Open Thoracoabdominal Repair in Connective Tissue Disease Patient

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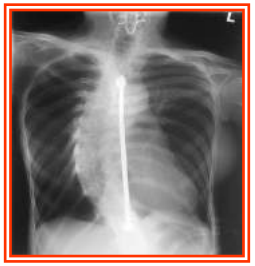
Disclosures

- A. Estrera Consultant Gore

Marfan Syndrome
FBN1 Mutations



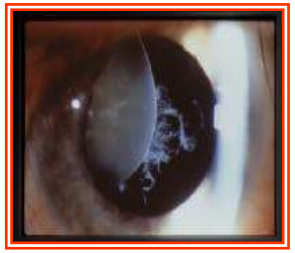
Skeletal

Pectus deformities

Reduced U/L segment

Wrist and thumb sign

Scoliosis

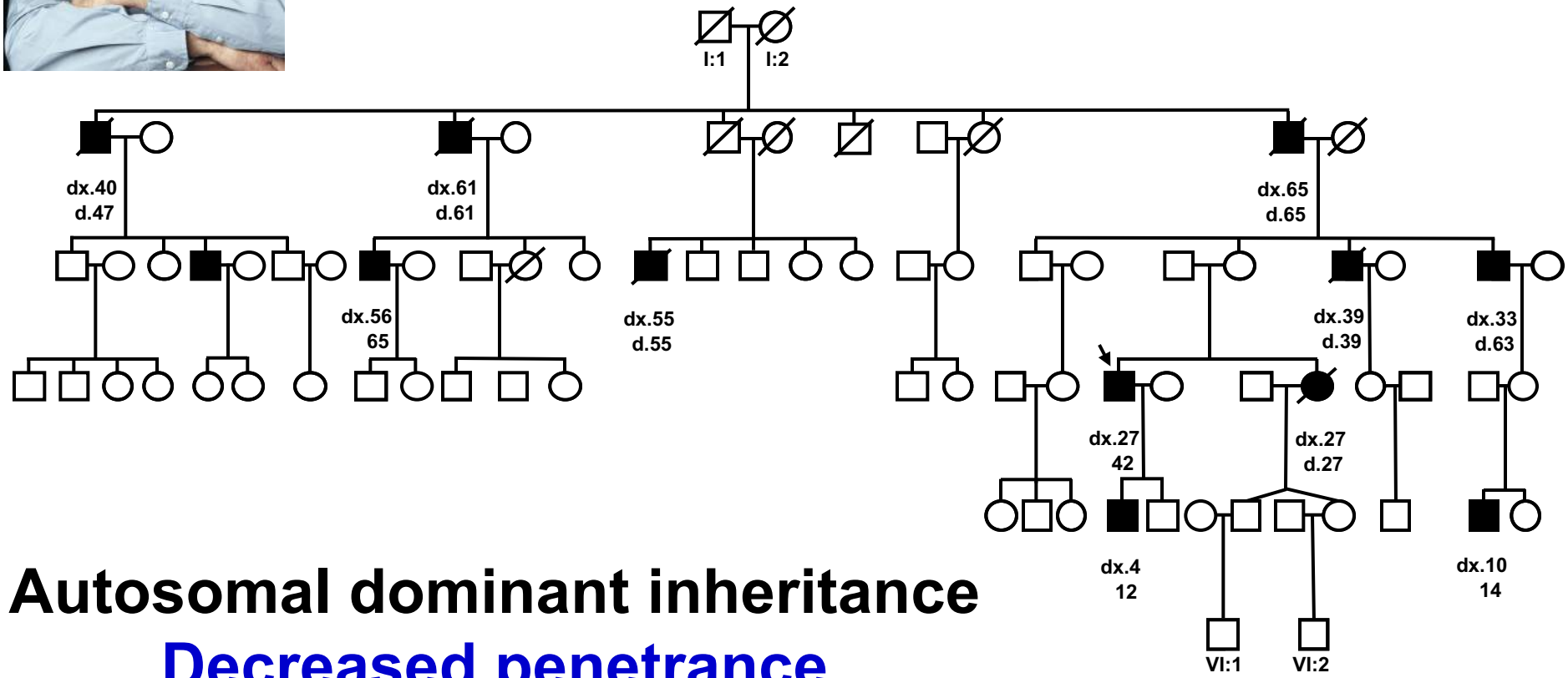


Ocular

Ectopia Lentis

Thoracic Aortic Aneurysms and Dissections

20% of patients with TAAD have a first-degree relative with TAAD



Autosomal dominant inheritance

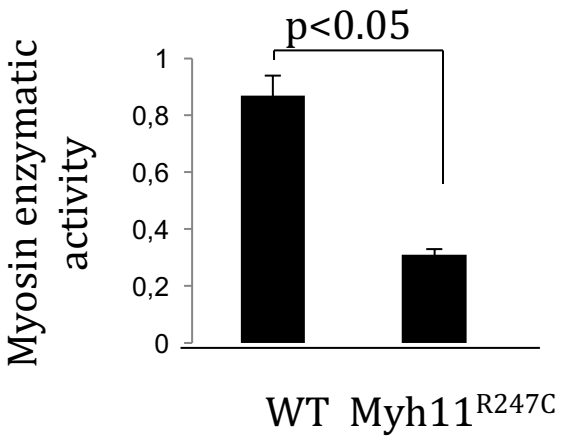
Decreased penetrance

Variable expression

R247C Variant Alters Myosin Function but Does Not Cause Aortic Disease

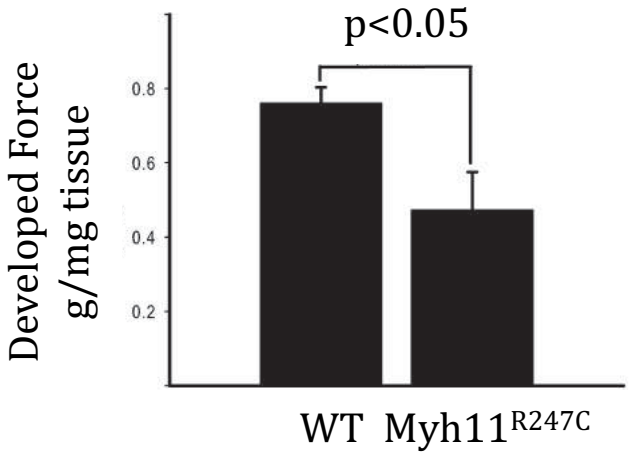
In vitro

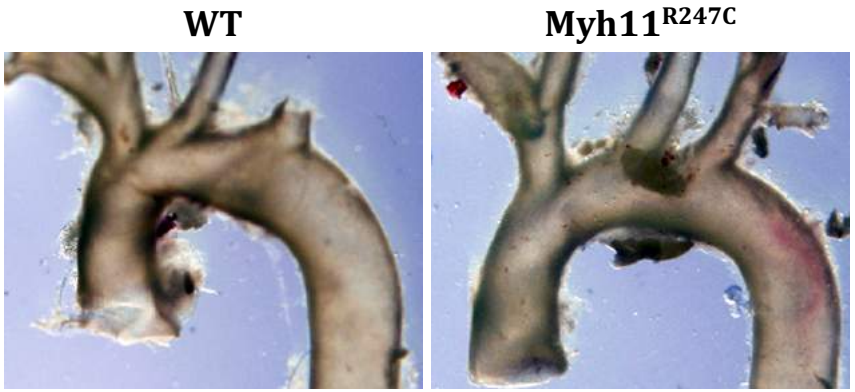
Baculovirus expression

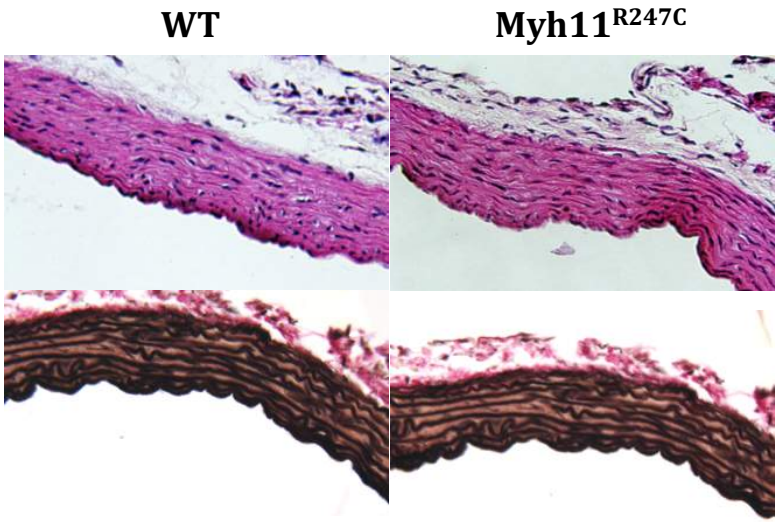


In vivo

Aortic Ring Contraction







In vitro assays- Sweeney lab (Penn), Aortic contractility- Stull lab (UTSW), Knockin model generation- Shao-Qing Kuang, PhD (UT Healt

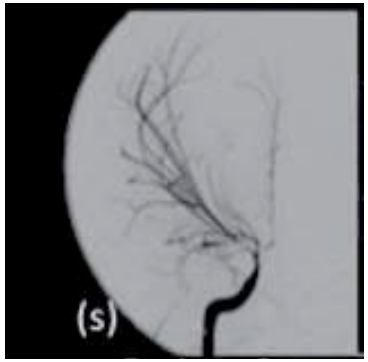
ACTA2 Mutations

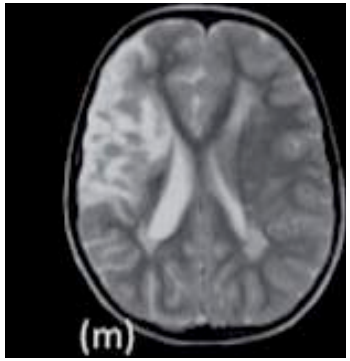
Responsible for 10 - 14% familial TAAD

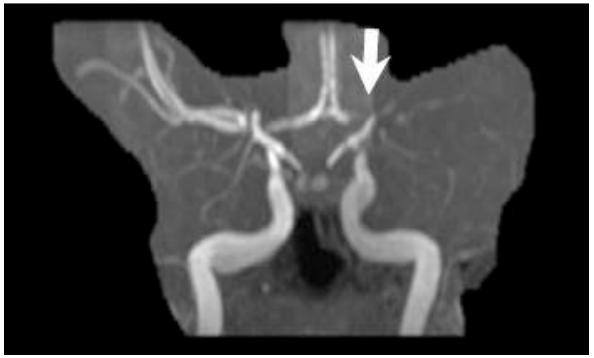
No Marfan-like syndromic features

PDA and other vascular diseases
Type A and B aortic dissections

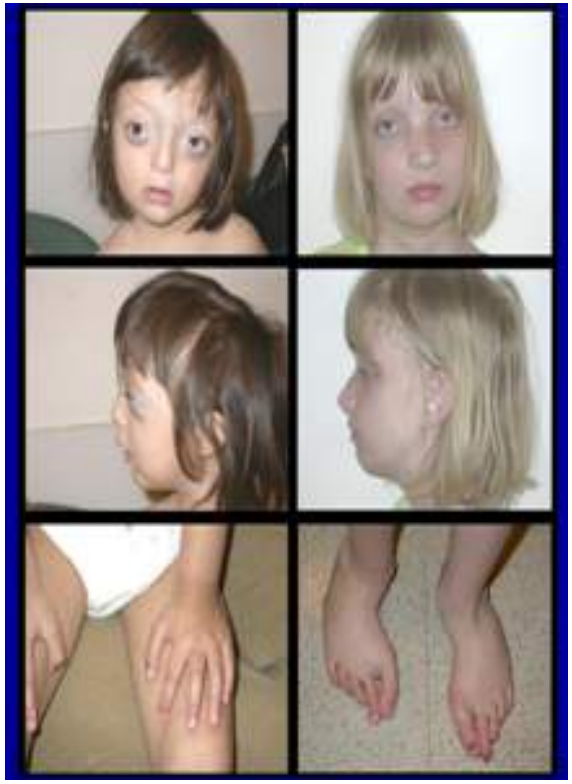
ACTA2 Mutations: Early Onset Coronary Artery Disease and Moyamoya Disease



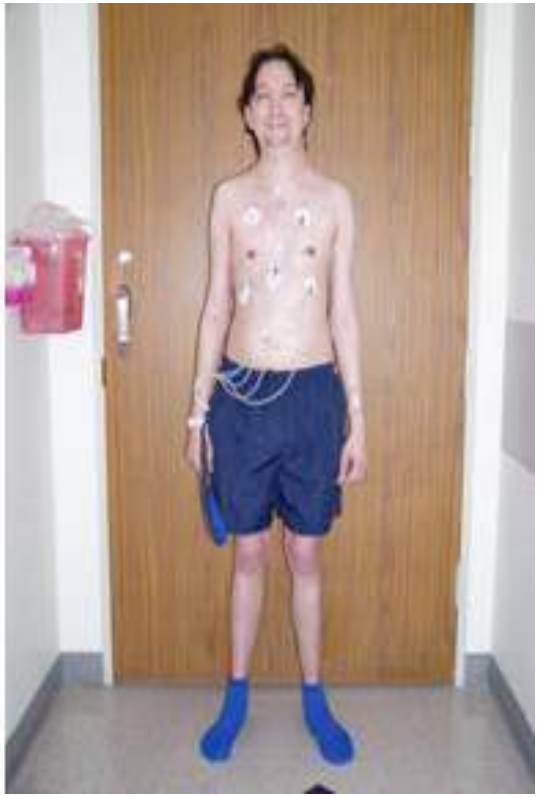




TGFBR2 and *TGFBR1* mutations: Variable spectrum of disease

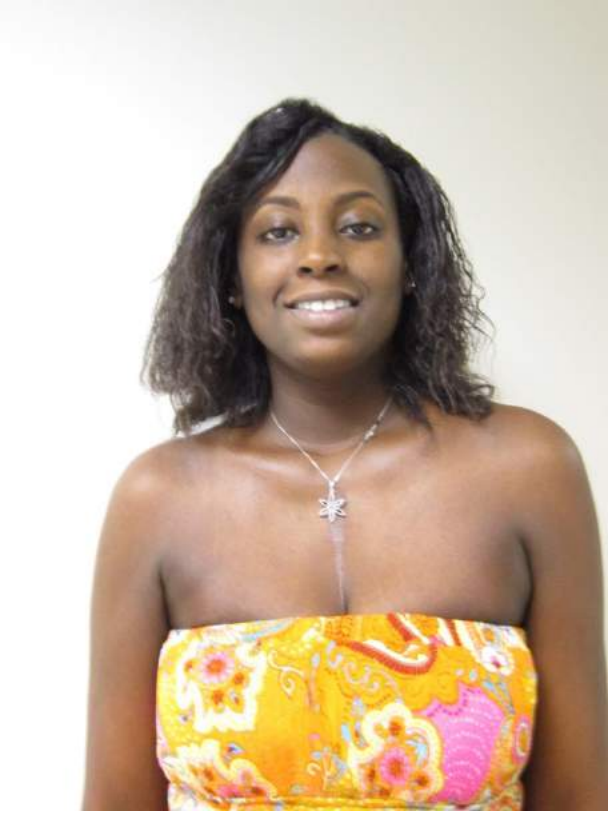


Loeys-Dietz Syndrome



Marfan Syndrome

"Marfan syndrome type 2"



Familial TAAD

No syndromic features

GenTac

National Heart, Lung, and Blood Institute

Accessible Search Form

NHLBI Entire Site | SEARCH

Public | Health Professionals | Researchers | Clinical Trials | News & Resources | About NHLBI

Home » Researchers » Research Resources » National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC)

Researchers

FUNDING

TRAINING & CAREER DEVELOPMENT

DIVISION OF INTRAMURAL RESEARCH

RESEARCH RESOURCES

RESEARCH MEETING SUMMARIES

TECHNOLOGY

National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC)

Home | About | The Team | Research | More...

The GenTAC Registry was established in 2006 to collect information from eligible patients with genetic conditions that predispose them for thoracic aortic aneurysms to assist physicians and researchers in understanding the link between genes, aortic aneurysms, and heart disease. The Registry includes de-identified medical data, clinical images, and biological samples of about 3,700 patients and is available for research at no cost to qualified investigators worldwide. The GenTAC Registry concluded in 2016. Several new registries formed to continue longitudinal data collection on GenTAC cohort and to enroll additional patients. Information about these registries is available here.

If you wish to use GenTAC data, images or biological samples, apply here via the BioLINCC.

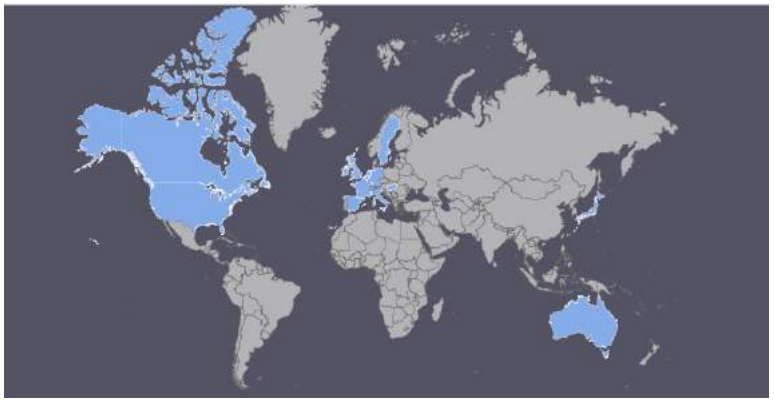
Scientists are learning more every day about how genes play a role in our health.

Our genetic makeup, or DNA, can influence whether we have a higher or lower risk of certain conditions, such as heart and cardiovascular disease.

View GenTAC podcasts that highlight genetics, imaging and surgery options for thoracic aortic disease, and research done using GenTAC data, biospecimens or images.

Montalcino Aortic Consortium (MAC)

MAC Sites and Investigators



Inclusion criteria:
Any patient or family member with a pathogenic or non-benign variant in the known HTAD genes

MAC Houston Administrative Center
Contact the Study Coordinator:
Ellen Hostetler
Tel 713 500 6843
Email ellen.m.hostetler@uth.tmc.edu

United States
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R Pyeritz, MD, PhD

A Braverman, MD
SA Morris, MD
RB Devereux, MD
J Grima, PhD
R Lacro, MD
SA LeMaire, MD
A Levin, MD

D Liang, MD, PhD

I Maumenee, MD
R Moran, MD
F Ramirez, PhD

P Robinson, MD

L Sakai, PhD
D Sallee, MD
S Shalhub, MD, MPH
A Yetman, MD

MN Singh, MD
ES Regalado, MS
MA Hofmann Bowman, MD, PhD
AM Crean, MD
J Bavaria, MD
A Psychogios, MD
V Kalahasti, MD

Europe
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A De Paepe, MD, PhD

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L Muiño-Mosquera, MD
G Jondeau, MD, PhD
C Boileau, PhD
F Labombarda, MD
L Faivre, MD, PhD

C Bouleti, MD, PhD

O Milleron, MD
Y von Kodolitsch
M Rybczynski, MD

Z Szabolcs, MD PhD MSc
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M Groenink, MD, PhD
A Evangelista, MD
G Teixido-Tura , MD, PhD
B Carlberg, MD, PhD

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A Pitcher, MRCP, PhD

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I El-Hamamsy, MD, PhD
D Chitayat, MD
B Fernandez, MD
G Horne, MD, PhD
N Poirier, MD
D Reinhardt, PhD
G Sandor, MD
D Human BA, BM. BCh
M Ouzounian , MD PhD

Australia
L Ades, MD
R Jeremy, MB BS PhD

Japan
H Morisaki, MD, PhD
T Morisaki, MD, PhD

MAC Aims: Evidence-based Diagnosis and Management of HTAD

- Establish a large **cohort** of patients with **mutations in the HTAD genes** and collect patient data
- Define the natural and clinical history of HTAD
- Characterize the **disease risk** associated with the HTAD **genes** and **mutations**
- Identify factors that **modify** risk
- Make the **MAC resource** available to investigators for further research and drug and device trials
- Address classification of disease genes

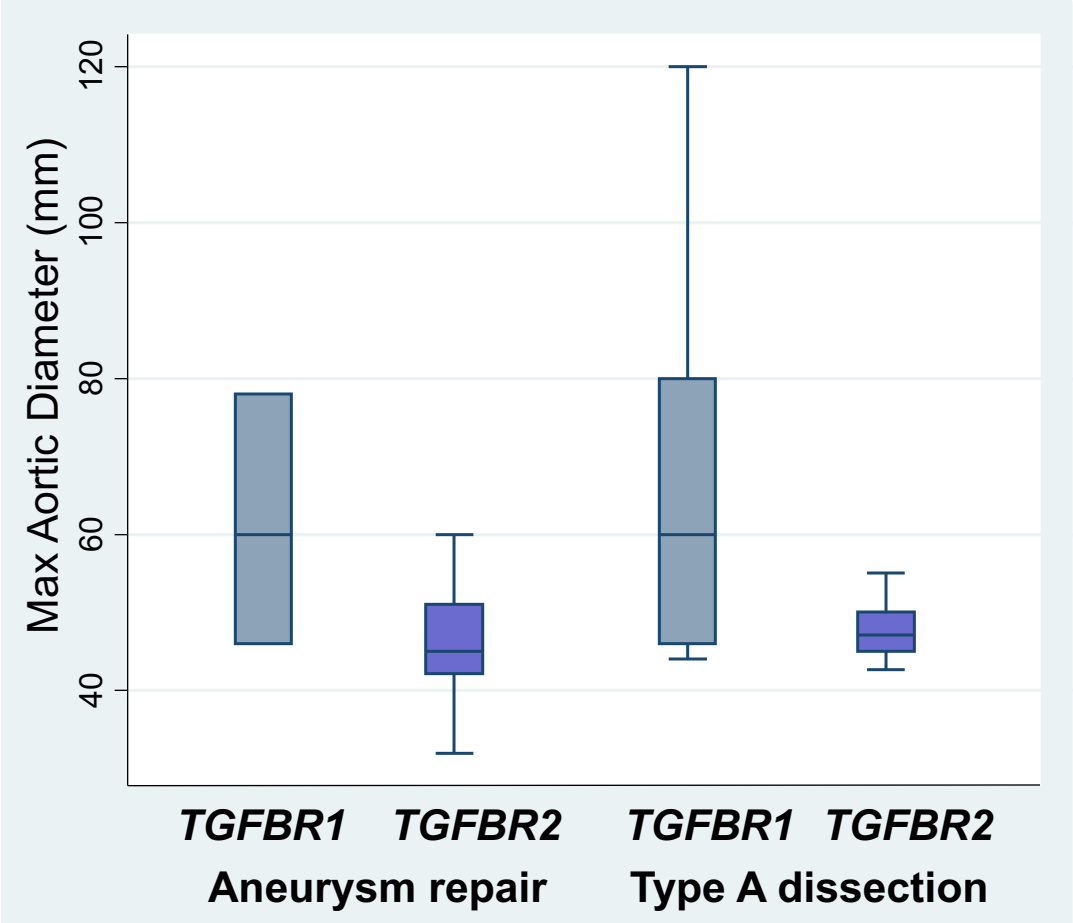
HTAD Cases in MAC
N = 987

Gene	Frequency
ACTA2	319 (32%)
PRKG1	37 (4%)
SMAD3	190 (19%)
TGFBR1	176 (18%)
TGFBR2	265 (27%)

Systemic features associated with *TGFBR1* and *TGFBR2* mutations

	TGFBR1	TGFBR2	p
Marfan systemic score mean (SD)	3.98 (3.44)	4.12 (2.94)	0.7
Systemic score >=7	28/128 (21.9%)	34/183 (18.6%)	0.6
Hypertelorism	36/138 (26%)	62/199 (31%)	0.3
Broad or bifid uvula	36/139 (26%)	72/219 (33%)	0.2
Arched palate	48/136 (35%)	109/229 (48%)	0.02
Craniosynostosis	11/118 (9%)	20/190 (11%)	0.8
Translucent skin	63/144 (43%)	78/227 (34%)	0.08
Wide scars	33/142 (23%)	62/218 (28%)	0.3
Head and neck arterial tortuosity	53/104 (51%)	72/133 (54%)	0.8
Cardiac defect (BAV, VSD, PDA)	13/154 (8.4%)	52/238 (21.8%)	<0.001
Mitral valve prolapse	36/156 (23%)	65/244 (27%)	0.5

Aortic Root Diameter at Surgery or Dissection (UTH data)



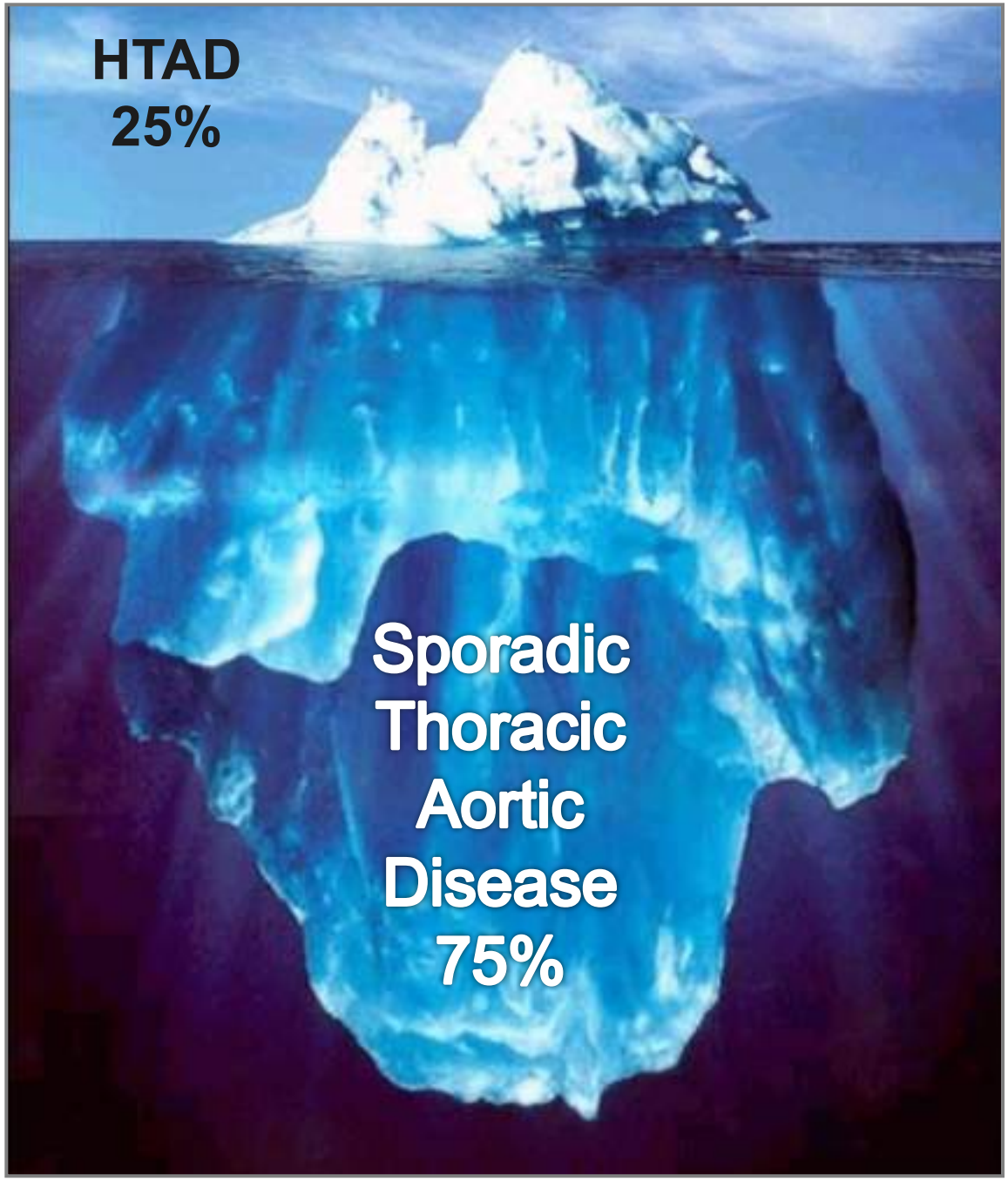
Does the Type of Aortic Event Differ Between Genes?

	FBN1	TGFBR1[6]	TGFBR2	ACTA2[7]	SMAD3
No. of individuals	243	176	265	277	190
Mean age (SD)	30 (16)			38 (20)	41 (17)
Aortic event	30%	40%	45%	48%	37%
Aortic dissection	42%	50%	47%	88%	74%
Type A‡	74%	89%	71%	61%	71%
Mean Age	39 ± 9		34 ± 17	36 ± 12	44 ± 16
Type B	26%	11%	29%	24%	12%
Mean Age	44 ± 10		38 ± 14	29 ± 12	53 yrs ± 15
Aneurysm repair	58%	50%	53%	12%	26%
Mean Age	39 ± 13	33 ± 16	26 ± 16	33 ± 18	46 ± 17
Cumulative risk of aortic event	74% at 60 yrs	100% at 80 yrs	100% at 90 yrs	76% at 85 yrs	86% at 81 yrs

Connective Tissue Disorder

Genetically Triggered Aneurysm (GenTac)

Heritable Thoracic Aortic Disease (HTAD)


HTAD
25%
Sporadic
Thoracic
Aortic
Disease
75%

TGF-β Pathway Gene

ECM Genes

5.0-5.5 cm (Standard)

ECM Genes	SMC Genes
BGN	*FLNA*
A2	*FOXE3*
A1	*MAT2A*
A2	TGF-β Pathway Genes
P2	*SKI*
N1	*SLC2A10*
2	*SMAD2*
	SMAD4
P5	*TGFB3*
	Other Genes
	NOTCH1

4.0-4.5

TGFBR1 (L

TGFBR2 (L

SMAD3 (L

≤ 5.0 cm

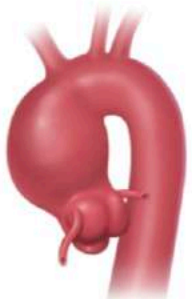
FBN1 (MFS)

COL3A1 (EDS)

3.5

Asce

5.5 cm



SMC Contractile Unit Genes

4.5-5.0 cm

ACTA2

MYH11

MYLK

PRKG1

TGF-β Pathway Genes

4.5-5.0 cm

TGFB2 (LDS 4)

stein, Elefteriades. Aorta. 2017, 5 (1):11-20

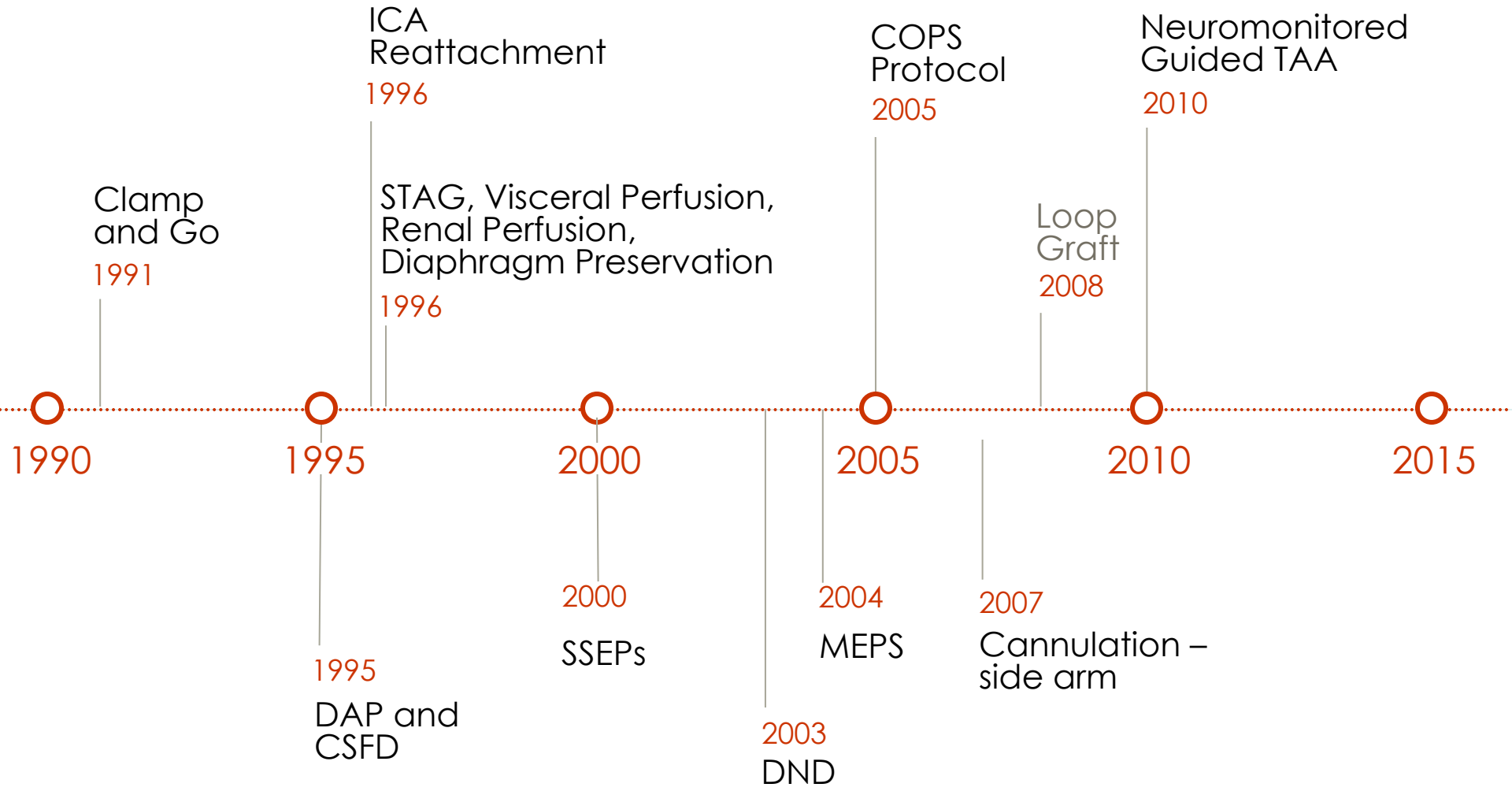
Although we don’t own the patient, we should own the disease.

Differences in outcomes when repairing TAAA in HTAD?

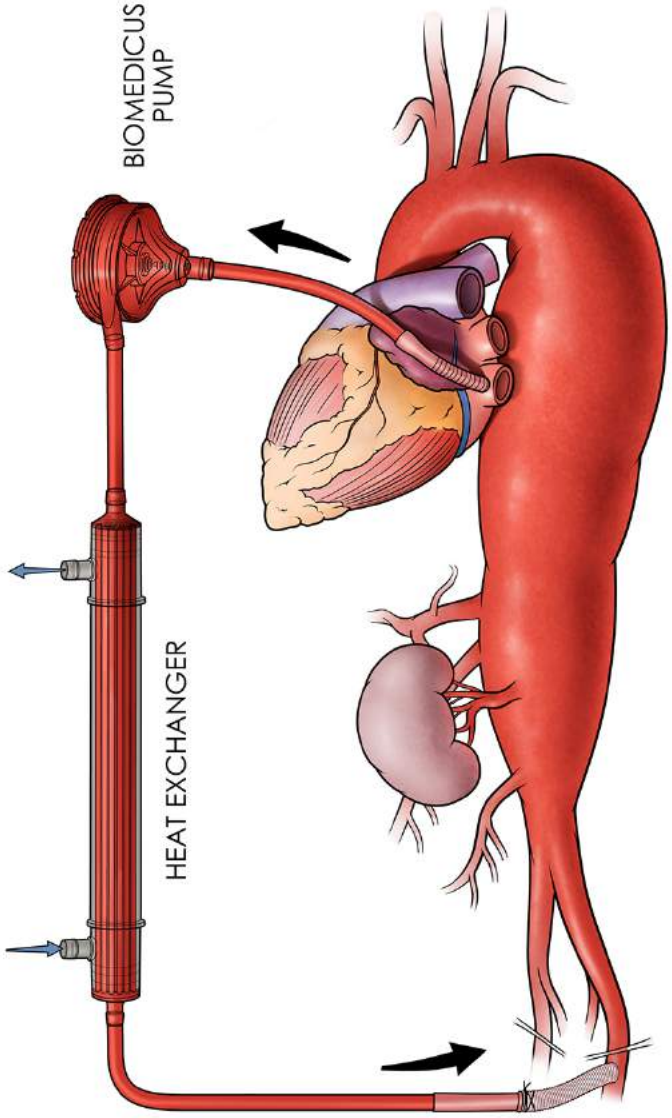
Marfan TAAA open surgical repair

Author	N	Dissection (acute)	Resp failure	Persistent SCI	Bleeding reop	In-hospital mortality	8-yr survival	8-yr Freedom From reop
Omura 2012 Japan	20	100% (0%)	5%	0%	5%	0%	91%	86%
Coselli 2016 USA	127	100% (9%)	38%	2%	8%	4%	75%	86%
Mommertz 2008 Netherlands	22	100% (0%)	9%	0%	5%	0%	100%	100%
UTH 2014 USA	78	100%	9%	4%	4%	5%	86%	88%

TAAA Modifications

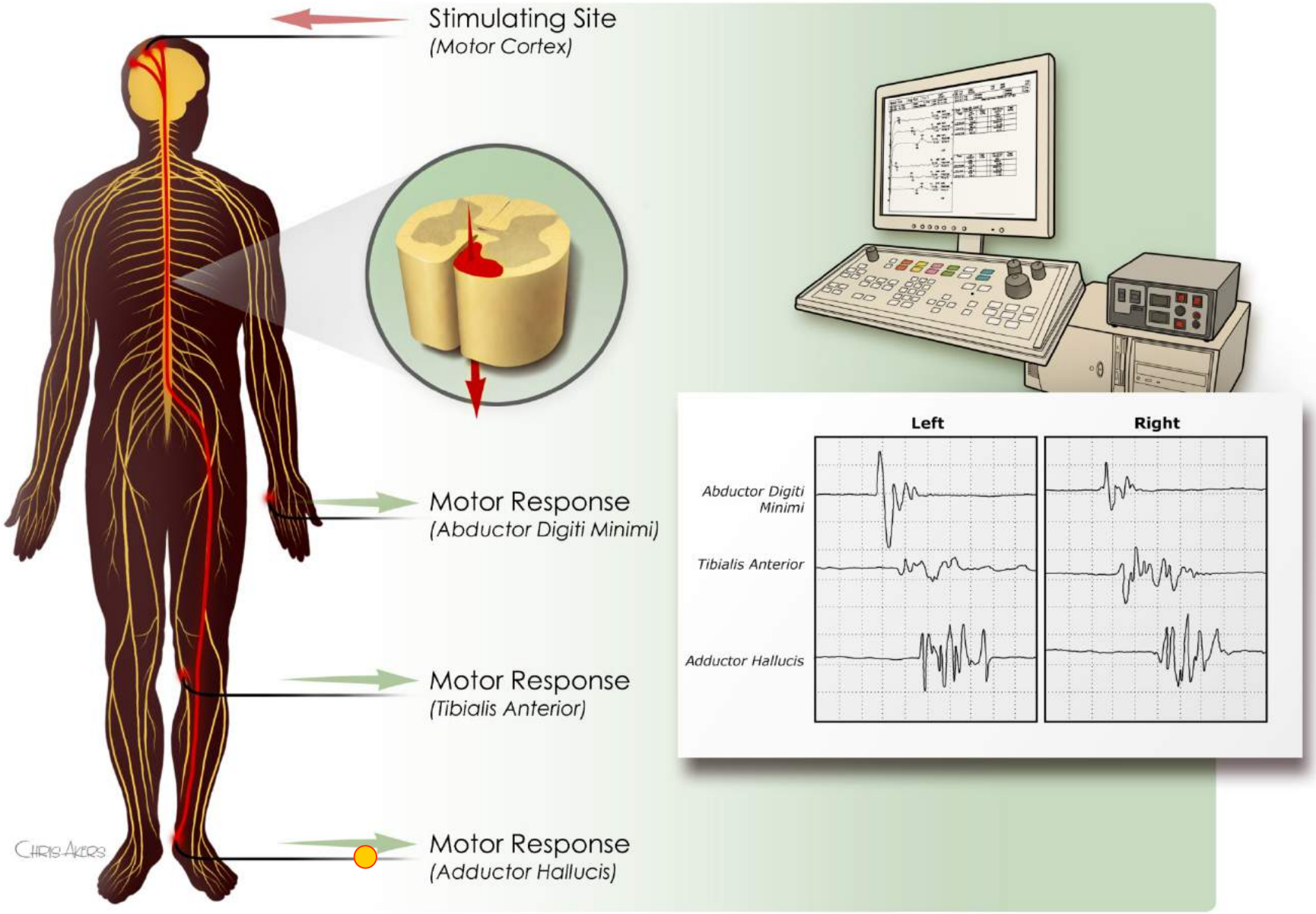


Approach

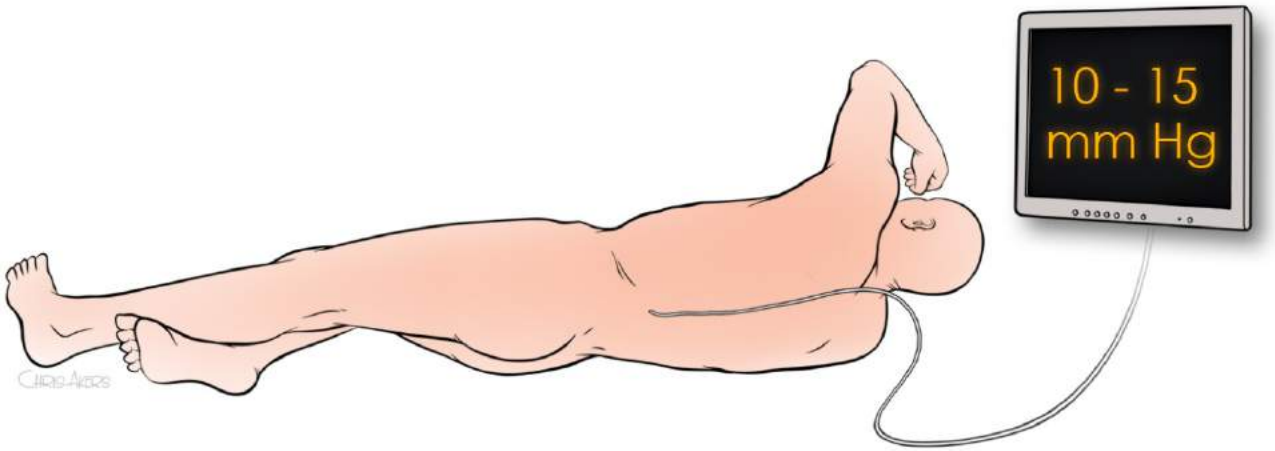


- CSFD
- DAP
- Moderate Hypothermia
- Sequential Clamp
- Reattach patent ICA 8-12

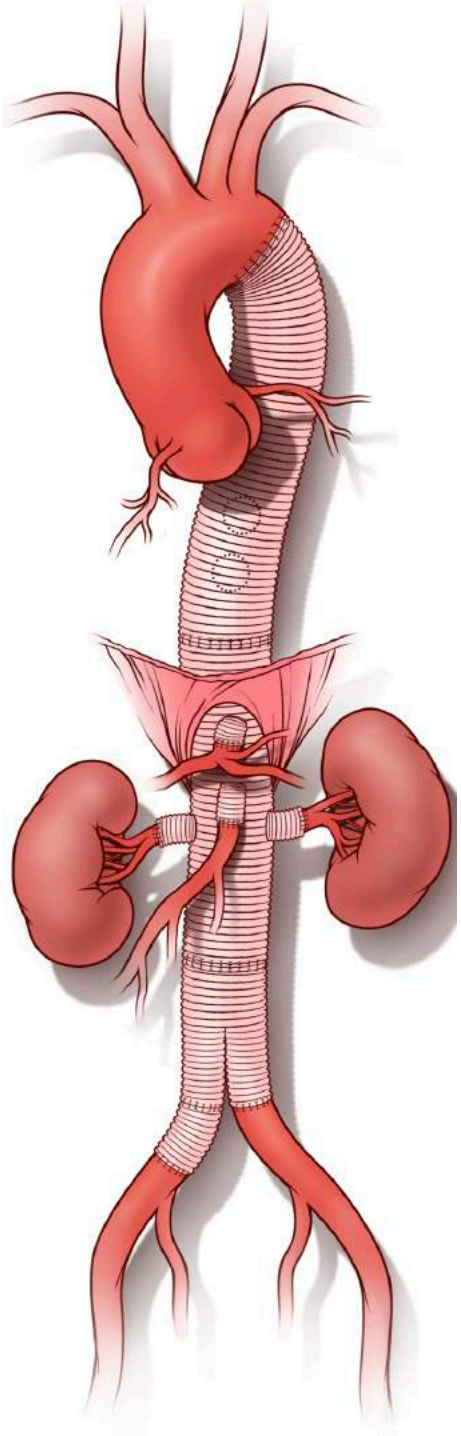
Motor


Stimulating Site
(Motor Cortex)
Motor Response
(Abductor Digiti Minimi)
Motor Response
(Tibialis Anterior)
Motor Response
(Adductor Hallucis)
Chris Akers
Left
Right
Abductor Digiti Minimi
Tibialis Anterior
Adductor Hallucis

Paraplegia Prevention: OR

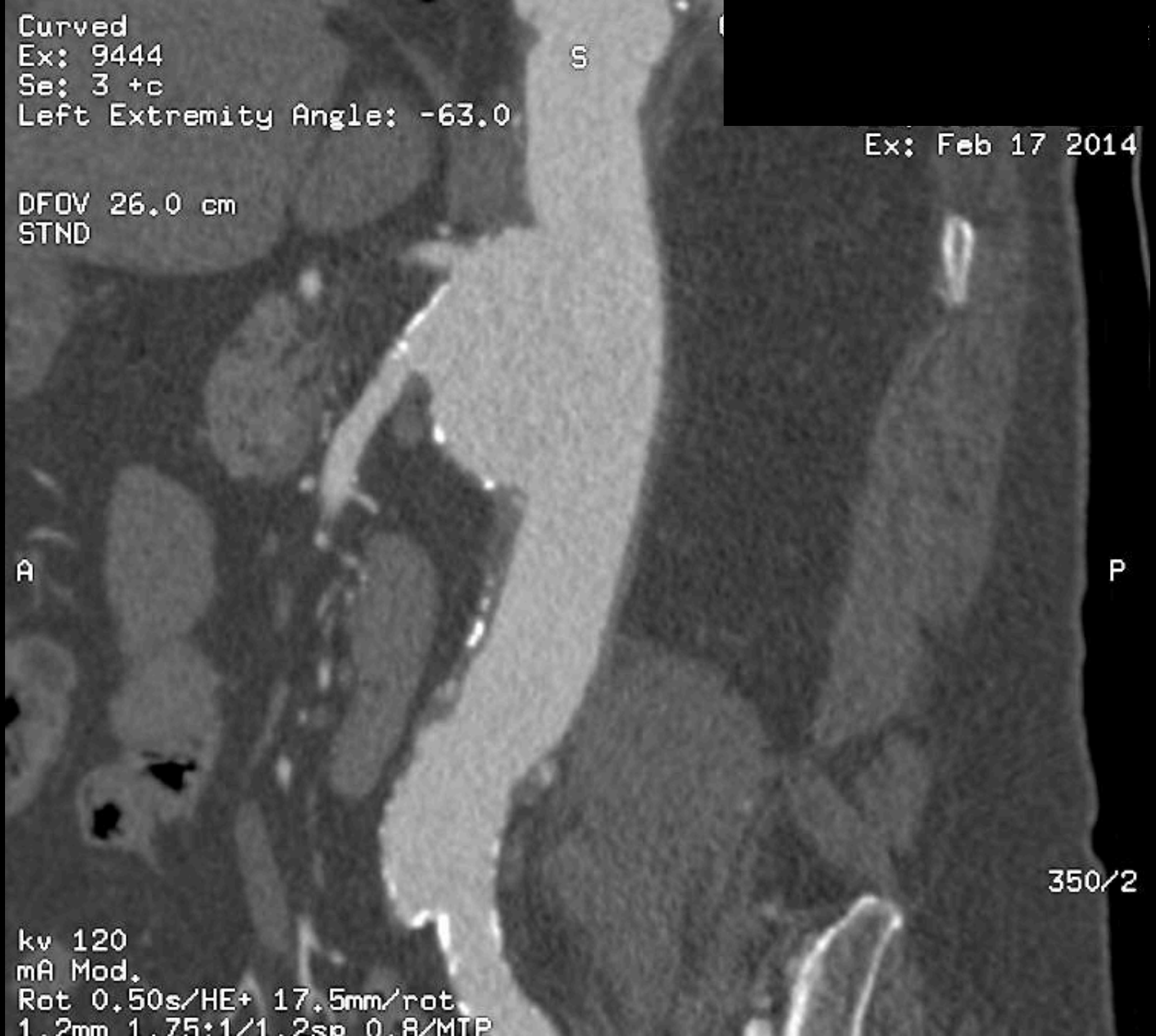


- Maintain CSF pressure <10 mmHg:
  - Intermittent manual gravity drainage
- Monitor SSEPs and MEPs
- Systolic BP >130 mmHg
- Maintain Spinal Cord Perfusion Pressure >120 mmHg



Conduct

- Proximal Anastomosis
- ICA reattachment
- Visceral/Renal
- Distal Anastomosis


Curved
Ex: 9444
Se: 3 +c
Left Extremity Angle: -63.0
S
Ex: Feb 17 2014
DFOV 26.0 cm
STND
A
P
350/2
kv 120
mA Mod.
Rot 0.50s/HE+ 17.5mm/rot
1.2mm 1.75:1/1.2sp 0.8/MIP

Redo Thoracoabdominal Aortic Aneurysm Repair: A Single-Center Experience Over 25 Years

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Department of Cardiothoracic and Vascular Surgery, McGovern Medical School at The University of Texas Health Science Center at Houston (UTHealth), Memorial Hermann Heart & Vascular Institute, Houston, Texas

Background. Aortic disease is a lifelong, progressive illness that may require repeated intervention over time. We reviewed our 25-year experience with open redo thoracoabdominal aortic aneurysm (TAAA) and descending thoracic aortic aneurysm (DTAA) repair. Our objectives were to determine patient outcomes after redo repair of DTAA/TAAA and compare them with nonredo repair. We also attempted to identify the risk factors for poor outcome.

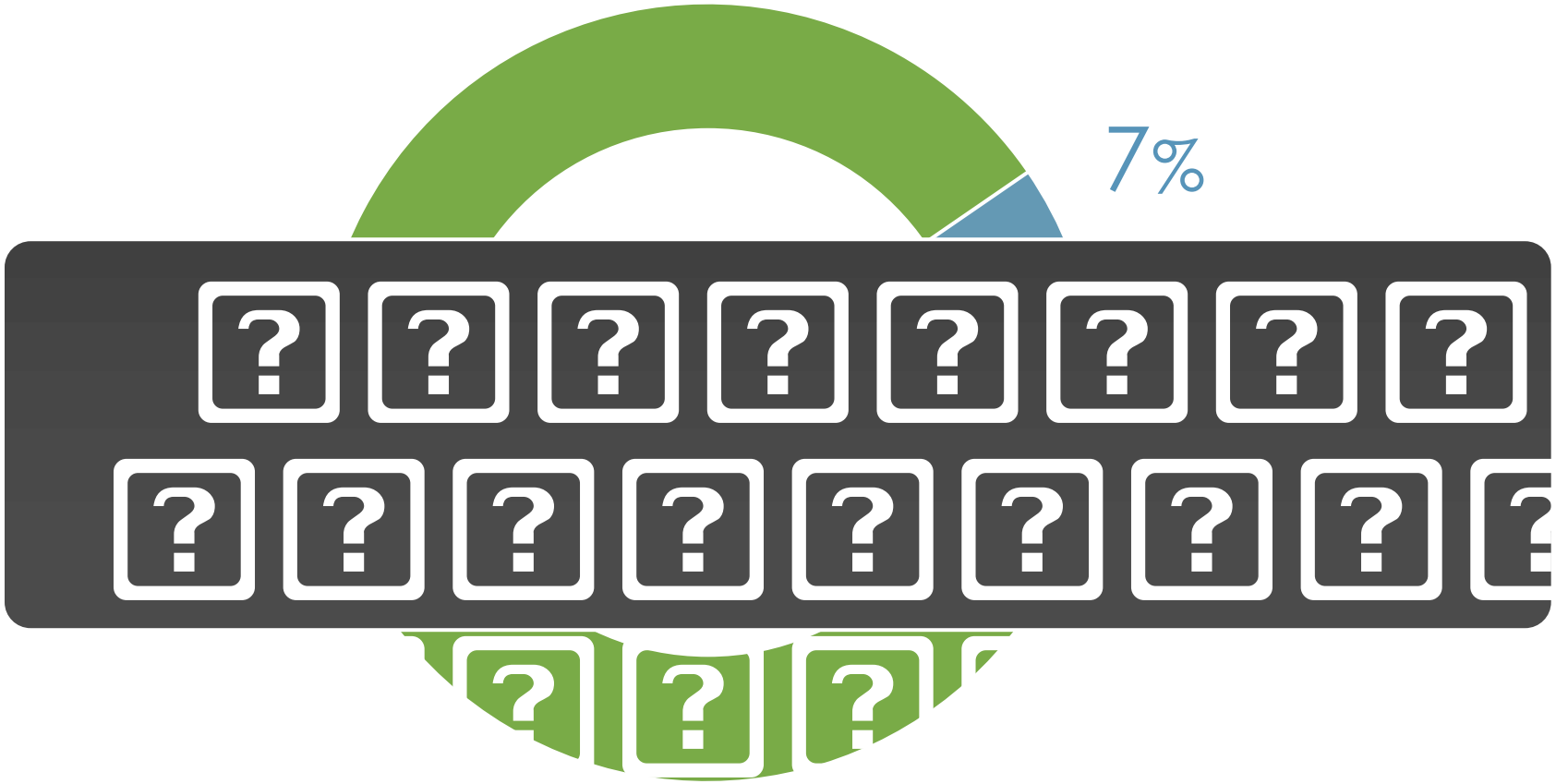
Methods. We reviewed all open redo TAAA and DTAA repairs between 1991 and 2014. Patient characteristics, preoperative, intraoperative variables, and postoperative outcomes were gathered. Data were analyzed by contingency table and by multiple logistic regression.

Results. We performed 1,900 open DTAA/TAAA repairs, with 266 (14%) being redos. Redos were associated with younger age (62 ± 16.4 years vs 64.5 ± 13.4 years, $p < 0.02$). Reasons for redo DTAA/TAAA were extension of the disease (86.8%), intercostal patch expansion (6.8%), visceral patch expansion (10.9%), infection (4.5%), anastomotic pseudoaneurysm (8.3%), and previous endovascular aortic repair complications (6.4%). Extent IV TAAA was predominantly involved in redos (42.8% redo vs 14.6% nonredo, $p < 0.0001$). The early mortality rate was significantly higher in redo (61 of 266 [23%]). Long-term survival was significantly lower among redo compared with nonredo DTAA/TAAAs. A multivariable analysis using the significant risk factors for early death from the risk factors on univariate analysis found four preoperative variables were significant (age >70 years, glomerular filtration rate <48 mL/min per 1.73m^2, extent III TAAA, and emergency presentation) for predicting early death. In the presence of all four risk factors in a redo patient, a maximal risk of 82% for early death was predicted.

Conclusions. The need for a redo operation in DTAA/TAAA repair is common and most often presents as an extension of the disease into an adjacent segment. A hybrid or completely endovascular treatment should be considered in high-risk patients.

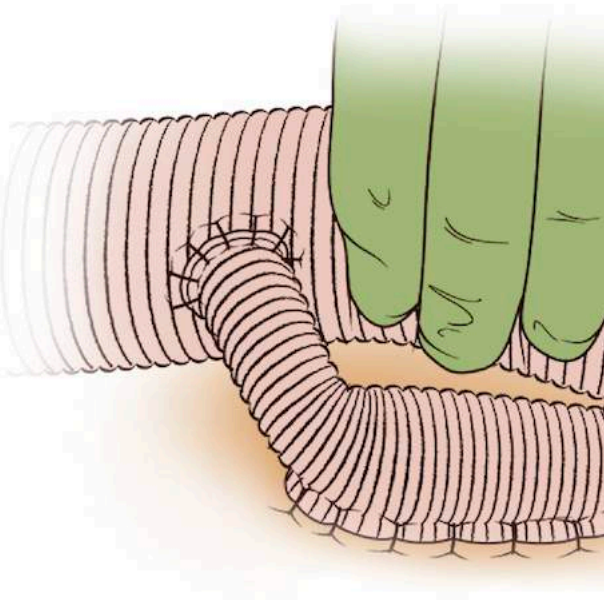
(Ann Thorac Surg 2017;103:1421–8)

Causes for Reoperation

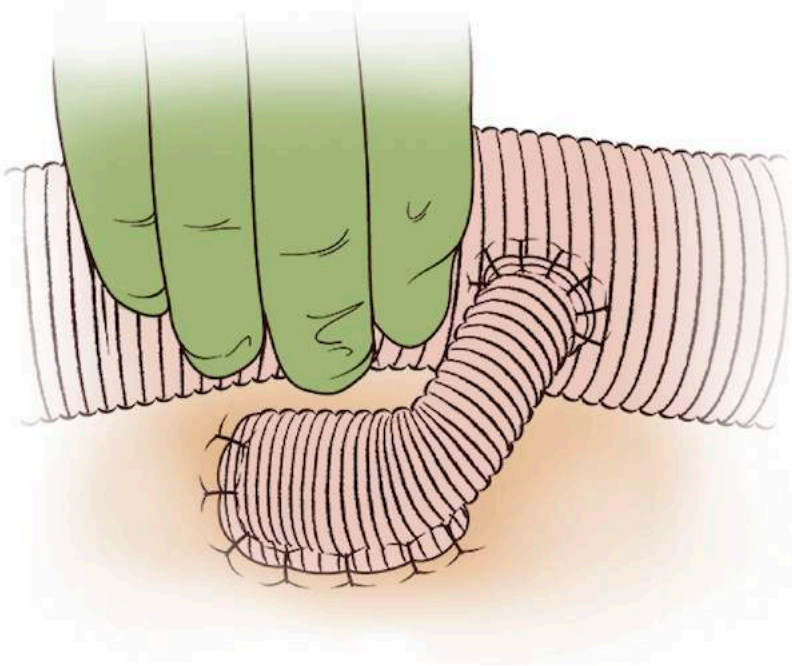


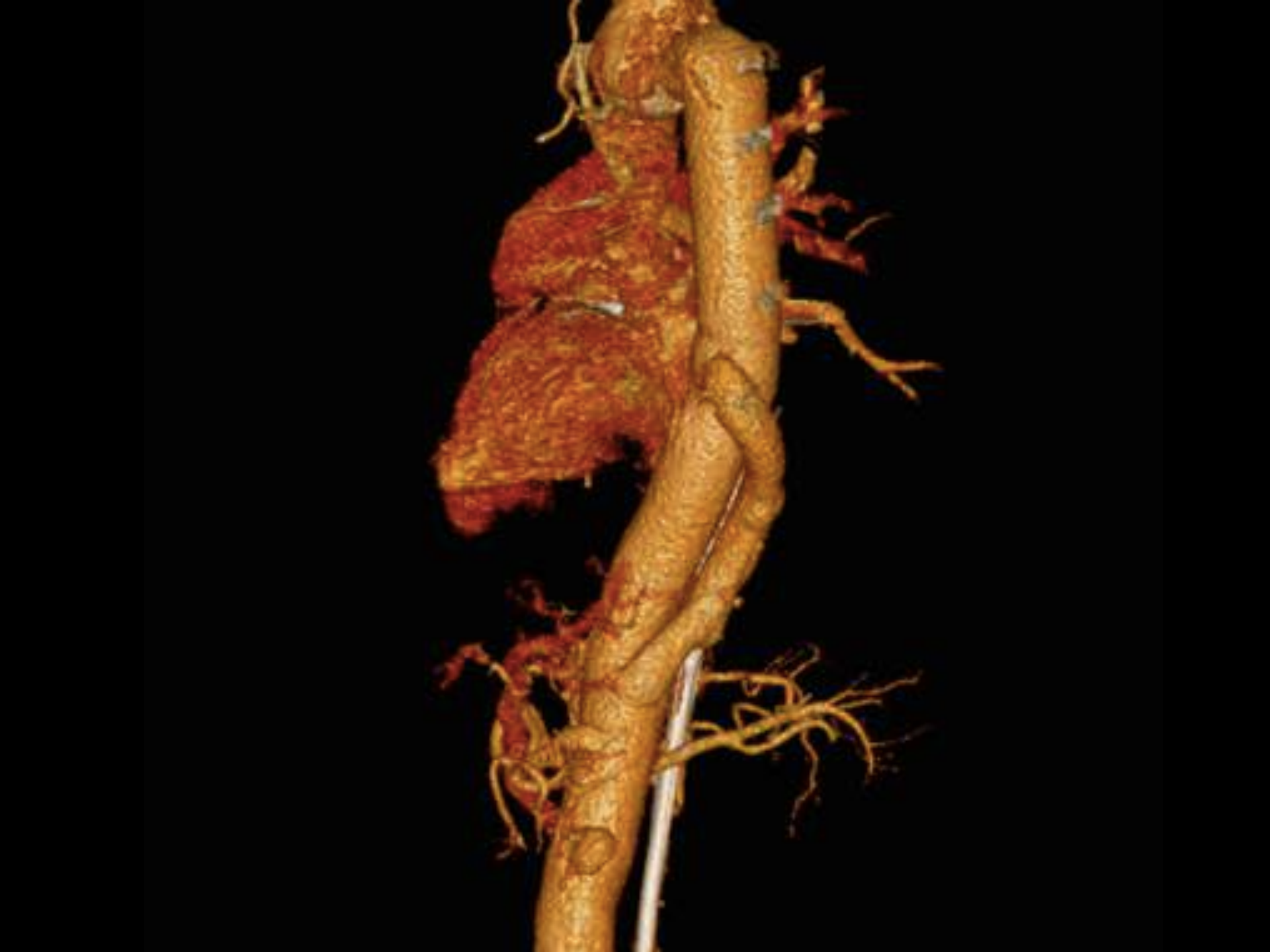
- Infective Pseudoaneurysm
- Pseudoaneurysm
- TEVAR Complication
- Aneurysmal Progression
- Intercostal Patch Enlargement
- Visceral Patch Enlargement

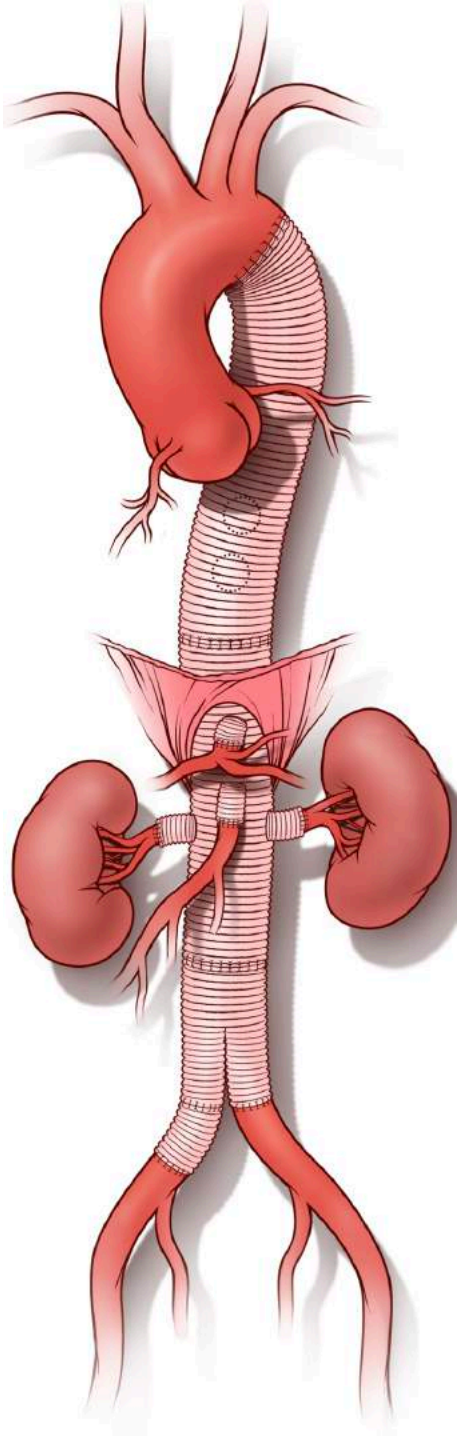
Intercostal Reattac a Loop Gr



Intercostal Reattachment with an End Graft



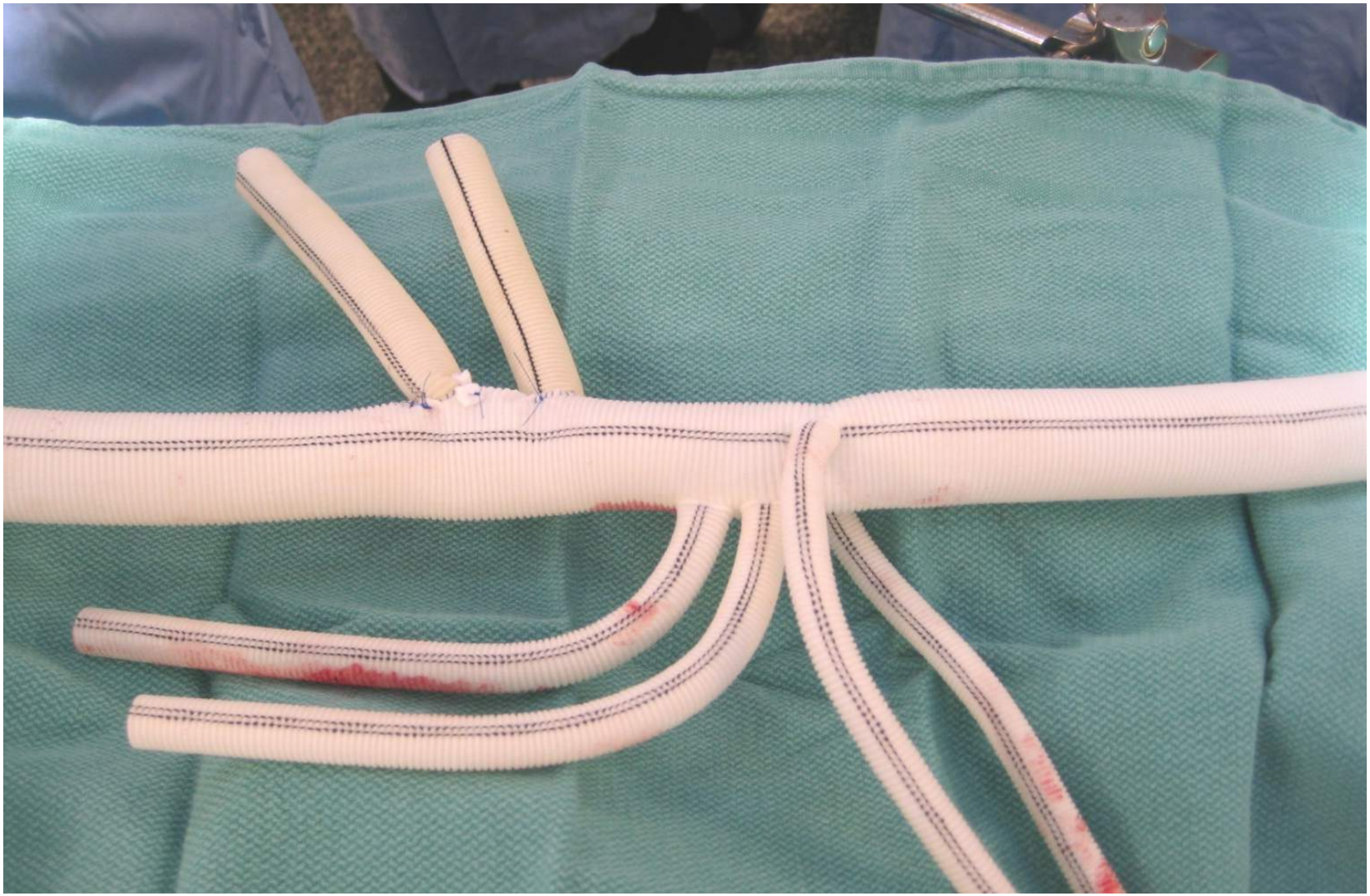




Conduct

- Proximal Anastomosis
- Distal Anastomosis
- Visceral/Renal
- ICA reimplant

STAG Graft



Eur J Vasc Endovasc Surg (2011) 41, 41—47

Operative Outcomes Using a Side-branched Thoracoabdominal Aortic Graft (STAG) for Thoraco-abdominal Aortic Repair

P. De Rango [a], A.L. Estrera [b,*], C. Miller III [b], T.-Y. Lee [c], K. Keyhani [b], S. Abdullah [b], H. Safi [b]

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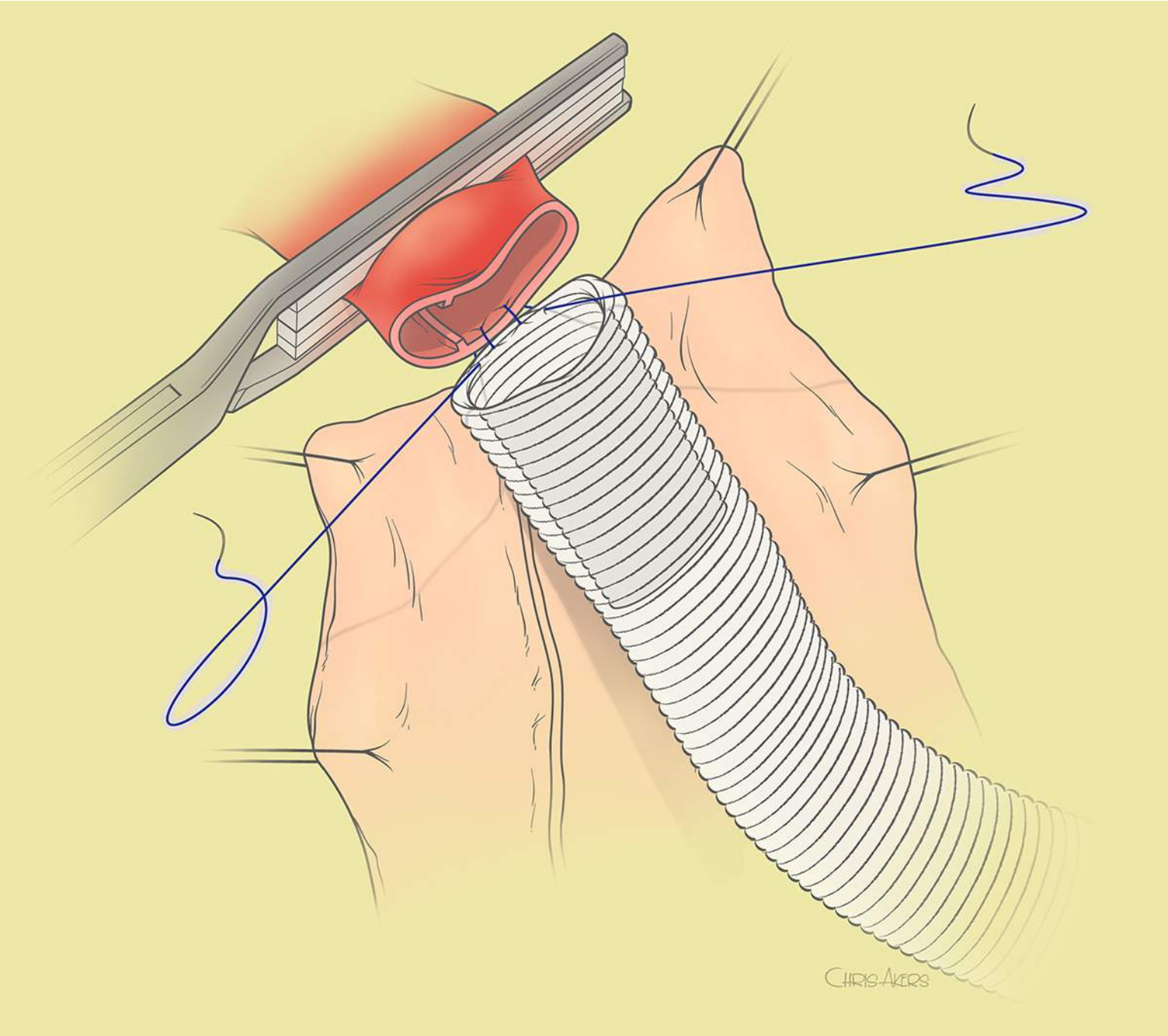
[c] *Department of Cardiovascular Surgery, Yonsei University College of Medicine, Seoul, South Korea*

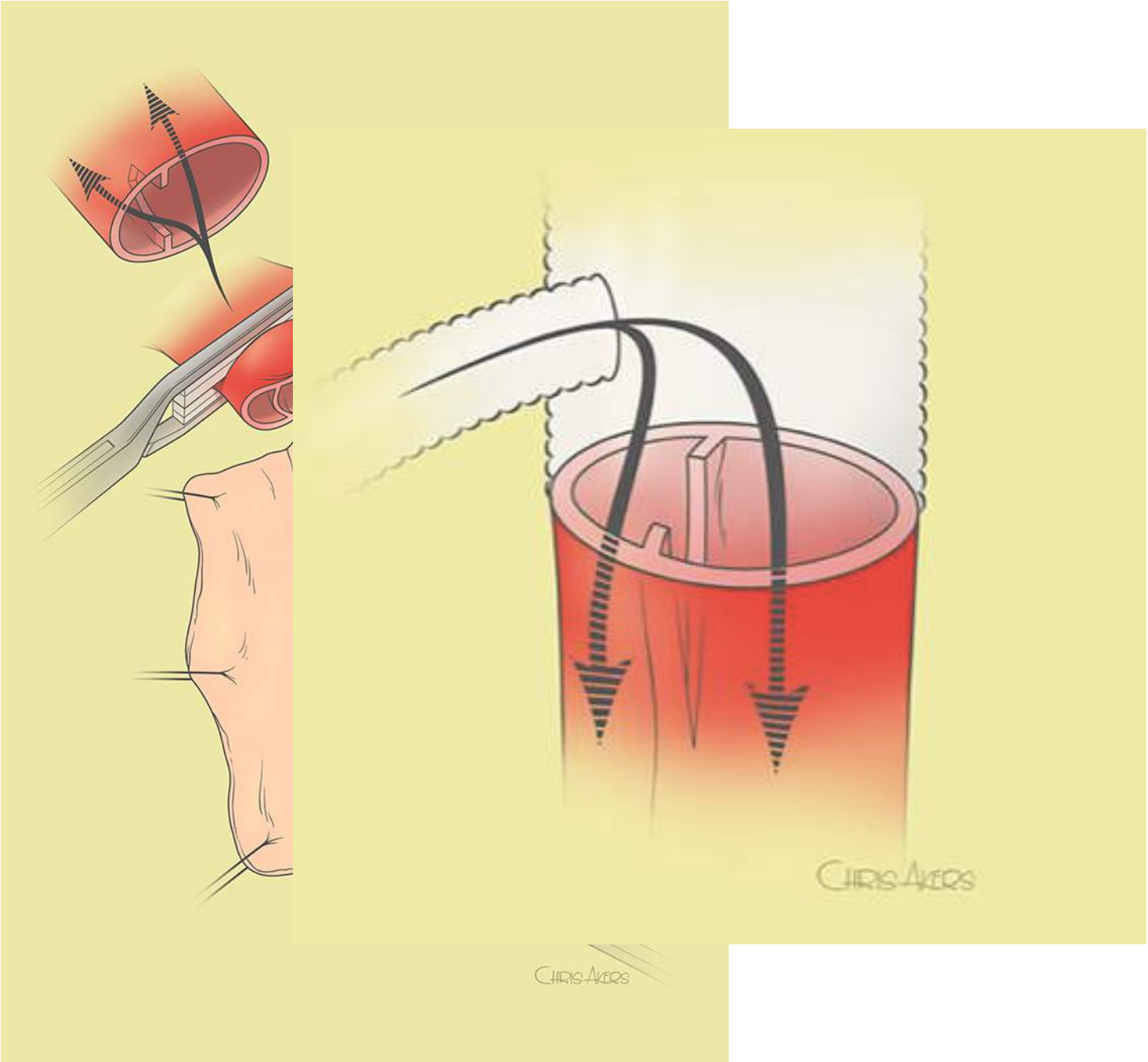
DeRango EJVES 2011

When to Use the STAG

- **TAAA Extent II, III, IV with:**
- **HTAD (Heritable Thoracic Aortic Disease)**
- **Young patients (Age < 70 years)**
- **Displaced Visceral & Renal Vessels**

  (>3 cm displacement)


CHRIS AKERS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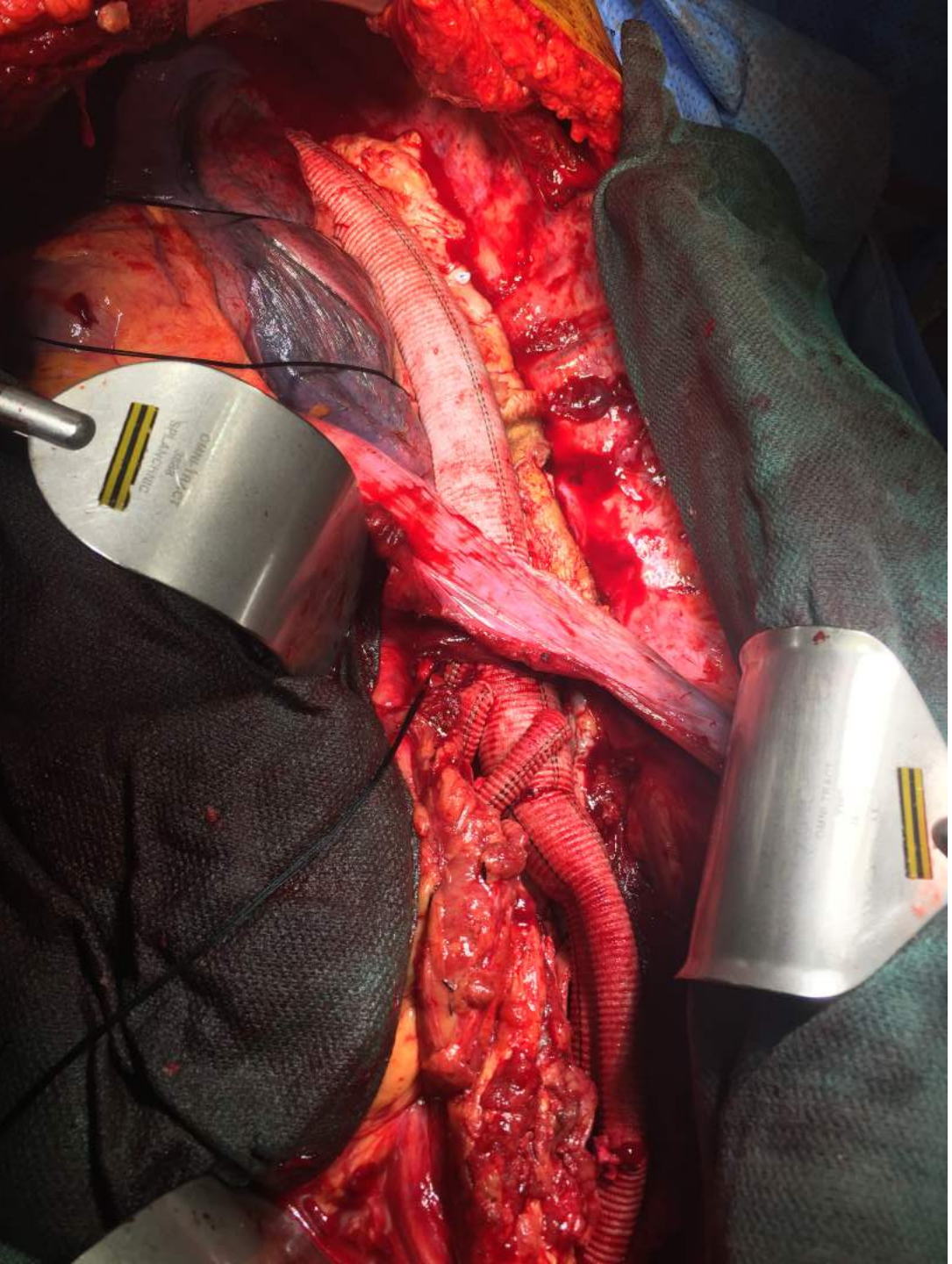
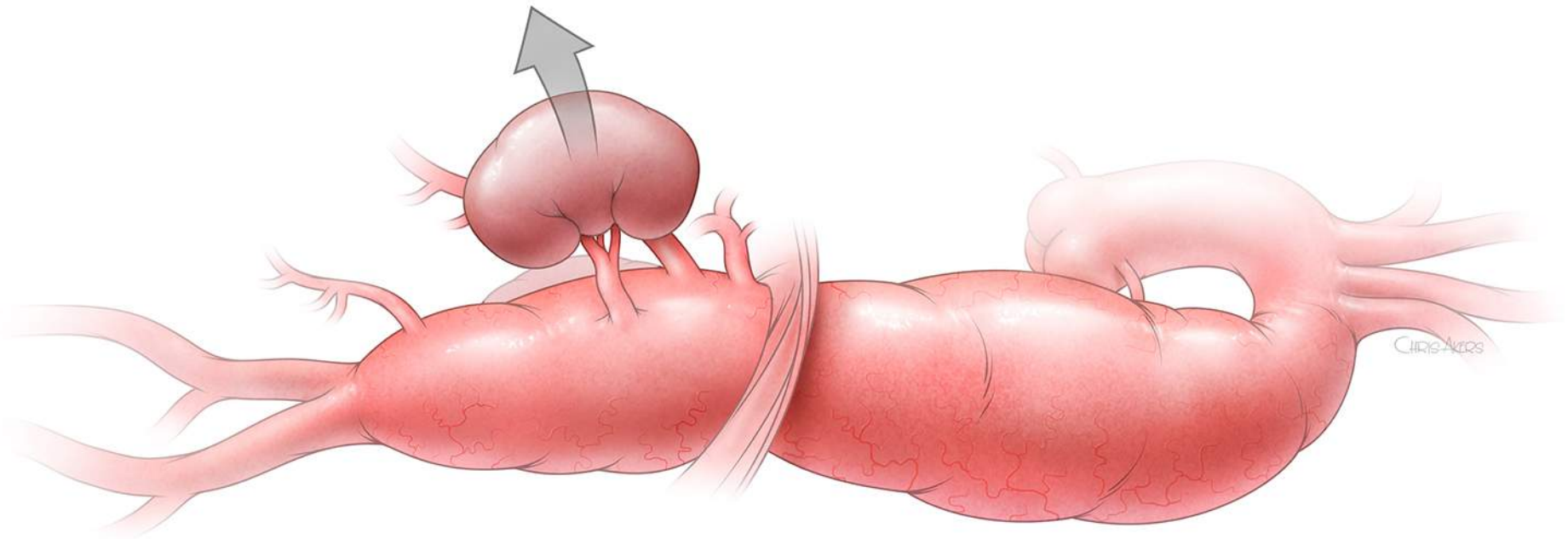
CHRIS AKERS



Prophylactic Repair

- Age
- Comorbidities
- Added Risks
- Risk of Reoperation
- TEVAR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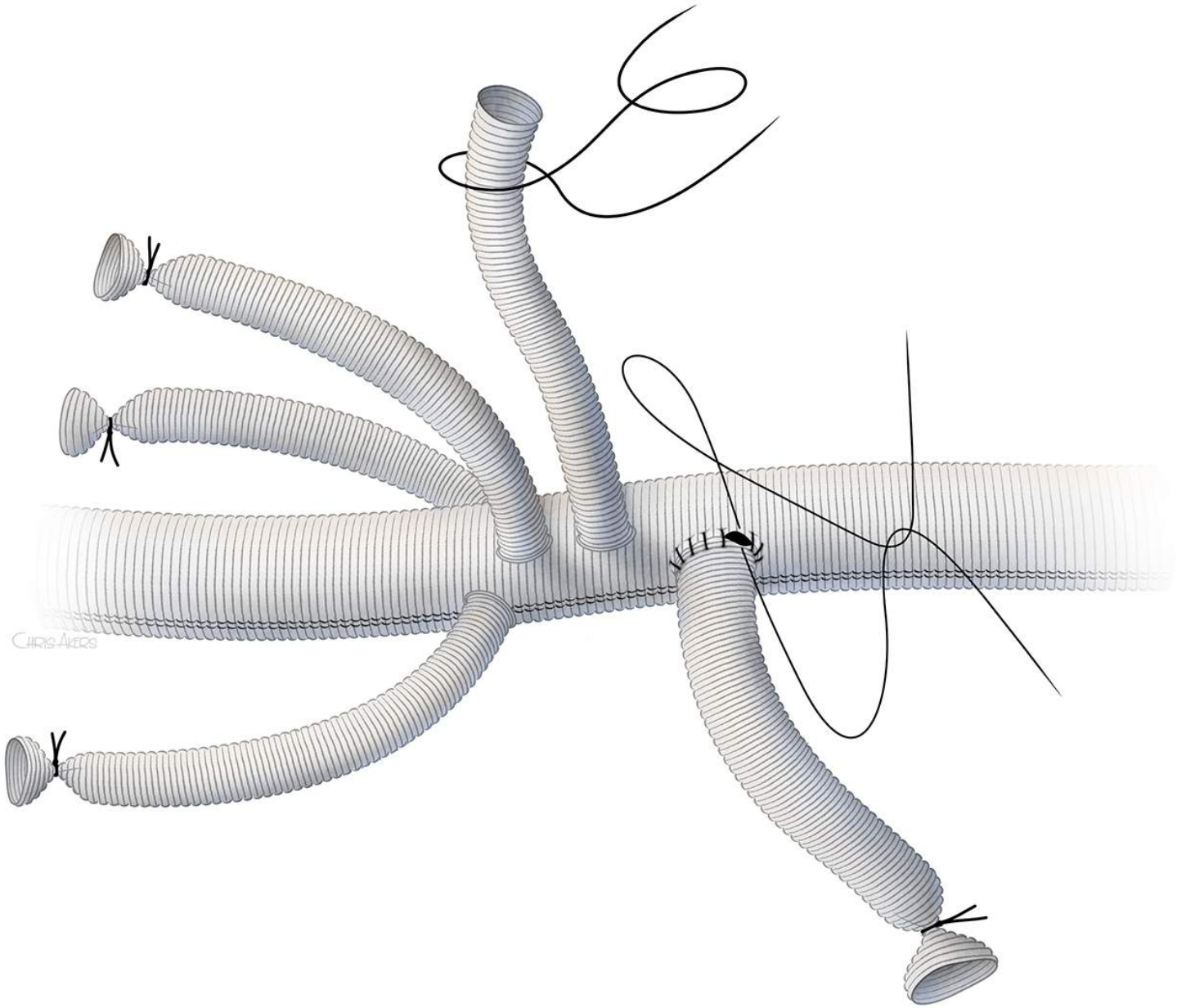
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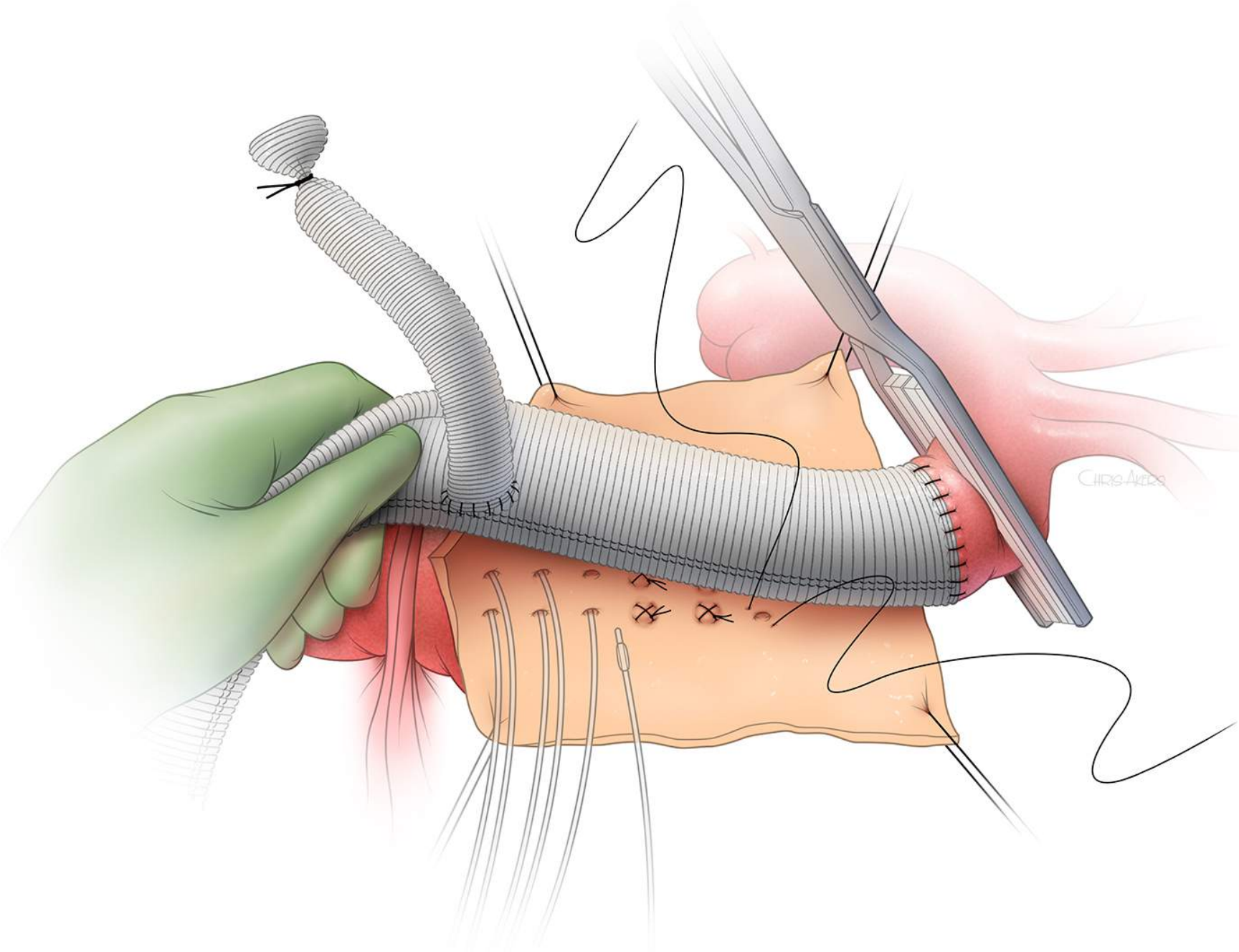
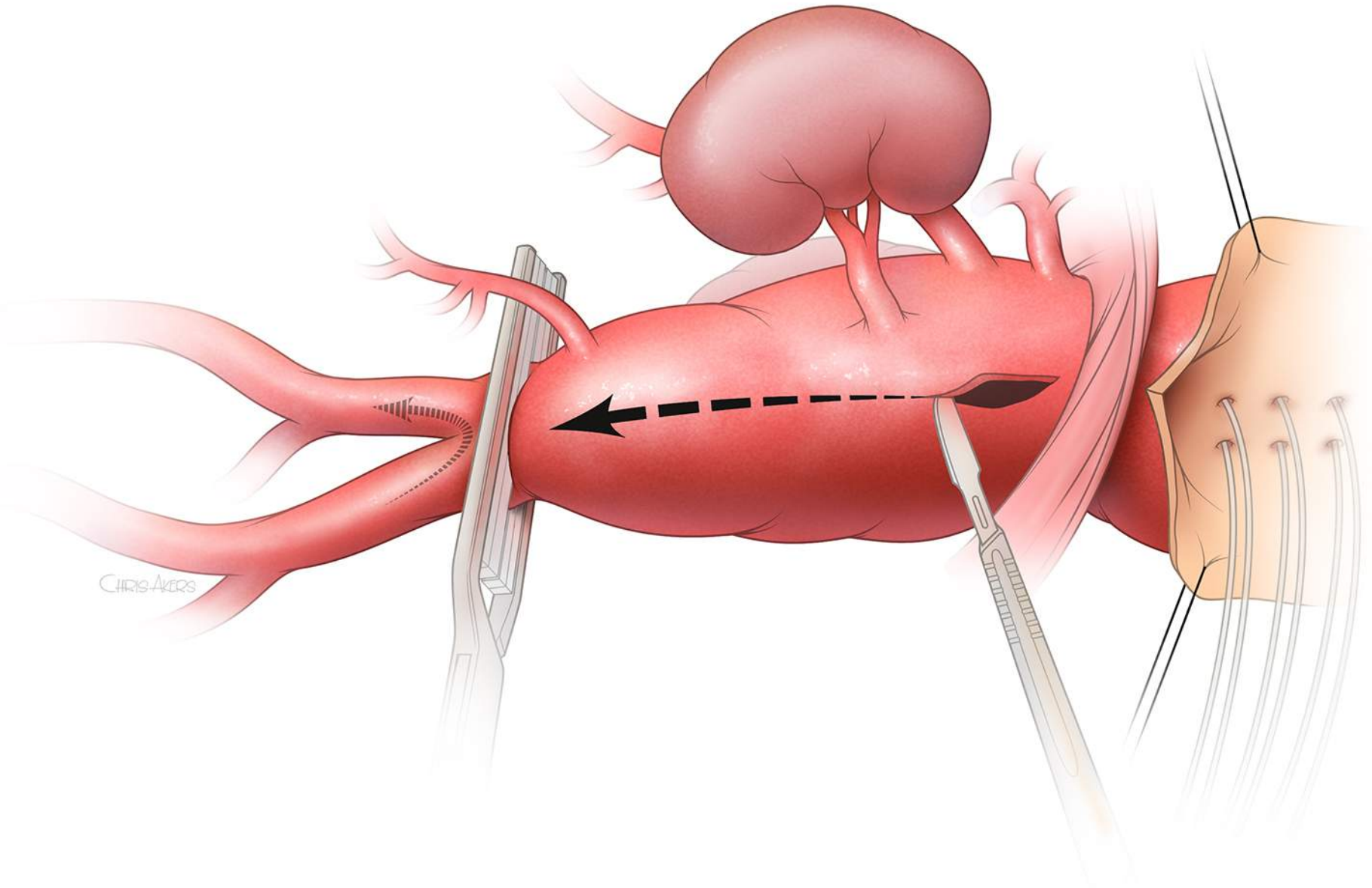

Chris Akers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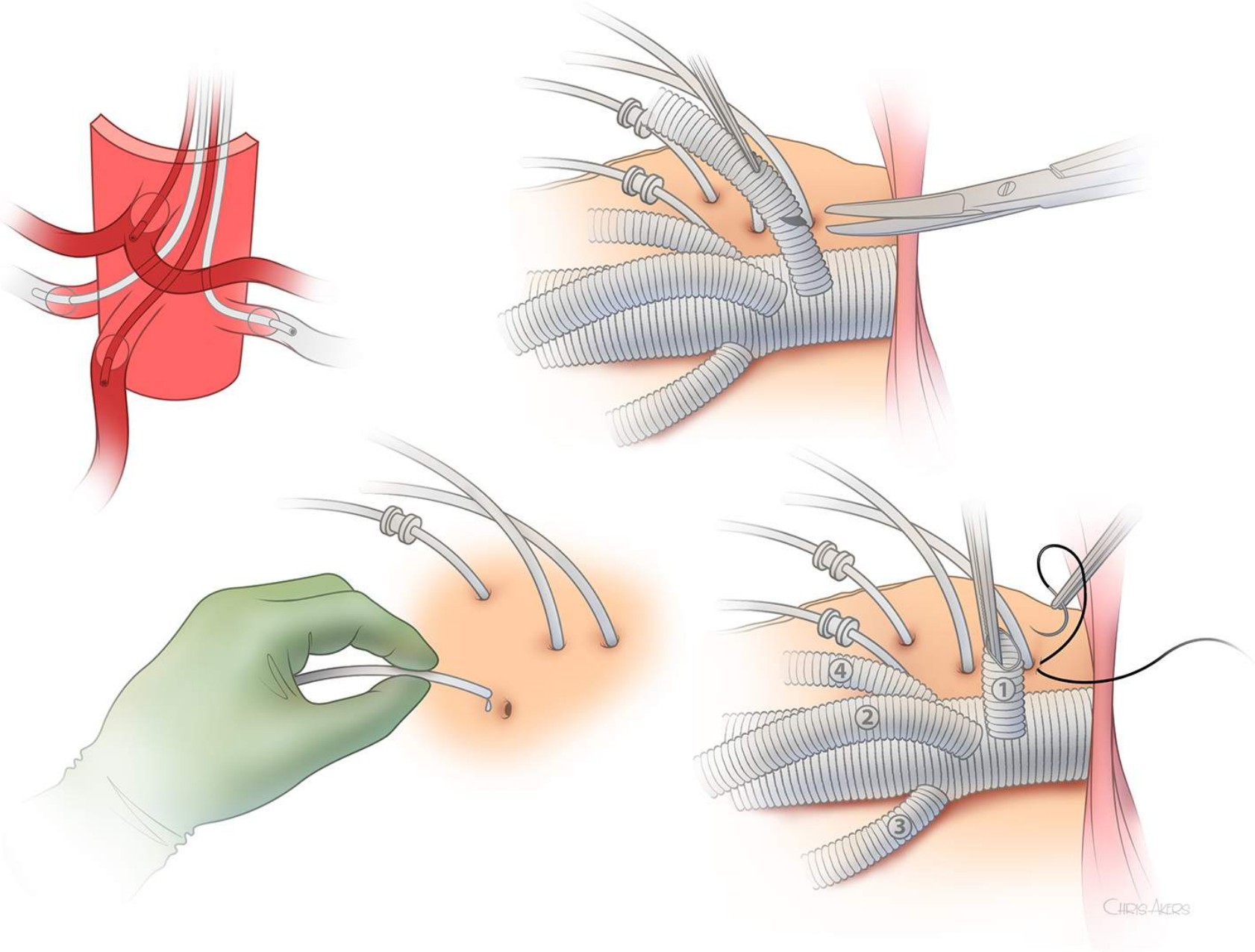
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2
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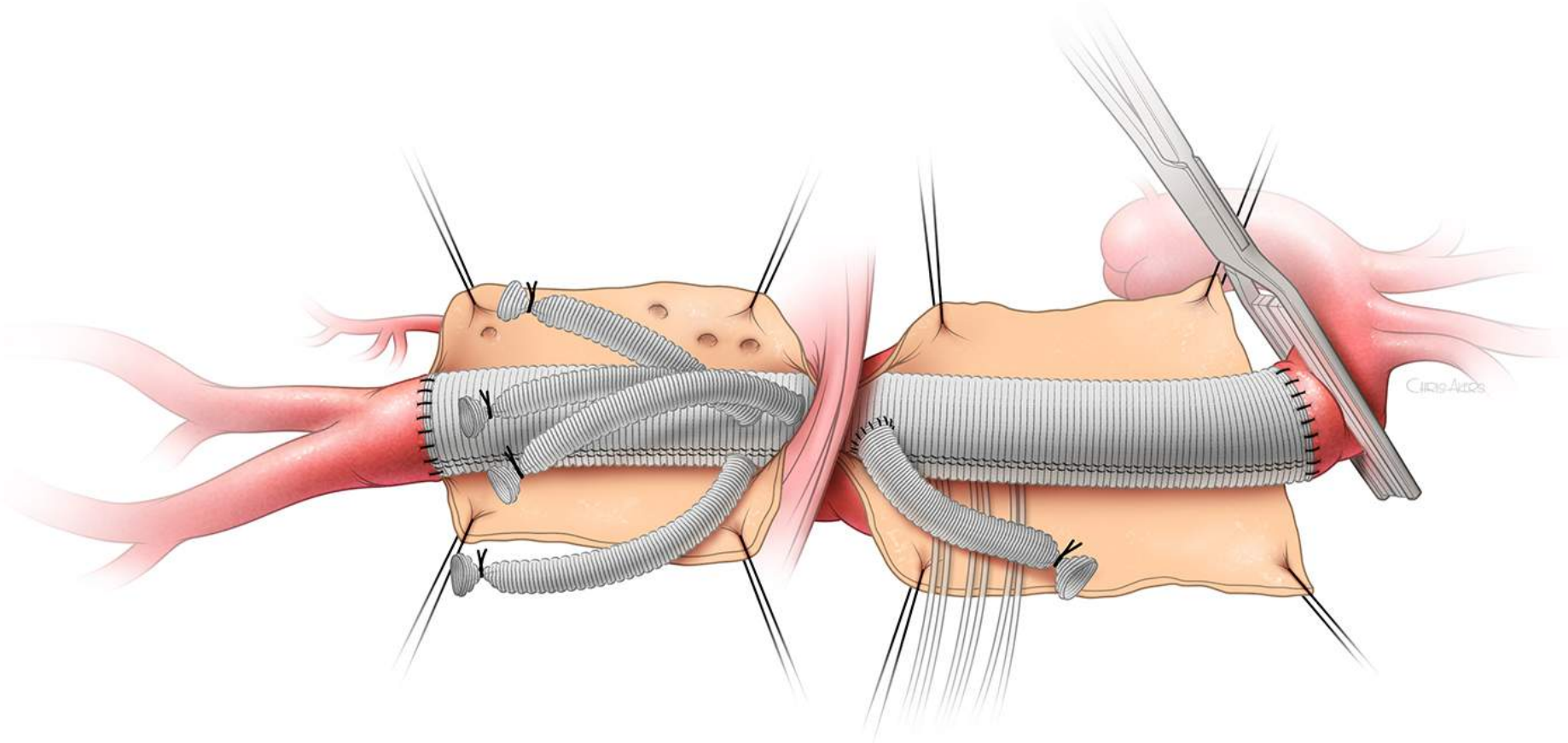
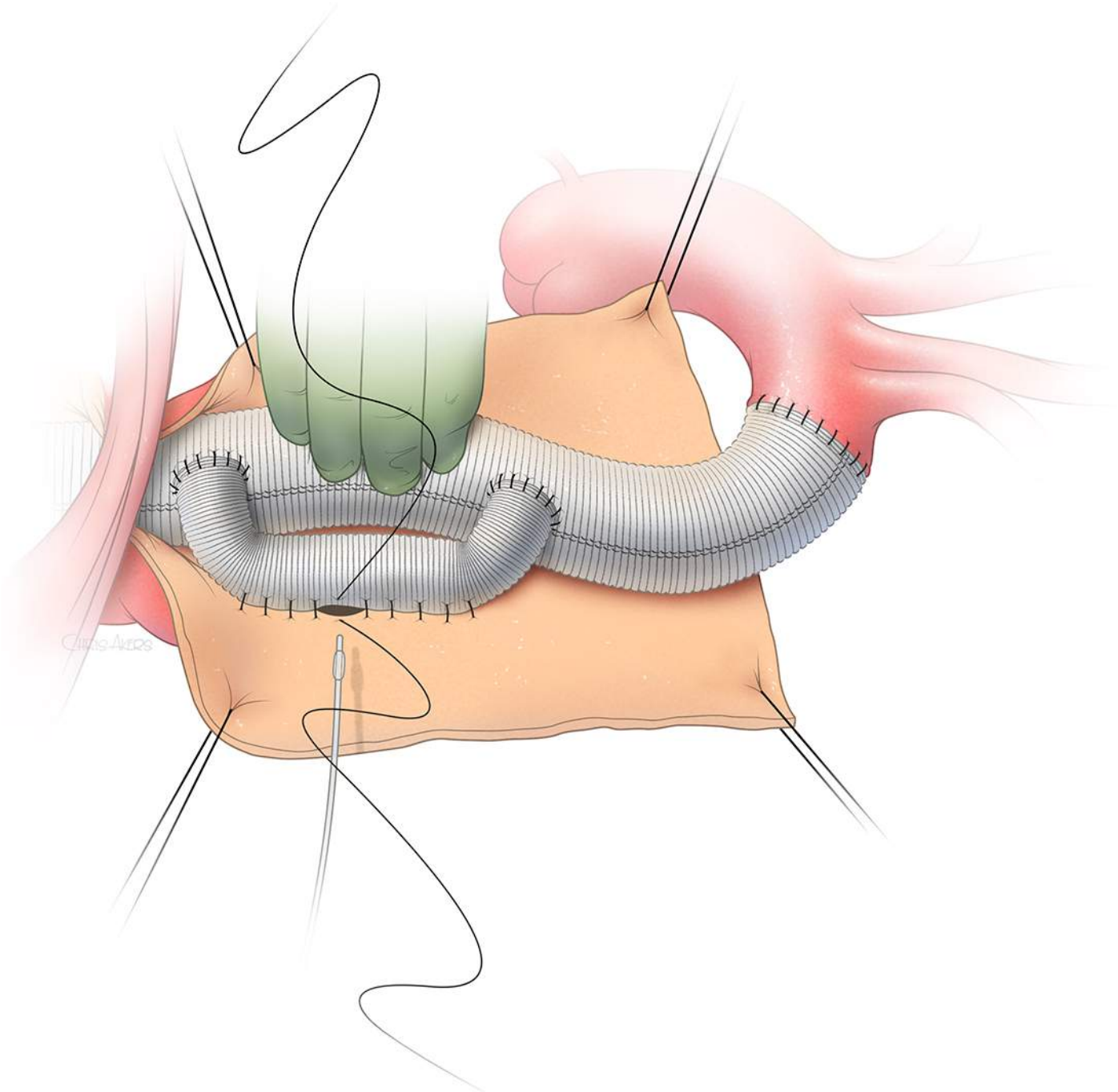
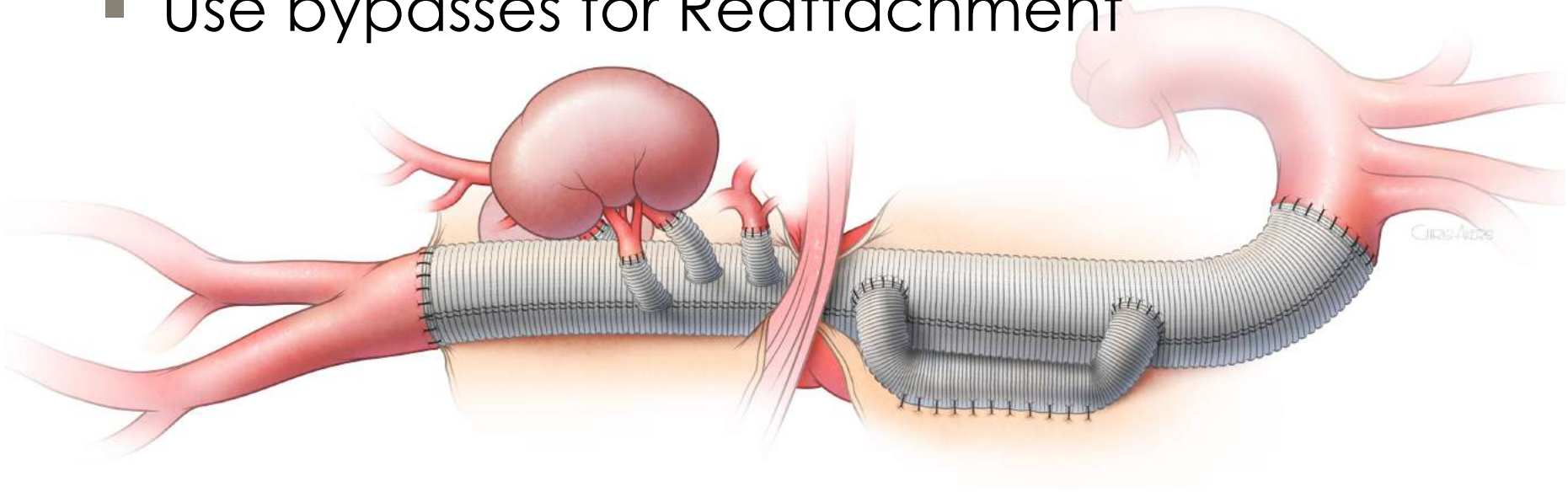
CHRIS AKERS


CIRS-ARTS



HTAD in TAAA

- Use bypasses for Reattachment



- Reversed Elephant trunk
- Frequently have chronic dissection
- Prophylactive repair

Conclusion

- Heritable Thoracic Aortic Disease: genetic specific management
- Open TAAA has good results in HTAD
- Technical considerations
- Although “we don’t own the patient”, we should own the disease.

Thank You