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Frontiers and advancements in open surgery and endovascular therapy for peripheral arterial disease

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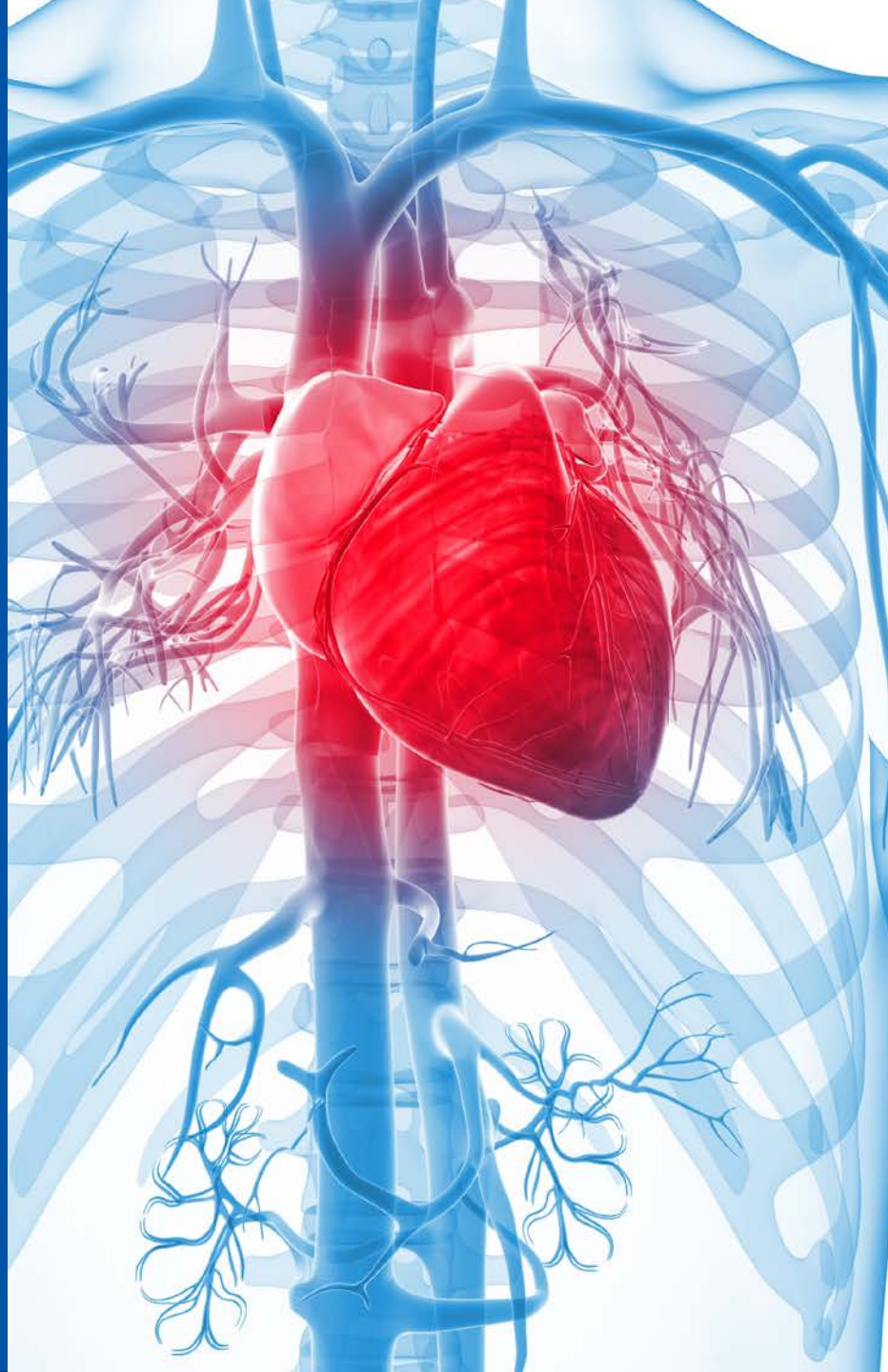

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Disclosures

None

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Education Need/Practice Gap

A major practice gap exists in the diagnosis and treatment of peripheral arterial disease (PAD). PAD is associated with cardiovascular morbidity and mortality. Providers need to be aware of the signs and symptoms of PAD.

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Learning Objectives

Upon completion of this learning activity, you will be able to:

1. Discus recent clinical research updates in peripheral arterial disease and implementation in practice.

2. Review current clinical trials.

3. Review horizons, frontiers, and current basic science for peripheral.

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Expected Outcome

The desired change/result in practice is to improve diagnosis and use of available treatment options in PAD.

Background - PAD is Actually Two Diseases

- Claudication vs CLTI
- Claudication is not an emergency and usually does not require procedural intervention
- Endo treatment for claudication should never be done in a smoker – bad for patients long-term waste of resources

Grade	Clinical features
0	Asymptomatic
1	Mild claudication
2	Moderate claudication
3	Severe claudication
4	Ischemic rest pain
5	Minor tissue loss - nonhealing diffuse pedal ischemia
6	Major tissue loss, functional f

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Claudication vs CLTI

- Claudicants are NOT at risk of losing their limbs - <5% progress to CLTI
- Treatment of claudication ultimately causes progression to CLTI**
- Rest pain CLTI R4
  - 13% one year MORTALITY
- Patients with tissue loss CLTI R5-6,
  - 20% one year MORTALITY
- CLTI is multilevel disease

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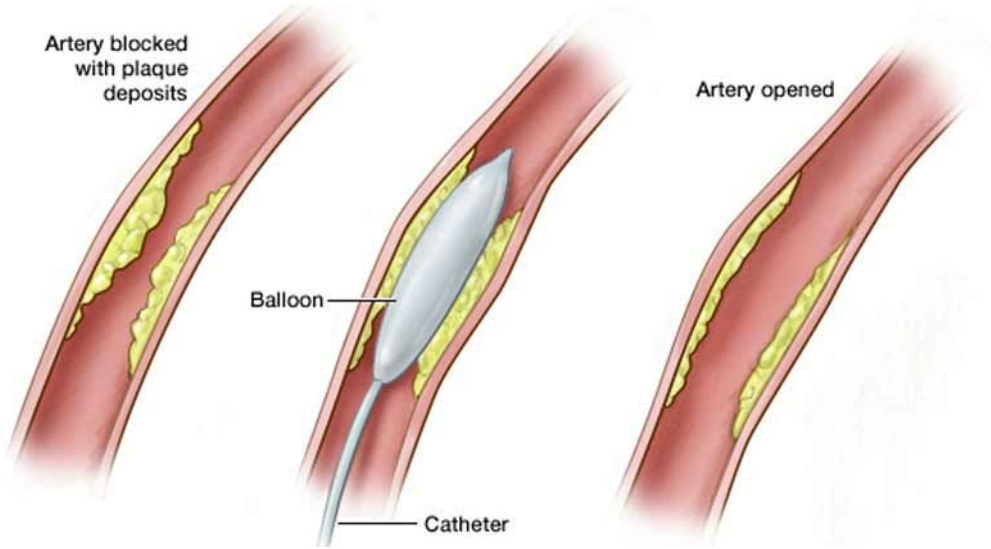
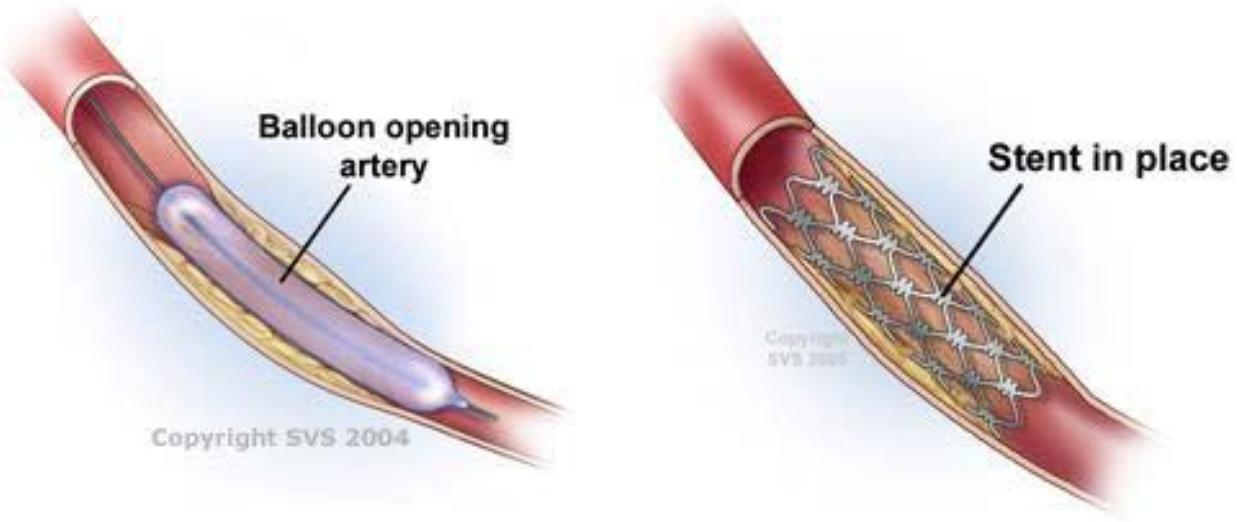
Endovascular Tx of PAD

- 60-70% of PAD is treated endo in USA,
- Balloon Angioplasty/Stent
- Atherectomy
- Anti-proliferative agents (DCB/DES)
- Endovascular “PQ” Bypass
- Venous Arterialization
- Hydration





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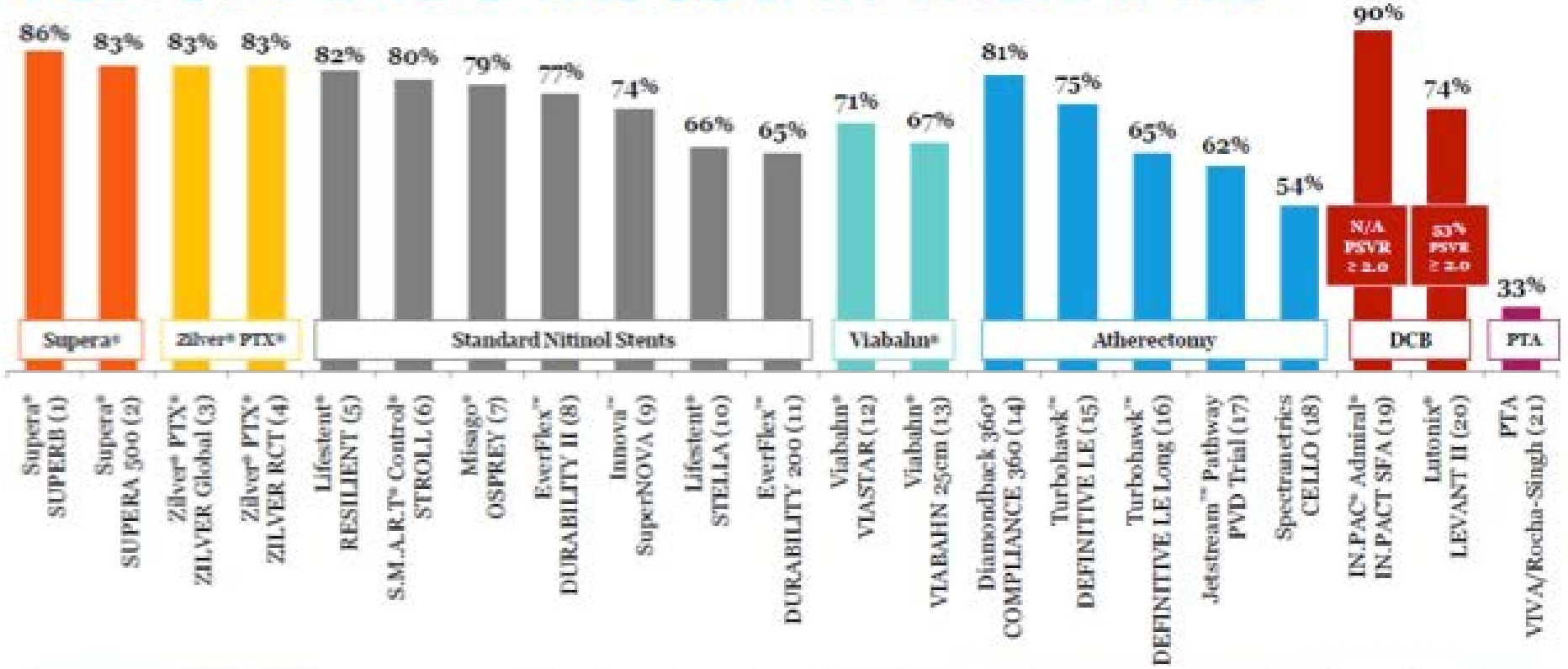
12-MONTH PRIMARY PATENCY (K-M) FOR SFA ENDOVASCULAR THERAPIES



n	264	470	787	241	134	250	261	287	299	58	100	72	71	25	671	232	172	65	220	316	307
cm	7.8	12.6	10	5.5	7.1	7.7	8.4	8.9	9.3	22	24	19	27	5.6	8.1	14.6	2.7	5.6	8.9	6.3	8.7
PSVR	2	2.4	2	2	2.5	2	2	2	2.4	2.4	2.4	2.5	N/A	2.5	2.4	2.4	2.4	N/A	2.4	2.5	N/A

See appendix for sources.
Data differences depicted between these trials may not be statistically significant or clinically meaningful and different clinical trials may include differences in the demographics of the patient populations.

Important Safety Information referenced within

Outcomes of Lower Extremity Bypass (LEB) for Claudication in Active Smokers

Vascular Study Group of New England database

1789 LEBs in 1689 patients (46% smokers)

Smokers undergoing LEB have worse outcomes than non-smokers:

Primary Patency At 2 Years	48%	vs. 61%
Assisted Primary Patency At 2 Years	59%	vs. 74%
Survival At 10 Years	69%	vs. 76%

CONCLUSION

Aim for smoking cessation before LEB for claudication to optimize graft patency and patient survival.

JVS Journal of Vascular Surgery
Official Publication of the Society for Vascular Surgery

Jones et. al. *J Vasc Surg September 2018*

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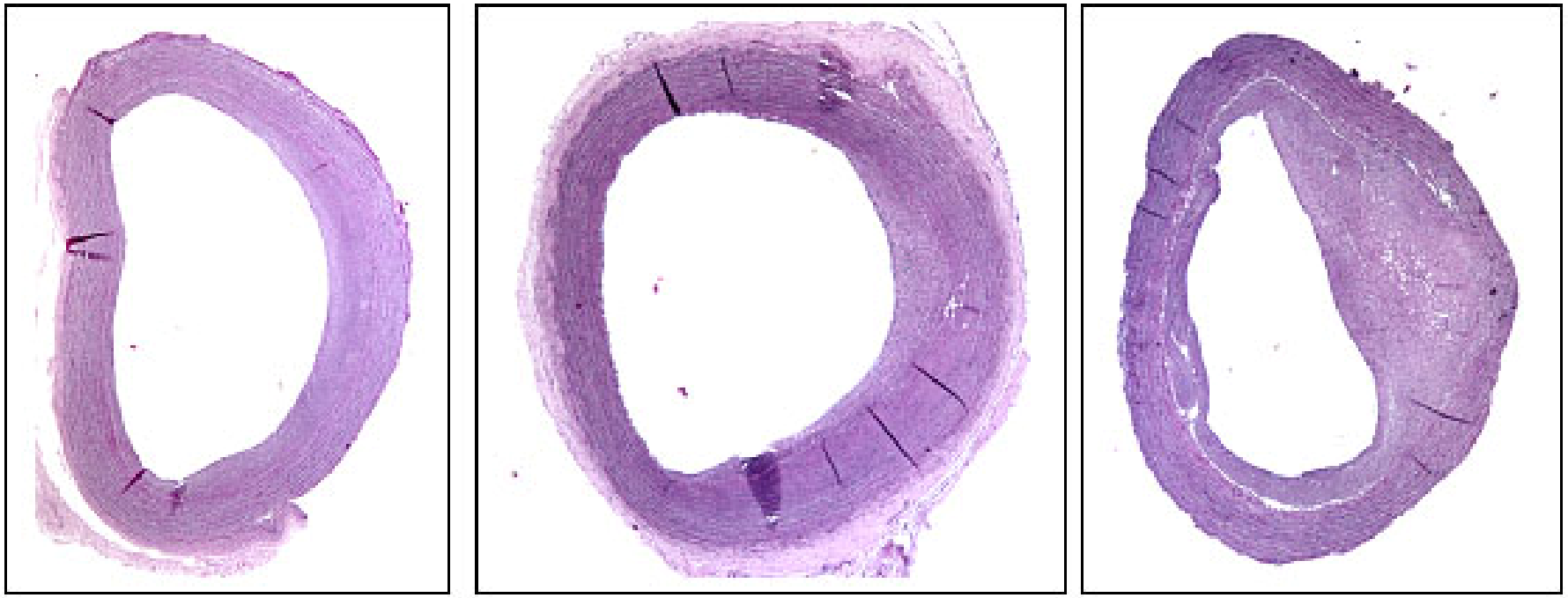
Why is Patency so BAD with Endo?

Intimal Hyperplasia



Progressive eccentric intimal hyperplasia with development of atherosclerosis in human arteries.

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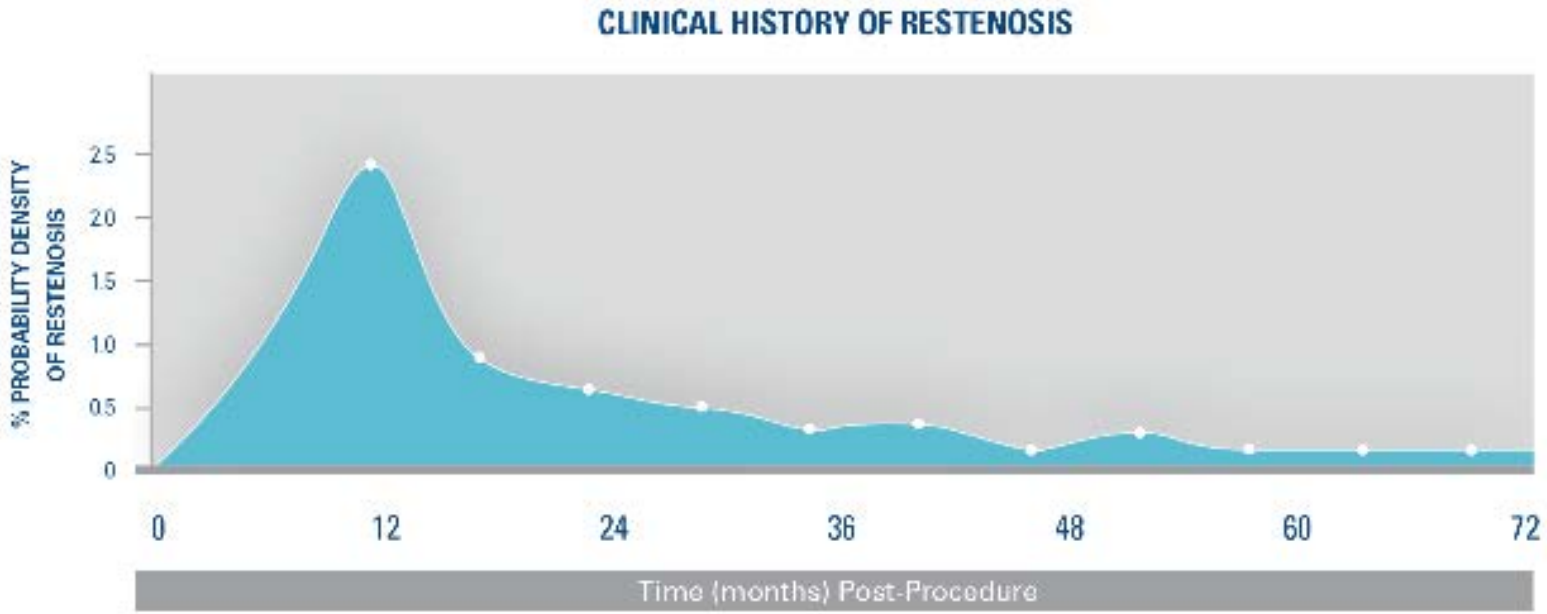
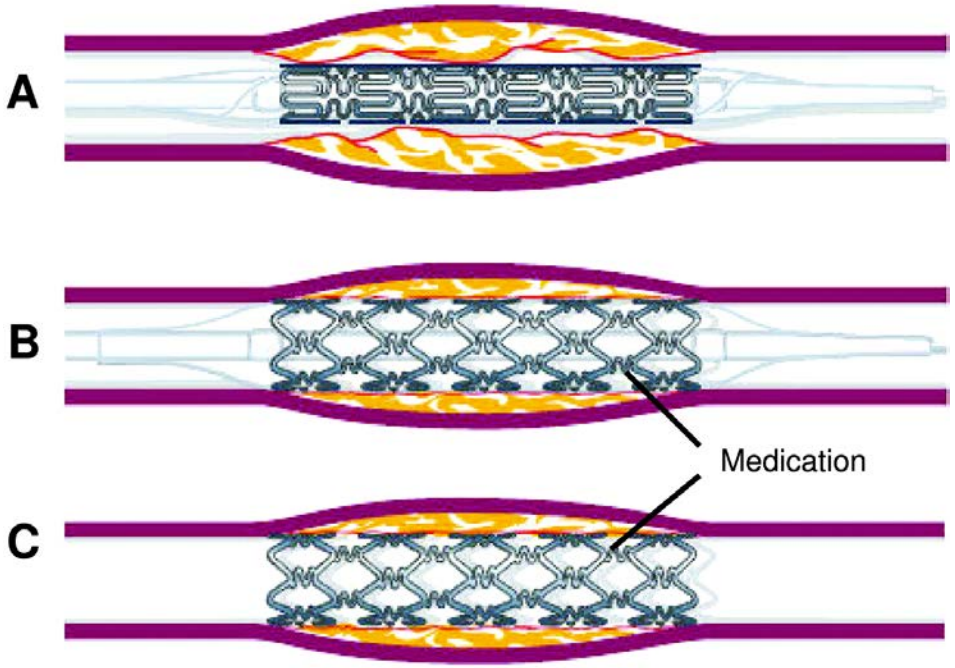
Restenosis following nitinol stenting in the SFA peaks at around 12 months



- Timing of SFA restenosis is longer compared to coronary stenting, which predominantly occurs within 6 months after stenting

How does a Drug Eluting Stent work?



Deliver chemotherapy agent to vessel wall for 2 years to decrease the cell proliferation that occurs during intimal hyperplasia.

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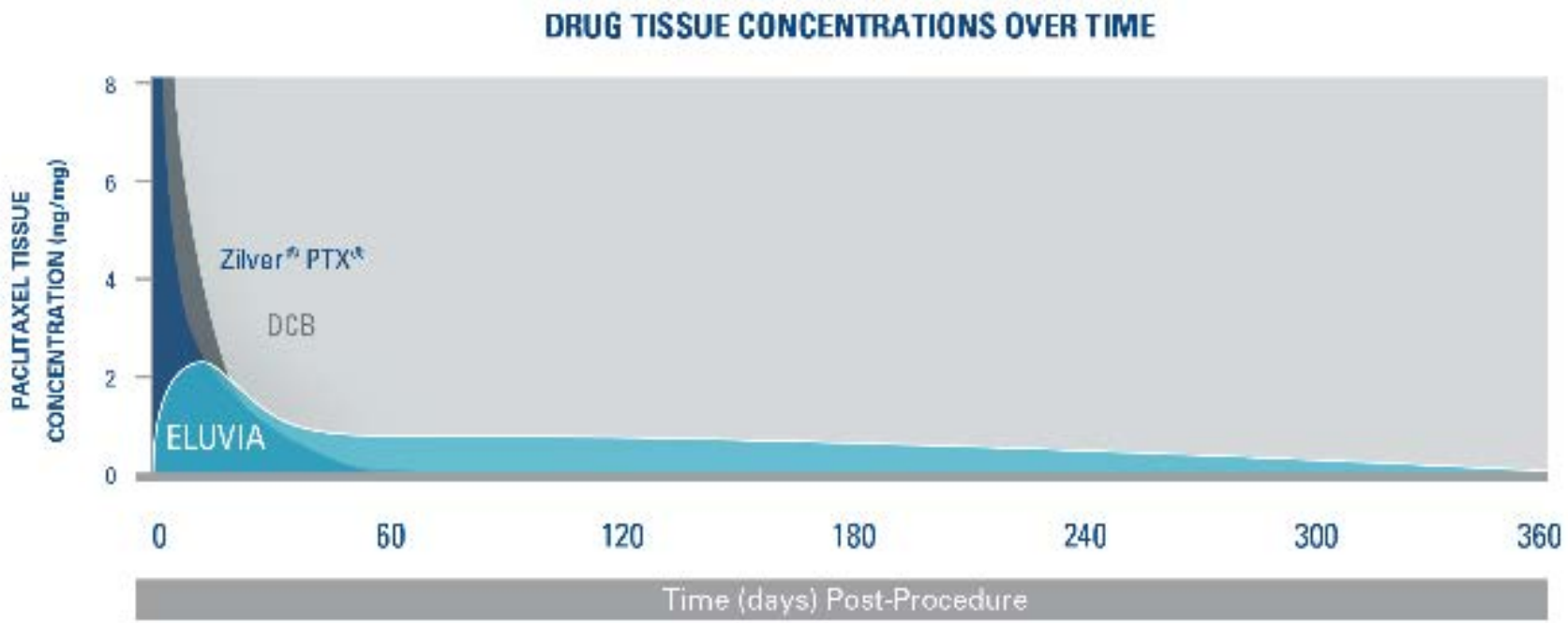
The ELUVIA™ stent system was designed to sustain drug release beyond 1 year



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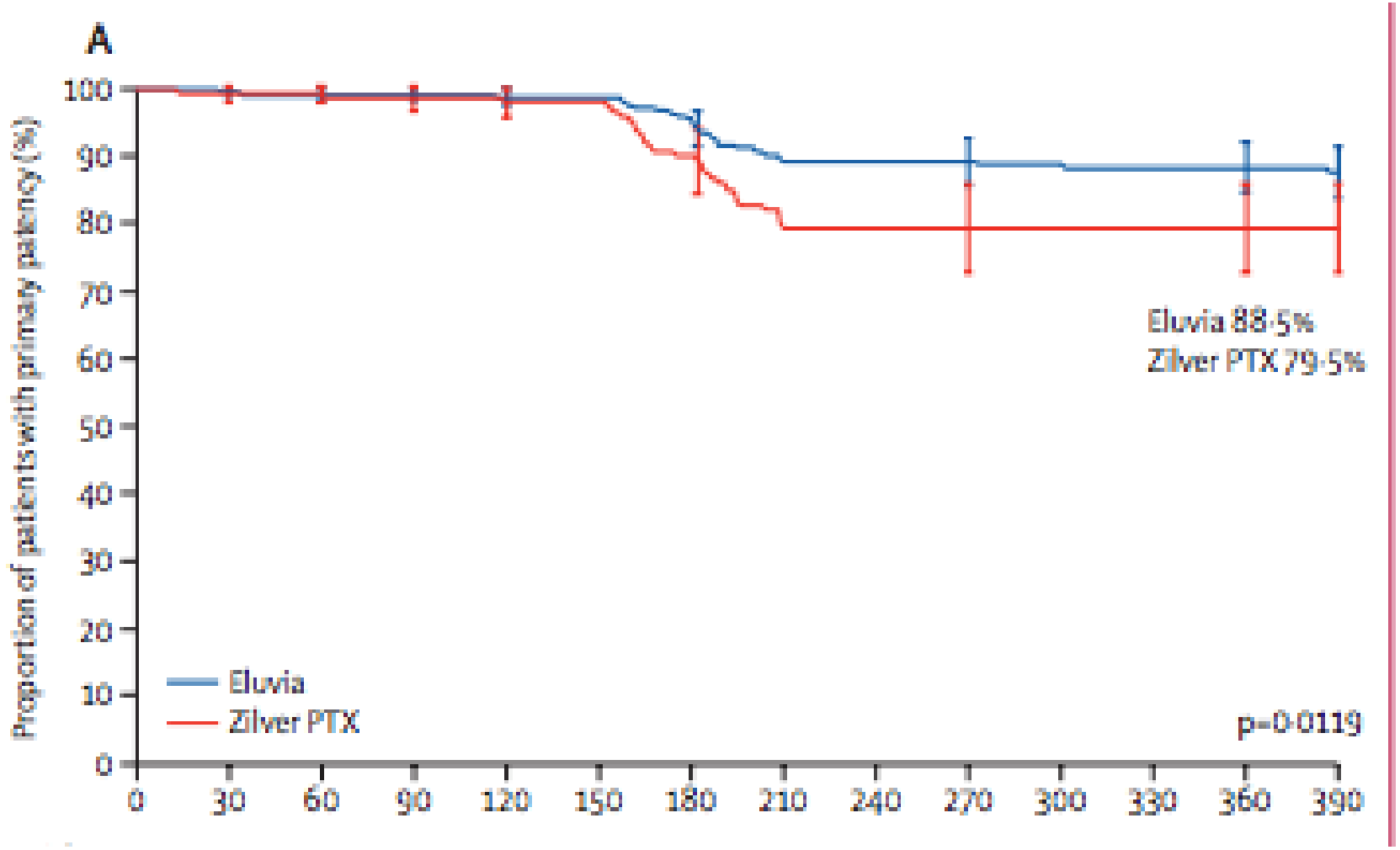
Elluvia Patency – 88.5% one year



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Disruption

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SYSTEMATIC REVIEW AND META-ANALYSIS

Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Konstantinos Katsanos, MD, PhD, MSc, EBIR; Stavros Spiliopoulos, MD, PhD; Panagiotis Kitrou, MD, PhD; Miltiadis Krokidis, MD, PhD; Dimitrios Karnabatidis, MD, PhD

Background—Several randomized controlled trials (RCTs) have already shown that paclitaxel-coated balloons and stents significantly reduce the rates of vessel restenosis and target lesion revascularization after lower extremity interventions.

Methods and Results—A systematic review and meta-analysis of RCTs investigating paclitaxel-coated devices in the femoral and/or popliteal arteries was performed. The primary safety measure was all-cause patient death. Risk ratios and risk differences were pooled with a random effects model. In all, 28 RCTs with 4663 patients (89% intermittent claudication) were analyzed. All-cause patient death at 1 year (28 RCTs with 4432 cases) was similar between paclitaxel-coated devices and control arms (2.3% versus 2.3% crude risk of death; risk ratio, 1.08; 95% CI, 0.72–1.61). All-cause death at 2 years (12 RCTs with 2316 cases) was significantly increased in the case of paclitaxel versus control (7.2% versus 3.8% crude risk of death; risk ratio, 1.68; 95% CI, 1.15–2.47; —number-needed-to-harm, 29 patients [95% CI, 19–59]). All-cause death up to 5 years (3 RCTs with 863 cases) increased further in the case of paclitaxel (14.7% versus 8.1% crude risk of death; risk ratio, 1.93; 95% CI, 1.27–2.93; —number-needed-to-harm, 14 patients [95% CI, 9–32]). Meta-regression showed a significant relationship between exposure to paclitaxel (dose-time product) and absolute risk of death (0.4±0.1% excess risk of death per paclitaxel mg-year; $P<0.001$). Trial sequential analysis excluded false-positive findings with 99% certainty (2-sided α, 1.0%).

Conclusions—There is increased risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the lower limbs. Further investigations are urgently warranted.

Clinical Trial Registration—URL: www.crd.york.ac.uk/PROSPERO. Unique identifier: CRD42018099447. (***J Am Heart Assoc.* 2018;7:e011245. DOI: 10.1161/JAHA.118.011245.**)

Key Words: balloon angioplasty • paclitaxel • paclitaxel-coated balloon • paclitaxel-eluting stent

SYSTEMATIC REVIEW AND META-ANALYSIS

American Heart Association | American Stroke Association

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Conclusions—There is increased risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the lower limbs. Further investigations are urgently warranted.

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At > 2 years

Paciltaxel Paradox

- Jan 2019 FDA
  - “the FDA believes that the benefits continue to outweigh the risks for approved paclitaxel-coated balloons and paclitaxel-eluting stents when used in accordance with their indications for use.”
- Jan 2019 – JACC pub
  - 1980 pts, DCB (9.3%) and percutaneous transluminal angioplasty (PTA) (11.2%) through 5 years
- Feb 2019 – Medtronic Data Error
  - “Due to a programming error, mortality data were inadvertently omitted from the summary tables included in the statistical analysis.”
  - The mortality in the DCB cohort was corrected from 9.30% to 15.12%. (P = .09).

Paciltaxel Paradox

- Feb 2019 – Cook Zilver PTX Circulation Paper 2016 correction
  - Mortality reporting error, these numbers were reversed and significantly higher in the paclitaxel-treated group (16.9% vs. 10.2%, P = .03).
- Feb 2019 – JAMA Cardiology
  - Patient level data analyzed 16,560, no evidence of paclitaxel related deaths, but mean f/u 389 days!
- March 2019 – FDA
  - consider that there may be an increased rate of long-term mortality in patients treated with paclitaxel-coated balloons and paclitaxel-eluting stents.

Paciltaxel Paradox

- March 2019 – FDA
  - 5 year data: 975 patients, and the risk of death was 20.1% in the paclitaxel group versus 13.4 % in the controls.
- Further patient level data analysis is needed.
- Cook patient level data
- “I know what I don’t know”

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References for DCB/DES

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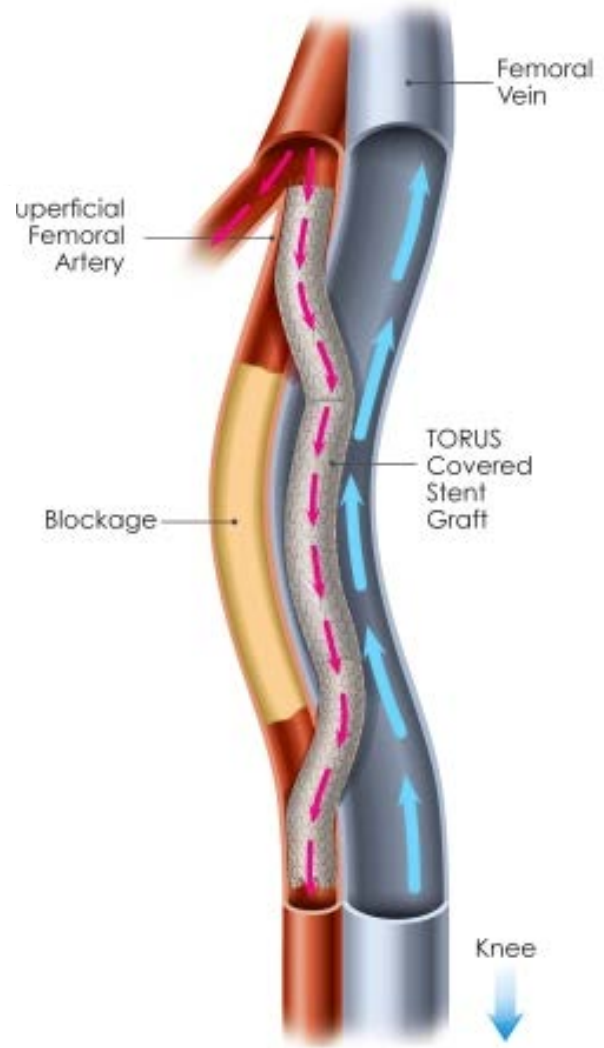
- 6. JAMA Cardiol. 2019 Feb 12. doi:10.1001/jamacardio.2019.0325.
- 7. www.fda.gov/MedicalDevices/Safety/LetterstoHealthCareProviders/ucm633614....

PQ Bypass



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PQ Bypass Video

- http://pqbypass.com/technology/
- https://vimeo.com/182166624

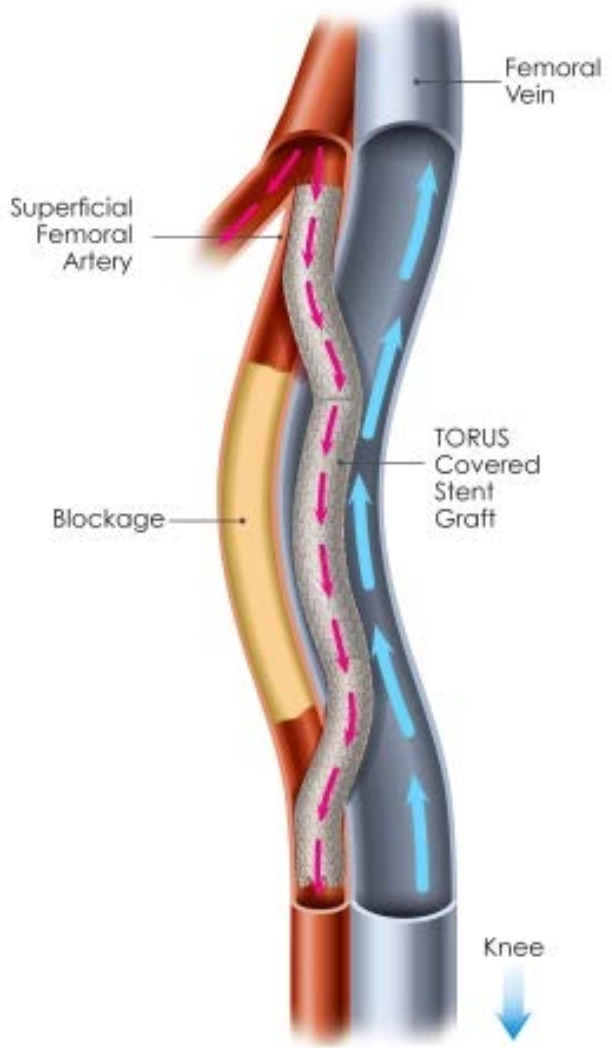
PQ Bypass results 18-months

- Primary patency was 67.6%
- Primary-assisted patency was 78.9%
- Secondary patency was 94.1%
- Survival 98.5%

- TLR 74.6%, Freedom from major amputation was 98.6%.

- NO INFO on claudicants vs CLI

- For a good Endo operator, limited clinical use



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Venous Arterialization

- Reserved for patients w no reconstructive option
- Superficial Surgical Venous Arterialization - GSV
- Deep Surgical Venous Arterialization -
- Percutaneous Venous Arterialization
- Hybrid Venous Arterialization

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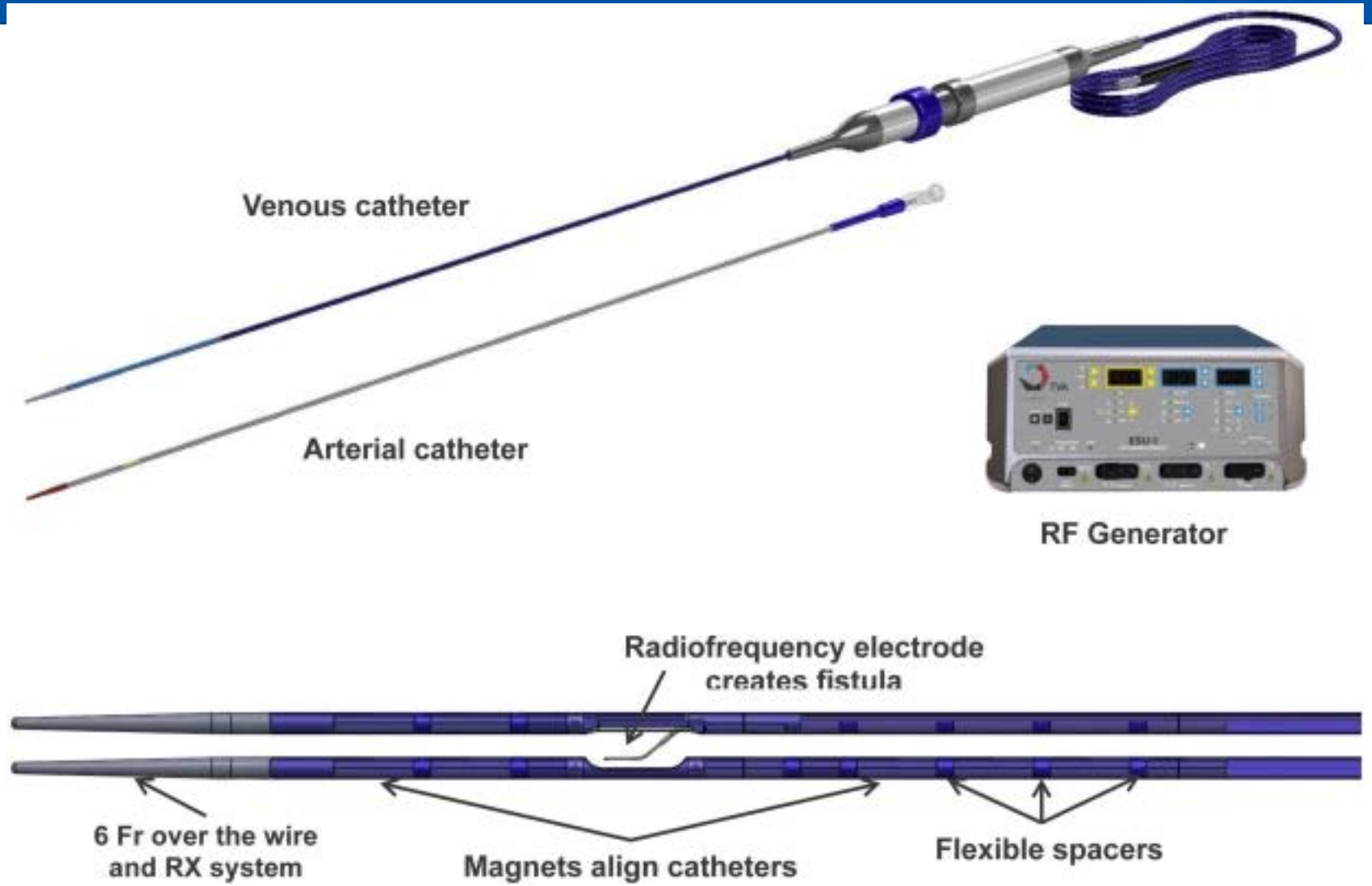

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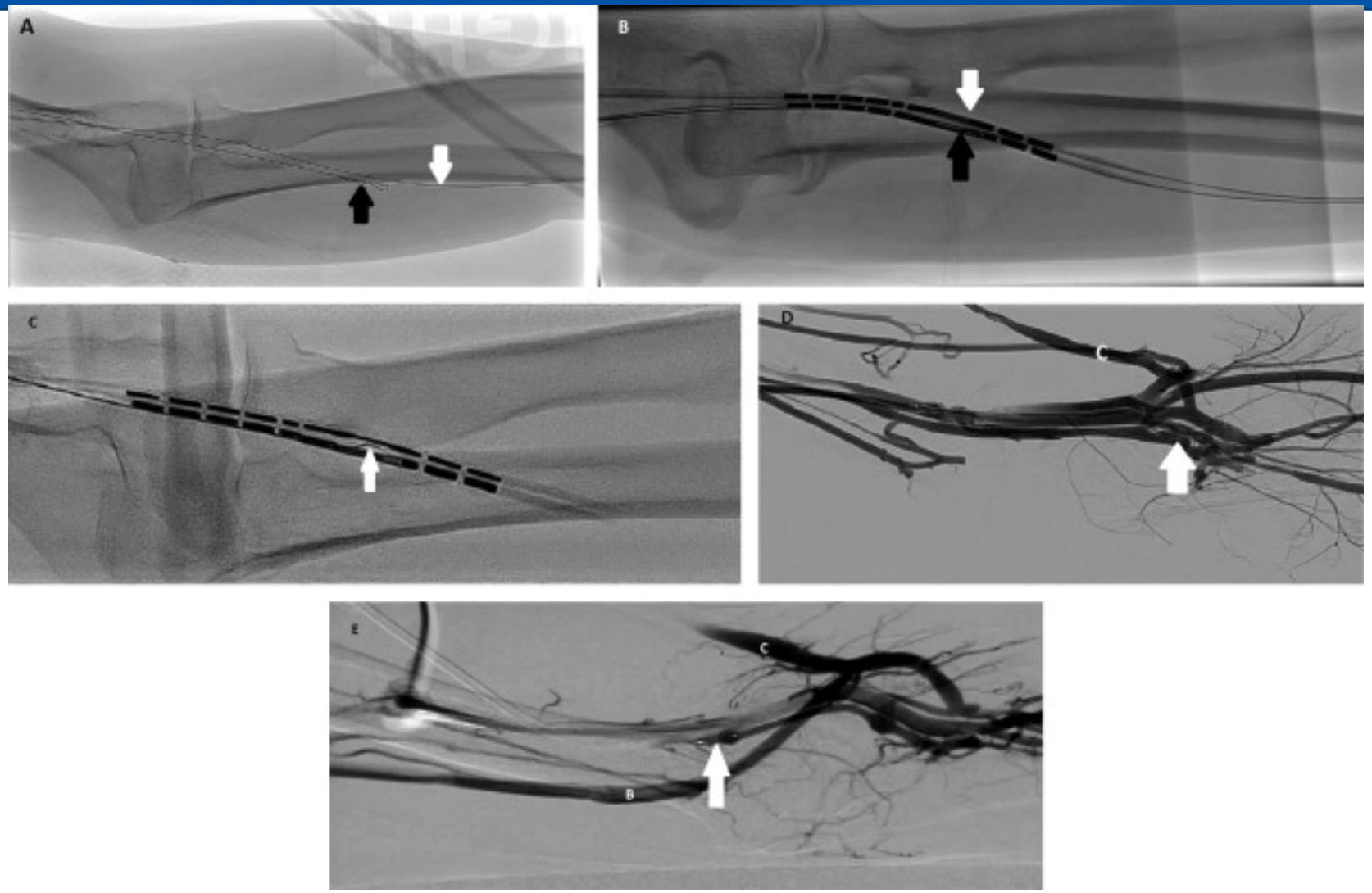

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https://www.youtube.com/watch?v=tAV9JV8-GxE

Venous Arterialization

- All patients CLTI
- All patients had undergone previous attempts at revascularization – 14 limbs (13 pts)
- Technical success was 93%.
- One patient died perioperatively.
- Primary patency at 30 days was 82%.
- 6 pts had relief of their rest pain and wound healing.
- 4 pts major amputation, and 2 have been offered amputation.

Venous Arterialization for Nonreconstructible Lower Extremity Arterial Disease: A Multicenter Case Series

Kyle A. Arsenault,[1] Leonard W. Tse,[2] Joel Gagnon,[1] David Kelton,[3] Keith Baxter,[1] Jerry Chen,[1] William Johnson,[4] Varun Kapila[2]. [1]Division of Vascular Surgery, University of British Columbia, Vancouver, BC, Canada; [2]Division of Vascular Surgery, William Osler Health System, Brampton, ON, Canada; [3]Division of Interventional Radiology, William Osler Health System, Brampton, ON, Canada; [4]Division of Vascular Surgery, Trillium Health Partners, Mississauga, ON, Canada

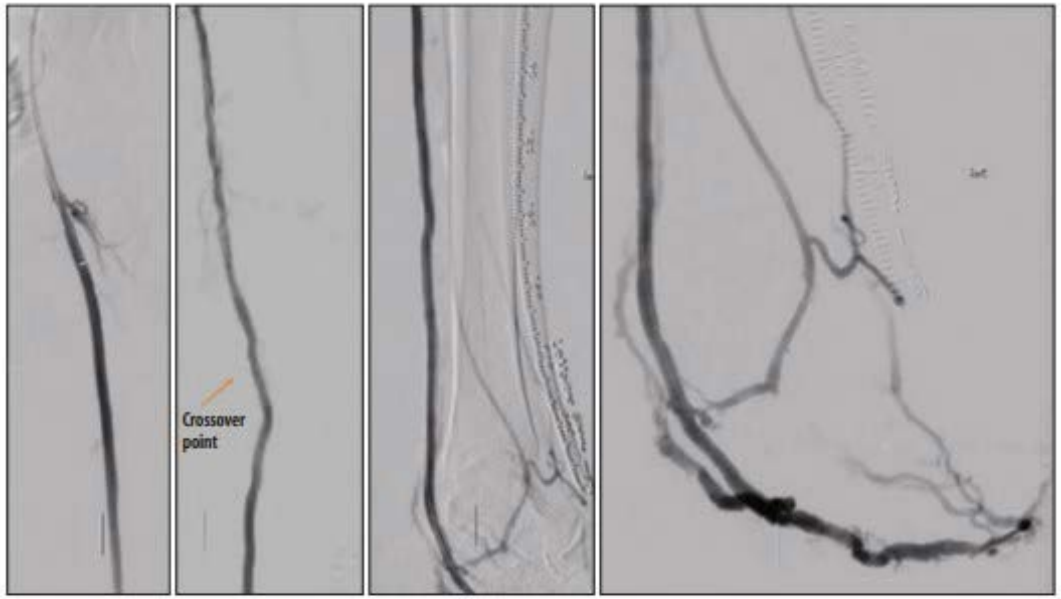

Figure 6. Angiogram showing the results immediately after the procedure was completed. The plantar venous arch is opacified.

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Hydration Cures PAD!!

- 32 claudicants, 4 rest pain
- 2.5L daily, 35/36 compliant
- ABI (from 0.60 to 0.76; P < 0.0001)
- skin temp from 29.95C to 30.0C, P < 0.001).
- Walking time: 1.25 to 6.25 min (P < 0.0001)
- Walking distance: 100 meters to 535 meters (P < 0.0001)

Reversal of Lower-Extremity Intermittent Claudication and Rest Pain by Hydration

Samuel Fernández,[1,2] Juan Carlos Parodi,[1,3,4,5] Fabián Moscovich,[1,6] and Camilo Pulmari,[1,7]
Buenos Aires and CABA, Argentina, Ann Arbor, Michigan

Background: Medical treatment of disabling intermittent claudication or critical limb-threatening ischemia causing rest pain often fails or has partial response.
Methods: In this pilot study, 36 patients (12 females) affected by disabling intermittent claudication or rest pain of the lower extremities were exposed to a daily 3-L water intake for up to 6 weeks. Cutaneous foot temperature, ankle/brachial index, time and distance of claudication, and pain intensity were recorded before and at the completion of the hydration period.
Results: Patients with a mean ± SE age of 71 ± 2 years (range, 40–86) had disabling claudication (less than 100 meters) for more than 5 months while 11% reported pain at rest. A 6-week water intake of more than 2,500 mL/24 hr was achieved in 35 of the 36 patients enrolled in the study. Increased water intake was associated with significant improvements in median ankle/brachial index (from 0.60 to 0.76; $P < 0.0001$) and skin temperature (first dorsal right toe, from 29.95°C to 30.0°C, $P < 0.001$). Time and distance to report claudication of supervised treadmill exercise improved from 1.25 to 6.25 min ($P < 0.0001$) and from 100 meters to 535 meters ($P < 0.0001$), respectively.
Conclusions: This study suggests that hydration attained by daily water consumption of more than 2.5 L has a robust impact on reducing the symptoms of disabling claudication and rest pain caused by peripheral vascular disease.

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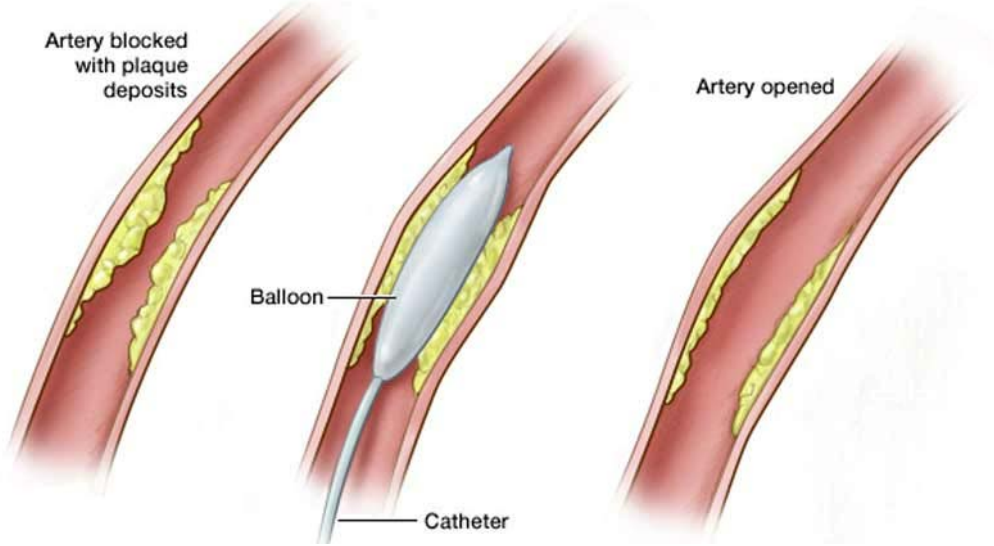
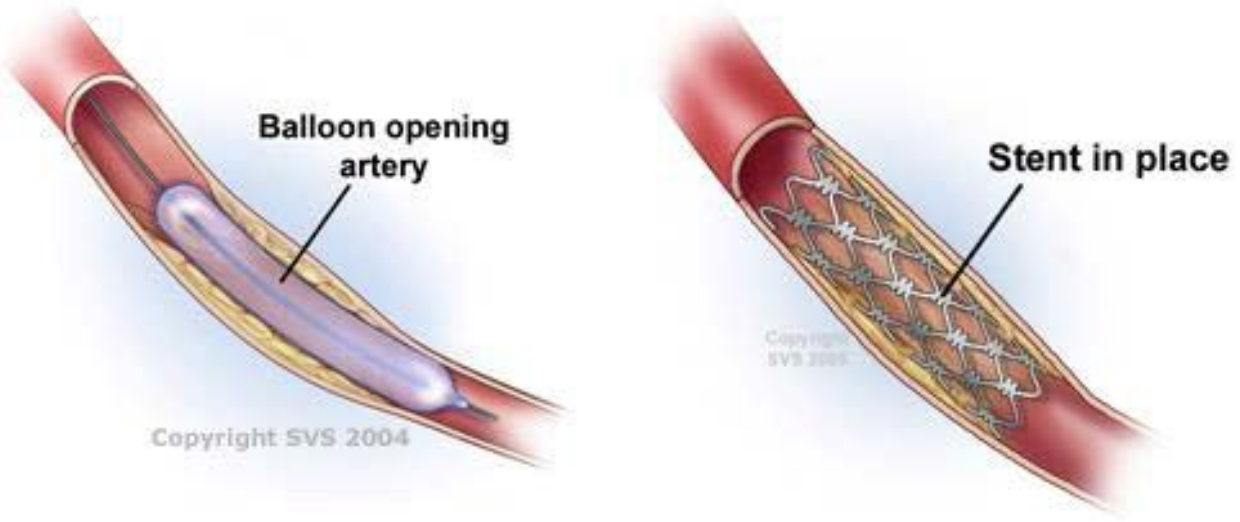
Endovascular Tx of PAD

- Balloon Angioplasty/Stent
- Atherectomy
- Anti-proliferative agents (DCB/DES)
- Endovascular “PQ” Bypass
- Venous Arterialization
- Hydration





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Thank You, Questions?

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