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## **Outcomes of Preventive embolization of the inferior mesenteric artery during EVAR**

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## **ABSTRACT**

**Purpose:** To evaluate the impact of preemptive inferior mesenteric artery (IMA) embolization on outcomes of endovascular abdominal aortic aneurysm repair (EVAR).

**Materials and Methods:** From Jan 2015 to July 2017, all patients undergoing elective EVAR or Fenestrated EVAR (F-EVAR) for asymptomatic AAA in a single tertiary hospital were retrospectively included. Three groups of patients were defined: patients with a chronically occluded IMA (group 1), those with a patent IMA who underwent embolization during EVAR/F-EVAR (group 2) and those with a patent IMA that did not undergo embolization during EVAR/F-EVAR (group 3). Preoperative aortic morphology, demographics and procedural details were recorded. Aneurysm growth ( $\geq 5\text{mm}$ ), reintervention and overall mortality rates were analysed using proportional hazard multivariate modelling. Propensity scores were constructed and inverse probability weighting applied to a new set of multivariate analyses to perform a sensitivity analysis.

**Results:** 266 patients (male, 95% (n=249) with a median age of 70 [65-77] were included, with FEVAR procedures comprising 87 (32.7%) of the interventions. There were 72 patients in group 1 and 52 and 142 in groups 2 and 3 respectively. Changes in aneurysmal sac size did not differ between groups, nor did overall survival or reintervention rates at 24 months. IMA embolization was not identified as an independently protective factor for aneurysm growth during follow-up (RR=2.82 [0.96; 8.28], p=0.060), while accessory renal arteries (RR= 5.07/mm [1.72-14.96] (p=0.003)) and a larger preoperative aneurysm diameter (RR= 1.09/mm [1.03; 1.15]; p=.004) were independent risk factors for sac enlargement.

**Conclusion:** Preventive embolization of the IMA during EVAR or FEVAR did not promote aneurysm sac shrinking or decrease the reintervention rate at 2-year follow-up.

## **INTRODUCTION**

Type II endoleaks (T2EL) occur in up to 45% of patients after endovascular aortic repair (EVAR) (1), and may account for up to 40% of aortic sac enlargement during follow-up (2,3). Very rarely cases of aortic rupture can be directly attributed to T2EL, but more frequently it is caused by the loss of proximal or distal sealing zones caused by rapid sac expansion. In some cases, other types of occult endoleak in addition to T2EL could contribute to aneurysmal sac expansion (4).

It has been suggested that preventive embolization of the inferior mesenteric artery (IMA) could prevent T2EL and therefore decrease the rate of long-term reintervention rate following EVAR (3,5).

A recently published meta-analysis (6) and randomized controlled trial (7) (RCT) suggested potential benefits of preventive IMA embolization during EVAR to lower incidence of T2EL and to achieve aneurysm sac shrinkage, and another RCT is underway (8). Nevertheless, real-world observational studies are valuable as confirmatory data.

This study aimed to evaluate the efficacy of selective preventive IMA embolization in reducing the occurrence of T2EL and therefore aneurysmal sac expansion size after EVAR in a high-volume aortic centre.

## **METHODS**

This study was approved by the Institutional Review Board of our institution.

From January 2015 to July 2017, all elective patients that received custom-made fenestrated endografts for juxta/pararenal aortic aneurysms (F-EVAR) or off-the-shelf infrarenal endografts (EVAR) in a single tertiary hospital were retrospectively included. Patients with isolated iliac aneurysms, previous open aortic repair, previous EVAR with fenestrated endograft proximal extension and emergency cases were excluded. Preoperative demographics data, clinical features and drug therapies were collected. Morphological data pertaining to aorta and iliac arteries were collected by a single endovascular operator experienced ( $\geq 15$  years) in endograft aortic planning on a dedicated 3D-workstation (Aquarius iNtuition Viewer imaging workstation, TeraRecon) from the preoperative computed tomography angiogram (CTA, with a maximum of 3mm-slice thickness). The analysis included lengths, diameters, angulations and the quality of the aortic wall (thrombus and calcification). All measures were performed after curvilinear reconstruction of the artery considered (Figure 1). The diameter and patency of the aortic branch arteries (accessory renal(s), IMA, lumbar(s)) were also reported (Appendix A).

All endovascular aortic repairs and adjunct procedures were performed by vascular surgeons that performed more than 100 EVAR cases each year. The repairs were conducted in accordance with the manufacturer's instructions for use criteria. The anatomical requirements detailed in the ESVS guidelines were also followed (9), including suitable proximal neck anatomy ( $\geq 15$  mm length and no major suprarenal or infrarenal angulation) with no hostile conditions such as severe calcification/thrombus and/or significant diameters' variations (i.e  $> 4$  mm) (10). All bifurcated endografts implanted were Zenith Flex stent graft or Zenith LP stent graft (Cook Medical, Bloomington, Ind) and all fenestrated endografts were Zenith Fenestrated AAA Endovascular Graft (Cook Medical, Bloomington, Ind).

Three groups of patients were compared:

- Group 1: Patients with patent IMA undergoing preventive embolization during EVAR/F-EVAR
- Group 2: Patients with patent IMA not undergoing preventive embolization during EVAR/F-EVAR
- Group 3: Patients with a chronically occluded IMA

Procedural details were collected from the patients' medical records. Technical success was defined according to the SVS reporting standards (11). Patients with patent IMA underwent embolization at the beginning of the endovascular aortic repair procedure after considering its anatomical configuration (take-off angle, patency and diameter) but procedural details were left to the discretion of the operator. A proximal IMA diameter  $\geq 3$ mm in the absence of ostial calcifications or significant stenoses were the indications used to perform the preventive embolization. All preventive IMA embolizations were performed in an antegrade fashion. A 5 or 4 Fr angiographic catheter was placed in the IMA ostium, then iodinate contrast injection was performed under a fluoroscopy to ensure its proper position. The IMA embolization was performed either with coils (Tornado Embolization Coil, Cook Medical or Concerto, Medtronic) or plugs (AMPLATZER Vascular Plug, AbbottVascular) in which case a 6Fr sheath had to be introduced into the IMA.

Patients provided informed consent to surgery and for being involved in such a study.

The primary endpoint was aneurysmal sac enlargement-free survival, which was defined as the time from the date of the index procedure until the earliest date on which a significant ( $\geq 5$ mm) sac enlargement was observed. The change in sac size was expressed as the absolute difference between the maximum pre-operative aneurysm diameter and the latest available diameter on CTA (If no CTA was available, the aortic diameter was collected from an unenhanced CT).

The variable was then dichotomised as stability/regression versus or enlargement, using a cut-off value of 5 millimetres ( $\geq 5$ mm) to define a significant increase in the aortic diameter.

To define all-cause reintervention the pre-operative aortic aneurysmal diameter before the reintervention was recorded to assess the primary outcome, and the patient was censored at the time of reintervention.

Secondary outcomes included overall survival, aortic-related and all-cause reinterventions and endoleak incidence. Where multiple mechanisms of endoleak were reported (Type 1 to 3), only the one considered to pose the highest risk (i.e, type 1 > type 3 > type 2) to sac stability was accounted for in the statistical analysis.

### ***Statistical analyses***

Statistical analyses were performed using SAS<sup>®</sup> software (SAS Institute version 9.4, Cary, NC, USA).

Continuous variables were quoted as the median (interquartile range (IQR)) and categorical variables were presented as absolute numbers (percentage).

Comparison of patient demographics, pre-operative morphological and intra-operative data between the three groups (i.e. chronic occluded IMA, patent IMA without preventive embolization and patent IMA with preventive embolization), were performed using Kruskal-Wallis test and Dunn's multiple comparison risk adjustment when necessary. The Chi-square or Fisher's tests were used for categorical covariates, according to theoretical groups' numbers.

Event-free survival curves were estimated by the Kaplan-Meier method and compared with the log-rank test, using Bonferroni correction for multiple comparisons adjustment. Median follow-up time was estimated with the reverse Kaplan-Meier method (12).

Univariate Cox analyses were performed to identify independent predictors of event (for all three main outcomes: sac enlargement, early mortality, and reintervention). The log-linearity assumption for continuous variables and the proportional hazard assumption were tested by Kolmogorov-type supremum tests as implemented in the PROC PHREG in SAS<sup>®</sup> (13). In case of violation of the former assumption, the continuous variable was dichotomised, the cut-off value being visually established and maximising the Akaike Information Criterion; in case of violation of the latter assumption, a

piecewise model was used to model the hazard ratio as a step function of time. Since the main objective of this article was to study the predictive value of the IMA status, interactions between the IMA status and the other covariates were systematically tested. In case of significant interaction, the main effects were maintained in the model even if not significant. Multivariate Cox models were built by including all relevant covariates on univariate analyses (defined as  $p < 0.20$ ) and performing a backward selection procedure with the IMA status being consistently forced into the model. All tests were two-sided, and  $P$ -values  $< .05$  were considered as significant.

As a sensitivity analysis, propensity scores were constructed and inverse probability weighting was assigned to account for imbalances between IMA status groups (i.e. chronic occluded, patent without preventive embolization, patent with preventive embolization IMA) (14). We used the TWANG macro for SAS® that allow propensity scores construction among  $> 2$  groups (15). The scores were tested for adequacy of overlap by plotting the propensity score distributions between the three groups. The propensity scores were used to create inverse probability weights (being the inverse of the probability to belong to a given IMA status group). After weighting, the standardised differences were all  $< 10\%$  (the usual threshold) for each covariate, indicating minimal imbalance and validating the procedure. Weighted Kaplan-Meier estimates and proportional hazard models were then calculated and compared to unweighted analyses. The combination of a design-based method of bias reduction (propensity score matching or weighting) with regression adjustment (Cox models) with the objective of obtaining a greater degree of bias reduction or a more robust estimate of treatment effect is called “doubly robust estimations” and is thought to achieve effect estimates superior to models based on either one of the approaches (16, 17).



## **RESULTS**

### *Baseline characteristics*

During the study period, 266 patients (95% of male, median age 70.3 [65.1-77.4]) were included: 52 in group 1 (patent IMA embolised during EVAR/F-EVAR), 142 in group 2 (patent IMA not embolised during EVAR/F-EVAR) and 72 in group 3 (chronically occluded IMA at the time of EVAR/F-EVAR). Twenty-three patients were excluded for missing data (the majority due to unavailable pre-operative CTA).

The three groups of patients exhibited similar preoperative features except for previous colonic surgery that was more frequent in the third group. Medications were also comparable between groups (Table 1).

Details of the preoperative morphological data of the 3 groups are reported in Table 1. Of note, there were significantly less juxta and para-renal aortic aneurysms that underwent preventive embolization of the IMA compared to infra-renal aneurysms ( $p=0.02$ ). The initial aortic diameter was significantly larger in group 3 ( $p<0.001$ ). The IMA diameter was significantly higher in the group where this was embolised ( $p<0.001$ ). Finally, the number of patent lumbar arteries depicted on the pre-operative CTA in group 3 was significantly lower compared to the 2 other groups ( $p<0.01$ ).

There was no significant difference between the three groups regarding intra-operative data except for the type of aortic endovascular repairs performed (Table 1).

All attempts to embolize the IMA were successful.

### *Primary outcome - Aneurysm sac enlargement*

Regarding the main outcome of the study, only a limited number of events occurred; 6 (11.5%) 9 (6.3%) and 1 (1.4%) in groups 1, 2 and 3, respectively ( $p=0.053$ ). The median time of follow-up was 14 months [IQR 12-16].

Weighted and unweighted univariable and multivariable associations with aortic sac enlargement are detailed in Table 2.

The relative risks (RR) [95% confidence intervals] of sac enlargement during follow-up for patients in group 1 was 9.88 [1.03; 94.81] ( $p=0.047$ ) when compared to patients in group 2 and 27.81 [2.44; 316.88] ( $p=0.007$ ) when compared to patients in group 3. Conversely, the RR comparing groups with a patent IMA and preventive embolization (group 1) vs. no embolization (group 2) was not significant (RR=2.82 [0.96; 8.28],  $p=0.060$ ).

The multivariate analysis also indicated that the initial diameter of the aneurysm and presence of an accessory renal artery below the proximal sealing zone were independent risk factors for sac enlargement during follow-up with RR respectively equal to 1.09 per millimetre ([1.03; 1.15];  $p=.004$  and RR= 5.07 per millimetre [1.72-14.96] ( $p=0.003$ ).

Aneurysmal sac enlargement remained associated with the IMA status ( $p=0.008$ ) and initial aortic aneurysm diameter ( $p<0.001$ ) when the sensitivity analysis was performed confirming the accuracy of the primary analysis.

No statistical association between the type of embolization devices implanted the IMA origin and the changes in aneurysmal sac size was demonstrated.

No significant sac enlargement was reported within the first 30 postoperative days in any of the 3 groups. Unadjusted Kaplan-Meier survival curves did not evidence significant differences in the sac enlargement rates between the three groups ( $p=0.051$ ) during follow-up, and due to the limited number of events, no median survival time could be estimated. The Kaplan-Meier two-year freedom from aortic sac enlargement was 95.0% [69.5-99.3] in group 2 and 92.0% [83.4-96.3] in group 3 (Figure 2, Table 3). However, when applying the inverse probability weighting in sensitivity analyses, the weighted log-rank test reached the significance cut-off ( $p=0.048$ ) (Figure 3).

#### *All-cause reintervention*

Regarding all-cause reintervention, 32 events occurred during follow-up, with 7 (13.5%), 20 (14.2%) and 5 (7.1%) respectively in groups 1, 2 and 3 ( $p=0.321$ ) (Table 4). No difference was observed between the groups regarding the freedom-from-reintervention survival rates in unadjusted analyses ( $p=0.344$ ). Corresponding 30-days rates were 98.0% [86.9; 99.7], 98.5% [94.3; 99.6], 97.1% [88.7; 99.3], and were estimated to be 85.0% [61.1; 94.8], 83.1% [74.9; 89.2] and 93.8% [80.4; 98.1], at 24 months, respectively in groups 1, 2 and 3 (Figure 4).

No significant change was observed by the sensitivity analyses when applying the inverse probability weighting (weighted log-rank test  $p=0.916$ ) (Figure 5).

In a multivariate analysis (Table 5), the IMA status was not significantly associated with reintervention ( $p=0.645$ ), while gender (female vs. male) and the presence of renal accessory artery appeared to be independent risk factors of reintervention (respective RRs of 4.12 [1.20; 14.17],  $p=0.025$  and 2.45 [1.17; 5.11],  $p=0.017$ ). An increasing rate of aneurysm sac thrombus was significantly associated with a decreased reintervention risk (RR 0.92 [0.86; 0.99],  $p=0.026$ ).

The inverse probability weighting exhibited limited changes in the multivariate analysis outputs, as the IMA group was still not associated with reintervention ( $p=0.861$ ). Of note, in weighted analyses, a larger diameter of the patent IMA in those with and no embolization (group 2) seemed to be protective against reintervention (RR per one-millimeter increment: 0.66 [0.44; 0.97],  $p=0.006$ ). The presence of a renal accessory artery and the thrombus importance remained significant risk factors of reintervention ( $p<0.001$  and  $p=0.045$ , respectively), whereas gender did not ( $p=0.078$ ).

### *Overall survival*

Regarding all-cause mortality, 18 patients died during follow-up, 4 (7.7%), 7 (4.9%) and 7 (9.7%) in groups 1, 2 and 3, respectively ( $p=0.356$ ). There was no significant difference between the 3 groups (all-cause and aortic-related) in unadjusted analyses ( $p=0.548$ ). The 30-days survival rates were 98.1% [87.1; 99.7], 96.4% [91.6; 98.5] and 98.6% [90.4; 99.8], while the overall survival at 24 months was estimated at 92.3% [87.8-97.3], 94.2% [87.8; 97.3] and 88.8% [76.0; 95.0] respectively in groups 1, 2 and 3 (Supplementary Figure 1). The differences in overall survival remained non-significant when applying the inverse probability weighting, although there was a tendency toward decreased survival in the first group (weighted log-rank test,  $p=0.088$ ) (Supplementary Figure 2). In a multivariate analysis, the IMA status group was not significantly associated with mortality ( $p=0.787$ ). Conversely, the type of procedure and advancing age appeared to be independent risk factors of overall mortality (RR, F-EVAR vs. EVAR: 3.73 [1.36; 10.26],  $p=0.011$  and per one-year increment 1.18 [1.06; 1.31],  $p=0.002$ , respectively) (Supplementary Table 1).

When applying inverse probability weighting to correct for demographic and aortic morphological imbalances between the three groups, the IMA status did not affect the overall mortality ( $p=0.126$ ), whereas the above-mentioned predictors did (type of procedure and an older age, respectively  $p=0.004$  and  $p<0.001$ ) (Supplementary Table 1).

## **DISCUSSION**

In this study IMA embolization during EVAR or F-EVAR failed to demonstrate any protective effect against aortic sac expansion at mid-term follow-up after multivariate analysis. There was an unexpected non-significant trend toward sac enlargement (RR=2.7; [0.9-8.1]; p=0.08) during follow-up in patients with initial patent IMA with embolization compared to those without.

Several retrospective cohorts studies have previously been performed to evaluate the impact of preventive IMA embolization on type II EL occurrence or reintervention rates after EVAR/F-EVAR (5, 18-21). In all those studies preventive IMA embolization appeared to decrease T2EL incidence and subsequent reintervention rate, but the aneurysm sac diameter was not directly independently analysed and followed up. In our study, the “sac enlargement  $\geq 5\text{mm}$ ” criterion was chosen as the primary endpoint since it was reproducible and is a broadly accepted cut-off for expansion.

Comprehensive evaluation of the effect of IMA embolization on T2EL incidence or reintervention rates is challenging, since the precise mechanism of EL often remains difficult to determine even with sensitive imaging techniques (22,23) and reintervention relies on physicians’ subjectivity (4). Of note the reported rates of T2EL in our cohort were similar during follow-up in groups 2 and 3.

In our cohort, preventive IMA embolization tended to promote sac enlargement, with 6 patients in the selective IMA embolization group exhibiting sac enlargement during follow-up. Reasons for sac enlargement were mostly due to a type 2 EL from lumbar arteries that require secondary embolization (in 5 out of 6 patients). This observation would suggest potential benefits from preventive embolization of lumbar arteries and/or other accessory renal arteries in conjunction of IMA embolization. It can be hypothesised that embolizing the IMA may compromise the “outflow” of a low pressure endoleak. This strategy was studied by Aoki and colleagues in 2017 (24) who embolised any collateral vessel with a diameter  $\geq 2\text{mm}$ . The post-operative CTA exhibited significantly

less T2EL in 24/56 patients that underwent preventive embolization (4.2% vs. 58.9% respectively ( $p < .0001$ ), but unfortunately no further follow-up data on sac enlargement was published. In our multivariate analysis, the presence of an accessory renal artery on the preoperative CTA was identified as an independent risk factor for sac enlargement (RR= 5.07 per millimetre [1.72-14.96] ( $p = 0.003$ )) whether the accessory renal artery was embolised or not during the index procedure.

We considered that embolization of small (<3mm) accessory renal arteries was acceptable, since it is generally not possible to preserve them during either open or endovascular repair; Malgor (25) and Greenberg (26) suggest that preventive embolization of accessory renal arteries along the proximal neck or in the aneurysm may reduce postoperative endoleak occurrence with no significant decline in renal function.

During the study period preventive embolization of IMA during EVAR/F-EVAR was not associated with any obvious additional procedural complications and no colonic ischemia, compromise to the digestive system or any other complications were reported during follow-up. In addition, no significant difference between the three groups with regards to volume of contrast media injected, radiation dose exposure, fluoroscopy time, or length of procedure was observed.

Another strategy that has been described to prevent T2EL is preemptive non selective sac embolization (27,28), and Fabre and colleagues (29) reported the use of this strategy in the setting of an RCT.

A meta-analysis published in 2020 (6) evaluated the impact of preventive IMA embolization. The authors highlighted a slight but significant increase in sac enlargement rate when aortic side branches (not limited to the IMA in most studies) were preventively embolized during EVAR (OR, 0.54; 95% CI, 0.29-1). Significant sac enlargement after EVAR was the primary outcome chosen. A further RCT (7) enrolled 106 patients considered at high risk of persistent T2EL, randomizing patients to receive concomitant IMA embolization or standard EVAR. Aortic sac shrinkage was only a secondary endpoint, and as a consequence the study was not powered to properly evaluate this. At a

mean follow-up period of 22 months, the IMA embolization appeared to significantly prevent both T2EL and sac enlargement.

Unfortunately, time to event data were not reported in their study, and would have been helpful to know if the 14 months follow-up of our study would be sufficient to depict the sac growth after EVAR. Another recent study entitled the “IMA Clarify project” is investigating if IMA embolization reduces the reintervention rate after EVAR (8). With these and other studies in the process of recruiting the evidence and guidelines regarding the management of the IMA during EVAR should evolve in the upcoming years, but longer term follow-up is mandatory.

One weakness of our present work was selection bias due to the fact that only accessible IMAs (the larger and the less diseased ones) were embolised. Although the preoperative anatomical appearance of the IMA and its configurations including the diameter of the IMA at its origin were the main inclusion criteria, this was ultimately left at the discretion of the operating physician.

Similarly, the patients in the second group where preventive embolization IMA was intended but eventually failed were not captured in the retrospective data collection process; these patients have been analysed and included in the second group of patients with a patent IMA without preventive embolization.

Diameters and lengths from the CTA were collected by a single operator without blinded control nor inter-observer agreement. The lack of validation of those measurements and potential measurement bias are limitations of the study, but the event: “aortic sac enlargement” was defined in the present study as a growth in the maximal diameter  $\geq 5$  mm which is unequivocally depicted by a well-trained operator.

Another limitation of our study was the median time of follow-up of 14 months of our cohort as most reinterventions due to endoleaks after EVAR occur after the 1<sup>st</sup> year (4). Nevertheless, a 14-month follow-up period seems adequate to properly evaluate the changes in aneurysmal sac size after the initial EVAR as some authors suggest that endoleaks associated with sac enlargement are usually

identified after the 1<sup>st</sup> year (30). A longer follow-up may have shown a more definitive trend relating to IMA embolization on the changes in aneurysmal sac size.



While preventive embolization of the IMA prior to endovascular aortic abdominal exclusion does not seem to increase the difficulty of the procedure or the risk of colonic ischemia, it also does not demonstrate any survival benefits or reduction in reintervention rates or sac enlargement. Results limited to this cohort even suggested that preventive IMA may increase the risk of sac enlargement during follow-up. Further prospective studies or multicentre registries would allow further evaluation of the impact of this technique on the occurrence of T2EL and subsequent changes in aneurysmal sac size.

## REFERENCES

1. Ultee KHJ, Büttner S, Huurman R, Bastos Gonçalves F, Hoeks SE, Bramer WM, et al. Editor's Choice - Systematic Review and Meta-Analysis of the Outcome of Treatment for Type II Endoleak Following Endovascular Aneurysm Repair. *Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg*. 2018;56:794-807
2. Avgerinos ED, Chaer RA, Makaroun MS. Type II endoleaks. *J Vasc Surg*. 2014;60:1386–91.
3. Yu HYH, Lindström D, A Wanhainen A, Tegler G, Hassan B, Mani K. Systematic Review and Meta-Analysis on Prophylactic Aortic Side Branch Embolization to Prevent Type II Endoleaks. *J Vasc Surg* 2020; S0741-5214(20)31236-2
4. Dijkstra ML, Zeebregts CJ, Verhagen HJM, Teijink JAW, Power AH, Bockler D, et al. Incidence, natural course, and outcome of type II endoleaks in infrarenal endovascular aneurysm repair based on the ENGAGE registry data. *J Vasc Surg* 2020; 71:780-789
5. Manunga JM, Cragg A, Garberich R, Urbach JA, Skeik N, Alexander J, et al. Preoperative Inferior Mesenteric Artery Embolisation: A Valid Method to Reduce the Rate of Type II Endoleak after EVAR? *Ann Vasc Surg*. 2017;39:40–7.
6. Yu HYH, Lindström D, Wanhainen A, Tegler G, Hassan B, Mani K. Systematic review and meta-analysis of prophylactic aortic side branch embolization to prevent type II endoleaks. *J Vasc Surg*. 2020;72:1783-1792.
7. Samura M, Morikage N, Otsuka R, Mizoguchi T, Takeuchi Y, Nagase T, et al. Endovascular Aneurysm Repair With Inferior Mesenteric Artery Embolization for Preventing Type II Endoleak: A Prospective Randomized Controlled Trial. *Ann Surg*. 2020;271:238-44.
8. Ichihashi S, Takahara M, Fujimura N, Nagatomi S, Iwakoshi S, Bolstad F, et al. Multicentre randomised controlled trial to evaluate the efficacy of pre-emptive inferior mesenteric artery embolisation during endovascular aortic aneurysm repair on aneurysm sac change: protocol of Clarify IMA study. *BMJ Open*. 2020;10:e031758.
9. Wanhainen A, Verzini F, Van Herzele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg*. 2019;57:8-93.
10. Greenberg RK, Sternbergh WC, Makaroun M, Ohki T, Chuter T, Bharadwaj P, et al. Intermediate results of a United States multicenter trial of fenestrated endograft repair for juxtarenal abdominal aortic aneurysms. *J Vasc Surg*. 2009;50:730-737.
11. 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.
12. Clark TG, Bradburn MJ, Love SB, Altman DG. Survival analysis part I: basic concepts and first analyses. *Br J Cancer*. 21 juill 2003;89:232-8
13. Lin DY, Wei L-J, Ying Z. Checking the Cox model with cumulative sums of martingale-based residuals. *Biometrika*. 1993;80:557-72.
14. Thabane L, Mbuagbaw L, Zhang S, Samaan Z, Marcucci M, Ye C, et al. A tutorial on sensitivity analyses in clinical trials: the what, why, when and how. *BMC Med Res Methodol*. 2013;13:92
15. Beth Ann Griffin, Greg Ridgeway, Andrew R. Morral, Lane F. Burgette, Craig Martin, Daniel Almirall, Rajeev Ramchand, Lisa H. Jaycox, Daniel F. McCaffrey. Toolkit for Weighting and Analysis of Non-

equivalent Groups (TWANG) Website. Santa Monica, CA: RAND Corporation, 2014.  
<http://www.rand.org/statistics/twang>

16. Joffe MM, Ten Have TR, Feldman HI, Kimmel SE. Model selection, confounder control, and marginal structural models: review and new applications. *Am Stat.* 2004;58:272-9.
17. Austin PC. Advances in propensity score analysis. *Stat Methods Med Res.* 2020;29:641-3.
18. Axelrod DJ, Lookstein RA, Guller J, Nowakowski FS, Ellozy S, Carroccio A, et al. Inferior Mesenteric Artery Embolisation before Endovascular Aneurysm Repair: Technique and Initial Results. *J Vasc Interv Radiol.* 2004;15:1263–7.
19. Nevala T, Biancari F, Manninen H, Matsi P, Mäkinen K, Ylönen K, et al. Inferior mesenteric artery embolisation before endovascular repair of an abdominal aortic aneurysm: effect on type II endoleak and aneurysm shrinkage. *J Vasc Interv Radiol.* 2010;21:181–5.
20. Ward TJ, Cohen S, Fischman AM, Kim E, Nowakowski FS, Ellozy SH, et al. Preoperative inferior mesenteric artery embolisation before endovascular aneurysm repair: decreased incidence of type II endoleak and aneurysm sac enlargement with 24-month follow-up. *J Vasc Interv Radiol.* 2013;24:49–55.
21. Burbelko M, Kalinowski M, Heverhagen JT, Piechowiak E, Kiessling A, Figiel J, et al. Prevention of type II endoleak using the AMPLATZER vascular plug before endovascular aneurysm repair. *Eur J Vasc Endovasc Surg.* 2014;47:28–36.
22. Martin SS, Wichmann JL, Weyer H, Scholtz JE, Leithner D, Spandorfer A, et al. Endoleaks after endovascular aortic aneurysm repair: Improved detection with noise-optimized virtual monoenergetic dual-energy CT. *Eur J Radiol.* 2017;94:125-132
23. Johnsen L, Hisdal J, Jonung T, Braaten A, Pedersen G. Contrast-enhanced Ultrasound Detects Type II Endoleaks During Follow-Up for Endovascular Aneurysm Repair. *J Vasc Surg* 2020; S0741-5214(20)30292-5.
24. Aoki A, Maruta K, Hosaka N, Omoto T, Masuda T, Gokan T. Evaluation and Coil Embolisation of the Aortic Side Branches for Prevention of Type II Endoleak after Endovascular Repair of Abdominal Aortic Aneurysm. *Ann Vasc Dis.* 2017;10:351–8.
25. Malgor RD, Oderich GS, Vrtiska TJ, Kalra M, Duncan AA, Gloviczki P, et al. A case-control study of intentional occlusion of accessory renal arteries during endovascular aortic aneurysm repair. *J Vasc Surg.* 2013;58:1467–75.
26. Greenberg JI, Dorsey C, Dalman RL, Lee JT, Harris EJ, Hernandez-Boussard T, et al. Long-term results after accessory renal artery coverage during endovascular aortic aneurysm repair. *J Vasc Surg.* 2012;56:291–6.
27. Fabre D, Fadel E, Brenot P, Hamdi S, Gomez Caro A, Mussot S, et al. Type II endoleak prevention with coil embolization during endovascular aneurysm repair in high-risk patients. *J Vasc Surg.* 2015;62:1–7
28. Mascoli C, Freyrie A, Gargiulo M, Gallitto E, Pini R, Faggioli G, et al. Selective Intra-procedural AAA sac Embolization During EVAR Reduces the Rate of Type II Endoleak. *Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg.* 2016;51:632-9
29. Fabre D, Mougin J, Mitilian D, Cochennec F, Garcia Alonso C, Becquemin J-P, et al. Prospective, Randomised Two Centre Trial of Endovascular Repair of Abdominal Aortic Aneurysm With or Without Sac Embolisation. *Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg.* 2021;6:201-9.

30. Zhou W, Blay Jr E, Varu V, Ali S, Jin MQ, Sun L, et al. Outcome and clinical significance of delayed endoleaks after endovascular aneurysm repair. *J Vasc Surg* 2014; 59:915-20

## **Tables/Figures legends**

Appendix A: Preoperative morphological parameters assessed (in mm) on preoperative computed tomography angiography

Table 1: Demographic and pre-operative morphological data of 266 patients undergoing EVAR/F-EVAR stratified by IMA preoperative patency and intraoperative preventive embolization

Table 2: Weighted and unweighted univariable and multivariable associations with aortic sac enlargement  $\geq 5$ mm after EVAR/F-EVAR with or without preemptive IMA embolization

Table 3: Freedom from aortic sac enlargement rate in patients with patent preoperative IMA

Table 4: Follow-up data of 266 patients undergoing EVAR/F-EVAR stratified by IMA preoperative patency and intraoperative preventive embolization

Table 5: Weighted and unweighted univariable and multivariable associations with all-cause reinterventions after EVAR/F-EVAR with or without preemptive IMA embolization

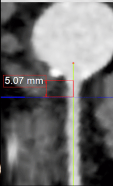
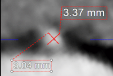
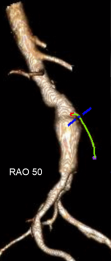
Figure 1: Method to measure the inner mean diameter of the inferior mesenteric artery (IMA) on a 3D workstation (bottom right corner) after curvilinear reconstruction (image on the right), the inner mean diameter is measured 5 mm after the ostium, the 3D volume rendering reconstruction is used to define the best working position used during procedure for IMA catheterization (top right corner)

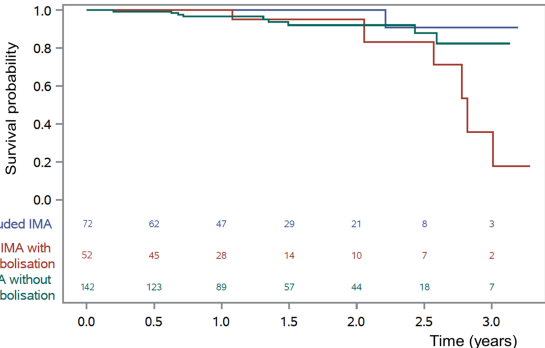
Figure 2: Unweighted Kaplan Meier curves presenting the comparison of freedom from aortic sac enlargement rates between groups

Figure 3: Propensity score weighted Kaplan Meier curves presenting the comparison of freedom from aortic sac enlargement rates between groups

Figure 4: Unweighted Kaplan Meier curves presenting the comparison of freedom from all-cause reintervention rates between groups

Figure 5: Propensity score weighted Kaplan Meier curves presenting the comparison of freedom from all-cause reintervention rates between groups



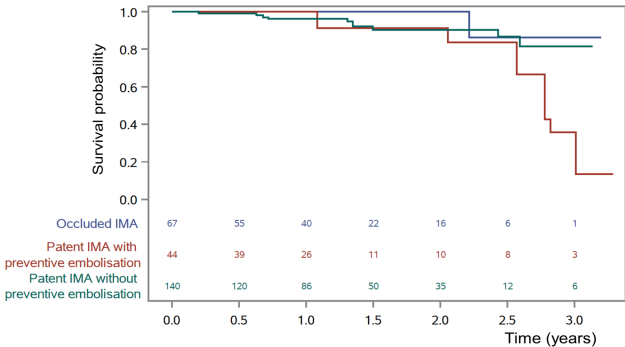


Occluded IMA

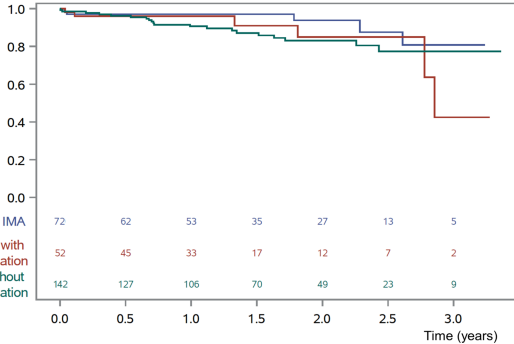
Patent IMA with preventive embolisation

Patent IMA without preventive embolisation





Survival probability



Occluded IMA

Patent IMA with preventive embolisation

Patent IMA without preventive embolisation

Survival probability

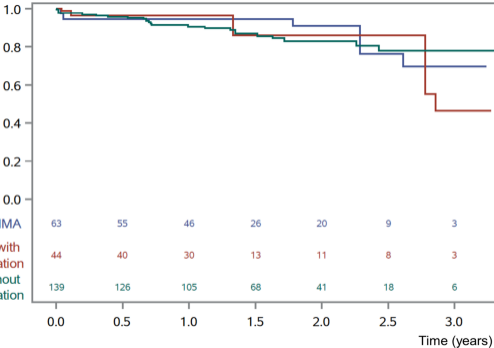


Table 1: Demographic and pre-operative morphological data of 266 patients undergoing EVAR/F-EVAR stratified by IMA preoperative patency and intraoperative preventive embolization

	Total (n=266)	Patent IMA with preventive embolization (n=52)	Patent IMA without preventive embolization (n=142)	Chronic Occluded IMA (n=72)	p-value
<u>Demographics data</u>					
Gender (male)	95.4% (249)	96.0% (48)	94.3% (132)	97.2% (69)	0.62
Age (years)	70.3 (65.1-77.4)	69.8 (66.5-78.0)	70.2 (64.6-77.1)	70.7 (65.6-78.3)	0.67
BMI (kg/m <sup>2</sup> )	27.7 (24.5-30.8)	28.1 (25.9-31.1)	27.3 (24.7-29.9)	27.7 (22.8-30.9)	0.41
Medical history of left colonic surgery	5.3% (14)	1.9% (1)	3.5% (5)	11.1% (8)	0.03
Oral anticoagulation	15.8% (42)	11.5% (6)	16.9% (24)	16.7% (12)	0.64
Anti-Platelet agents	96.2% (256)	94.2% (49)	97.9% (139)	94.4% (68)	0.32
<u>Morphological data</u>					
Initial aneurysm diameter (mm)	55.0 (52.0-60.0)	54.5 (51.0-57.5)	55.0 (52.0-60.0)	59.0 (53.0-66.0)	<0.001
Juxta/Para-renal/Thoracoabdominal aneurysms	31.2% (83)	38.5% (20)	23.9% (34)	40.3% (29)	0.02
IMA diameter (mm)	3.6 (2.9-4.2)	4.3 (4.0-5.0)	3.6 (3-4.2)	2.8 (2.3-3.2)-	<0.001*
Aortic bifurcation diameter (mm)	30.0 (25.0-39.0)	27.0 (22.0-36.0)	32.0 (27.0-40.0)	30.0 (24.5-40.5)	0.01
Number of patent lumbar arteries/patient	5.0 (4.0-6.0)	5.0 (4.0-6.0)	5.0 (4.0-6.0)	4.0 (3.0-5.0)	<0.001
Maximal diameter of the largest patent lumbar artery (mm)	3.0 (2.6-3.4)	3.1 (2.8-3.6)	3.0 (2.7-3.5)	2.9 (2.4-3.3)	0.09
Patient with at least one accessory renal artery	26.3% (69)	33.3% (17)	25.2% (35)	23.6% (17)	0.44
Neck morphology					0.31
- straight	93.5% (244)	98.0% (49)	94.2% (131)	88.9% (64)	
- funnel shape	4.6% (12)	2.0% (1)	3.6% (5)	8.3% (6)	
- reversed funnel shape	1.9% (5)	0.0% (0)	2.2% (3)	2.8% (2)	
Calcified neck	4.2% (11)	0.0 (0)	7.2% (10)	1.4% (1)	0.04
% Thrombus	12 (8.0-17.0)	14 (10.0-18.0)	11 (8.0-16.0)	13 (9.0-19.0)	0.07
<u>Intra-operative data</u>					
Contrast (mL)	76.5 (60.0-110.0)	80 (60.0-120.0)	75.0 (60.0-110.0)	78.0 (60.0-107.5)	0.88
Radiation Dose (Gy.cm <sup>2</sup> )	34.1 (18.4-66.4)	38.8 (20.1-70.1)	33.4 (18.0-61.0)	31.7 (18.9-74.3)	0.91
Time of fluoroscopy (min)	18 (11-42)	24 (15-46)	15 (9-36)	15 (11-45)	0.38
Time of procedure (min)	100.0 (80-173)	120 (80-180)	95.0 (80-150)	120 (75-180)	0.27
F-EVAR procedure	32.7% (87)	40.4% (21)	25.4% (36)	41.7% (30)	0.02
<u>Techniques of IMA embolization</u>					
- Coils		46.2% (24)			
- Plugs		51.9% (27)			
- Both		1.9% (1)			

Technical Success	97.4% (258)	98.1% (51)	97.2% (137)	97.2% (70)	0.94
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IMA= inferior mesenteric artery; BMI =Body Mass Index; Calcified neck = more than 50% of aortic neck was calcified; % Thrombus= ratio between thrombosed aortic surface and total at the level of the IMA's origin; F-EVAR = fenestrated endovascular aneurysm repair.

Continuous data are presented as the median (interquartile range) and categorical data as counts (percentage).

Table 2 Weighted and unweighted univariable and multivariable associations with aortic sac enlargement  $\geq 5$ mm after EVAR/F-EVAR with or without preemptive IMA embolisation

Univariable associations	Unweighted		Weighted		<i>p</i> value
	RR (95% CI)	<i>p</i> value	RR	95% CI	
IMA group		0.086			0.047
2 vs 1	3.89 (0.49-30.77)	0.198	2.98 (0.48-18.56)		0.242
3 vs 1	8.68 (1.04-72.45)	0.046	6.66 (1.17-38.04)		0.033
2 vs 3	0.45 (0.16-1.27)	0.130	0.45 (0.17-1.18)		0.104
Gender (Female vs Male)	3.70 (0.83-16.52)	0.087	6.62 (2.09-21.03)		0.001
Oral anticoagulation	2.31 (0.84-6.37)	0.107	3.30 (1.39-7.79)		0.007
Anti-Platelet Agents	0.17 (0.02-1.43)	0.103	0.08 (0.02-0.35)		0.001
AAA type (Juxta/Para-renal vs Infra-renal)	0.59 (0.17-2.07)	0.408	0.39 (0.10-1.51)		0.172
Patent renal accessory artery	4.88 (1.71-13.94)	0.003	2.78 (1.08-7.14)		0.034
FEVAR	0.71 (0.23-2.19)	0.545	0.39 (0.11-1.40)		0.148
Age (years)*	1.06 (0.99-1.13)	0.095	1.08 (1.02-1.14)		0.010
BMI (kg/m <sup>2</sup> )*	0.997 (0.86-1.15)	0.965	0.99 (0.88-1.11)		0.835
Thrombus (%)*	0.87 (0.78-0.98)	0.019	0.89 (0.80-0.98)		0.023
Initial max aortic sac diameter (mm)*	1.04 (0.99-1.08)	0.147	1.05 (1.00-1.09)		0.034
IMA max diameter (mm)*	1.26 (0.80-1.97)	0.320	1.35 (0.88-2.06)		0.167
Aortic bifurcation diameter (mm)*	0.995 (0.95-1.04)	0.831	1.03 (0.99-1.07)		0.201
Number of patent lumbar artery*	1.07 (0.78-1.45)	0.693	0.87 (0.67-1.14)		0.315
Maximal diameter of the largest patent lumbar artery (mm)*	0.98 (0.56-1.71)	0.941	1.05 (0.63-1.72)		0.861
Medical history of left colonic surgery	1.05 (0.14-8.03)	0.961	0.99 (0.28-3.59)		0.992
<b>Multivariable associations</b>					
Initial max aortic sac diameter (mm)*	1.09 (1.03-1.15)	0.004	1.11 (1.05-1.17)		<0.001
IMA group		0.018			0.008
2 vs 1	9.88 (1.03-94.81)	0.047	7.20 (0.98-52.94)		0.052
3 vs 1	27.81 (2.44-316.88)	0.007	21.50 (2.69-171.86)		0.004
3 vs 2	2.82 (0.96-8.28)	0.060	2.99 (1.04-8.54)		0.041

Group 1 Patent IMA with preventive embolization

Group 2 Patent IMA without preventive embolization

Group 3 Chronic Occluded IMA

\* per-one unit increment

AAA = abdominal aortic aneurysm; BMI = body mass index; CI = confidence intervals; EVAR = endovascular aneurysm repair; F-EVAR = fenestrated endovascular aneurysm repair; IMA = inferior mesenteric artery; RR = risk ratio

Table 3: Freedom from aortic sac enlargement rate in patients with patent preoperative IMA

Follow-up (months)	6	12	24	36*
Patent IMA with preventive embolization				
Survival	100%	100%	95.0%	35.6%
[IC95%]			[69.5-99.3]	[5.5-69.2]
Events	0	0	1	5
Patent IMA without preventive embolization				
Survival	99.2%	96.6%	92.0%	82.3%
[IC 95%]	[94.6-99.9]	[91.3-98.7]	[83.4-96.3]	[62.9-92.2]
Events	1	4	7	9

\*Not enough patients at 36 months to conclude

Table 4: Follow-up data of 266 patients undergoing EVAR/F-EVAR stratified by IMA preoperative patency and intraoperative preventive embolization

	Total (n=266)	Patent IMA with preventive embolization (n=52)	Patent IMA without preventive embolization (n=142)	Chronically Occluded IMA (n=72)	p-value
Aortic Sac Enlargement $\geq 5$ mm at any term	6.0 % (16)	11.5% (6)	6.3% (9)	1.4% (1)	0.05
Patients with EL of any type	27.2% (67)	35.4% (17)	34.1% (45)	7.6% (5)	<0.001
Prominent Endoleak type					<0.001
- No EL	75.2% (200)	65.4% (34)	69.1% (98)	94.4% (68)	
- Type Ia	0.8% (2)	1.9% (1)	0.7% (1)	0.0% (0)	
- Type Ib	0.8% (2)	3.9% (2)	0.0% (0)	0.0% (0)	
- Type II	23.3% (62)	28.9% (15)	30.3% (43)	5.6% (4)	<0.001
Colonic Ischemia	1.9% (5)	3.9% (2)	2.1% (3)	0	0.29
Digestive resection	0.7% (2)	1.9% (1)	0.7% (1)	0	0.47
Reintervention rate	12.2% (32)	13.5% (7)	14.2% (20)	7.1% (5)	0.14
Delay between index procedure and reintervention (months)	15.7 (11.6-25.7)	13.4 (8.7-23.1)	16.2 (11.9-26.7)	18.9 (12.2-26.2)	0.19

IMA = inferior mesenteric artery; EL = endoleak

Continuous data are presented as the median (interquartile range) and categorical data as counts (percentage)



Table 5 Weighted and unweighted univariable and multivariable associations with all-cause reinterventions after EVAR/F-EVAR with or without preemptive IMA embolization

Univariable associations	Unweighted		Weighted	
	RR (95% CI)	<i>p</i> value	RR (95% CI)	<i>p</i> value
IMA group		0.359		0.906
2 vs 1	1.97 (0.74-5.24)	0.177	1.21 (0.51-2.84)	0.667
3 vs 1	2.12 (0.67-6.76)	0.204	1.17 (0.47-2.88)	0.738
2 vs 3	0.93 (0.39-9.86)	0.865	1.03 (0.46-2.35)	0.936
Gender (Female vs Male)	2.95 (0.89-9.86)	0.078	2.24 (0.65)	0.188
Oral anticoagulation	1.67 (0.75-3.74)	0.210	1.23 (0.51)	0.648
AAA type (Juxta/Para-renal vs Infra-renal)	1.51 (0.73-3.11)	0.265	2.11 (1.06-4.21)	0.044
Patent renal accessory artery	2.46 (1.19-5.11)	0.015	2.77 (1.36-5.65)	0.005
FEVAR	1.52 (0.75-3.11)	0.250	1.98 (0.98- 3.92)	0.061
Age (years)*	0.98 (0.93-1.02)	0.279	0.97 (0.93-1.01)	0.172
BMI (kg/m <sup>2</sup> )*	1.03 (0.99-1.08)	0.137	1.04 (1.01-1.08)	0.020
Thrombus (%)*	0.93 (0.86-0.99)	0.029	0.95 (0.89-1.01)	0.125
Initial max aortic sac diameter (mm)*	1.01 0.98-1.04	0.963	0.99 (0.95-1.05)	0.950
IMA max diameter (mm)*	0.94 0.67-1.32)	0.724	0.97 (0.70-1.36)	0.859
Aortic bifurcation diameter (mm)*	1.01 (0.98-1.04)	0.446	1.01 (0.98-1.04)	0.619
Number of patent lumbar artery*	1.15 (0.92-1.44)	0.223	1.05 (0.84-1.32)	0.655
Maximal diameter of the largest patent lumbar artery (mm)*	1.17 (0.75-1.83)	0.487	1.46 (0.96-2.21)	0.076
Medical history of left colonic surgery	0.64 (0.09-4.68)	0.657	0.98 (0.26-3.63)	0.970
Calcified neck	1.54 (0.37-6.46)	0.558		
<b>Multivariable associations</b>				
Gender (Female vs male)	4.12 (1.20-14.17)	0.025	2.30 (0.91-5.78)	0.078
Renal accessory	2.45 (1.17-5.11)	0.017	2.75 (1.79-4.23)	<.0001
Initial max aortic sac diameter (mm)*	0.92 (0.86-0.99)	0.026	0.96 (0.93-0.99)	0.045
IMA group		0.645		0.861
2 vs 1	1.60 (0.60-4.32)	0.351	1.06 (0.63-1.76)	0.839
3 vs 1	1.52 (0.45-5.13)	0.498	0.92 (0.92-0.53)	0.763
3 vs 2	0.95 (0.37-2.43)	0.917	0.87 (0.87-0.53)	0.585

Group 1 Patent IMA with preventive embolization

Group 2 Patent IMA without preventive embolization

Group 3 Chronic Occluded IMA

\* per-one unit increment

AAA = abdominal aortic aneurysm; BMI = body mass index; CI = confidence intervals; EVAR= endovascular aneurysm repair; F-EVAR = fenestrated endovascular aneurysm repair; IMA = inferior mesenteric artery; RR = risk ratio