Post-operative Surveillance and Long Term Outcome after Endovascular Aortic Aneurysm Repair in Patients with an Initial Post-operative Computed Tomography Angiogram Without Abnormalities

ODYSSEUS study group; Geraedts, Anna C.M.; Mulay, Sana; Vahl, Anco C.; Verhagen, Hence J.M.; Wisselink, Willem; de Mik, Sylvana M.L.; van Dieren, Susan; Koelemay, M. J.W.; Balm, Ron

Published in:
European Journal of Vascular and Endovascular Surgery

DOI:
10.1016/j.ejvs.2021.11.018

Publication date:
2022

Eur J Vasc Endovasc Surg (2022) 63, 390—399

Editor's Choice – Post-operative Surveillance and Long Term Outcome after Endovascular Aortic Aneurysm Repair in Patients with an Initial Post-operative Computed Tomography Angiogram Without Abnormalities: the Multicentre Retrospective ODYSSEUS Study

Anna C.M. Geraedts [a], Sana Mulay [a], Anco C. Vahl [b], Hence J.M. Verhagen [c], Willem Wisselink [a], Sylvana M.L. de Mik [a], Susan van Dieren [a], Mark J.W. Koelemay [a], Ron Balm [a,*], on behalf of the ODYSSEUS study group [†]

[a] Amsterdam University Medical Centres, Amsterdam Cardiovascular Sciences, Department of Surgery, Amsterdam, The Netherlands
[b] OLVG, Department of Surgery, Amsterdam, The Netherlands
[c] Erasmus Medical Centre, Department of Vascular Surgery, Rotterdam, The Netherlands

WHAT THIS PAPER ADDS

Endovascular aneurysm repair (EVAR) has become the predominant modality for the treatment of infrarenal abdominal aortic aneurysms (AAAs) in The Netherlands. There are concerns regarding the long term durability of EVAR, lifelong follow up routines, and adherence to these surveillance programmes. This study has highlighted that discontinued imaging surveillance post EVAR is common in The Netherlands. Moreover, discontinued yearly follow up in patients with initial post-operative computed tomography angiography without abnormalities is not associated with poor outcomes (in terms of mortality or secondary interventions), suggesting that less frequent surveillance may be envisaged. Future prospective studies are indicated to determine in which patient groups follow up can be safely reduced.

Objective: Lifelong imaging surveillance is recommended following endovascular aneurysm repair (EVAR). This study aimed to examine the association between adherence to post-operative surveillance and survival and secondary interventions in patients with an initial post-operative computed tomography angiogram (CTA) without abnormalities.
Methods: All consecutive patients undergoing EVAR for intact abdominal aortic aneurysm (AAA) in 16 hospitals between 2007 and 2012 were identified retrospectively, with follow up until December 2018. Patients were included if the initial post-operative CTA showed no types I — III endoleak, kinking, infection, or limb occlusion. Discontinued follow up was defined as at least one 16 month period in which no imaging surveillance was performed. Primary outcomes were aneurysm related mortality and secondary interventions, and secondary outcome all cause mortality. Kaplan—Meier analysis was used to estimate survival, and Cox regression analyses to identify the association between independent variables and outcome. Sensitivity analyses were performed by varying the definition of continued yearly follow up. The study protocol was published (bmjopen-2019-033584).
Results: 1 596 patients (552 continued, 1 044 discontinued follow up) were included with a median (interquartile range) follow up of 89.1 months (52.6). Cumulative aneurysm related, overall, and intervention free survival was 99.4/94.8/96.1%, 98.5/72.9/85.9%, and 96.3/45.4/71.1% at 1, 5, and 10 years, respectively. American Society of Anesthesiologists (ASA) classification (ASA IV hazard ratio [HR] 3.810, 95% confidence interval [CI] 1.296 — 11.198), increase in AAA diameter (HR 3.299, 95% CI 1.408 — 7.729), and continued follow up (HR 3.611, 95% CI 1.780 — 7.323) were independently associated with aneurysm related mortality. The same variables and age (HR 1.063 per year, 95% CI 1.052 — 1.074) were significantly associated with all cause mortality. No difference in secondary interventions was observed between patients with continued *vs.* discontinued follow up (89/552; 16% *vs*. 136/1044; 13%; $p = .091$). Sensitivity analyses showed worse aneurysm related and overall survival in patients with continued follow up.
Conclusion: Discontinued follow up is not associated with poor outcomes. Future prospective studies are indicated to determine in which patients imaging follow up can be safely reduced.

Keywords: Abdominal aortic aneurysm, Endovascular procedures, Vascular surgical procedures
Article history: Received 2 February 2021, Accepted 14 November 2021, Available online 16 February 2022

[†] Members of the collaboration group listed in Appendix B section

* Corresponding author. Amsterdam University Medical Centres, University of Amsterdam, Amsterdam Cardiovascular Sciences, Department of Surgery, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
E-mail address: r.balm@amsterdamumc.nl (Ron Balm).
1078-5884/
https://doi.org/10.1016/j.ejvs.2021.11.018

INTRODUCTION

In current practice, endovascular aneurysm repair (EVAR) is the preferred surgical treatment of asymptomatic infrarenal abdominal aortic aneurysms (AAAs). In The Netherlands, 79% of elective AAA repairs are performed using EVAR.[1,2] EVAR offers important procedural benefits compared with open surgical repair (OSR), i.e., lower peri-operative mortality, fewer complications, and quicker post-operative recovery.[3,4] However, there is a difference in durability between EVAR and OSR. Long term results of previous clinical trials reveal equal overall survival rates, but significantly more secondary interventions in patients treated by EVAR.[5–7] Due to a continued risk of endograft related complications and rupture following EVAR, strict imaging surveillance is considered mandatory for all patients, and recommended by current international guidelines[8,9] and endograft manufacturer's instructions for use (IFU). However, adherence to strict yearly follow up protocols is often suboptimal and inconsistent.[10,11] Previous research has not demonstrated any beneficial effect on survival when comparing patients with continued and discontinued imaging surveillance; however, increased secondary intervention rates were observed in patients with continued follow up.[10,12,13]

The initial post-operative computed tomography angiogram (CTA) guides patient stratification during follow up. This scan either shows complications, such as endoleaks, occlusion, or endograft malposition, or the absence thereof. If the initial CTA shows no abnormalities the risk of a secondary intervention is low.[14–16] Doubts remain as to whether yearly imaging surveillance is essential for all EVAR patients, and if patients whose initial post-operative CTA showed no abnormalities could be considered for less intensive follow up, as suggested by the European Society for Vascular Surgery (ESVS) guidelines.[8]

It is hypothesised that there would be no difference in aneurysm related mortality between patients with continued *vs.* discontinued follow up, and that patients with continued imaging surveillance undergo more secondary interventions.

MATERIALS AND METHODS

This multicentre retrospective observational study was performed in accordance with the STROBE guidelines,[17] and complied with the Declaration of Helsinki. The study was approved by the local Institutional Review Board (W18_102#18.130), registered with The Netherlands Trial Registration (NL6953), and the protocol was published.[18] In accordance with the Dutch Code of Civil Procedure, the opt out procedure was used; by default patient records were used for research, unless the patient objected to participation within four weeks of notification.

Study population

All consecutive patients at 16 academic and teaching hospitals in The Netherlands (one hospital did not participate) with an AAA who underwent elective EVAR between January 2007 and January 2012 were included. This selection provided a maximum follow up of 6 — 11 years on 1 December 2018. Inclusion criteria were the presence of an intact infrarenal aortic or aorto-iliac aneurysm treated by standard EVAR, and a CTA without abnormalities (no type I — III endoleak, kinking, infection or limb occlusion) performed within 90 days of the initial procedure. Patients with ruptured or isolated iliac aneurysms or requiring chimney or fenestrated EVAR were excluded.

Data collection

Data were collected from patient medical records by two investigators (A.G., S.M.) and entered into an electronic database built with Castor EDC (ISO 27001 and NEN 7510 certified).[19] Baseline characteristics included age, sex, American Society of Anesthesiologists (ASA) classification and endograft type. Anatomical characteristics included pre-operative AAA diameter, neck length, neck angulation, and iliac artery diameters. Follow up data comprised all imaging studies (duplex ultrasonography [DUS], CTA, magnetic resonance angiography) including the AAA diameter, abnormal findings, interventions, and death. Also, imaging studies made for other reasons outside protocol were used. Data were censored at the date when either the patient died or when the end of follow up on 1 December 2018 was reached. Deaths were ascertained by linking the records of the study population and the National Death Register based on sex, name, and date of birth.

Surveillance programmes

All participating centres provided their respective surveillance protocol (Table 1). These local surveillance protocols dated from 2018 and earlier. Follow up protocols varied per institution, in the first year CTA and DUS were most frequently used and usually DUS annually thereafter.

Definitions

Continued follow up was defined as undergoing imaging surveillance at least once every 16 months throughout the entire follow up period, as most patients were rescheduled within three to four months if they missed their annual follow up visit (consensus decision of the study group). Patients missing at least one follow up visit (imperfect follow up) were included as discontinued to imaging follow up. The reasons why patients missed their follow up visit could not be retrieved from their medical files. Imaging studies were evaluated by radiologists from participating centres and not re-analysed for the purpose of this study. Abnormal radiological findings during follow up were recorded as follows: type I — IV endoleak, endograft migration $>$ 10 mm, endograft infection, endograft kinking, limb occlusion, or sac growth (anteroposterior [AP] diameter).[20,21] Patients were distributed over three groups depending on the reported aneurysm diameter over time:

Table 1. Surveillance programmes after endovascular repair of an intact abdominal aortic aneurysm in participating centres in The Netherlands

Centre	First imaging	Yearly thereafter
1	A CT angiogram (CTA) after 4–6 w and clinical visit. No abnormalities: yearly duplex ultrasound (DUS). Abnormalities: CTA is repeated. Endoleak type I/III: intervention	DUS
2	Two weeks clinical visit. A CTA, plain film Xray and clinical review at3 mo post-procedure. CTA at 12 mo. DUS + plain film Xray at year 2, 3, and 5. CTA at 5 y post procedure	DUS, 1/5 y CTA
3	6 week CTA. No abnormalities: DUS after 6 mo and thereafter annually. Type I endoleak: intervention or strict surveillance, type II: normal follow up	DUS, CTA if new endoleak and/or sac size increase
4	First day after discharge consult via phone. Clinical visit after two weeks. Six weeks clinical review + CTA	DUS
5	CTA after 4 w	DUS + ABI + biplanar plain film Xray. CTA if new endoleak and/or sac size increase
6	Clinical visit + DUS 6–8 w. DUS after 3 mo.	DUS + plain film Xray every 2 y
7	CTA at 6 w, colour flow DUS at 6 mo	Colour flow DUS On indication: CTA
8	CTA at 4 w and 12 mo	DUS
9	CTA at 4 w and 12 mo	DUS
10	CTA at 4 w and 12 mo	DUS, 1/5 y CTA
11	6 w clinical visit + CTA	DUS or CTA every 5 years
12	CTA at 6 w, CTA or DUS + plain film Xray at 6 mo	DUS + plain film Xray
13	6 w clinical visit + DUS, DUS at 3 mo	DUS
14	CTA at 4 w and 12 mo. No abnormalities: yearly DUS. Abnormalities: CTA at 3 mo, endoleak I/III: intervention	DUS
15	CTA at 6 w + biplanar plain film Xray. DUS at 6 mo	DUS, CTA if sac size increase
16	Pre-discharge: biplanar plain film Xray. CTA at 6 weeks, CTA at 12 months + biplanar plain film Xray	DUS, CTA if new endoleak and/or sac size increase
	Abnormalities first CTA: • Type I endoleak: intervention • Type II endoleak: strict follow up protocol • After 6 mo: biplanar plain film Xray + CT, if sac size increase >10% → CTA • After 12 mo: biplanar plain film Xray + CT	
	No abnormalities first CTA: • Minimal follow up • After 12 mo: biplanar plain film Xray + CT	

CT = computed tomography; CTA = computed tomography angiography; DUS = duplex ultrasonography; ABI = ankle brachial index.

increased, stable, or decreased. Sac growth and shrinkage were determined as an increase or decrease of > 5 mm between two consecutive imaging studies, or if there was > 5 mm growth or shrinkage in comparison with the initial post-operative AAA diameter. The aneurysm diameter was recorded as stable if less than 5 mm sac growth or shrinkage occurred.[20] Secondary interventions were defined as procedures to fix endograft related complications that were detected on imaging studies.[20]

Outcomes

The primary outcome parameters of this study were aneurysm related death and secondary interventions. Secondary outcomes included all cause mortality, radiological findings during follow up and aneurysm rupture.

Statistical analysis

The sample size calculation was based on a superiority design for secondary interventions and non-inferiority for aneurysm related mortality.[18] In patients with a post-operative CTA without abnormalities and to correct for 10% incomplete or missing data, a total of 1 598 (1 438/0.9) patients were required to detect a 7% difference for the outcome secondary interventions, and 1 451 (1 306/0.9) patients for aneurysm related death with a non-inferiority limit of 3%.[18] The Shapiro–Wilk test, Q-Q plots, and histograms were used to determine whether continuous data were normally distributed. Continuous variables were presented as mean and standard deviation (SD) for normally distributed data, or median and inter-quartile range (IQR) for non-normally distributed data. Differences between groups were assessed using Student's *t* test or Mann–Whitney U test, as appropriate. Categorical variables were presented as counts and percentages, differences between groups were analysed using the Pearson χ^2 test or Fisher's exact test. The Kaplan–Meier method was used to estimate survival, and the log rank test to compare survival estimates between groups. Time to aneurysm related and all cause mortality was calculated

between start of follow up and time of death or December 2018. Secondary interventions were censored at the last contact with the hospital for imaging. To account for missing data, ten imputed datasets were constructed using multiple imputation by predictive mean matching and pooled with Rubin's rule. Cox regression analyses controlling for ASA classification, age, sex, endograft type, initial AAA diameter, neck length, angulation, maximum iliac diameter, and change in AAA diameter were used to determine the hazard ratio (HR) and 95% confidence interval (CI) of the variables associated with death and secondary interventions. Continued follow up was investigated in Cox regression analyses to adjust the effect of continued imaging surveillance by possible confounders. To correct for misclassification and because of progressive insight, sensitivity analyses were performed by varying the definition of continued follow up. In this first sensitivity analysis, all patients were reclassified and allocated as continued with imaging surveillance if they underwent at least 80% of their required follow up visits. In the second sensitivity analysis continued follow up rates in the participating centres were divided into low, medium or high continued follow up rates to evaluate strategies instead of patients. With these new variables (continued follow up 80% and continued follow up participating centres) Cox regression analyses were repeated. The level for statistical significance was set at a two sided $p < .050$. All statistical analyses were calculated with SPSS software version 26 and RStudio 3.6.1.

RESULTS

In total, 1 596 patients were included (Supplementary Figure S1), 552 patients had continued yearly imaging surveillance according to the definition, and 1 044 patients discontinued. The mean (SD) age was 73.5 years (7.8) and there was preponderance of males ($n = 1\,425$; 89%). Patient characteristics are presented in Table 2. The amount of imputed missing data ranged from 0.1% to 37.5%. Neck angulation was missing from > 50% of the radiology reports, and therefore excluded from further analyses. Adherence to yearly imaging surveillance varied widely between participating centres from 15.8% to 54.7% (Supplementary Table S1). The percentage of follow up visits declined in later years following primary EVAR (Supplementary Table S2). The 30 day mortality rate following primary EVAR was 0.4% (7/1 596).

Primary outcomes

As of 1 December 2018, there were 807 deaths of 1 596 EVAR patients: 320 patients died of non-aneurysm related causes, 34 patients of aneurysm related causes (20 with continued and 14 with discontinued follow up), and in 453 patients the cause of death was unknown. The median (IQR) follow up until death or December 2018 for the entire cohort was 89.1 months (52.6). The median (IQR) follow up for patients with continued follow up was 75.4 months (66.1), while for patients with discontinued follow up it was 92.4 months (41.4), $p < .001$. Freedom from aneurysm related death was 96.9% and 92.0% at five and 10 years for patients with continued follow up, and 99.7% and 98.0% at five and 10 years for patients with discontinued follow up (log rank; $p < .001$, Fig. 1).

There was no difference between the two groups in the number of patients undergoing secondary interventions (89/552; 16% *vs.* 136/1 044; 13%; $p = .091$). Also, no

Table 2. Baseline characteristics in 1 596 patients with continued vs. discontinued follow up after endovascular aneurysm repair of an intact abdominal aortic aneurysm (AAA)

Variable	Missing	Continued follow up ($n = 552$)	Discontinued follow up ($n = 1\,044$)	*p* value
Age − y	0	73.4 ± 0.314	73.6 ± 0.248	.52
Male sex	0	495 (89.7)	930 (89.2)	.86
AAA diameter − cm	2	6.1 ± 0.041	6.0 ± 0.030	.39
ASA classification	0			.91
I		6 (1.1)	7 (0.7)	
II		225 (40.9)	424 (40.7)	
III		283 (51.5)	543 (52.1)	
IV		36 (6.5)	68 (6.5)	
Unknown		2 (0.4)	2 (0.2)	
Endograft	0			.032
Endurant (Medtronic)		240 (43.5)	383 (36.7)	
Zenith (Cook)		175 (31.7)	381 (36.5)	
Excluder (Gore)		70 (12.7)	115 (11.0)	
Talent (Medtronic)		22 (4.0)	74 (7.1)	
Powerlink (Endologix)		2 (0.4)	6 (0.6)	
Anaconda (Vascutek)		4 (0.7)	2 (0.2)	
Other/Unknown		39 (7.0)	83 (7.9)	
Neck length − cm	468	3.1 ± 0.062	3.0 ± 0.041	.053
Neck angulation − degrees	1 336	48.3 ± 2.95	54.8 ± 2.87	.12
Maximum iliac diameter − cm	598	1.9 ± 0.060	1.9 ± 0.041	.46

Data are presented as *n* (%) or mean ± standard error of the mean. ASA = American Society of Anesthesiologists.

difference was observed in numbers of acute secondary interventions (symptomatic presentation) between patients with continued and discontinued follow up (16/89; 18% *vs*. 30/136; 22%; $p = .48$). The median (IQR) time to a secondary intervention was 56 months (61.7). The most common indications were type I endoleak and limb occlusion (Table 3). The median (IQR) follow up for the entire cohort until last contact with the hospital was 65 months (61.0), and no difference in follow up duration was observed between patients with continued or discontinued imaging follow up ($p = .33$). Freedom from secondary interventions was higher in patients with discontinued follow up (Log rank; $p = .003$) (Fig. 2). Cumulative intervention free survival was 96.1%, 85.9%, and 71.1% at one, five, and 10 years, respectively.

Secondary outcomes

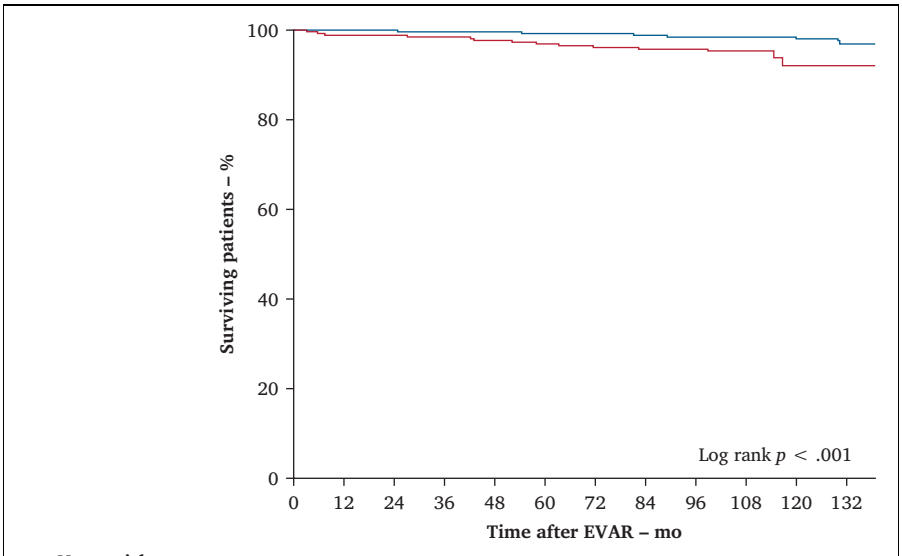
Overall survival was higher in patients with discontinued imaging follow up (log rank; $p < .001$) (Supplementary Figure S2). The overall survival rates were 94.8%, 72.9%, and 45.4% at one, five, and 10 years, respectively. Overall survival was 80.3% and 49.6% at five and 10 years for patients with discontinued imaging follow up, and 58.6% and 35.5% at five and 10 years for patients with continued follow up.

When comparing patients with continued *vs.* discontinued follow up, abnormal radiological findings were seen more often in the "continued follow up" group (192/552; 35% *vs*. 226/1 044; 22%, $p < .001$) (Table 4). On imaging many patients had multiple abnormal findings, so this resulted in 739 abnormal findings during follow up. The commonest abnormal radiological findings in patients with continued follow up were sac growth and type II endoleak.

Twenty-nine patients (1.8%) presented with aneurysm rupture, equally divided between the groups (10/552; 1.8% *vs*. 19/1044; 1.8%). The causes of aneurysm rupture were: type I endoleak in 15 patients (3/15 previously detected on imaging surveillance), type II endoleak in three patients (2/3 previously detected), one patient with type III endoleak (not previously detected), two patients with endograft kinking (not previously detected), and in eight patients no cause or previously detected abnormalities were recorded. The median (IQR) time to rupture was 73 months (44.7). The median diameter (IQR) at the time of rupture was 7.8 cm (1.9). The majority of ruptures (18/29; 62%) occurred more than five years after the primary procedure. The cumulative freedom from AAA rupture was 98.9% and 94.5% at five and 10 years, respectively.

Cox regression analyses

Table 5 gives results of the Cox regression analyses for both primary outcomes. In multivariable analysis, ASA classification (ASA IV HR 3.810, 95% CI 1.296 — 11.198), change in AAA diameter (increase HR 3.299 per cm, 95% CI 1.408 — 7.729, decrease HR 0.256 per cm, 95% CI 0.096 — 0.688) and continued follow up (HR 3.588, 95% CI 1.760-7.314) were significantly related to aneurysm related death.



No. at risk												
Discontinued follow up	1017	973	946	914	868	809	724	561	377	236	122	36
Events	3	1	1	0	2	0	3	2	0	1	1	0
Censored	54	28	23	40	53	61	109	211	153	128	98	72
Continued follow up	542	491	432	384	345	305	268	209	130	66	25	6
Events	7	0	2	2	3	2	1	0	1	2	0	0
Censored	21	66	52	40	35	39	30	86	73	52	27	11

Figure 1. Cumulative Kaplan—Meier estimate of aneurysm related mortality in 1 596 patients with continued and discontinued imaging surveillance after endovascular aneurysm repair (EVAR) of an intact abdominal aortic aneurysm.

Table 3. Complications and secondary interventions within five years and in total in 552 and 1 044 patients with continued *vs.* discontinued follow up following endovascular aneurysm repair of an intact abdominal aortic aneurysm

Radiological finding	Interventions in patients with continued follow up		Interventions in patients with discontinued follow up	
	5 years (n = 58)	Total (n = 89)	5 years (n = 104)	Total (n = 136)
Endoleak type I	11	18	16	21
Endoleak type I + sac growth	4	5	6	8
Endoleak type I + migration	1	2	1	1
Endoleak type I + kinking	0	1	0	0
Endoleak type II	8	11	14	15
Endoleak type II + sac growth	3	6	0	4
Endoleak type II + migration	1	1	0	0
Endoleak type II + kinking	1	1	0	0
Endoleak type II + limb occlusion	1	3	1	1
Endoleak type III	0	5	1	5
Endoleak type III + sac growth	1	1	4	4
Endoleak type IV	0	0	0	1
Endograft migration	1	2	4	4
Endograft kinking	3	6	3	3
Endograft kinking + sac growth	0	0	2	2
Endograft kinking + limb occlusion	4	4	4	5
Limb occlusion	14	20	28	36
Endograft infection	2	2	7	7
Sac growth	4	9	10	14
Other	4	5	10	13
No abnormal finding previous imaging	13	18	29	32
Rupture endovascular repair (open repair)	6	8 (1)	2 (3)	17 (9)
Total	82	129	145	202

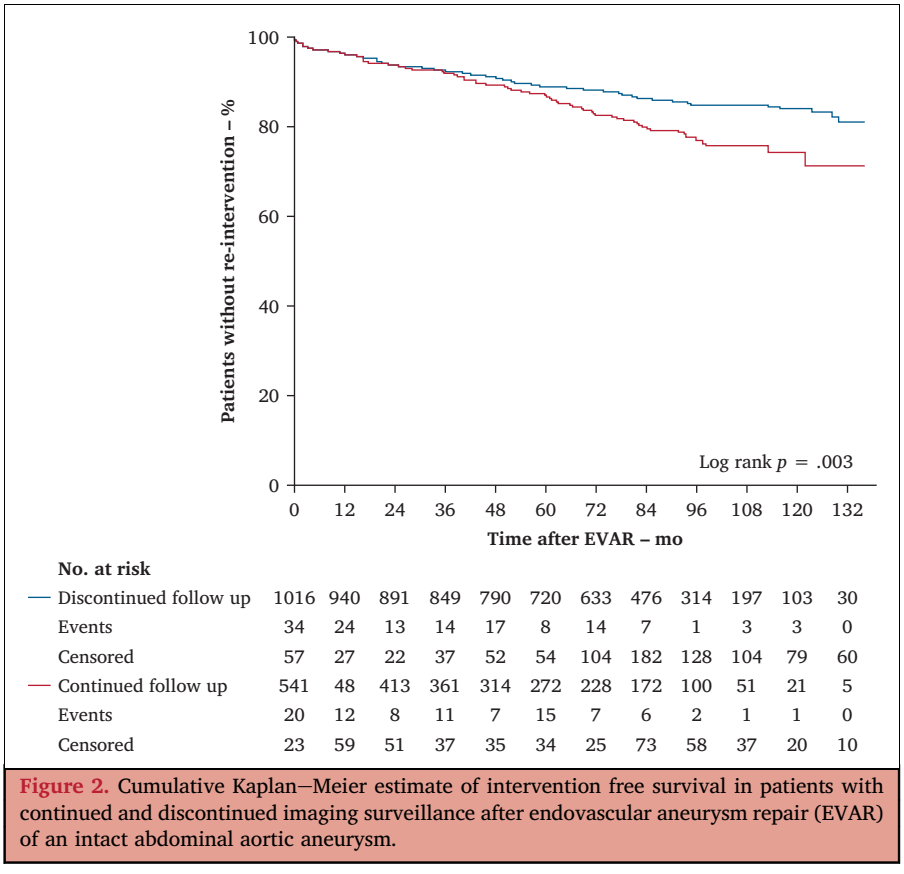


Figure 2. Cumulative Kaplan–Meier estimate of intervention free survival in patients with continued and discontinued imaging surveillance after endovascular aneurysm repair (EVAR) of an intact abdominal aortic aneurysm.

Table 4. Number of abnormal findings during surveillance imaging linked to adherence to imaging follow up in 552 and 1 044 patients with continued vs. discontinued follow up following endovascular aneurysm repair of an intact abdominal aortic aneurysm

Abnormal finding in imaging	Continued follow up (n = 552)	Discontinued follow up (n = 1 044)	p value
Endoleak type I	40 (7.2)	56 (5.4)	.13
Endoleak type II	80 (14.5)	63 (6.0)	.001
Endoleak type III	14 (2.5)	17 (1.6)	.21
Endoleak type IV	1 (0.2)	2 (0.2)	.96
Endograft migration	10 (1.8)	13 (1.2)	.37
Endograft kinking	18 (3.3)	20 (1.9)	.094
Limb occlusion	27 (3.7)	41 (3.9)	.36
Sac growth	88 (15.9)	119 (11.4)	.010
Endograft infection	12 (2.2)	9 (0.9)	.029
Other abnormalities	52 (9.4)	57 (5.5)	.003
Total	342	397	

Data are presented as n (%).

In multivariable analysis pre-operative AAA diameter (HR 1.255 per cm, 95% CI 1.108 — 1.422), maximum iliac diameter (HR 1.171 per cm, 95% CI 1.018 — 1.347), increase in AAA diameter (HR 7.335 per cm, 95% CI 4.608 — 11.677), age (HR 0.962 per year, 95% CI 0.945 — 0.978), endograft type (Gore Excluder HR 0.558, 95% CI 0.326 — 0.958), and continued follow up (HR 1.368, 95% CI 1.021-1.831) were significantly associated with secondary interventions.

In univariable analysis of all cause mortality age, AAA diameter, ASA classification, endograft type, maximum iliac diameter, change in AAA diameter, and continued follow up were statistically significant. In multivariable analysis, age (HR 1.063 per year, 95% CI 1.052 — 1.074), ASA classification (ASA IV HR 1.498, 95% CI 1.136 — 1.975), change in AAA diameter (increase HR 0.495 per cm, 95% CI 0.385 — 0.637, decrease HR 0.418 per cm, 95% CI 0.357— 0.489), and continued follow up (HR 1.957, 95% CI 1.688 — 2.268) were significantly associated with all cause mortality. All analyses before imputation are displayed in Supplementary Table S3.

Sensitivity analyses

After applying the alternative definition of continued follow up in which patients were classified as continued imaging surveillance if they had 80% of their follow up visits, 1 018 patients had continued follow up and 578 discontinued. In multivariable analysis, maximum iliac diameter (HR 1.370 per cm, 95% CI 1.030 — 1.821), decrease in AAA diameter (HR 0.299, 95% CI 0.095 — 0.943), and continued follow up, 80% (HR 4.706, 95% CI 1.371 — 16.152) were significantly associated with aneurysm related mortality. In multivariable analysis AAA diameter (HR 1.346 per cm, 95% CI 1.164 — 1.556), maximum iliac diameter (HR 1.316 per cm, 95% CI 1.123 — 1.543), increase in AAA diameter (HR 7.161, 95% CI 3.871 — 13.247), age (HR 0.967, 95% CI 0.946 — 0.989), and continued follow up, 80% (HR 1.774, 95% CI 1.157 — 2.719) were significantly associated with secondary interventions. Multivariable analysis showed that age (HR 1.067, 95% CI 1.055 — 1.078), ASA classification (ASA IV HR 1.511, 95% CI 1.144 — 1.995), change in AAA diameter (increase HR 0.440 per cm, 95% CI 0.341 — 0.567, decrease HR 0.392 per cm, 95% CI 0.334 — 0.459), and continued follow up 80% (HR 1.932, 95% CI 1.651 — 2.260) were significantly associated with all cause mortality (Supplementary Table S3). There was a significant difference between the two groups in the proportion of patients undergoing secondary interventions (168/1 018; 17% *vs.* 57/578; 10%; $p < .001$).

Continued imaging follow up in participating centres was classified as low (up to 26%), medium (up to 36%) or high (up to 55%). Multivariable analyses showed no significant association between this distribution of continued follow up rates in participating centres and all outcomes (aneurysm related mortality, secondary interventions, and all cause mortality) (Supplementary Table S3).

DISCUSSION

The current study has endeavoured to address the evidence gap regarding the value of imaging surveillance in post-EVAR patients whose initial post-operative CTA shows no abnormalities. All participating hospitals used their own surveillance protocol with many similarities to the ESVS guidelines.[8] Most patients who underwent EVAR did not undergo yearly imaging. There was no difference in the number of secondary interventions between patients with continued and discontinued imaging follow up. However, secondary interventions were seen earlier in the group with continued post-EVAR surveillance. This was confirmed after correcting for confounders by multivariable Cox regression. Finally, in the univariable analysis it was found that continued imaging surveillance was associated with decreased survival, an outcome that remained consistent after adjusting for confounders.

The value of the initial post-operative imaging has been investigated before, demonstrating the risk of complications and interventions is low if no abnormalities are shown on initial imaging.[14–16] In this study, patients with continued imaging surveillance underwent 3% more secondary interventions. This is less than the expected difference of 7%, which may be explained by the fact that physicians have become more restrained in intervening nowadays. These findings suggest that not all complications require secondary intervention but may be monitored. It is not known whether if abnormalities are seen on imaging, patients tend to undergo stricter follow up.[13,22] However, in sensitivity analysis, including the continued follow up 80% variable, patients with continued imaging surveillance underwent more secondary interventions. This finding was similar to Garg *et al.*,[15] who found more interventions (10% *vs.* 1.4%) in patients with complete against incomplete surveillance. The intervention free survival rates were in line with previous studies.[4,23]

The results showed poor survival outcomes in patients with continued imaging surveillance. Overall survival was

Table 5. Cox regression univariable and multivariable analyses of the effect of different variables on aneurysm related mortality and secondary interventions in 1 596 patients following endovascular aneurysm repair of an intact abdominal aortic aneurysm (AAA)

	Univariable analysis		Multivariable analysis	
	AAA mortality HR (95% CI)	Interventions HR (95% CI)	AAA mortality HR (95% CI)	Interventions HR (95% CI)
Age (per year)	1.014 (0.970–1.060)	0.966 (0.951–0.982)		0.962 (0.945–0.978)*
Sex	1.212 (0.426–3.444)	0.773 (0.484–1.237)		
ASA classification				
ASA I/II	1	1	1	
ASA III	1.592 (0.740–3.423)	1.018 (0.777–1.333)	1.489 (0.685–3.236)	
ASA IV	3.881 (1.324–11.372)	1.269 (0.747–2.199)	3.810 (1.296–11.198)	
Endograft				
Endurant (Medtronic)	1	1		1
Zenith Flex (Cook)	0.838 (0.383–1.831)	0.693 (0.507–0.948)		0.721 (0.516–1.008)
Talent (Medtronic)	1.376 (0.443–4.280)	1.084 (0.661–1.776)		0.792 (0.458–1.370)
Excluder (Gore)	0.407 (0.092–1.804)	0.516 (0.308–0.863)		0.558 (0.326–0.958)*
Other	0.595 (0.135–2.623)	1.206 (0.788–1.847)		0.963 (0.594–1.560)
AAA diameter − cm	1.319 (0.977–1.781)	1.262 (1.119–1.423)		1.255 (1.108–1.422)*
Neck length − cm	0.847 (0.593–1.209)	0.847 (0.593–1.209)		
Max. iliac diameter − cm	1.226 (0.962–1.562)	1.227 (0.963–1.563)		1.171 (1.018–1.347)*
Continued follow up	3.529 (1.771–7.032)	1.497 (1.147–1.955)	3.611 (1.780–7.323)*	1.368 (1.021–1.831)*
Change AAA diameter				
Stable	1	1	1	1
Increase	3.896 (1.672–9.078)	3.896 (1.672–9.078)	3.299 (1.408–7.729)*	7.335 (4.608–11.677)*
Decrease	0.291 (0.109–0.778)	0.291 (0.109–0.778)	0.256 (0.095–0.688)*	1.080 (0.684–1.706)

ASA = American Society of Anaesthesiologists; HR = hazard ratio; CI = confidence interval; Max = maximum.
* Significant difference.

49.6% at 10 years for patients with discontinued follow up *vs.* 35.5% for patients with continued follow up. Aneurysm related survival was also worse: 98.0% and 92.0% for patients with discontinued and continued follow up, respectively. This is an intriguing fact that needs to be looked at carefully and which, considering the non-inferiority study design, was unexpected. Multiple explanations for this finding may be proposed. First, patients with continued follow up could have multiple comorbidities and have imaging studies for other reasons, and therefore attend the hospital more often. Second, symptomatic patients and patients with abnormalities seen on imaging surveillance tend to adhere better to their surveillance programme. This finding was robust in the sensitivity analysis in which similar variables were independently associated with all cause mortality. However, other factors were associated with aneurysm related mortality which is probably explained by the low incidence of recorded aneurysm related deaths. High rates of continued follow up in participating centres did not lead to better outcomes. Current guidelines focus on assessment of AAA diameter with DUS and recommend CTA if the diameter increases. Contrary to what might be expected, it was found that an increase in AAA diameter was associated with lower all cause mortality. There is no explanation for this finding, which might be due to other comorbidities that were not included in the dataset (residual confounding). During follow up, some patients had several abnormal radiological findings, or even findings that usually require secondary interventions. Yet these scenarios failed to encourage adherence to surveillance protocols, as only 50% of patients underwent yearly imaging surveillance in the first five years following primary EVAR.[24] This may be explained by the fact that patients who have undergone AAA repair feel disease free[25] or the physician had indicated that the imaging frequency could be reduced in patients too frail to undergo a secondary intervention.

The study showed that 73.0% of patients survived more than five years after EVAR, while 45.6% survived more than 10 years after EVAR, equivalent to another long term study.[23] As life expectancy is rising, long term endograft durability is of major importance. Based on the present study, the durability of the implanted devices is satisfactory, as the intervention free survival was 71.1% at 10 years. However, newer generation stent grafts will need strict surveillance as their long term results are still unknown, and new technology failures must be avoided as evidenced by a device that was designed to provide ”endovascular aneurysm sealing”.[26]

This study has limitations including its retrospective observational study design with a risk of information bias. It was unclear if patients were lost to follow up, if imaging studies had been discontinued after uncomplicated surveillance, or if patients had undergone imaging surveillance elsewhere. Nonetheless, the long term results of a treatment method also require retrospective analysis, since not all potential problems can be foreseen. Patients were included until 2012, limiting the ability to draw

conclusions from more recent devices and in more EVAR experienced vascular surgeons. Another important issue to address is that there were no clear protocols as to when a patient might be discharged from further follow up. This could have modified the outcome that patients would automatically be considered as patients with (dis) continued follow up. However, this may affect both groups equally. No analysis was performed whether patients were treated in accordance with the IFU. Another major limitation of this study is the missing information on cause of death, and therefore the primary outcome regarding aneurysm related mortality should be interpreted with caution. Autopsy to confirm cause of death is not routinely performed in The Netherlands, and therefore it is likely that the proportion of aneurysm related deaths has been underestimated. Another limitation was that the reasons why patients were no longer under surveillance imaging were not noted, and therefore it can only be speculated what happened in the long interval between last imaging and time of death. This may have resulted in a distorted view as patients could have been referred back to their initial hospital, and therefore be misclassified as discontinued to imaging follow up.

The strengths of this study include the use of population based data with long term follow up and the accuracy of verifying deaths through the National Death Register. It also comprises all imaging studies made following EVAR, and thus provides a complete overview of national practice and adherence to the ESVS guidelines.

The results show that no EVAR related abnormalities were detected during follow up in the majority of patients (74%). In this multicentre study, discontinued imaging follow up was not associated with worse outcomes. This signals an important opportunity for increasing the efficiency of the post-EVAR follow up programme. Yearly imaging surveillance may not always be necessary if initial post-operative CTA shows no abnormalities. This suggestion should be validated in future prospective studies to determine in which patients imaging surveillance can be safely postponed. Incorporating risk stratification based on pre-operative variables into the development of surveillance protocols may reduce over-treatment. Since patients with no abnormalities at their initial post-EVAR CTA may be considered as low risk, imaging surveillance could be delayed until five years after the initial repair, as proposed by the ESVS guidelines. This would save on healthcare system resources without endangering patient safety, while at the same time increasing adherence among those who do need surveillance.

CONFLICTS OF INTEREST

None.

FUNDING

This study was funded by The Netherlands Organisation for Health Research and Development (ZonMw; grant number 843004119).

ACKNOWLEDGEMENTS

The authors thank N. Wolfhagen for the statistical assistance with Rstudio.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2021.11.018.

APPENDIX B.

ODYSSEUS study group: R. Balm, J.W. Elshof, B.H.P. Elsman, J.F. Hamming, M.J.W. Koelemay, R.H.J. Kropman, P.P. Poyck, G.W.H. Schurink, A.A.E.A de Smet, S.M. van Sterkenburg, C. Ünlü, A.C. Vahl, H.J.M. Verhagen, P.W.H.E. Vriens, J.P.P.M. de Vries, J.J. Wever, W. Wisselink, C.J. Zeebregts

REFERENCES

1 Dutch Surgical Aneurysm Audit. Available at: https://dica.nl/dsaa [Accessed 24 February 2020].
2 Lijftogt N, Vahl AC, Wilschut ED, Elsman BHP, Amodio S, van Zwet EW, et al. Adjusted hospital outcomes of abdominal aortic aneurysm surgery reported in the Dutch Surgical Aneurysm Audit. *Eur J Vasc Endovasc Surg* 2017;**53**:520–32.
3 Lederle FA, Freischlag JA, Kyriakides TC, Matsumura JS, Padberg FT, Kohler TR, et al. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med* 2012;**367**:1988–97.
4 Schermerhorn ML, Buck DB, O'Malley AJ, Curran T, McCallum JC, Darling J, et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *N Engl J Med* 2015;**373**:328–38.
5 De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven ELG, Cuypers PWM, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2010;**362**:1881–9.
6 Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *Lancet* 2016;**388**:2366–74.
7 Lederle FA, Kyriakides TC, Stroupe KT, Freischlag JA, Padberg Jr FT, Matsumura JS, et al. Open versus endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2019;**380**:2126–35.
8 Wanhainen A, Verzini F, van Herzeele I, 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.
9 Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA, et al. The society for vascular surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg* 2018;**67**:2–77.
10 AbuRahma AF, Yacoub M, Hass SM, AbuRahma J, Mousa AY, Dean LS, et al. Compliance of postendovascular aortic aneurysm repair imaging surveillance. *J Vasc Surg* 2016;**63**:589–95.
11 De Mestral C, Croxford R, Eisenberg N, Roche-Nagle G. The impact of compliance with imaging follow-up on mortality after endovascular abdominal aortic aneurysm repair: a population based cohort study. *Eur J Vasc Endovasc Surg* 2017;**54**:315–23.
12 Godfrey AD, Morbi AH, Nordon IM. Patient compliance with surveillance following elective endovascular aneurysm repair. *Cardiovasc Intervent Radiol* 2015;**38**:1130–6.
13 Wu CY, Chen H, Gallagher KA, Elisaon JL, Rectenwald JE, Coleman DM. Predictors of compliance with surveillance after endovascular aneurysm repair and comparative survival outcomes. *J Vasc Surg* 2015;**62**:27–35.
14 Bastos Gonçalves F, van de Luijtgaarden KM, Hoeks SE, Hendriks JM, Ten Raa S, Rouwet EV, et al. Adequate seal and no

endoleak on the first computed tomography angiography as criteria for no additional imaging up to 5 years after endovascular aneurysm repair. *J Vasc Surg* 2013;**57**:1503–11.
15 Garg T, Baker LC, Mell MW. Postoperative surveillance and long-term outcomes after endovascular aneurysm repair among Medicare Beneficiaries. *JAMA Surg* 2015;**150**:957–63.
16 Baderkhan H, Haller O, Wanhainen, Björck M, Mani Kl. Follow-up after endovascular aortic aneurysm repair can be stratified based on first postoperative imaging. *Br J Surg* 2018;**105**:709–18.
17 Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;**370**:1453–7.
18 Geraedts ACM, de Mik S, Ubbink DT, Koelemay M, Balm R. Postoperative surveillance and long-term outcome after endovascular aortic aneurysm repair in the Netherlands: study protocol for the retrospective ODYSSEUS study. *BMJ Open* 2020;**10**:e033584.
19 Castor EDC. *Castor electronic data capture*. 2019. Available at: https://castoredc.com. [Accessed 21 April 2020].
20 Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, et al. Reporting standards for endovascular aortic aneurysm repair. *J Vasc Surg* 2002;**35**:1048–60.
21 Lyons OT, Baguneid M, Barwick TD, Bell RE, Foster N, Homer-Vanniasinkam S, et al. Diagnosis of aortic graft infection: a case definition by the management of aortic graft infection collaboration (MAGIC). *Eur J Vasc Endovasc Surg* 2016;**52**:758–63.
22 Grima MJ, Karthikesalingam A, Holt PJ, EVAR-SCREEN collaborators. Multicentre post-EVAR surveillance evaluation study (EVAR-SCREEN). *Eur J Vasc Endovasc Surg* 2019;**57**:521–6.
23 Väärämäki S, Salenius JP, Pimenoff G, Uurto I, Suominen V. Systematic long-term follow up after endovascular abdominal aortic aneurysm repair with the Zenith stent graft. *Eur J Vasc Endovasc Surg* 2019;**58**:182–8.
24 Schanzer A, Messina LM, Ghosh K, Simons JP, Robinson 3rd WP, Aiello FA, et al. Follow-up compliance after endovascular abdominal aortic aneurysm repair in Medicare beneficiaries. *J Vasc Surg* 2015;**61**:16–22.
25 Lee R, Jones A, Woodgate F, Bellamkonda K, Killough N, Fulford-Smith L, et al. The experience of patients during the clinical management pathway of abdominal aortic aneurysms at a NHS trust. *J Patient Exp* 2017;**4**:202–9.
26 Singh AA, Benaragama JS, 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.