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# Preemptive AAA Sac embolization - Do we need it and does the embolic agent matter?


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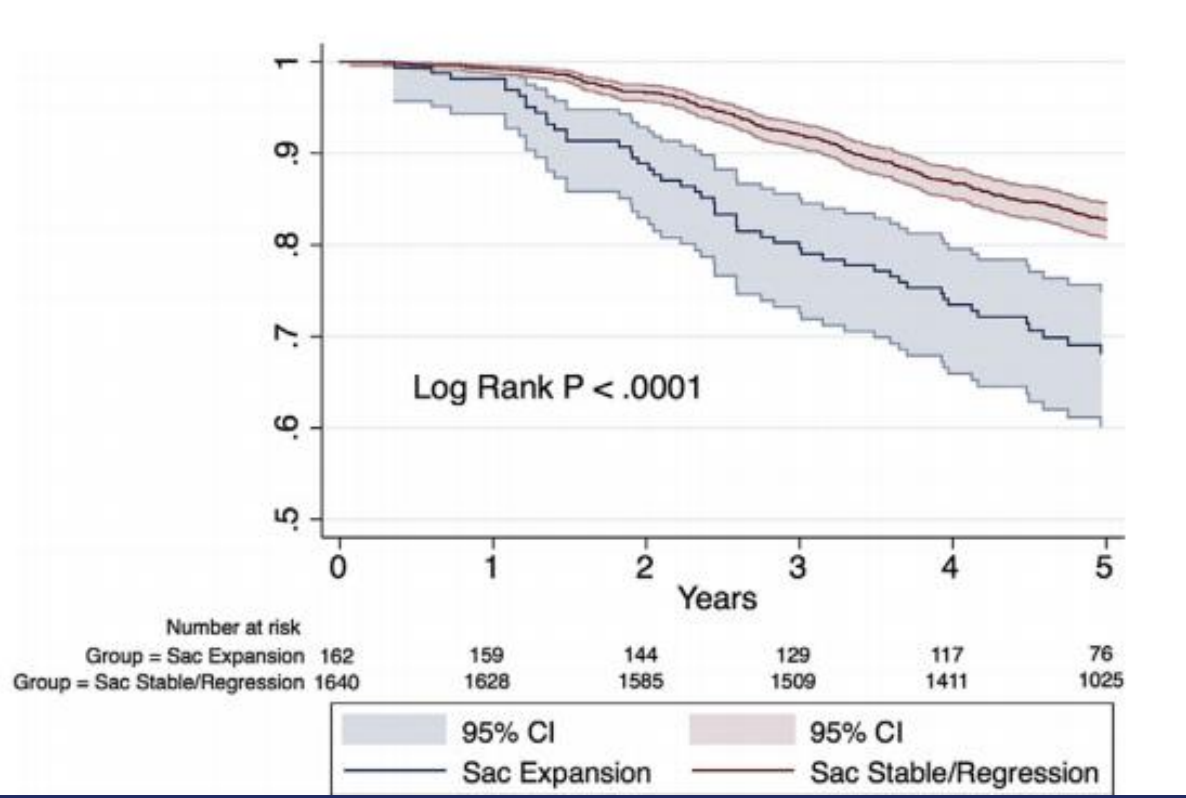
Harvard Medical School


Critical Issues in Aortic Endografting, 22/03/24

# Disclosures

- National Principal Investigator, AAA-SHAPE Pivotal Trial
- Financial: No personal income

# AAA sac failure to regress post-EVAR: a significant unmet need

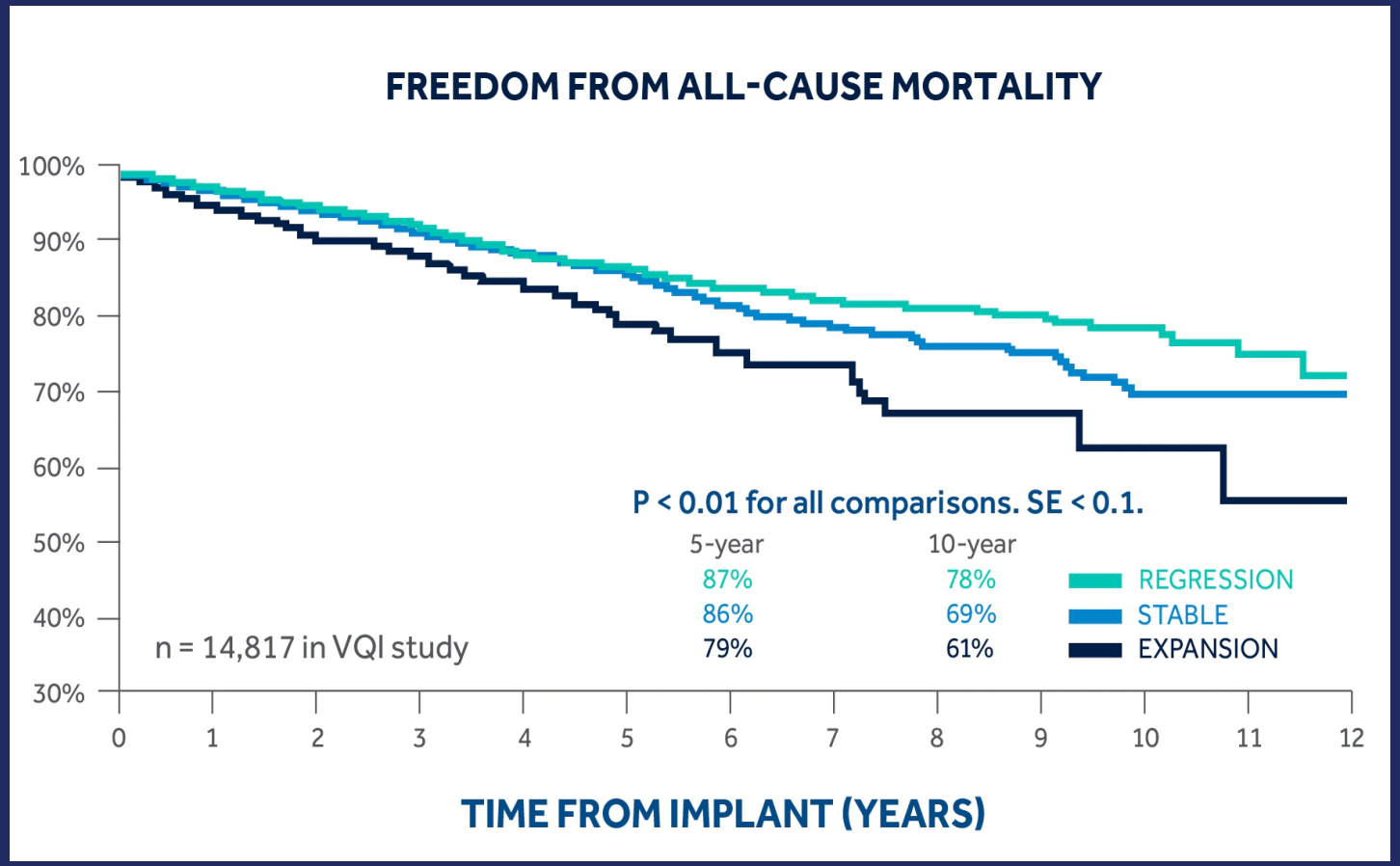



All patients (N=2,437) undergoing EVAR, VSGNE 2003 - 2011

Sac expansion (≥5 mm) at 1 year was independently associated with late mortality, regardless of the presence or absence of endoleak.

Deery SE, Ergul EA, Schermerhorn ML, et al.. *J Vasc Surg* 2018;67:157-64

# AAA sac failure to regress post-EVAR: a significant unmet need




**40% Regress** → **Survival** 87% at 5y, 78% at10y

**35% Stable** → **Survival** 86% at 5y, 69% at10y

**25% Expand** → **Survival** 79% at 5y, 61% at10y

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O'Donnell TFX, Deery SE, Boitano LA, et al. *J Vasc Surg* 2019;69(2):415-21.

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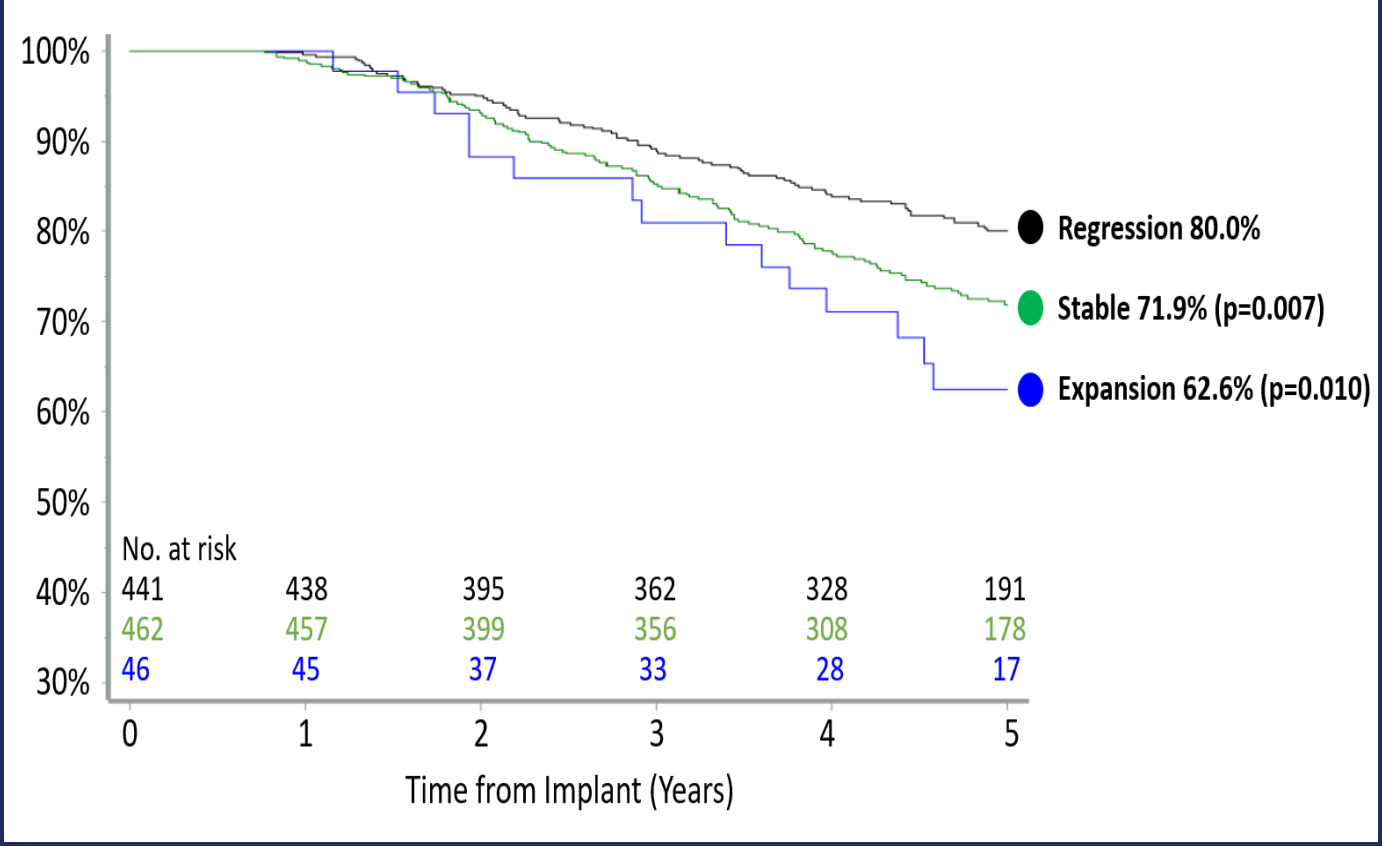
# AAA sac failure to regress post-EVAR: ENGAGE Registry




All patients (N=949) with 30-day and 1-year imaging following EVAR, 2009 - 2011

- Sac expansion (>5 mm) and stable sac at 1 year were independently associated with late mortality

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Li et al. ENGAGE Registry. Accepted for publication.

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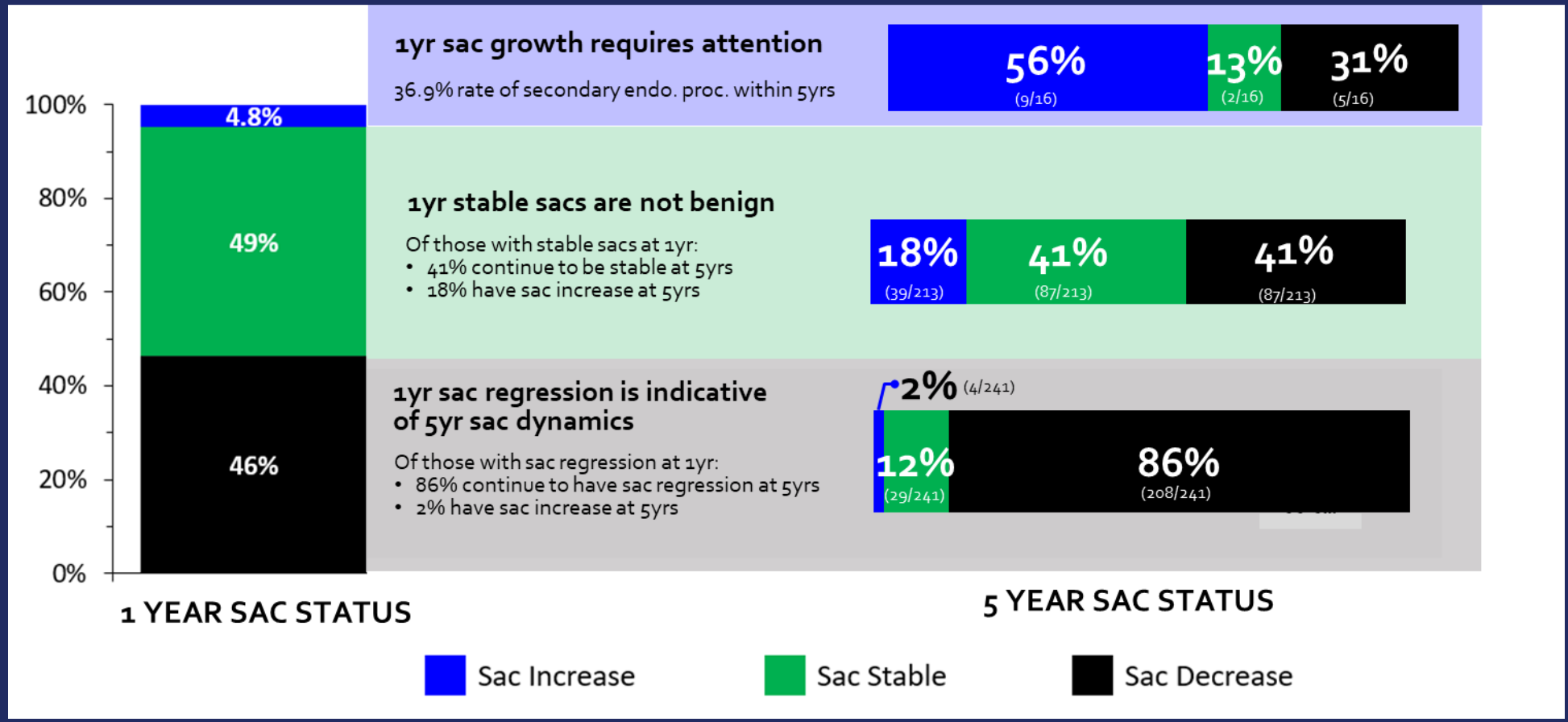
# One year-status of sac behavior is predictive of future sac behavior

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Li et al. ENGAGE Registry. Accepted for publication.

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+



N=16,102 intact EVAR

Outcomes: Late rupture, Re-Intervention, Survival

Categorized by Diameter change at one-year imaging:

| | |
|---|---|
| Sac Regression (≥5mm) | 49% |
| Stable Sac (<5mm) | 44% |
| Sac Expansion (≥5mm) | 6.7% |

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Rastogi V, O'Donnell TFX, Marcaccio CL, et al. *J Vasc Surg* 2024 Feb;79(2):269-279

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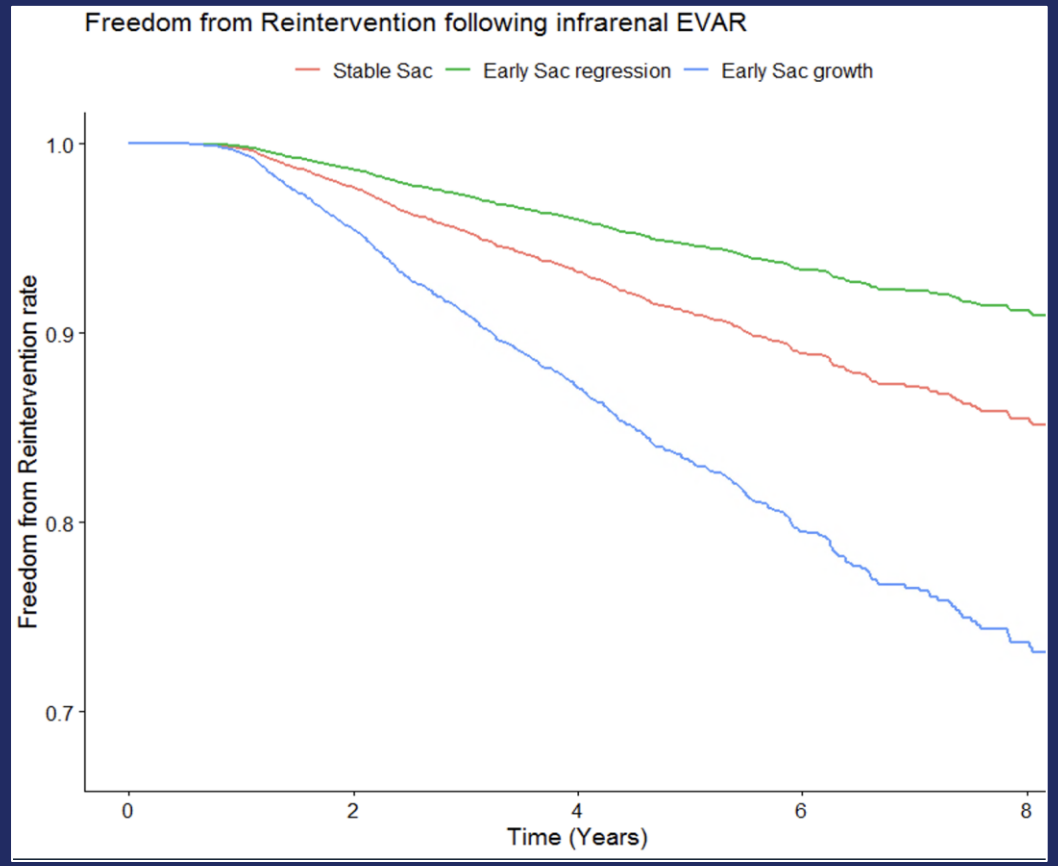
# 8-Year Reintervention




**Sac Regression HR: 0.58 [95%CI: 0.50-0.68], p<.001**

**Ref: Stable Sac**

**Sac Expansion HR: 1.98 [95%CI: 1.57-2.51], p<.001**

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Rastogi V, O'Donnell TFX, Marcaccio CL, et al. *J Vasc Surg* 2024 Feb;79(2):269-279

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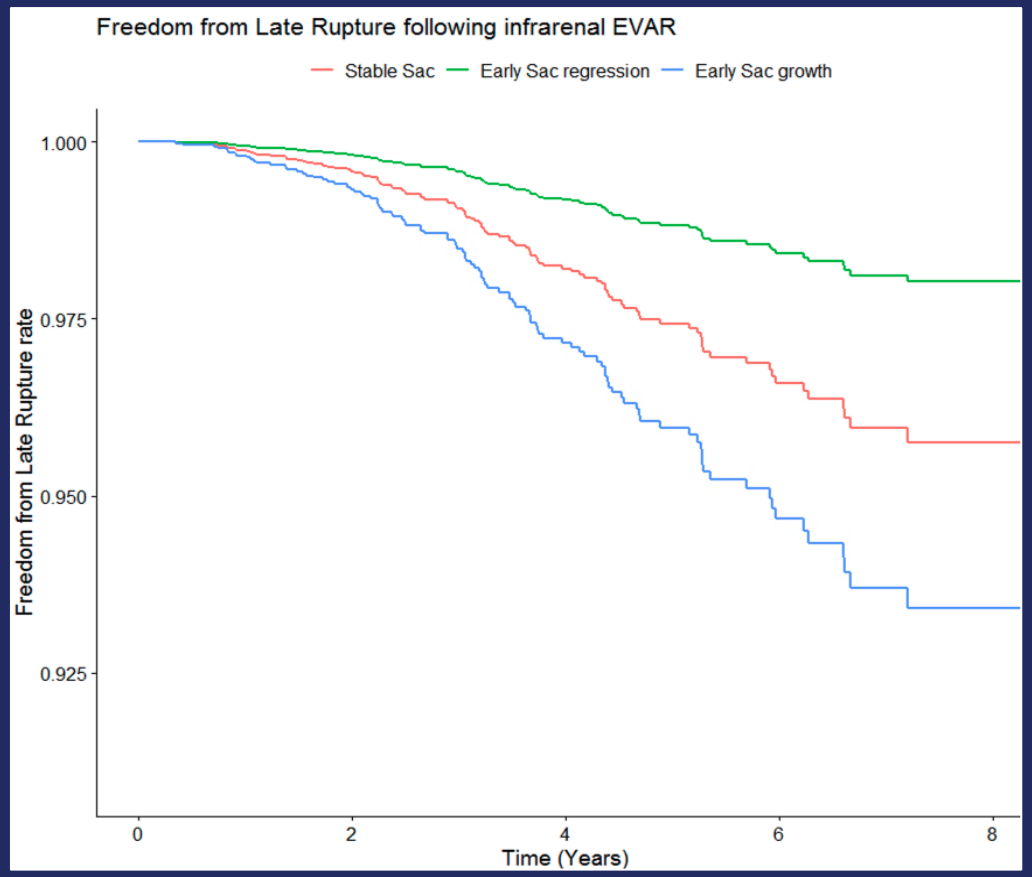
# 8-Year Rupture




**Sac Regression HR: 0.45 [95%CI: 0.29-0.69], p<.001**

**Ref: Stable Sac**

**Sac Expansion HR: 1.61 [95%CI: 0.88-2.96], p=.12**

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Rastogi V, O'Donnell TFX, Marcaccio CL, et al. *J Vasc Surg* 2024 Feb;79(2):269-279

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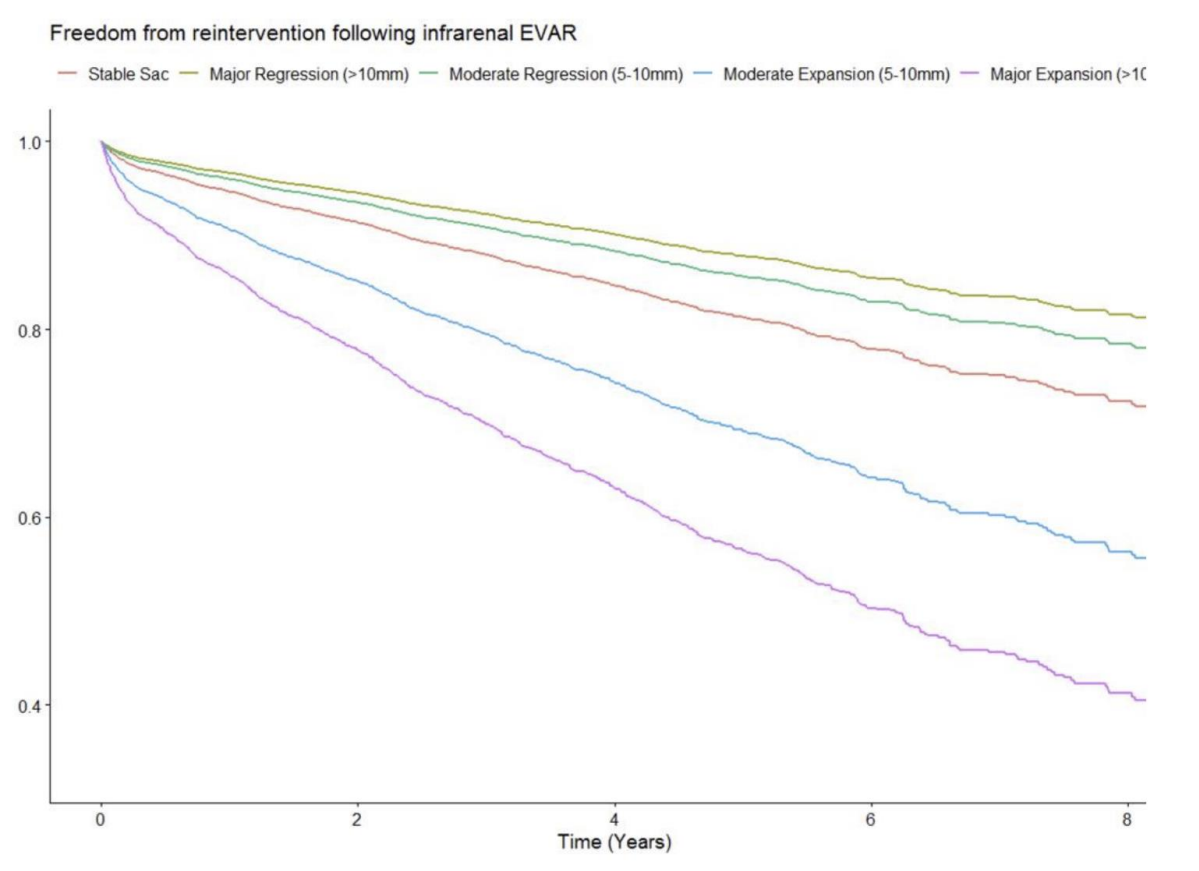
# Following Sub-stratification…

## Reintervention-Free Survival following Infrarenal EVAR




# The amount of regression matters

| 8-year Reintervention | Hazard Ratio (HR) | 95% CI | P-value |
|---|---|---|---|
| Ref: Stable Sac | - | - | - |
| **Major Regression (>10mm)** | **0.62** | **0.53-0.73** | **<.001** |
| **Moderate Regression (5-10mm)** | **0.74** | **0.64-0.86** | **<.001** |
| **Moderate Growth (5-10mm)** | **1.79** | **1.43-2.24** | **<.001** |
| **Major Growth (>10mm)** | **2.81** | **2.11-3.74** | **<.001** |

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Rastogi V, O'Donnell TFX, Marcaccio CL, et al. *J Vasc Surg* 2024 Feb;79(2):269-279

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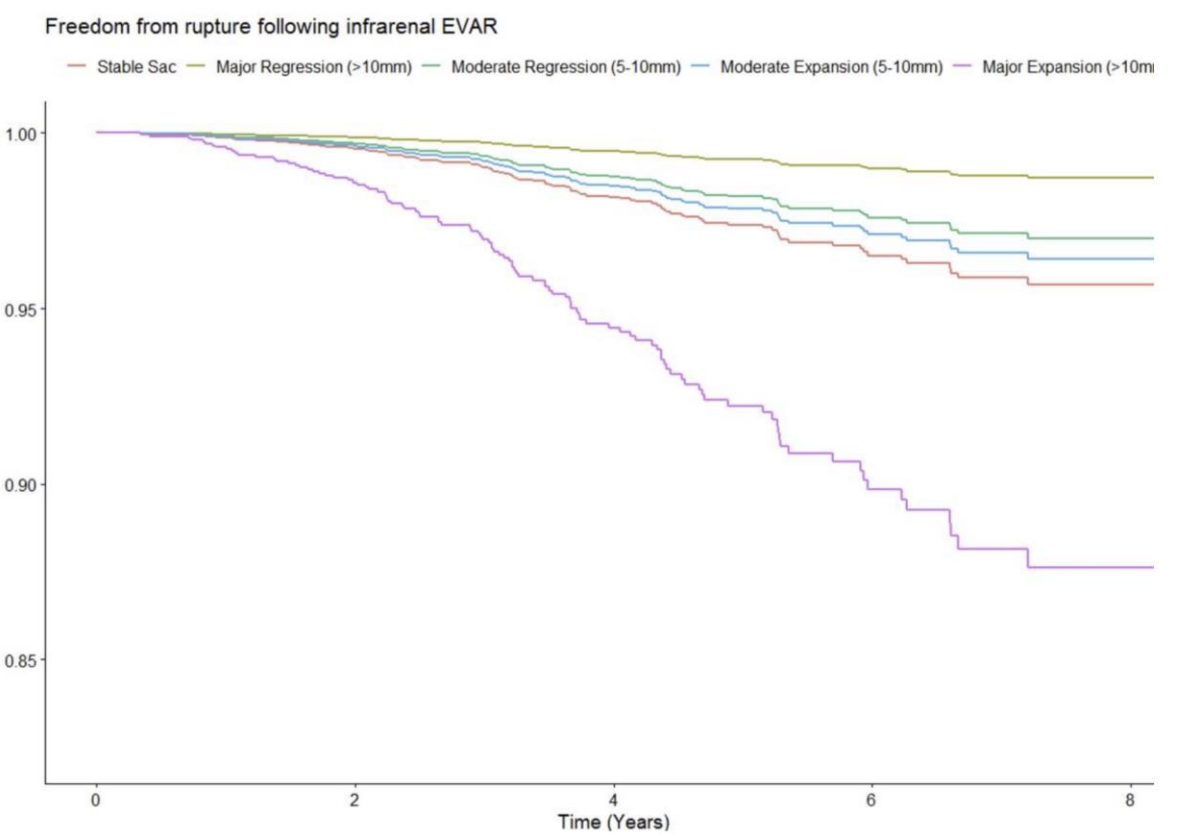
# Following Sub-stratification…

## Rupture-Free Survival following Infrarenal EVAR




# The amount of regression matters

| 8-year Rupture | Hazard Ratio (HR) | 95% CI | P-value |
|---|---|---|---|
| Ref: Stable Sac | - | - | - |
| **Major Regression (>10mm)** | **0.28** | **0.15-0.50** | **<.001** |
| Moderate Regression (5-10mm) | 0.68 | 0.42-1.09 | .11 |
| Moderate Expansion (5-10mm) | 0.82 | 0.33-2.05 | .67 |
| **Major Expansion (>10mm)** | **3.25** | **1.51-6.98** | **.003** |

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Rastogi V, O'Donnell TFX, Marcaccio CL, et al. *J Vasc Surg* 2024 Feb;79(2):269-279

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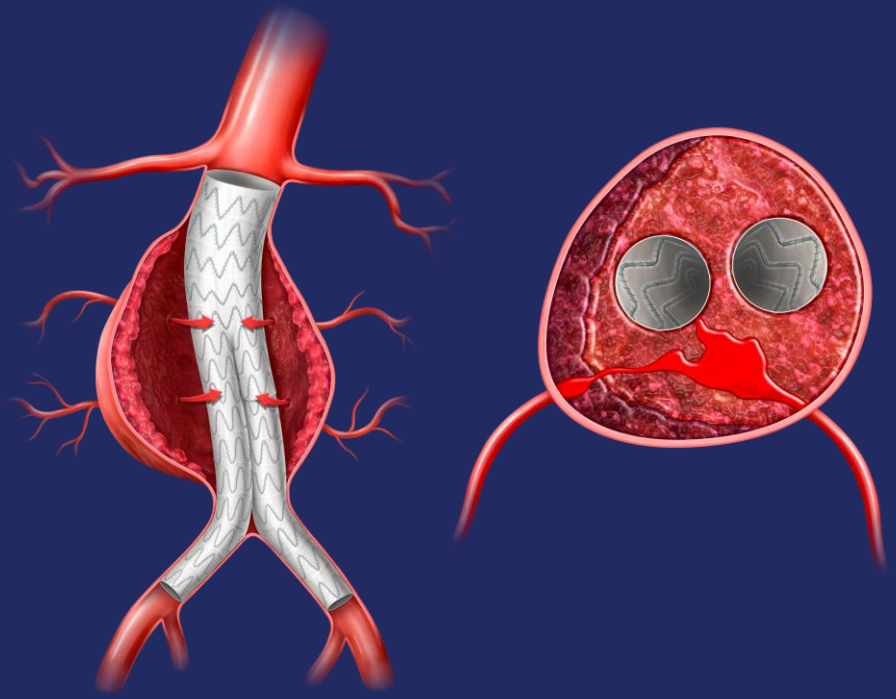
# Failure to Regress Risk Factors

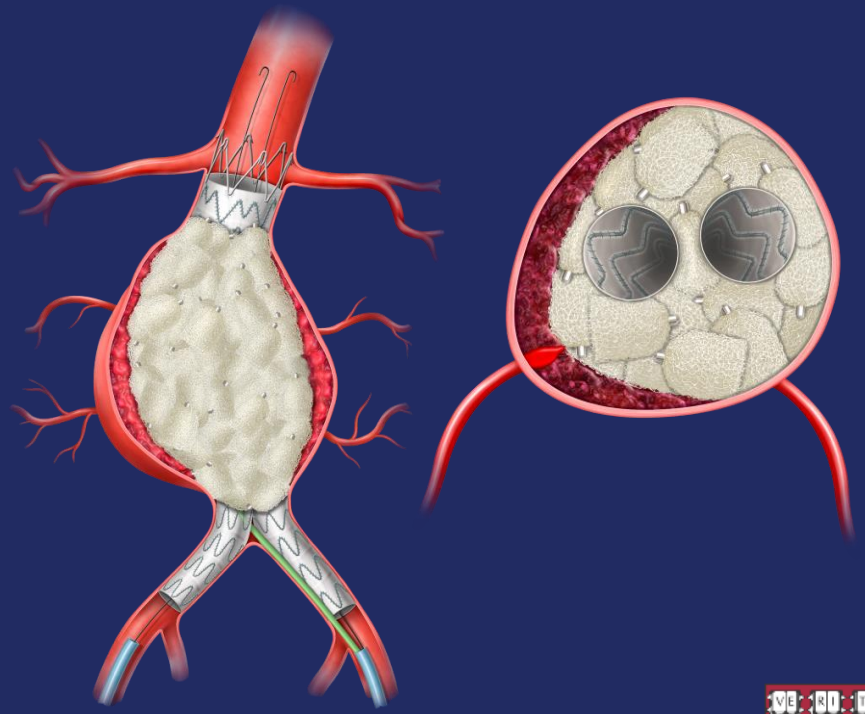
- Medical history and CV risk factors
- Aneurysm morphology
  - Preoperative diameter
  - Neck characteristics
  - Thrombus characteristics
- Endograft design
- Endoleak
  - Type I/III
  - Type II

# Preemptive AAA Sac embolization - Do we need it?

**EVAR**
excludes the sac



**EVAR + Shape Memory Polymer**
intended to manage the sac



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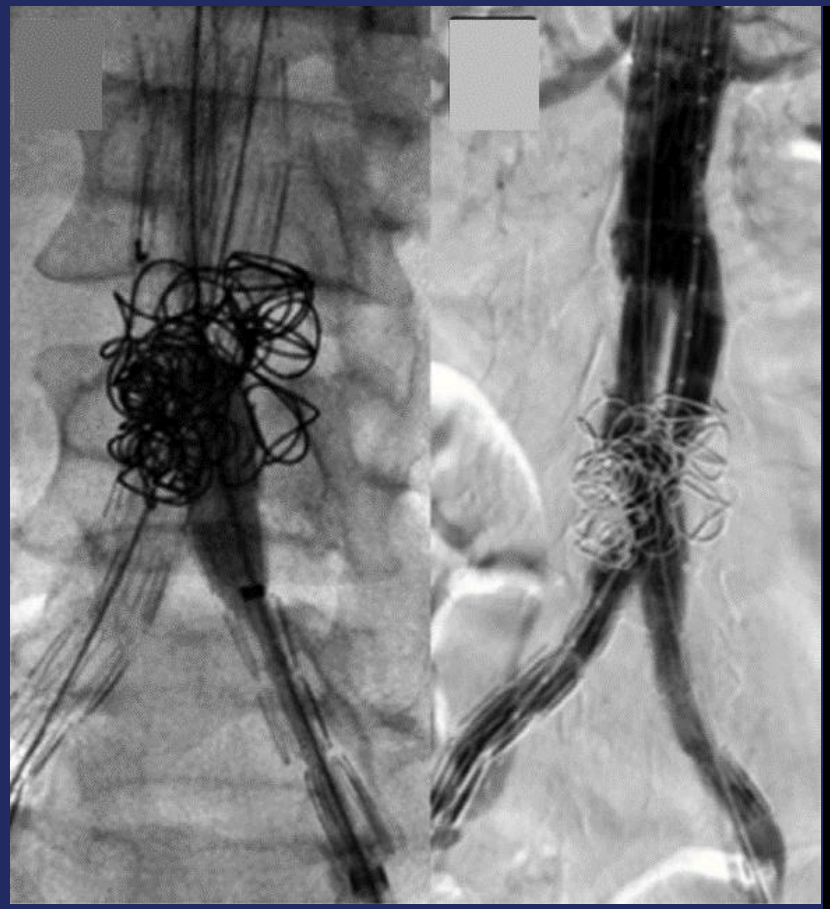
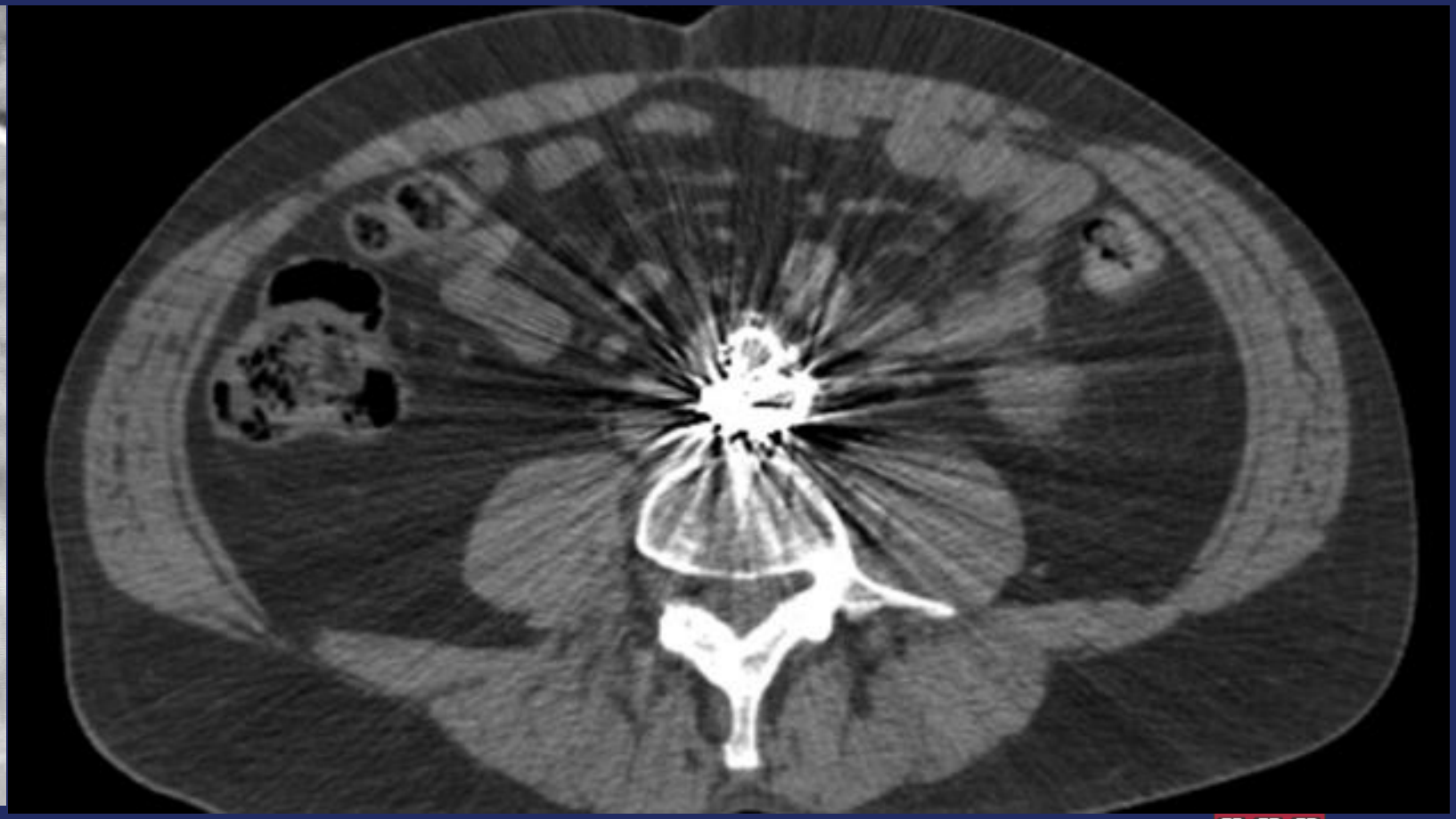
# Preemptive Coil Embolization



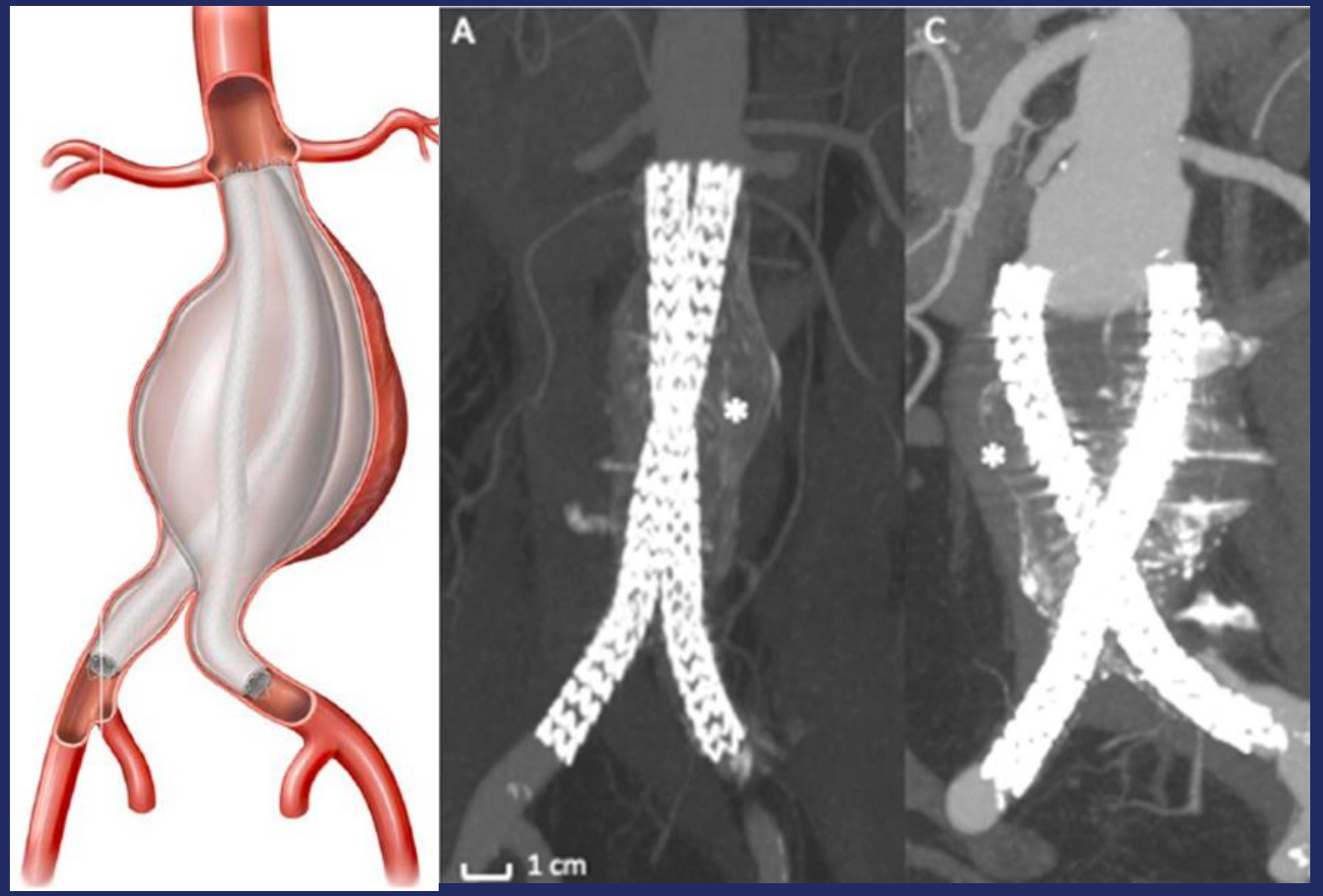




Dosluoglu, J Vasc Surg 2019;69:1736-46.

# Endovascular Aneurysm Sealing (EVAS) with Nellix

- Flexible cobalt chromium stent grafts
- Integrated polymer-filled endobags
- Low profile; Simple to deploy
- EVAS Clinical Trials
  - Low type 2 endoleak rate
  - **Early signals of lower all cause mortality**
  - Mid-term device failures
    - Type 1 endoleak with migration
    - Sac expansion
    - Secondary AAA rupture

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Singh AA. EJVES 2021, O'Donnell Ann Vasc Surg 2020, Rastogi JVS 2023

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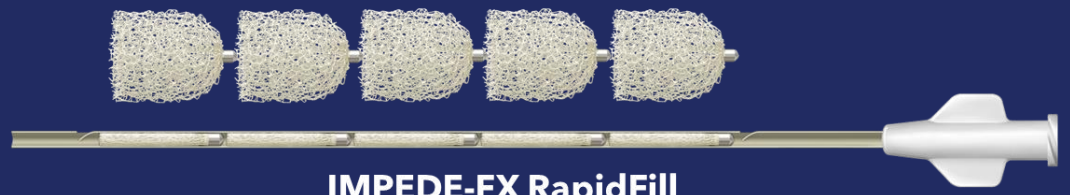
# Preemptive Sac Management with Shape Memory Polymer - Goals

- High volume filling of AAA sac
  - Compliant material, low radial force
- Stable clot formation and thrombosis
- Improve imaging visibility
- Increase rate of sac regression
- Reduce reintervention for T2 endoleak
- Avoid chronic inflammation



IMPEDE-FX RapidFill

Investigational. Not available for sale in the U.S.

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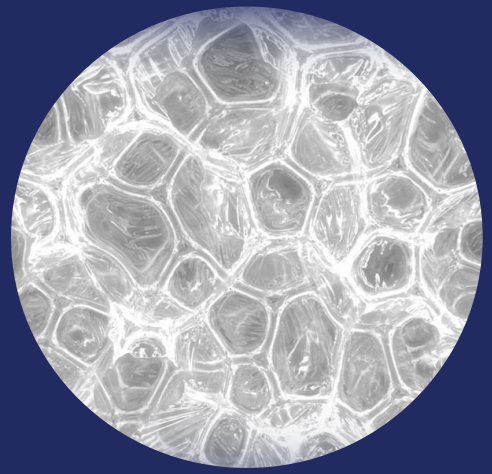
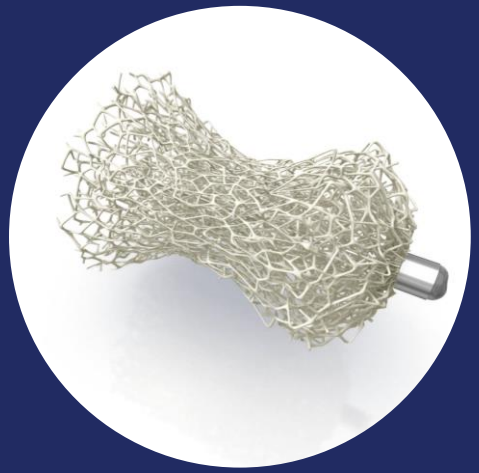
# Shape Memory Polymer

**Porous, polyurethane foam**



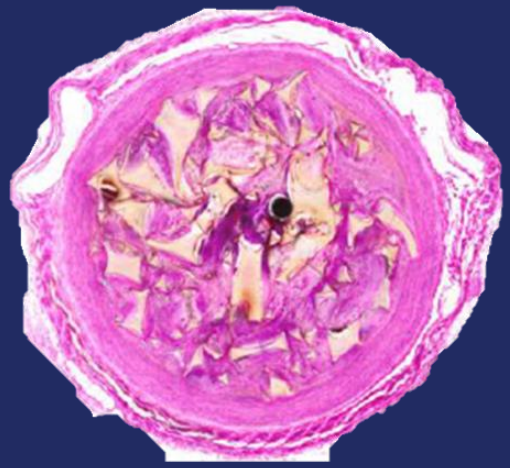
**Open scaffold Stable clot formation**

**Soft Conformable**



**Radiolucent material**

**Cellular growth Tissue infiltration‡**



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‡ Pre-clinical data: Jessen SL, Friedemann MC, Ginn-Hedman AM, et al. ACS Biomater Sci Eng 2020 6 2588–2599

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# AAA-SHAPE Early Feasibility Studies

- Prospective, multicenter
  - New Zealand, 2 centers (NCT04227054)
  - The Netherlands, 3 centers (NCT04751578)
- 35 patients
- Primary outcomes: Technical success, 30d MAE
- Secondary outcomes (through 5 years)
  - MAEs, SAEs
  - Endoleak, sac diameter/volume, AAA-related secondary intervention, conversion to open repair

## AAA-SHAPE NZ

Andrew Holden, Andrew Hill
*Auckland City Hospital, Auckland*

Manar Khashram
*Waikato District Health Board, Hamilton*

## AAA-SHAPE NLD

Michel Reijnen
*Rijnstate Hospital, Arnhem*

Jan Heyligers
*St. Elisabeth Hospital, Tilburg*

Arno Wiersema
*Dijklander Hospital, Hoorn*

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Holden A, Hill A, Khashram M, et al. J Vasc Surg. 2024. Epub Ahead of Print.

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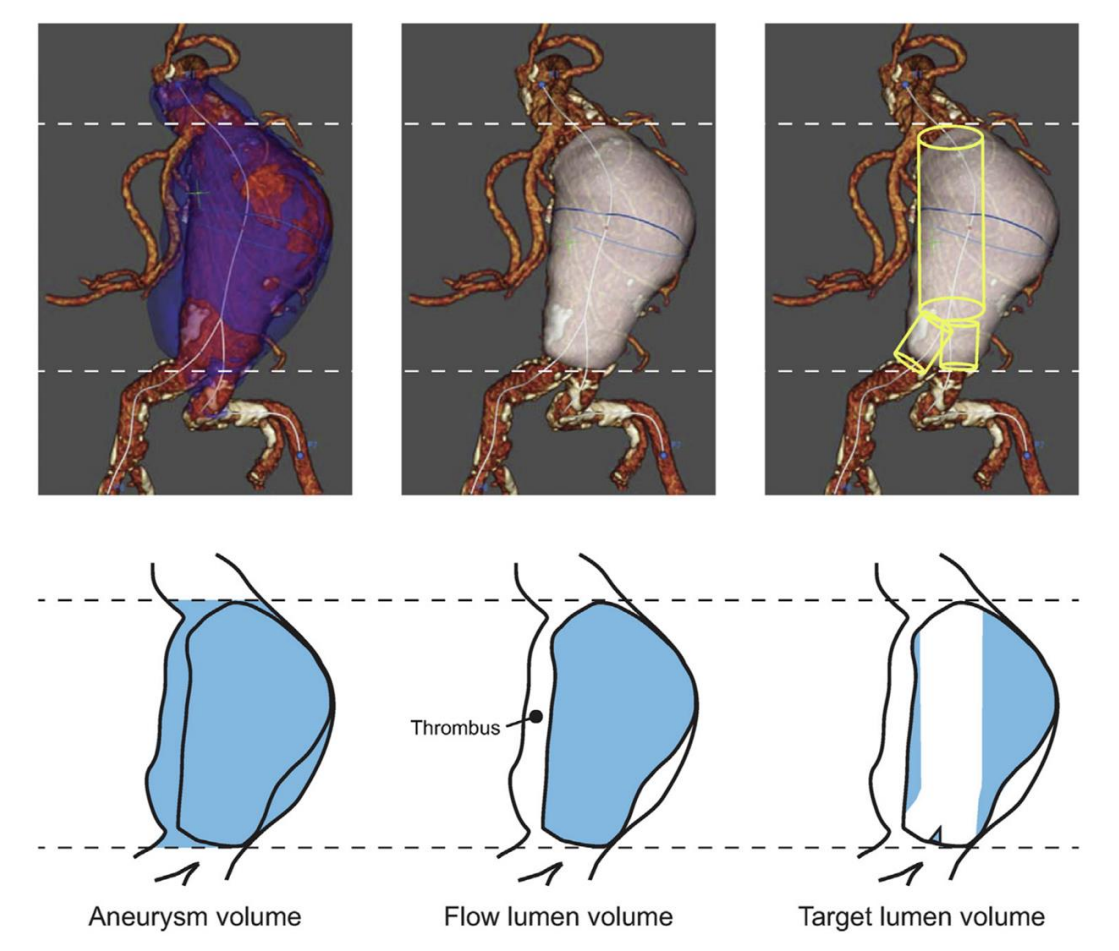
# Pre-procedure Volume Estimations




Estimated Number of IMPEDE-FX RapidFills =

$$\left( \frac{\text{Target Lumen Volume}}{6.25} \right) \times 1.5$$

Each IMPEDE-FX RapidFill contains **6.25 mL** embolic material

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Holden A, Hill A, Khashram M, et al. J Vasc Surg Cases Innov Tech. 2023 Jun 12;9(3):101241.

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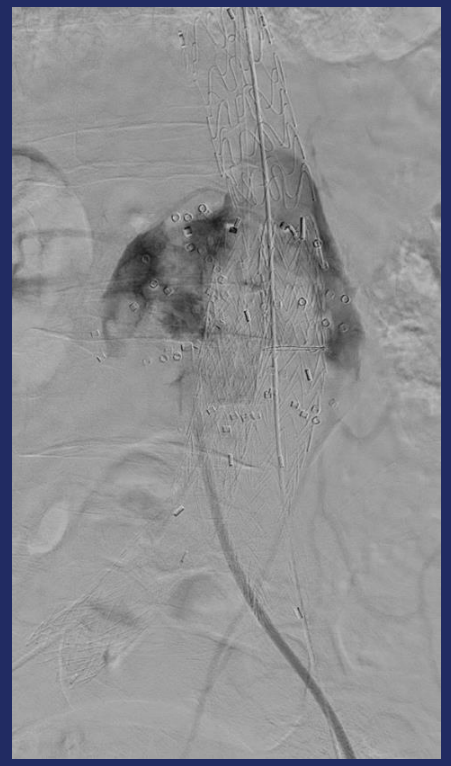
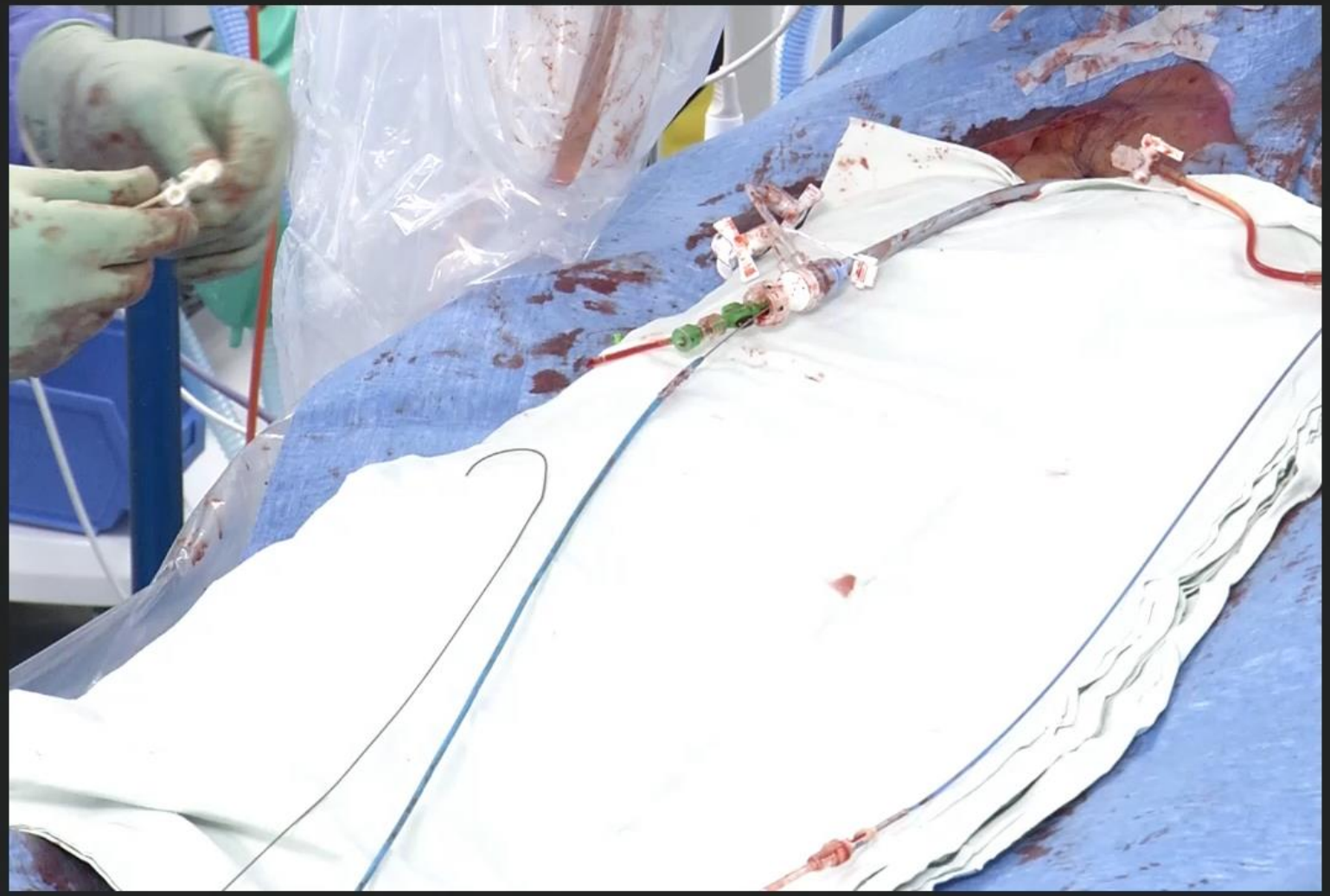
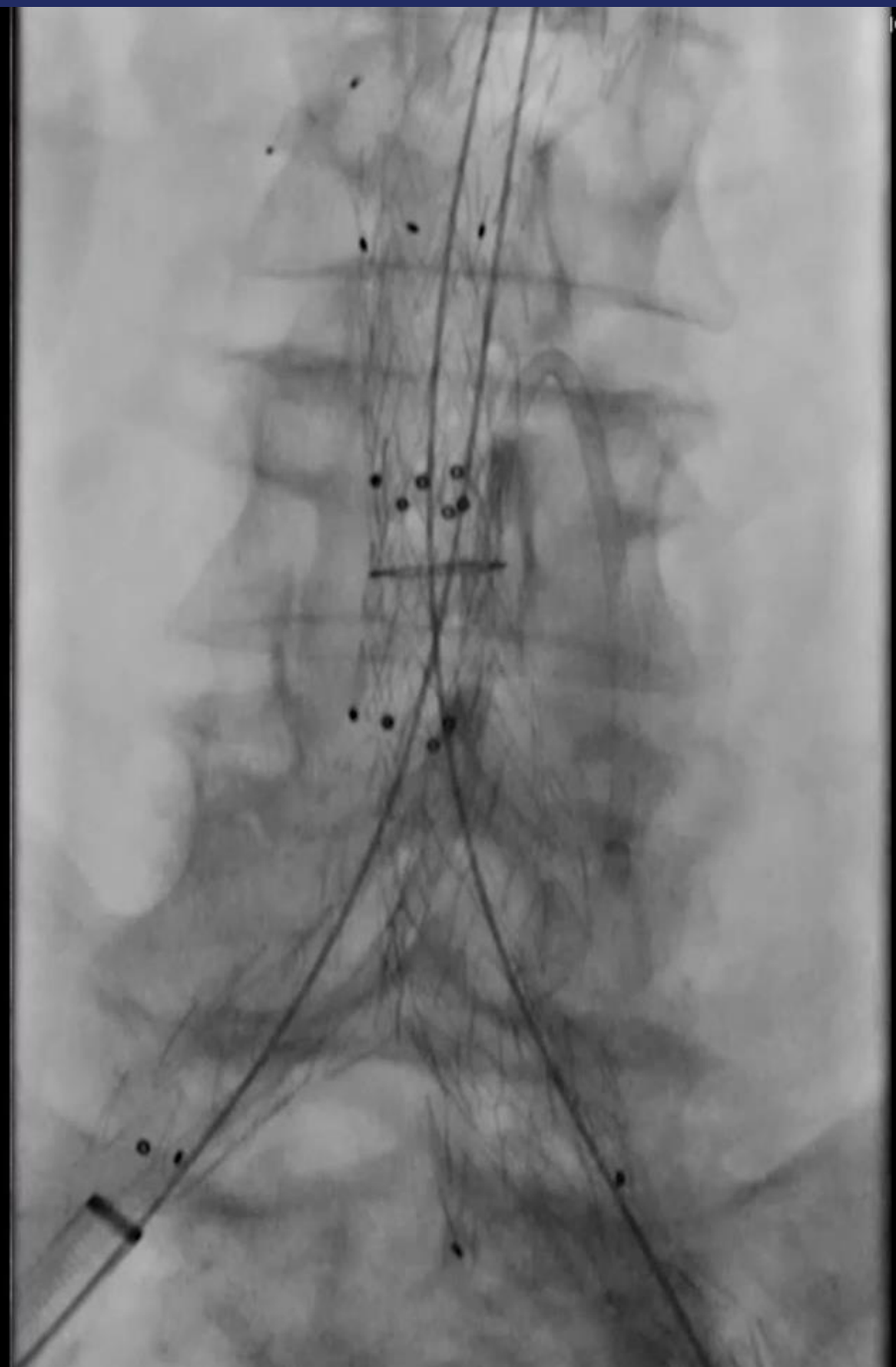
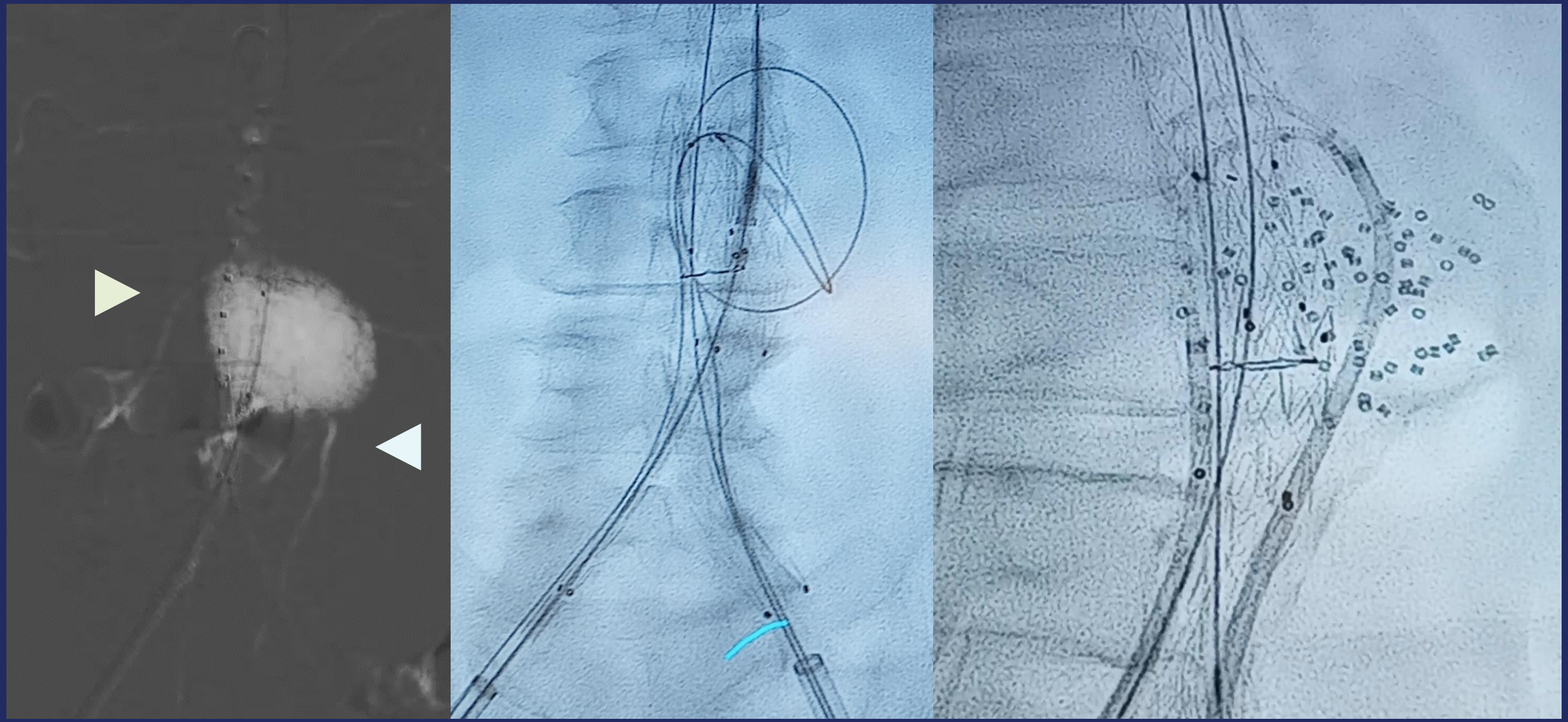
# Case Example

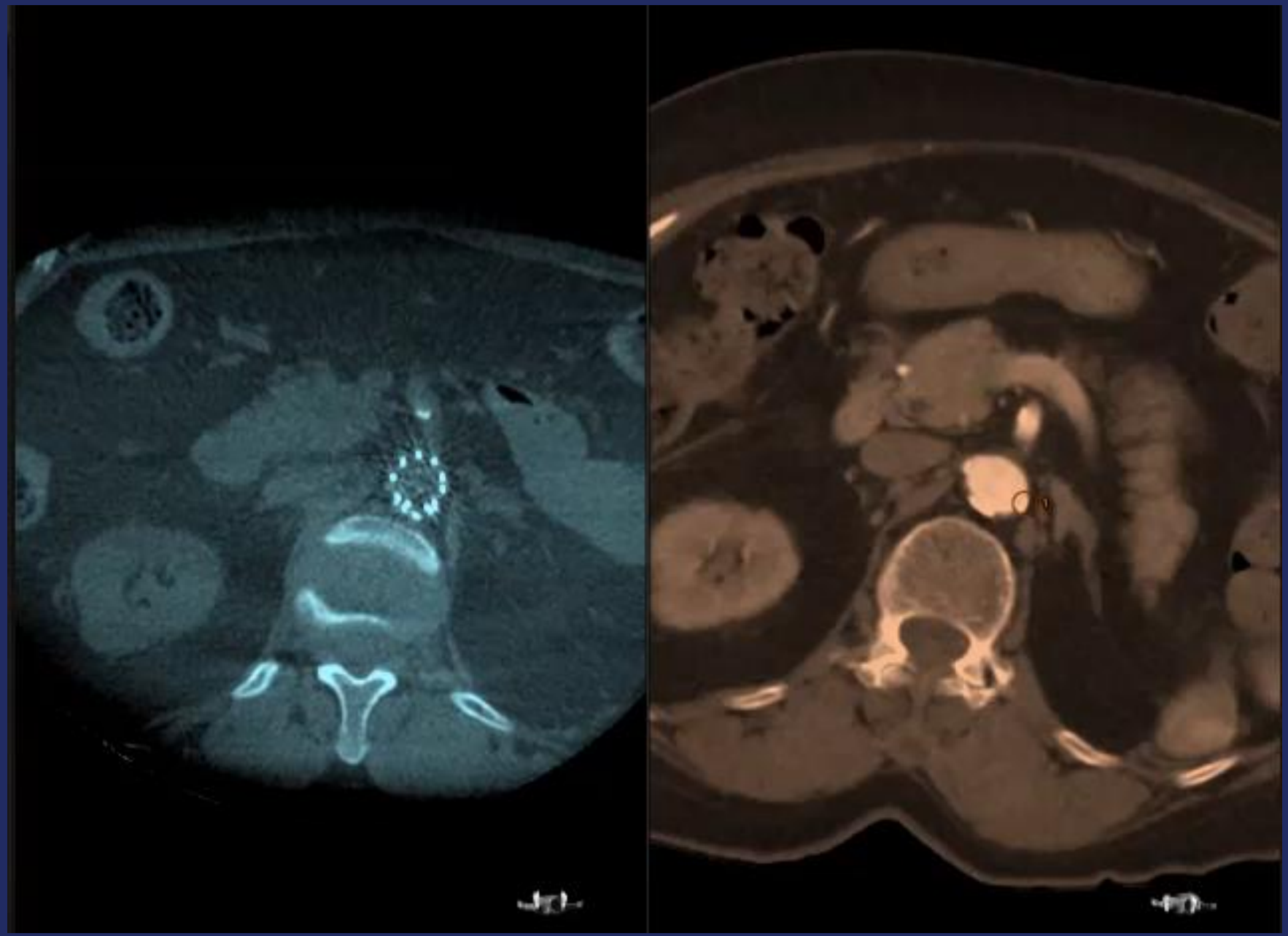












# Demographics, Aneurysm Characteristics (N=34)

| | |
|---|---|
| Age, years | 75.5 ± 7.3 |
| Male sex, n (%) | 29 (85.3%) |
| ASA Grade, n (%) | |
| I | 0 (0%) |
| II | 6 (17.6%) |
| III | 27 (79.4%) |
| IV | 1 (2.9%) |

| | |
|---|---|
| Aneurysm Diameter, mm | 60.8 (57.8 to 63.9) |
| Aneurysm Volume, mL | 181.4 (150.7 to 212.1) |
| Thrombus Volume, mL | 83.2 (56.3 to 110.1) |
| Thrombus Volume, % | 41.7 (35.5 to 47.8) |
| Blood Lumen Volume, mL | 98.2 (88.4 to 108.1) |
| Patent IMA ≥3 mm, n (%) | 10 (29.4%) |
| Patent Renal Accessory Arteries, n (%) | 5 (14.3%) |
| Patent Lumbar Arteries ≥1, n (%) | 31 (91.2%) |

Data presented as mean ± standard deviation or 95% confidence interval for continuous variables unless stated otherwise or number (%) for categorical variables.
*One subject was excluded from analysis due to pre-existing inflammatory aneurysm.

Holden A, Hill A, Khashram M, et al. J Vasc Surg Cases Innov Tech. 2023 Jun 12;9(3):101241.

# Procedure Data (N=34)

| | |
|---|---|
| Endografts, n (%) | |
| Medtronic Endurant II/IIs | 17 (50) |
| Gore Excluder | 12 (35.3) |
| Gore Excluder Conformable | 5 (14.7) |
| Sac Management Approach, n (%) | 34 |
| Ipsilateral | 20 (58.8) |
| Contralateral | 14 (41.2) |

| | |
|---|---|
| Target Lumen Volume, mL<br>(Blood Lumen Vol – Endograft Vol) | 56.3 (46.9 to 65.8) |
| Technical Success | 100% |
| IMPEDE-FX RapidFill Devices | 11 (7 to 15) |
| Shape Memory Polymer Volume / Target Lumen Volume Ratio | 1.4 ± 0.3 |
| Additional Procedure Time, min | 27 ± 14 |
| Additional Radiation Time, min | 135 seconds (n=6) |

Data presented as mean ± standard deviation or 95% confidence interval for continuous variables unless stated otherwise or number (%) for categorical variables.
One subject was excluded from analysis due to pre-existing inflammatory aneurysm.

# Adverse Events through 1y

- No device- or procedure-related MAEs
  - Procedural blood loss >1000mL, od (Femoral access, resolved without sequalae)
  - CHF, 177d: death
  - COVID-19, 185d, death
- Four device/study procedure-related SAEs
  - Arrhythmia, 1d
  - Post implantation syndrome, 1d
  - Constipation, 2d
  - Abdominal pain, 5d



Preliminary data from an ongoing clinical investigation, data subject to change.
Device AEs refer to investigational device, IMPEDE-FX RapidFill
Holden A, Hill A, Khashram M, et al. J Vasc Surg. 2024. Epub Ahead of Print.

# Adverse Events through 1y

- Four AAA-related reinterventions for:
  - EVAR limb stenosis
  - EVAR limb occlusion
  - Partial coverage LRA with EVAR graft
  - Type 1a endoleak
- One AAA perforation (iatrogenic)
  - Guidewire perforated AAA during index procedure; no clinical sequalae, sac decrease
- No conversion to open repair through 1y
  - Conversion for Type 2 endoleak with expansion at 2y

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Preliminary data from an ongoing clinical investigation, data subject to change.
Device AEs refer to investigational device, IMPEDE-FX RapidFill
Holden A, Hill A, Khashram M, et al. J Vasc Surg. 2024. Epub Ahead of Print.

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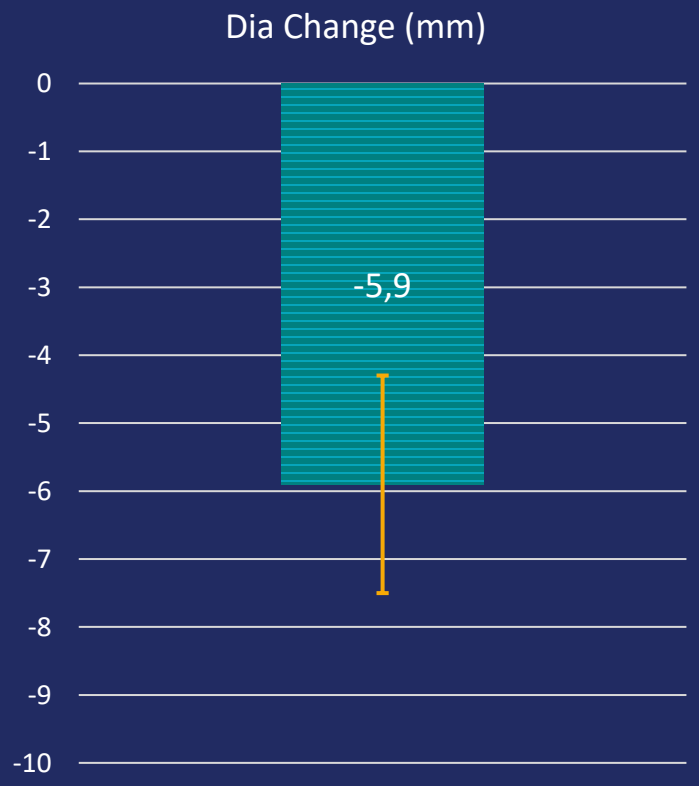
# Sac Changes at 1y Compared to 30d Baseline (Core Lab)

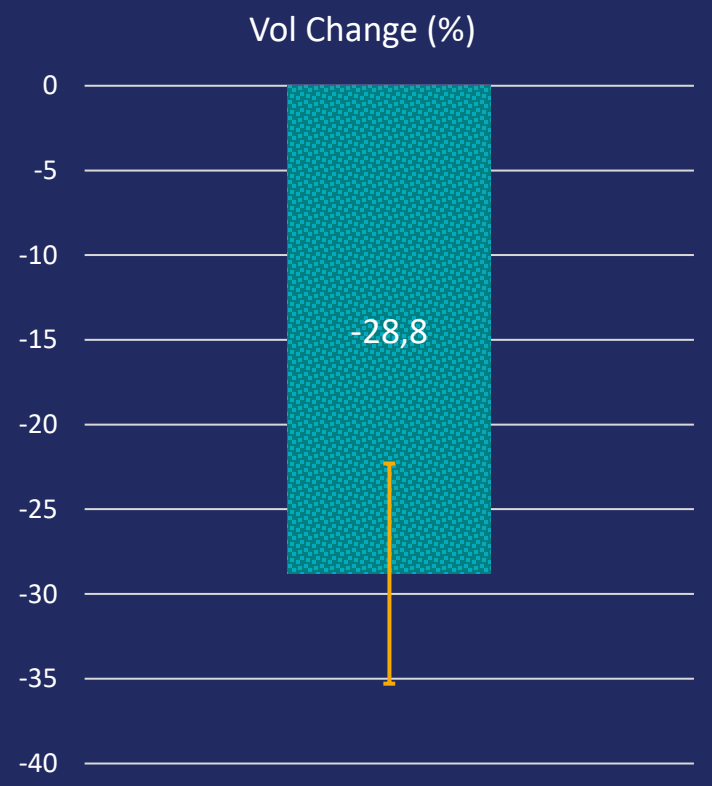
**-6 mm mean diameter change at 1y**

95% CI, -7.5 to -4.4 mm, P<.001




**-29% mean volume change at 1y**

95% CI, -35.3 to -22.4, P<.001

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Holden A, Hill A, Khashram M, et al. J Vasc Surg. 2024. Epub Ahead of Print.

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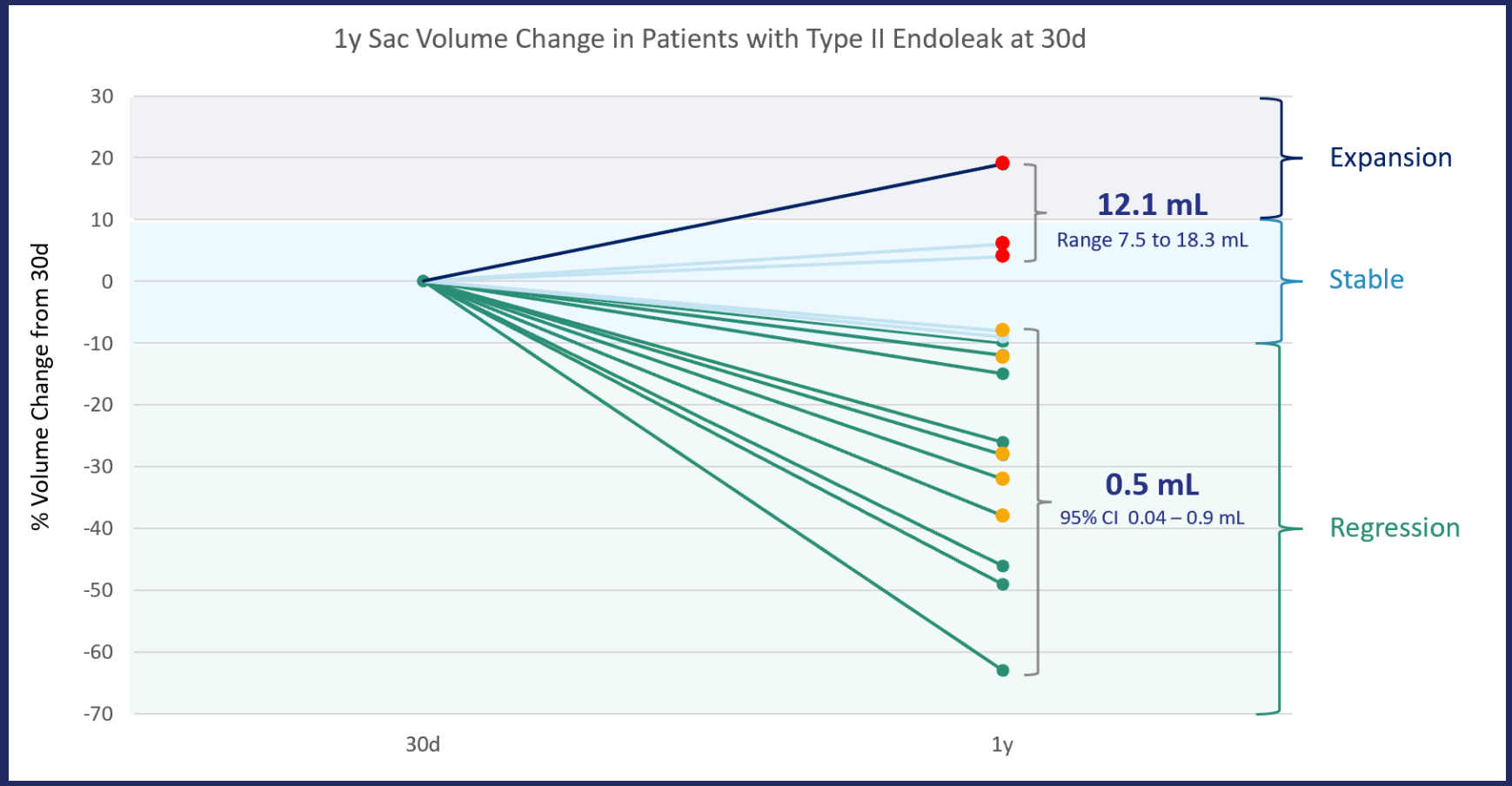
# Sac Changes at 1y in Presence of 30d Type 2 Endoleak (Core Lab)




- Persistent EL, High Vol*
- Persistent EL, Low Vol*
- Resolved EL

*Categorized according to EL volume ≥2.4 mL and <2.4 mL. Based on a cutoff derived from published analysis of need for reinterventions for T2 EL

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Holden A, Hill A, Khashram M, et al. J Vasc Surg. 2024. Epub Ahead of Print.
*Dudeck O, Schnapauff D, Herzog L, et al. Cardiovasc Intervent Radiol. 2015;38:45-52

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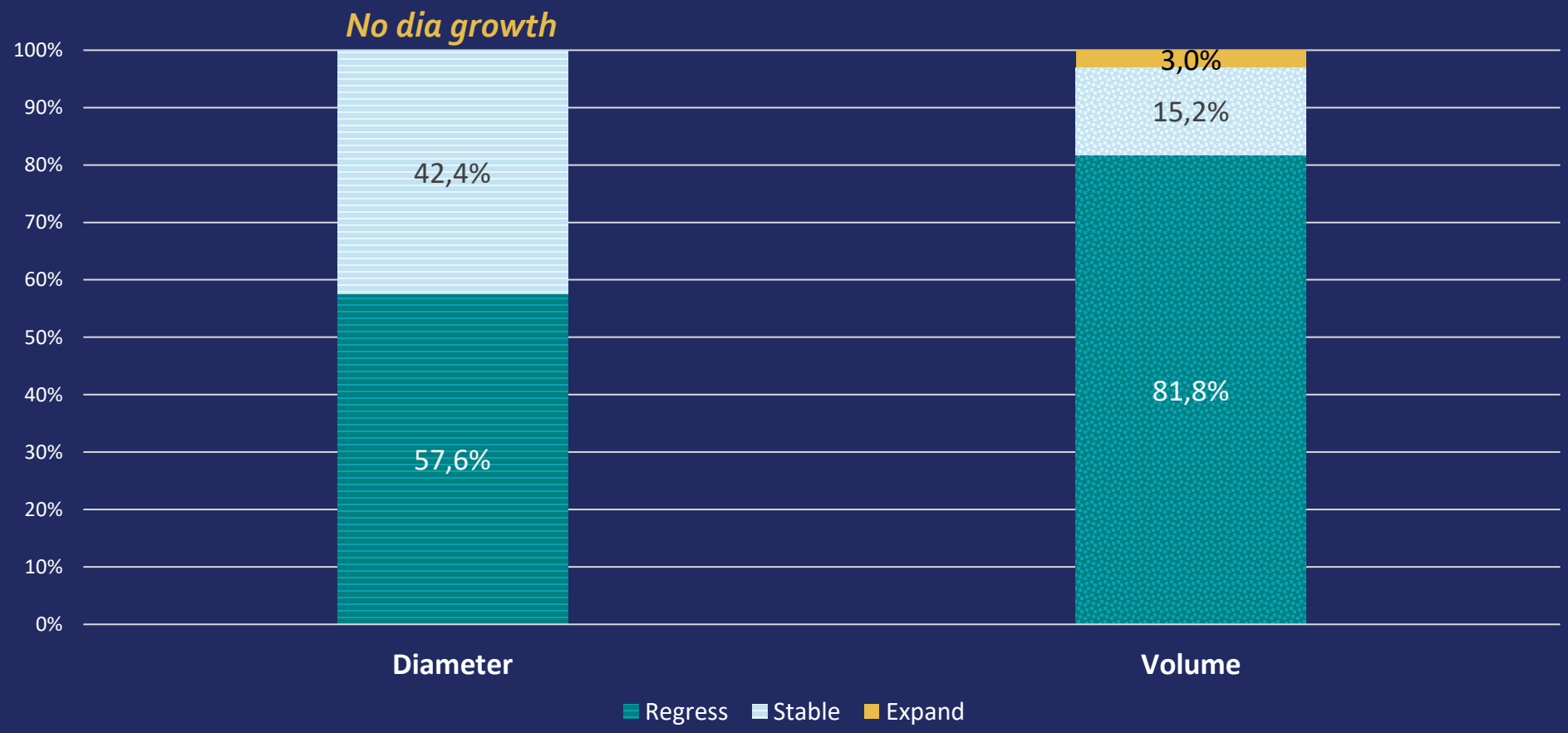
# % Patients, Sac Change at One Year (Compared to 30d Baseline)

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Holden A, Hill A, Khashram M, et al. J Vasc Surg. 2024. Epub Ahead of Print.

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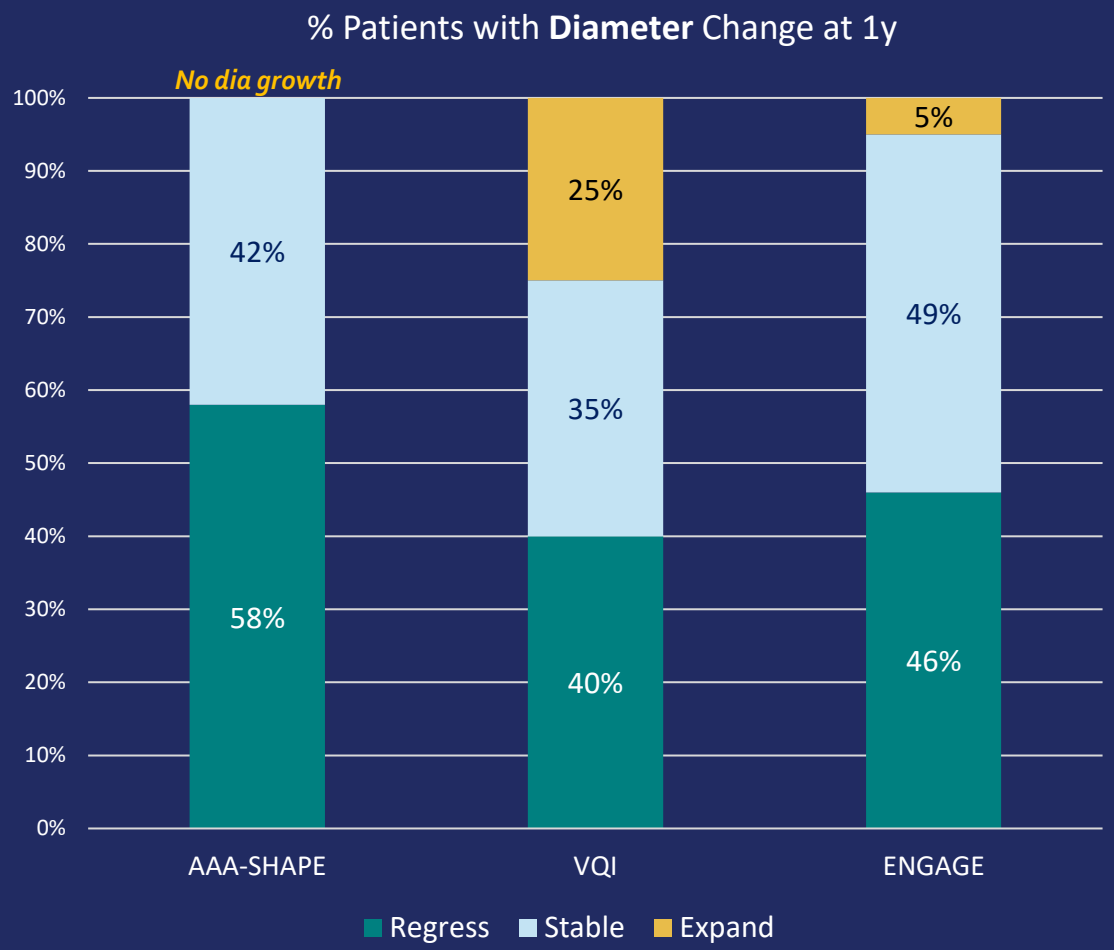
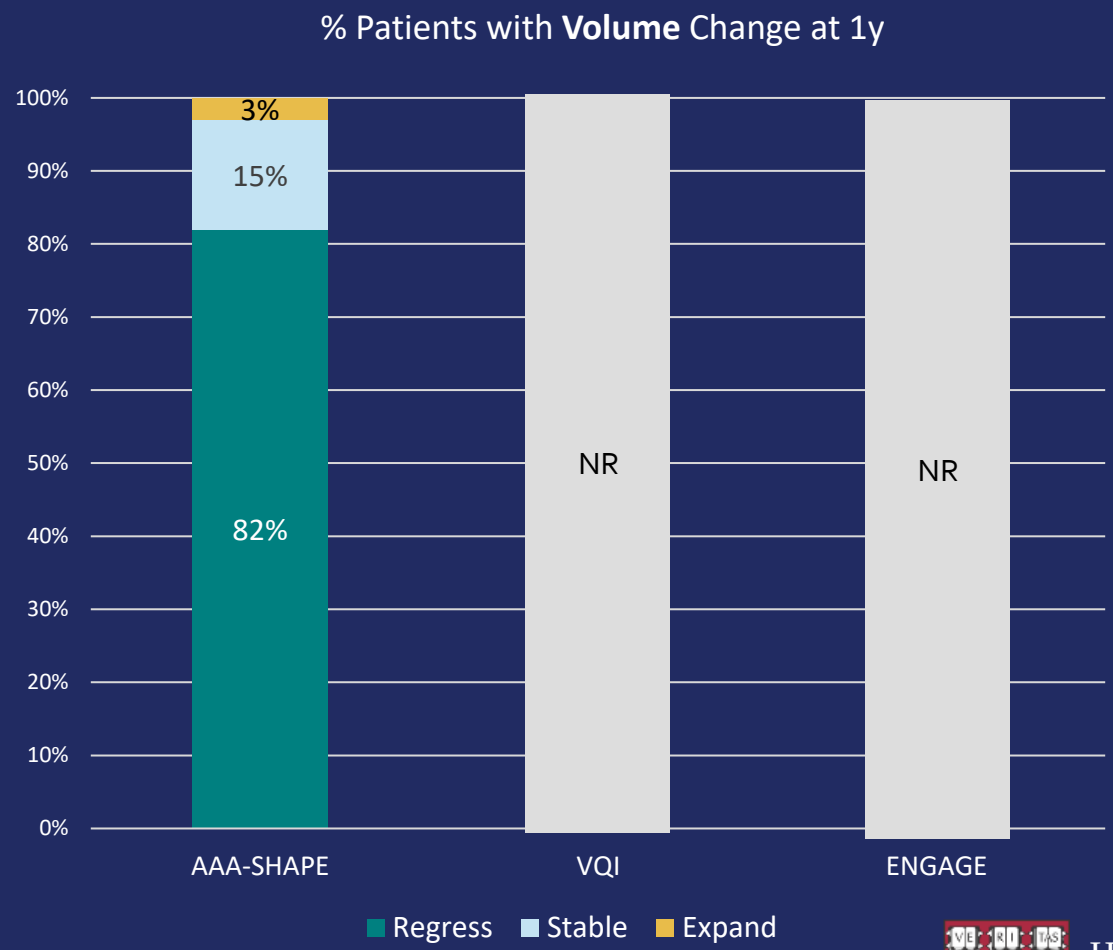
# % Patients, Sac Change at One Year Compared to Standard EVAR

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Holden A, Hill A, Khashram M, et al. J Vasc Surg. 2024. Epub Ahead of Print.
VQI: O'Donnell TFX et al. *J Vasc Surg* 2019;69(2):414-422; ENGAGE: Li J, et al. ENGAGE Registry. Accepted for publication.

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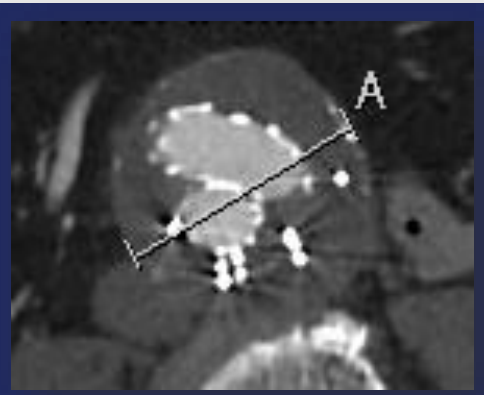
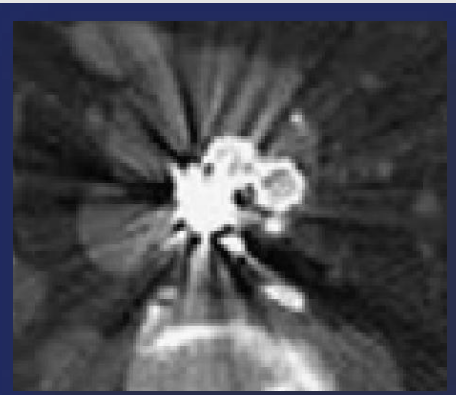
# % Sac Volume Change Compared to EVAR +/- Preemptive Coil Embo

| | | Randomized Controlled Trial | | |
|---|---|---|---|---|
| | AAA-SHAPE | EVAR + COIL EMBO* | VS | STANDARD EVAR* |
| Patients (n) | 33 | 52 | | 55 |
| Population Treated | 68% at risk of T2 EL | All patients at risk of T2 EL | | All patients at risk of T2 EL |
| % volume regression, 6m | **-18%** (-24% to -11%), P<.001 | **-7.5%** ± 11%, P=.02 | | **-1.7%** ± 15%, P=.02 |
| % volume regression, 1y | **-29%** (-35% to -22%), P<.001 | **-14%** ± 17%, P=.02 | | **-2.0%** ± 27%, P=.02 |



*Piazza M, Squizzato F, Zavatta M, et al. J Vasc Surg 2016;63:32-8.

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# AAASHAPE

**A**bdominal **A**ortic **A**neurysm **S**ac **H**ealing **a**nd **P**revention of **E**xpansion

## Randomized Controlled Pivotal Trial

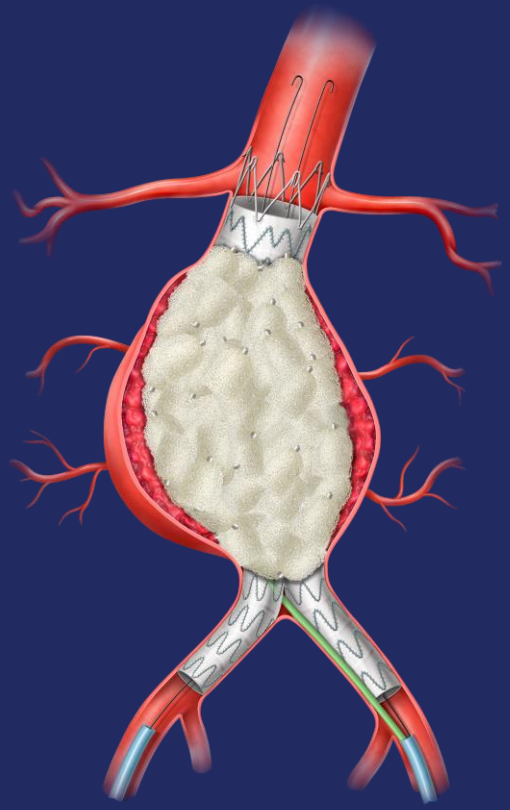
180 total subjects

Up to 50 sites (40 in US; 10 in EU/NZ)

Follow-up through 5y

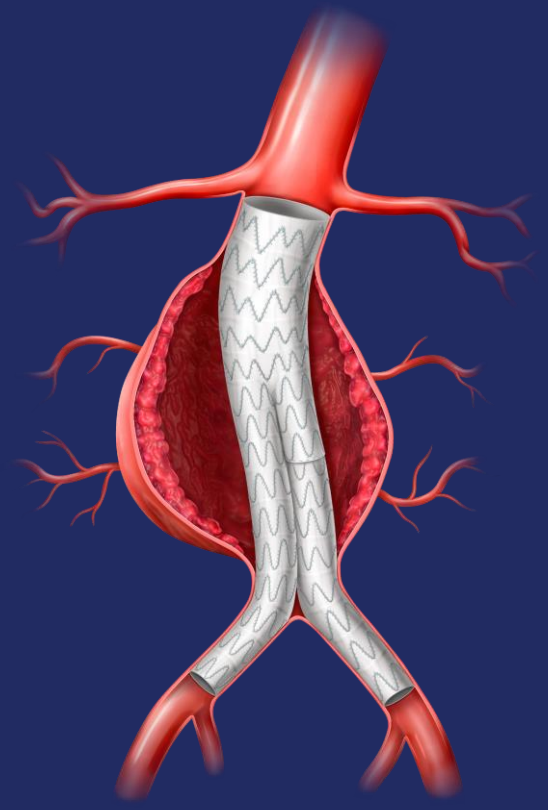
## Primary Efficacy Endpoint

*% patients with ≥10% sac volume reduction at 1y and no AAA-related intervention through 1y*



EVAR *plus*
IMPEDE-FX RapidFill

vs



Standard
EVAR

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Thank You