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Midterm Outcomes of the Nellix Endovascular Aneurysm Sealing System: A Dual-Center Experience

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Abstract

Purpose: To report midterm outcomes of the Nellix Endovascular Aneurysm Sealing (EVAS) System in the treatment of abdominal aortic aneurysm (AAA). **Methods:** Between September 2013 and July 2014, 64 AAA patients (mean age 76.6±6.8 years; 61 men) were treated with the EVAS system at 2 centers (only procedures performed at least 12 months prior to the analysis were included). Most patients were treated for a stable AAA, while 1 patient was treated for a ruptured aneurysm. Mean aneurysm diameter was 57.3±9.3 mm. The proximal neck measured a mean 21.5±3.3 mm in diameter and 27.0±12.1 mm long; the neck angle was 16.9°±19.3°. Eleven (17.2%) patients were treated outside the instructions for use (IFU). **Results:** Technical success was achieved in 63 (98.4%) of 64 patients; 1 type Ia endoleak was treated intraoperatively. One (1.6%) aneurysm-related death occurred at 4 months due to a secondary aortoenteric fistula. Overall, endoleaks occurred in 3 (4.7%) patients (2 type Ia, 1 type II). The estimated rates for 18-month overall survival, freedom from aneurysm-related death, and freedom from secondary interventions were 92.7%, 98.4%, and 95.0%, respectively. Patients treated outside the IFU had a significantly higher incidence of device-related complications (p=0.03). **Conclusion:** The use of the Nellix device in everyday clinical practice is safe and offers promising midterm results. The risk of secondary aortoenteric fistula requires further analysis. Longer follow-up is needed to assess the actual efficacy of the device, although the risk of migration with late endoleak seems low.

Keywords

abdominal aortic aneurysm, balloon-expandable stent, endoleak, endovascular aneurysm sealing, sac anchoring stent-graft

Introduction

Endovascular aneurysm sealing (EVAS) using the Nellix device (Endologix Inc, Irvine, CA, USA) has been recently introduced for the treatment of abdominal aortic aneurysm (AAA), with promising results.[1,2] The different concept of EVAS seems to expand the possibilities of endovascular treatment of aortic aneurysm disease and reduce the risk of type II endoleaks after treatment.[1] Two clinical trials and one investigational device exemption (IDE) pivotal trial have been published[1–3] to test the efficacy and safety of the Nellix device. Since these studies were designed as first in human or as IDE trials, selected patients were enrolled. More recent data regarding the outcome of the Nellix device in everyday clinical practice have been reported in 2 multicenter and 3 single-center studies,[4–8] all reporting a rather low incidence of type I and II endoleak (2%–8%) and a high clinical success rate (98%–100%), even in ruptured AAAs.[8] However, all reports have a short (<12 months) mean follow-up, and data on midterm outcome are still scarce. As the real-world use of this new device is expanding rapidly, we report the midterm outcome of a group of patients with >12 months' follow-up treated at 2 vascular centers.

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Methods

Study Design

Data on all patients treated with the Nellix device at 2 participating centers between September 2013 and July 2014 were retrospectively analyzed based on the intention-to-treat principle; only procedures performed at least 12 months prior to the analysis were included. Patients were eligible for endovascular repair with an infrarenal AAA >5 cm in axial diameter or with rapid growth (>1 cm in the last 12 months). The instructions for use (IFU) list the appropriate anatomy for the Nellix device as a nonaneurysmal aortic neck ≥10 mm long with a diameter between 18 and 32 mm, a maximum aortic blood flow lumen diameter ≤60 mm, a maximum common iliac artery (CIA) diameter between 9 and 35 mm, and a <60° angle from neck to sac, but these were not considered strict inclusion criteria. At the beginning of the EVAS experience at both centers, patients were considered for EVAS if their anatomy complied with the IFU and they were older than average AAA patients. The decision to treat older patients with shorter life expectancy was based on the lack of data on the long-term performance of the device. Later, after the learning curve, patients not complying with the IFU were also included according to the treating physician's decision.

Follow-up visits were completed according to each center's internal policy. Minimal follow-up was a clinical examination (with duplex imaging) at 30 days and computed tomography angiography (CTA) at 3 months after the procedure in both centers. Thereafter, 1 center used duplex and the other used CTA surveillance imaging at 6 and 12 months unless endoleaks or other problems warranted an accelerated schedule. All patients were given a full explanation of the procedure and signed a consent form with authorization to release anonymized data.

EVAS Procedure

The Nellix device and the EVAS procedure have been described in previous publications.[1,2] In brief, femoral access was obtained either percutaneously or with surgical exposure, according to the operator's preference. Intraoperative aortography was performed to identify the renal arteries and then access wires were exchanged for a 0.035-inch extra-stiff wire [Lunderquist (Cook Medical Inc, Bloomington, IN, USA) or Backup Meier (Boston Scientific, Marlborough, MA, USA)]. The 2 components of the Nellix system were inserted and the endoframes were expanded. Contrast-enhanced saline was injected in the endobags under fluoroscopic guidance to determine the volume required to fill the aneurysm sac. The endobags were then filled with polymer, with a mean fill pressure ~50 mm Hg higher than the patient's systolic pressure, not exceeding 200 mm Hg. Secondary fills were performed when necessary. The delivery catheters were then released from the implant and removed after the polymer had cured.

Table 1. Demographic Variables and Aneurysm Characteristics of the 64 Study Patients.

Age, y	76.6±6.8
Men	61 (95.3)
Diabetes	9 (14.1)
Hypertension	55 (85.9)
Dyslipidemia	32 (50)
Smoking habit	38 (59.4)
Chronic kidney disease[b]	8 (12.5)
History of AMI	16 (25)
Peripheral artery disease	7 (10.9)
CAD	19 (29.7)
COPD	29 (45.3)
ASA II	39 (60.9)
ASA III/IV	24 (37.5)
ASA V	1 (1.6)
Aneurysm diameter, mm	56.4±11.3
Blood lumen diameter, mm	37.7±10.2
Proximal neck diameter, mm	21.5±3.3
Neck length, mm	27.0±12.1
Neck angle, deg	16.9±19.5
CIA diameter, mm	13.9±3.7
Patients outside of the IFU	11 (17.2)
Aortic neck angle >60°	3
Aortic neck <10 mm	3
Aortic neck diameter <18 mm	4
CIA diameter <8 mm	1

Abbreviations: AMI, acute myocardial infarction; ASA, American Society of Anesthesiologists; CAD, coronary artery disease; CIA, common iliac artery; COPD: chronic obstructive pulmonary disease; IFU, instructions for use.
[a]Continuous data are presented as the means ± standard deviation; categorical data are given as the counts (percentage).
[b]Defined as serum creatinine >1.5 mg/dL.

Patient Population

During the observation period, 64 patients (mean age 76.6±6.8 years; 61 men) were treated with the EVAS system (1 with a ruptured aneurysm). Mean aneurysm diameter was 57.3±9.3 mm, with a mean blood lumen diameter of 37.8±10.1 mm. Mean proximal neck diameter was 21.5±3.3 mm, with a mean neck length of 27.0±12.1 mm; the neck angle was 16.9°±19.3°. CIA diameter was 13.9±3.7 mm. Eleven (17.2%) patients were treated outside the current IFU. Patient demographics and aneurysm characteristics are given in Table 1.

Outcome Measures

Outcomes are reported according to the reporting standards for endovascular aortic aneurysm repair.[9] Technical success was defined as the successful deployment of the device in the

planned position with aneurysm sealing and no type I endoleak or stent thrombosis. Assisted primary technical success referred to the unplanned use of endovascular procedures as necessary, such as balloons other than those of the device or the insertion of stents to address endoleak. Clinical success was defined as successful deployment of the device at the intended location without major adverse events (MAEs), type I endoleak, graft infection or thrombosis, aneurysm expansion or rupture, and conversion to open repair. Major adverse events included all-cause mortality, bowel ischemia, myocardial infarction (MI), renal failure (requiring dialysis or elevated serum creatinine 2 times baseline), respiratory failure (need for >24 hour mechanical ventilation postoperatively or reintubation for any reason), and stroke.

Statistical Analysis

Results are presented as mean ± standard deviation or median and absolute range, as appropriate. Comparison of categorical data was performed using the Fisher exact test. Kaplan-Meier estimates of overall mortality, freedom from aneurysm-related mortality, and freedom from secondary procedures are expressed with the 95% confidence interval (CI). The incidence of device-related complications was compared between patients treated within vs outside the IFU; results are reported as the odds ratio (OR) and 95% CI. Statistical significance was indicated by a 2-tailed $p<0.05$. GraphPad Prism (version 6; GraphPad Software, La Jolla, CA, USA) was used for data analyses.

Results

Procedure Outcomes

Technical success was achieved in 63 (98.4%) patients; 1 intraoperative type Ia endoleak was detected at completion angiography and treated (100% assisted primary technical success). The procedure was performed under general (40, 62.5%) or local anesthesia (24, 37.5%) according to operator preference. The mean procedure time was 97.9±29.6 minutes (range 56–182), during which 117±66.1 mL of contrast were used for fluoroscopy (mean 8±2 minutes). The mean intraoperative blood loss was 201±138 mL. A mean 74.5±27 mL of polymer was delivered at a mean inflation pressure of 186±15 mm Hg. In one case a concomitant hypogastric aneurysm was treated without complications. No patients required intensive care. Mean hospital stay from the date of the procedure was 3.3±4.6 days (range 1–35, median 2). Procedure data are shown in Table 2.

Table 2. Variables in the 64 EVAS Procedures.[a]

Procedure time, min	97.9±29.6
Fluoroscopy time, min	8±2
Local anesthesia	24 (37.5)
Contrast volume, mL	117±66.1
Blood loss, mL	201±138
Volume of polymer, mL	69.5±27
Hospital LOS, d	3.3±4.6
Percutaneous procedures	46 (71.8)
Intraoperative endoleaks	1 (1.6)
Unplanned procedures	1 (1.6)

Abbreviations: EVAS, endovascular aneurysm sealing; LOS, length of stay.
[a]Continuous data are presented as the means ± standard deviation; categorical data are given as the counts (percentage).

Clinical Outcomes

There were no perioperative major adverse events or other major complications at 30 days. Minor complications included 3 (4.7%) cases of postoperative fever and 3 access complications (inguinal hematoma, dehiscence of the inguinal cutdown) not requiring surgical treatment.

Including the intraoperative type Ia endoleak, there were 3 (4.7%) endoleaks encountered during the observation period. Another type Ia endoleak was detected and corrected at 15 months from the index operation. Both the type I endoleaks occurred in cases treated outside the current IFU. The intraoperative leak was due to an 80° proximal neck angulation in an 18-mm-diameter, 10-mm-long neck; the second was due to a small neck diameter (17 mm, 11 mm in length). Both patients were successfully treated with the deployment two 12×41-mm Advanta V12 (Maquet Getinge Group, Göteborg, Sweden) covered stents in the first and two 11×15-mm Viabahn covered stents (W. L. Gore & Associates, Flagstaff, AZ, USA) in the second. The only type II endoleak, detected at 3-month CTA control, is under surveillance, without aneurysm growth.

At 2 months, 1 (1.6%) patient was diagnosed with thrombosis of the external iliac artery (EIA) distal to the landing zone of the device, which remained patent. This patient underwent surgical embolectomy, complicated by distal embolization, with complete recovery and without further adverse events during follow-up.

Median follow-up for the group was 17 months (absolute range 2–22). All patients had at least 1 follow-up CTA within the first 3 months after the procedure. Aneurysm-related mortality was 1.6%. One patient was treated for a secondary aortoduodenal fistula (ADF) occurring 4 months after EVAS, resulting in death on the 24th postoperative day. This patient was treated outside the IFU (proximal neck angle 70°). The overall mortality was 6.2%. Besides the aforementioned case, the 3 additional deaths were all considered unrelated to the aneurysm. One patient died at 6 months due to acute pancreatitis, another at 16 months due to respiratory failure secondary to pulmonary infection, and the third died at 2 months due to acute MI. All these patients had at least 1 CTA showing complete exclusion of the aneurysm, without endoleak.

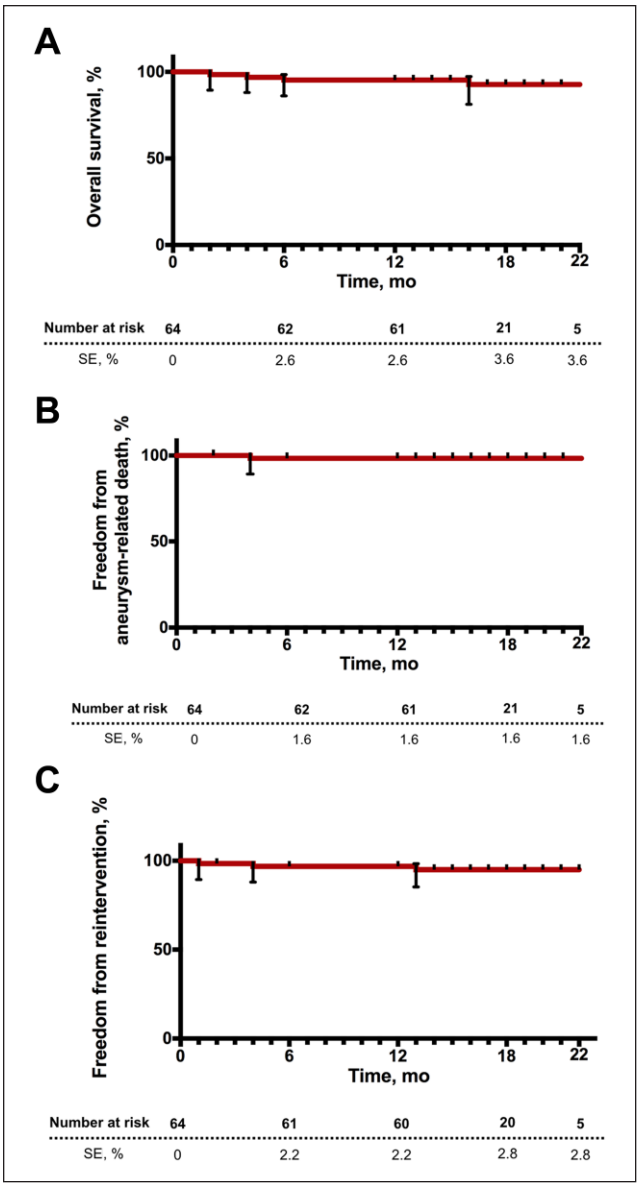

Figure 1. Kaplan-Meier analyses of (A) overall survival, (B) freedom from aneurysm-related death, and (C) freedom from reintervention. SE, standard error.

There have been no aneurysm ruptures, no device migration, and no aneurysm enlargement. The Kaplan-Meier estimate for overall survival at 18 months was 92.7% (95% CI 81.2 to 97.2), while freedom from aneurysm-related death was 98.4% (95% CI 89.3 to 99.8), with the 1 device-related death. The estimate for freedom from reintervention was 95.0% (95% CI 85.3 to 98.3), with 1 type Ia endoleak, 1 EIA occlusion, and 1 case ADF (Figure 1).

Aneurysm diameter reduction or increase >5 mm was not detected in any patient. Patients treated outside the IFU had a significantly higher incidence of device-related complications (OR 9.6, 95% CI 1.38 to 66.5, p=0.03) owing to 1 ADF and 2 type Ia endoleaks vs 1 type II endoleak and 1 EIA thrombosis in the IFU-compliant patients.

Discussion

Our study reports the midterm results of a group of patients treated with the Nellix device in a real world setting. Our 30-day results are in line with those reported by other groups[1,5–8] and seem to confirm that EVAS is a safe and effective procedure, with a low incidence of perioperative MAEs, a short procedure time, and no intraoperative deaths. Our not negligible overall mortality (6.2%) is in our opinion related mostly to the older age of the study group, with 3 of the 4 deaths unrelated to the aneurysm or procedure.

We experienced only 1 type II endoleak, an incidence that is in line with other studies.[1,5–8] It is believed that type II endoleaks in EVAS are caused by inadequate unfurling of the endobags,[10] which are therefore unable to reach and seal the lumbar arteries. In our case, we actually detected a severely calcified plaque encompassing the ostia of the lumbar arteries feeding the endoleak. Although this consideration remains speculative, the plaque might have prevented optimal apposition of the bag to the aortic wall.

Treatment of type Ia endoleak after EVAS has usually been achieved with direct embolization,[11] while spontaneous resolution has also been reported.[5] Both patients with type Ia endoleak had a small proximal neck, with tight angulation in 1 case. Treatment with covered stents aimed to improve apposition of the Nellix stents and endobags against the aortic wall and to occupy a greater portion of the transverse area of the proximal neck. The goal was therefore to divert more flow into the Nellix stents, hoping that the remaining flow would be slow enough to obtain thrombosis.

Harvey et al[11] also had similar ideas regarding the role of proximal extensions to change the flow pattern of type Ia endoleaks. The authors described a technique for type Ia endoleak based on n-butyl cyanoacrylate embolization associated with proximal extension of the Nellix stent lumen with covered stents, reporting that the use of covered stents actually changed the flow pattern of type Ia endoleaks from high-velocity flow to a low-flow situation. In our 2 cases, the change in flow pattern was enough to resolve the endoleaks, although we still consider direct embolization in case of recurrence (both patients are under close clinical surveillance).

As previously stated, both type Ia endoleaks occurred in patients with suboptimal proximal necks, either for angulation and/or diameter. As reported by other authors,[4,6] we also believe that factors such as proximal neck angulation, stomach-shaped aneurysms, and large blood lumens should be thoroughly evaluated when planning an EVAS procedure. Due to the stiffness of the system, these features seem to favor migration of the Nellix stents during inflation of the

endobags, leading to a more distal deployment than originally intended with the risk of type Ia endoleaks. Brownrigg et al[6] suggest keeping the Nellix balloons inflated during polymer injection to stabilize the system and minimize this risk, although the actual efficacy of this technique is yet to be proven.

No type Ib endoleak occurred although 1 patient suffered from EIA occlusion. The reported incidence of device or iliac artery stenosis/occlusion has a variable incidence, ranging between 2% and 8%.[5–7] These events can be related to the fact that the Nellix is a low-profile device, and if patients with small and calcified iliac arteries are treated, the risk of access complications may be increased. Consistent with these considerations, a not negligible rate of limb stenosis/occlusion has also been reported with other ultra-low profile devices.[12]

A second and more specific cause of limb occlusion is the straightening of the aortoiliac anatomy caused by the stiffness of the Nellix graft. This straightening causes the displacement of angulations from inside to outside the distal end of the graft,[7,10] meaning that, in a tortuous distal landing zone, all curves become more heightened in the arterial segments that are free from the device, with possible misalignments or kinks. Although no striking misalignment was evident at completion angiography in the patient who suffered from EIA thrombosis, we actually believe that distal landing zone tortuosity, associated with poor compliance with the recommended antiplatelet therapy, might have played a role in the development of this event. The use of adjunctive self-expanding stents is suggested to reduce and modulate the tightness of eventual distal bends,[6,10] although its efficacy was not proven in the large multicenter registry by Böckler et al.[5]

The most important device-related complication in our study was an ADF 4 months after implant.[13] Only one other case of secondary ADF has been recently reported in the literature, also 4 months after the procedure.[14] Although the possible mechanism of fistula formation remains speculative, erosion of the stiff polymer-filled endobags into the aortic wall and then into the duodenum cannot be excluded. The early occurrence (4 months) of both cases is, however, peculiar. Secondary aortoenteric fistulas are known to be time-dependent, with a higher incidence late in follow-up. Both reported cases instead occurred within the first 12 months from the procedure, and no other has been so far reported. On the other hand, this short interval is also compatible with a primary infection of the endograft, leading to aortic rupture and fistula formation.[13,14] In this event, the ADF would be only a consequence of graft infection and not the initial cause. This second hypothesis might be supported by another early infection case (at 8 months) described by Tolenaar et al,[14] which caused aortic rupture (without fistula formation). Ferrero et al[13] also suggested that aortic thrombus may protect against secondary ADF, with patients having less thrombus being at greater risk. Further evidence is needed to evaluate the actual incidence of this complication and the factors that might favor this event.

An interesting aspect of our study is that all but one complication occurred within 6 months after implant. One possible explanation, as also pointed out by other authors,[10] is that the device tends to stabilize the AAA anatomy, meaning that a device-related complication has to occur early as the aorta-device geometry will not change over time. Consistent with this eventuality, we detected only 1 late type Ia endoleak (at 15 months), supporting a low tendency to migration of the device, at least in the midterm.

Patients treated outside the IFU in our cohort had a statistically higher incidence of device-related complications. This is in contrast with the results of the largest multicenter registry of EVAS procedures, where Böckler et al[5] did not find a higher frequency of type Ia or Ib endoleak, device occlusion, or reintervention in patients treated outside the IFU.

Although the list of anatomical requirements for EVAS includes several parameters, we believe that proximal neck features (angulation and small diameter) remain among the most stringent, as all the most important complications of the present study occurred in this subgroup of patients. This same outcome has also been reported by other authors.[4,6] Böckler et al[5] performed no specific analysis in this regard as all patients not complying with the IFU were analyzed together. Future analyses should be directed to better characterizing the role of the proximal neck as a predictor of failure.

Conclusion

The use of the Nellix device in everyday clinical practice is safe and offers promising midterm results. The low number of endoleaks and the stabilization of the aneurysm seem to provide a durable solution, with a low incidence of reinterventions. Caution should be used in the setting of small, angulated proximal necks, as they seem to be associated with a higher risk of complications. Longer follow-up is awaited to assess the actual efficacy of the device.

Declaration of Conflicting Interests

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