient on chronic pharmacologic therapy and/or have a FEVI less than 75 percent of predicted value.

Chronic Renal Insufficiency: Indicate if the patient has a history of chronic renal insufficiency, defined
1. Kidney damage for ≥3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either pathological abnormalities; or markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests.
2. GFR <60 mL/min/1.73 m² for ≥3 months, with or without kidney damage.

Iatrogenic:
Indicate if aortic dissection was a result of any form of medical treatment and specifically resulted from cardiac catheterization, percutaneous coronary angioplasty, cardiac surgery, or other treatment during hospitalization
- Cath/PTCA: Catheterization, angiography or percutaneous transluminal coronary angiography.
- Cardiac surgery: Any cardiac surgery other than catheterization/PTCA.
- Other: other treatment than the two listed above.

Prior Cardiac Surgery: Select any / all options that apply.

Cath/angiography: Indicate if the patient had a catheterization or imaging of the circulation of the myocardium by injection of contrast medium.
PTCI: Indicate whether the patient has had a percutaneous transluminal coronary intervention of any type (balloon angioplasty, atherectomy, stent, thrombectomy or other).
CABG: Indicate whether the patient has had a previous coronary artery bypass surgery by any approach.
Aortic Aneurysm/Dissection: Indicate if the patient had in the past undergone surgery for aneurysm or dissection.
AVR: Indicate whether the patient had a previous aortic valve replaced with a prosthetic valve.
MVR: Indicate whether the patient had a previous mitral valve replaced with a prosthetic valve.
Other: Any cardiac surgery other than the above. Please specify.

§ Presenting Symptoms

Chest pain: Indicate if the patient had chest pain and the site of location as either the front (anterior) or back (posterior) of the chest where pain was manifest as the initial symptom. Indicate both anterior and posterior if warranted.
- Back pain is not the same as posterior chest pain; Back pain refers to pain in the lower back, and posterior chest pain refers to pain behind the chest (upper back).

Pain severity: Indicate mild if pain not extreme in any way, severe if extremely painful and worst ever, if pain intensity was as intense as possibly perceived.

Pain in head or neck: Indicate if pain was felt in the region of the body above the clavicles.
Back pain: Indicate if the pain was felt in the posterior aspect of the body.
Abdominal pain: Indicate if pain was felt in the region between the costal margin and the hip joint.
Radiating: Indicate if the pain branched out from its area of origin.
Migrating: Indicate if the pain changed location.
Leg pain: Indicate if the pain was felt below the hip joint.
Quality of pain: Select any / all options that apply. Indicate the characteristic that best describes the pain.
• Tearing/Ripping
• Sharp
• Pressure
• Burning

**Abrupt onset of pain:** Indicate if the onset of pain was sudden and unexpected.

*Syncope:* Indicate if there was a sudden loss of consciousness, including loss of postural tone. Patient may experience syncope when supine. If symptoms of syncope are not explicitly stated, please mark no.

**Febrile:** Indicate whether the patient was feverish at presentation, either at the primary or tertiary site.

**Abnormal CXR w/o associated pain:** Indicate if the chest X-ray showed an abnormality in the absence of pain as a presenting symptom.

§ **Signs of Aortic Dissection**

**Presenting hemodynamics:** Indicate the SBP on admission as **Hypertensive** (BP \(\geq\) 150/90mmHg), **Normotensive** (SBP between 100-149 mmHg), **Hypotensive** (SBP < 100mmHg), or as

**Shock:** Indicate if patient has a maximum systolic blood pressure \(\leq\) 80 mmHg for at least 30 minutes or pump failure, even after correction of contributing extra myocardial factors (hypovolemia, arrhythmia, pain, vasovagal reactions), as manifested by either a cardiac index < 2.2 and a PCWP > 18 mm Hg, or signs of hypoperfusion (peripheral vasoconstriction, urine output < 30 cc/hr or altered sensorium) or as

**Cardiac tamponade:** Indicate if there was fluid in the pericardial space compromising cardiac filling, with evidences of pericardial fluid either by typical hemodynamics, pericardiocentesis or cardiac echo.

**First BP:** Indicate the first measurement of systolic and diastolic pressures taken in mm of Hg.

**Murmur of aortic insufficiency:** Indicate if a murmur is noted by auscultation or echocardiography:

**Grade:**
I: (mild) Murmur so faint that it is heard only with special effort.
II: (mild to moderate) Murmur is soft and readily detected.
III: (moderate) Murmur is prominent but not loud.
IV: (severe) Murmur is loud and usually palpable.

**Pulse deficits checked?** *Indicate if pulse deficits were determined.*

**Pulse deficits present:** Indicate if there is a diminution or absence of pulse at each site of the deficit.

• Right carotid
• Left carotid
• Right brachial
• Left brachial
• Right femoral
• Left femoral

**Pericardial friction rub:** Indicate if scratching, grating high pitched sounds arising from friction between the roughened pericardial and epicardial surfaces were heard.

**Ischemic peripheral neuropathy:**
Indicate if vascular compromise lead to sensory or motor abnormalities.

**Ischemic spinal cord damage:** Indicate if spinal cord damage producing paraparesis or paraplegia resulted from compromised spinal perfusion.

**Cerebralvascular accident (CVA)/Stroke:** Indicate if there was loss of neurological function caused by a disturbance in cerebral blood supply with residual symptoms 24 hours after onset.

**Ischemic lower extremity:** Indicate if any of the following were seen below the waist as a sign of aortic dissection e.g. pain, pulselessness, pallor of the foot on elevation, rubor on dependency, necrosis, paralysis, paresthesia, intermittent claudication, rest pain or impotence.

**Coma/altered consciousness:** Indicate if patient experienced complete or partial mental unresponsiveness (beyond that expected from anesthesia) or no evidence of psychological or physiologically appropriate responses to stimulation.

**Congestive Heart Failure (CHF):** Indicate if the patient has evidence of heart failure as a sign of aortic dissection. Physician should have CHF documented in the record or there should be a history of fluid retention during that same period although this is not an absolute requirement. Patient should have received diuretics or cardiac medication to treat the failure. There should be a history of one or more of the following: paroxysmal nocturnal failure (PND), dyspnea on exertion or at rest due to heart failure, pulmonary congestion on x-ray, ventricular S3 gallop. Bilateral pedal edema or dyspnea alone is not diagnostic.

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**§ CXR (Chest X-ray) Findings**

**Chest X-ray done:** Indicate whether a chest x-ray was done or not.

**Site:** Indicate whether the chest x-ray findings noted herein were performed at the tertiary or referring (i.e., primary) site.

**Normal Findings:** Indicate whether the CXR was diagnosed as “normal” and as unremarkable to the indications listed below or other abnormal indications.

**Widened mediastinum:** Indicate if there was presence of apical cap, displacement of NG tube to the right of midline, displacement of left main stem bronchus or left sided pleural effusion.

**Abnormal aortic contour:** Indicate if the aortic arch in the frontal view is more than 2.0± 1.0 cm. in the absence of a right sided aortic arch, widening of the aortic silhouette or presence of a localized bulge over the site of origin.

**Abnormal cardiac contour:** Indicate if the cardiothoracic ratio is > 0.5.

**Displacement/calcification of aorta:** Indicate in the presence of calcification, separation of the intimal calcification from the outer aortic soft tissue border by > 1.0cm.

**Pleural effusion (> minor):** Indicate if the costophrenic angle is obliterated in a frontal projection.

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**§ ECG Findings**
ECG done: Indicate whether an electrocardiogram was done or not. For the following information, the ECG done closest to presentation (generally in the ER) should be used.

Site: Indicate whether the electrocardiogram findings noted herein were performed at the tertiary or referring (i.e., primary) site.

Normal: Indicate whether the ECG was diagnosed as “normal” and as unremarkable to the indications listed below or other abnormal indications.

Ischemia: Indicate if horizontal or downsloping ST segment depression $\geq 1$ mm in two or more contiguous leads that reverses after ischemia disappears is seen, or T wave flattening or inversion reversing with disappearance of ischemia; rarely ST elevation with transmural ischemia or coronary spasm.

Infarction, new Q’s or ST elevation: Indicate if there is a myocardial infarction with the development of new Q waves that are 0.03 seconds in width and/or $\geq$ one third of the QRS complex in two or more contiguous leads and/or ST elevation $> 1.0$mm.

Infarction, old Q’s: Indicate if the patient had a documented ECG evidence of greater than 7 days of Q waves that are 0.03 seconds in width and/or one third of the total QRS complex in two or more contiguous leads.

Non-specific ST-T changes: Indicate if ST segment and T wave changes do not lead to a specific diagnosis.

Left ventricular hypertrophy: Indicate if the QRS voltage criteria for LVH are present e.g. $R_1 + S_{III}$ $> 2.5$mV, $R$ in $aV_L$ $> 1.2$mV, $R$ in $avF$ $> 2.0$mV, $S$ in $V_1 > 2.4$mV, $R$ in $V_5$ or $V_6 > 2.6$mV and $R$ in $V_5$ or $V_6 + S$ in $V_1 > 3.5$mV or sum of $R$ wave in $avL$ and $S$ wave in $V_3$ (Cornell index) exceeding 35mm.

Low voltage: Indicate if the QRS voltage was less than 5 mV in precordial or less than 10 mV in limb leads.

§ Initial Medical Therapy (at your center)

ACE Inhibitor: Indicate if an Angiotension- Converting Enzyme Inhibitor was administered, a class of drugs that block the conversion of angiotension I to angiotension II.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benazepril</td>
<td>Lotensin</td>
</tr>
<tr>
<td>Benazepril+HCTZ</td>
<td>Lotensin HCT</td>
</tr>
<tr>
<td>Captopril</td>
<td>Capoten</td>
</tr>
<tr>
<td>Captopril+HCTZ</td>
<td>Capozide</td>
</tr>
<tr>
<td>Enalapril</td>
<td>Vasotec</td>
</tr>
<tr>
<td>Enalapril+HCTZ</td>
<td>Vaseretic</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>Monopril</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>Zestril</td>
</tr>
<tr>
<td>Lisinopril+HCTZ</td>
<td>Prinzide, Zestoretic</td>
</tr>
<tr>
<td>Moexipril</td>
<td>Univasc</td>
</tr>
<tr>
<td>Quinapril</td>
<td>Accupril</td>
</tr>
<tr>
<td>Ramipril</td>
<td>Altace</td>
</tr>
<tr>
<td>Trandolapril</td>
<td>Mavik</td>
</tr>
<tr>
<td>ACE I + CA Blockers</td>
<td>Lotrel</td>
</tr>
</tbody>
</table>
**ARB:** Indicate if an Angiotensin II Receptor Antagonist was administered, a class of drugs that bind with angiotensin receptors, thus preventing access of angiotension II to the receptor.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irbesartan</td>
<td>Avapro</td>
</tr>
<tr>
<td>Candesartan</td>
<td>Atacand</td>
</tr>
<tr>
<td>Epiosartan</td>
<td>Teveten</td>
</tr>
<tr>
<td>Losartan</td>
<td>Cozaar</td>
</tr>
<tr>
<td>Valsartan + HCTZ</td>
<td>Diovan</td>
</tr>
<tr>
<td>Losartan +HCTZ</td>
<td>Hyzaar</td>
</tr>
<tr>
<td>Olmesartan Medoxomil</td>
<td>Benicar</td>
</tr>
<tr>
<td>Telmisartan</td>
<td>Micardis</td>
</tr>
</tbody>
</table>

**Beta-blocker:** Indicate if the drugs administered belonged to a class of drugs that act by inhibiting the beta receptor activity of secretion of autonomic nerves and adrenal glands on certain organs and tissues.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acebutolol</td>
<td>Sectral</td>
</tr>
<tr>
<td>Atenolol</td>
<td>Tenormin</td>
</tr>
<tr>
<td>Atenolol+Chlorthalidone</td>
<td>Tenoretic</td>
</tr>
<tr>
<td>Betaxolol</td>
<td>Kerlone</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>Zebeta</td>
</tr>
<tr>
<td>Bisoprolol+HCTZ</td>
<td>Ziac</td>
</tr>
<tr>
<td>Carteolol</td>
<td>Cartrol</td>
</tr>
<tr>
<td>Labetalol</td>
<td>Trandate</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>Lopressor</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>Toprol</td>
</tr>
<tr>
<td>Metoprolol+HCTZ</td>
<td>Lopressor HCT</td>
</tr>
<tr>
<td>Nadolol</td>
<td>Corgard</td>
</tr>
<tr>
<td>Nadolol+Bendroflumethiazide</td>
<td>Corzide</td>
</tr>
<tr>
<td>Penbutolol</td>
<td>Levatol</td>
</tr>
<tr>
<td>Pindolol</td>
<td>Visken</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Inderal</td>
</tr>
<tr>
<td>Propranolol+HCTZ</td>
<td>Inderide</td>
</tr>
<tr>
<td>Timolol</td>
<td>Blocadren</td>
</tr>
<tr>
<td>Timolol+HCTZ</td>
<td>Timolide</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>Coreg</td>
</tr>
</tbody>
</table>

**Calcium channel blocker:** Indicate if drugs that act by inhibiting the calcium channels in the myocardium were used.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bepridil</td>
<td>Vascor</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Cardizem</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Dalacor</td>
</tr>
<tr>
<td>Diltiazem HCL</td>
<td>Cartia</td>
</tr>
<tr>
<td>Felodipine</td>
<td>Plendil</td>
</tr>
<tr>
<td>Isradipine</td>
<td>Dynacirc</td>
</tr>
</tbody>
</table>
Nicardipine Cardene
Nifedipine Adalat
Nifedipine Procardia
Verapamil Calan
Verapamil Isoptin
Verapamil Verelan

**Diuretic:** Indicate if the class of drugs administered act by increasing the amount of urine excreted.

<table>
<thead>
<tr>
<th><strong>Generic Name</strong></th>
<th><strong>Trade Name</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiloride</td>
<td>Midamor</td>
</tr>
<tr>
<td>Amiloride+HCTZ</td>
<td>Moduretic</td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td>Diuril</td>
</tr>
<tr>
<td>Ethacrynic acid</td>
<td>Edecrin</td>
</tr>
<tr>
<td>Furosemide</td>
<td>Lasix</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Esiotin</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Hydrodiuril</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Oretic</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Diuercardin</td>
</tr>
<tr>
<td>Indapamide</td>
<td>Lozol</td>
</tr>
<tr>
<td>Methyclothiazide</td>
<td>Enduron</td>
</tr>
<tr>
<td>Metolazone</td>
<td>Mykrox</td>
</tr>
<tr>
<td>Metolazone</td>
<td>Zaroxolyn</td>
</tr>
<tr>
<td>Quinethazone</td>
<td>Hydromox</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>Aldactone</td>
</tr>
<tr>
<td>Spironolactone+HCTZ</td>
<td>Aldactazide</td>
</tr>
<tr>
<td>Torsemide</td>
<td>Demedex</td>
</tr>
<tr>
<td>Triamterene</td>
<td>Dyrenium</td>
</tr>
<tr>
<td>Triamterene+HCTZ</td>
<td>Dyazide</td>
</tr>
<tr>
<td>Triamterene+HCTZ</td>
<td>Maxzide</td>
</tr>
</tbody>
</table>

**Nitroprusside:** Indicate if sodium nitroprusside was used as initial treatment.

**Other Vasodilator:** Indicate if the initial therapy consisted of drugs (other than nitroprusside) that cause blood vessels in the body to become wider by relaxing the smooth muscles in the vessel wall, or vasodilation. Examples include (but are not limited to) nesiritide (Natrecor) and nitroglycerin.

**Statin:** Indicate if the initial therapy consisted of cholesterol-lowering drugs whose generic names all end in “-statin”.

<table>
<thead>
<tr>
<th><strong>Generic Name</strong></th>
<th><strong>Trade Name</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>Lipitor</td>
</tr>
<tr>
<td>Cerristatin</td>
<td>Baycol</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>Lescol</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Mevacor</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Pravachol</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Zocor</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Crestor</td>
</tr>
<tr>
<td>Lovastatin + Niacin</td>
<td>Advicor</td>
</tr>
<tr>
<td>Atorvastatin + CA Blockers</td>
<td>Caduet</td>
</tr>
<tr>
<td>Simvastatin + Ezetimibe</td>
<td>Vytoral</td>
</tr>
</tbody>
</table>
Vasopressor: Indicate if the initial treatment consisted of drugs that raise blood pressure by causing constriction of blood vessels. Examples include (but are not limited to) dobutamine, dopamine, epinephrine, inamrinone, midodrine, milrinone, norepinephrine, phenylephrine, and vasopression (Pitressen).

Other: Indicate if any other type of pharmacological treatment apart from those listed above was used as the initial mode of treatment. Please specify the medication administered.

§ Chronic medical therapy at time of discharge:

Indicate what class(es) of drugs (see above) was(were) prescribed on a continued basis for long term use at time of discharge from the current hospitalization. Also, indicate systolic, diastolic blood pressures in mm of Hg and the heart rate at time of discharge.

§ Imaging studies

Methods: Only diagnostic imaging studies (versus intra-procedural studies) should be included.

- TEE: Transesophageal echocardiography
- TTE: Transthoracic echocardiography (Note: report TTE if the results reported are primary from a TTE done alone or with a TEE. If the TEE results predominate, report method as TEE.)
- CT: Computerized tomography
- MRI: Magnetic resonance imaging
- Aortogram: Imaging of the aorta by injecting radio-opaque contrast directly into the aorta.

Order performed: Indicate the order in which these studies were performed as 1 or 2 or 3 or 4, regardless of site.

Site of study: For each modality, indicate the site at which the study, whose results are noted herein, was performed. IRAD centers are considered TERTIARY SITES. All referring hospitals are considered PRIMARY SITES.

Extent of Imaging Modality Details:

Normal: Indicate if the imaging study showed no abnormalities.
Dissection: Indicate if a tear was seen in the aortic intima.

Intramural hematoma: Indicate if there is evidence of new hematoma formation without evidence of an intimal tear.

Aneurysm: Indicate if there was a localized dilation or enlargement of the aorta at any site along its length (from aortic annulus to aortoiliac bifurcation.)

Intimal Flap: Indicate if a diagnostic study has been able to identify a tear in the intima as a result of shear forces.

Double Lumen: Indicate if the blood filled space within the layers of the aortic wall produces a true and false lumen.

Site of most proximal extension of dissection flap or hematoma: Indicate if the diagnostic study has been able to identify the most proximal site of the dissection
or hematoma. Only one site is to be entered. **Site of most distal extension of dissection flap or hematoma:**

Indicate the most distal site of the aorta (one choice only) to which the dissection is confined.

**False lumen patency:** Indicate if the blood filled space between the layers of the aortic wall has a laminar flow (patent), partial laminar flow (partial thrombosis), or no laminar flow (complete thrombosis).

**Site of intimal tear:** If site of tear is known, indicate the site where the breach in the intima was identified; one choice only. If re-entry tear, exclude this site.

**Abdominal vessel involvement:** Indicate if the dissection flap extended into the ostium of any abdominal vessel. If abdominal vessels are involved, select the specific vessel, complete, or not available (see below). If no abdominal vessel involvement, leave this section blank.

**Abdominal vessel involvement site:** Select any / all options that apply. Indicate the site or sites of compromise of the abdominal vasculature by the dissection process. Complete indicates involvement of all the branches of the aorta including celiac axis, mesenterics, renals and iliac bifurcation.

**Distal communication:** Indicate if there is an additional communication between the false and true lumen of a dissected aorta. Usually distal location refers to one or more than one reentry/reentries at the abdominal level of a thoracoabdominal dissection.

**Arch vessel involvement:** Indicate if the aortic pathology includes the level of the left subclavian artery or any more proximally originating arch vessels.

**Pericardial effusion:** Indicate if the diagnostic study was able to identify a collection of fluid between the visceral and parietal pericardium.

**Periaortic hematoma:** Indicate if the diagnostic imaging study was able to identify a localized collection of blood between the layers of the aortic wall.

**Aortic regurgitation:** Indicate if incomplete closure of the cups was noted on a static image (non-Doppler or contrast), or if aortic regurgitation was recorded as a score of moderate or greater.

**Coronary arteries compromised:** Indicate if the imaging study was able to detect proximal coronary narrowing as a result of the dissection, due to occlusion of the ostia by the intimal flap.

§ **Aortic Measurements:**

Enter the widest diameter of various sites of the aorta as measured by any of the imaging studies.

§ **Management:**

**Angiography prior to consideration of surgery:** Indicate whether the patient had imaging of the circulation of the myocardium by injection of contrast medium whether surgery was eventually performed or not.

§ **Management-Surgical:**
If surgical management was opted, indicate the reason/s for doing so (choose all that apply):

*Type A:*
- Intramural hematoma in the ascending aorta.

*Type B:*
- Recurrent pain
- Refractory pain: Pain not controlled by optimal medical treatment
- Limb ischemia
- Visceral ischemia: Ischemia of the abdominal viscera
- Extension of dissection beyond the original site
- Refractory hypertension: Hypertension not controlled by optimal medical treatment
- Aortic rupture
- Acute renal failure

**Date and time of surgery mm/dd/yy:** Indicate the month, date and year when patient was operated on for acute aortic dissection during the current hospitalization.

**Time started hr:min:** Indicate the time in hours and minutes on a 24 hour time scale of the commencement of this surgery.

**Was surgery delayed beyond 24 hours of presentation?** Refers to presentation to the tertiary hospital for advanced care.

**Why was surgery delayed?** If delayed, indicate why the surgery was delayed beyond 24 hours after presentation:
- to obtain another confirmatory imaging study,
- to perform coronary angiography,
- unavailability of the surgeon or operating room, and/or
- comorbid medical condition: whether other comorbidities like smoking, diabetes, Hx CHF, PVD, significant valve disease, malperfusion syndrome, current or recent GI bleed, COPD, atrial fibrillation, previous MI or revascularization, (notably pulmonary emphysema) existed to account for the delay in surgical treatment.

**Open placement of stent graft in desc. thoracic aorta:** Indicate if the patient underwent a surgical stent graft in the descending aorta either in conjunction with, or as the primary surgical procedure. The descending aorta is the portion of the aorta between the arch and the abdomen.

**Open visceral segment fenestration:** Indicate if the origin of the celiac trunk, SMA, and/or renal arteries have been surgically repaired opening the dissection septum to permit flow in both false and true lumen.

**Open AAA repair:** Indicate if the patient underwent an abdominal aortic aneurysm repair.

**Peripheral vessels:** Indicate if the patient had a procedure treating peripheral vessels in conjunction with the primary surgical procedure. This would include the celiac axis, superior mesenteric artery, renal, iliac, or femoral arteries.

**Coronary Artery Bypass Graft (CABG):** Indicate if the patient had at least one coronary artery bypass graft placed concomitant to the aortic dissection procedure.

**Number of CABG grafts:** Indicate the number of coronary artery bypass grafts.

**MVR:** Indicate if the mitral valve was replaced with prosthetic valve, any kind, in suprannular or annular position.
AVR: Indicate if the aortic valve was removed and a new valve implanted.
Re-op: Indicate if this surgery was done before and had to be redone.
Details of surgery unknown: Select this option if details about the surgery are not known/not available.

Surgical methods
Cerebral perfusion: Indicate if during hypothermic circulatory arrest, the brain has been perfused.
Hypothermic circulatory arrest: Indicate if the patient was supported by artificial circulation (e.g. aortopulmonary bypass/cardiopulmonary bypass).

Circulatory arrest time: If circulatory arrest was used, indicate the total circulatory arrest time in minutes. Circulatory arrest time is recorded in the perfusion record or operative record and indicates the time the patient was supported by artificial circulation (e.g. aortopulmonary bypass/cardiopulmonary bypass). If more than one period of circulatory arrest required during this surgical procedure, the sum of these periods is equal to the total duration of circulatory arrest. If circulatory arrest was not used, leave blank.

Complications at surgery or endovascular procedure: Events at Surgery
Hypotensive/shock: Indicate whether the patient was in a clinical state of hypoperfusion on entry to the OR according to any of the following criteria:
- Hypotension as defined by systolic blood pressure SBP < 90 mm Hg
- IV inotropes, IV vasoactive agents, or mechanical support required to maintain blood pressure as defined above.
- Cardiac index < 1.8 L/min/M2
- Patient in a state of compensated shock as evidenced by all of the following:
  - decreased peripheral pulses,
  - decreased capillary refill,
  - cool skin temperature.
- pH < 7.2 and/or lactate > 4 mmol/L
Normotensive: Indicate whether the patient was normotensive on entry to the OR as defined by systolic blood pressure SBP between 100-149 mmHg.
LV dysfunction: Indicate if there was any abnormal or difficult function in the left ventricle.
RV dysfunction: Indicate if there was any abnormal or difficult function in the right ventricle.
Lower extremity ischemia: Indicate whether the patient had any complication producing anemia in the lower extremity due to mechanical obstruction of the blood supply.
Other complication: Indicate whether the patient had any other complication at surgery.

Replacement of:
Ascending: Indicate if the patient underwent replacement of the ascending aorta either in conjunction with, or as the primary surgical procedure. The ascending aorta begins at the sinotubular junction and ends at the origin of the innominate artery where the aorta continues as the transverse arch.
Root: Indicate if the patient underwent replacement of the aortic root (that portion of the aorta between the aorto-ventricular junction and the sinotubular junction; it gives rise to the coronary arteries)
If root replaced, indicate if it was a(n):

- **Interposition graft**: Indicate if aortic continuity, after resection, was reestablished by interposing a proximal sleeve graft between the two ends of the aorta.
- **Homograft (allograft)**: Indicate if the root prosthesis was harvested from a human cadaver.
- **Composite mechanical graft**: Indicate if the reconstruction was with a mechanical prosthesis attached directly to a Dacron graft.

**Arch repair/replacement**: Indicate if the patient underwent repair or replacement of the arch of the aorta either in conjunction with, or as the primary surgical procedure. The arch begins at the origin of the innominate artery and ends beneath the left subclavian artery. It is the portion of the aorta at the top of the heart that gives off three important blood vessels; the innominate artery, the left carotid artery and the left subclavian artery.

  - **Partial**: Indicate if only the proximal or distal portion of the arch was replaced with reimplantation of at least one of the brachiocephalic vessels. The arch reconstruction has left some of the aortic arch tissue.
  - **Complete**: Indicate if no arch tissue is left after the arch reconstruction.

**Descending**: Indicate if the patient underwent replacement of the descending aorta either in conjunction with, or as the primary surgical procedure. The descending aorta is the portion of the aorta between the left subclavian artery and the diaphragm.

### § Management-Endovascular:

If endovascular management was opted, indicate the reason/s for doing so (choose all that apply):

**Type B**:

- **Malperfusion**
  - Limb ischemia
  - Visceral ischemia
  - Renal ischemia
- **Refractory pain**
- **Refractory Hypertension**
- **Rupture**
  - Contained rupture
  - Free rupture
- **Extension of dissection**
- **Type B dissection with aneurysm > 5.0 cm**

**Date and time of endovascular procedure mm/dd/yy**: Indicate the month, date and year when the endovascular procedure for the acute aortic dissection was first begun.

  Time started hr:min: Indicate the time in hours and minutes on a 24 hour time scale of the commencement of this procedure.

**Endovascular Procedures**

**Dissection flap fenestration**: Indicate if the dissection septum was opened to permit flow in both false and true lumen.
Root aortic stent graft: Indicate if a stent was placed in the aortic root; defined as the area including the root at the sinus of valsalva, the annulus, or the sinotubular junction.

Ascending aortic stent graft: Indicate if a stent was placed in the ascending aorta. The ascending aorta is the area from the tubular area to just proximal to the brachiocephalic trunk/innominate artery.

Arch aortic stent graft: Indicate if a stent was placed in the aortic arch, which extends from the area just proximal to the brachiocephalic trunk/innominate artery to the area just distal to the left subclavian artery.

Descending thoracic aortic stent graft: Indicate if a stent was placed in the descending thoracic aorta. The descending aorta is the portion of the aorta between the arch and the abdomen.

Thoracoabdominal aortic stent graft: Indicate if a stent was placed in the thoracoabdominal aorta. The thoracoabdominal aorta is the portion of the aorta from the origin of the left subclavian artery to the aortic bifurcation or can involve only one or more segments of the abdominal aorta.

Infrarenal stent graft: Indicate if a stent was placed in the abdominal aorta, below the region of the renal arteries.

Celiac artery stent: Indicate if a stent was placed in the origin of the celiac artery.

SMA stent: Indicate if a stent was placed in the origin of the superior mesenteric artery.

Renal artery stent: Indicate if a stent was placed in the origin of the renal arteries.

Iliac artery stent: Indicate if a stent was placed in the origin of the iliac artery.

§ Management-Medical:

If Medical management was opted, indicate the reason/s for doing so (choose all that apply):
- Type B
- Age
- Comorbid illness
- Patient refusal
- Intramural hematoma – descending
- Intramural hematoma – arch

§ In Hospital Complications

Pre-procedure new neurological deficit:
Indicate if prior to surgery/endovascular procedure (or while assigned medical treatment) the patient developed a neurological abnormality that was not present before. Also indicate if this neurological abnormality of function was transient (lasted < 24 hours) or “permanent” (lasted > 24 hours).

Coma:
Indicate if patient experienced complete mental unresponsiveness (beyond that expected from anesthesia) and no evidence of psychological or physiologically appropriate responses to stimulation.

CVA:
Cerebrovascular accident representing a loss of neurological function (loss or slurring of speech, altered state of consciousness) caused by an ischemic event. Confirmed by either computed tomography or magnetic resonance imaging.
Spinal cord ischemia: Indicate if there is evidence of occlusion of the radicular arteries of the spinal cord with loss of function to the lower extremities with or without bowel/bladder involvement.

Transient neurological deficit: Indicate if the patient had evidence of a transient neurological deficit, defined as a brief episode of neurological dysfunction resulting from focal cerebral ischemia not associated with permanent cerebral infarction.

Post-procedure new neurological deficit: Indicate if the patient developed a new abnormality in neurological function after surgery/endovascular procedure for aortic dissection. This includes the entire postoperative period up to discharge. Also indicate if this neurological abnormality of function was transient (lasted < 24 hours) or “permanent” (lasted > 24 hours).

Pre-procedure or Medical Rx/ Post-procedure: Indicate if the following complications were seen either before or after surgery/endovascular procedure for aortic dissection or occurred while the patient was assigned a medical treatment.

Myocardial complications: Indicate if the patient had any of the following cardiac complications. Yes must be marked here for any of the subcategories to be considered.

Myocardial ischemia: Indicate if reduced coronary perfusion is evident without enzymatic or ECG evidence of infarction.

Myocardial infarction: Indicate if the patient had a myocardial infarction documented in the medical record by history, ECG or cardiac enzymes. Documented evidence of a MI includes at least two of the following four criteria:
1. Clinical history of prolonged “typical” chest pain (> 20 minutes not relieved by rest and/or nitrates)
2. Enzyme level elevation, specifically:
   - CK-MB >= 5% of total CK
   - CK greater than two times normal
   - LDH subtype 1 > LDH subtype 2
   - Troponin > two times normal
3. New wall motion abnormalities
4. Serial ECG tracings (at least two) showing changes from baseline or serially in ST-T and/or Q waves that are 0.03 seconds in width and/or > one third of the total QRS complex in two or more contiguous leads.

Low output syndrome: Indicate if the patient had evidence of low output syndrome, defined by the usage of catecholamines, or a cardiac index of ≤ 2.2 L/min/m² and a low ejection fraction (below 50%).

Mesenteric ischemia/infarct: Indicate if there is evidence of decreased perfusion through the superior mesenteric and inferior mesenteric arteries with decreased viability or necrosis of the gut, with or without lactic acidosis, pain or abdominal distension.

Acute renal failure: Indicate if there was a sudden, rapid, deterioration in renal function associated with a 3-fold increase in serum creatinine, a 75% decrease in glomular filtration rate, a serum creatinine value ≥ 4 mg/dl, urine output < .3 ml/kg/h over 24 hours, or anuria for 12 or more hours.
• A short-term increase in creatinine is normal after procedures. However, if levels do not return to baseline within 48 hours, then mark “yes”.

**Requiring dialysis:** Please indicate whether or not the patient had to undergo dialysis as a result of acute renal failure.

**Temporary or Permanent:** If the patient required dialysis, please specify whether the dialysis was temporary, defined as having been done until renal function is restored/until renal function returns to baseline, or permanent.

**Extension of dissection:** Indicate if compromise of additional arteries like the renal, mesenteric, iliac resulted as a sequelae of the dissection.

**Hypotension:** Indicate if systolic BP decreased below 90mmHg from an earlier higher recording.

**Cardiac tamponade:** Indicate if there are signs of hypotension requiring treatment, with evidences of pericardial fluid either by typical hemodynamics, pericardiocentesis or cardiac echo.

**Limb ischemia:** Indicate whether the patient had any complication producing anemia in the extremities due to mechanical obstruction of the blood supply. This may include upper or lower limb ischemia. Indicate if any of the following were seen as a complication of aortic dissection e.g. pain, pulselessness, pallor of the foot on elevation, rubor on dependency, necrosis, paralysis, paresthesia, intermittent claudication, rest pain or impotence.

**Respiratory insufficiency:** Indicate whether the patient had respiratory insufficiency following intervention, defined as ventilatory support $\geq 3$ days, and/or a tracheostomy, and/or pneumonia.

**Bleeding requiring re-thoracotomy:** Indicate whether the patient had post-intervention bleeding requiring a re-thoracotomy.

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**§ Outcome**

**Patient Outcome:**

• **Discharged to home:** Indicate whether the patient was alive at discharge and was discharged to home. Include the month, date and year when patient was discharged from THIS tertiary site to complete acute hospitalization of the incident event.

• **Discharged to tertiary hospital or care facility:** Indicate whether the patient was alive at discharge and was transferred to another hospital or care facility. Include the time of discharge from THIS tertiary site in mm/dd/yyyy.

• **Mortality:** Indicate whether the patient has been declared dead within this hospital. This includes all causes of death. Also indicate the date and time of death (on a 24 hour time scale).

• **Time of death hr:min:** Indicate the time on a 24 hour time scale of the time of death.

**Patient died while awaiting anticipated surgery or endovascular procedure:** Indicate if surgery or endovascular management was the planned treatment, but the patient died before
the operation.

**Major cause of death**: Indicate the PRIMARY cause of death, i.e. the first significant abnormal event which ultimately led to death; choose one of the following:

- Neurologic
- Tamponade
- Visceral Ischemia
- Bleeding
- Multi-Organ Failure
- Cardiac
- Rupture
- Unknown
- Other (please specify)

Note: Sites have added additional information on cause of death on the bottom margin of the page or on a separate page.
Appendix 5

IRAD registration form follow-up
IRAD Follow-up Form V7.0

Follow Up Mark:
☐ 6m  ☐ 1  ☐ 2  ☐ 3  ☐ 4  ☐ 5

Hospital_______________________________ Date of Admission: __ __ / __ __ / __ __ __ __

IRAD Acute Case ID Number: __________ Date of Birth: __ __ / __ __ / __ __ __ __

Date of Follow-up Visit: __ __ / __ __ / __ __ __ __ Consent Denied: ☐ y  ☐ n
Date Lost to Follow-Up: __ __ / __ __ / __ __ __ __ SSDI Only: ☐ y  ☐ n

Health Status During Follow-Up Period
Reurrence of old symptoms or new symptoms: ☐ y  ☐ n  ☐ n/a
If yes, symptoms related to acute dissection: ☐ y  ☐ n  ☐ n/a
If yes, chest pain: ☐ y  ☐ n  ☐ n/a
back pain: ☐ y  ☐ n  ☐ n/a
abdominal pain: ☐ y  ☐ n  ☐ n/a
other pain: ☐ y  ☐ n  ☐ n/a
Limb ischemia: ☐ y  ☐ n  ☐ n/a
New or persistent hypertension: ☐ y  ☐ n  ☐ n/a
Renal failure: ☐ y  ☐ n  ☐ n/a  If yes, requiring dialysis? ☐ y  ☐ n

Medications at time of Clinic Visit
Date of visit listing medications: __ __ / __ __ / __ __ __ __
ACE: ☐ y  ☐ n  ☐ n/a  Ca Block: ☐ y  ☐ n  ☐ n/a
ARB: ☐ y  ☐ n  ☐ n/a  Diuretics: ☐ y  ☐ n  ☐ n/a
Other antihypertensive: ☐ y  ☐ n  ☐ n/a
Betablock: ☐ y  ☐ n  ☐ n/a  Vasodilators: ☐ y  ☐ n  ☐ n/a
Anticoagulants: ☐ y  ☐ n  ☐ n/a

Imaging Studies
Modalities used during the current follow-up period (number performed):
TEE  ☐ 0  ☐ 1  ☐ 2  ☐ >2  CT  ☐ 0  ☐ 1  ☐ 2  ☐ >2  MRI  ☐ 0  ☐ 1  ☐ 2  ☐

Initial after discharge

Vessel size:

Maximum diameter:
Root
Sinotubular junction
Ascending
Arch
Descending thoracic
Proximal descending
Distal descending
Suprarenal abdominal
Infrarenal abdominal

Initial after discharge only:
Post-operative sites of intimal tear:
☐ N/A  ☐ Root  ☐ Ascending  ☐ Arch  ☐ Descending
☐ Suprarenal abdominal  ☐ Infrarenal abdominal
False lumen patency:
☐ N/A  ☐ Patent  ☐ Partial thrombosis  ☐ Complete thrombosis

Consent Denied: ☐ y  ☐ n

Blood pressure at date of follow-up visit:
___ ___ / ___ ___ mmHg
Heart rate: ___ ___ ___ beats/min
Highest blood pressure during follow-up period:
___ ___ / ___ ___ mmHg

Statins: ☐ y  ☐ n  ☐ n/a
Other antihypertensive: ☐ y  ☐ n  ☐ n/a

Date of study (month/day/year): __ __ / __ __ / __ __ __ __

Most recent (closest to f/u mark): TEE  ☐  CT  ☐  MRI  ☐
(prefer CT>MRI>TEE, when available)
___ ___ / ___ ___ mmHg
**Imaging Studies**

Looking at all studies in the follow-up period:

- New dissection: □ Yes □ No □ N/A
  - If yes, dissection type: □ Type A □ Type B
  - If yes, most proximal extension of dissection or hematoma: □ Root □ Sinotubular junction □ Ascending □ Arch □ Left subclavian level □ Descending thoracic □ Suprarenal □ Infrarenal

- Progression of incident dissection: □ Yes □ No □ N/A
  - If yes, date: _____ / _____ / ________

- New aneurysm: □ Yes □ No □ N/A
  - If yes, date: _____ / _____ / ________

- Prior aneurysm: □ Yes □ No □ N/A
  - If yes, location: □ Root □ Ascending □ Arch □ Descending □ Suprarenal □ Infrarenal

- Increased total aortic diameter: □ Yes □ No □ N/A
  - If yes, date: _____ / _____ / ________

- False lumen patency *(most thrombosed)*: □ Patent □ Partial thrombosis □ Complete thrombosis □ N/A

- Aortic Regurgitation *(maximum reported on any imaging, including TEE/TTE)*: □ Yes □ No □ N/A
  - If yes, grade: □ 1 □ 2 □ 3 □ 4 □ N/A

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**Change in Management?**

- Change to surgical? □ y □ n □ n/a
  - Postpone planned surgery? □ y □ n □ n/a

- Change to endovascular? □ y □ n □ n/a
  - Postpone planned endovascular? □ y □ n □ n/a

---

**Adverse Events**

- Death: □ y □ n □ n/a
  - If yes, date: _____ / _____ / ________
  - □ cardiac □ non-cardiac
  - If mortality is unknown, what was last day known alive?: _____ / _____ / ________

- CVA: □ y □ n □ n/a
  - If yes, date: _____ / _____ / ________
  - □ embolic □ hemorrhagic □ other □ n/a

- Aortic Rupture: □ y □ n □ n/a
  - If yes, date: _____ / _____ / ________

- Rehospitalization: □ y □ n □ n/a
  - If yes, date: _____ / _____ / ________

- Related to Incident Dissection: □ y □ n □ n/a
  - If yes, date: _____ / _____ / ________

- Reoperation:
  - □ y □ n □ n/a
  - If yes, date: _____ / _____ / ________
  - If yes, was reoperation planned?: □ y □ n □ n/a

- Patient is not a surgical candidate: □ y □ n □ n/a

- Intervention Related to Aorta
  - (Unrelated to Incident Dissection): □ y □ n □ n/a
  - If yes, date: _____ / _____ / ________

- Reintervention: □ y □ n □ n/a
  - If yes, surgical conversion:
  - □ y □ n □ n/a
  - If yes, additional stent graft placement: □ y □ n □ n/a

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**STENT GRAFT PATIENTS ONLY**

- Stent-graft Endoleak: □ y □ n □ n/a
  - If yes, □ Type I □ Type II □ Type III □ Type IV □ Indeterminate

- Stent Graft Migration: □ y □ n □ n/a
  - If yes, was intervention required? □ y □ n

- Stent Graft Compression: □ y □ n □ n/a
  - If yes, was intervention required? □ y □ n

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**Form Completion**

- Initials: ______
- Date: _____ / _____ / ________
Appendix 6

Data definitions for IRAD registration form follow-up
IRAD FOLLOW-UP v7.0 LEXICON

Variables marked with an asterisk are required [*].

Follow-up mark*: This is the date from which follow-up is performed, which is 6 months, or 1, 2, 3, 4, or 5 years away from the index date of admission (found on the IRAD acute form). These marks represent the perspectives in time follow-up data abstraction should be completed from.

Current follow-up period: These windows delineate the time frame from which information can be taken for each follow-up period. This is determined by the Follow-up Mark (FUM). The time constraints are shown here:
- **FUM = 6 months** after the index date of admission:
  - Follow-up period = From the date of discharge to the FUM to 3 months after the FUM.
- **FUM = 1 year** after the index date of admission:
  - Follow-up period = 3 months before the FUM to 6 months after the FUM.
- **FUM = 2, 3, 4, or 5 years** after the index date of admission:
  - Follow-up period = 6 months before the FUM to 6 months after the FUM.

§ Patient Identification

Hospital: Name of IRAD center.
Online acute case ID number: IRAD index record number.
Date of admission: Date of admission to the referring hospital.
Date of birth: Patient’s birthdate (mm/dd/yyyy).

§ Consent and Date of Follow-up

Consent denied: Indicate if consent was or was not obtained for the current follow-up period.
SSDI only: If a comprehensive death index was available and used to determine mortality for this follow-up period, mark yes. This should only be selected if no other records are found within the current follow-up period.

Date of follow-up visit: Record the date of the note closest to the follow-up mark (from which information in the current health status section is taken); date should be within 6 months before and after the ideal follow-up mark.
- *Exception: For the 6 month follow-up form, the visit referred to can be within 6 months before and 3 months after that mark.
- *Exception: For the 1 year follow-up form, the visit referred to can be within 3 months before and 6 months after that mark.
- The date of an imaging study can be used, if no other notes or follow-up information is found.
Date lost to follow-up: Record the date of ideal follow-up for periods where no clinic notes or imaging information is available.

§ Current Health Status (Date of Clinic Visit)

Recurrence of old symptoms or new symptoms: Indicate if symptoms suggesting recurrence, extension or change in dissection reported during the current f/u period. Symptoms can be either similar to those at the patient’s original dissection or new.

- If yes, symptoms related to acute dissection: If symptoms were noted above, record whether or not they were attributed to changes in the incident dissection.
  - Chest pain: Indicate if chest pain suggesting recurrence, extension or change in dissection was reported during the current f/u period.
  - Back pain: Indicate if back pain suggesting recurrence, extension or change in dissection aorta was reported during the current f/u period.
  - Abdominal pain: Indicate if abdominal pain suggesting recurrence, extension or change in dissection in the aorta was reported during the current f/u period.
  - Other pain: Indicate if the patient had pain related to dissection in an area other than those listed above.

Limb ischemia: Indicate if any of the following signs or symptoms indicative of limb ischemia were seen during the current f/u period:

- pain
- pulselessness
- pallor of the foot on elevation (extreme or unnatural paleness)
- rubor on dependency (redness when legs are in dependent position - hanging down)
- necrosis
- paralysis
- paresthesia (abnormal skin sensations – tingling, tickling, itching, burning)
- intermittent claudication (pain, tension, weakness, cramps in legs – limped walking)
- rest pain (burning pain of the lower leg, aggravated by reclining, relieved by sitting or standing – intermittent claudication is a risk factor of rest pain).
- impotence (weak, feable, lacking strength in limbs)

New or persistent hypertension: Indicate if the patient during the current f/u period had a documented case of new hypertension:

- diagnosed and treated with medication, diet and/or exercise by a physician;
- or, diagnosed by BP >140 systolic or >90 diastolic on two occasions
- or, on antihypertensive meds when previously not taking these meds
- or, current medication regimen was changed to improve hypertension management.
**Renal failure:** Indicate if there was a sudden, rapid, deterioration or chronic deterioration of normal renal function associated with:

- **Nephropathy requiring dialysis:** decrease in renal function requiring peritoneal dialysis or hemodialysis as a result of contrast induced nephropathy.
- **Contrast nephropathy:** acute renal insufficiency resulting in an increase in serum creatinine to more than 1.5mg/dl or a 50% or greater increase over abnormal baseline prior to procedure.

Indicate new cases of renal failure and existing cases that have significantly worsened during the current f/u period.

- If renal insufficiency is noted, renal failure can be marked “yes”.
- A short-term increase in creatinine is normal after procedures. However, if levels do not return to baseline within 48 hours, then mark “yes”.

Also indicate if dialysis was required.

**Blood pressure at follow-up appointment:** Provide the systolic and diastolic blood pressures (mmHg) as determined during the follow-up visit.

**Heart rate:** Provide the heart rate (beats per minute) as determined during the follow-up visit.

**Highest blood pressure during follow-up period:** Provide the highest blood pressure noted during the current f/u period.

**§ Meds at time of Clinic Visit**

Record which medications the patient was on at the time of the clinic visit and the date used to determine current medical therapy.

- **ACE:** Angiotensin-Converting Enzyme Inhibitor
- **ARB:** Angiotensin II Receptor Blocker
- **Beta Blocker**
- **CA Blocker:** Calcium Channel Blocker
- **Diuretics**
- **Vasodilators**
- **Statins**
- **Other anti-hypertensive medications?** If yes, specify them. *(Aspirin and Warfarin are NOT considered “other” meds.)*

**§ Imaging**

**Modalities used since last contact (number performed during the follow-up period):** Indicate initial (and any secondary) imaging methods that were used and how many times each study was performed during the current f/u period.

**Initial imaging study after discharge:** Select the first post-discharge study performed, and record the modality (CT or MRI only) and the date of the study. This should only be filled out on the 6 month follow-up form.
**Maximum diameter:** Provide the widest diameter, in centimeters, for the aortic root, sinotubular junction, ascending aorta, arch, descending (can further specify proximal and/or distal descending measurements), suprarenal, and infrarenal aorta, as determined by the initial post-discharge study.

**Post-operative sites of intimal tear:** List the location(s) of any residual tear sites noted on the initial post-discharge study.

**False lumen patency:** Record the extent of false lumen thrombosis as seen on the first study after discharge.

**Date of imaging study done closest to the date of follow-up:** Indicate the date and type of the imaging study performed closest to the ideal date of follow-up. The study can be a CT, MRI or TEE, but CT then MRI is preferred if multiple modalities are available. *(imaging that does not visualize the aorta or does not use contrast should not be used)*

**Maximum diameter:** Provide the widest diameter, in centimeters, for the aortic root, sinotubular junction, ascending aorta, arch, descending (can further specify proximal and/or distal descending measurements), suprarenal, and infrarenal aorta, as determined by the most recent imaging study in the follow-up period.

**Looking at all studies in the follow-up period:** The presence of any of the variables listed below on any imaging study in the follow-up period should be recorded here.

**New dissection:** Indicate if a new dissection occurred at a site other than the index dissection.
- Provide the **date** of dissection.
- Record the **type** of new dissection using the Stanford classification criteria.
- Additionally, please specify the **most proximal extension** of dissection or intramural hematoma (aortic root, sinotubular junction, ascending, arch, left subclavian level, descending, suprarenal or infrarenal aorta).

**Progression of incident dissection:** Indicate if there has been retrograde/antegrade growth of the original dissection.
- Specify the anatomical **direction of progression** (retrograde/antegrade).

**New aneurysm:** Indicate if the patient has aortic dilatation, referred to as ectasia or an aneurysm, at a site not previously noted.
- Provide the **date** the new aneurysm was noted.
- Indicate whether the **maximal diameter**.
- Record the **location** of the aneurysm (root, ascending, arch, descending, suprarenal or infrarenal aorta).

**Prior aneurysm:** Indicate if the patient has a pre-existing aortic aneurysm, or previous history of aortic aneurysm.
- Indicate whether the aneurysm has enlarged in size (progression of aneurysm).
- Record the location of the aneurysm (root, ascending, arch, descending, suprarenal or infrarenal aorta).

**Increased total aortic diameter:** Indicate if the aortic diameter has increased significantly in size (more than 0.5 cm) during the current f/u period.
- Provide the date aortic growth was noted.
- Note the location of the increase (root, ascending, arch, descending, suprarenal, or infrarenal aorta).

**False lumen patency:** Indicate if the false lumen is patent, partially thrombosed, or completely thrombosed.
- If more than one imaging study provides information about thrombosis, list the greatest extent of thrombosis if there is a discrepancy.

**Aortic insufficiency (regurgitation) noted on follow-up:** Indicate if a murmur of aortic insufficiency is noted by auscultation or echocardiography on follow-up exam. Record the maximum grade listed.
- Grade I: (mild) Murmur so faint that it is heard only with special effort
- Grade II: (mild to moderate) Murmur is soft and readily detected.
- Grade III: (moderate) Murmur is prominent but not loud.
- Grade IV: (severe) Murmur is loud and usually palpable.

§ Change in Management

**Change to surgical management:** Indicate if a patient who was originally managed medically or with endovascular treatment underwent a surgical procedure to treat the original dissection.

**Change to endovascular management:** Medical or surgical treatment for the index event was changed to endovascular intervention during the current f/u period.

**Date of procedure:** If a change in management occurred, record the date of the procedure detailed in this section.

**Postpone planned Surgery:** Surgery for re-exploration or repair of an existing dissection has been postponed during the current f/u period.

**Postpone planned endovascular treatment:** Endovascular treatment for re-exploration or repair of an existing dissection has been postponed during the current f/u period.

§ Adverse Events

**Death:** Indicate if the patient has died during the current follow-up period, and indicate the date of death (MM/DD/YYYY)
- Indicate if the death was primarily due to a cardiovascular-related or non-cardiovascular-related event or cause.
- **If mortality is unknown, what was last day known alive?** If mortality status for this patient is unknown, please record the date of last contact with the patient.

**CVA (Cardiovascular Accident)/Stroke:** Indicate if the patient suffered a stroke during the follow-up period, and indicate the **date** of occurrence (MM/DD/YYYY). Also, indicate if the CVA was either:

- Embolic
- Hemorrhagic
- Other
- Not known

**Aortic rupture:** Indicate if the aorta ruptured during the follow-up period, and indicate the **date** of occurrence (MM/DD/YYYY).

**Rehospitalization Related to Incident Dissection:** Indicate if an acute, unplanned hospitalization occurred during the current follow-up period due to a problem related to the aorta or a complication, progression, or recurrence to the incident dissection. Record the **date** of hospitalization.

**Reoperation:** Indicate if a patient who had previous surgical management of their dissection was taken back to the operating room for any reason related to the incident dissection. Also record the **date** of reoperation.

- Please select whether the reoperation was a **planned** intervention or emergent procedure.

**Intervention related to aorta (unrelated to incident dissection):** Indicate if a surgical or endovascular procedure was performed on any other part of the aorta, NOT on the incident dissection. Record the **date** of the intervention (*examples include surgery for an abdominal aortic aneurysm, or an aortic valve replacement in a patient whose dissection did not include root involvement.*).

**§ Stent Graft Patients Only**

**Reinterventions:** Indicate if any surgical or endovascular procedure was performed on the incident dissection of a patient who originally underwent endovascular management. Also specify the date of reintervention. Patients who were managed via fenestration or stenting and fenestration should also list any reinterventions.

- **Surgical Conversion:** Indicate if an endovascular patient underwent a surgical procedure on the incident dissection, either with or without explantation of the original stent graft.
- **Additional Stent Graft Placement:** Indicate if an endovascular patient had to have an additional stent graft placed to treat the incident dissection.
**Stent-graft endoleak:** Blood flow perfusing the false lumen within the margins of the stent-graft at any time after endovascular repair.

- **Type I:** Endoleak arising from the proximal or distal sealing zone of the stent-graft perfusing the false lumen from the true lumen.
- **Type II:** Endoleak arising from a patent branch vessel perfusing the false lumen, e.g., lumbar or interior mesenteric branch.
- **Type III:** Inter-Device Junction: Endoleak arising from the component junction(s) of the stent-graft or due to damage to the graft material.
- **Type IV:** Graft Porosity: Endoleak arising through the graft fabric.
- **Indeterminate:** Endoleak detected with unknown source. (Also known as Type V).

**Stent-graft migration:** Displacement of all or part of the stent-graft that causes another complication (e.g. endoleak); or longitudinal movement of all or part of the stent-graft relative to anatomical landmarks post-implant for a distance > 1 cm as confirmed by CT scan or x-ray. Abdominal x-rays should be compared, with images performed immediately post-implant, to assess the position of the stent-graft.

**Stent-graft compression:** Stent-graft infolding or collapse following complete device deployment resulting in an overall reduction in the luminal diameter. Device compression may be sustained or transient in nature.
Appendix 7

IRAD registration form interventional treatment
## IRAD INTERVENTIONAL DATA FORM

<table>
<thead>
<tr>
<th>Hospital Code</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dissection Type</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Definitive Management</td>
<td>Surgical</td>
<td>Endovascular</td>
</tr>
<tr>
<td>IRAD Acute Case ID Number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date of Birth (mm/dd/yyyy)</td>
<td></td>
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</tbody>
</table>

### Surgical Procedures (ascending/arch)

<table>
<thead>
<tr>
<th>Ascending aortic Cross-Clamp</th>
<th></th>
<th>Y</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open Procedure</td>
<td></td>
<td>Y</td>
<td>N</td>
</tr>
</tbody>
</table>

#### Type of Operation

| Non-Coronal Sinus Replacement |   | Y | N |
| Aortic Valve Sparing Technique |   | Y | N |
| Remodelling                  |   |   |   |
| Reimplantation               |   |   |   |
| Comissural Resuspension      |   | Y | N |
| Bentall                      |   | Y | N |
| Cabrol                       |   | Y | N |
| Classic                      |   |   |   |
| Classic                      |   |   |   |
| Button                       |   |   |   |
| Separated grafts             |   |   |   |

### Surgical Procedures (descending/thoracoabdominal)

| Use of cardiopulmonary bypass |   | Y | N |
| Left heart bypass             |   | Y | N |
| Open procedure                |   | Y | N |
| Clamp between Left Carotid and Left Subclavian artery |   | Y | N |
| Clamp after Left Subclavian artery |   | Y | N |

#### Extent of repair

| Entire Descending Aortic Replacement |   | Y | N |
| Proximal 1/3                        |   | Y | N |
| Proximal 2/3                        |   | Y | N |
| Entire Thoracoabdominal Aortic Replacement |   | Y | N |
| Abdominal Aortic Replacement        |   | Y | N |
| Thoracic Aortic Fenestration        |   | Y | N |
| Supra-renal Abdominal Aortic Fenestration |   | Y | N |
| Infra-renal Abdominal Aortic Fenestration |   | Y | N |
| Axillo-bifemoral Bypass             |   | Y | N |

#### Other:

<table>
<thead>
<tr>
<th>Graft size</th>
<th></th>
<th>mm</th>
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</thead>
<tbody>
<tr>
<td>Additional graft sizes (if applicable):</td>
<td></td>
<td>mm</td>
</tr>
<tr>
<td>Use of Glue</td>
<td></td>
<td>Y</td>
</tr>
<tr>
<td>Glue Type</td>
<td></td>
<td>Biologic</td>
</tr>
<tr>
<td>Reinforce aortic anastomosis with teflon felt</td>
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<td>Y</td>
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<tr>
<td>Coronary ostium repair</td>
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<td>Y</td>
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<tr>
<td>Concomitant CABG</td>
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<td>Y</td>
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<td>Number of CABG</td>
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<td>Coronary stenting</td>
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<td>Left</td>
<td>Right</td>
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<tr>
<td>MV Replacement</td>
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<td>Y</td>
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<tr>
<td>MV Repair</td>
<td></td>
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</tr>
<tr>
<td>TV Replacement</td>
<td></td>
<td>Y</td>
</tr>
<tr>
<td>TV Repair</td>
<td></td>
<td>Y</td>
</tr>
</tbody>
</table>

#### Aortic Valve Replacement

| Homograft | Mechanical | Biological | Stentless |
| AV Graft Size |   | mm | Stented |

### Spinal cord protection and Adjuncts

| Reimplant intercostal arteries |   | Y | N |
| CSF drainage                  |   | Y | N |
| Monitoring somatosensory evoked potentials |   | Y | N |
| Monitoring motor-evoked potentials |   | Y | N |
| Selective visceral perfusion |   | Y | N |
| Selective renal perfusion |   | Y | N |

#### Hybrid surgical and endovascular treatment

| Yes | No | If yes, frozen elephant trunk? | Y | N |

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## Endovascular Treatment

### Vascular Access:
- Femoral
- Proximal Stent Graft Zone
  - Ascending Aorta
  - Aortic Arch
    - Zone 0
    - Zone 1
    - Zone 2
    - Zone 3
  - Descending Aorta
    - Above T6
    - Below T6
  - Abdominal Aorta
- Distal Stent Graft Zone
  - Descending Aorta
    - Above T6
    - Below T6
  - Thoraco-Abdominal Aorta
    - Intra-Renal
    - Iliac Arteries

### Adjunctive Procedure: Surgical
- Total Debranching
- Innominate to Carotid to Subclavian Bypass
- Carotid to Subclavian Bypass
- Abdominal Branch Vessel Revascularization
- Femoro=Femoral Bypass
- Thoracic Fenestration
- Abdominal Fenestration
- Other:

### Adjunctive Procedure: Interventional
- Embolization
- Celiac Artery Stent
- SMA Stent
- Renal Artery Stent
- Iliac Artery Stent
- Fenestration
- Uncovered True Lumen Stenting
- Other:

### Closure of all Thoracic Entries:
- Y
- N

### Type of stent graft
- Medtronic
- Bolton
- Gore
- Endomed
- Cook
- Djumbodis
- Jotec

### Model:

### Proximal Flare:
- Y
- N

### Proximal Free Flow:
- Y
- N

### Extracorporeal circulation

#### Arterial line
- Right axillary artery
- Left axillary artery
- Right femoral artery
- Left femoral artery
- Apex left ventricle
- Aorta
- Carotid
- Innominate Artery
- Other, specify

#### Rewarming

#### Cooling

#### Vent line
- Right Atrium
- SVC
- IVC
- Left Femoral Vein
- Right Femoral Vein
- Pulmonary Artery
- Left Atrium

#### Using Left Heart Bypass

- Left Pulmonary Veins

#### Hypothermic Circulatory Arrest
- Y
- N

#### EEG
- Y
- N

#### Cerebral Perfusion
- Antegrade
- Retrograde

#### Cardiac Perfusion Time

#### Cerebral Ischemia Time

#### Visceral Ischemia Time

#### Clamping Time

#### Cardiac Arrest Time

#### Clamping Time / Cardiac Arrest Time

#### Total Cardiopulmonary Bypass Time

#### Left Heart Bypass Time

#### Visceral Perfusion Time

#### Renal Perfusion Time

### Minimum temperature
- Farenheit/Celsius
  - Esophageal
  - Rectal
  - Bladder
  - Tympanic
  - Nasal

### Selective Visceral Perfusion
- Y
- N

### Selective Renal Perfusion
- Y
- N

### Cardioplegia
- Systemic K+
  - Y
  - N
- Antegrade
  - Y
  - N
- Retrograde
  - Y
  - N
- Warm
  - Y
  - N
- Cold
  - Y
  - N

### Blood
- Y
  - N
- Crystalloid
  - Y
  - N
- Intermittent
  - Y
  - N
- Continuous
  - Y
  - N
- None

### Drugs used during circulatory arrest time
- Steroids
  - Y
  - N
- Barbiturates
  - Y
  - N
- Nitric oxide
  - Y
  - N
- Mg++
  - Y
  - N
- Mannitol
  - Y
  - N

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**Version 6.2**

05/02/2013

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Appendix 8

Data definitions IRAD registration form interventional treatment
§ Patient Identification Section

Hospital Code:
Unique ID:
Dissection Type: A B
Definitive Management: Surgical Endovascular Hybrid
Date of Birth:

§ Surgical Procedures (ascending/arch)

Ascending aortic cross-clamp: indicate “yes” if the distal aortic anastomosis was constructed with a clamp applied on the aorta. If a clamp was used during the cooling period only and then removed, a “no” will be indicated. Cross-clamp time is myocardial arrest time or cardiac arrest time i.e. no blood flow to the heart.

Open procedure: Indicate if the distal anastomosis was constructed without a clamp on the aorta (i.e. Open distal anastomosis) using circulatory arrest.

Type of operation

Non coronary sinus replacement: Removal of the noncoronary sinus down to the level of the aortic annulus and replacement of the sinus by graft material.

Aortic valve sparing technique: Removal of all aortic tissue but preservation of the aortic valve.

Remodelling: Indicate if a Yacoub technique has been performed, with the aortic graft shaped on the anatomy of the aortic valve.

Reimplantation: Indicate if a David technique has been performed, with the aortic valve sutured into the aortic graft.

Commissural resuspension: Reconstruction of the aortic root with gluing or suturing together of the dissected root tissue (also with the use of reinforcing between-layer grafts or felt)

Bentall: Total root replacement with prostheses, including a mechanical or biological valve and graft tissue. The coronaries have been sewn directly to the graft.

Classic: The coronary ostia are sutured to two small holes in the graft; the graft is wrapped with aortic wall.

Button: All diseased aortic tissue is resected, except for small buttons of aorta surrounding the coronary ostia. These buttons are sewn directly to the graft. Native aorta is not wrapped around the graft.
**Cabrol:** Instead of direct suturing of the coronaries to the graft, an interposition graft is used between the coronaries and the ascending graft.

**Classic:** A Dacron graft is sutured to the left and right coronary arteries, and then anastomosed side-to-side to the composite graft.

**Separated Grafts:** Two separate Dacron grafts are attached one or both coronary arteries, and then connected to the composite graft. If one coronary artery does not use a Cabrol graft, a button procedure is done to attach it to the composite graft instead.

**Ascending aortic replacement:** The aortic graft is used from the level of the sinotubular junction (supracommissural) and to a level below the brachiocephalic trunk.

**Hemi-arch arch replacement:** Indicate if only the underside of the arch was replaced.

**Partial arch replacement:** indicate if only the proximal or distal portion of the arch was replaced with reimplantation of at least one of the brachiocephalic vessels

**Complete arch replacement:** Indicate if the patient underwent complete replacement of the arch of the aorta. No aortic arch tissue is left after the arch reconstruction. The arch begins at the origin of the innominate artery and ends immediately beyond the left subclavian artery. It is the portion of the aorta that gives off three important blood vessels; the innominate artery, the left carotid artery and the left subclavian artery.

**Single arterial button for supra-aortic vessels:** All arch vessel sewn into the graft in one Carel patch.

**Use of branched graft:** An aortic graft with separate branches to the brachiocephalic trunk, the left carotid and possibly to the left subclavian. **Does not mean side branch for cannulation preattached to the aortic graft.**

**Elephant trunk:** Extension of the aortic graft beyond the distal anastomosis for a secondary procedure

**Other:**

**Graft size:** (If more than one graft is used, multiple sizes can be entered).

**Use of Glue:**

**Glue Type:**

- Biologic:
- Synthetic:
Reinforce aortic anastomosis with Teflon felt: Whether or not felt was applied within or around the anastomosis.

Coronary ostium repair: Whether or not the coronary ostia have been repaired by suture or patching.

Concomitant CABG
Number of CABG (coronary aortic bypass grafting): Give the number of peripheral anastomoses

Coronary stenting: Indicate if a coronary stent has been deployed during the surgical procedure.

MV Replacement: Indicate if the mitral valve was replaced with prosthetic valve, any kind, in suprannular or annular position.

MV Repair: Indicate if the mitral valve was repaired.

TV Replacement: Indicate if the tricuspid valve was replaced with prosthetic valve.

TV Repair: Indicate if the tricuspid valve was repaired

Aortic Valve Replacement: Indicate if the aortic valve was replaced.

- Homograft (allograft): Indicate if the root prosthesis was harvested from a human cadaver.

- Mechanical: Indicate if the reconstruction was with a mechanical prosthesis attached directly to a dacron graft.

- Biological: Indicate if the reconstruction was with a stented biological valve sewn directly to a dacron graft.

- Stented: Indicate if the reconstruction was with a biological valve sewn directly to a dacron graft.

- Stentless: xenograft (heterograft). Indicate if the reconstruction was with a commercially available xenograft root prosthesis

Aortic graft size: Indicate aortic valve prosthesis size.

$Surgical procedures – (descending and thoracoabdominal)$

Use of cardiopulmonary bypass: Bypass including an oxygenator

Left heart bypass: Bypass with no oxygenator
**Open procedure:** Indicate if the anastomosis at the level of the left subclavian artery was constructed without a clamp on the aorta using circulatory arrest.

**Clamp between Left Carotid and Left Subclavian artery:** Indicate if the aortic clamp has been positioned between the origin of the left carotid artery and left subclavian artery

**Clamp after Left Subclavian artery:** Indicate if the aortic clamp has been positioned after the origin of the left subclavian artery

**Extent of repair**

**Entire Descending aortic replacement:** Indicate if the patient underwent a complete replacement of the descending aorta. The descending aorta is the portion of the aorta between the left subclavian artery and the diaphragm.

**Proximal 1/3:** Indicate if the patient underwent a replacement of proximal 1/3 of the descending aorta.

**Proximal 2/3:** Indicate if the patient underwent a replacement of proximal 2/3 of the descending aorta.

**Entire Thoracoabdominal Aortic Replacement:** Indicate if the entire thoracoabdominal aorta was replaced from the origin of the left subclavian artery to the aortic bifurcation.

**Abdominal Aortic Replacement:** Indicate if the aorta was replaced below the origin the origin of the renal arteries.

**Thoracic Aortic Fenestration:** Indicate if surgical removal of the dissection septum to permit flow in both false and true lumen has been performed in the descending aorta.

**Supra-renal Abdominal Aortic Fenestration:** Indicate if surgical removal of the dissection septum to permit flow in both false and true lumen has been performed between the origin of the celiac trunk and the origin of the renal arteries.

**Infra-renal Abdominal Aortic Fenestration:** Indicate if surgical removal of the dissection septum to permit flow in both false and true lumen has been performed in the abdominal aorta, below the origin of the renal arteries.

**Axillobifemoral bypass:** Indicate if a bypass graft between the right and/or left axillary artery and the femoral arteries has been performed to revascularize the lower extremities.

**Reinforce aortic anastomosis with teflon felt:** Whether or not felt was applied within or around the anastomosis.

**Need for visceral vessel repair (no graft):** Indicate whether or not the origin of the celiac trunk, and/or SMA, and/or renal arteries have been repaired by suture or patching.
Need for visceral vessel reimplant: Indicate whether or not the origin of the celiac trunk, and/or SMA, and/or renal arteries have been repaired by suture or patching and directly re-anastomosized on the aorta or on the aortic graft.

Need for visceral vessel fenestration: Indicate whether or not the origin of the celiac trunk, and/or SMA, and/or renal arteries have been surgically repaired opening the dissection septum to permit flow in both false and true lumen.

Use of branched graft: Indicate if it has been used an aortic graft with separate branches to the celiac trunk, and/or SMA, and/or renal arteries. Does not mean side branch for cannulation preattached to the aortic graft.

Visceral and peripheral vessels treated: Indicate whether or not one or more of the following anatomic arterial segments have been surgically treated. DO NOT CONSIDER ENDOVASCULAR TREATMENT IN THIS SECTION.

- Celiac Axis
- SMA: superior mesenteric artery
- Renal
- Iliac
- Femoral

Aorto-Distal Bypass Graft: Indicate if a bypass graft between the abdominal aorta and the iliac/or femoral arteries has been performed.

Femoro-Femoral Bypass Graft: Indicate if a bypass graft between the right femoral artery and the left femoral artery (or vice versa) has been performed.

Spinal cord protection and Adjuncts

Reimplant intercostal arteries: Indicate if the origin of some intercostals arteries has been anastomosized to the aortic graft by suture or patching.

CSF draining: Indicate if cerebral spinal fluid was drained, to lessen the decrease in perfusion to the spinal cord seen during aortic clamping.

Monitoring somatosensory evoked potentials: Indicate if detection of somatosensory evoked potentials has been done during the operation.

Monitoring motor-evoked potentials: Indicate if detection of motor evoked potentials has been done during the operation.
Selective visceral perfusion: Indicate if a perfusion of the celiac trunk and/or the superior mesenteric artery and/or the renal arteries has been conducted using cardiopulmonary bypass or left heart bypass.

Selective renal perfusion: Indicate if a perfusion of the renal arteries has been conducted using cardiopulmonary bypass or left heart bypass.

**Hybrid Surgical and Endovascular Treatment**

Frozen elephant trunk: Indicate if a frozen elephant trunk procedure was done to create a blood-tight seal between the surgical and endovascular grafts.

**Endovascular Treatment**

Vascular access:

- **Femoral**: Indicate if the endovascular procedure was done through the femoral artery

- **Iliac**: Indicate if the endovascular procedure was done though the iliac artery

- **Axillary**: Indicate if the endovascular procedure was done though the axillary artery

Closure of all thoracic entries: Indicate if all intimal entry tears were closed at the end of the procedure.

Type of stent graft:

- Medtronic
- Gore
- Cook
- Bolton
- Jotec
- Endomed
- Djumbodis
  - Model
• **Proximal Flare:** Indicate whether the proximal portion of the stent was flared to anchor it in position.

• **Proximal Free Flow:** Indicate if the proximal portion of the stent was bare metal, to allow proper stent fixation without occluding any vessels.

**Proximal Stent Graft Zone**

• **Ascending Aorta:** Begins at the sinotubular junction and ends at the origin of the innominate artery where the aorta continues as the transverse arch.

• **Aortic Arch:** Begins at the origin of the innominate artery and ends immediately beyond the left subclavian artery. It is the portion of the aorta that gives off three important blood vessels; the innominate artery, the left carotid artery and the left subclavian artery.
  - Zone 0: The ascending aorta, including the innominate artery
  - Zone 1: The portion of the aortic arch from which the left common carotid artery stems
  - Zone 2: The portion of the aortic arch that includes the origin of the left subclavian artery
  - Zone 3: The curved portion of the aortic arch distal to the left subclavian artery

• **Descending thoracic aorta:** The portion of the aorta between the left subclavian artery and the diaphragm.
  - Above T6
  - Below T6

**Distal Stent Graft Zone**

• **Descending thoracic aorta:** The portion of the aorta between the left subclavian artery and the diaphragm.
  - Above T6
  - Below T6

• **Thoraco-abdominal aorta:** The portion of the aorta caudal to the diaphragm and cranial to the aortic bifurcation.
  - **Infrarenal:** The portion of the aorta caudal to the level of the renal arteries.

**Adjunctive Procedure: Surgical**

• Indicate if any supplementary surgical procedures were performed before or during the endovascular procedure

• **Total debranching:** Indicate if all arteries that would be covered by the stent were severed and then revascularized after stent placement.
• **Innominate to carotid to subclavian bypass:** Indicate if these arteries were bypassed to allow stent deployment up to the origin of the innominate artery.

• **Carotid to subclavian bypass:** Indicate if these arteries were bypassed to allow stent deployment up to the origin of the carotic artery.

• **Abdominal branch vessel revascularization:** Indicate whether the patient received revascularization to prevent visceral artery occlusion, which can occur as a result of stent placement.

• **Femoro-Femoral Bypass:** Indicate whether the two femoral arteries were connected with a graft to maintain adequate limb perfusion.

• **Thoracic Fenestration:** Indicate whether the thoracic aorta received surgical fenestration to allow adequate artery perfusion.

• **Abdominal Fenestration:** Indicate whether the abdominal aorta (from below the diaphragm to the aortic bifurcation) received surgical fenestration to allow adequate visceral and renal artery perfusion.

**Adjunctive Procedure: Interventional**

• **Embolization:** Indicate whether an embolus was introduced into an artery to occlude blood flow.

• **Branch vessel stenting:** Indicate whether additional stent grafts were placed in the arteries branching from the aorta listed below:
  - Celiac artery stent
  - SMA stent: Superior mesenteric artery
  - Renal artery stent
  - Iliac artery stent

• **Fenestration:** Indicate whether endovascular fenestration was done to allow for adequate artery perfusion.

• **Uncovered true lumen stenting:** Indicate if a stent (NOT a stent graft) was placed in the true lumen of the aorta.

**Number of grafts:** Indicate the number of endovascular grafts that has been used during the procedure.

**Proximal graft size:** Indicate the proximal size of endovascular graft that has been used during the procedure.
**Distal graft size:** Indicate the distal size of endovascular graft that has been used during the procedure. In case of deployment of multiple grafts, indicate the distal size of the more distal endovascular graft deployed.

**Total graft length.** Indicate the total length of the endovascular prosthesis deployed during the procedure. DO NOT CONSIDER THE OVERLAPPED SEGMENT OF SUPPLEMENTAL ENDOGRAFTS.

**§Extracorporeal circulation**

**Arterial line, Cooling- Rewarming:** For cooling and rewarming the patients, indicate the artery that has been used for arterial blood in-flow.

- Right axillary artery
- Left axillary artery
- Right femoral artery
- Left femoral artery
- Apex left ventricle
- Aorta
- Carotid arteries
- Innominate Artery
- **Graft:** aortic graft or a side branch graft.
- **Other, specify**

**Venous line:** Indicate the anatomic site that has been used for the venous blood drainage.

- Right Atrium
- SVC: superior vena cava
- IVC: inferior vena cava
- Left Femoral Vein
- Right Femoral Vein
- Pulmonary Artery

Using **Left Heart Bypass: Left Atrium, Left Pulmonary Veins:** In case of patients with descending or thoracoabdominal surgical procedures in whom has been used the Left Heart Bypass, indicate if the anatomic site for the blood drainage has been the left atrium or the left pulmonary veins

**Vent line:** Indicate the anatomic site that has been used for the heart blood drainage.

- Right Superior Pulmonary Vein
- Pulmonary Artery
- Apex
- Through aortotomy
- None
Minutes cooling: Indicate minutes that have been necessary to reach the lowest temperature.

Minimum temperature: Indicate the lowest temperature during the operation and the site where it has been detected. Use Celsius degrees.

- Esophageal
- Rectal
- Bladder
- Tympanic
- Nasal

Hypothermic Circulatory Arrest: Indicate if hypothermic circulatory arrest has been adopted during the surgical operation.

EEG: Indicate if during hypothermic circulatory arrest brain activity has been monitored using electroencephalogram.

Cerebral Perfusion: Indicate if during hypothermic circulatory arrest, the brain has been perfused

- Antegrade Indicate if during hypothermic circulatory arrest, the brain has been perfuse with selective antegrade blood flow from right axillary artery and/or innominate artery and left common carotid artery.

- Retrograde Indicate if during hypothermic circulatory arrest the brain has been perfuse with retrograde blood flow from the superior vena cava.

Cerebral Perfusion Time: Indicate the interval time during which the brain had an antegrade and/or retrograde cerebral perfusion. Includes time the brain was receiving retrograde cerebral perfusion.

Cerebral Ischemia Time: Indicate the interval time during which the brain had no antegrade cerebral perfusion.

Visceral Ischemia Time: Indicate the interval time during which the visceral organs had no perfusion.

Clamping Time / Cardiac Arrest Time: Cross-clamp time in ascending/arch aortic operations is myocardial arrest time or cardiac arrest time, with no blood flow to the heart.
- In case of ascending aortic cross-clamp, when the distal aortic anastomosis was constructed with a clamp applied on the aorta, indicate the interval time between positioning and removal of aortic clamp.
- In case of ascending open procedure, when the distal anastomosis was constructed without a clamp on the aorta using circulatory arrest, indicate the interval time between the beginning and the end of the circulatory arrest.
- In case of descending/thoracoabdominal surgical procedures, if the anastomosis at the level of the left subclavian artery was constructed without a clamp on the aorta using circulatory arrest, indicate the interval time between the beginning and the end of the circulatory arrest.
- In case of descending/thoracoabdominal surgical procedures, if the anastomosis at the level of the left subclavian artery was constructed with a clamp on the aorta, indicate the interval time between positioning and removal of aortic clamp.

**Total Cardiopulmonary Bypass Time:** Indicate the time of use extracorporeal circulation for both ascending/arch surgical procedures and descending/thoracoabdominal surgical procedures, when bypass including an oxygenator was adopted.

**Left Heart Bypass Time:** Indicate the time of use a bypass with no oxygenator during descending/thoracoabdominal surgical procedures.

**Visceral Perfusion Time:**
- In case of ascending/arch surgical procedures, during hypotermic circulatory arrest, if descending/thoracoabdominal low-flow perfusion is performed from the femoral arteries or supplemental arterial lines, indicate the interval time of its use. IN THIS SPECIFIC CASE, THE INTERVAL TIME OF VISCERAL AND RENAL PERFUSION WILL BE THE SAME.
- In case of descending/thoracoabdominal surgical procedures, during cardiopulmonary bypass or left heart bypass with a selective visceral perfusion of the celiac trunk and/or the superior mesenteric artery, indicate the interval time of its use.

**Renal Perfusion Time:**
- In case of ascending/arch surgical procedures, during hypotermic circulatory arrest, if descending/thoracoabdominal low-flow perfusion is performed from the femoral arteries or supplemental arterial lines, indicate the interval time of its use. IN THIS SPECIFIC CASE, THE INTERVAL TIME OF VISCERAL AND RENAL PERFUSION WILL BE THE SAME.
- In case of descending/thoracoabdominal surgical procedures, during cardiopulmonary bypass or left heart bypass with a selective renal perfusion, indicate the interval time of its use.

**§Cardioplegia**

**Systemic K⁺:** Indicate if systemic potassium cardioplegia has been administered.

**Antegrade:** Indicate if cardioplegia has been infused from coronaries ostii

**Retrograde:** Indicate if cardioplegia has been infused from venues sinus

**Warm:** Indicate if cardioplegia utilized had temperature superior to 37* Celsius

**Cold:** Indicate if cardioplegia utilized had temperature inferior to 37* Celsius

**Blood:** Indicate if blood has been used as cardioplegia

**Crystalloid:** Indicate if a crystalloid solution has been used as cardioplegia
**Intermittent:** Indicate if cardioplegia has been infused as antegrade and/or retrograde at determined interval times.

**Continuous:** Indicate if cardioplegia has been infused as retrograde in a continuous way.

**None:** Indicate if no cardioplegia has been infused during operation.

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**§Drugs Used During Circulatory Arrest Time**

- Steroids
- Barbiturates
- Mannitol
- Nitric oxid
- Mg++
Appendix 9

IRAD informed consent form for the University Hospital North Norway.
FORESPØRSEL OM INFORMERT SAMTYKKE

Kjære

Jeg ber med dette om din tillatelse til å bruke informasjon om din helsetilstand i et internasjonalt register som tar sikte på å øke kunnskapen om en sykdomstilstand i hovedpulsåren (aortadisseksjon), da du har vært innlagt på vårt sykehus på grunn av en slik tilstand.

Det meste av informasjonen vil bli framskaffet fra dine journaler. Vi vil også gjerne kontakte ditt lokalsykehus, din fastlege og eventuelt også deg pr. telefon med ½ - 1 års mellomrom for å få opplysninger om din helse i inntil 5 år etter at du ble utskrevet fra sykehuset.

Din deltakelse i dette registeret er frivillig. Dersom du samtykker til å delta, kan du trekke deg ut når som helst.

Målet med registeret er å dokumentere medisinske detaljer om pasienter med denne tilstanden fra ulike sykehus i dette og andre land, i den hensikt å framskaffe mer kunnskap om tilstanden.

All informasjon som blir innsamlet behandles konfidensielt.

Du vil ikke selv ha noen direkte fordeler av studien, men informasjonen som framskaffes kan forhåpentligvis bidra til å bedre behandlingen for andre pasienter med samme tilstand i framtiden. Du kan avslå å delta i studien uten at dette vil få konsekvenser for kontroll eller behandlingsopplegg.

Studien innebærer ikke noen endring i oppfølgning eller behandling.

Resultatene fra undersøkelsene vil bli publisert i fagtidsskrifter, uten at noen av pasientenes navn nevnes. Dersom du har spørsmål, må du gjerne kontakte meg på følgende adresse:

Kristian Bartnes, Avdeling for hjerte-, lunge- og karkirurgi, Boks 102, Universitetssykehuset Nord-Norge. E-post: kristian.bartnes@unn.no Tlf. 77 62 60 00. Fax. 77 62 82 98
Dersom du er villig til å la oss bruke opplysninger om deg for dette registeret, er vi takknemlig om du signerer brevet og returnerer det til oss i vedlagte adresserte konvolutt.

Med vennlig hilsen

Tromsø, 21.05.07

Kristian Bartnes
Lege
Avd. for hjerte-, lunge- og karkirurgi
Universitetsklinikken i Nord-Norge

Navn:

Fødselsdato:

Jeg samtykker i at data som anført ovenfor brukes i prosjektet "The International Registry of Acute Aortic Dissections".

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signatur        sted, dato