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Endovascular Repair of Descending Thoracic Aortic Aneurysm

An Evidence-Based Analysis

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Executive Summary

Objective

To conduct an assessment on endovascular repair of descending thoracic aortic aneurysm (TAA).

Clinical Need

Aneurysm is the most common condition of the thoracic aorta requiring surgery. Aortic aneurysm is defined as a localized dilatation of the aorta. Most aneurysms of the thoracic aorta are asymptomatic and incidentally discovered. However, TAA tends to enlarge progressively and compress surrounding structures causing symptoms such as chest or back pain, dysphagia (difficulty swallowing), dyspnea (shortness of breath), cough, stridor (a harsh, high-pitched breath sound), and hoarseness. Significant aortic regurgitation causes symptoms of congestive heart failure. Embolization of the thrombus to the distal arterial circulation may occur and cause related symptoms. The aneurysm may eventually rupture and create a life-threatening condition.

The overall incidence rate of TAA is about 10 per 100,000 person-years. The descending aorta is involved in about 30% to 40% of these cases.

The prognosis of large untreated TAAs is poor, with a 3-year survival rate as low as 25%. Intervention is strongly recommended for any symptomatic TAA or any TAA that exceeds twice the diameter of a normal aorta or is 6 cm or larger. Open surgical treatment of TAA involves left thoracotomy and aortic graft replacement. Surgical treatment has been found to improve survival when compared with medical therapy. However, despite dramatic advances in surgical techniques for performing such complex operations, operative mortality from centres of excellence are between 8% and 20% for elective cases, and up to 50% in patients requiring emergency operations. In addition, survivors of open surgical repair of TAAs may suffer from severe complications. Postoperative or postprocedural complications of descending TAA repair include paraplegia, myocardial infarction, stroke, respiratory failure, renal failure, and intestinal ischemia.

The Technology

Endovascular aortic aneurysm repair (EVAR) using a stent graft, a procedure called endovascular stent-graft (ESG) placement, is a new alternative to the traditional surgical approach. It is less invasive, and initial results from several studies suggest that it may reduce mortality and morbidity associated with the repair of descending TAAs.

The goal in endovascular repair is to exclude the aneurysm from the systemic circulation and prevent it from rupturing, which is life-threatening. The endovascular placement of a stent graft eliminates the systemic pressure acting on the weakened wall of the aneurysm that may lead to the rupture. However, ESG placement has some specific complications, including endovascular leak (endoleak), graft migration, stent fracture, and mechanical damage to the access artery and aortic wall.

The Talent stent graft (manufactured by Medtronic Inc., Minneapolis, MN) is licensed in Canada for the treatment of patients with TAA (Class 4; licence 36552). The design of this device has evolved since its clinical introduction. The current version has a more flexible delivery catheter than did the original system. The prosthesis is composed of nitinol stents between thin layers of polyester graft material. Each stent is secured with oversewn sutures to prevent migration.

Review Strategy

Objectives

- To compare the effectiveness and cost-effectiveness of ESG placement in the treatment of TAAs with a conventional surgical approach
- To summarize the safety profile and effectiveness of ESG placement in the treatment of descending TAAs

Measures of Effectiveness

Primary Outcome

- Mortality rates (30-day and longer term)

Secondary Outcomes

- Technical success rate of introducing a stent graft and exclusion of the aneurysm sac from systemic circulation
- Rate of reintervention (through surgical or endovascular approach)

Measures of Safety

Complications were categorized into 2 classes:

- Those specific to the ESG procedure, including rates of aneurysm rupture, endoleak, graft migration, stent fracture, and kinking; and
- Those due to the intervention, either surgical or endovascular. These include paraplegia, stroke, cardiovascular events, respiratory failure, real insufficiency, and intestinal ischemia.

Inclusion Criteria

- Studies comparing the clinical outcomes of ESG treatment with surgical approaches
- Studies reporting on the safety and effectiveness of the ESG procedure for the treatment of descending TAAs

Exclusion Criteria

- Studies investigating the clinical effectiveness of ESG placement for other conditions such as aortic dissection, aortic ulcer, and traumatic injuries of the thoracic aorta
- Studies investigating the aneurysms of the ascending and the arch of the aorta
- Studies using custom-made grafts

Literature Search

The Medical Advisory Secretariat searched The International Network of Agencies for Health Technology Assessment and the Cochrane Database of Systematic Reviews for health technology assessments. It also searched MEDLINE, EMBASE, Medline In-Process & Other Non-Indexed Citations, and Cochrane CENTRAL from January 1, 2000 to July 11, 2005 for studies on ESG procedures. The search was limited to English-language articles and human studies.

One health technology assessment from the United Kingdom was identified. This systematic review included all pathologies of the thoracic aorta; therefore, it did not match the inclusion criteria. The search yielded 435 citations; of these, 9 studies met inclusion criteria.

Summary of Findings

Mortality

- The results of a comparative study found that in-hospital mortality was not significantly different between ESG placement and surgery patients (2 [4.8%] for ESG vs. 6 [11.3%] for surgery).
- Pooled data from case series with a mean follow-up ranging from 12 to 38 months showed a 30-day mortality and late mortality rate of 3.9% and 5.5%, respectively. These rates are lower than are those reported in the literature for surgical repair of TAA.
- Case series showed that the most common cause of early death in patients undergoing endovascular repair is aortic rupture, and the most common causes of late death are cardiac events and aortoesophageal or aortobronchial fistula.

Technical Success Rate

- Technical success rates reported by case series are 55% to 100% (100% and 94.4% in 2 studies with all elective cases, 89% in a study with 5% emergent cases, and 55% in a study with 42% emergent cases).

Surgical Reintervention

- In the comparative study, 3 (7.1%) patients in the ESG group and 14 (26.5%) patients in the surgery group required surgical reintervention. In the ESG group, the reasons for surgical intervention were postoperative bleeding at the access site, paraplegia, and type 1 endoleak. In the surgical group, the reasons for surgery were duodenal perforation, persistent thoracic duct leakage, false aneurysm, and 11 cases of postoperative bleeding.
- Pooled data from case series show that 9 (2.6%) patients required surgical intervention. The reasons for surgical intervention were endoleak (3 cases), aneurysm enlargement and suspected infection (1 case), aortic dissection (1 case), pseudoaneurysm of common femoral artery (1 case), evacuation of hematoma (1 case), graft migration (1 case), and injury to the access site (1 case).

Endovascular Revision

- In the comparative study, 3 (7.1%) patients required endovascular revision due to persistent endoleak.
- Pooled data from case series show that 19 (5.3%) patients required endovascular revision due to persistent endoleak.

Graft Migration

- Two case series reported graft migration. In one study, 3 proximal and 4 component migrations were noted at 2-year follow-up (total of 5%). Another study reported 1 (3.7%) case of graft migration. Overall, the incidence of graft migration was 2.6%.

Aortic Rupture

- In the comparative study, aortic rupture due to bare stent occurred in 1 case (2%). The pooled

incidence of aortic rupture or dissection reported by case series was 1.4%.

Postprocedural Complications

- In the comparative study, there were no statistically significant differences between the ESG and surgery groups in postprocedural complications, except for pneumonia. The rate of pneumonia was 9% for those who received an ESG and 28% for those who had surgery (P = .02). There were no cases of paraplegia in either group. The rate of other complications for ESG and surgery including stroke, cardiac, respiratory, and intestinal ischemia were all 5.1% for ESG placement and 10% for surgery. The rate for mild renal failure was 16% in the ESG group and 30% in the surgery group. The rate for severe renal failure was 11% for ESG placement and 10% for surgery.
- Pooled data from case series show the following postprocedural complication rates in the ESG placement group: paraplegia (2.2%), stroke (3.9%), cardiac (2.9%), respiratory (8.7%), renal failure (2.8%), and intestinal ischemia (1%).

Time-Related Outcomes

- The results of the comparative study show statistically significant differences between the ESG and surgery group for mean operative time (ESG, 2.7 hours; surgery, 5 hours), mean duration of intensive care unit stay (ESG, 11 days; surgery, 14 days), and mean length of hospital stay (ESG, 10 days; surgery, 30 days).
- The mean duration of intensive care unit stay and hospital stay derived from case series is 1.6 and 7.8 days, respectively.

Ontario-Based Economic Analysis

In Ontario, the annual treatment figures for fiscal year 2004 include 17 cases of descending TAA repair procedures (source: Provincial Health Planning Database). Fourteen of these have been identified as "not ruptured" with a mean hospital length of stay of 9.23 days, and 3 cases have been identified as "ruptured," with a mean hospital length of stay of 28 days. However, because one Canadian Classification of Health Interventions code was used for both procedures, it is not possible to determine how many were repaired with an EVAR procedure or with an open surgical procedure.

Hospitalization Costs

The current fiscal year forecast of in-hospital *direct* treatment costs for all in-province procedures of repair of descending TAAs is about $560,000 (Cdn). The forecast in-hospital *total* cost per year for in-province procedures is about $720,000 (Cdn). These costs include the device cost when the procedure is EVAR (source: Ontario Case Costing Initiative).

Professional (Ontario Health Insurance Plan) Costs

Professional costs per treated patient were calculated and include 2 preoperative thoracic surgery or EVAR consultations.

The professional costs of an EVAR include the fees paid to the surgeons, anesthetist, and surgical assistant (source: fee service codes). The procedure was calculated to take about 150 minutes.

The professional costs of an open surgical repair include the fees of the surgeon, anesthetist, and surgical assistant. Open surgical repair was estimated to take about 300 minutes.

Services provided by professionals in intensive care units were also taken into consideration, as were the costs of 2 postoperative consultations that the patients receive on average once they are discharged from the hospital. Therefore, total Ontario Health Insurance Plan costs per treated patient treated with EVAR are on average $2,956 (ruptured or not ruptured), as opposed to $5,824 for open surgical repair and $6,157 for open surgical repair when the aneurysm is ruptured.

Conclusions

- Endovascular stent graft placement is a less invasive procedure for repair of TAA than is open surgical repair.
- There is no high-quality evidence with long-term follow-up data to support the use of EVAR as the first choice of treatment for patients with TAA that are suitable candidates for surgical intervention.
- However, short- and medium-term outcomes of ESG placement reported by several studies are satisfactory and comparable to surgical intervention; therefore, for patients at high risk of surgery, it is a practical option to consider. Short- and medium-term results show that the benefit of ESG placement over the surgical approach is a lower 30-day mortality and paraplegia rate; and shorter operative time, ICU stay, and hospital stay.

Abbreviations

AAA	Abdominal aortic aneurysm
CCI	Canadian Classification of Health Interventions
ICD	International Statistical Classification of Disease and Related Health Problems
Endoleak	Endovascular leak
ESG	Endovascular stent-graft
EUROSTAR	European Collaborators on Stent Graft Techniques for Thoracic Aortic Aneurysm and Dissection Repair
EVAR	Endovascular aortic aneurysm repair
FSC	Fee service code
ICU	Intensive care unit
OCCI	Ontario Case Costing Initiative
OHIP	Ontario Health Insurance Plan
OSR	Open surgical repair
TAA	Thoracic aortic aneurysm

Objective

To conduct an assessment on endovascular repair of descending thoracic aortic aneurysm (TAA).

Background

Clinical Need: Target Population and Condition

Most diseases of the thoracic aorta are serious or life-threatening conditions (1) that can present in either an acute or chronic setting. Thoracic aortic aneurysms, aortic dissections, and penetrating ulcers of the aorta pose a major risk of death to the patient. The optimal approach for the repair of aorta in these pathologies poses a challenge for vascular and cardiothoracic surgeons. Most of these pathologies occur in the elderly. Moreover, comorbid conditions like hypertension, coronary artery disease, obstructive pulmonary disease, and congestive heart failure are often seen in these patients.

Surgical treatment for these conditions is associated with a high mortality rate that increases with emergency cases. (1) With the development and refinement of endovascular techniques to treat these pathologies, many patients previously turned down for surgery due to co-existing illnesses are now referred and treated with an endovascular stent-graft (ESG) procedure. The application of the technology now is shifting toward offering ESG procedures as an alternative treatment for patients with TAAs and other pathologies of the thoracic aorta.

Studies show that the rates of associated comorbid conditions, including paraplegia, renal failure, and cardiac and pulmonary complications are significantly lower with ESG procedures than with conventional "open" surgical treatment or repair. (2) This allows for faster recovery, shorter intensive care unit and hospital stays, and better midterm survival. (2)

Atherosclerosis

Atherosclerosis is a leading cause of morbidity and death in older people. It affects various regions of the circulatory system and yields distinct clinical manifestations depending on the particular circulatory bed affected. After a prolonged "silent" period, atherosclerosis may clinically manifest as myocardial infarction (a heart attack), angina pectoris, stroke or transient ischemic attack, intermittent claudication, mesentric ischemia, and renal failure. (3)

Patients with severe atherosclerosis (plaques > 4 mm deep) of the ascending aorta and the arch have a high prevalence of atheromatous emboli in the cerebral circulation, which may lead to stroke. (4-6) They are also at high risk of embolization and stroke after manipulation of the ascending aorta during coronary artery bypass graft surgery and other cardiac procedures. (5;7;8) The presence of severe atheromatous disease in the distal aortic arch and the descending aorta can cause embolization to the visceral, renal, and peripheral arteries.

The aorta is the main arterial trunk of the systemic circulation. It ascends for about 5 cm from the upper part of the left ventricle where it is about 3 cm in diameter, then arches to the left and backward over the root of the left lung. It then descends within the thorax on the left side of the vertebral column, enters the abdominal cavity through the aortic hiatus in the diaphragm, and diminishes in size to about 1.75 cm in diameter. It finally bifurcates into the right and left common iliac arteries. (9)

The most common diseases or conditions that affect the thoracic aorta are TAA, aortic dissection, aortic ulcer, and traumatic aortic rupture.

Thoracic Aortic Aneurysm

Not all manifestations of atherosclerosis result from stenosis (abnormal narrowing) or occlusion (blockage). Development of an aneurysm in an aorta, for example, is another form of lesion evolution that accounts for variability in the clinical expression of atherosclerotic disease. Vessels affected by atherogenesis tend to increase in diameter, a phenomenon known as compensatory enlargement. Therefore, due to arterial remodeling, an atheroma (a mass of plaque) will not cause stenosis that can limit blood flow until the plaque exceeds about 40% of the arterial lumen.

Aneurysm is the most common condition of the thoracic aorta that requires surgery. (10) Aortic aneurysm is defined as a localized dilatation of the aorta. Most aneurysms of the thoracic aorta are asymptomatic and discovered incidentally. (11) However, aneurysms tend to enlarge progressively and compress surrounding structures causing symptoms such as chest or back pain, dysphagia (difficulty swallowing), dyspnea (breathlessness), cough, stridor (a harsh, high-pitched breath sound), and hoarseness. Significant aortic regurgitation causes symptoms of congestive heart failure. Embolization of the thrombus to the distal arterial circulation may occur and cause related symptoms. The aneurysm may eventually rupture and create a life-threatening condition.

The prognosis of large, untreated TAAs is poor, with a 3-year survival rate as low as 25%. (12) Therefore, surgical treatment is justified unless comorbid medical illnesses contraindicate it. Reasonable indications for surgery include symptomatic TAA, aneurysm diameter of 6 cm or greater, an aneurysm that enlarges under observation, and one in a patient with poorly controlled hypertension.

Aortic Dissection

Aortic dissection results when blood separates the layers of aortic wall, usually through a tear in the intima, the layer that is in direct contact with the flow of blood. This tear occurs most commonly in the ascending aorta, adjacent to the aortic valve. It can also occur in the arch and the descending thoracic aorta. (10) Hypertension is the most important risk factor for thoracic aortic dissection. Dissection may extend to the adjacent aortic wall, or an aneurysm may develop weeks after the dissection due to the weak outer wall of the dissected aorta.

Two classifications of aortic dissection are widely used: The DeBackey classification, which includes 3 types (types 1 to 3), and the Stanford classification, which includes 2 types, A and B. Type A includes all cases in which the ascending aorta is involved, with or without involvement of the arch or the descending aorta. Type B includes cases in which the descending thoracic aorta is involved, with or without proximal or distal extension. (10)

Most early deaths from all types of aortic dissection are due to rupture of the aorta into the pleural cavity or pericardium. (10) Death may also occur due to the obstruction of the origin of the coronary artery, brachiocephalic artery, or visceral arteries by the dissecting hematoma. (13;14)

Aortic Ulcer

Atherosclerotic lesions of the thoracic aorta may ulcerate and penetrate the aortic wall. (10) This may result in separation of the media and formation of intramural hematoma. Penetrating atherosclerotic ulcers

occur most commonly in the descending aorta.

Traumatic Aortic Rupture

Severe blunt trauma to the chest can lead to aortic transection or rupture. Traumatic aortic rupture leads to death immediately after the injury in 85% of cases. About 20% to 30% further mortality occurs in those who reach an emergency room and undergo emergency operation. (2) However, those who survive may have significant morbidity due to accompanying head injury, abdominal injury, and fractures. Paraplegia, paralysis of the lower limbs and trunk, is the most devastating complication that can occur following aortic cross-clamping during surgical repair. High-volume trauma centres usually adopt techniques to prevent spinal cord ischemia to decrease paraplegia rates.

Clinical Symptoms of Thoracic Aortic Aneurysm and Aortic Dissection

In many patients, aneurysms are detected during testing for other disorders. Thoracic aortic aneurysms may remain asymptomatic until the enlargement of the aorta results in compression on the adjacent structures. Dysphagia results from pressure on the lumen of the esophagus, dyspnea results from compression of the lung, hoarseness results from stretching of the left recurrent laryngeal nerve, stridor results from compression of the trachea, and plethora and edema result from compression of the superior vena cava. Patients may have symptoms of aortic regurgitation and congestive heart failure due to dilatation of the aortic valve annulus and aortic valve regurgitation. Patients may also present with pain in their neck and jaw, scapular area, or with left-sided pleuritic pain. Patients with a thoracoabdominal aneurysm may present with abdominal pain and pain in the left shoulder due to the irritation of the left hemidiaphragm. (10)

Typical symptoms of acute aortic dissection include sharp pain in the anterior part of the chest, neck, or between the shoulders. Other symptoms may be present due to compression of branches of aorta. This includes acute myocardial infarction, stroke or ischemic neurologic deficits, paraplegia, renal failure, intestinal ischemia, and ischemia of the arms and legs.

Existing Treatments Other Than Technology Being Reviewed

Surgical Treatment of Thoracic Aortic Pathologies

Open surgical treatment of TAA involves left thoracotomy and aortic graft replacement. Surgical treatment has been found to improve survival when compared with medical therapy. (15) Recent 5-year survival rates range from 60% to 70%. (2) However, despite dramatic advances in surgical techniques for performing such complex operations, operative mortality from centres of excellence are between 8% and 20% for elective cases, (2) and up to 50% in patients requiring emergency operation. (16) In addition, survivors of open surgical repair of TAAs may suffer from severe complications.

Although surgical indications for TAA repair are relatively straightforward, the optimal therapy for type B dissection remains somewhat controversial. (17) In some institutions, medical therapy with aggressive antihypertensive medications and ß-blockers is used, and operative treatment is reserved for cases in which life-threatening complications such as progression of the dissection, end-organ ischemia, or rupture are present. (2;17)

Treatment of the acute penetrating aortic ulcer is similar to that of dissection. Persistent or recurrent pain and rapidly expanding aortic diameter are indications for surgical intervention. However, risk of rupture is higher for penetrating aortic ulcers than for type B dissections (40% vs. 4%); (2) therefore, it is important to diagnose and treat the pathology appropriately.

Evaluation of Patients for Surgical Procedures

The American Society of Anesthesiologists' (ASA) physical status classification is routinely used as a guide to estimate the clinical condition of the patient. (18) (See Table 1.)

Table 1: American Society of Anesthesiologists' Physical Status Classification

Class 1	Normal healthy patient
Class 2	Patient with mild systemic disease
Class 3	Patient with severe systemic disease
Class 4	Patient with severe systemic disease that is a constant threat to life
Class 5	Morbid patient who is not expected to survive without the operation
Class 6	Brain dead patient (patient whose organs are being removed for donor purposes)

This scale indicates the patient's overall physical health prior to selecting the anesthesia technique and performing surgery. Surgery to repair TAA is invasive and high-risk. It requires thoracotomy, aortic cross-clamping, and left-sided heart bypass. Therefore, patients with severe morbidities (ASA class 3 and 4) are poor surgical candidates at higher risk of mortality or postoperative morbidity.

Indications for Intervention

Intervention is strongly recommended for any symptomatic TAA or any TAA that exceeds twice the diameter of a normal aorta, or is 6 cm or larger. (16) An analysis of 1,600 patients with TAA and dissection with 3,000 patient-years of follow-up showed that the aortic size at which rupture or dissection occurred was 6 cm for the ascending aorta and 7 cm for the descending aorta. (19) Therefore, intervention was recommended for the ascending aorta at 5.5 cm and for the descending aorta at 6.5 cm. For Marfan disease, intervention was recommended at 5 cm for the ascending and 6 cm for the descending aorta.

Complications Following Repair of Thoracic Aortic Aneurysm

Postoperative or postprocedural complications of descending TAA repair include paraplegia, myocardial infarction, stroke, respiratory failure, renal failure, and intestinal ischemia.

Paraplegia

During the surgical repair or EVAR of descending TAA, intercostal arteries that supply the anterior spinal cord may be sacrificed, resulting in spinal cord ischemia and injury. The incidence of neurological deficits following surgical repair of thoracic aneurysms varies from 4% to 38%. (20) The risk of this complication was shown to be greatest in patients with extensive lesions, aortic rupture, and aortic dissection. (21) One of the risk factors for developing paraplegia after ESG placement is a history of abdominal aortic aneurysm (AAA) repair. (22)

During surgery, several factors contribute to the development of paraplegia. These include the aortic cross-clamp time, the exclusion of the critical intercostals arteries, and the extension of the replaced aortic segment. (23)

Biglioli et al. (23) compared the incidence of paraplegia and mortality following 3 different methods to prevent spinal cord ischemia during operations on descending TAAs. Patients were divided into 3 groups: atriodistal bypass (group 1), simple clamping (group 2), and quick simple clamping (group 3). The incidence of paraplegia was 4.8%, 14.3%, and 0% in the 3 groups, respectively ($P < .05$; group 3 vs.

group 2). Multivariate logistic regression showed a powerful effect of aortic cross-clamping time as a risk factor for paraplegia ($P < .008$, odds ratio, 1.03/minute), and in-hospital mortality ($P < .001$, odds ratio, 2.5/minute). Patients were followed-up for a mean 65 months. The mortality rate was significantly lower in group 3 compared with groups 1 and 2 ($P < .05$).

An increase in cerebrospinal fluid pressure may result in a decrease in spinal cord perfusion pressure. This is the physical principle and the rational for the use of cerebrospinal fluid drainage before surgical repair of TAA. A systematic review and meta-analysis have provided evidence that the use of cerebrospinal fluid drainage is effective when used in centres with experience in the management of TAA. (24)

Specific Complications of Endovascular Repair of Thoracic Aortic Aneurysm

Endovascular leak

Endovascular leak (endoleak) is defined as the persistence of blood flow within the aneurysm sac outside of the lumen of the stent graft. (25) Endoleaks are classified into 5 types. Type 1 involves a leak around the stent graft at the proximal or distal fixation sites due to incomplete seal. Type 2 is the retrograde flow into the aneurysm from collateral arteries. Type 3 is due to the leaks through fabric defects or through graft-to-graft attachment sites. Types 4 and 5 refer to graft porosity or endotension. (25;26)

There are distinct differences between various types and frequencies of endoleaks after stent grafting of TAAs and AAAs. There is a clear indication that endoleaks occur less frequently after repair of TAAs. (25;26) It is generally accepted that a type 1 endoleak is a more serious condition than a type 2 endoleak. (26) In type 1 endoleak, the effect from the forces of aortic arterial pressure is transmitted directly to the aneurysm after graft replacement and is a potentially lethal condition. Aggressive endovascular or surgical intervention is recommended if type 1 or 3 endoleaks occur more than 2 to 4 weeks following stent graft replacement. (26)

Graft Migration

Graft migration is the downward slippage of the graft, and it occurs at an incidence of 0% to 30%. (25) Higher rates have been associated with earlier designs and multiple overlapping of endografts. (25)

Mechanical Damage to the Aortic Wall

Acute retrograde type A dissection can occur during or after the ESG procedure (27) and may have been underreported. (27) Retrograde extension of the dissections that originate in the descending aorta may lead to aortic valve regurgitation, cerebrovascular ischemia, cardiac temponade, and obstruction of the coronary artery.

Additionally, the use of stent graft oversizing to achieve secure proximal sealing may contribute to intimal injuries. (28;28) Forced and repeated balloon dilatation of the aorta to form a tight seal is another important factor that contributes to intimal injuries. (28) For patients with anatomical tortuosity of the aorta, surgical repair or using more flexible devices is recommended.

Epidemiology

Atherosclerosis is the most common cause of aneurysmal disease. Presently, the incidence of AAAs greatly exceeds that of TAAs owing to the decline in the incidence of syphilitic aneurysms. (10) The overall incidence of TAAs is estimated to be 10 per 100,000 person-years. (2;29) The descending aorta is

involved in about 30% to 40% of these cases. (29)

A Swedish study (30) scrutinized autopsy records from 1958 to 1985 and calculated prevalence and incidence according to age and sex. The overall incidence of TAA was 489 per 100,000 autopsies in men and 437 per 100,000 autopsies in women. The median age at which the TAA was verified at autopsy was 77.7 years for men and 85.3 for women ($P < .05$). The rate of thoracoabdominal aneurysms was 5.3%, and there were no differences attributed to sex. Asymptomatic TAA was highest among men aged 75 to 79 years, whereas the peak occurrence in women appeared 10 years later. The incidence of rupture was 0.9 per 100,000 for men and 1.0 per 100,000 for women.

The mortality rate associated with ruptured TAAs is high. A retrospective analysis of compiled data from multiple registries in Sweden showed the overall rate of ruptured TAAs to range from 70% to 100%. Clouse et al. (29) reported that the 5-year risk of rupture as a function of aneurysm size at diagnosis is 0% for aneurysms less than 4 cm in diameter, 16% (95% confidence interval, 4%–28%) for those 4 to 5.9 cm, and 31% (95% confidence interval, 5%–56%) for aneurysms 6 cm or more.

New Technology Being Reviewed

Endovascular aortic aneurysm repair using an ESG is a new alternative to the traditional surgical approach. It is less invasive, and initial results from several studies (25) suggest that it may reduce the rates of mortality and morbidity associated with repair of descending TAAs.

The goal of EVAR is to exclude the aneurysm from systemic circulation and prevent it from rupturing, which is life threatening. The endovascular placement of a stent graft eliminates the systemic pressure acting on the weakened wall of the aneurysm that may lead to a rupture. A primary technical success rate is defined on an intention-to-treat basis and requires the successful introduction and deployment of the graft in the absence of the following: (31)

- Mortality
- Surgical conversion
- Persistent endoleak (type 1 or 2)
- Significant twist, kinks, or obstruction

Before the procedure, all patients have routine examinations. These include computed tomography scans and computed tomography angiography to determine the anatomical feasibility for the procedure, location and size of the aneurysm; and the relationship between the aneurysm and aortic branches, such as the left subclavian artery and the celiac trunk.

The procedure takes place in an operating room and is visualized under fluoroscopy. Different anesthetic techniques have been described for aortic stent graft placement. Choice of anesthetic technique depends on the planned intervention and the patient's comorbid conditions. Some procedures may take longer. In these cases, a general anesthesia may be administered to increase a patient's compliance. Regional anesthesia, including an epidural, continuous epidural, spinal anesthesia, and local anesthetic supplemented by sedation, may be used. Because of the possibility of acute aortic rupture during the procedure, the anesthesiology and operating room team must be prepared for an open surgical procedure.

During the procedure, an access site is created by surgical cut-down of the femoral artery. Other vascular access, for example, via the common iliac artery or an infrarenal aorta, is also possible. Through the arteriotomy, a guide wire is introduced and positioned in the descending aorta. The delivery catheter is

then introduced over the guide wire to access the implant location. The prosthesis is collapsed over the distal segment of the delivery catheter and maintained on a packed configuration. Once the stent graft is properly positioned, usually within 1 to 3 cm of the proximal landing zone, the overlying sheath is slowly withdrawn. After deployment, the graft expands and lines the aortic wall. The delivery catheter is then removed, and a balloon is introduced to expand the graft fully and seal the proximal and distal necks.

The length of the proximal and distal "landing zones" is important for graft deployment. The proximal landing zone has to be distal to the left subclavian artery; therefore, in situations where this artery is expected to be covered by the graft, a carotid to subclavian artery transposition or bypass is performed prior to the procedure. During the procedure, the location of proximal and distal landing zones can be confirmed by transesophageal ultrasound.

Types of Endovascular Stent-Grafts and Regulatory Status

Stent-grafts are available in a range of diameters and lengths, and custom fabrication of prosthesis is possible. The most widely used commercial devices are these ones:

- Talent (manufactured by Medtronic Inc., Minneapolis, MN)
- Excluder (manufactured by W.L. Gore and Associates, Flagstaff, AZ)
- Zenith TX2 TAA endovascular graft (manufactured by William Cook Europe)
- Endofit (manufactured by Endomed, Flagstaff, AZ)
- The Vanguard (manufactured by Boston Scientific, Natick, MA)
- AneuRX stent-graft system (manufactured by Medtronic AVE, CA)

The Talent stent is the only one Health Canada has licensed for use in Canada for the treatment of patients with TAA (Class 4; licence 36552). The design of this device has evolved since its clinical introduction. The current version has a more flexible delivery catheter than did the original system. (26) The prosthesis is composed of nitinol stents between thin layers of polyester graft material. Each stent is secured with oversewn sutures to prevent migration, but they are not connected to one another, and there are segments of unsupported graft interposed between the stents. This design allows independent stent motion and confers a degree of longitudinal flexibility. The Talent stent has 2 longitudinal wires to provide stabilization and prevent longitudinal compression. (26)

Anatomical characteristics must be considered when choosing a graft. For example, the Excluder is better suited for patients with severely angled anatomy or iliofemoral arteries that are tortuous, small, or calcified, while the Talent device may be preferred in TAA cases with short proximal necks or in aortic dissection where the primary artery tear is very close to the subclavian artery. (26)

Larger diameter devices are used in the thoracic aorta, as compared to those used in the AAA (32) which may become problematic in elderly patients with coexisting occlusive disease within the iliofemoral arteries. If 2 or more grafts are needed for complete aneurysm exclusion, an overlapping zone of 2 to 3 cm will be considered.

Objectives

There were 2 main objectives: to compare the effectiveness and cost-effectiveness of ESG placement in the treatment of TAAs with the conventional surgical approach, and to summarize the safety profile and effectiveness of ESG placement in the treatment of descending TAAs.

Questions Asked

- How do outcomes of treatment with ESG in descending TAA compare with those with obtained with conventional open surgical techniques?
- Is there any risk associated with the use of ESG placement for the treatment of descending TAAs?

Methods

Measures of Effectiveness

Mortality rates (30-day and longer term) were the primary outcome of interest in this category.

Technical success rates of introducing a stent graft and exclusion of the aneurysm sac from systemic circulation, and rates of reintervention (through surgical or endovascular approach) were the secondary outcomes of interest.

Measures of Safety

Complications were categorized into 2 classes:

- Those specific to the ESG procedure, including aneurysm rupture, endovascular leak, graft migration, stent fracture, and kinking; and
- Those due to the intervention, either surgical or endovascular, including paraplegia, stroke, cardiovascular events, respiratory failure, real insufficiency, and intestinal ischemia.

Inclusion Criteria

- Studies comparing the clinical outcomes of ESG placement with surgical approaches
- Studies reporting on the safety and effectiveness of the ESG procedure for the treatment of descending TAAs

Exclusion Criteria

- Studies investigating the clinical effectiveness of ESG placement for other conditions, such as aortic dissection, aortic ulcer, and traumatic injuries of the thoracic aorta
- Studies investigating aneurysms of the ascending aorta and the arch of the aorta
- Studies using custom-made grafts

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Literature Search

The Medical Advisory Secretariat searched The International Network of Agencies for Health Technology Assessment and the Cochrane Database of Systematic Reviews for health technology assessments. It also searched MEDLINE, EMBASE, MEDLINE In-Process & Other Non-Indexed Citations, and Cochrane CENTRAL from January 1, 2000, to July 11, 2005 for studies on ESG procedures. The search was limited to English-language articles and human studies

Results of Literature Review

One health technology assessment from the United Kingdom was identified. This systematic review

included all pathologies of the thoracic aorta; therefore, it was excluded. The search yielded 435 citations. Nine studies met inclusion and exclusion criteria.

Grading the Evidence

To grade the strength of the body of evidence the grading system formulated by the GRADE Working Group (33) and adopted by the Medical Advisory Secretariat was applied. The grading system classifies quality of evidence as high (grade A), moderate (grade B), or low (grade C) according to 4 key elements: study design, study quality, consistency across studies, and directness. (See Appendix 3.)

Summary of Medical Advisory Secretariat Review

Types of Included Studies

One retrospective study (34) compared the outcomes of ESG placement with those of the surgical approach. Seven case series included 5 cohort studies (35-39) and 2 retrospective studies. (40;41) One (35) of the cohort studies was a large multicentre trial. One (42) was a small cohort study that compared the outcomes of ESG treatment with a historical group of patients who underwent surgical repair of TAA. Data from this study was analyzed for the ESG group only, given that there was no indication of comparability between the 2 groups. Most of the outcomes of interest were documented.

Comparative Study by Glade et al.

Glade et al. (34) conducted a multicentre case-control study and compared the results of ESG placement with the results of open surgery for repair of descending TAA. Ninety-five consecutive patients with a mean age of 67 years (range 39–81 years) who underwent either surgical repair or EVAR of TAA were included. There was no statistically significant difference between the open surgical repair and ESG groups in age and preoperative risk factors including hypertension, smoking, chronic obstructive pulmonary disease, diabetes, angina pectoris, previous myocardial infarction, previous coronary artery bypass graft surgery, renal failure, stroke, and previous carotid surgery. There were 9 patients in the open surgical group and 7 in the ESG group who were symptomatic. Fifty-three patients underwent open surgical repair; 42 patients received an ESG. A mean 2.1 (range, 1–4) endografts per patient were implanted. Patient characteristics, devices used, and duration of follow-up are shown in Table 2.

Table 2: Patient Characteristics, Devices Used, and Length of Follow-up in Glade et al.*†

Patients, n	95 Endovascular stent-graft: 42 Surgery: 53
Symptomatic TAA	Endovascular stent-graft: 7 (17%) Surgery: 9 (17%)
Physical status	Endovascular stent-graft vs. surgery: Hypertension: 86% vs. 75% COPD/smoking: 60% vs. 81% Diabetes: 12% vs. 6% Angina pectoris: 21% vs. 11% Previous myocardial infarction: 25% vs. 15% Previous coronary artery bypass graft surgery: 17% vs. 8% Renal failure: 14% vs. 13% TIA/CVA/previous carotid surgery: 19% vs. 9% None were significant
Aneurysm diameter, mean (range), mm	Endovascular stent-graft: 61 (40–80) Surgery: 65 (45–90)
Age, mean (range)	67 (39–81)
Gender	Male: 59 Female: 36
Stent graft, n	Talent: 24 Excluder: 17 AneuRX: 1
ESG implanted, mean (range)	2.1 per patient (1–4)
Cerebrospinal fluid drainage	Was performed routinely
Concomitant repair of AAA, no. (%)	0 (0)
Duration of follow-up, mean (range), months	Endovascular stent-graft: 15 (1–48) Surgery: 26 (3–82)

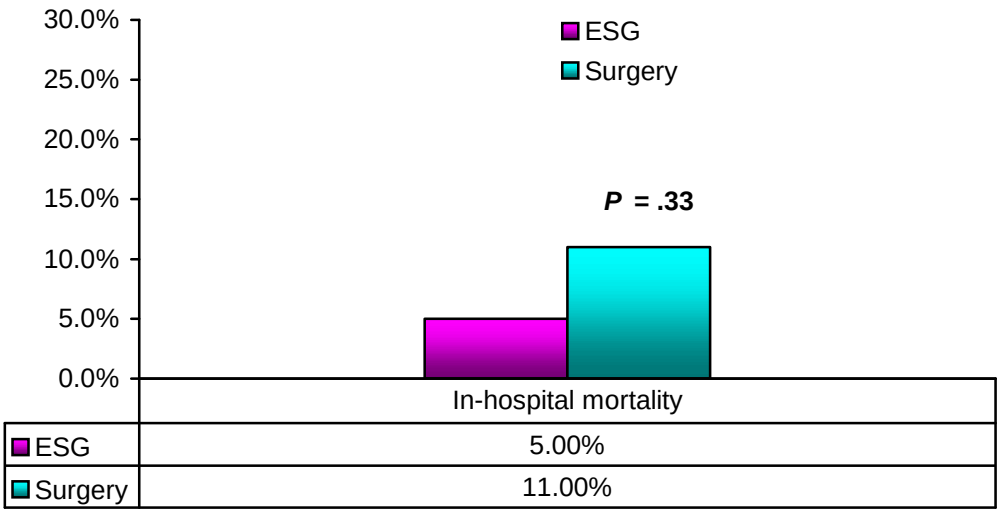
*COPD indicates chronic obstructive pulmonary disease; CVA, cerebrovascular accident; TIA, transient ischemic attack.
† Glade et al. (34)

Results: Primary and Secondary Outcomes

The rate of technical success was not reported.

Two (5%) patients in the ESG group, and 6 (11%) patients in the surgical group died in hospital; this difference was not statistically significant (Figure 1 on the next page).

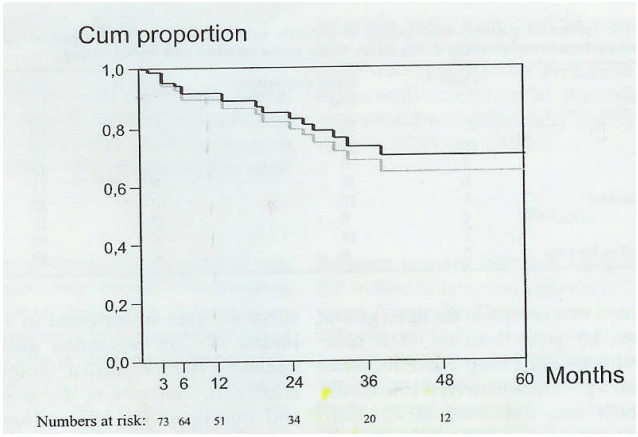
Figure 1: In-Hospital Mortality Rates in the Endovascular and Open Surgical Repair Groups in Glade et al. (34)



	In-hospital mortality
ESG	5.00%
Surgery	11.00%

Survival after a mean follow-up of 15 months (range, 1–48) for the ESG group and 26 months (range, 3–82) for the open surgical repair group was not significantly different. The proportion of survivors was 92% after 1 year and 73% after 3 years (Figure 2).

Figure 2: Survival Rates for Patients Undergoing Endovascular and Surgical Repair of Descending Thoracic Aortic Aneurysm in Glade et al. (34)



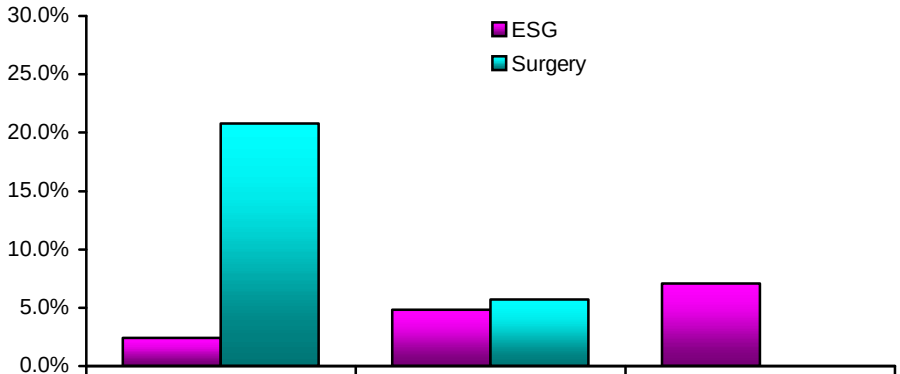
Reprinted from the European Journal of Vascular & Endovascular Surgery, 29(1), Glade GJ, Vahl AC, Wisselink W, Linsen MA, Balm R. Mid-term survival and costs of treatment of patients with descending thoracic aortic aneurysms; endovascular vs. open repair: a case-control study, 28–34. Copyright 2005, with permission from Elsevier.

This study used a model to predict the influence of preoperative risk factors (heart failure, renal failure, acute aneurysm, diameter of the aneurysm, and smoking) and postoperative risk factors (reoperation, occurrence of pneumonia, paraplegia, cardiac or intestinal ischemia, time of anesthesia, duration of intensive care unit [ICU] stay, and length of hospital admission) on midterm survival. None of these factors proved to be significantly associated with the midterm survival in either group.

Looking at reintervention, reoperation during the same admission was performed in 13 patients in the open surgical repair group compared with 2 in the ESG group. Reasons for reoperation in the surgery group were postoperative bleeding (n = 11), duodenal perforation (n = 1), and persistent thoracic duct leakage (n = 1). The reasons for the 2 reoperations in the ESG group were postoperative bleeding at access site and paraplegia. During follow-up, 1 reoperation in the open surgical group was performed after 1.5 years because of a false aneurysm. In the ESG group, 1 patient had a type 1 endoleak and was converted to an open procedure.

In the ESG group, 3 patients required additional stent graft implantation. Early type 1 endoleaks in 2 patients and contained perforation caused by bare stent after 4.5 months in 1 patient required additional stent graft implantation. Rates of reoperation and restenting are shown in Figure 3.

Figure 3: Rates of Reoperation and Restenting in Glade et al. (34)



	Surgery for postoperative bleeding	Surgery for aneurysm related complications*	Endovacular revision
ESG	2.4%	4.8%	7.1%
Surgery	20.8%	5.7%	0.0%

*In the ESG group, 2 patients had surgery (1 for paraplegia and 1 for type 1 endoleak). In the surgery group, 3 patients had surgery (1 for duodenal perforation, 1 for persistent thoracic duct leakage, and 1 for false aneurysm).

Results: Specific Complications of Endovascular Grafting

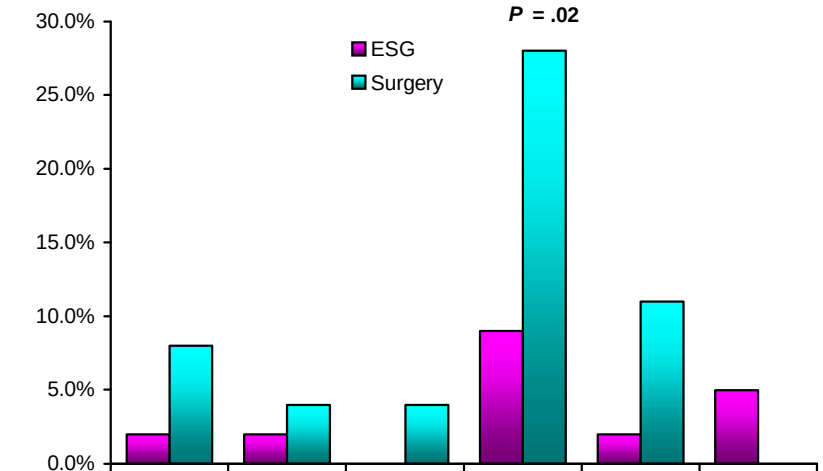
This study did not report whether there were cases of endoleak or graft migration that did not require further intervention. Three patients had endovascular reintervention (2 for type 1 endoleaks and 1 for contained perforation caused by a bare stent).

Results: Postprocedural Morbidities

The rate of pneumonia was significantly lower in the ESG group than in the open surgical repair group (9% vs. 28%, *P* = .02). The rates of myocardial infarction, stroke, and renal failure were also lower in the ESG group, but the rate of intestinal ischemia was lower in the surgery group. None of these differed significantly between groups.

The incidence of paraplegia was 2% in the ESG group and 8% in the open surgical repair group, but this was not statistically significant either. Of 14 patients in the open surgical group who were operated on without distal perfusion, 3 (21%) developed paraplegia, versus 1 (2.6%) of 39 patients who was operated on with distal perfusion (*P* < .01). Figure 4 shows the incidence of postprocedural complications.

Figure 4: Rates of Postoperative Complications for Endovascular and Surgical Methods in Glade et al. (34)

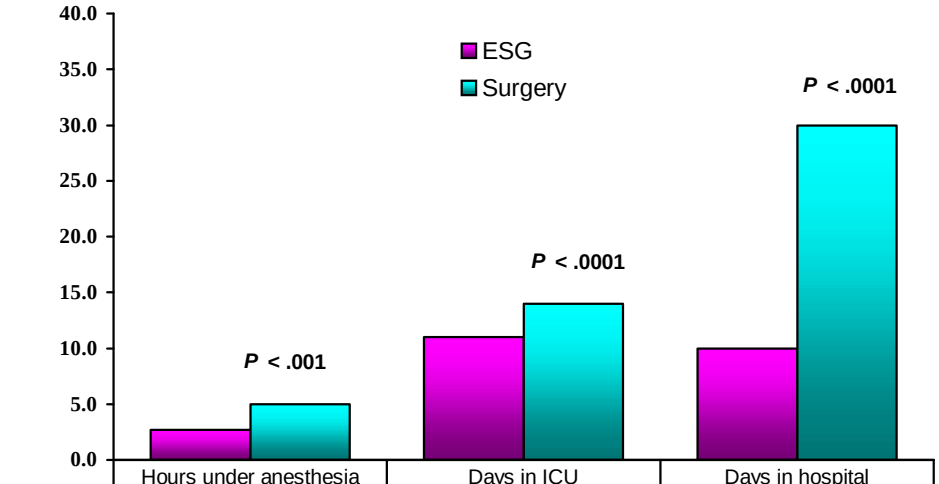


	Paraplegia	MI	Stroke	Pneumonia	Renal failure	Intestinal ischemia
ESG	2.00%	2.00%	0.00%	9%	2%	5%
Surgery	8.00%	4.00%	4.00%	28%	11%	0%

Results: Time-Related Outcomes

The mean anesthesia time, duration of ICU stay, and duration hospital stay were significantly shorter for patients in the ESG group than for those in the open surgical repair group (Figure 5).

Figure 5: Mean Anesthesia Time, ICU Stay, and Hospital Stay for Endovascular and Open Surgical Groups in Glade et al. (34)



	Hours under anesthesia	Days in ICU	Days in hospital
ESG	2.7	11.0	10.0
Surgery	5.0	14	30.0

The findings of Glade and colleagues' study support the results of an earlier case-control study on the repair of TAAs. Ehrlich et al. (43) reported on a series of 68 patients with a mean age of 51 years and a mean aneurysm size of 7 cm. Ten patients received ESG placement (9 atherosclerotic aneurysm, and 1 chronic dissection), and 58 patients had conventional surgical treatment. The 30-day mortality rate in the ESG group was 10%. It was 31% in the conventional surgery group. There was no spinal cord injury in the ESG group compared with an incidence of 12% in the conventional surgery group. However, due to the small number of patients in the ESG group, the difference in the mortality and paraplegia rates did not reach significance. Mean intervention time was 320 minutes in the ESG group and 150 minutes in the surgery group ($P < .05$). Mean duration of ICU stay was also shorter in ESG group (4 days in ICU and 6 days on the ward, compared with 13 days in ICU and 10 days on the ward; $P < .05$).

Results of Case Series

Graft Deployment

Deployment of the device was reported by 7 studies. The data show that in 95% to 100% of cases, the device was successfully deployed (Table 3).

Table 3: Rates of Successful Graft Deployment in Case Series Reviewed*

Study, Year	Patients	Mean Follow-up, Months	Symptomatic TAA, No. (%)	Successful Deployment, No. (%)
Makaroun et al., 2005 (35)	142	24.0	0 (0.0)	139 (98)
Bortone, 2004 (40)	41	21.0	5 (12.0)	NR
Neuhauser, 2004 (36)	31	15.0	13 (42.0)	30 (97)
Czerny et al., 2004 (41)	54	38.0	0 (0.0)	54 (100)
Lepore et al., 2003 (37)	21	17.0	7 (33.3)	21 (100)
Schoder et al., 2003 (38)	28	22.7	0 (0.0)	28 (100)

Study, Year	Patients	Mean Follow-up, Months	Symptomatic TAA, No. (%)	Successful Deployment, No. (%)
Najibi et al., 2002 (42)	19	12.0	1 (5.3)	18 (95)
Heijmen et al., 2002 (39)	27	21.0	5 (18.5)	26 (96)
Total, all studies	363		31 (8.5)	

*TAA indicates thoracic aortic aneurysm; NR, not reported.

Technical Success

Four studies reported technical success rates. The lowest rate of technical success was reported by Neuhauser et al. (36) This study had also the highest rate of emergency cases. Table 4 shows technical success rates for all case series.

Table 4: Technical Success Rates in Case Series Reviewed*

Study, Year	Patients, No.	Mean Follow-up, Months	Symptomatic TAA, No. (%)	Technical Success Rate, %
Makaroun et al., 2005 (35)	142	24.0	0 (0.0)	NR
Bortone, 2004 (40)	41	21.0	5 (12.0)	NR
Neuhauser, 2004 (36)	31	15.0	13 (42.0)	55.0
Czerny et al., 2004 (41)	54	38.0	0 (0.0)	94.4
Lepore et al., 2003 (37)	21	17.0	7 (33.3)	NR
Schoder et al., 2003 (38)	28	22.7	0 (0.0)	100
Najibi et al., 2002 (42)	19	12.0	1 (5.3)	89.0
Heijmen et al., 2002 (39)	27	21.0	5 (18.5)	NR
Total, all studies	363		31 (8.5)	

*TAA indicates thoracic aortic aneurysm; NR, not reported.

Mortality

About 36% of the early deaths were due to the causes that cannot be attributed directly to the procedure. The cause of late death was unrelated to the procedure in 75 % of the patients. However, stroke, cardiac events, respiratory failure, and metastatic cancer naturally occur in an older population, and it is difficult to determine whether these events are related to the procedure or not. Many patients die of non-aneurysm related causes, because TAAs occur in an older population that has a life expectancy less than that of the general population. The pooled early mortality rate was 3.9%; the pooled late mortality rate was 5.5%.

Table 5 shows pooled data for early and late mortality.

Table 5: Early and Late Mortality Rates for 363 Patients in Case Series Reviewed*

Study, Year	Patients, No.	Mean Follow-up, Months	Symptomatic TAA, No. (%)	30-Day Mortality, No. (%)	Late Mortality, No. (%)
Makaroun et al., 2005 (35)	142	24.0	0 (0.0)	2 (1.4)	2 (1.5)
Bortone, 2004 (40)	41	21.0	5 (12.2)	1 (2.4)	0 (0.0)
Neuhauser, 2004 (36)	31	15.0	13 (42.0)	6 (19.3)	7 (22.6)
Czerny et al., 2004 (41)	54	38.0	0 (0.0)	2 (3.7)	3 (5.6)
Lepore et al., 2003	21	17.0	7 (33.3)	2 (10.0)	3 (14.0)

(37)					
Schoder et al., 2003 (38)	28	22.7	0 (0.0)	0 (0.0)	3 (11.0)
Najibi et al., 2002 (42)	19	12.0	1 (5.3)	1 (5.3)	1 (5.0)
Heijmen et al., 2002 (39)	27	21.0	5 (18.5)	0 (0.0)	1 (3.7)
Total, all studies	363		31 (8.5)	14 (3.9)	20 (5.5)

*TAA indicates thoracic aortic aneurysm.

The highest mortality rates were reported in the study by Neuhauser et al., (36) in which 42% of the patients were symptomatic. The 30-day mortality rate was 6 (19%) of 31patients, and about one-half of these were directly aneurysm related. In 2 patients, the aortic diameter was large, resulting in failure to exclude the aneurysm and consequent endoleak. This resulted in compression and finally erosion of the tracheobronchial system in one patient and aneurysm rupture in another (confirmed by autopsy). Failed aneurysm exclusion resulted in rupture into the pleural cavity and death in the third patient. The cause of death in 1 of 7 patients who died during the follow-up was also aneurysm related.

The details of causes of early and late mortality are shown in Table 6 (next page).

Table 6: Causes of Early and Late Mortality in Case Series Reviewed*

Study, Year	Early Death, Number	Late Death, Number
Makaroun et al., 2005 (35)	**2** 1: Cardiac 1: Stroke	**2** 1: Aortoesophageal fistula and respiratory failure 1: Reoperation for aneurysm enlargement and suspected infection → the patient was found to have aortoesophageal fistula → the fistula was repaired successfully → on postoperative day 13, the patient experienced respiratory arrest and anoxic brain injury
Bortone, 2004 (40)	**1:** Unexplained	**0**
Neuhauser, 2004 (36)	**6** 2: The ostium of the left carotid artery was covered with bare springs → surgery was impossible due to comorbid conditions and further ESG procedures were impossible due to anatomical limitations → hemorrhage of aortobronchial fistula in one and aneurysm rupture in another. 1: Failed aneurysm exclusion → aneurysm rupture into the pleural cavity 2: Myocardial infarction 1: Respiratory failure	**7** 1: Aortic rupture 6: Unrelated death
Czerny et al., 2004 (41)	**2** 1: Dislocation of the stent into aneurysm sac → aneurysm rupture 1: Narrowing of the celiac axis → multiorgan failure	**3** 1: Myocardial infarction 1: Liver failure 1: Metastatic colon cancer
Lepore et al., 2003 (37)	**2** 1: Embolic intestinal necrosis → The patient had concomitant repair of AAA and also received 4 thoracic ESGs) 1: Multiorgan failure → the patient had 4 prior cardiac surgeries → was on artificial ventilation and had renal insufficiency at the time of operation → had a ruptured TAA → died at day 4 from multiorgan failure.	**3** 1: Myocardial infarction and abdominal ischemia requiring bowel resection 1: Sudden death due to aortic rupture (the patient had undergone emergency grafting because of a ruptured TAA and received 5 stent grafts [2 GORE, 3 Talent] covering all the thoracic portion of the descending aorta during a long and troublesome procedure → Aortic rupture due to bare stent of the device. 1: Heart failure
Schoder et al., 2003 (38)	**0**	**3** 1: Hepatic 1: Heart failure 1: Metastatic colon cancer
Najibi et al., 2002 (42)	**1:** No conclusion was made	**1:** No conclusion was made
Heijmen et al., 2002 (39)	**0**	**1:** Stroke

*ESG indicates endovascular stent-graft; TAA, thoracic aortic aneurysm.

The most common cause of early death was aortic rupture. The most common causes of late death were cardiac events and aortoesophageal or aortobronchial fistula. Certain causes of death could be attributed to the procedure. During the 30 days after the procedure, 3 patients died of aortic rupture. Narrowing of celiac and embolic intestinal necrosis caused the deaths of 2 patients. One patient died of aortobronchial fistula that resulted in hemorrhage. Two patients died of aortoesophageal or aortobronchial fistula, and aortic rupture in 2 patients was fatal. Therefore, overall, 10 (29%) of 34 deaths were procedure related. The remaining causes of death could not be attributed directly to the procedure.

Survival Data

Five studies reported survival rates for patients who underwent ESG procedures (Table 7).

Table 7: Survival Rates for Endovascular Stent-Graft Procedures in Case Series Reviewed

Study, Year	1-Year Survival Rate, %	2-Year Survival Rate, %	3-Year Survival Rate, %
Makaroun et al., 2005 (35)	—	Aneurysm-related: 97 Overall: 75	—
Czerny et al., 2004 (41)	—	—	Event-free: 63
Neuhauser et al., 2004 (36)	61.1	47.4	—
Lepore et al., 2003 (37)	81 (SD, 8.6)	73.6 (SD, 10.5)	—
Schoder et al., 2003 (38)	Cumulative: 96.1 (SD, 3.8)	Actuarial: 90.9 (SD, 6.2)	Actuarial: 80.2 (SD, 11.5)

Specific Complications of Endovascular Grafting

Aortic Rupture

The incidence of aortic rupture or dissection across 8 case series was 1.4% (Table 8).

Table 8: Endovascular Stent-Graft Placement: Rates of Aortic Rupture or Dissection

Study, Year	Patients, N	Mean Follow-up, Months	Aortic Rupture/Dissection, No. (%)
Makaroun et al., 2005 (35)	142	24.0	0 (0.0)
Bortone, 2004 (40)	41	21.0	0 (0.0)
Neuhauser, 2004 (36)	31	15.0	3 (9.7)
Czerny et al., 2004 (41)	54	38.0	1 (1.9)
Lepore et al., 2003 (37)	21	17.0	1 (4.8)
Schoder et al., 2003 (38)	28	22.7	0 (0.0)
Najibi et al., 2002 (42)	19	12.0	0 (0.0)
Heijmen et al., 2002 (39)	27	21.0	0 (0.0)
Total, all studies	363		5 (1.4)

Endovascular Leak

The most common type of endovascular leak (endoleak) was type 1. Overall, the incidence of any endoleak was 18.4%. Table 9 shows the incidence of different types of endoleak reported by studies on ESG placement. Across all studies and types of endoleak, there were 67 (18.4%) endoleaks.

Table 9: Endovascular Stent-Graft Placement: Rates of Endovascular Leakage

Study, Year	Patients	Mean Follow-up, Months	Type 1, No. (%)	Type 2, No. (%)	Type 3, No. (%)	Type Not Specified, No. (%)
Makaroun et al., 2005 (35)	142	24	1 (0.7)	4 (2.8)	0 (0.0)	4 (2.8)
Bortone, 2004 (40)	41	21	0 (0.0)	0 (0.0	0 (0.0)	0 (0.0)
Neuhauser, 2004 (36)	31	15	13 (41.9)	4 (12.9)	3 (9.7)	0 (0.0)
Czerny et al., 2004 (41)	54	38	7 (13.0)	7 (13.0)	4 (7.4)	0 (0.0)

Lepore et al., 2003 (37)	21	17	4 (19.0)	0 (0.0)	0 (0.0)	0 (0.0)
Schoder et al., 2003 (38)	28	22.7	5 (17.9)	4 (14.3)	0 (0.0)	0 (0.0)
Najibi et al., 2002 (42)	19	12	0.0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Heijmen et al., 2002 (39)	27	21	2 (7.4)	4 (14.8)	0 (0.0)	1 (3.7)
Total, all studies	363		32 (8.8)	23 (6.3)	7 (1.9)	5 (1.4)

Thirty-two (8.8%) type 1, 28 (6.3%) type 2, and 7 (1.9%) type 3 endoleaks were reported for 363 patients. There were 5 (1.4%) endoleaks for which type was not specified. Table 10 shows the rates and methods of reintervention to treat these endoleaks.

Table 10: Fate of Endoleaks

Study, Year	Type of Endoleak	Number of Endoleaks	Treatment of Endoleak
Makaroun et al., 2005 (35)	Early endoleak	Type 1: 1 Type 2: 4	- 1 was treated by endovascular revision and insertion of an additional stent. The patient had another revision after 24 months. - 4 were treated conservatively.
	Late endoleak	Type not specified: 4	- 3 were treated by endovascular revision (total of 4 revisions). - 1 surgical conversion.
Bortone et al., 2004 (40)	Early endoleak	0	
	Late endoleak	0	
Neuhauser et al., 2004 (36)	Early endoleak	Type 1: 7 Type 2: 4 Type 3: 2	- 1 underwent surgery. - 2 treated by additional stent graft. - 2 patients were unsuitable for either endovascular or surgical treatment; both died. - 1 patient declined further therapy. - 1 patient developed a stroke on the first postoperative day and declined further therapy. (Both patients who declined further therapy survived 12 and 30 months after stent grafting.) - 2 sealed spontaneously. - 2 had stable aneurysm diameter and remained under observation. - 1 was treated with an additional stent graft. - 1 died on the first postoperative day due to aorto-bronchial fistula
	Late endoleak	Type 1: 6 Type 3: 1	- 4 were treated by additional stent grafts. - 2 patients declined further therapy. - 1 was treated by an additional stent graft.
Czerny et al., 2004 (41)	Early endoleak	Type 1: 3	- 1 healed spontaneously. - 1 treated by additional stent. - 1 treated by radiation.

Study, Year	Type of Endoleak	Number of Endoleaks	Treatment of Endoleak
	Late endoleak	Type 1: 4	- 1 treated by additional stent. - 1 treated by performing thoracoabdominal replacement of the entire aorta with left heart bypass. - 2 were under observation.
		Type 2: 7	- 1 sealed spontaneously. - 1 was embolized. - 5 were being observed because there was no increase in aneurysm diameter.
		Type 3: 4	- 1 healed spontaneously. - 3 were being observed because of the small size aneurysm
Lepore et al., 2003 (37)	Early endoleak	Type 1: 4	- 1 was restented successfully on fourth postoperative day. -1 was restented twice at 4 and 14 days after the procedure. - 2 had trivial leaks that were treated conservatively.
	Late endoleak	0	
Schoder et al., 2003 (38)	Early endoleak	Type 1: 5	- 3 were sealed spontaneously. - 1 was treated by an extension graft. - 1 was treated with reballooning.
		Type 2: 3	- 3 were under observation; this persisted at 1year follow-up.
	Late endoleak	Type 2: 1	- 1 was successfully treated by embolization of the intercostals arteries.
Najibi et al., 2002 (42)	Early endoleak	0	
	Late endoleak	0	
Heijmen et al., 2002 (39)	Early endoleak	Type 2: 4	- All 4 were treated conservatively.
	Late endoleak	Type 1: 2	- 2 were treated with the extension.
		Type not specified: 1	- This was treated conservatively.

Nineteen (5.2%) patients required reintervention through insertion of an additional stent graft (14 for type 1, and 2 for type 3 endoleaks; in 3 cases, the type of endoleak was not specified). Three of these patients were restented twice. Three (0.8%) patients required open surgery (2 for type 1, and 1 for unspecified type). Four (1.1%) patients required other treatment to treat endoleaks (2 required an embolization [for type 2 endoleaks]; 1, radiation therapy; and 1, reballooning [for type 1]).

Four of 32 type 1 endoleaks sealed spontaneously, 4 were treated conservatively or went under observation, 14 were restented, 2 underwent surgery, 1 was treated by radiation therapy, 1 was treated by reballooning, 2 were unsuitable for endovascular or surgical intervention (patients eventually died). Four patients with endoleak declined further therapy.

Most of the type 2 endoleaks did not require treatment; however, 2 cases were treated by embolization of the associated arteries. Of the 7 type 3 endoleaks, 1 healed spontaneously, 3 were small and went under observation, and 2 required restenting. One patient with a type 3 endoleak died on the first postoperative day due to aortobronchial fistula. Of the 5 endoleaks for which type was not specified (4 in the study by Makaroun et al. (35)), 3 were restented, 1 underwent surgery, and 1 was treated conservatively.

Graft Migration

Two studies reported on graft migration. The overall incidence of graft migration was 2.6% (Table 11). Makaroun et al. (35) reported 3 proximal and 4 component migrations without associated clinical events.

Table 11: Rate of Graft Migration*

Study, Year	Patients	Mean Follow-up, Months	Graft Migration, No. (%)
Makaroun et al., 2005 (35)	142	24.0	7 (5.0)
Bortone, 2004 (40)	41	21.0	0 (0.0)
Neuhauser, 2004 (36)	31	15.0	NR
Czerny et al., 2004 (41)	54	38.0	0 (0.0)
Lepore et al., 2003 (37)	21	17.0	0 (0.0)
Schoder et al., 2003 (38)	28	22.7	NR
Najibi et al., 2002 (42)	19	12.0	0 (0.0)
Heijmen et al., 2002 (39)	27	21.0	1 (3.7)
Total, all studies	363		8 (2.2)

*NR indicates not reported.

Stent Fracture

Makaroun et al. (35) reported 20 stent fractures in 19 patients. However, only 1 patient required treatment. Most of the fractures (18 of 20) occurred at the longitudinal spine of the stent. However, the original device used in this study was discontinued in 2001 after a report detailing high rates of stent fractures was released. (www.FDA.gov) The device was redesigned and re-entered the market in 2004.

Reintervention

Ten (2.8%) cases required surgery following ESG procedures (3 [1.1%] patients due to endoleaks). Nineteen (5.2%) patients with endoleaks required additional stent grafting, and 4 (1.1%) were treated by radiation, embolization, or reballooning (Table 12).

Table 12: Rates of Reintervention

Study, Year	N	Mean Follow-up, Months	Early Endovascular Revision, No.	Late Endovascular Revision, No.	Early Reoperation, No.	Late Reoperation, No.	Other Intervention, No.
Makaroun et al., 2005 (35)	142	24	1*	3*	1†	2 (1*, 1‡)	0
Bortone, 2004 (40)	41	21	0	0	0	0	0
Neuhauser, 2004 (36)	31	15	0	8*	1*	1§	0
Czerny et al., 2004 (41)	54	38	1*	1*	0	1*	2 (1‖, 1¶,)
Lepore et al., 2003 (37)	21	17	2*	0	0	0	0
Schoder et al., 2003 (38)	28	22.7	1*	0	0	0	2 (1‖, 1#)
Najibi et al., 2002 (42)	19	12	0	0	2 (1**, 1††)	0	0
Heijmen et al., 2002 (39)	27	21	0	2*	2‡‡	0	0

Study, Year	N	Mean Follow-up, Months	Early Endovascular Revision, No.	Late Endovascular Revision, No.	Early Reoperation, No.	Late Reoperation, No.	Other Intervention, No.
Total, No. (%)	363		5 (1.4)	14 (3.9)	6 (1.7)	4 (1.1)	4 (1.1)

* For endoleak.
† For extraction of the misplaced device.
‡ For aneurysm enlargement and suspected infection.
§ For aortic dissection.
‖Embolization for endoleak.
¶ Radiation for endoleak.
# Reballooning for endoleak.
** For pseudoaneurysm of common femoral artery.
†† For evacuation of hematoma and ileofemoral bypass.
‡‡ For graft migration.

Postprocedural Morbidity

The incidences of postprocedural complications are shown in Table 13.

Table 13: Rates of Complications After Endovascular Stent-Graft Placement*

Study, Year	N	Stroke, No. (%)	Cardiac, No. (%)	Respiratory, No. (%)	Renal Failure, No. (%)	Intestinal Ischemia, No. (%)
Makaroun et al., 2005 (35)	142	5 (3.5)	4 (2.8)	14 (10.0)	0 (0.0)	1 (0.7)
Bortone, 2004 (40)	41	1 (2.4)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Neuhauser, 2004 (36)	31	1 (3.2)	2 (6.5)	3 (9.7)	1 (3.2)	0 (0.0)
Czerny et al., 2004 (41)	54	NR	NR	NR	NR	NR
Lepore et al., 2003 (37)	21	2 (9.5)	2 (9.5)	3 (14.3)	1 (4.8)	1 (4.8)
Schoder et al., 2003 (38)	28	1 (3.6)	0 (0.0)	3 (10.7)	1 (3.6)	0 (0.0)
Najibi et al., 2002 (42)	19	1 (5.3)	1 (5.3)	1 (5.3)	5 (26.3)	1 (5.3)
Heijmen et al., 2002 (39)	27	1 (3.7)	0 (0.0)	2 (7.4)	NR	NR
Total, all studies†	363	12 (3.9)	9 (2.9)	27 (8.7)	8 (2.8)	3 (1.0)

*NR indicates not reported.
†The total for some outcomes is less than 363. The proportions calculated reflect this.

Paraplegia

Paraplegia is one of the most feared postoperative complications of an open surgical approach. (2) The incidence of paraplegia has ranged from 20% to 30% in earlier studies of surgical repair, (2) but has improved recently with numerous adjunctive advances in spinal cord protection. (44) The incidence of neurological deficits following surgical repair of thoracic aneurysms ranges from 4% to 38%. (20) It has been shown that aortic cross-clamping is a risk factor for paraplegia. (34) The pooled incidence of paraplegia from recent studies comprising mainly patients treated for descending TAA is 6.1% in 604 patients who have had open surgery and 2.4% in 544 patients who have had an ESG procedure. (34)

Spinal cord ischemia can result from interruption of critical intercostals and lumbar arteries, thrombosis and embolism of lumbar arteries, distal aortic hypotension after aortic occlusion, and hypotension or hypoxemia. (20) There is no opportunity to implant intercostal arteries with this new technique. Covering of the intercostal arteries with the stent graft is much important in distal descending thoracic repair than the proximal part. For example, an earlier study (43) that compared the outcomes of endovascular grafting with surgical repair reported no paraplegia with ESG placement compared with a rate of 12% of

paraplegia in the surgery group. This result is not surprising, because all of the patients in the ESG group in this study had proximal descending aneurysms.

Table 14 shows the incidence of paraplegia in the case series reviewed.

Table 14: Incidence of Paraplegia After Endovascular Stent-Graft Placement

Study, Year	Patients, No.	Mean Follow-up, Months	Symptomatic Thoracic Aortic Aneurysm, No.	Paraplegia, No. (%)
Makaroun et al., 2005 (35)	142	24.0	0	4 (2.8)
Bortone, 2004 (40)	41	21.0	5	0 (0.0)
Neuhauser, 2004 (36)	31	15.0	13	2 (6.5)
Czerny et al., 2004 (41)	54	38.0	0	0 (0.0)
Lepore et al., 2003 (37)	21	17.0	7	2 (9.5)
Schoder et al., 2003 (38)	28	22.7	0	0 (0.0)
Najibi et al., 2002 (42)	19	12.0	1	0 (0.0)
Heijmen et al., 2002 (39)	27	21.0	5	0 (0.0)
Total, all studies	363		31	8 (2.2)

The pooled incidence of paraplegia (2.2%) is lower in studies of thoracic endografting compared with rates reported in the literature for patients who underwent surgery. Five of 8 case series reported no paraplegia.

The highest incidence of paraplegia (2 cases [9.5%]) was reported by Lepore et al. (37) In their study, patients whose lower part of the thoracic aorta (segment T8-L1) was planned to be covered by the stent graft were treated by spinal drainage preoperatively and during the first 48 hours postoperatively. One of these 2 cases was a patient who was stented for rupture of the aneurysm and had received 5 stent grafts to cover an aneurysm that engaged the entire descending aorta.

In Neuhauser's study, (36) 2 (6%) patients had paraplegia. Retrospectively, both patients had an increased risk for developing neurological deficits. One patient developed a bilateral leg weakness on the third day after placement of a single stent graft for proximal descending TAA repair. In this patient, the orifice of the left subclavian artery was fully covered by the stent graft, resulting in reduced blood supply to the spinal cord through the anterior spinal artery. Further intercostal arteries were also lost due to a coexisting 5 cm infrarenal aortic aneurysm. This patient gained partial recovery through physiotherapy. The other patient had had an AAA repair 4 years earlier. The left subclavian artery was covered by bare springs, and vital intercostal arteries were covered by 3 thoracic stent grafts. This patient suffered from complete paraplegia without recovery. Techniques to prevent paraplegia were not used in Neuhauser's study.

In Makaroun and colleagues' study, (35) spinal drainage was not routinely used during the procedure. Four (3%) patients developed spinal cord events. Three of these had more than 1 device implanted (one had 2; one had 3; and one had 4). The rate of spinal cord events was higher in patients who had had previous abdominal aortic replacement, compared with those who had not (4.7% vs. 2%, $P = .36$). One patient developed bilateral lower extremity weakness after the intervention; despite receiving a spinal drainage immediately after the intervention, her deficits persisted. The second patient had a hypotensive episode during the procedure and developed paraplegia 6 hours after the intervention. The symptoms improved after the patient was stabilized and a spinal drainage was performed. At the last follow-up, this patient was able to walk using a walker. The third patient exhibited lower extremity weakness and numbness 1 day after the procedure. However, her symptoms improved by the time of discharge and were near the baseline at 1-month follow-up. The fourth patient had less strength in the proximal muscles of the

leg 1 day after the procedure. This patient was treated with aggressive blood pressure support and improved within 24 hours.

Time-Related Outcomes

Table 15 shows the duration of hospital and ICU stay. Across studies, the mean length of hospital stay was 7.8 days; the mean ICU stay was 1.6 days.

Table 15: Length of Stay in the Intensive Care Unit and Hospital*

Study, Year	Patients, No.	Mean Follow-up, Months	No. Days in Hospital, Mean	No. Days in ICU, Mean
Makaroun et al., 2005 (35)	142	24.0	7.6	2.6
Bortone, 2004 (40)	41	21.0	NR	NR
Neuhauser, 2004 (36)	31	15.0	NR	NR
Czerny et al., 2004 (41)	54	38.0	9.2	3.4
Lepore et al., 2003 (37)	21	17.0	NR	NR
Schoder et al., 2003 (38)	28	22.7	9.0	0.4
Najibi et al., 2002 (42)	19	12.0	6.2	0.8
Heijmen et al., 2002 (39)	27	21.0	7.0	1.0
Mean no. days, across studies			7.8	1.6

*ICU indicates intensive care unit; NR, not reported.

Change in Aneurysm Size

Change in aneurysm size or diameter was reported on by 6 studies. Follow-up data show that aneurysm size decreased in most patients (Table 16).

Table 16: Changes in Aneurysm Size*

Study, Year	Patients, No.	Mean Follow-up, Months	Aneurysm Diameter, Mean (SD; Range), mm	Change in Aneurysm Size/Diameter
Makaroun et al., 2005 (35)	142	24.0	64.1 (15.4; 20–110)	Decreased: in 38% Increased: in 17%
Bortone, 2004 (40)	41	21.0	NR	NR
Neuhauser, 2004 (36)	31	15.0	Median, 65 (22; 25–110	NR
Czerny et al., 2004 (41)	54	38.0	73 (61–93)	Decreased: Year 1: -9.1%, *P* = .002 Year 2: -10.7%, *P* = .002
Lepore et al., 2003 (37)	21	17.0	> 50	NR
Schoder et al., 2003 (38)	28	22.7	65.6 (11.3; 50–96)	Decreased: in 67% Increased: in 11% Unchanged: in 22% Decreased significantly in patients without apparent endoleak at any time (-10.4%, *P* = .001)
Najibi et al., 2002 (42)	19	12.0	68 (22)	Decreased: -19 (SD,10 mm); *P* < .01
Heijmen et al., 2002 (39)	27	21.0	66 (15)	Stable or decreased slightly over time in all but 1 patient who had evidence of endoleak

*NR indicates not reported.

Pooled data from case series were compared to the data from a large European registry. The European Collaborators on Stent Graft Techniques for Thoracic Aortic Aneurysm and Dissection Repair (EUROSTAR) and the United Kingdom Thoracic Endograft Registries have published their combined experience on endovascular grafting for pathologies of thoracic aorta. (45) Four hundred and forty-three patients underwent endovascular repair of thoracic aortic disease between September 1997 and August 2003 (EROSTAR: 340 patients; United Kingdom registry: 103 patients). Patients represented 4 major disease groups (n = 249, degenerative aneurysm; n =131, aortic dissections; n = 13, false aneurysm; and n = 50, traumatic aortic injuries). Results were reported separately for each category. Table 17 lists the clinical outcomes of endovascular repair for TAA reported by the European registry aligned with the pooled outcomes derived from case series included in this assessment.

Table 17: Report From European Registries: Endovascular Repair of Atherosclerotic Aneurysms*

	EUROSTAR and United Kingdom Registry† (Duration of Follow-up, 12 Months)	Case Series‡ (Duration of Follow-up, 12–38 Months)
Technical success, %	87	55–100
Early mortality, %	Overall: 10.4 Elective: 5.3 Emergent: 28 (*P* < .0001)	Overall: 3.9
Late mortality, %	At I year: 10	5.5
Type 1 endoleak, %	Early: 7.6 At I year: 4.2	8.8
Graft migration, %	0	2.6
Aneurysm rupture, %	1	1.7
Reintervention, %	5.2	9 (via surgery: 2.8; via ESG placement 5.2; via other methods 1)
Paraplegia/paresis, %	4	2.2
Stroke, %	2.8	3.9

*ESG indicates endovascular stent-graft.
†(45)
‡(35-42)

In the category of aortic aneurysm, many patients (52%) had serious comorbid conditions. They were classified as ASA greater than 3 and therefore unsuitable candidates for open surgery. Patients had a mean age of 71 years. Emergency procedures were performed in 24% of the cases. Most of the outcomes reported by the European registry concord with the pooled outcomes derived from the case series. Early mortality was 5.3% for elective cases and 28% for emergent cases. One-year survival was 80%. The highest mortality rates were reported by 2 studies (36;37) that also had the highest number of symptomatic patients. Endoleak was usually type 1 with an incidence of 7.6%. Type 2 endoleaks were relatively uncommon. Aneurysm rupture occurred in 1% of the patients. Graft migration was not reported during the relatively short follow-up of 1 year.

Summary of Findings

Mortality

- The results of 1 comparative study show that in-hospital mortality was not significantly different for ESG placement and surgery patients (2 [4.8%] for ESG, vs. 6 [11.3%] for surgery).
- Pooled data from case series with a mean follow-up ranging from 12 to 38 months shows a 30-day mortality rate and late mortality rate of 3.9% and 5.5%, respectively. These rates are lower than are those reported in the literature for surgical repair of TAA. (2)

- Case series show that the most common cause of early death in patients undergoing endovascular repair is aortic rupture. The most common causes of late death are cardiac events and aortoesophageal or aortobronchial fistula.

Technical Success

- Technical success rates reported by case series range from 55% to 100% (100% and 94.4% in 2 studies (38;41) with all elective cases, 89% in a study (42) with 5% emergent cases, and 55% in a study (36) with 42% emergent cases.

Surgical Reintervention

- In the comparative study, 3 (7.1%) patients in the ESG group and 14 (26.5%) patients in the surgery group required surgical reintervention. In the ESG group, the reasons for surgical intervention were postoperative bleeding at access site, paraplegia, and type 1 endoleak. In the open surgical repair group, the reasons for surgery were duodenal perforation, persistent thoracic duct leakage, false aneurysm, and 11 cases of postoperative bleeding.
- Pooled data from case series show that 9 (2.6%) patients required surgical intervention. The reasons for surgical intervention were endoleak (3 cases); aneurysm enlargement and suspected infection (1 case); aortic dissection (1 case); pseudoaneurysm of common femoral artery (1 case); evacuation of hematoma (1 case); graft migration (1 case); and injury to the access site (1 case).

Endovascular Revision

- In the comparative study, 3 (7.1%) patients required endovascular revision due to persistent endoleak.
- Pooled data from case series show that 19 (5.3%) patients required endovascular revision due to persistent endoleak.

Graft Migration

- Two case series reported graft migration. In the study by Makaroun et al., 3 proximal and 4 component migrations were noted at 2 year follow-up (total of 5%). Heijmen et al. reported 1 case (3.7%) of graft migration. Overall, the incidence of graft migration was 2.6%.

Aortic Rupture

- In the comparative study, aortic rupture due to bare stent occurred in 1 case (2%). Pooled incidence of aortic rupture/dissection reported by case series was 1.4%.

Postprocedural Complications

- In the comparative study, there were no statistically significant differences between the ESG and surgery groups on postprocedural complications, except for pneumonia. The rate of pneumonia was 9% for patients that received an ESG placement and 28% for those that had surgery (P = .02). There were no cases of paraplegia in either group. The rate of other complications, including stroke, cardiac, respiratory, and intestinal ischemia, were each 5.1% for those that received ESG treatment and 10% for those who had surgery. The rate for mild renal failure was 16% in the ESG placement group and 30% in the open surgical repair group. For severe renal failure, it was 11% in the ESG placement group and 10% in the surgery group.

- Pooled data from case series show the following rates for postprocedural complications: paraplegia (2.2%), stroke (3.9%), cardiac (2.9%), respiratory (8.7%), renal failure (2.8%), and intestinal ischemia (1%).

Time-Related Outcomes

- The comparative study found statistically significant differences between the ESG group and surgery group for mean operative time (ESG placement, 2.7 hours; surgery, 5 hours), mean length of ICU stay (ESG placement, 11 days; surgery, 14 days), and mean duration of hospital stay (ESG placement, 10 days; surgery, 30 days).
- Pooled data from case series show that the mean duration of ICU stay was 1.6 days and the mean duration of hospital stay was 7.8 days.

Strength of the Body of Evidence

According to the grading system formulated by the GRADE Working Group, (33) the grade score for the body of evidence on ESG placement to treat the descending TAA is low. (See Appendices 2 and 3.)

Conclusion

- Endovascular stent grafting is a less invasive alternative for repair of TAA.
- There is no high-quality evidence with long-term follow-up data to support the use of endovascular TAA as the first choice of treatment for patients with TAA that are suitable candidates for surgical intervention
- However, short- and medium-term outcomes of ESG placement reported by several studies are satisfactory and comparable to surgical intervention; therefore, for patients that are not suitable candidates for surgery, it is a practical option to consider. Short- and medium-term results show that the benefit of ESG placement over the surgical approach is a relatively lower 30-day mortality and paraplegia rate; and shorter operative time, ICU stay, and hospital stay.

Economic Analysis

Results of Literature Review on Economics

Glade et al. (34) compared the results of open surgery ESG repair of descending TAA. They did a retrospective multicentre study of 95 patients (with a median age of 67 years) undergoing TAA repair (42 received stent grafts; 53 had open surgical repair). They assessed postoperative complications, mid-term survival, and costs. They calculated the mean costs for each patient from the mean outcome values of the study cohort, and they included the costs of the diagnostic process (radiological investigations and laboratories), operative procedure (including anesthesia and specialists), implants, and adjunctive procedures (intensive care, ward, and paraplegia rehabilitation).

The hospital cost of open surgical repair was 33,770 Euros, which is 40% more than that of the endovascular procedure, which was 20,663 Euros. The authors did not calculate the costs of follow-up for patients with an endograft. However, they explained that the costs of serial computed tomography scans would be just a small percentage of the hospital costs. The authors concluded that endografting of descending thoracic aneurysms can be performed with less perioperative morbidity, and at lower hospital costs, despite the higher costs of prosthetic material, but with equal midterm life expectancy, compared with open grafting.

Ontario-Based Economic Analysis

Notes & Disclaimer

The Medical Advisory Secretariat uses a standardized costing methodology for all of its economic analyses of technologies. The main cost categories and the associated methodology from the province's perspective are as follows.

Hospital: Ontario Case Costing Initiative (OCCI) cost data is used for all program costs when there are 10 or more hospital separations, or one-third or more of hospital separations in the ministry's data warehouse are for the designated International Classification of Diseases-10 diagnosis codes and Canadian Classification of Health Interventions procedure codes. Where appropriate, costs are adjusted for hospital-specific or peer-specific effects. In cases where the technology under review falls outside the hospitals that report to the OCCI, PAC-10 weights converted into monetary units are used. Adjustments may need to be made to ensure the relevant case mix group is reflective of the diagnosis and procedures under consideration. Due to the difficulties of estimating indirect costs in hospitals associated with a particular diagnosis or procedure, the Medical Advisory Secretariat normally defaults to considering direct treatment costs only. Historical costs have been adjusted upward by 3% per annum, representing a 5% inflation rate assumption less a 2% implicit expectation of efficiency gains by hospitals.

Non-Hospital: These include physician services costs obtained from the Provider Services Branch of the Ontario Ministry of Health and Long-Term Care, device costs from the perspective of local health care institutions, and drug costs from the Ontario Drug Benefit formulary list price.

Discounting: For all cost-effective analyses, discount rates of 5% and 3% are used as per the Canadian Coordinating Office for Health Technology Assessment and the Washington Panel of Cost-Effectiveness, respectively.

Downstream cost savings: All cost avoidance and cost savings are based on assumptions of utilization, care patterns, funding, and other factors. These may or may not be realized by the system or individual institutions.

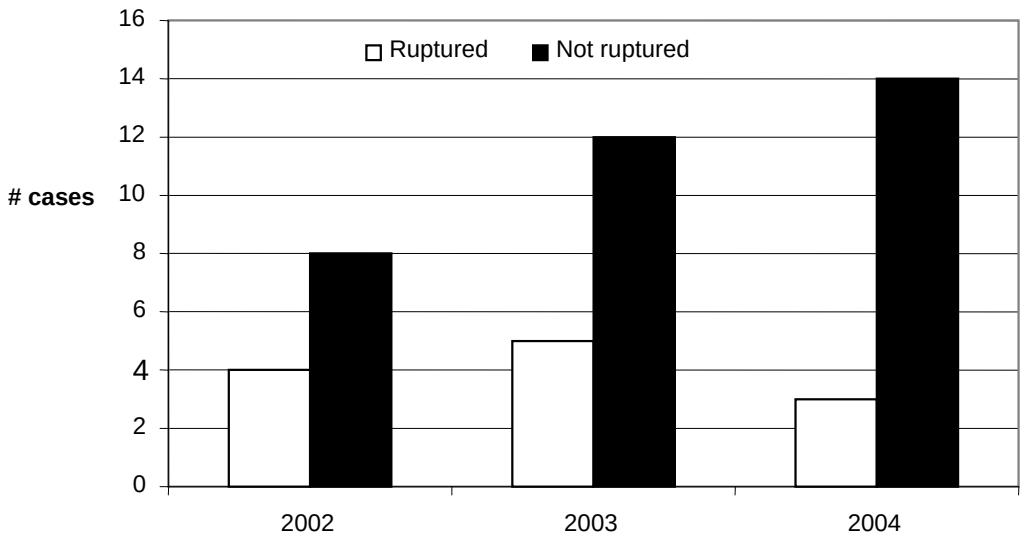
In cases where a deviation from this standard is used, an explanation has been given as to the reasons, the assumptions and the revised approach.

The economic analysis represents an estimate only, based on assumptions and costing methods that have been explicitly stated above. These estimates will change if different assumptions and costing methods are applied for the purpose of developing implementation plans for the technology.

Cases in Ontario

In Ontario, the annual treatment figures for the fiscal year 2004 include 17 cases of descending thoracic aneurysm repair procedures (source: Provincial Health Planning Database). Of these, 14 have been identified as not ruptured; the mean length of hospital stay for these is 9.23 days. Three cases were identified as ruptured; the mean length of hospital stay for these was 28 days.[1] Of these 17, it is impossible to determine how many were repaired with an EVAR or open surgical repair, because both procedures are still classified under the same CCI code (1.IC.80 Repair Thoracic [Descending] Aorta). The number of procedures has remained stable: in fiscal year 2002 there were 12 cases; in 2003, there were 17 cases.

Figure 6: Number of Cases in Ontario of Thoracic Descending Aortic Aneurysm Repair



Hospitalization Costs

The current fiscal year forecast of in-hospital *direct* treatment costs for all in-province procedures of thoracic descending aortic aneurysm repairs is about $560,000 (Cdn). The forecast in-hospital *total* cost per year for in-province procedures is about $720,000 (Cdn). These costs include the device cost when the procedure is an EVAR (source: OCCI).

Professional (Ontario Health Insurance Plan) Costs

Professional costs per treated patient were calculated and include 2 preoperative thoracic surgery or EVAR consultations.

The professional costs of an EVAR include the fees paid to the surgeons, anesthetist, and surgical assistant (source: fee service codes [FSC]). The procedure was estimated to take about 150 minutes.

The professional costs of an open surgical repair include the fees of the surgeon, anesthetist and surgical

[1] The ICD-10CA codes that were used to identify these cases were I71.1: thoracic aneurysm ruptured, and I71.2: thoracic aneurysm without mention of rupture.

assistant. Open surgical repair was estimated to take about 300 minutes.

The costs of services provided by professionals in ICUs were also considered, as were those of the 2 postoperative consultations that patients receive on average once they are discharged from the hospital. Therefore, total OHIP costs per treated patient treated with EVAR are on average $2,956 (ruptured or not ruptured), compared with $5,824 for open surgical repair, and $6157 for open surgical repair when the aneurysm is ruptured. (All figures are in Canadian currency.)

Table 18: Services and Fees Related to Endovascular Repair and Open Surgical Repair of Thoracic Aortic Aneurysms in Ontario*

Service	Fee, $Cdn
2 preoperative thoracic surgery or EVAR consultations (FSC A645)	164
EVAR (FSC code #R875) surgeon + anesthetist + surgical assistant (mean, 150 minutes)	2,042
OSR nor ruptured (FSC R801) surgeon + anesthetist + surgical assistant (mean, 300 minutes)	2,892
OSR ruptured (FSC R801 and #E667) surgeon + anesthetist + surgical assistant (mean, 300 minutes)	3,125
1st day in intensive care unit (FSC G557)	308
2nd to 10th day in intensive care unit per diem (FSC G558)	192
2 post-operative subsequent visits (FSE C642)	58
Total OHIP costs per treated patient for EVAR	2,956
Total OHIP costs per treated patient for OSR	5,824
Total OHIP costs per treated patient for OSR when ruptured	6,157

*EVAR indicates endovascular repair; FSC, fee service code; OHIP, Ontario Health Insurance Plan; OSR, open surgical repair.

Summary

- Starting in 2006, there will be a separate FSC code for EVAR; therefore, it will be possible to tell both procedures apart when doing further studies.
- The results obtained so far show that doing an EVAR procedure instead of open surgical repair for descending TAAs would result in savings of professional costs of about $1,500 (Cdn).
- Based on a study of abdominal EVAR versus open surgical repair performed by the Program for Assessment of Technology in Health (46), abdominal EVAR was about 14% more expensive per treated patient. The expectation is that this difference is smaller for thoracic aneurysm repair owing to the relatively higher costs of open surgical repair for the thoracic area, while the EVAR costs to repair abdominal and thoracic aneurysms are expected to be similar. The offset of EVAR versus open surgical repair is less time in hospital, the operating room, and the ICU.

Appraisal

Policy Considerations

Patient Outcomes – Medical, Clinical

No randomized controlled trial has compared the ESG procedure with conventional open surgical approaches, and no quality of life studies are available yet. Most of the studies are case series. Only one comparative study has compared ESG placement with an open surgical approach. It showed that in-hospital mortality and 1-year survival rates did not differ between the surgical and endovascular groups. In addition, the rate of pneumonia, mean operative time, mean duration of ICU stay, and mean length of

hospital stay were significantly lower or shorter in the ESG group. This study concluded that despite the cost of ESG material, the cost of treatment with ESG is 61% less than for open surgery. The mean hospital cost per patient who received an ESG was 20,663 Euros, versus 33,770 Euros for a patient who had an open procedure.

Overall, the case series have provided a clear safety profile for ESG treatment. Moreover, pooled outcomes from case series were mostly in line with the outcomes reported by a large European Registry on endovascular stent grafting of TAA.

In terms of crucial outcomes, a 30-day mortality rate of 3.9% and late mortality rate of 5.5% for a mean follow-up ranging from 12 to 38 months seems to be satisfactory compared with the rates reported for operative techniques in the literature. The pooled rate of paraplegia from case series (2.2%) is much lower than the rate for surgical patients reported in the literature (6%). The incidences of most serious postoperative complications including paraplegia (2.2%), cardiac events (2.9%), stroke (3.3%), respiratory insufficiency (8.7%), and renal failure (2.8%) are about what would be expected, and do not exceed the rates reported for open surgical approach.

Ethics

Endovascular stent grafting is an alternative to conventional surgical intervention. The graft provides minimally invasive treatment in many patients with TAA; therefore, it results in fewer patients dying of ruptured TAA. It is important that surgeons have the best treatment available for patients who have extremely limited treatment options with no chance of surviving open surgery.

The important issue is what would be the alternative option for patients with TAA at high risk of rupture, or ruptured, if they are not suitable for surgery. This fact mandates consideration of ESG treatment for this subset of patients. A technique that is potentially less invasive and less risky than conventional operative techniques, in the context of patient populations described above, has the potential to treat such a life-threatening condition and save many lives. However, for ESG placement to become the treatment of choice for repair of TAAs, long-term follow-up is mandatory to investigate aneurysm-related mortality and the rate of rupture due to material used.

The Talent thoracic stent graft licensed in Canada is still an investigational device in the United States. A large prospective non-randomized controlled trial in the United States (the VOLAR trial) is investigating the safety and efficacy of the Talent thoracic stent graft. (47)

Diffusion – International, National, Provincial

Endovascular stent grafting of TAA is performed and funded by the Quebec government as part of hospitals' budgets. Sherbrooke, Quebec, was granted authorization to have a modern interventional vascular catheter lab that can convert to a surgical room if it becomes mandatory to perform open surgery during a percutaneous procedure. Other provinces in Canada do not fund the procedure.

The United States Food and Drug Administration (48) issued a premarket approval for the Gore Tag device in March 2005. It concluded that 2 studies on Gore Tag, Tag 99-01 and Tag 03-03, provide reasonable assurance of the safety and effectiveness of the Gore Tag thoracic endoprosthesis for the treatment of descending TAA. The Food and Drug Administration also indicated that patients treated with the Gore Tag endoprosthesis experienced a greater probability of remaining free from major adverse events than those treated with open surgical repair. In addition, these 2 studies showed that the incidence of major device-related events was low. Patients treated with the Gore Tag endoprosthesis lost less blood during the procedure, had a shorter hospital and ICU stay, and took less time to return to normal daily

activities than did patients treated with open surgical repair.

Appendices

Appendix 1: Patient Characteristics and Study Details for Case Series

Table 1: Synopsis of Marakoun et al. and Bortone*

Study, year	Makaroun et al., 2005	Bortone 2004
Study design	Prospective cohort, multicentre	Retrospective
Patients, n	142	41
Physical status/ASA classification	Patients were surgical candidates	NR
Symptomatic TAA, no. (%)	0 (0)	5 (12)
Aneurysm diameter, mean (SD; range), mm	64.1 (15.4; 20–110)	NR
Age, mean	71 (range, 30–86)	67.66 (SD, 9.88)
Gender	Male: 82 Female: 60	NR
Stent graft, number	GORE TAG: 237	Talent: 29 Excluder: 14 Zenith: 8 Endofit: 2
Endovascular stent-grafts implanted, number	237 1 device: 62 (44%) 2 devices: 61 (43%) 3 devices: 11 (8%) 4 devices: 5 (4%)	53
Adjunctive techniques for prevention of spinal ischemia	Not routinely used	NR
Concomitant repair of AAA, no. (%)	0 (0)	5 (12)
Duration of follow-up, mean, months	24 (range, 3 days–53 months)	20.82 (SD, 10)
Clinical Results of Stent Grafting of Thoracic Aortic Aneurysm		
Successful deployment, no. (%)	139 (98)	NR
Technical success rate	NR	NR
Conversion to surgery, no. (%)	1 (0.7)	0 (0)
Intraoperative blood loss, mL	506 (SD, 945; range, 0–8,000)	NR
Injury to access site, no. (%)	20 (14)	NR
Changes in aneurysm diameter, cm, mean	Decreased: 24 of 64 patients (38%) Increased: 11 (17%)	NR
Endovascular leak, no. (%)	Early: Type 1: 1 (0.7) Type 2: 4 (2.8) Type not specified: 4 (2.8) Follow-up: Observed endoleaks: Year 1: 7/97 (7) Year 2: 6/68 (9)	0 (0)
Graft migration, no. %)	1-year: Proximal: 0/97 (0) Components: 1/84 (1) 2-year: Proximal: 3/68 (4) Components: 4/61 (6)	0 (0)

Stent fracture, no. (%)	20 in 19 patients (14) 18 in the longitudinal spine of the stent 2 in the apical nitinol support rings Only 1 patient required treatment)	0 (0)
Reintervention, no. (%)	Early: Endovascular revision: 1 (0.7) Surgery: 1 (0.7) Late: Endovascular revision: 3 (2.1) Surgery: 2 (1.4)	0 (0)
Aortic rupture or dissection, no. (%)	0 (0)	0 (0)
Hospital stay, days (SD; range)	7.6 (18; 1–190)	NR
ICU stay, days (SD; range)	2.6 (14.6; 0–167)	NR

Morbidity and Mortality in Patients who Treated by Endovascular Stent Graft for Thoracic Aortic Aneurysm

30-day/in-hospital mortality, no. (%)	Perioperative: 2 (1.5)	1 (2.4)
TAA-related death. no. (%)	0 (0)	NR
TAA-unrelated death, no. (%)	2 (1.5)	NR
Late mortality, no. (%)	Late: 2 (1.5)	0 (0)
TAA-related death, no. (%)	2 (1.5)	0 (0)
TAA-unrelated death	0 (0)	0 (0)
Paraplegia, no. (%)	4 (3); 75% had more than 1 device implanted	0 (0)
Stroke, no. (%)	5 (4), clustered in patients with proximal aneurysm who underwent a carotid subclavian bypass	1 (2.4)
Renal failure, no. (%)	0 (0)	0 (0)
Cardiac, no. (%)	4 (2.8)	0 (0)
Bronchopulmonary or respiratory insufficiency, no. (%)	14 (10)	1 (2.4)
Vascular, no. (%)	NR	0 (0)
Intestinal ischemia, no. (%)	1 (0.7)	0 (0)
Wound infection, no. (%)	NR	NR

*AAA indicates abdominal aortic aneurysm; ASA, American Society of Anesthesiologists; ESG, endovascular stent-graft; ICU, intensive care unit; NR, not reported; TAA, thoracic aortic aneurysm.

Table 2: Details of Neuhauser et al. and Czerny et al.*

Study, year	Neuhauser et al., 2004	Czerny et al., 2004
Study design	Prospective cohort	Retrospective review
Patients, n	31	54
Physical status/ASA classification	Class 3 or 4: 100%	NR
Symptomatic TAA, no. (%)	13 (42)	0 (0)
Aneurysm diameter, mean (range), mm	Median 65±22, range (25–110)	73 (61–93)
Age, mean (range), years	73 (65–81)	68 (33–87)
Gender	Male: 25 Female: 6	Male: 38 Female: 16
Stent graft, no.	Talent: 44 Excluder: 13 Vanguard: 2	Talent: 21 Excluder: 33
Endovascular stent-grafts implanted, no.	59 1 device: 12 (39%) 2 devices: 12 (39%) 3 devices: 6 (19%) 5 devices: 1 (3%)	Mean 2.4 (1–6)
Adjunctive techniques for prevention of spinal ischemia	Not used	NR
Concomitant repair of AAA, no. (%)	2 (6)	0 (0)
Duration of follow-up, mean (range), months	Median, 15.1 (4–69)	38 (1–72)
Clinical Results of Stent Grafting of Thoracic Aortic Aneurysm		
Successful deployment, no. (%)	30 (97)	54 (100)
Technical success rate, no. (%)	17 (55)	51 (94.4)
Conversion to surgery, no. (%)	0 (0)	0 (0)
Intraoperative blood loss, ml	NR	NR
Injury to access site, no. (%)	3 (9.7)	NR
Change in aneurysm diameter, cm, mean	NR	Year 1: -0.8 (SD, 0.6) (-9.1%, *P* = .002) Year 2: Additional decrease: -0.7 (SD, 0.6) (-10.7%, *P* = .002)

Endovascular leak, no. (%)	Early: Overall: Type 1: 7 (22.6) Type 2: 4 (12.9) Type 3: 2 (6.5) Talent: Early: Type 1: 4 (12.9) Type 2: 2 (6.5) Type 3: 2 (6.5) Excluder: Type 1: 3 (9.7) Type 2: 2 (6.5) Late: Overall: Type 1: 6 (19.4) Type 3: 1 (3.2) Talent: Type 1: 5 (16.1) Excluder: Type 1: 1 (16.1) Type 3: 1 (16.1)	Early: Type 1: 3 (type of the device not specified) Late: Type 1: 4 (7.4) Type 2: 7 (13) Type 3: 4 (7.4) Talent: Type 1: 4 (7.4) Type 2: 0 (0) Type 3: 3 (5.6) Excluder: Type 1: 0 (0) Type 2: 7 (13) Type 3: 1 (1.9) There was no difference in the number of endoleaks between the different types of stent grafts.
Graft migration, no. (%)	NR	0 (0)
Stent fracture, no. (%)	0 (0)	0 (0)
Reintervention, no. (%)	Early: Additional ESG: 0 (0) Surgery: 1 (3.2) Late: Additional ESG: 8 (26) Surgery: 1 (3.2)	Early: Additional ESG: 1 (1.9) Surgery: 0 (0) Radiation: 1 (1.9) Late: Additional ESG: 1 (1.9) Surgery: 1 (1.9) Embolization: 1 (1.9)
Aortic rupture or dissection, no. (%)	3 (9.7)	1 (1.9)
Hospital stay, mean days (range)	NR	9.2 (4–35)
ICU stay, mean days (range)	NR	3.4 (1–31)

Morbidity and Mortality in Patients who were Treated by Endovascular Stent Graft for Thoracic Aortic Aneurysm

30-day mortality, no. (%)	Overall: 6 (19.3) Elective: 3 (16.7) Emergency: 3 (23)	2 (3.7)
TAA-related death, no. (%)	3 (9.6)	2 (3.7)
TAA-unrelated death, no. (%)	3 (9.6)	0 (0)
Late mortality, no. (%)	Overall: 7 (23) Elective: 5 (27.8) Emergency: 2 (15.4)	3 (5.6)
TAA-related death, no. (%)	1 (3.2)	0 (0)
TAA-unrelated death, no. (%)	6 (19.4)	3 (5.6)
Paraplegia or spinal cord ischemia, no. (%)	2 (6) Permanent: 1 Partial recovery: 1	0 (0)
Stroke, no. (%)	1 (3)	NR
Renal failure, no. (%)	1 (3)	NR

Cardiac, no. (%)	Myocardial infarction: 2 (6.5)	NR
Bronchopulmonary or respiratory insufficiency, no. (%)	Aortobronchial fistula: 2 (6.5) Respiratory failure: 1 (3)	NR
Vascular, no. (%)	2 (6.5)	NR
Intestinal ischemia, no. (%)	0 (0)	1 narrowing of celiac axis with consequent multiorgan failure
Wound infection, no. (%)	2 (6.5)	NR

*AAA indicates abdominal aortic aneurysm; ASA, American Society of Anesthesiologists; ESG, endovascular stent-graft; ICU, intensive care unit; NR, not reported; TAA, thoracic aortic aneurysm.

Table 3: Details of Lepore et al. and Schoder et al.*

Study, year	Lepore et al., 2003	Schoder et al., 2003
Study design	Prospective cohort	Prospective
Patients, n	21	28
Physical status/ASA classification	High surgical risk indicated stent grafting whenever anatomic criteria were satisfied	71% of the patients were unsuitable for surgery
Physical status	High surgical risk patients indicated stent grafting whenever anatomical criteria were satisfied (6 [29%] patients had undergone 11 previous cardiovascular operations)	Unsuitability for open surgical: 20 (71%)
Symptomatic TAA, no. (%)	7 (33)	0 (0)
Aneurysm diameter, mean (SD; ragne), mm	> 50	65.6 (11.3; 50–96)
Age, mean (SD; range), years	73 (6; 60–82)	71.6 (53–82)
Gender	Male: 13 Female: 8	Male: 17 Female: 11
Stent graft, number	Talent: 16 Excluder: 36	Excluder: 58
Endovascular stent-grafts implanted, number	52	58
Adjunctive techniques for prevention of spinal ischemia	Was performed for patients in whom segments T8-L1 was involved	NR
Concomitant repair of AAA, number (%)	2 (10)	0 (0)
Duration of follow-up, mean (SD; range), months	17 (8; 0–32) 100% complete	22.7 (11–47)
Clinical Results of Stent Grafting of Thoracic Aortic Aneurysm		
Successful deployment, no. (%)	21 (100)	NR
Technical success rate, no. (%)	NR	(100)
Conversion to open surgery, no. (%)	0 (0)	0 (0)
Intraoperative blood loss	NR	NR
Injury to access site, no. (%)	NR	2 (7.1)
Change in aneurysm diameter, cm, mean	Unchanged or diminished	At 1 year follow-up: For patients without an apparent endoleak at any time: -6.6 (SD, 6.4) (-10.4%, *P* = .001) ➢ Decreased in 12 of 18 (67%) ➢ Remained unchanged in 4 of 18 (22%) ➢ Increased in 2 of 18 (11%)

		No significant interval decrease between the 1- and 2-year follow-ups At 3-year follow-up: Decreased: 1 (20%) Unchanged: 3 (60%) Increased: 1 (20%)
Endovascular leak, no. (%)	Early: Type 1: 4 (19) Late: 0 (0)	Early: Type 1: 5 (17.9) Type 2: 3 (10.7) Late: Type 2: 1 (3.6)
Graft migration, no. (%)	0 (0)	NR
Stent fracture, no. (%)	NR	NR
Reintervention, no. (%)	Additional ESG: 2 (9.5) Surgery: 0 (0)	Additional stent: 1 (3.6) Surgery: 0 (0) Embolization: 1 (3.6) Reballooning: 1 (3.6)
Aortic rupture or dissection, no. (%)	1 (4.8) due to the bare stent of the device	0 (0)
Hospital stay, mean (SD; range) days	NR	9 (3.2; 4–20)
ICU/recovery room stay, mean hours	NR	0.4

Morbidity and Mortality in Patients who Treated Endovascular Stent Graft for Thoracic Aortic Aneurysm

30-day mortality, no. (%)	2 (10)	0 (0)
TAA-related death, no. (%)	0 (0)	0 (0)
TAA-unrelated death, no. (%)	2 (10)	0 (0)
Late mortality, no. (%)	3 (14)	3 (11)
TAA-related death, no. (%)	1 (4.5)	0 (0)
TAA-unrelated death, no. (%)	2 (9.5)	3 (11)
Paraplegia or spinal cord ischemia, no. (%)	2 (9.5)	0 (0)
Stroke, no. (%)	2 (9.5)	1 (3.6)
Renal failure, no. (%)	1 (4.8)	1 (3.6)
Cardiac, no. (%)	Myocardial infarction: 1 (4.8) Heart failure: 1 (4.8)	0 (0)
Bronchopulmonary or respiratory insufficiency, no. (%)	3 (14.3)	2 nontransient atelectasis 1 nontransient pleural effusion
Vascular, no. (%)	0 (0)	3 (11)
Intestinal ischemia, no. (%)	1 (4.8)	0 (0)
Wound infection, no. (%)	NR	NR

*AAA indicates abdominal aortic aneurysm; ASA, American Society of Anesthesiologists; ESG, endovascular stent-graft; ICU, intensive care unit; NR, not reported; TAA, thoracic aortic aneurysm.

Table 4: Details of Najibi et al. and Heijmen et al.*

Study, year	Najibi et al., 2002	Heijmen et al., 2002
Study design	Prospective cohort	Prospective cohort
Patients, n	ESG: 19 Surgery: 10	27
Physical status/ASA classification	74% had acceptable medical risk profiles for open surgical repair and 26% did not have this condition.	All but one patient were candidates for open surgical procedure.
Symptomatic TAA, no. (%)	ESG: 1 (5) Surgery: 3 (30)	5 (18.5)
Aneurysm diameter, mean (SD; range), mm	ESG: 68 (22; 47–130) Surgery: 73 (22; 40–110)	66 (15)
Age, mean (SD; range)	ESG: 70.6 (5.3; 59–78) Surgery: 70.1 (4.5; 67–75)	70 (50–82)
Gender, no. (%)	ESG: Male: 15 (79) Female: 4 (21) Surgery: Male: 3 (30) Female: 10 (70)	Male: 17 Female: 10
Stent graft, no.	Talent: 5 Excluder: 14	Talent: 9 Excluder: 13 AneurX: 6
Endovascular stent-grafts implanted, no.	ESG: 19 Surgery: N/A	41 (1.5 per patient) 2 stents: 43 3 stents: 1
Adjunctive techniques for Prevention of spinal ischemia	Was not used	NR
Concomitant repair of AAA, no. (%)	Endovascular group: 0 (0) Surgery: 0 (0)	0 (0)
Duration of follow-up, mean (range), months	ESG: 12 (3–22)	Median: 21 (1–49)
Clinical Results of Stent Grafting of Thoracic Aortic Aneurysm		
Successful deployment, no. (%)	ESG: 18 (95) Surgery: N/A	26 (96)
Conversion to surgery, no. (%)	ESG: 0 (0) Surgery: N/A	1 (3.7)
Technical success rate	17/19 (89%)	NR
Intraoperative blood loss, mean, (SD), ml	ESG: 325 (353) Surgery: 1205 (1493)	Median, 200 (range, 50–1,500)
Injury to access site	NR	NR
Change in aneurysm diameter, cm, mean (SD)	At 1 year follow-up: ESG: -19 (10), $P < .01$ Surgery: NR	Unchanged/decreased: 26 Increased: 1
Endovascular leak, no. (%)	ESG: 0 (0) Surgery: N/A	Early: Type 2: 4 (14.8) Late: Type 1: 2 (7.4) Type not specified: 1 (3.7)
Graft migration, no. (%)	ESG: 0 (0) Surgery: N/A	1 (3.7)
Stent fracture, no. (%)	ESG: 1 (5.3) (Excluder) Surgery: N/A	0 (0)
Reintervention, no. (%)	ESG: 0 (0) Surgery: 0 (0)	Additional stent: 2 (7.4) Surgery: 2 (7.4)

Aortic rupture or dissection, no. (%)	ESG: 1 (5.3) Surgery: 0 (0)	0 (0)
Hospital stay, mean (SD) days	ESG: 6.2 (3.3; range, 1–13) Surgery: 16.3 (6.7; *P* = .002)	7 (range, 3–36)
ICU/recovery room stay, mean (SD) hours	ESG: 0.8 (1.0) Surgery: 11 (12; *P* = .03)	1 (range, 1–5)

Morbidity and Mortality in Patients Treated With Endovascular Stent Graft for Thoracic Aortic Aneurysm

30-day mortality, no. (%)	ESG: 1 (5.3) Surgery: 1 (10)	0 (0)
TAA-related death, no. (%)	ESG: 1 (5.3) Surgery: 1 (10)	0 (0)
TAA-unrelated death, no. (%)	ESG: 0 (0) Surgery: 0 (0)	0 (0)
Late mortality, no. (%)	ESG: 1 (5.3) Surgery: 2 (20)	1 (3.7)
TAA-related death, no. (%)	ESG: Unknown Surgery: 1	0 (0)
TAA-unrelated death, no. (%)	ESG: Unknown Surgery: 1	1 (3.7)
Paraplegia/spinal cord Ischemia, no. (%)	ESG: 0 (0) Surgery: 0 (0)	0 (0)
Stroke, no. (%)	ESG: 1 (5.3) Surgery: 1 (10)	1 (3.7)
Renal failure, no. (%)	Mild: ESG: 3 (16) Surgery: 3 (30) Severe: ESG: 2 (11) Surgery: 1 (10)	NR
Cardiac, no. (%)	Myocardial infarction: ESG: 1 (5.3) Surgery: 1 (10)	0 (0)
Bronchopulmonary or respiratory insufficiency, no. (%)	ESG: 1 (5.3) Surgery: 1 (10)	2 (7.4)
Vascular, no. (%)	ESG: 2 (10.5) Surgery: 0 (0)	1 (3.7)
Intestinal ischemia, no. (%)	ESG: 1 Surgery: 1 (10)	NR
Wound infection, no. (%)	NR	4 (14)

*AAA indicates abdominal aortic aneurysm; ASA, American Society of Anesthesiologists; ESG, endovascular stent-graft; ICU, intensive care unit; NR, not reported; TAA, thoracic aortic aneurysm.

Appendix 2: Assessment of the Quality of the Observational Studies

Domains of the quality		Glade et al. 2005	
			Score
Patients	Were the patients enrolled into the study in a consecutive manner?	Yes	(1)
	Were the inclusion/exclusion criteria clearly stated/applied consistently?	Yes	(1)
	Did the investigator report on the number of elective/urgent cases?	Yes	(1)
Setting &skills	Was the environment appropriate for performing the procedure?	Yes	(1)
	Did the staff have skills and experience to perform the procedure?	Yes	(1)
Comparability	Did the study have a prospective design?	No	(0)
	Was the comparison made between contemporaneous controls?	Yes	(1)
	Were the procedures done on similar anatomical location in the body?	Yes	(1)
	Were the groups comparable on their baseline characteristics?	Yes	(1)
Outcome assessment	Did the investigator follow a standardized procedure?	Yes	(1)
	Did the study defined and measured the important outcomes?	Yes	(1)
	Did the investigators create the main outcome of interest?	No	(1)
Statistical methodology	Did the study have adequate power to detect a significant effect?	Yes	(1)
	Did the investigator use appropriate statistical methods?	Yes	(1)
Follow-ups	Were all the patients accounted for in the analysis?	Yes	(1)
	Was the duration of follow-up long enough to demonstrate the effect?	No	(0)
	Did the investigator use a valid assessment tool during the follow-ups?	Yes	(1)
	Did the number of lost to follow-up reported?	No	(0)
Reporting	Did the author validate the conclusions by presenting data from literature?	Yes	(1)
	Did the study report funding from sources without financial interest in the technology or did the author have financial interest in the technology?	No	(1)
Total scores Overall quality[1]		17/20 High	

[1] 80% to 100% = High, 60% to 79% = Moderate, < 60%=Low

Appendix 3: Grade Score for the Body of Evidence on Endovascular Stent Grafting of Descending Thoracic Aortic Aneurysm*

Number of Studies	Study Design	Quality of Studies	Consistency	Directness	Other Modifying Factors
N	Randomized controlled trial = High Observational = Low Any other evidence = Very low	Serious limitation (-1) Very serious limitation (-2)	Important inconsistency (-1)	Same uncertainty (-1) Major uncertainty (-2)	❑ Association Strong (+1) Very strong (+2) ❑ Dose response gradient (+1) ❑ All plausible confounders would have reduced the effect (+1) ❑ Imprecise or sparse data (-1) ❑ High of reporting bias (-1)

*Source: Grade Working Group (33)

Grading System Applied to the Studies

Number of Studies	Study Design	Quality of Studies	Consistency	Directness	Other Modifying Factors	Overall Quality of Evidence
1	Observational = Low	High	Consistent with case series	Same direction as case series	Not applicable	Low

Appendix 4: Grading System for Recommendations by the American College of Chest Physicians*

Grade of Recommendation	Benefit Versus Risk and Burdens	Methodological Strength of Supporting Evidence	Implications
Strong recommendation, High quality evidence 1 A	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Strong recommendation, Moderate quality evidence 1 B	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	
Strong recommendation, Low or very low quality evidence 1 C	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
Weak recommendation, High quality evidence2 A	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Weak recommendation, Moderate quality evidence 2 B	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	
Weak recommendation, Low or very low quality evidence 2 C	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

*Developed by a task force convened in 2005: Guyatt G, Gutterman D, Baumann MH. Grading Strength of Recommendations and Quality of Evidence in Clinical Guidelines. Report from an American College of Chest Physicians Task Force. *CHEST.* In Press. (49)

http://www.chestnet.org/education/guidelines/development/q7.php

References

1. Therasse E, Soulez G, Giroux MF, Perreault P, Bouchard L, Blair JF et al. Stent-graft placement for the treatment of thoracic aortic diseases. Radiographics 2005; 25(1): 157-173

2. Lee JT, White RA. Current status of thoracic aortic endograft repair. Surg Clin North Am 2004; 84(5): 1295-1318

3. Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. Harrison's principles of internal medicine. 15th ed. New York: McGraw-Hill Professional; 2001.

4. Amarenco P, Duyckaerts C, Tzourio C, Henin D, Bousser MG, Hauw JJ. The prevalence of ulcerated plaques in the aortic arch in patients with stroke. N Engl J Med 1992; 326(4): 221-225

5. Blauth CI, Cosgrove DM, Webb BW, Ratliff NB, Boylan M, Piedmonte MR et al. Atheroembolism from the ascending aorta. An emerging problem in cardiac surgery. J Thorac Cardiovasc Surg 1992; 103(6): 1104-1111

6. Karalis DG, Chandrasekaran K, Victor MF, Ross JJ, Jr., Mintz GS. Recognition and embolic potential of intraaortic atherosclerotic debris. J Am Coll Cardiol 1991; 17(1): 73-78

7. Wareing TH, Davila-Roman VG, Daily BB, Murphy SF, Schechtman KB, Barzilai B et al. Strategy for the reduction of stroke incidence in cardiac surgical patients. Ann Thorac Surg 1993; 55(6): 1400-1407

8. Katz ES, Tunick PA, Rusinek H, Ribakove G, Spencer FC, Kronzon I. Protruding aortic atheromas predict stroke in elderly patients undergoing cardiopulmonary bypass: experience with intraoperative transesophageal echocardiography. J Am Coll Cardiol 1992; 20(1): 70-77

9. Gray H. Gray's anatomy. 37th ed. Edinburgh (Scotland): Churchill Livingstone; 1989.

10. Kouchoukos NT, Dougenis D. Surgery of the thoracic aorta. N Engl J Med 1997; 336(26): 1876-1888

11. Textbook of cardiovascular medicine. 2nd ed. Philadelphia: Lippincott, Williams & Wilkins; 2002.

12. Bickerstaff LK, Pairolero PC, Hollier LH, Melton LJ, Van Peenen HJ, Cherry KJ et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982; 92(6): 1103-1108

13. Lindsay J, Jr., Hurst JW. Clinical features and prognosis in dissecting aneurysm of the aorta. A re-appraisal. Circulation 1967; 35(5): 880-888

14. Svensson LG, Crawford ES. Aortic dissection and aortic aneurysm surgery: clinical observations, experimental investigations, and statistical analyses. Part I. Curr Probl Surg 1992; 29(11): 817-911

15. Crawford ES, DeNatale RW. Thoracoabdominal aortic aneurysm: observations regarding the natural course of the disease. J Vasc Surg 1986; 3(4): 578-582

16. Dake MD, Miller DC, Mitchell RS, Semba CP, Moore KA, Sakai T. The "first generation" of endovascular stent-grafts for patients with aneurysms of the descending thoracic aorta. J Thorac Cardiovasc Surg 1998; 116(5): 689-703

17. Umana JP, Miller DC, Mitchell RS. What is the best treatment for patients with acute type B aortic dissections--medical, surgical, or endovascular stent-grafting? Ann Thorac Surg 2002; 74(5): S1840-S1843

18. American Society of Anaesthesiologists. ASA Physical status classification system [homepage on the Internet]. 2005. [cited Feb. 2006]. Available from: http://www.asahq.org/clinical/physicalstatus.htm

19. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. Ann Thorac Surg 2002; 74(5): S1877-S1880

20. Mauney MC, Blackbourne LH, Langenburg SE, Buchanan SA, Kron IL, Tribble CG. Prevention of spinal cord injury after repair of the thoracic or thoracoabdominal aorta. Ann Thorac Surg 1995; 59(1): 245-252

21. Crawford ES, Crawford JL, Safi HJ, Coselli JS, Hess KR, Brooks B et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. J Vasc Surg 1986; 3(3): 389-404

22. Kahn RA, Moskowitz DM. Endovascular aortic repair. J Cardiothorac Vasc Anesth 2002; 16(2): 218-233

23. Biglioli P, Spirito R, Porqueddu M, Agrifoglio M, Pompilio G, Parolari A et al. Quick, simple clamping technique in descending thoracic aortic aneurysm repair. Ann Thorac Surg 1999; 67(4): 1038-1043

24. Cina CS, Abouzahr L, Arena GO, Lagana A, Devereaux PJ, Farrokhyar F. Cerebrospinal fluid drainage to prevent paraplegia during thoracic and thoracoabdominal aortic aneurysm surgery: a systematic review and meta-analysis. J Vasc Surg 2004; 40(1): 36-44

25. Sayed S, Thompson MM. Endovascular repair of the descending thoracic aorta: evidence for the change in clinical practice. Vascular 2005; 13(3): 148-157

26. Dake MD. Endovascular stent-graft management of thoracic aortic diseases. Eur J Radiol 2001; 39(1): 42-49

27. Pasic M, Bergs P, Knollmann F, Zipfel B, Muller P, Hofmann M et al. Delayed retrograde aortic dissection after endovascular stenting of the descending thoracic aorta. J Vasc Surg 2002; 36(1): 184-186

28. Neuhauser B, Czermak BV, Fish J, Perkmann R, Jaschke W, Chemelli A et al. Type A dissection following endovascular thoracic aortic stent-graft repair. J Endovasc Ther 2005; 12(1): 74-81

29. Clouse WD, Hallett JW, Jr., Schaff HV, Gayari MM, Ilstrup DM, Melton LJ, III. Improved prognosis of thoracic aortic aneurysms: a population-based study. JAMA 1998; 280(22): 1926-1929

30. Svensjo S, Bengtsson H, Bergqvist D. Thoracic and thoracoabdominal aortic aneurysm and dissection: an investigation based on autopsy. Br J Surg 1996; 83(1): 68-71

31. Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM et al. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg 2002; 35(5): 1048-1060

32. Carroccio A, Ellozy S, Spielvogel D, Marin ML, Hollier L. Endovascular stent grafting of thoracic aortic aneurysms. Ann Vasc Surg 2003; 17(4): 473-478

33. GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004; 328(7454): 1490

34. Glade GJ, Vahl AC, Wisselink W, Linsen MA, Balm R. Mid-term survival and costs of treatment of patients with descending thoracic aortic aneurysms; endovascular vs. open repair: a case-control study. Eur J Vasc Endovasc Surg 2005; 29(1): 28-34

35. Makaroun MS, Dillavou ED, Kee ST, Sicard G, Chaikof E, Bavaria J et al. Endovascular treatment of thoracic aortic aneurysms: results of the phase II multicenter trial of the GORE TAG thoracic endoprosthesis. J Vasc Surg 2005; 41(1): 1-9

36. Neuhauser B, Perkmann R, Greiner A, Steingruber I, Tauscher T, Jaschke W et al. Mid-term results after endovascular repair of the atherosclerotic descending thoracic aortic aneurysm. Eur J Vasc Endovasc Surg 2004; 28(2): 146-153

37. Lepore V, Lonn L, Delle M, Mellander S, Radberg G, Risberg B. Treatment of descending thoracic aneurysms by endovascular stent grafting. J Card Surg 2003; 18(5): 436-443

38. Schoder M, Cartes-Zumelzu F, Grabenwoger M, Cejna M, Funovics M, Krenn CG et al. Elective endovascular stent-graft repair of atherosclerotic thoracic aortic aneurysms: clinical results and midterm follow-up. Am J Roentgenol 2003; 180(3): 709-715

39. Heijmen RH, Deblier IG, Moll FL, Dossche KM, van den Berg JC, Overtoom TT et al. Endovascular stent-grafting for descending thoracic aortic aneurysms. Eur J Cardiothorac Surg 2002; 21(1): 5-9

40. Bortone AS, De Cillis E, D'Agostino D, Schinosa LL. Stent graft treatment of thoracic aortic disease. Surg Tech Int 2004; 12: 189-193

41. Czerny M, Cejna M, Hutschala D, Fleck T, Holzenbein T, Schoder M et al. Stent-graft placement in atherosclerotic descending thoracic aortic aneurysms: midterm results. J Endovasc Ther 2004; 11(1): 26-32

42. Najibi S, Terramani TT, Weiss VJ, Mac Donald MJ, Lin PH, Redd DC et al. Endoluminal versus open treatment of descending thoracic aortic aneurysms. J Vasc Surg 2002; 36(4): 732-737

43. Ehrlich M, Grabenwoeger M, Cartes-Zumelzu F, Grimm M, Petzl D, Lammer J et al. Endovascular stent graft repair for aneurysms on the descending thoracic aorta. Ann Thorac Surg 1998; 66(1): 19-24

44. Hamilton IN, Jr., Hollier LH. Adjunctive therapy for spinal cord protection during thoracoabdominal aortic aneurysm repair. Semin Thorac Cardiovasc Surg 1998; 10(1): 35-39

45. Leurs LJ, Bell R, Degrieck Y, Thomas S, Hobo R, Lundbom J et al. Endovascular treatment of thoracic aortic diseases: combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. J Vasc Surg 2004; 40(4): 670-679

46. Bowen J, De Rose G, Hopkins R, Novick T, Blackhouse G, Tarride J-E. Systematic review and cost-effectiveness analysis of elective endovascular repair compared to open surgical repair of abdominal aortic aneurysms. Interim report. [report on the Internet]. July 2005. Hamilton, Ontario: Program for Assessment of Technology in Health. [cited 2006 Feb. 3]. Available from: http://path-hta.ca/EVAR%20Interim%20Report%20Jul%202005.pdf.

47. Medtronic. Medtronic completes enrollment of VALOR clinical trial evaluating the Talent™ thoracic stent graft system [homepage on the Internet]. 2005. [cited Nov. 2005]. Available from: http://wwwp.medtronic.com/Newsroom/NewsReleaseDetails.do?itemId=1118927845069&lang=en_US

48. United States Food and Drug Administration. New device approval. GORE TAG thoracic endoprosthesis - P040043 [homepage on the Internet]. 2005. [cited Dec. 2005]. Available from: http://www.fda.gov/cdrh/mda/docs/p040043.html

49. Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. Chest 2006; 129(1): 174-181