The Morphological Applicability of a Novel Endovascular Aneurysm Sealing (EVAS) System (Nellix) in Patients with Abdominal Aortic Aneurysms


a Department of Outcomes Research, St George’s Vascular Institute, London, UK
b Department of Cardiovascular Sciences, University of Leicester, Leicester, UK

WHAT THIS PAPER ADDS
A novel endovascular technique for the management of abdominal aortic aneurysm (AAA) is assessed. Morphological applicability is assessed in a range of patients who have undergone traditional infrarenal endovascular aortic repair (EVR), open repair (OR), fenestrated endovascular repair (FEVR) or non-operative management. The anatomical applicability of this new technology in these patients is assessed and compared with other endograft devices currently in use. It is concluded that EVAS (Nellix) technology appears to be widely applicable to contemporary infrarenal AAA practice, and provides an additional solution for patients currently being treated by EVR outside current devices’ instructions for use.

Objective: Endovascular aneurysm sealing (EVAS) using the Nellix system is a promising alternative to endovascular repair (EVR) and open surgery for abdominal aortic aneurysms (AAA). The aim of this study was to investigate the proportion of patients with AAA who are morphologically suitable for treatment with Nellix.

Methods: Patients presenting with AAA were investigated at two regionalised vascular units. Separate cohorts were identified, who had undergone infrarenal EVR, open aneurysm repair, fenestrated endovascular repair (FEVR) or non-operative management. Pre-operative morphology was quantified using three-dimensional computed tomography according to a validated protocol. Each aneurysm was assessed for compliance with the instructions for use (IFU) of Nellix.

Results: 776 patients were identified with mean age 75 ± 9 years. 730/776 (94.1%) had undergone infrarenal EVR, 6/776 (0.8%) open repair, 27/776 (3.5%) FEVR and 13/776 (1.7%) had been managed non-operatively. 544/776 (70.1%) of all AAA were morphologically suitable for Nellix. 533/730 (73.0%) of patients who had undergone infrarenal EVR were compliant with Nellix IFU, compared with 497/730 (68.1%), 379/730 (51.9%) and 214/730 (29.3%) with the IFU for Medtronic Endurant (p = .04) or Cook Zenith (p < .01) and Gore C3 Excluder (p < .01) endografts respectively.

Conclusions: Nellix technology appears widely applicable to contemporary infrarenal AAA practice, and may provide an option for patients that are outside current EVR device instructions for use. However, formal outcomes study is still required, and will ultimately dictate the clinical relevance of this feasibility study. The major limitation to anatomic suitability for Nellix is currently the maximum patent lumen diameter of large AAA.

© 2013 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

Article history: Received 13 April 2013, Accepted 19 June 2013, Available online 1 August 2013

Keywords: Morphology, Endovascular, Abdominal aortic aneurysm, EVAS, Nellix

INTRODUCTION
The advent of endovascular aneurysm repair (EVR) has permitted management of abdominal aortic aneurysm (AAA) with significantly lower perioperative risk than open repair (OR). The long-term results of EVR are equivalent to open repair,1 and continue to improve with increasing experience, developing technology, and greater attention to surveillance and reintervention.2 Patients prefer minimally invasive surgery3 and EVR has supplanted open repair as the most common management of AAA. However, aneurysm morphology remains a key challenge for EVR, and is a key determinant of long-term success.4,5 For each device, manufacturers’ instructions for use (IFU) guide the operator with regards to the limits of aneurysm morphology. Current stent-grafts are often used outside IFU according to clinical need, although this may be associated with a greater need for secondary intervention.6 Close monitoring for aortic complications (type 1 or 3 endoleak, device migration or sac expansion) is mandatory.3,7

Adverse aneurysm morphology remains an important obstacle to the universal use of EVR for AAA. The development of fenestrated (FEVR) and branched devices has
extended the endovascular approach to patients with more complex aneurysm morphology, with disease involving the renal artery origins (suprarenal aneurysms) or coeliac and superior mesenteric origins (Crawford type IV thoraco-abdominal aneurysms). However, this technique is relatively novel and technically challenging, while there remains uncertainty regarding the optimum use of FEVR in juxtarenal (JRA), suprarenal (SRA), or type IV thoraco-abdominal (TAA) aneurysms.\(^8,9\)

The Nellix device\(^10\) employs a novel approach to AAA; achieving aneurysm exclusion by EVAS (endovascular aneurysm sealing). The device consists of two flow channels supported by bilateral balloon-expandable stents, with surrounding EndoBags that are filled with a polymer solution that cures in situ. The polymer filling step is performed under pressure monitoring until the EndoBags expand and occupy the blood lumen space within the aneurysm sac, allowing sealing of side branch flow\(^11\) (Fig. 1). The expanded polytetrafluoroethylene (ePTFE)-covered, cobalt chromium (CoCr) alloy balloon-expandable stents provide biocompatible structural support to the flow lumens. The polyurethane EndoBags unwrap when filled with polymer solution and conform to the aneurysm blood lumen to provide sealing of the entire aortoiliac segment being treated. The low viscosity polymer delivered to the EndoBags is intended to form a biocompatible, biodurable, solid polyethylene glycol (PEG)-based hydrogel in situ within minutes of delivery. The 17Fr Nellix Catheter is compatible with 0.035" guidewires. After the system is advanced via femoral artery access, the integrated catheter sheaths are retracted, exposing the implants. The Nellix Accessory Kit and Dispenser facilitate single-operator application of bilateral Nellix Catheters. The Accessory Kit contains a console, mixers and separately pouched Mirador Biomedical Compass GP pressure transducer. Quick connectors on the console allow for attachment to mating connectors on each of the Nellix catheters. Ports on the console permit simultaneous management of the two catheters in the following steps: (a) drawing a vacuum through the system to the EndoBags, verifying EndoBag and fill-line integrity, (b) simultaneous balloon expansion of the stents, (c) introduction of the mixed polymer solution under in-line pressure monitoring to the EndoBags, and (d) angiography performed through the catheter tips.

The IFU of this device allow greater morphological variability than those for the current generation of EVR stent-grafts, potentially expanding the proportion of patients with AAA that may be offered an endovascular solution. However, it remains unknown whether this theoretical advantage translates to clinical practice. The aim of this study was to quantify the applicability of Nellix, by reporting the proportion of patients presenting with AAA that were morphologically suitable for treatment with the Nellix device.

**METHODS**

Four patient groups were identified: patients who had undergone EVR for infrarenal AAA (infrarenal EVR), open aneurysm repair (OR) for infrarenal or juxtarenal AAA, fenestrated endovascular repair (FEVR) for juxtarenal AAA, and patients with AAA selected for non-operative management.

Two prospectively maintained databases, which included all patients undergoing EVR of infra-renal AAA, were interrogated at two tertiary vascular centres. These databases contained details of operative procedure, patient demographics, comorbidity, and follow-up. Patients who had undergone OR, FEVR, or non-operative management were identified retrospectively at a single tertiary vascular centre over differing time periods, and data regarding patient demographics, comorbidity, and follow-up were collated.

**Inclusion criteria**

All EVR for infrarenal AAA were studied at Leicester Royal Infirmary (LRI) and St George’s Vascular Institute (SGVI) between January 2004 and June 2010. All cases of open AAA repair and FEVR were studied at St George’s Vascular Institute (SGVI) between January 2010 and July 2012. AAA managed non-operatively at SGVI were studied between January 2008 and January 2009. Different temporal cohorts were chosen for convenience, based on the availability of complete morphological data for existing databases and the centre of treatment received by each group of patients. Data collection and study design were adherent to recent reporting standards for endovascular aneurysm repair.\(^12\) Cases were excluded from this study if non-luminal volume segmentation failed during automated image analysis. Patients with ruptured AAA were excluded.
A. Karthikesalingam et al.

Table 1. Instructions for use for Nellix and contemporary endovascular aortic repair devices.

<table>
<thead>
<tr>
<th></th>
<th>Nellix</th>
<th>Cook Zenith</th>
<th>Medtronic</th>
<th>Gore</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-aneurysmal AN length</td>
<td>≥10 mm</td>
<td>≥15 mm</td>
<td>≥10 mm</td>
<td>≥15 mm</td>
</tr>
<tr>
<td>Non-aneurysmal AN diameter</td>
<td>18–32 mm</td>
<td>18–32 mm</td>
<td>19–32 mm</td>
<td>19–29 mm</td>
</tr>
<tr>
<td>Maximum aortic blood lumen diameter</td>
<td>≤60 mm</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Maximum common iliac artery diameter</td>
<td>8–35 mm</td>
<td>7.5–20 mm</td>
<td>8–25 mm</td>
<td>8–18.5 mm</td>
</tr>
<tr>
<td>Angle from neck to sac</td>
<td>&lt;60</td>
<td>&lt;45</td>
<td>If AN length 10–15 mm, then &lt;45</td>
<td>—</td>
</tr>
<tr>
<td>Angle from suprarenal aorta to neck</td>
<td>—</td>
<td>&lt;60</td>
<td>If AN length 10–15 mm, then &lt;60</td>
<td>≤60</td>
</tr>
</tbody>
</table>

AN = aortic neck.

Image analysis

Pre-operative CT images were acquired in the DICOM (Digital Image and Communication in Medicine) format from the hospital archive and analyzed using CT reconstruction software (3Surgery; 3Mensio Medical Imaging B.V., Bilthoven, The Netherlands). All image sets had a slice thickness of less than 3 mm and each image extended from the thoracic inlet to the common femoral artery bifurcation. Intravenous injection of 90 mL of Omnipaque 300 (Iohexol 300/Omnipaque 300; Sanofi-Winthrop, New York, NY) was used as standard. All measurements were taken orthogonally to a semi-automatically installed central luminal line. 3D morphological assessment was performed utilising a validated protocol with acceptable inter- and intra-observer variability.

Outcome measures

The primary outcome measure for each of the four procedure groups was compliance with anatomical instructions for use supplied by the manufacturers of one EVAS system (Endologix Nellix10) and three EVR devices (Cook Zenith,14 Medtronic Endurant,15 and Gore Excluder16). Criteria for the Nellix IFU required a non-aneurysmal aortic neck length of ≥10 mm, non-aneurysmal aortic neck diameter of 18–32 mm, maximum aortic blood lumen diameter of ≤60 mm, and common iliac artery diameter of 8–35 mm (Table 1).

Statistical analysis

All analyses were performed using SPSS v.19 (IBM). Dichotomous data were compared using the chi-squared or Fisher’s Exact tests.

RESULTS

The study population consisted of 776 patients who had an identifiable AAA between January 2004 and July 2012 in a non-continuous series at two regional vascular units: 730/776 (94.1%) patients underwent infrarenal EVR, 6/776 (0.8%) underwent open repair, 27/776 (3.5%) underwent FEVR and 13/776 (1.7%) underwent non-operative management (Table 2). Thirty-one patients were excluded because automated volumetric processing was not possible.

Morphological compliance with IFU for EVAS

Of all patients, 70.1% (544/776) were suitable for treatment with Nellix under standard IFU of the Nellix system. This differed significantly (p < .001) across each procedure group. Of those who underwent infrarenal EVR, 73.0% (533/730) were compliant with Nellix IFU. Of those who had undergone open repair, 50% (3/6) would have been morphologically suitable for Nellix. Of patients treated by FEVR, 7.4% (2/27) were within the limits of the Nellix IFU, and 46.2% (6/13) of patients managed non-operatively would have been morphologically suitable for Nellix (Fig. 2).

Table 2. Demographics.

<table>
<thead>
<tr>
<th></th>
<th>Infraerial EVR</th>
<th>OR</th>
<th>FEVR</th>
<th>Non-operative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>649 (88.9)</td>
<td>6  (100)</td>
<td>24  (88.9)</td>
<td>7  (53.8)</td>
</tr>
<tr>
<td>Mean age, n (%)</td>
<td>74.7 ± 9.04</td>
<td>72.7 ± 7.97</td>
<td>73.5 ± 7.73</td>
<td>80.1 ± 7.20</td>
</tr>
<tr>
<td>Smoking:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker, n (%)</td>
<td>156 (21.4)</td>
<td>0  (0)</td>
<td>5   (18.5)</td>
<td>1  (0.77)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>350 (47.9)</td>
<td>3  (50.0)</td>
<td>7   (25.9)</td>
<td>5  (38.5)</td>
</tr>
<tr>
<td>Ex-smoker, n (%)</td>
<td>224 (30.7)</td>
<td>3  (50.0)</td>
<td>15  (55.5)</td>
<td>7  (53.8)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>495 (67.8)</td>
<td>5  (83.3)</td>
<td>22  (81.5)</td>
<td>12 (92.3)</td>
</tr>
<tr>
<td>IHD, n (%)</td>
<td>336 (46.0)</td>
<td>2  (33.3)</td>
<td>17  (62.9)</td>
<td>8  (61.5)</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>183 (25.1)</td>
<td>1  (8.3)</td>
<td>7   (25.9)</td>
<td>5  (38.5)</td>
</tr>
<tr>
<td>Dyslipidaemia, n (%)</td>
<td>459 (62.9)</td>
<td>4  (66.7)</td>
<td>21  (77.8)</td>
<td>10 (76.9)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>104 (14.2)</td>
<td>0  (0)</td>
<td>0   (0)</td>
<td>1  (0.8)</td>
</tr>
<tr>
<td>Maximum patent AAA lumen diameter (mm)</td>
<td>48.74 ± 17.65</td>
<td>46.07 ± 11.15</td>
<td>43.43 ± 11.02</td>
<td>48.69 ± 11.86</td>
</tr>
<tr>
<td>Neck length (mm)</td>
<td>32.40 ± 15.28</td>
<td>15.03 ± 14.16</td>
<td>2.63 ± 4.76</td>
<td>15.61 ± 18.83</td>
</tr>
<tr>
<td>Neck diameter (mm)</td>
<td>25.89 ± 4.32</td>
<td>29.40 ± 4.67</td>
<td>38.51 ± 9.12</td>
<td>31.04 ± 8.15</td>
</tr>
<tr>
<td>Maximum CIA diameter (mm)</td>
<td>21.22 ± 12.30</td>
<td>17.10 ± 2.95</td>
<td>17.32 ± 5.58</td>
<td>21.48 ± 7.08</td>
</tr>
</tbody>
</table>

AAA = abdominal aortic aneurysm; CIA = common iliac artery; COPD = chronic obstructive pulmonary disease; EVR = endovascular aortic repair; FEVR = fenestrated endovascular repair; IN = ischaemic heart disease; OR = open repair.
Morphological compliance with Nellix IFU compared with current EVR devices

Nellix was more widely applicable than current EVR devices: 497/730 (68.1%) of the infrarenal EVR group were morphologically compliant with the Medtronic Endurant device IFU ($p = \cdot 04$), 379/730 (51.9%) compliant with the IFU for the Cook Zenith device ($p < \cdot 001$), and 214/730 (29.3%) for the Gore C3 Excluder ($p < \cdot 001$) (Fig. 3). Of the subgroup of patients treated by EVR outside device IFU for existing endografts, Nellix also appeared a useful option: 116/233 (49.8%) of patients who underwent EVR outside the IFU for the Medtronic Endurant device were compliant with IFU for Nellix, 215/351 (61.3%) of patients treated by EVR outside the IFU for the Cook Zenith device would have been compatible with IFU for Nellix, and 347/516 (67.2%) treated by EVR outside of the IFU for the Gore Excluder would have been compatible with the IFU for Nellix.

Morphological compliance with each Nellix IFU component in each procedure group

**Infrarenal EVR:** The maximum AAA patent lumen diameter was suitable for Nellix in only 615/730 (84.2%) cases, representing the most common barrier to the use of Nellix (Fig. 4, Table 2). Neck length was within the IFU for Nellix, 215/351 (61.3%) of patients treated by EVR outside the IFU for the Medtronic Endurant device were compliant with IFU for Nellix, and 347/516 (67.2%) treated by EVR outside of the IFU for the Gore Excluder would have been compatible with the IFU for Nellix.

**Open repair patients:** Neck length and neck diameter were suitable for Nellix in 4/6 (66.7%) cases. The maximum AAA patent lumen diameter fell within Nellix IFU in 5/6 (83.3%) cases and maximum common iliac artery diameter was suitable for Nellix in all cases.

**FEVR repair patients:** Neck length was within the limits of Nellix IFU in 2/27 (7.4%) cases and neck diameter was suitable for Nellix in 10/27 (37.0%) cases. Twenty-five of twenty-seven (92.6%) cases had a suitable maximum AAA patent lumen diameter for Nellix, and the maximum common iliac artery diameter was compatible with Nellix IFU in 26/27 (96.3%).

**Non-operative patients:** Neck length was compatible with Nellix in 7/13 (53.8%) cases. Aneurysm neck diameter was suitable for Nellix in 9/13 (69.2%) cases, and the maximum AAA patent lumen diameter was within Nellix IFU in 11/13 (84.6%) cases. All cases were found to have a maximum common iliac artery diameter suitable for Nellix.

**DISCUSSION**

Nellix technology was widely applicable in a contemporary series of patients with infrarenal AAA, and the main finding of this study was that 70% of all aneurysms assessed were suitable for treatment within the device’s IFU. Nellix appeared to be applicable to a wider range of aortic morphology than EVR devices currently in use. A notable finding was that many patients who had undergone EVR outside the IFU of current stent-grafts would have been suitable for EVAS within the Nellix device IFU. This finding is of particular importance in light of the higher incidence of sac expansion observed in patients treated by EVR outside manufacturers’ IFU.$^{17,18}$

Individual assessment of each morphological criterion revealed that the most common obstacle to the use of Nellix was the presence of a large maximum patent lumen diameter within the AAA sac. Device development to enable relaxation of this criterion therefore represents an
important area for future generations of this technology. Conversely, wide aneurysm neck diameter, short neck length, increased neck angulation or a large common iliac artery diameter were rarely obstacles to the potential deployment of a Nellix device. These features are often a considerable challenge for modern EVR technology, and patients with large AAA remain a considerable challenge. It has been suggested that morphological hostility in these cases might be attributable to the increasing wall stress present at greater maximal aneurysm diameter, which leads to morphological deterioration. It has previously been shown that large AAA diameter is the greatest impediment to the suitability for traditional endovascular therapy, whereas the presence of sac thrombus is of greater importance for EVAS. The Nellix device cannot currently be utilised in AAA in which the maximum patent lumen diameter exceeds 60 mm, as each endobag has a finite capacity for expansion to obliterate the aneurysm sac and this may limit its use in larger diameter aneurysms at present.

Almost half (46.2%) of patients managed non-operatively were morphologically suitable for Nellix. Nellix might offer a compassionate solution for this group, but the selection of patients for non-operative management is often made for reasons other than aneurysm morphology. Extensive medical comorbidity and patient preference is usually the dominant factor in non-operative management of large AAA, and in such cases anatomical suitability for novel endovascular devices may be of limited relevance.

Nellix was morphologically applicable in most infrarenal AAAs and might be of greatest use in patients that currently undergo EVR outside the IFU for contemporary stent-grafts, of whom many were suitable for Nellix. However, this benefit did not extend to patients with juxtarenal AAA. Patients currently undergoing open AAA repair with revascularisation of renal or visceral vessels would not have been treatable within the current limitations of Nellix, and this restriction applied equally to many patients selected for FEVR. The further development of Nellix for use in these more complex aneurysms is likely to follow evidence of its safety and efficacy in infrarenal AAA.

Clinical data are required to describe the performance of Nellix in terms of its procedural complexity, short-term morbidity, mid-term sequelae, and long-term safety. Currently, reintervention is necessary in 20% of EVR patients over 5 years, with the majority entailing minimally invasive endovascular procedures with little morbidity. It remains to be seen how Nellix technology will compare with this benchmark, particularly with regard to the need for surveillance and options for reintervention after aneurysm sealing. Estimates of the applicability of Nellix in non-operative, FEVR and open surgery patients should be interpreted with caution; further study is required in these populations and detailed, case-specific evaluation is needed before usage of the device can be considered. Most notably, clinical data are currently lacking for this device.

CONCLUSION

Emerging Nellix technology was widely applicable in a contemporary series of patients with AAA, and may be particularly feasible in infrarenal AAA treated by EVR outside existing devices’ IFU. The major limitation to the use of Nellix is currently the maximum patent lumen diameter of large AAA. Further studies are required to document the clinical performance of Nellix and its longer-term sequelae.

CONFLICT OF INTEREST

Professor Matthew Thompson provides consultancy to Endologix, Cook and Medtronic. No other author has any conflict of interest.

FUNDING

Alan Karthikesalingam is a National Institute for Health Research (NIHR) Doctoral Research Fellow supported by the Circulation Foundation Surgeon Scientist Award. Edward Choke is a NIHR Clinical Lecturer; Peter Holt is an NIHR Clinician Scientist. The views expressed in this publication are those of the authors and not necessarily those of the NIHR, NHS or Department of Health.

REFERENCES


14 Cook Medical. Zenith® AAA endovascular graft with the h & l-bone-shot™ introduction system; August 2006.

15 Medtronic Inc.. The endurant™ stent graft system instructions for use (en); 2009.

16 Gore Medical. GORE® EXCLUDER® AAA endoprosthesis featuring C3 delivery system (en); July 2011.


