Endoleak as a predictor of outcome after endovascular aneurysm repair: AneuRx multicenter clinical trial

Christopher K. Zarins, MD,a Rodney A. White, MD,b Kim J. Hodgson, MD,c Donald Schwarten, MD,d and Thomas J. Fogarty, MD,a for the AneuRx Clinical Investigators, Stanford and Torrance, Calif, Springfield, Ill, and Indianapolis, Ind

Objective: The purpose of this study was to determine whether evidence of blood flow in the aneurysm sac (endoleak) is a meaningful predictor of clinical outcome after successful endovascular aneurysm repair.

Methods: We reviewed all patients in Phase II of the AneuRx Multicenter Clinical Trial with successful stent graft implantation and predischarge contrast computed tomographic (CT) imaging. The clinical outcome of patients with evidence of endoleak was compared with the outcome of patients without evidence of endoleak. The CT endoleak status before hospital discharge at 6, 12, and 24 months was determined by each clinical center as well as by an independent core laboratory. Endoleak status at 1 month was assessed with duplex scanning examination or CT at each center without confirmation by the core laboratory.

Results: Centers reported endoleaks in 152 (38%) of 398 patients on predischarge CT, whereas the core laboratory reported endoleaks in 50% of these patients (P < .001). The center-reported endoleak rate decreased to 13% at 1 month. Follow-up extended to 2 years (mean, 10 ± 4 months). One patient had aneurysm rupture and underwent successful open repair at 14 months. This patient had a Type I endoleak at discharge but no endoleak at 1 month or at subsequent follow-up times. There were no differences between patients with and patients without endoleak at discharge in the following outcome measures: patient survival, aneurysm rupture, surgical conversion, the need for an additional procedure for endoleak or graft patency, aneurysm enlargement more than 5 mm, the appearance of a new endoleak, or stent graft migration. Despite a higher endoleak rate identified by the core laboratory, neither the endoleak rate reported by the core laboratory nor the endoleak rate reported by the center at discharge was significantly related to subsequent outcome measures. Patients with endoleak at 1 month were more likely to undergo an additional procedure for endoleak than patients without endoleaks. Patients with Type I endoleaks at discharge and patients with endoleak at 1 month were more likely to experience aneurysm enlargement at 1 year. However, there was no difference in patient survival, aneurysm rupture rate, or primary or secondary success rate between patients with or without endoleak. Actuarial survival of all patients undergoing endovascular aneurysm repair was 96% at 1 year and was independent of endoleak status. Primary outcome success was 92% at 12 months and 88% at 18 months. Secondary outcome success was 96% at 12 months and 94% at 18 months.

Conclusions: The presence or absence of endoleak on CT scan before hospital discharge does not appear to predict patient survival or aneurysm rupture rate after endovascular aneurysm repair using the AneuRx stent graft. Although the identification of blood flow...
in the aneurysm sac after endovascular repair is a meaningful finding and may at times indicate inadequate stent graft fixation, the usefulness of endoleak as a primary indicator of procedural success or failure is unclear. Therefore, all patients who have undergone endovascular aneurysm repair should be carefully followed up regardless of endoleak status. (J Vasc Surg 2000;32:90-107.)

Complete aneurysm exclusion with no endoleak is considered a primary end point of endovascular aneurysm repair. Successful aneurysm exclusion has been achieved in 50% to 90% of cases with the use of a variety of endovascular grafts. Continued blood flow in the aneurysm sac (endoleak) has been reported in 15% to 52% of patients after endovascular repair and is regarded as evidence that the risk of aneurysm rupture has not been eliminated. Conversely, absence of blood flow in the aneurysm sac is viewed as evidence that the patient is no longer at risk for aneurysm rupture. Although aneurysm ruptures have been reported in patients with endoleak after endovascular aneurysm repair, ruptures have also been reported in patients with no endoleak and decreasing aneurysm size. Thus, the risk of rupture in patients with evidence of perigraft flow is unknown. The purpose of this investigation was to determine whether evidence of blood flow in the aneurysm sac after successful endovascular aneurysm repair is a meaningful predictor of clinical outcome.

METHODS

All patients treated during Phase II of the multicenter clinical trial of endovascular aneurysm repair with the Medtronic AneuRx stent graft system (Santa Rosa, Calif) were reviewed. Details of the study design, patient eligibility, and inclusion and exclusion criteria have been previously reported. Thirteen clinical sites participated in this study (see addendum), and all patients were entered into the trial between April 1997 and October 1998. Each study site received Institutional Review Board approval, and all patients gave informed consent.

Each patient met the inclusion criteria of an abdominal aortic aneurysm with an infrarenal neck length of at least 10 mm and a neck diameter between 18 and 26 mm with a maximum distal iliac diameter of 15 mm. Patients were treated with the modular, bifurcated AneuRx stent graft in the operating room or endovascular radiology suite with completion angiographic imaging. Before hospital discharge, contrast computed tomographic (CT) angiography was performed on all patients to document the position of the stent graft and to evaluate the size of the aneurysm and the presence or absence of perigraft flow in the aneurysm sac (endoleak). One month after endovascular repair, patients underwent imaging of the aneurysm and stent graft with the use of either duplex ultrasound scanning or contrast CT or both, as determined by each center. Patients were thereafter imaged with contrast CT at 6 months, 12 months, and 24 months. Abdominal radiographs were taken before discharge at 1 month, 6 months, 12 months, and annually thereafter to evaluate device integrity and migration. Additional imaging was performed as clinically indicated.

Full data sets and selected cross-sectional images of noncontrast- and contrast-infused spiral CT scans were evaluated by the radiologists and investigators at each study site (centers) before hospital discharge and at each subsequent follow-up interval and reported to the AneuRx clinical database. Selected cross-sectional images of the predischARGE CT, 6-month CT, and 12-month CT, along with abdominal radiographs, were sent for blinded reading to an independent radiology group (core laboratory), which had no involvement with any of the clinical investigation sites.

Aneurysm and neck diameter and length, stent graft patency and configuration, evidence of perigraft contrast in the aorta or aneurysm sac (endoleak), and position of the stent graft in relation to the native aorta and L1 vertebral body were recorded. Endoleaks were classified by the core laboratory as to location: proximal, distal, or junctional attachment site (Type I); branch vessel flow (Type II); and undetermined. An increase or decrease in maximum aneurysm diameter by more than 5 mm compared with predischARGE CT imaging at any time during the follow-up or between any two consecutive follow-up intervals was considered to be a significant diameter change.

Patients were grouped according to whether an endoleak was present, and analysis was performed according to endoleak status as defined by (a) investigational site (centers) report of endoleak based on predischARGE CT, (b) core laboratory report of endoleak based on review of same predischARGE CT scans as in (a), and (c) investigational site (centers) report of endoleak at 1 month determined by CT or duplex scan. Outcome related to endoleak type was based on core laboratory classification of Type I and Type II endoleaks. The following outcome measures were
used: death, aneurysm rupture, conversion to open surgical repair, stent graft patency, additional procedure for endoleak or nonpatency, aneurysm enlargement, new endoleak, and stent graft migration.

Results are reported as the mean and SD. Statistical differences between groups were evaluated with the 2-tailed Student t test, Wilcoxon rank sum test, x^2 analysis, Fischer exact test, and McNemar test, as appropriate. Differences are reported as significant if the P value was equal to or less than .05.

RESULTS

Among the 425 patients entered into Phase II, the AneuRx bifurcation stent graft was successfully deployed in 414 (97%). In three patients, no treatment attempt was made. In eight patients (2%) the iliac arteries were too small or tortuous to introduce the device. Six patients died in the hospital (hospital mortality rate, 1%), and five underwent open surgical repair (surgical conversion rate, 1%). Postimplantation CT imaging was not obtained or unavailable for review in nine patients. Thus, there were 398 Phase II patients with successful implantation and predischARGE CT imaging available for analysis.

Endoleak evaluation

Predischarge CT scans were performed within 2 days of stent graft insertion in 89% of patients, within 4 days in 95% of patients, and within 1 week in 98% of patients. Investigational sites (centers) reported endoleaks in 152 (38%) of 398 patients and no endoleaks in 246 (62%) of 398 patients on the basis of noncontrast- and contrast-infused CT scans before hospital discharge. The core laborato-

![Kaplan-Meier Survival Curve](image)

**Fig 1.** Kaplan-Meier survival curves for patients with and without endoleak after successful endovascular aneurysm repair. A, Endoleak status before hospital discharge.
ry reported endoleaks in 175 (50%) of 350 patients and no endoleaks in 175 (50%) of 350 patients on the basis of its review of selected images of the same predischarge contrast CT. The core laboratory endoleak rate was significantly higher ($P < .001$) than that reported by the centers.

Endoleak status at 1 month was documented with the use of either duplex ultrasound scanning or contrast CT as determined by each center. CT scans were not required by the study protocol, and no evaluation by the core laboratory was performed. One-month evaluation was performed with duplex ultrasound scanning in 254 patients (67%), contrast CT scans in 124 patients (33%), and magnetic resonance angiography in one patient. Endoleak was documented in 51 (13%) of 379 patients, and no endoleak was present in 328 (87%) of 379 patients. Mean time to last follow-up was 10 months with a range of 1 to 25 months. There were 242 patients (61%) who had 1-year follow-up data, and seven patients had 2-year follow-up data.

**Patient characteristics**

Baseline patient characteristics and risk factors were recorded before endovascular treatment. Patients with or without endoleak on predischarge CT as defined by the centers are shown in Table I. Patients with endoleak were slightly older, had a higher rate of treatment of coronary artery disease, had a higher rate of alcoholism, and had a more frequent history of prior abdominal or pelvic radiation. There were no differences in other baseline (preoperative) risk factors or patient characteristics. Multivariate analysis to control for these differences
in baseline characteristics did not alter the results of group comparisons.

When patients were grouped according to endoleak status as defined by the core laboratory reading of the predischarge CT, there were no differences between patients with endoleak (n = 175) and those without endoleak (n = 175), except for a higher rate of alcoholism in the endoleak group (P = .048). Multivariate analysis to control for this difference in baseline characteristics did not alter the results of group comparisons.

When patients were grouped according to endoleak status at 1 month as determined by the centers, there were no significant differences in baseline patient characteristics between patients with and those without endoleak, with the exception of increased smoking history in patients without endoleak (85%) than in those with endoleak (73% P = .03). Statistical adjustment for this baseline difference did not alter the outcome analysis of the 1-month patient analysis.

**Endoleaks after endovascular aneurysm repair**

The endoleak rate before hospital discharge was 38% as reported by the centers and 50% as reported by the core laboratory (P < .001). The endoleak rate at 1 month was determined by the centers to be 13%. The endoleak rate reported by the centers was 16% at 6 months and 13% at 1 year, compared with an endoleak rate of 27% at 6 months and 20% at 1 year reported by the core laboratory (P < .001) (Table III). Although there was a consistently higher endoleak rate reported by the core laboratory, there was no difference in the rate of detection of new endoleaks (6%), stent graft migration (2%), or aneurysm enlargement (6%) between the center and core laboratory readings.

Endoleaks were classified by the core laboratory as Type I (attachment site) in 54 patients (31%), Type II (branch flow) in 70 patients (40%), and undetermined in 51 patients (29%). Among the 54 Type I endoleaks, there were 16 proximal (30%), 3 distal (6%), 22 junctional (40%), and 13 extender cuff (24%) endoleaks. Among the 70 Type II

**Preoperative aneurysm morphology**

There were no differences in preoperative aneurysm morphology between patients with endoleak and without endoleak as defined by either the centers or core laboratory (Table II). Morphologic features evaluated included aneurysm diameter, neck diameter, neck length and aneurysm length, and the degree of calcification and thrombus. Also evaluated was whether the aneurysm was localized to the aorta alone (Class A and B) or involved the iliac arteries (Class C, D, and E) (Table II).
endoleaks, 67 (96%) were primarily related to lumbar arteries, whereas three (4%) were primarily related to the inferior mesenteric artery.

Deaths

Twenty patients have died during the follow-up period. No patient died of aneurysm rupture. There was no difference in the mortality rate for patients with endoleak (5%) on predischarge CT compared with patients without endoleak (5%). There was no difference in mortality rate between center-defined and core laboratory-defined endoleak. There was no difference in the mortality rate between patients with or without endoleak at 1 month (Table IV). Ten patients have died of cardiac causes, 2 of strokes, 1 of pneumonia, 5 of cancer, and 2 of gastrointestinal disorders. Life table/Kaplan-Meier analysis reveals no difference in survival of patients, with or without predischarge endoleak as defined by the centers or core laboratory (Fig 1). There was no difference in life table survival between patients with or without endoleak at 1 month.

Aneurysm rupture

One patient had aneurysm rupture 14 months after endovascular aneurysm repair. This man was aged 80 years and had severe coronary artery disease and a 6.8-cm abdominal aortic aneurysm before endovascular repair. One day after successful placement of the stent graft, contrast CT revealed a minor endoleak at the iliac junction, by both center and core laboratory reading. One month later the center reported no endoleak, and aneurysm size was unchanged. The core laboratory reviewed this CT scan and confirmed the findings. The CT scan performed at 6 months revealed no endoleak and no change in aneurysm size. At the 1-year follow-up, the patient refused CT scanning. Duplex ultrasound scanning revealed no endoleak. Two months later the patient experienced back pain, and a CT scan demonstrated rupture of the aneurysm, which now measured 7.5 cm with endoleak and contrast extravasation (Fig 2). The patient underwent emergent operation with successful open repair of his aneurysm. At operation insecure proximal fixation of the stent graft in a short angulated neck was identified as the cause of rupture. The iliac junction, the source of the early endoleak, was intact.

Open surgical repair

Two patients (0.5%) underwent open surgical repair (surgical conversion) during the follow-up period. No patient died of aneurysm rupture. There was no difference in the mortality rate for patients with endoleak (5%) on predischarge CT compared with patients without endoleak (5%). There was no difference in mortality rate between center-defined and core laboratory-defined endoleak. There was no difference in the mortality rate between patients with or without endoleak at 1 month (Table IV). Ten patients have died of cardiac causes, 2 of strokes, 1 of pneumonia, 5 of cancer, and 2 of gastrointestinal disorders. Life table/Kaplan-Meier analysis reveals no difference in survival of patients, with or without predischarge endoleak as defined by the centers or core laboratory (Fig 1). There was no difference in life table survival between patients with or without endoleak at 1 month.
period. One was the patient with rupture, described above. A second patient had endoleak at discharge, at 1 month, and at 6 months because of a proximal Type I endoleak with no change in aneurysm size. The patient declined a recommendation to place a proximal extender cuff and chose to undergo elective open surgical repair.

**Additional procedures**

Twenty-two patients (6%) underwent secondary treatments during the follow-up period for endoleak or nonpatency. Of these, 15 were for endoleak, and seven were for graft limb occlusion.

**Endoleak.** Fifteen patients (4%) with endoleak were treated with a secondary endovascular procedure from 2 weeks to 16 months after the initial stent graft repair. Most were treated more than 6 months after stent graft placement. Of these, nine had endoleak at hospital discharge, and six had no endoleak. At 1 month, eight continued to have endoleak, and seven had no endoleak. Nine patients were treated for persisting endoleaks at 2 weeks to 13 months (mean, 6 months); five patients were treated with proximal extender cuffs, three with distal extender cuffs, and one with both proximal and distal extenders. The endoleak was successfully sealed in three patients and persists in six patients.

Six patients had no endoleak at hospital discharge, and five of the six had no endoleak at 1 month. New endoleaks were identified at 1 month in one patient and between 8 and 16 months (mean, 12 months) in five patients. All six were successfully
treated with elimination of the leak. Three patients had proximal extender cuffs, two had distal extender cuffs, and one had both proximal and distal extenders.

**Nonpatency.** Seven patients (2%) had occlusion or obstruction of one limb of the stent graft 1 week to 6 months after stent graft repair. Of these patients, three had endoleak, and four had no endoleak at the time of hospital discharge. At 1 month, none had evidence of endoleak. Five patients were treated within 1 month, one was treated at 6 weeks, and one was treated at 6 months to restore blood flow. Graft patency was restored in four patients, three with thrombectomy and femoral artery revision and one with thrombolysis, angioplasty, and stent placement. In two patients, flow was restored with femoral-femoral bypass grafting, and in one patient flow was restored with an axillopopliteal bypass graft. Thus, primary graft patency was 98% and secondary graft patency was 99%. Flow was restored to the lower extremities in all patients. There was no difference in the rate of additional procedures performed on the basis of endoleak status as determined by either the centers or core laboratory before hospital discharge (Table IV). Patients with endoleak at 1 month were more likely to undergo an additional procedure during the follow-up period (16%) compared with patients with no endoleak at 1 month (4%, \( P < .01 \)).

**New endoleaks**

A new endoleak was defined as contrast enhancement of the aneurysm sac on CT scan in a patient with no evidence of endoleak on the previous study. A new endoleak during the course of the study was documented by the centers in 9% of patients and by the core laboratory in 6% of patients. There was no differ-
ference in the appearance rate of new endoleaks between patients with and without endoleak at hospital discharge as determined by the centers or the core laboratory. There was no difference in new endoleak between patients with and without endoleak at 1 month (Table IV). Among the 32 patients with new onset endoleak identified by the centers, six (19%) had an additional procedure that successfully treated the endoleak; three of these new endoleaks were related to stent graft migration described below.

**Aneurysm enlargement**

Aneurysm enlargement was defined as an increase in maximum aneurysm diameter by more than 0.5 cm from predischarge imaging at any time during the follow-up period or between any two consecutive follow-up intervals. Aneurysm diameter on the predischarge CT was used as the baseline for comparison of aneurysm diameter changes during the follow-up period. This baseline was selected because the predischarge CT was performed, on average, 2 days after endovascular repair, whereas there was considerable variability in the time interval (sometimes several month delays) between the preoperative CT and placement of the stent graft. In addition, the preprocedure CT was often done at an outside referring hospital, which was different from the study center with variability in technique.

Six months after endovascular repair, aneurysm diameter had not changed in 88% to 89% of patients (Table V). In 2% to 4% of patients, aneurysm diameter increased more than 5 mm, and in 7% to 10% of patients aneurysm diameter decreased more than 5 mm. There was no statistical difference in diameter changes between patients with and those without endoleak at hospital discharge as determined by the centers or the core laboratory. There was no difference between patients with center-defined and core laboratory-defined endoleaks.

After 12 months, aneurysm diameter was increased by more than 5 mm in 1% to 8% of patients, was decreased by more than 5 mm in 14% to 25% of patients, and was unchanged in approximately 75% of patients. There were no significant differences in aneurysm diameter changes between patients with and those without endoleak at hospital discharge as determined by the centers or the core laboratory. There was no difference in new endoleak between patients with and without endoleak at 1 month (Table IV). Among the 32 patients with new onset endoleak identified by the centers, six (19%) had an additional procedure that successfully treated the endoleak; three of these new endoleaks were related to stent graft migration described below.

**Table II. Aneurysm morphology: preoperative CT imaging**

<table>
<thead>
<tr>
<th>AAA diameter (cm)</th>
<th>Centers (n = 398)</th>
<th>Core laboratory (n = 350)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Endoleak (n = 152)</td>
<td>No endoleak (n = 246)</td>
<td></td>
</tr>
<tr>
<td>AAA diameter (cm)</td>
<td>5.6 ± 1.0</td>
<td>5.5 ± 0.9</td>
<td>ns</td>
</tr>
<tr>
<td>Neck diameter (cm)</td>
<td>2.2 ± 0.3</td>
<td>2.2 ± 0.2</td>
<td>ns</td>
</tr>
<tr>
<td>Neck length (cm)</td>
<td>2.7 ± 1.4</td>
<td>2.8 ± 1.3</td>
<td>ns</td>
</tr>
<tr>
<td>Calcification</td>
<td>77%</td>
<td>76%</td>
<td>ns</td>
</tr>
<tr>
<td>Thrombus</td>
<td>81%</td>
<td>85%</td>
<td>ns</td>
</tr>
<tr>
<td>AAA class</td>
<td></td>
<td></td>
<td>ns</td>
</tr>
<tr>
<td>A</td>
<td>26%</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>47%</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>16%</td>
<td>11%</td>
<td>ns</td>
</tr>
<tr>
<td>D</td>
<td>5%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td></td>
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</table>

AAA, Abdominal aortic aneurysm; ns, not significant.

**Table III. Endoleaks after endovascular aneurysm repair: posttreatment CT imaging**

<table>
<thead>
<tr>
<th>Endoleak at Hospital discharge</th>
<th>Centers (N = 398)</th>
<th>Core laboratory (N = 350)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAA diameter (cm)</td>
<td>5.6 ± 1.0</td>
<td>5.6 ± 0.9</td>
<td>ns</td>
</tr>
<tr>
<td>Neck diameter (cm)</td>
<td>2.2 ± 0.3</td>
<td>2.2 ± 0.2</td>
<td>ns</td>
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<td>2.7 ± 1.4</td>
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<td>26%</td>
<td>15%</td>
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<td>B</td>
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<td>16%</td>
<td>11%</td>
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<td>D</td>
<td>5%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td></td>
<td></td>
<td>ns</td>
</tr>
</tbody>
</table>

Center data verified by external auditors and entered into central database. Core laboratory independent blinded review. *Comparison of center vs core laboratory reading. ns, Not significant.
discharge as defined by the core laboratory. Among patients without endoleak as defined by the centers at 12 months, mean aneurysm diameter decreased more (–2.6 ± 5.1 mm) than in patients with endoleak (–0.7 ± 4.0 mm) (P < .02) (Table V).

Patients with endoleak at 1 month as defined by the centers had an increased risk of aneurysm enlargement (12%) at 12 months, compared with patients without endoleak (4%) (P < .05) (Table IV).

In addition, patients with Type I endoleaks at discharge had an increased likelihood of aneurysm enlargement (15%) compared with patients with no Type I endoleak (5% P > .01, Table VI). However, only 22 patients (6%) had an increase in aneurysm diameter of 5 mm or greater at any time (Table III), and of these, only 15 (68%) had an endoleak at any time. Among 342 patients with no increase in aneurysm diameter, 103 (30%) had an endoleak reported at some time during the course of the study. Thus, detection of an endoleak was poorly correlated to increase in aneurysm size.

### Stent graft migration

Seven patients had radiologic evidence of stent graft movement relative to the native aorta during the course of the study. Three patients were successfully treated with an additional endovascular procedure at the time of appearance of a new endoleak and are described among the additional procedures for endoleak. Three patients have never had an endoleak, and one had an endoleak at discharge and has a continuing endoleak with no change in aneurysm size.

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**Fig 4.** Kaplan-Meier secondary outcome estimates (no death, no aneurysm rupture, and no conversion to open surgical repair) for patients with and those without endoleaks at (A) hospital discharge.

<table>
<thead>
<tr>
<th>Endoleak</th>
<th>Time</th>
<th>discharge to 6 months</th>
<th>6 months to 1 year</th>
<th>1 year to 18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td># at Risk</td>
<td>152</td>
<td>149</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td># Events</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td># Censored</td>
<td>1</td>
<td>29</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Kaplan-meier estimates</td>
<td>0.987</td>
<td>0.952</td>
<td>0.932</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No Endoleak</th>
<th>Time</th>
<th>discharge to 6 months</th>
<th>6 months to 1 year</th>
<th>1 year to 18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td># at Risk</td>
<td>246</td>
<td>236</td>
<td>201</td>
<td></td>
</tr>
<tr>
<td># Events</td>
<td>9</td>
<td>1</td>
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</tr>
<tr>
<td># Censored</td>
<td>1</td>
<td>34</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Kaplan-meier estimates</td>
<td>0.963</td>
<td>0.959</td>
<td>0.934</td>
<td></td>
</tr>
</tbody>
</table>
Stent graft migration at any time during the course of the study was identified in 3% of patients with endoleaks at discharge and in 2% of patients with no endoleak before hospital discharge. There was no difference between patients with endoleak and without endoleak as defined by the centers or core laboratory. There was no difference in stent graft migration rate between patients with and without endoleak at 1 month.

**Primary outcome success**

Primary outcome success was defined as no death, no aneurysm rupture, no conversion to open surgical repair, and no additional procedure for endoleak or nonpatency of the stent graft. There was no difference in Kaplan-Meier primary outcome estimates between patients with and without endoleak before hospital discharge as defined by the centers (Fig 3, A). There were no differences when these results were adjusted for baseline group differences by the Cox proportional model or if the analysis was carried out using the core laboratory definition of endoleak. Primary outcome was decreased (P < .001) in patients with endoleak at 1 month compared with patients without endoleak (Fig 3, B) because of the increase in additional procedures for endoleak and nonpatency.

**Secondary outcome success**

Secondary outcome success was defined as no death, no aneurysm rupture, and no conversion to open surgical repair. There was no difference in secondary outcome between patients with and without endoleak before hospital discharge (Fig 4, A) and no difference in secondary outcome between patients with and without endoleak at one month (Fig 4, B). There were no differences when these results were adjusted for baseline group differences by the Cox proportional model or if the analysis was carried out using the core laboratory definition of endoleak.
adjusted for baseline group differences by the Cox proportional model or if the analysis was carried out using the core laboratory definition of endoleak.

Outcome by endoleak type

Outcome by endoleak type as determined by the core laboratory is presented in Table VI. There were no differences in death from any cause or aneurysm rupture rate between patients with Type I or Type II endoleaks and those with no endoleaks. Patients with Type I endoleaks were more likely to undergo surgical conversion and experience aneurysm enlargement compared with patients with no Type I endoleak (P < .05). Patients with Type II endoleak were less likely to experience a new endoleak compared with patients without Type II endoleaks (P < .05). There were no significant differences in primary or secondary outcome success in patients with Type I or Type II endoleaks and those with no endoleaks.

DISCUSSION

Endovascular aneurysm repair has been shown to have significant short-term benefits compared with open surgical repair with reduced blood loss, reduced hospital stay, reduced morbidity, and earlier return to function. However, the long-term effectiveness of endovascular repair in preventing aneurysm rupture and death is unknown. Endoleaks have been identified in 15% to 52% of patients after endovascular repair and have been related to aneurysm rupture. But rupture has also been observed in patients who have not had endoleaks after endovascular repair. Although endoleak has been called “the major complication of endovascular aneurysm repair,” there is little evidence that endoleak in and of itself represents an adverse event of the procedure. Rather, endoleak is an indicator of continued blood flow in the aneurysm sac after endovascular repair. Presumably, the blood flow in the aneurysm sac is less than it was before the stent graft was placed in the aneurysm. How this alters the natural history of the aneurysm is still undefined. Thus, the significance of endoleaks and the determinants of long-term outcome are unknown.

Because the primary outcome of aortic aneurysm repair is to prevent aneurysm rupture and death from rupture, we considered a successful primary outcome after endovascular aneurysm repair to be rupture-free survival with a patent stent graft, no conversion to open surgical repair, and no need for an additional endovascular procedure. A successful primary outcome after stent graft repair by Kaplan-Meier analysis was achieved in 92% of patients at 12 months and 88% of patients at 18 months in this study. There was no significant difference in primary outcome between patients with and those without endoleak at the time of hospital discharge. This was true whether the center or core laboratory determination of endoleak was used for the analysis.

Rupture-free survival with a patent graft and no conversion to open surgical repair were achieved with the use of additional procedures to treat endoleak or nonpatency of the graft in 6% of patients. This resulted in a secondary outcome success of 96% at 12 months and 94% at 18 months. There was no difference in secondary outcome between patients with and those without endoleak at the time of hospital discharge. This was true whether the center or core laboratory determination of endoleak was used for the analysis.
a reduced primary outcome success rate. In patients with no endoleak at 1 month, primary success was 95% at 12 months and 92% at 18 months, whereas patients with endoleak had a primary success rate of 86% at 12 months and 77% at 18 months (P < .001). This difference was due entirely to the additional endovascular procedures performed in the patients with endoleak. The decision to treat endoleaks was investigator determined and subject to investigator bias as to the significance of the endoleak. Among the nine patients with endoleak at discharge who underwent additional endovascular treatment for the endoleak, six continued with endoleaks after the additional treatment. However, the six patients with no endoleak at discharge who had new onset endoleaks during the follow-up period were all successfully treated with endovascular techniques to eliminate the endoleak. There was no difference in the secondary success rate at 18 months between patients with endoleak at 1 month (91%) and those without endoleak at 1 month (96%).

There is wide variability in the reported rate of endoleak and lack of uniformity in classification and quantification of endoleak.11,26,27,28 The endoleak rate reported in this study is higher than the endoleak rate reported in the first 150 patients treated with the AneuRx stent graft.4 This may be due to the fact that the earlier report included the Phase I feasibility study, which did not have the same focus on postoperative imaging with independent core laboratory review. Patient selection was more restricted in Phase I and included only four study sites, whereas this report of Phase II study patients included 13 investigational sites. Endoleaks in this study were evaluated by each clinical center as well as by an independent, central core laboratory. Endoleak classification was determined by the core laboratory to ensure that consistency and criteria for Type I and Type II endoleaks were maintained throughout the study. Several refinements of endoleak classification have been proposed since this study was begun,24,26,28 but the reliability and accuracy of precisely defining the endoleak source have not been defined. In this study, the source of endoleak could not be determined in 29% of CT scans. Perhaps more precise imaging techniques will reduce the number of "undetermined" endoleaks in the future. Although attachment site endoleaks are meaningful and usually prompt additional treatment, 89% of predischarge Type I endoleaks in this

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**Fig 5.** CT scan at 6 months of patient with aneurysm rupture at 14 months (same patient as in Fig 2) demonstrating short, angulated neck with eccentric fixation of proximal stent graft. A, Infrarenal aortic segment with tortuosity apparent at level of left renal artery. B, Eccentric fixation of proximal portion of stent graft in tortuous infrarenal segment. C, Body of stent graft within aneurysm with no endoleak. D, Bifurcation portion of stent graft with no endoleak.
study were not treated. Although no significant relationship between endoleak type and outcome was identified in this study, the follow-up period is relatively short. Longer-term follow-up may well identify certain endoleak types as meaningful predictors of outcome.

The endoleak rate reported by the study centers was significantly lower than the endoleak rate reported by the core laboratory according to the evaluation of the same contrast-infused CT scans. There are several possible explanations including a potential bias to underread endoleaks by the centers and a potential bias to overread endoleaks by the core laboratory. In addition, the data set for evaluation was not identical. The study sites had the advantage of real-time access to the complete data set of spiral CT images with both precontrast and postcontrast infusion images as well as delayed images. The center radiologist could order additional images and adjust contrast technique as necessary to make a determination. Hard copy CT film images may be printed at variable intervals, such as every fourth image, and the core laboratory had access to only those films that it received. Noncontrast CT images help differentiate calcium in the mural thrombus or aneurysm wall from contrast in the aneurysm sac. On occasion only the contrast CT images, but not the noncontrast images, were sent to the core laboratory. Thus, the higher reading of endoleak in the core laboratory may be due, in part, to interpretation of calcium as endoleak. This highlights the difficulty in classification and quantification of endoleaks with precision. Nonetheless, regardless of the difference in overall endoleak rate, there was no difference in evaluation of clinically significant features such as the appearance of a new endoleak, change in aneurysm size, or evidence of stent graft migration between the centers and the core laboratory. Most important, there was no difference in the analysis of clinical outcome that was based on whether the center or core laboratory assessment of endoleak was used.

Changes in aneurysm size have been related to the presence or absence of endoleak. An increase in aneurysm size has been related to the presence of endoleak, whereas absence of an endoleak has been associated with a decrease in aneurysm size. In this study the presence of endoleak before hospital discharge was not associated with an increased likelihood of increase in aneurysm size, nor was the absence of endoleak associated with an increased likelihood of decrease in aneurysm size. Most aneurysms did not change and remained within 0.5 cm of their original diameter at 12 months. However, all endoleaks are not the same, and certain endoleak types, such as those related to device attachment or fixation (Type I), have greater significance. In this study, patients with Type I endoleaks had a threefold increased likelihood of experiencing aneurysm enlargement at 1 year than those without Type I endoleaks. Endoleaks that persisted longer than 1 month also had an increased likelihood of aneurysm enlargement at 1 year. However, only 6% of patients had any aneurysm enlargement during the follow-up period, and 42% of these patients had no endoleak of any type at any time during the study. Thus, endoleak was not a reliable indicator of a propensity for aneurysm enlargement.

The low predictive value of the postprocedure contrast CT suggests that CT scans may not always be essential before hospital discharge. Duplex ultrasound scanning can potentially be used before dis-
charge to image the aortic aneurysm and stent graft, to record aneurysm size, and to identify endoleaks.\(^{30}\) Timing of the postprocedure contrast CT at 1 month after the procedure offers the advantage of avoiding an additional contrast load to the patient within a short time of the endovascular procedure, particularly if there is borderline or compromised renal function. Second, at the 1-month time period, many early endoleaks will be closed. Endoleak status at 1 month appears to be more meaningful than endoleak status at hospital discharge, and elimination of the predischarge CT would reduce procedure-related hospital costs.

A number of investigators have focused on endoleaks, identifying them as the primary failure mode of endovascular repair, and have closely related them to risk of aneurysm rupture.\(^{10,11,24}\) However, many reports include a variety of stent grafts with differing reasons for failure, including endovascular devices in the early stages of development and those that are no longer manufactured.\(^{10,11}\) Some of the ruptures and failures have been related to fabric or device structural failure,\(^{29,32-35}\) which may not occur in improved stent graft designs. Although failures have been linked to endoleaks, the endoleak may simply be the method by which the failure was identified and demonstrated, rather than providing evidence that flow in the aneurysm sac is the prerequisite cause of rupture.

Untreated aneurysms all have large endoleaks, and not all aneurysms rupture. The risk of rupture of untreated aneurysms is related to aneurysm size. Aneurysm enlargement and rupture may be determined by factors other than whether there is blood flow in the aneurysm sac.\(^{36}\) The annual expansion rate of aneurysms ranges from 6.5% to 20.6% of diameter per year.\(^{37}\) If one assumes an average increase in diameter of 10% per year and the average aneurysm diameter in this series was 56 mm, then the expected increase in aneurysm diameter at 1 year would have been 5.6 mm. We observed that aneurysm size did not change or decreased in 92% of patients with endoleaks, suggesting that despite continued blood flow in the aneurysm sac the natural tendency for aneurysms to enlarge was altered in most patients. Similarly, 98% of patients without endoleak had no change or a decrease in aneurysm diameter. However, 2% of patients without endoleak had an increase in diameter of more than 5 mm, indicating that diameter changes are possible without evidence of endoleak.

Consideration of endoleak as a primary end point of treatment rather than prevention of aneurysm enlargement and rupture may lead to significant adverse patient outcome. A focus on endoleak and the elimination of endoleak as an end point of treatment may expose the patient to an increased risk of aneurysm rupture.\(^{34,38}\) Clinical treatment of aneurysms in the past has been guided by aneurysm size and changes in diameter or symptoms, and there is no evidence that there should be a change in favor of endoleaks.

Furthermore, absence of endoleak is no assurance that the patient is free of the risk of rupture. This is illustrated by the patient in this series who had aneurysm rupture at 14 months. This patient had an endoleak at hospital discharge related to the modular iliac junction site. This was sealed at 1 month and remained sealed for 1 year with no endoleak. The aneurysm ruptured at 14 months because of dislodgment of proximal fixation in a short, angulated infrarenal neck (Fig 5), a site remote from the source of the earlier endoleak.

One additional patient treated with an AneuRx stent graft has experienced aneurysm rupture during this follow-up period. This second patient was among the 40 patients treated in Phase I of the AneuRx Clinical Trial.\(^4\) This patient was aged 70

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### Table VI. Outcome by endoleak type

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Type I (N = 54)</th>
<th>Type II (N = 70)</th>
<th>No endoleak (N = 175)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (any cause)</td>
<td>2 (4%)</td>
<td>3 (4%)</td>
<td>7 (4%)</td>
</tr>
<tr>
<td>Aneurysm rupture</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Surgical conversion</td>
<td>2* (4%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Additional procedure</td>
<td>4 (7%)</td>
<td>1 (1%)</td>
<td>7 (4%)</td>
</tr>
<tr>
<td>Aneurysm enlargement</td>
<td>8* (15%)</td>
<td>5 (7%)</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>New endoleak</td>
<td>3 (2%)</td>
<td>0† (0%)</td>
<td>10 (6%)</td>
</tr>
<tr>
<td>Migration</td>
<td>1 (2%)</td>
<td>2 (3%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>Primary success</td>
<td>46 (85%)</td>
<td>66 (94%)</td>
<td>161 (92%)</td>
</tr>
<tr>
<td>Secondary success</td>
<td>50 (93%)</td>
<td>67 (96%)</td>
<td>168 (96%)</td>
</tr>
</tbody>
</table>

*P < .05 compared with no Type I endoleak.
†P < .05 compared with no Type II endoleak.
years and had a 5.5-cm aneurysm at the time of endovascular repair. The aneurysm was successfully excluded with no endoleak at hospital discharge and no endoleak at 1 month, 6 months, and 12 months. Aneurysm diameter was unchanged and measured 5.5 cm at 6 months and 12 months. At 23 months, the patient had back pain and underwent successful open repair of a ruptured aortic aneurysm. Review of morphologic features of this aneurysm also revealed a short angulated neck, raising the possibility that this anatomic feature may identify patients with less secure proximal fixation who may need closer follow-up. It highlights the fact that aneurysms may rupture after endovascular repair with no evidence of endoleak and that other measures such as aneurysm size changes and stent graft fixation configuration may be more important than endoleak status in identifying patients at risk for future adverse events.

Considering both Phase I and Phase II data, it appears that the aneurysm rupture rate after AneuRx stent graft repair of 5.6-cm abdominal aneurysms is 0.5% up to 2 years. This can be compared with an expected rupture rate of approximately 11% per year for 5- to 6-cm aneurysms that are untreated. Thus, endovascular repair markedly reduces, but does not entirely eliminate, the risk of aneurysm rupture. Endoleak, however, does not appear to be a reliable predictor of those patients who may be at future risk of rupture. Thus, all patients, regardless of endoleak status, should be followed up closely.

The 18-month cumulative survival rate of 94% in this study compares favorably with an 86% 2-year cumulative survival rate reported by the French Vanguard Trial and an 88% 2-year survival rate reported by May et al. It also compares favorably with long-term survival after open surgical repair. The 18-month survival rate free of reintervention in this study was 88% compared with a 67% 2-year cumulative survival free of intervention reported by the multicenter French Vanguard Trial.

In conclusion, endoleak is commonly seen after endovascular repair, but is a poor predictor of the most important clinical outcome measures such as death or aneurysm rupture. Thus, the usefulness of endoleak as a primary indicator of success or failure of endovascular aneurysm repair is uncertain. A primary focus on endoleak and its treatment or prevention may divert attention from potentially more important considerations such as adequate stent graft fixation and changes in aneurysm size. It is well known that aneurysm size and change in size are closely related to the risk of rupture. Patients with known, untreated aortic aneurysms are followed up with periodic aneurysm imaging focused primarily on determining aneurysm size. The same strategy with modification to evaluate endovascular device morphology and fixation might be used in patients who have undergone endovascular aneurysm repair. Physicians with knowledge of the natural history of aneurysms and an understanding of the spectrum of endovascular and open surgical treatment strategies should be involved with the ongoing care, long-term follow-up, and management of patients with aortic aneurysms.

We thank the AneuRx Clinical Investigators and the Medtronic AneuRx Clinical support team, Tami Crabtree for statistical evaluation, and Rita Wedell for preparation of the manuscript.

REFERENCES


Submitted Jan 25, 2000; accepted May 2, 2000.

ADDENDUM

Since completion of this analysis and presentation of these data at the Western Vascular Society Meeting on September 22, 1999, there have been five additional patients with aneurysm ruptures after AneuRx stent graft repair. Thus, there have been a total of seven aneurysm ruptures (0.7%) following successful implantation among 1046 patients in Phases I, II, and III of the AneuRx Clinical Trial that began in June 1996. Three of these patients were described in the March 2000 issue of the Journal of Vascular Surgery (Politz J, Newman VS, Stewart M T. Late abdominal

Of note is the fact that among these seven patients, three had endoleak at hospital discharge, and four had no endoleak. At 1 month two patients had endoleak, and five had no endoleak. The two patients with endoleak refused recommended endovascular or open surgical treatment and ruptured 15 and 24 months later. The five patients without endoleak continued to be free of endoleak at the time of the last examination before rupture. Retrospective review of abdominal radiographs and CT scans identified insecure stent graft attachment or fixation in each of the five patients. Each could potentially have been corrected with endoluminal extender cuffs.

This experience confirms the observation in this study that the presence of an endoleak is not a reliable predictor of subsequent outcome events. Furthermore, the absence of an endoleak does not ensure that the patient is free of the risk of aneurysm rupture. Although the risk of aneurysm rupture is small, all patients with endovascular aneurysm repair regardless of endoleak status should be followed up by periodic imaging. If insecure stent graft fixation or attachment is suspected or if there is evidence of aneurysm enlargement or if there is new onset endoleak, further treatment should be considered.

DISCUSSION

Dr Christopher Zarins. Thank you, Dr Taylor, for your discussion.

Regarding the patient who ruptured, we analyzed that patient both ways. The patient had an endoleak at the time of discharge, and we analyzed that patient in the endoleak group. The patient did not have an endoleak at the time of the 1-month study, and thus we analyzed the patient in that analysis in the no-endoleak group. Whichever way you analyzed it, it made no difference. The outcome was the same. Whether or not you had an endoleak was not a predictor of what was going to happen in the future.

Regarding the type of endoleak, overall we had 30% Type I endoleaks, 40% Type II endoleaks, and 30% undetermined. On CT scan it may be hard to be precise in the definition of what is a Type I and what is a Type II endoleak. To a large extent that is a subjective interpretation. For this analysis we relied on the core laboratory interpretation and classification. Certainly on an individual patient basis when you see an attachment site defect, that is a significant finding that merits more attention.

Regarding the question of what we really do, how we evaluate patients, and what needs to be looked at to follow patients, I think that the criterion that we really can follow is aneurysm size. After all, that is the criterion that we always have followed as we have looked and thought about aneurysms. We have always taken the risk benefit analysis of aneurysm size versus patient comorbidities and considered the risks of open repair versus no treatment. It is a complex algorithm that we as vascular surgeons have done all of our professional lives, and I think we should continue to use that same algorithm and approach.

The problem that I see is a focus on endoleak as a primary outcome measure. Some people think that we are here to fix endoleaks, and, in fact, that approach can be dangerous. Patients have ruptured their aneurysms because of that approach. There are published reports in the literature of repeated efforts to seal endoleaks despite increasing aneurysm size with ultimate rupture. The problem was the focus on the endoleak rather than the progressive enlargement.

So how do we evaluate the success of endovascular repair? We usually compare endovascular grafts to open surgical repair. Perhaps we should also compare endografts to nonoperative treatment where we consider the natural history of aneurysms. The annual risk of rupture of untreated aneurysms of the size treated in this study is perhaps 10% per year. After we place an endograft, the risk is reduced to less than half of 1%.

From our data there is no evidence that the presence or absence of an endoleak will predict those at continuing risk of rupture. Subsequent outcome is primarily dependent on patient comorbidities according to our data analysis.