

CLINICAL PRACTICE GUIDELINES ALERT!

Editor's Choice – Focused Update on Patients Treated with the Nellix EndoVascular Aneurysm Sealing (EVAS) System from the European Society for Vascular Surgery (ESVS) Abdominal Aortic Aneurysm Clinical Practice Guidelines

Jonathan R. Boyle ^a, Nikolaos Tsilimparis ^b, Isabelle Van Herzele ^c, Anders Wanhainen ^{d,*}, on behalf of the ESVS AAA Guidelines Writing Committee [‡], the ESVS Guidelines Steering Committee [§]

^a Cambridge Vascular Unit, Cambridge University Hospitals NHS Trust & Department of Surgery, University of Cambridge, Cambridge, UK

^b Department of Vascular Surgery, Ludwig-Maximilian University Hospital, Munich, Germany

^c Department of Thoracic and Vascular Surgery, Ghent University Hospital, Ghent, Belgium

^d Department of Surgical Sciences, Vascular Surgery, Uppsala University, Uppsala, Sweden and Department of Surgical and Peri-operative Sciences, Surgery, Umeå University, Umeå, Sweden

WHAT THIS PAPER ADDS

European Society for Vascular Surgery (ESVS) Guidelines are renewed regularly, usually every five years. ESVS Guidelines Focused Updates are issued to convey important new data that have emerged between the publication of full guidelines that affect patient safety or that in a decisive way impact decision making or patient management. This Focused Update provides guidance on surveillance and management of patients who had undergone abdominal aortic aneurysm repair with an EndoVascular Aneurysm Seal (EVAS) device.

Objective: After alerts on EndoVascular Aneurysm Seal (EVAS) failure were raised, the European Society for Vascular Surgery (ESVS) Abdominal Aortic Aneurysm (AAA) Clinical Practice Guidelines Writing Committee (WC) initiated a task force with the aim to provide guidance on surveillance and management of patients with implanted EVAS devices.

Methods: Based on a scoping review of risk for late serious aortic-related adverse events in patients treated with EVAS for AAA, the ESVS AAA Guidelines WC agreed on recommendations graded according to the European Society of Cardiology (ESC) grading system.

Results: EVAS has a very high incidence of late endograft migration resulting in proximal type 1 endoleak with risk of rupture, requiring open conversion with device explantation. The reported mortality rate for elective explantation varies between 0% and 14%, while acute conversion for rupture has a very dismal prognosis with a 67 – 75% mortality rate.

Conclusion: It is recommended that all patients in whom a Nellix device has been implanted should be identified, properly informed, and enrolled in enhanced surveillance. If device failure is detected, early elective device explantation should be considered in surgically fit patients.

Keywords: Abdominal aortic aneurysm, Endovascular Aneurysm Sealing, EVAS, Nellix, Endoleak, Guidelines

Article history: Received 12 October 2022, Accepted 28 December 2022, Available online 7 January 2023

© 2023 The Author(s). Published by Elsevier B.V. on behalf of European Society for Vascular Surgery. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

[‡] ESVS AAA Guidelines Writing Committee: Frederico Bastos-Gonçalves (Lisbon, Portugal), Sergi Bellmunt-Montoya (Barcelona, Spain), Xavier Berard (Bordeaux, France), Mario D'Orta (Trieste, Italy), Carlota Prendes (Munich, Germany), Christos Karkos (Thessaloniki, Greece), Arkadiusz Kazimierzak (Szczecin, Poland), Mark Koelemay (Amsterdam, the Netherlands), Tilo Köbel (Hamburg, Germany), Kevin Mani (Uppsala, Sweden), Germano Melissano (Milan, Italy), Janet Powell (London, UK), Santi Trimarchi (Milan, Italy).

[§] ESVS Guidelines Steering Committee: George Antoniou (Manchester, UK), Raphael Coscas (Paris, France), Nuno Dias (Malmö, Sweden), Philippe Kolh (Liege, Belgium), Sandro Lepidi (Trieste, Italy), Barend Mees (Maastricht, the Netherlands), Tim Resch (Copenhagen, Denmark), Jean Baptiste Ricco (Poitiers, France), Riikka Tulamo (Helsinki, Finland), Chris Twine (Bristol, UK), Martin Björck (Uppsala, Sweden).

* Corresponding author. Department of Surgical Sciences, Vascular Surgery, Uppsala University, Uppsala, Sweden and Department of Surgical and Peri-operative Sciences, Surgery, Umeå University, Umeå, Sweden.

E-mail address: anders.wanhainen@surgsci.uu.se (Anders Wanhainen).

1078-5884/© 2023 The Author(s). Published by Elsevier B.V. on behalf of European Society for Vascular Surgery. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

<https://doi.org/10.1016/j.ejvs.2022.12.031>

INTRODUCTION

The European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the management of abdominal aorto-iliac artery aneurysms recommended that conceptual new technologies, such as Endovascular Aneurysm Sealing (EVAS), should only be used within studies approved by research ethics committees and with informed consent until properly evaluated. The reportedly higher rates of leaks around the Nellix implant (Endologix, Inc., Irvine, CA, USA), endograft migration, and aneurysm sac enlargement further strengthened the position that EVAS was not suitable for use in clinical practice,¹ and subsequently, the manufacturer ended its production (Endologix, Nellix End of Life Communication, 10 May 2022). However, there was no clear guidance on surveillance and management of patients who had already undergone abdominal aortic aneurysm (AAA) repair with an EVAS device.

The ESVS AAA Guidelines Writing Committee therefore initiated a literature review, and the current accumulated knowledge suggests that patients treated with EVAS for AAA may be at high risk of serious aortic related adverse events, which justifies updated guidance on the surveillance and management of patients already treated with EVAS. It is also appropriate to reiterate the ESVS 2019 AAA Clinical Practice Guidelines Recommendation 58.¹

ESVS 2019 AAA Guidelines Recommendation 58		
New techniques/concepts (such as endovascular aneurysm sealing with endobags) are not recommended in clinical practice and should only be used with caution, preferably within the framework of studies approved by research ethics committees, until adequately evaluated		
Class	Level	References
III	C	Wanhainen <i>et al.</i> 2019

METHODS

A Scoping Review of the risk of late serious aortic related adverse events and follow up routines in patients treated with EVAS for AAA was performed based on a literature search in PubMed up to 7 December 2022 using the title search terms Endovascular Aneurysm sealing, EVAS, and Nellix. Reference checking and manual searching by members of the writing committee added other relevant literature. Full text original articles and published abstracts were included.

Based on a synthesis of the available evidence, the ESVS AAA Guidelines Writing Committee agreed on recommendations. The recommendations are graded according to the European Society of Cardiology (ESC) grading system, where the strength (class) of each recommendation is graded from I to III and the letters A to C mark the level of evidence. As per standard ESVS Guidelines procedure, this document has been reviewed and approved by the members of the ESVS Guidelines Steering Committee.

RESULTS

Endovascular Aneurysm Sealing failure mechanism

The main mechanisms of EVAS failure result from caudal migration of the stent grafts and separation of the endobags leading to type 1a endoleak, sac pressurisation, and aneurysm expansion.^{2–4} Failure of these endografts often occurs beyond two years from implant.^{2–5} In a recent systematic review and meta-analysis including 703 patients from seven studies with a mean follow up of more than two years (range 24 – 72 months), the pooled estimated incidence of type 1 endoleak, migration, and re-intervention was 25%, 22%, and 27% respectively,⁵ and by four years up to 100% of patients may demonstrate AAA sac expansion.⁶ Furthermore, it has become apparent that the failure mechanisms persisted despite refinement of the instructions for use of EVAS.⁷ Device migration and proximal type 1 endoleak may lead to secondary AAA rupture with an incidence of 9.3% with two thirds of patients not surviving the event.³

Endovascular Aneurysm Sealing surveillance

Experience from centres where large numbers of EVAS procedures were performed, initially prioritised the identification of all patients in whom these devices had been implanted and then enrolled them in enhanced surveillance programmes including initial computed tomography angiography (CTA), clinical assessment, and subsequent duplex imaging every six months, and plain abdominal radiographs to identify sac expansion, device migration, and endoleaks. If problems were identified, an additional CTA was performed to provide a more detailed assessment.

It is important that clinicians actively inform their patients in a clear and transparent manner regarding the high mid- and long term failure rates of EVAS, and a frank face to face consultation should be undertaken to explain the need for enhanced surveillance and potential problems that may occur. A formal “duty of candour” process with written communication to all patients is advocated.²

Management of device migration and endoleak

The management of a failing Nellix device presents a number of challenges compared with standard EVAR. The small stent calibre and the two flow lumens through separate devices prevent the use of proximal extension cuffs. Proximal extension with further Nellix devices often described as Nellix-in-Nellix application (NINA), with or without the addition of chimney parallel grafts (ChNINA) to the visceral arteries, did show some initial promise with reasonable one year results.⁸ However, much like the early attempts to embolise proximal type 1a endoleaks,^{3,9} the NINA approach has not been demonstrated to be durable at preventing device migration during extended follow up.^{2,4} Finally, Endologix recently announced in a targeted communication that the production of Nellix devices and its accessories has been ended, which prevents any further

secondary intervention or bailout treatment with these systems going forward (Endologix, Nellix End of Life Communication, 10 May 2022). Proximal extension with a fenestrated or branched EVAR device may be an alternative option, but, due to limited data, this method needs further evaluation.^{10,11}

Open conversion with device explantation is the treatment of choice for patients with a failing EVAS if they are deemed fit enough to undergo the intervention.^{3,4} The Nellix devices are relatively easy to remove from the proximal neck as there is no active fixation; however, the balloon expandable stent grafts in the iliac arteries may be more challenging to remove and care must be taken to avoid intimal dissection. Alternatively, they can be partially resected with the distal end left in situ and incorporated into the distal anastomoses. The mortality rate associated with device explantation can, however, be significant. A series of 21 explants including four for ruptured AAA reported no in hospital mortality and similar results were reported in another series of eight elective explants, although the explantation mortality rate in ruptured AAA patients in the same centre was 67%.^{3,12} In a recent single centre report from Norway, 29% (40/137) of patients treated with EVAS had open conversion due to type 1 endoleak with sac expansion after mean of 39 months follow up. The overall peri-operative (30 day) mortality was 20% (8/40), 75% (3/4) among emergency conversions, and 14% (5/36) among elective conversions.¹³ A further contemporary series of 44 explantations for various indications also identified significantly poorer outcomes in urgent or emergency cases.¹⁴ Therefore, these data would support early explantation of failing devices in fit patients in an elective setting.

CONCLUSION

The ESVS AAA Guidelines Writing Committee decided that it was important to publish this Focused Update before the fully updated guidelines will be available in 2024 to highlight the issues with EVAS failure to promote patient safety and to encourage clinicians to identify all patients in whom a Nellix device has been implanted. These patients should be enrolled in enhanced surveillance programmes and, if device failure is detected, be offered early elective device explant. It is recognised that in elderly, frail, and comorbid patients not suitable for explant, a conservative management strategy or alternative complex endovascular techniques may be more appropriate.

Recommendation 1

Patients who have undergone Endovascular Aneurysm Sealing with the Nellix (Endologix) prosthesis should be identified, properly informed and enrolled in enhanced surveillance.

Class	Level	References
I	C	Consensus

Recommendation 2

Explantation of failing Endovascular Aneurysm Sealing Nellix prostheses (Endologix) is recommended as the preferred treatment in surgically fit patients.

Class	Level	References
I	C	Consensus

REFERENCES

- 1 Wanhainen A, Verzini F, Herzelee IV, Allaire E, Bown M, Cohnert T, et al. European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg* 2019;**57**:8–93.
- 2 Harrison SC, Winterbottom AJ, Coughlin PA, Hayes PD, Boyle JR. Editor's Choice – Mid-term migration and device failure following endovascular aneurysm sealing with the Nellix stent graft system – a single centre experience. *Eur J Vasc Endovasc Surg* 2018;**56**:342–8.
- 3 Singh AA, Benaragama KS, Pope T, Coughlin PA, Winterbottom AP, Harrison SC, et al. Progressive device failure at long term follow up of the Nellix EndoVascular Aneurysm Sealing (EVAS) System. *Eur J Vasc Endovasc Surg* 2021;**61**:211–8.
- 4 Stenson KM, de Bruin JL, Loftus IM, Holt PJE. Migration and sac expansion as modes of midterm therapeutic failure after endovascular aneurysm sealing. *J Vasc Surg* 2020;**71**:457–69.
- 5 Kouvelos G, Nana P, Brodis A, Spanos K, Tasoudis P, Katsargyris A, et al. A meta-analysis of mid-term outcome of endovascular aneurysm sealing. *J Endovasc Ther* 2022. doi: 10.1177/15266028221098706 [Epub ahead of print].
- 6 Yafawi A, McWilliams RG, Fisher RK, England A, Karouki M, Uhanowita, et al. Aneurysm growth after endovascular sealing of abdominal aortic aneurysms (EVAS) with the Nellix endoprosthesis. *Eur J Vasc Endovasc Surg* 2020;**60**:671–6.
- 7 Carpenter JP, Lane 3rd JS, Trani J, Hussain S, Healey C, Buckley CJ, et al. Nellix Investigators. Refinement of anatomic indications for the Nellix System for endovascular aneurysm sealing based on 2-year outcomes from the EVAS FORWARD IDE trial. *J Vasc Surg* 2018;**68**:720–30.
- 8 Zoethout AC, Zerwes S, Zeebregts CJAM, Heyligers JMM, De Vries JPJM, Oberhuber A, et al. Preliminary outcome of Nellix-in-Nellix extensions in patients treated with failed endovascular aneurysm sealing. *J Vasc Surg* 2019;**70**:1099–106.
- 9 van den Ham LH, Holden A, Savlovskis J, Witterbottom A, Ouriel K, Reijnen MMPJ, EVAS Type IA Endoleak Study Group. Editor's Choice – Occurrence and classification of proximal type I endoleaks after endovascular aneurysm sealing using the Nellix™ device. *Eur J Vasc Endovasc Surg* 2017;**54**:729–36.
- 10 Pleban E, Michalak J, Iwanowski J, Szopinski P. The dilemma after sealing an endovascular aortic aneurysm – three ways out. *Zentralbl Chir* 2021;**146**:498–505.
- 11 Kasprzak PM, Pfister K, Kuczmik W, Schierling W, Sachsamanis G, Oikonomou K. Novel technique for the treatment of type Ia endoleak after endovascular abdominal aortic aneurysm repair. *J Endovasc Ther* 2021;**28**:519–23.
- 12 Mortola L, Ferrero E, Quaglino S, Ferri M, Viazzo A, Manzo P, et al. Management of Nellix migration and type Ia endoleak from proximal endovascular aneurysm sealing relining to late open conversion. *J Vasc Surg* 2021;**74**:1204–13.
- 13 Mathisen SR, Berge ST. Resultater etter konvertering av EVAS. Presented at the Norwegian annual meeting 24–28 October 2022. Available at https://issuu.com/brataas/docs/vitenskapelige_forhandlinger_2022_v3?fr=sMjRkYzIyNTg5Njc [accessed 28 December 2022].
- 14 Zerwes S, Kiessling J, Liebetau D, Jakob R, Gosslau Y, Bruijnen HK, et al. Open conversion after endovascular aneurysm sealing: technical features and clinical outcomes in 44 patients. *J Endovasc Ther* 2021;**28**:332–41.