MANAGEMENT OF ANEURYSMS IN CONNECTIVE TISSUE DISORDER PATIENTS

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PRESENTER DISCLOSURE

I have no current relationships with commercial entities or conflicts of interest to declare.

AGENDA

- Connective Tissue Disorders
  - Marfan Syndrome
  - Vascular Ehlers-Danlos Syndrome
  - Loeys-Dietz Syndrome
  - Familial TAAD
- Open Surgical Technique in CTDs

CONNECTIVE TISSUE DISORDERS

- Connective Tissue Disorders, CTDs, are genetic diseases involving collagen or elastin assembly.
- Predisposes to vascular degeneration, loss of structural integrity, consequent aneurysm formation, and/or spontaneous vascular dissection and rupture.
- CTDs with severe vascular manifestations:
  - Marfan Syndrome (MFS),
  - Vascular-Type Ehlers-Danlos Syndrome (vEDS),
  - Loeys-Dietz Syndrome (LDS),
  - Familial Thoracic Aortic Aneurysm and Dissection (TAAD).

Works Cited: Roseborough GS and Williams GM, 2000

MARFAN SYNDROME

- ~1-20 per 100,000 Individuals, Autosomal dominant though 25% of cases are *de novo*.
- *FBN1* → Fibrillin-1 → Required for maintenance of normal elastic fibres through the downregulation of TGF-β activity.
- Cardinal Manifestation: Aortic complication.
- Medical management:
  - Beta-blockade and antihypertensives;
    - Resting HR < 70, Exercise HR_{max} < 100,
    - Resting BP < 120/80 mmHg.
  - Lifestyle modifications

Works Cited: Groth et al., 2015; Milewicz et al., 2021; Ammash et al., 2008; Chobanian et al., 2003; Doyle et al., 2015

MARFAN SYNDROME

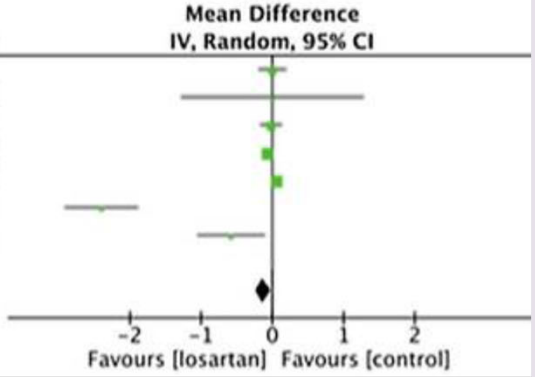
- Losartan:
  - Indirect inhibitor of TGF-β
  - Meta-analysis of seven RCTs demonstrated a significantly smaller change in aortic root diameter in the losartan group. Retrospective data suggests clinically significant reduction in risk of Type B Aortic Dissection.

Change in aortic root diameter in losartan versus control groups (mm)

	Losartan			Control				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Teixido 2018	0.4	0.6	61	0.4	0.5	58	15.1%	0.00 [-0.20, 0.20]	2018
Mosquero 2017	1	0.93	10	1	1.85	10	0.7%	0.00 [-1.28, 1.28]	2017
Bhatt 2015	-0.06	0.17	17	-0.04	0.28	17	18.4%	-0.02 [-0.18, 0.14]	2015
Milleron 2015	0.44	0.07	146	0.51	0.06	146	28.6%	-0.07 [-0.08, -0.06]	2015
Lacro 2014	0.75	0.04	267	0.69	0.04	268	28.7%	0.06 [0.05, 0.07]	2014
Chiu 2013	0.3	0.7	15	2.7	0.7	13	4.0%	-2.40 [-2.92, -1.88]	2013
Groenink 2013	0.77	1.36	78	1.35	1.55	67	4.6%	-0.58 [-1.06, -0.10]	2013
Total (95% CI)			594			579	100.0%	**-0.13 [-0.24, -0.02]**	

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 332.32$, df = 6 ($P < 0.00001$); $I^2 = 98\%$

Test for overall effect: $Z = 2.25$ ($P = 0.02$)



Works Cited: Elbadawi et al., 2019

MARFAN SYNDROME – SURGICAL INDICATIONS

- Traditional threshold for surgical repair of aortic root is 50mm in MFS, some recommendations as low as 45mm.
- Aortic Arch and Descending thoracoabdominal aneurysms → Threshold of 55-60mm or rapid growth.

Works Cited: Loeys et al., 2010

MARFAN SYNDROME – ENDOVASCULAR

- Aortic stent grafts are traditionally avoided as primary treatment in CTD.
- Primary concern: Persistent radial force of the stent graft
- Up to 60% primary failure rate of endovascular therapy in this context.
- Most common complication in TEVAR is retrograde Type A dissection.
- Value remains in endovascular therapy for temporization, and in treating in a graft-to-graft fashion.
- Avoid excessive oversizing.

Works Cited: Shalhub et al., 2018; Liu et al., 2022

VASCULAR EHLERS-DANLOS SYNDROME

- 1 in 50,000-200,000, Autosomal dominant, though 50% represent *de novo* mutations.
- *COL3A1* gene which encodes for a procollagen molecule.
- Wide spectrum of disease severity.
- More frequently present with acute ruptures and dissections.
- Medical Management:
  - Beta-blockade, ARB, statins, and lifestyle modifications.
  - Avoidance of arterial and central lines.

Works Cited: Byers et al., 2017; Demirdas et al., 2024; Eagleton MJ, 2016; Bowen et al., 2023

VASCULAR EDS – SURGICAL INDICATIONS

- Traditional approach: Surgical Intervention only if risking imminent death otherwise.
    - Mortality in open vascular procedures reported as high as 20-60%.
- Recent data favouring elective repair create a more nuanced patient-individualized discussion.
    - Consider individual tissue fragility. Increased risk if:
        - Vascular event at age < 20 years.
        - Multiple asymptomatic dissections or aneurysms apart from the index vascular lesion.
        - Spontaneous abdominal bleeding without identifiable source.

Works Cited: Byers et al., 2017; Bergqvist et al., 2013

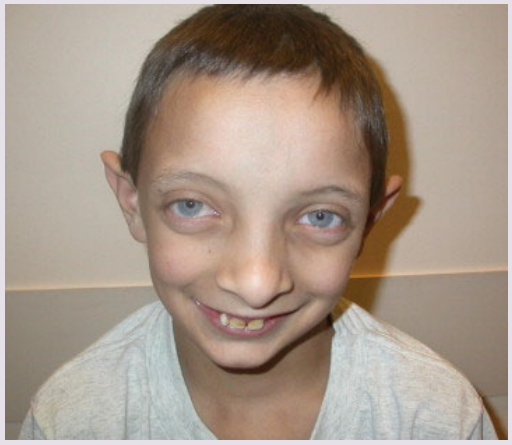
VASCULAR EDS – ENDOVASCULAR

- Often useful for coil embolization aortic branch vessels and other medium sized arteries.
- Arterial access can precipitate femoral rupture and pseudoaneurysm formation.
- Otherwise, open surgery is typically preferred.

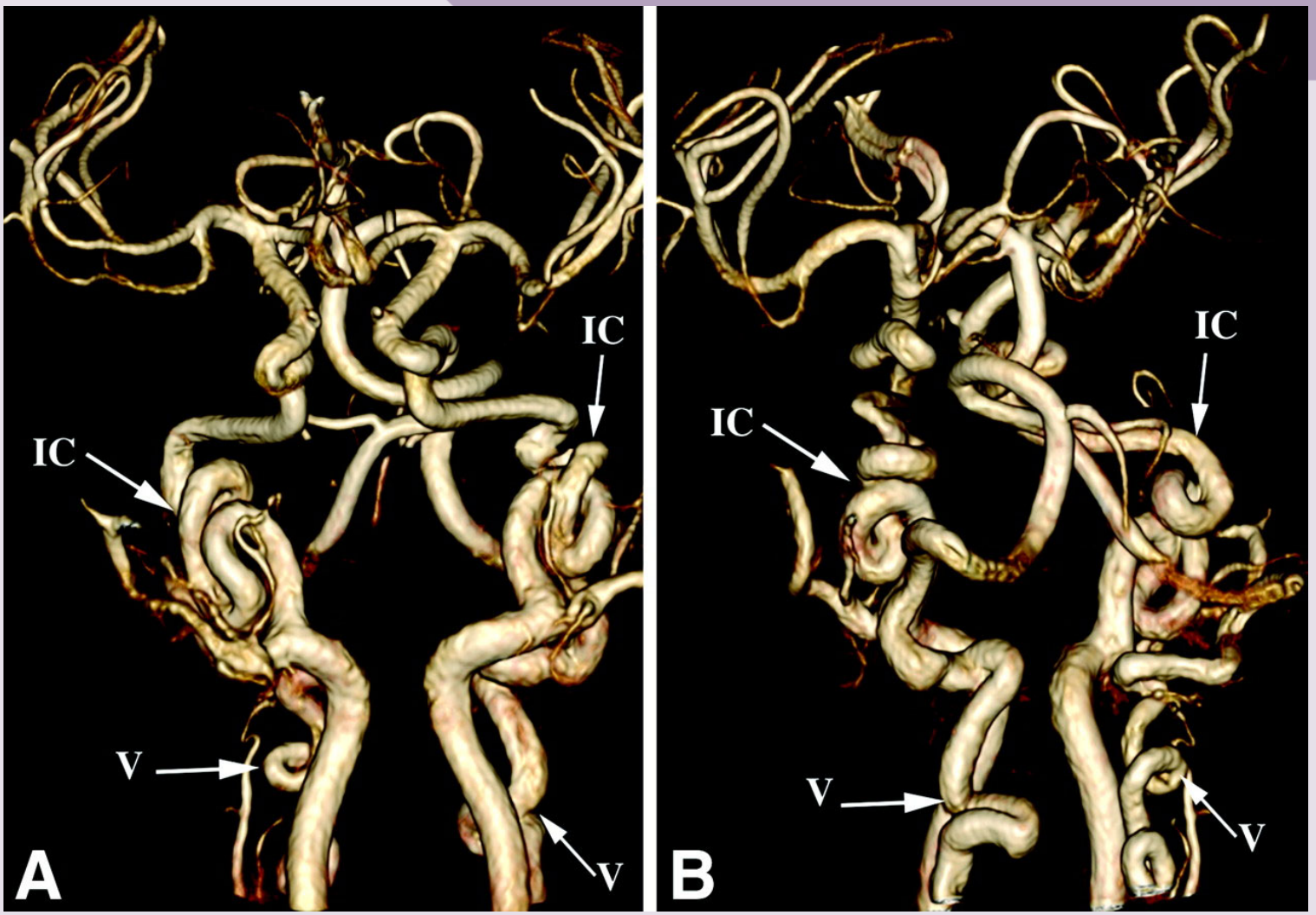
Works Cited: Bergqvist et al., 2013

LOEYS-DIETZ SYNDROME

- Prevalence of ~1-2 in 100,000.
- Caused by mutations affecting proteins within the TGF-β signalling pathway.
  - I: *TGFBR1*, II: *TGFBR2*, III: *SMAD3*, IV: *TGFB2*, V: *TGFB3*
- Cardinal manifestation is in the aortic root, which dissects or ruptures at small diameters and in childhood.
- Distinct triad of hypertelorism, arterial tortuosity, and bifid uvula.
- **Must** distinguish LDS from vEDS.
- Similar medical management as MFS and vEDS.
  - Consider Losartan.



Works Cited: Velchev et al., 2021; Williams et al., 2007



Works Cited: Dhouib et al., 2012

LOEYS-DIETZ SYNDROME – SURGICAL INDICATIONS

- More aggressive nature of aneurysms in LDS.
- Severity of craniofacial manifestations can be used to predict severe cardiovascular manifestations.
- Ascending aortic aneurysm/aortic root repair thresholds:
  - LDS I and II → Once aortic annulus is > 99th percentile and can accommodate adult-size graft for children. In adolescents/adults, threshold of 40mm.
  - LDS III and IV → Threshold of 45mm.
  - LDS V → Threshold of 50mmm.
- Descending thoracic aorta → 45-50mm threshold or rapid expansion.
- Remainder of aneurysmal disease requires personalized decision making.

Works Cited: Schoenhoff et al., 2013

FAMILIAL THORACIC AORTIC ANEURYSM AND DISSECTION

- Catch-all for familial inheritance of thoracic aortic aneurysm and dissection.
- Autosomal dominant with decreased penetrance and variable expression.
- Older population for vascular events.
- Treatment recommendations follow typical sporadic thresholds except in those with family history of rupture at smaller diameters.
- Similar concern for endovascular treatment as other CTDs.

Works Cited: Albornoz et al., 2006

OPEN SURGICAL TECHNIQUE IN CONNECTIVE TISSUE DISORDERS

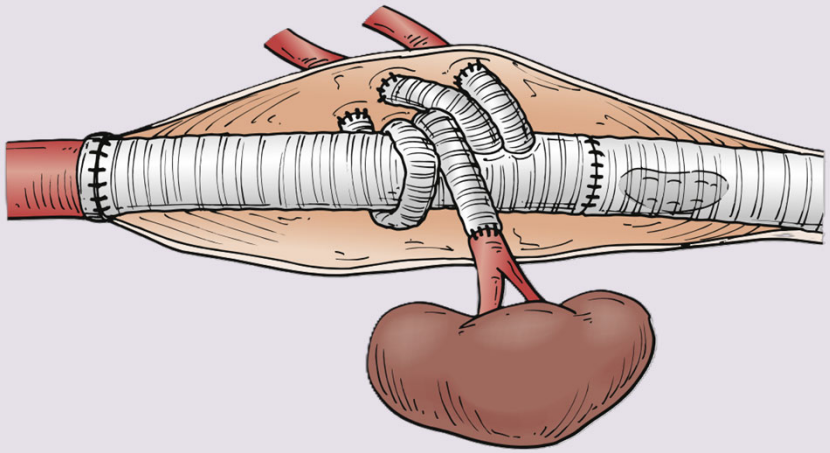
SURGICAL TECHNIQUE IN CTDS

- Techniques are suited towards compromised integrity of vascular tissue and for prevention of further degeneration.
- Use padded clamps and avoid repeated clamp applications.
- Aim for systemic hypotension during clamping, target of SBP < 70-80 mmHg.
- Prioritize gentle tissue handling and minimizing manipulation.
- Avoid ‘parachuting’ when tissue is especially friable.

Works Cited: European Society for Vascular Surgery (ESVS) 2026 Clinical Practice Guidelines on the Management of Descending Thoracic and Thoraco-Abdominal Aortic Diseases

SURGICAL TECHNIQUE IN CTDS

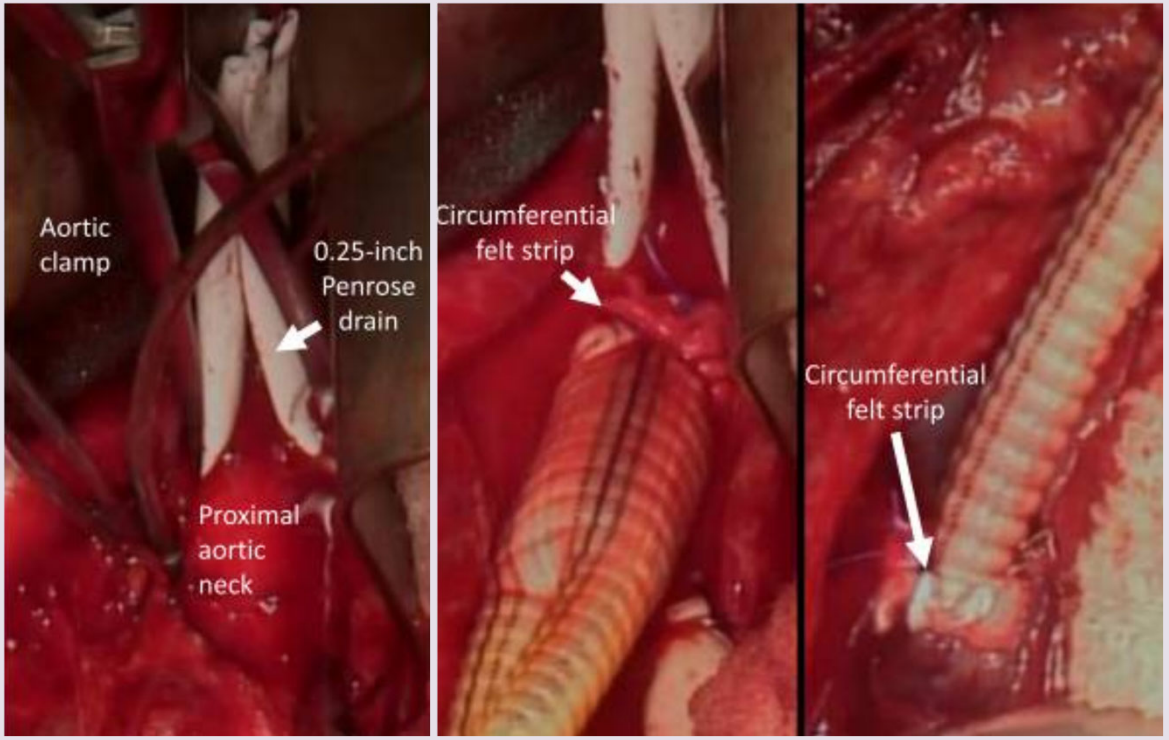
- Favour pre-fabricated branched prosthetic as opposed to patching.
- If patching (i.e.intercostals), minimize the size of Carrel patch to minimize likelihood of degeneration.



Works Cited: Rutherford's vascular surgery and endovascular therapy. 10th ed, 2018. p.1858-1876.

SURGICAL TECHNIQUE IN CTDS

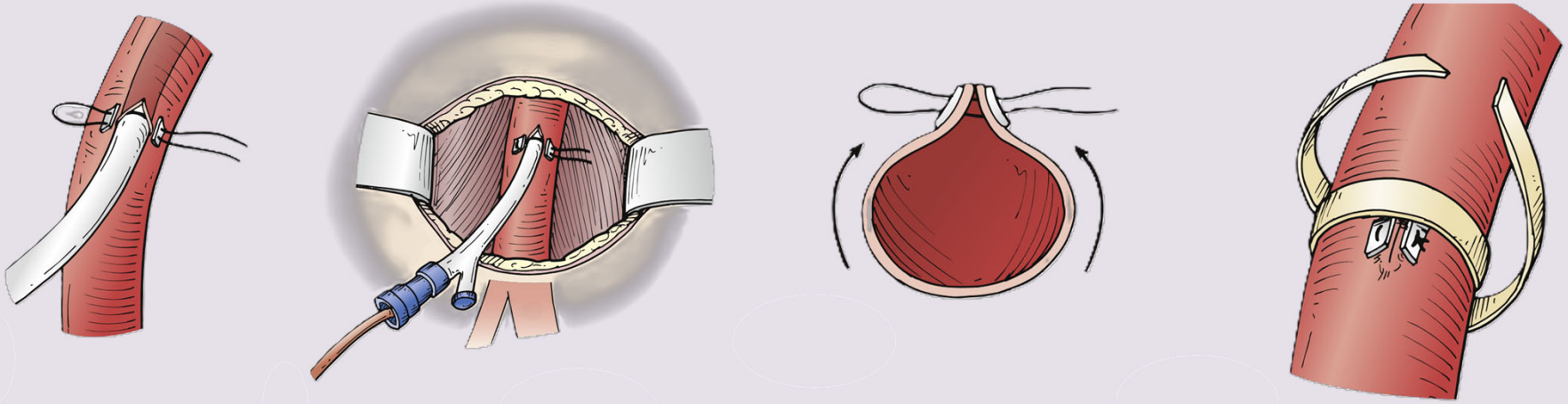
- Circumferentially reinforce anastomoses with felt strips or bovine pericardium. Use pledgets liberally.
- Use Penrose drains instead of umbilical tape and vessel loops.



Works Cited: Dittman et al., 2023

SURGICAL TECHNIQUE IN CTDS

- Consider open repair of any puncture with the use of pledgeted suture and buttressed bovine pericardium.



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CONCLUSIONS

- The management of aneurysms in patients with connective tissue disorder is complex and varied depending on the disorder and the individual patient.
- Medical management consistently includes beta blockade, ARBs, and lifestyle adjustments.
- Surgical technique requires delicate handling of tissue with steps taken to minimize trauma and tension upon vasculature.
- Surveillance → MRA or CTA from head to pelvis to identify aneurysms and tortuosity, lifelong echocardiography to follow aortic root.

THANK YOU

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