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Disappointing results with a new commercially available thoracic endograft

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Introduction: **New devices for endovascular treatment of thoracic aortic diseases were recently approved for clinical use by European authorities, obtaining the Conformité Européenne (CE) mark. In all patients who underwent endovascular treatment of a thoracic aortic disease in 2002, we used a new CE-marked device, the Endofit stent graft. The device is constituted of nitinol stents and polytetrafluoroethylene fabric, and has a simple design and delivery system.**
Methods: **During 2002, 11 patients (mean age, 75 years; range, 66-85 years) underwent treatment of atherosclerotic aneurysm (n = 9), chronic type B dissection (n = 1), and intramural hematoma (n = 1). Disease involved the descending thoracic aorta in 7 patients and the distal aortic arch in 4 patients.**
Results: **In all cases the Endofit stent grafts were successfully deployed in the intended position. No postoperative paraplegia or paraparesis was recorded. There were two in-hospital deaths: 1 patient died in the operating room (postmortem examination showed a kinked graft); and the other patient died in the intensive care unit on postoperative day 30, after an intraoperative stroke. One surgical conversion was performed 2 weeks after the procedure, because of total collapse of the graft due to rupture of three stents. Other graft-related complications included type I endoleak (n = 2), type II endoleak (n = 1), and incomplete opening of the device (n = 1).**
Conclusion: **Endovascular treatment of thoracic disease with the Endofit graft in this small heterogeneous group of patients resulted in several complications, which may arise from both the delivery system and the graft itself. At present, other commercially available endografts may be safer for endovascular treatment of thoracic aortic diseases. (J Vasc Surg 2004;39:124-30.)**

The feasibility and safety of stent-graft therapy for thoracic aortic aneurysms was initially investigated by Dake et al[1] in 1992, using homemade devices that combined polyester grafts and modified Gianturco Z-stents. This therapeutic concept proved successful, not only in treatment of aneurysm, but also other aortic diseases, such as dissection,[2] intramural hematoma (IMH),[3] penetrating ulcer,[4,5] traumatic injury,[6-8] and anastomotic aneurysm.[9] Both ready-made and custom-made grafts soon became commercially available.

The most popular commercially manufactured thoracic stent grafts were the Talent (AVE/Medtronic, Santa Rosa, Calif) and Excluder (W. L. Gore & Associates, Flagstaff, Ariz) stent grafts. However, structural problems with the Excluder graft were detected during follow-up, and in November 2001 the manufacturer voluntarily withdrew this product from the market.[10]

Other stent grafts have become commercially available in recent years, such as the Zenith (William Cook Europe, Bjaeverskov, Denmark) and Endofit (Endomed, Phoenix, Ariz) grafts, which obtained Conformité Européenne (CE) marking in June 2001.[10] To our knowledge, phase 1 of the US Food and Drug Administration (FDA) approval process for the Endofit graft is currently under way at several US centers. The simple design and delivery system, reduced cost, and favorable preliminary results presented to us by the manufacturer induced us to implant the Endofit graft in our patients in 2002. The purpose of this study was to evaluate the clinical results of endovascular treatment of diseases of the thoracic aorta with this new commercially available and CE-marked stent graft.

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MATERIAL AND METHODS

During 2002 at our institution, 11 patients underwent treatment of thoracic aortic disease with the Endofit graft. Demographic data are presented in the Table. All patients were men, with mean age 75 years (range, 66-85 years). Disease involved the distal arch in 4 patients and the descending aorta in 7 patients. One patient had chronic dissection, one patient had an intramural hematoma, and the remaining nine patients had atherosclerotic aneurysms (mean diameter, 6.8 cm).

This series comprises all patients with thoracic aortic disease treated with an endovascular approach in 2002 at our institution. Over the same period, 16 patients underwent open surgical treatment of disease involving the thoracic aorta, and 3 patients were observed with medical therapy alone, because we believed they were too sick to undergo either open surgical or endovascular procedures.

In three procedures the graft was implanted after administration of subarachnoid anesthesia, and in eight procedures the patient was under general anesthesia. The preferred access site was the right common femoral artery, possible in nine patients. In one of the remaining patients, we used right common iliac artery access through a retroperitoneal approach, and in the other patient we used the

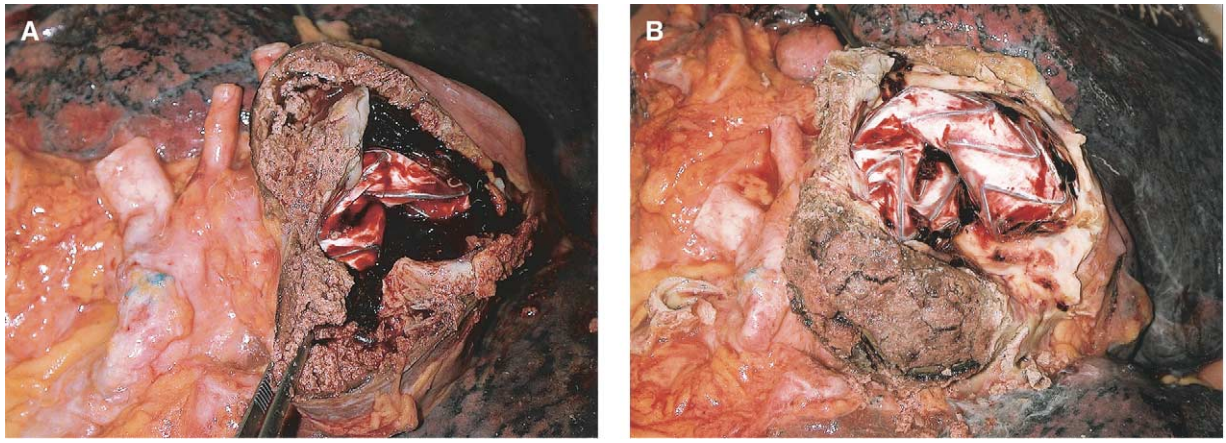

Fig 1. Case 1. Photographs obtained at postmortem examination. **A,** After removal of thrombus, new thrombosis formed around the stent graft. Note kinking of the graft within the aneurysmal sac. **B,** Endograft after complete removal of old and fresh thrombi.

Demographic data

Patients	*Sex*	*Age (y)*	*Lesion*	*Graft size (mm)*	*In-hospital outcome*
No. 1	Male	71	Distal arch aneurysm	40 × 140	Graft migration, intraoperative death
No. 2	Male	77	Distal arch aneurysm	36 × 140	Type I endoleak; discharged
No. 3	Male	69	DTAA	38 × 220	Asymptomatic incomplete graft release; discharged
No. 4	Male	85	DTAA	40 × 140	Discharged
No. 5	Male	75	Dissected DTAA	30 × 140	Discharged
No. 6	Male	81	Distal arch aneurysm	36 × 140	Discharged
No. 7	Male	79	DTAA	36 × 140	Type II endoleak; discharged
No. 8	Male	74	IMH of descending aorta	32 × 140	Stroke, perioperative death
No. 9	Male	66	DTAA	36 × 140	Discharged
No. 10	Male	77	DTAA	34 × 140	Type I endoleak; discharged
No. 11	Male	71	Distal arch aneurysm	36 × 180	Discharged; subsequent open surgery because of collapse of graft, due to fracture of three stents; discharged; alive and well

DTAA, Distal thoracic aortic aneurysm; *IMH,* intramural hematoma.

left branch of a previous aortobiiliac bypass graft, also through a retroperitoneal approach. Control angiographs were obtained with a 6-8F introducer sheath inserted through the contralateral femoral artery or the left brachial artery in 2 patients.

All procedures were performed in the operating room, under fluoroscopic control with a mobile digital C-arm image intensifier (OEC Medical Systems Inc, Salt Lake City, Utah). A bolus of heparin (70 IU/kg) was administered at deployment of the graft, and controlled systemic hypotension was induced pharmacologically by the anesthesiologist with a bolus of fast-acting venous or arterial vasodilator, such as nitrate or urapidil. Nitroprusside or adenosine-induced asystole were never used.

The Endofit device is composed of nitinol stents combined with expandable polytetrafluoroethylene (ePTFE) fabric, with an uncovered proximal stent, and comes loaded in a cartridge. Each stent is separated from the others, and only the top "free-flow" stent is linked to the first covered stent. All stents except the proximal free-flow stent are sandwiched between two layers of ePTFE in a thermal process of encapsulation that avoids the need for sutures. Therefore, there is no interface of metallic stent with either the blood or the aortic wall. No longitudinal structures for columnar support are present.

A 24F introducer sheath with tapered conic dilator is inserted over a guide wire up to the site intended for deployment of the graft or above it. The dilator is then withdrawn, and the stent graft is inserted into the sheath and advanced all the way up with a pusher. At this point, however, the sheath can no longer be safely advanced forward, because its tip is no longer tapered; it can only be withdrawn, if necessary. The stent graft is simply deployed by holding still on the pusher as the sheath is

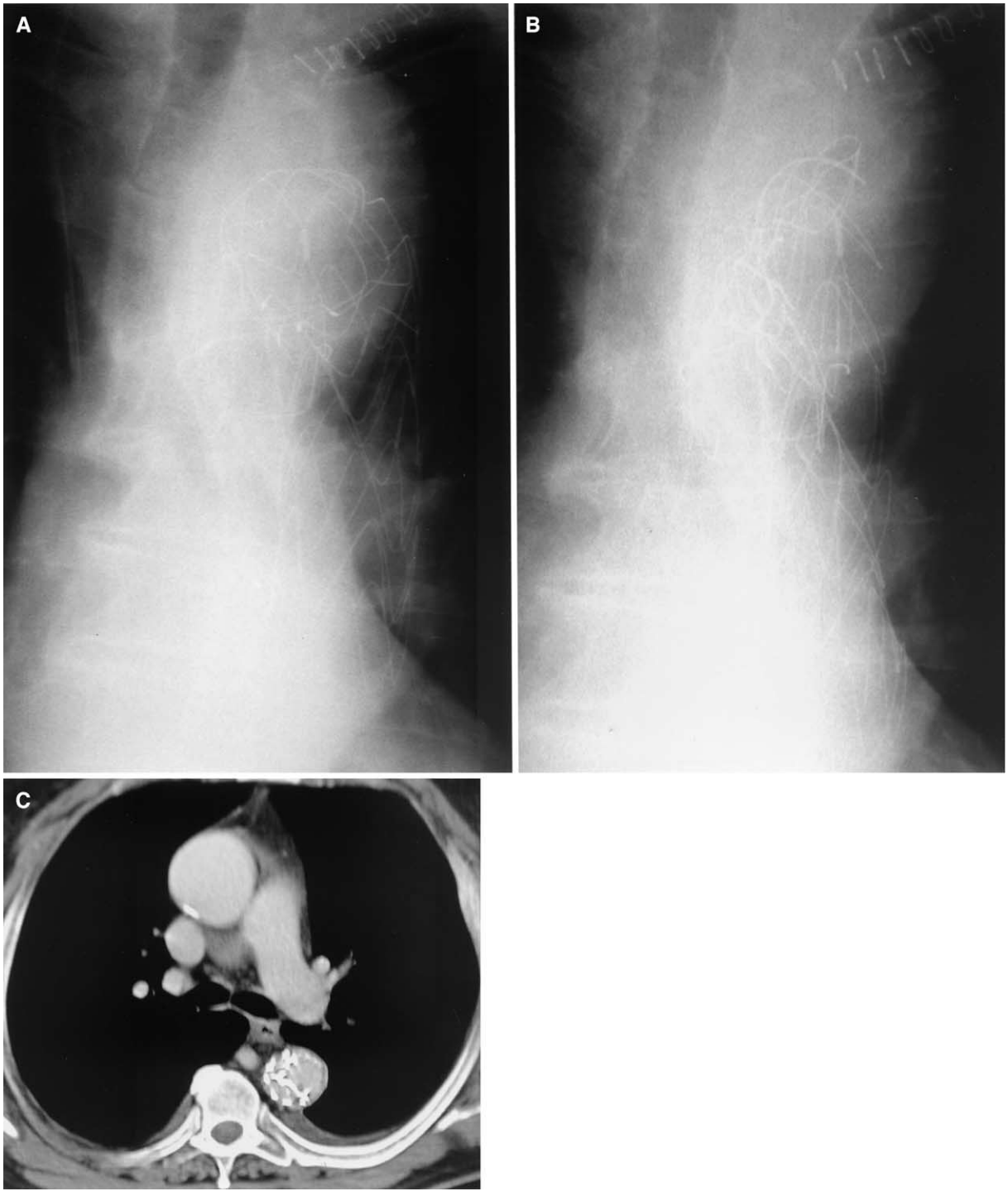

Fig 2. Case 11. **A,** Early postoperative x-ray film shows correct endograft deployment. **B,** X-ray film obtained 2 weeks later shows total collapse of the graft. **C,** CT scan obtained 2 weeks after graft implantation.

withdrawn. Control aortograms are obtained. Visibility of the nitinol stents is good, and the graft usually does not require balloon expansion. Postoperative computed tomography (CT) scans were obtained in all patients but one, before discharge from the hospital. Follow-up CT scans were obtained every 6 months for the first year; additional aortograms were also obtained in patients with endoleak.

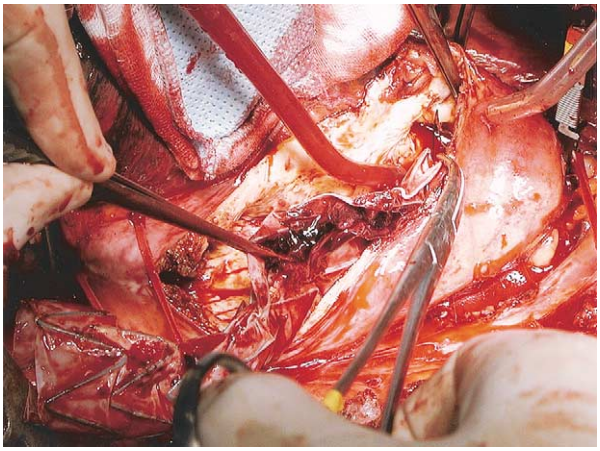

Fig 3. Case 11. Surgical removal of collapsed endograft during open surgical repair with partial left atriofemoral bypass with centrifugal pump.

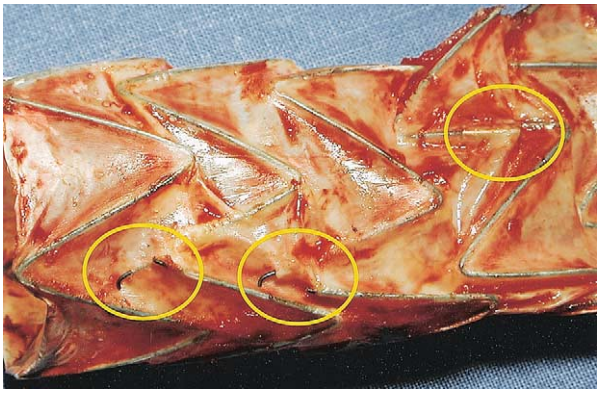

Fig 4. Case 11. Direct examination of the device shows rupture of three stents.

RESULTS

In all 11 patients, the Endofit stent grafts were successfully deployed in the intended position.

There were no complications related to the access site or to anesthesia, and no postoperative paraplegia or paraparesis. Two in-hospital deaths (18%) occurred: one patient died in the operating room; the other patient died in the intensive care unit on postoperative day 30, due to intraoperative stroke.

The patient who died in the operating room was admitted for treatment of a distal arch saccular aneurysm with maximum diameter 7.5 cm. The history included hypertension, myocardial infarction, coronary artery bypass graft implanted 10 years previous but no longer patent, abdominal aortic aneurysm repair, pacemaker implantation, and obstructive pulmonary disease. An aortogram revealed a proximal neck 36 mm in diameter and 30 mm long between the left common carotid artery and the left subclavian artery. The stent graft was delivered at the intended site without complications, and a completion aortogram

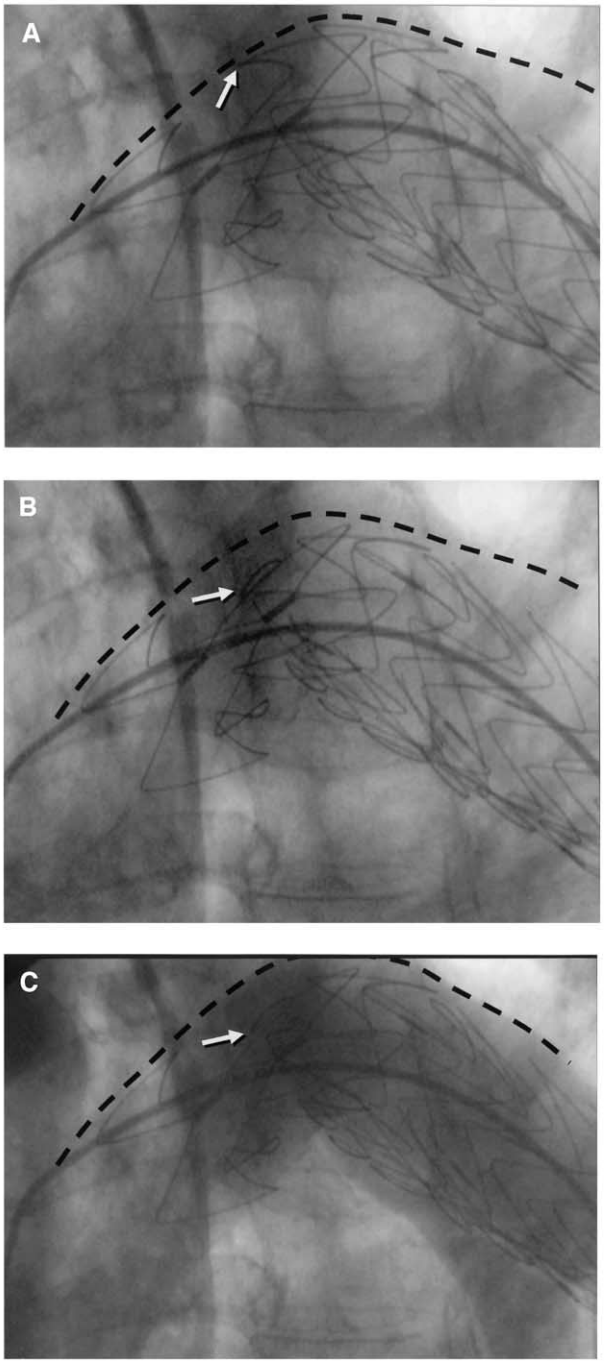

Fig 5. Case 2. Fluoroscopic examination shows proximal covered stent (*arrows*) adherent to aortic wall (*dashed line*) during diastole (**A**) and diverging from aortic wall during systole (**B**). Angiogram shows a type I endoleak during systole (**C**).

showed complete exclusion of the aneurysm and no endoleak. No balloon expansion was performed. One hour after completion of the procedure, the patient had severe hypotension and cardiac arrest. Cardiopulmonary resuscitation was attempted for 45 minutes, and defibrillation was

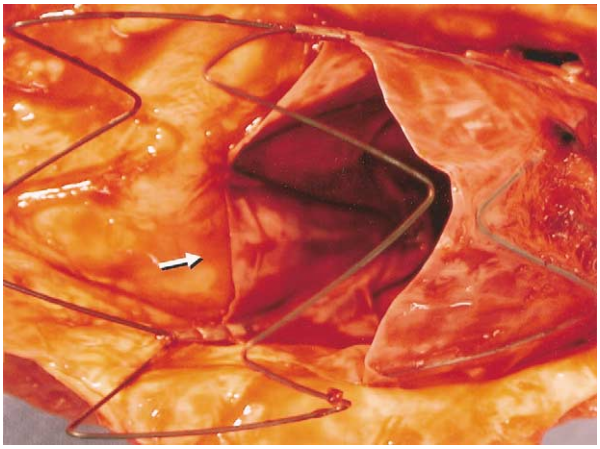

Fig 6. Case 8. At postmortem examination the proximal end of the expandable polytetrafluoroethylene fabric of the stent graft was not adherent to the aortic wall.

performed several times without result. Postmortem examination revealed severe pulmonary congestion, left ventricular hypertrophy and dilatation, and, to our surprise, that the stent graft was completely kinked within the aneurysm (Fig 1). The proximal end was between the left common carotid artery and the left subclavian artery.

The other patient who died underwent treatment of an intramural hematoma, and intraoperative stroke occurred. CT scans showed that it was caused by a cerebellar ischemic infarction with mass effect. Despite emergent external ventricular drainage, severe hydrocephalus developed. The patient was admitted to the intensive care unit, but never recovered. He was comatose and required prolonged respiratory assistance and tracheotomy, and died on postoperative day 30.

Postmortem examination showed that the stent graft was intact and well-expanded. The aortic arch, especially in the area of the origin of the supra-aortic trunks, was atheromatous. Emboli may well have originated from this area during stent-graft positioning and deployment.

In another patient, with a distal arch aneurysm, the graft was deployed successfully (Fig 2, *A*). However, 2 weeks after the procedure a routine chest x-ray study (Fig 2, *B*) and CT scan (Fig 2, *C*) showed total collapse of the graft, as a result of fracture of three stents that perforated the e-PTFE. The patient had no symptoms. Femoral pulses were decreased but still palpable, because flow was present between the collapsed graft and the aortic wall. Open surgery was performed, with partial left atriofemoral bypass with a centrifugal pump. The aorta was clamped proximally between the left common carotid artery and the left subclavian artery. The stent graft was easily removed (Fig 3), and graft replacement was performed with routine technique. Direct examination of the device confirmed rupture of the three stents (Fig 4). The postoperative course was uneventful, and the patient was discharged on postoperative day 6.

In the 2 patients with type I endoleak, it was determined that leakage originated from the proximal neck. At fluoroscopy (Fig 5, *A-C*), the first covered stent was observed to move in and out from the aortic wall during the cardiac cycle, and it was not fully adherent to the proximal neck during systole. Further treatment will be needed in these patients.

Fig 6, obtained at postmortem examination in the patient who died perioperatively, clearly demonstrates that at this level the PTFE fabric is not adherent to the aortic wall and that during systole the force of the blood may produce movement of the stent, as in the patient in Fig 5. In this patient, however, the indication for the procedure was intramural hematoma, and therefore no endoleak was present, which was probably not relevant to the final outcome.

The single type II endoleak was small, and probably due to intercostal branches. One of the middle stents did not open completely (Fig 7); however, this did not seem to be clinically relevant, because the proximal end distal stents sealed the aneurysm satisfactorily. We were not able to observe a stent rupture in this case. We are closely observing all patients with endoleak.

DISCUSSION

Open surgical repair of distal arch and descending thoracic aortic diseases with graft placement is a reliable and durable treatment for aneurysms and other serious conditions. However, morbidity and mortality may be as high as 25% to 28%.[11] Patient age and preoperative comorbid conditions, such as cardiac, respiratory, renal, and neurologic disease, may greatly increase risk. Because it is less invasive, endovascular treatment is an attractive alternative, especially in patients at high risk.[12] The technique may be performed with the patient under locoregional anesthesia[13]; we generally use subarachnoid anesthesia. The procedure is associated with much less hemodynamic alteration, blood loss, and ischemia to the splanchnic, renal, and spinal regions.[14] It also seems to limit immune cell activation and the systemic inflammatory response syndrome associated with open surgical repair of aneurysm.[15]

On the other hand, little is known about long-term safety and durability of the stent grafts that we are implanting. Therefore, in younger patients with good surgical risk, open surgery may still be the best choice.

The Excluder device, for example, which produced good short-term results,[16] is no longer available, because the manufacturer voluntarily withdrew it from the market after mechanical failure was discovered in several patients at follow-up.[10] Patients with these devices are now scrutinized closely to determine the clinical relevance of these failures. As of March 10, 2003, spinal fracture was found in 26 devices worldwide, of the more than 2500 devices implanted in more than 2000 patients. Thus far, no fracture has resulted in any adverse clinical sequelae. The fracture rate in the United States is approximately 10% (19 of 207 patients). To date, only eight fractures have been found in patients outside of the United States (M. Nilson, W. L.

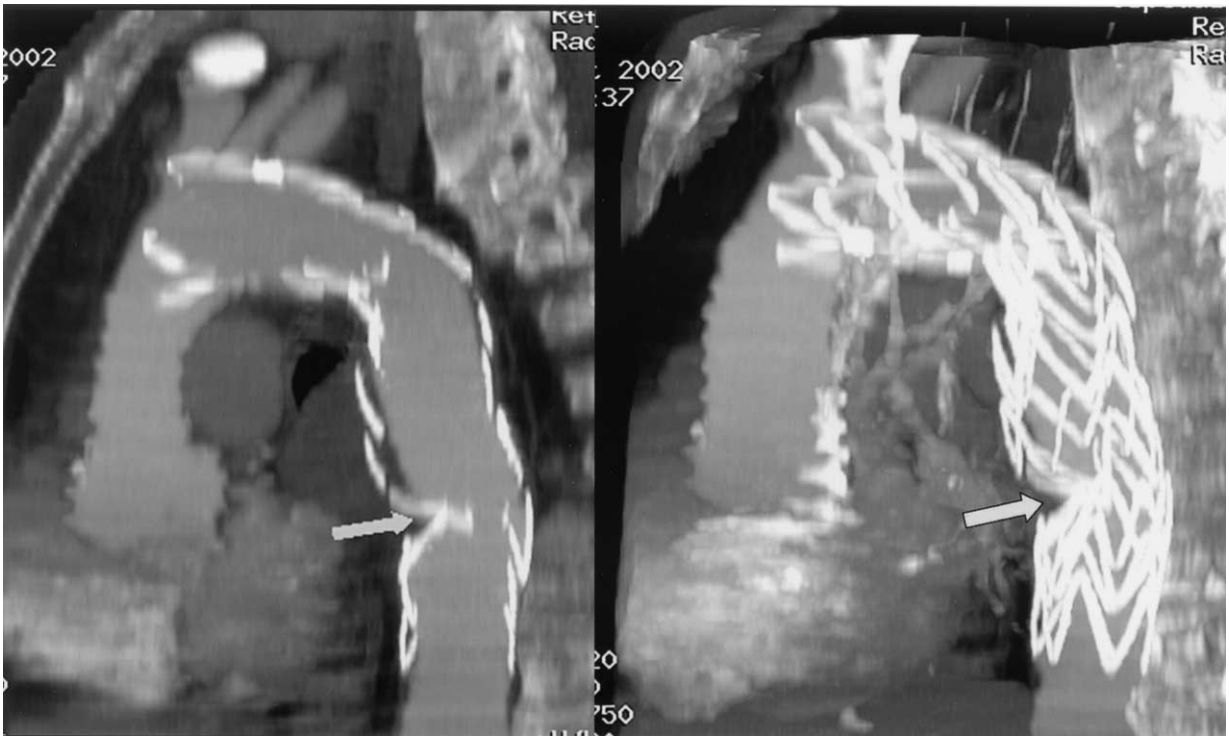

Fig 7. Case 3. *Left,* Spiral computed tomography scan *(sagittal view)* shows incomplete opening of stent *(arrow)* in the distal third of the endograft. *Right,* However, proximal end distal stents sealed the aneurysm satisfactorily.

Gore & Associates, Flagstaff, Ariz, personal communication, March 2003).

Our policy has been to use endovascular treatment for diseases of the distal arch and descending thoracic aorta in patients who are poor candidates for surgery. In 2002, 16 patients underwent open treatment and 11 patients received a stent graft. In the same period only three patients at our institution were believed to be unfit for either procedure and were observed with medical therapy only. Until definitive results from randomized surgical trials are available, we believe this prudent attitude is acceptable.

All patients with endografts must be followed up carefully over time, because previous experience has demonstrated the possibility of aortic rupture despite absence of endoleak on postoperative CT scans.[17]

The Endofit stent graft is a CE-marked product. The CE mark (abbreviation of a French phrase, Conformité Européenne) is affixed by the manufacturer to certain products for access to the European market (consisting of 18 countries; also referred to as the European Economic Area). It is a visual identifier that the product meets the requirements of one or more European directives. What is a directive? To facilitate free trade and ensure the safety of certain products, European countries, through the European Commission, have developed a series of standards, or directives, as they are referred to, that manufacturers must meet to legally export their products to European member countries. These directives replace individual country standards because they relate principally to product safety. Compliance with these directives is mandatory; it is a legal obligation on the part of the manufacturer or the manufacturer's agent. The Medical Devices Directive (MDD: 93/42/EEC) is concerned with all medical devices. To obtain the CE mark, a product must fulfill certain essential safety and environmental requirements; however, the CE mark is basically a measure that the European Union has adopted to establish a single market and foster economic development for member states, permitting products manufactured (or imported) by a member state that do not present a health, safety, or environmental threat to travel freely among the other states.

Detailed information on CE marking can be found on the official website of the European Union: http://europa.eu.int/index_en.htm. In particular, the directive concerning implantable medical devices can be found at the following link (Annex 7 focuses on clinical evaluation of the devices): http://europa.eu.int/eur-lex/en/consleg/pdf/1990/en_1990L0385_do_001.pdf.

Insofar as the properties of the Endofit stent graft are concerned, it is of note that the delivery system is as simple as possible, being made up of a guide wire and a 24F introducer sheath with its dilator, which is also used as a pusher. However, once the graft is inserted into the introducer sheath, it cannot be advanced safely in the aorta because the tip of the sheath is no longer tapered. Therefore, if at this point of the procedure one realizes that the

graft is too low in the aorta, the introducer sheath with the graft must be withdrawn and the procedure started all over again with a new introducer sheath, which may be cumbersome and is time-consuming. The one intraoperative stroke in this series might have been caused by atheromatous dislodgment with the guide wire and introducer during deployment of the stent graft.

During deployment, the upper stents of the device open first; therefore a "parachute effect" is present, and controlled systemic hypotension is advisable.[1] Once the proximal stent is open, corrections in positioning of the stent graft are no longer safe, and the rest of the device should be withdrawn from the sheath rapidly to avoid involuntary displacement.

Initial deployment of the stent grafts in the desired landing zone did not seem to be a problem; in fact, it was successful in all patients. However, when the stent graft was deployed in the distal aortic arch, a great deal of force was needed, both to advance the device up to the desired position and, in particular, to retract the introducer sheath for deployment. Positioning and deployment in the descending aorta was straightforward and much easier.

Regarding our learning curve, our previous experience with endovascular exclusion of thoracic aortic disease comprised 29 patients who underwent treatment between June 1999 and October 2001 with the Excluder graft and 2 patients who received the Talent graft. Despite less experience with endovascular exclusion of aneurysms, the initial results were definitely better. We recorded no 30-day mortality (1 death at 3 months in a patient with chronic dissection), no major morbidity, one type I endoleak in a distal arch aneurysm (sealed spontaneously at 1 month), no surgical conversion, and no graft migration. At mean follow-up of 23 months, we have found no evidence of stent rupture in the Excluder grafts.

Available devices are far from ideal, and several manufacturers are increasing their efforts to produce safer, but also simpler and cheaper, devices. New devices have been made commercially available in an attempt to overcome the problems of existing devices; however, this is not always the case.

In conclusion, endovascular treatment of thoracic diseases with the Endofit graft in this small heterogeneous group of patients demonstrated several problems that may arise both from the delivery system and from the graft itself. At present, we believe that other commercially available endografts may be safer for endovascular treatment of thoracic aortic disease.

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