Structural Heart Disease & Peripheral Arterial Disease Update!

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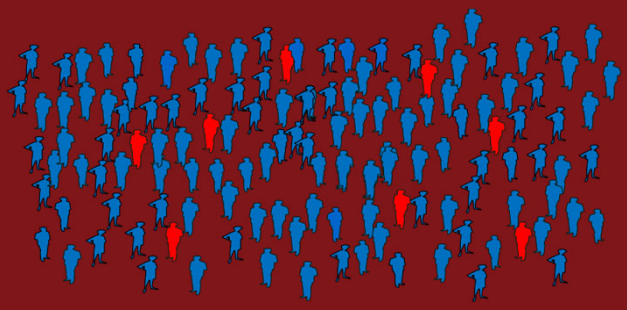
Scope

- Definition and Prevalence
- Clinical Manifestation
- Diagnosis
- Medical Therapy
- Endovascular Therapy
- Critical Limb Ischemia
- Transpedal Access
- Future

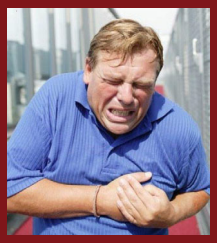
Prevalence(How many people have PAD)

- The worldwide prevalence of lower extremity peripheral artery disease (PAD) is between 3 to 12 percent
- In Europe and North America, an estimated 27 million individuals



Symptoms of PAD

- Asymptomatic PAD
  - < 50 % of PAD patients and ~30 percent of their physicians are aware that PAD is present
  - PAD increased the risk of heart attack, stroke and death



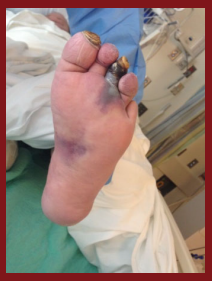
Symptoms of PAD

- Intermittent Claudication*** most common***
  - reproducible pain with ambulation that is relieved

Different from neuropathic claudication which walking improve pain

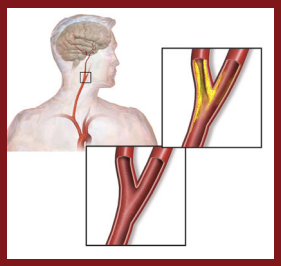
Symptoms of PAD

- Critical limb ischemia
  - Tissue loss such as skin ulceration or gangrene

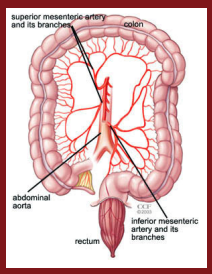


PAD can happens anywhere

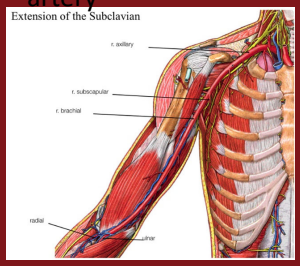
Carotid artery



Abdominal artery



Subclavian(arms) artery



Risk factors SAME AS coronary artery disease

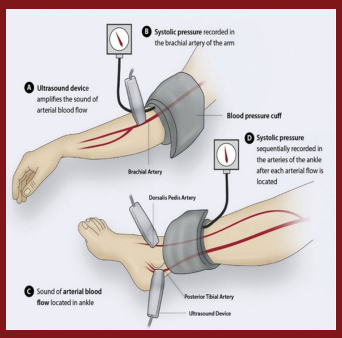
- Age above 45 years for men and above 55 years for women
- Family history of premature CAD:
- First degree relative male < 55 years or female <65 years.
- Hypercholesterolemia
- Hypertension
- Cigarette smoking
- Diabetes mellitus
- Obesity

Diagnosis

- **Non invasive**

ABI(ankle brachial index)**

- We measure the blood pressure in the arms and legs
- The differences between arms and legs

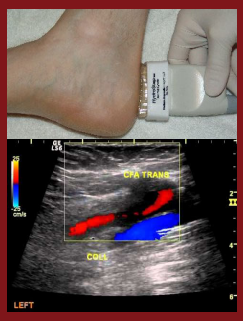


ABI Value	Interpretation	Recommendation
Greater than 1.4	Calcification / Vessel Hardening	Refer to vascular specialist
1.0 - 1.4	Normal	None
0.9 - 1.0	Acceptable	
0.8 - 0.9	Some Arterial Disease	Treat risk factors
0.5 - 0.8	Moderate Arterial Disease	Refer to vascular specialist
Less then 0.5	Severe Arterial Disease	Refer to vascular specialist

Stanford Medicine 25

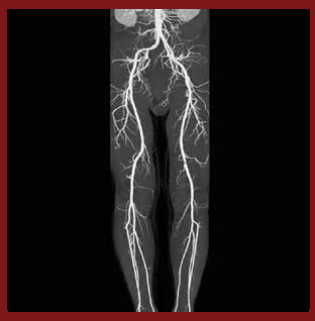
Diagnosis-non invasive

Duplex Ultrasound***



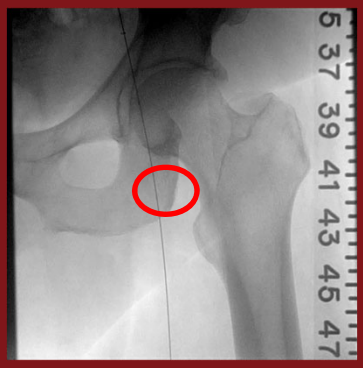
CT/ MRI

- radiation and contrast



Diagnosis-minimally invasive

- Angiogram-injecting contrast to see the flow and blockade

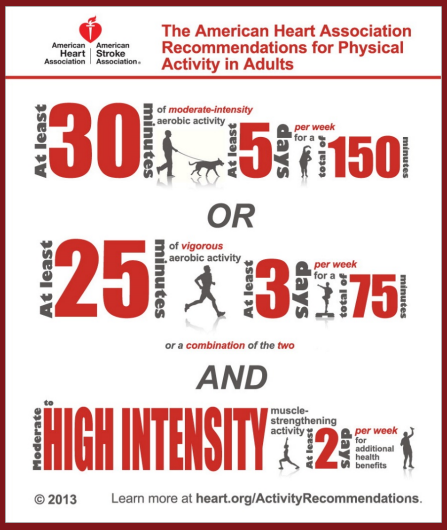


Life style modification-DIET

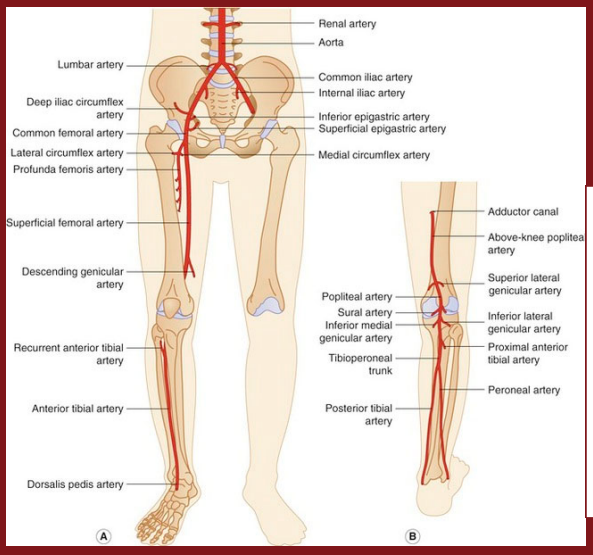
- Reduce saturated fat to no more than 5-6 percent of total calories
- Minimize mono-unsaturated fats (oleic acid found in olive oil) and trans-fats (found in milk, animal fats and some vegetable oils). These types of fats are specified in most foods lists of calorie sources.
- Restrict sodium intake to no more than 1.5 to 2 grams per day (approximately 6 grams salt/day)
- Increas[illegible] to 25-30 grams per day

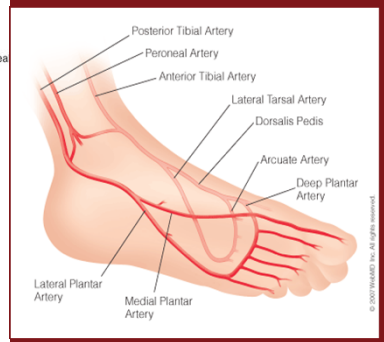
Health.Clevelandclinic.org

Exercise



Anatomy





Definition and Prevalence

- Atherosclerosis of aorta, iliac and lower extremities arteries
- Significant morbidity and mortality
- 200 million people lives with PAD
- ~ 30% increased prevalence in low and middle income countries
- 13.1% increase high-income country – 10 year period

Patel et al. JACC 2015
Fowkes et al. 2013

Prevalence

- 6% of Americans over 40 years of age
- High-risk population (DM, HTN, CAD): 30%
- Prevalence and severity: higher among African Americans and Hispanics

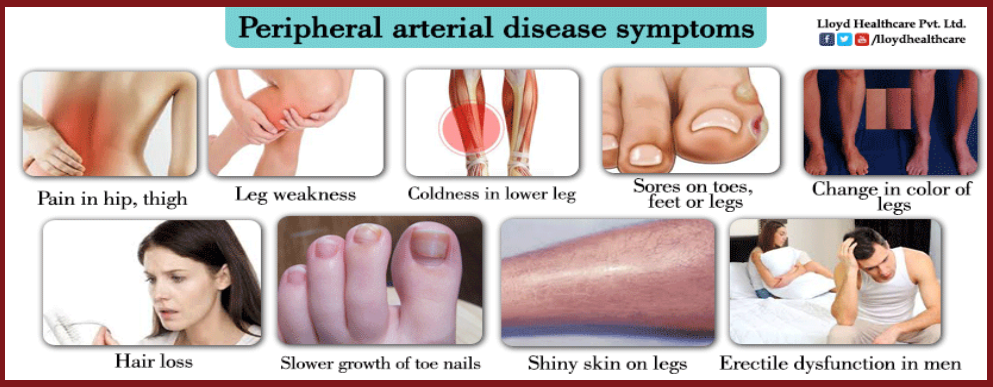
Selvin et al. Circulation 2004

Risk Factors

- Positive family history
- DM2 – main risk factors
- Smoking – main risk factors
- Chronic kidney disease
- Hypertension
- Hyperlipidemia

Joosten et al. JAMA 2012

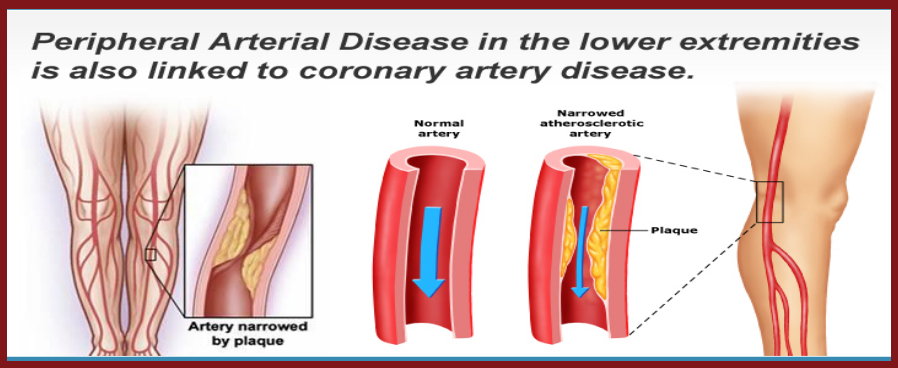
Clinical Presentation



- Classic claudication (10% to 30%)
- Atypical leg pain (20-40%)
- Asymptomatic (nearly 50%)

Rooke et al. JACC 2015

Clinical Presentation

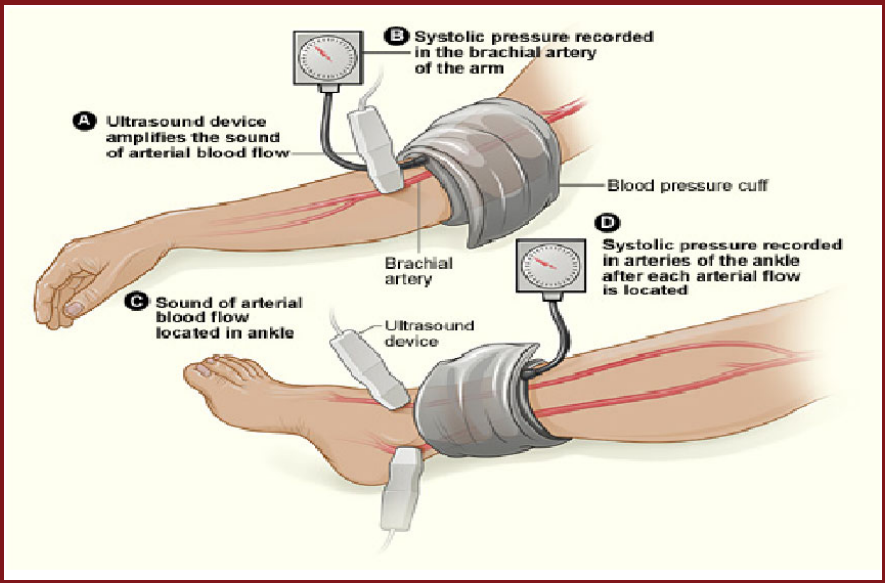


- Function decline and associated CV disease:

1. 10% Fatal AMI/Stroke
2. 25% Limb amputation

Diagnosis

- Ankle brachial index:
- Continuous-wave doppler: higher of 2 systolic pressures in the dorsalis pedis and posterior tibial artery in each leg
- Divide by the higher of the brachial artery systolic blood pressure in each arm
- Normal: between 1.0 and 1.40
- Abnormal ≤ 0.90
- Values > 1.4 = very calcified vessels
- Toe brachial index should be used (< 0.70 - abnormal)



Role of screening and biomarkers

- Patients ≥ 65 years old
- Patients ≥ 50 years with DM2 or smoking
- High-sensitivity C-reactive protein
- Beta 2 microglobulin
- Cystatin C

Hirsch et al. JAMA 2001
Hiatt et al. Circ Res. 2015

The role of Exercise

- Mainstay treatment for symptomatic PAD – Class Ia recommendation
- Well-established benefit after 12-week exercise
- It modifies the pathophysiology of the disease:

1. Skeletal muscle metabolism
2. Endothelial function
3. Gait biomechanics

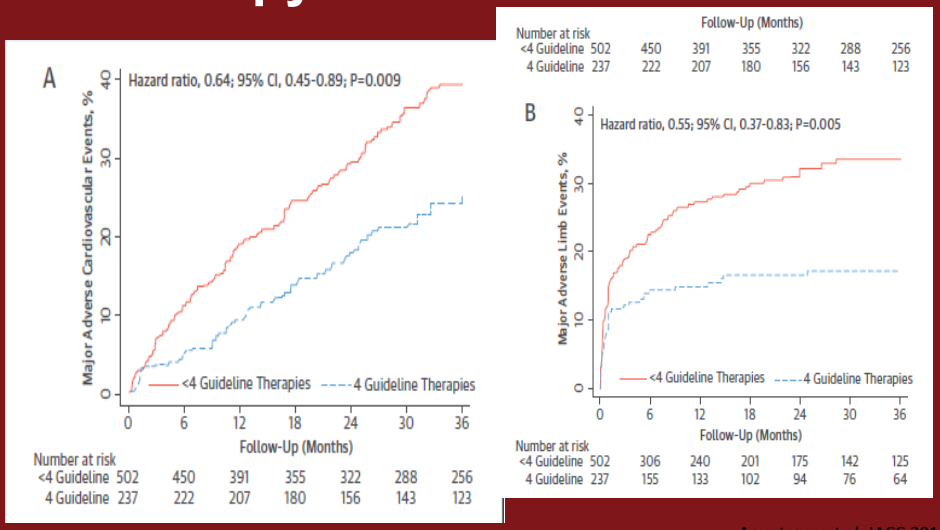
- Associated with decreased all-cause mortality and morbidity ~ 10%

Hiatt et al. J Appl Physiol 1996
Hiatt et al. Circulation 1990

Decrease the Risk of MI, Stroke, and CV Death	Improve Symptoms, Quality of Life, and Prevent Amputation
• Discontinue Tobacco Use	• Discontinue Tobacco Use
• Walking Program	• Walking Program
• Control Blood Pressure to Goal -ACE Inhibitor	• Cilostazol
• High-Dose Statin Therapy	• Good Foot Care -Moisturizing cream, nail care, treat and prevent tinea, orthotics to prevent abnormal pressure points
• Antiplatelet Therapy	• Revascularization

Olin et al. JACC 2016

Adherence to Guideline-Recommended Medical Therapy



Armstrong et al. JACC 2014

Pharmacotherapy to improve claudication symptoms

Cilostazol
50% absolute improvement of claudication symptoms
Low Adherence (> 60 % discontinuation at 3 years)
Contra-indicated in heart failure patients (EF < 40%)
Recommended dose is 100 mg po 2x/day for at least 4 months

Ostergren et al. Eur Heart J 2004
Westin et al. JACC 2014
Kumbhani et al. Eur Heart J 2014

ACEI's

HOPE trial : ~ 4100 PAD patients randomized to Ramipril or placebo

Composite cardiac death, AMI and stroke 14.3% in Ramipril vs. 22% placebo

Should be used for both symptomatic and asymptomatic patients

Westin et al. JACC 2014

Statins

High-intensity statin (Atorvastatin 80 mg or rosuvastatin 40 mg)

Reduction in adverse limb outcomes: 10% :amputation at 4 years follow up

Improvement of 1 year of limb salvage, primary and secondary patency after endovascular treatment

Kumbhani et al. Eur Heart J 2014

Antiplatelet Therapy

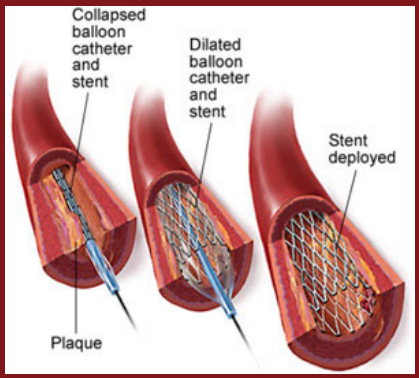
Aspirin
Mainstay drug therapy
Data is not well established for PAD patients
POPADAD and AAA trials failed to prove aspirin benefit for low-risk patients (ABI < 0.95)
Meta-Analysis showed no difference on MACCE (8.2% aspirin vs. 9.6% placebo)
Currently class Ia for symptomatic PAD patients
IIa for asymptomatic PAD and ABI < 0.90

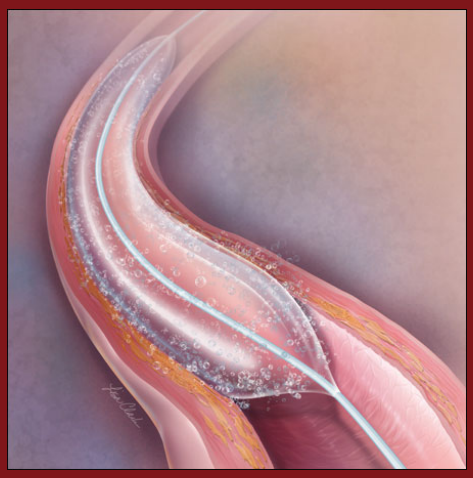
CAPRIE trial, Lancet 1996

Dual anti-platelet therapy with Clopidogrel
Can be an alternative to ASA for antiplatelet monotherapy
DAPT should be indicated for high risk symptomatic patients
Significant less AMI (2.3% vs. 3.7%, hospital admission 16.5% vs. 20.1%)
Minor bleeding is increased but not moderate, severe or fatal bleeding
Novel anti-coagulants and new antiplatelets are currently being investigated

Bhatt NEJM 2006

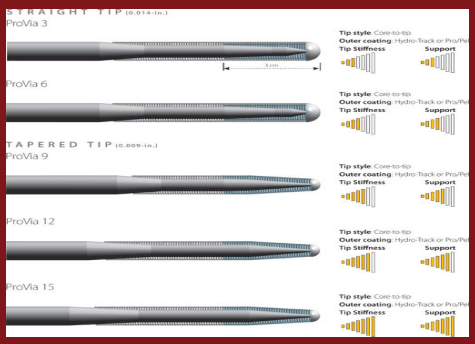
Endovascular Therapy

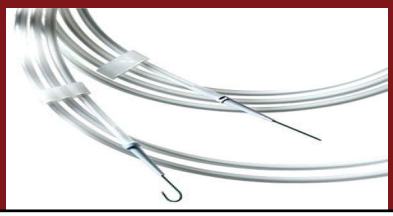


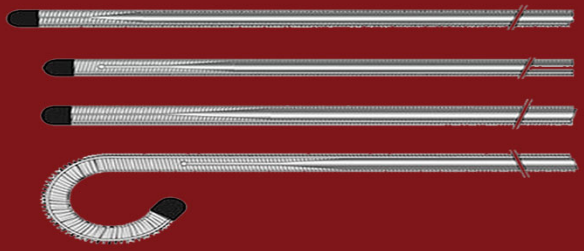


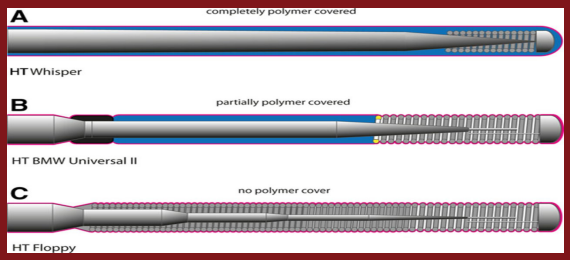
Team approach to CLI	
Wound care/Podiatry	Wound care and debridement
Infectious Disease	Infection control
Endocrinology	Diabetes management
Primary care	Smoking cessation and exercise program program
Interventional Cardiology	Endovascular revascularization
Nutrition	Nutrition evaluation
Vascular surgery	Open revascularization
Orthopedic surgery	Minor or major amputation
Plastic Surgery	Limb reconstruction

Wires

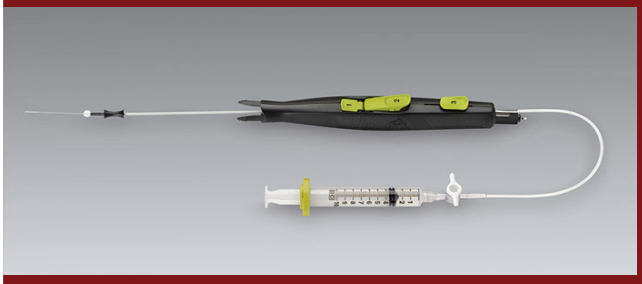




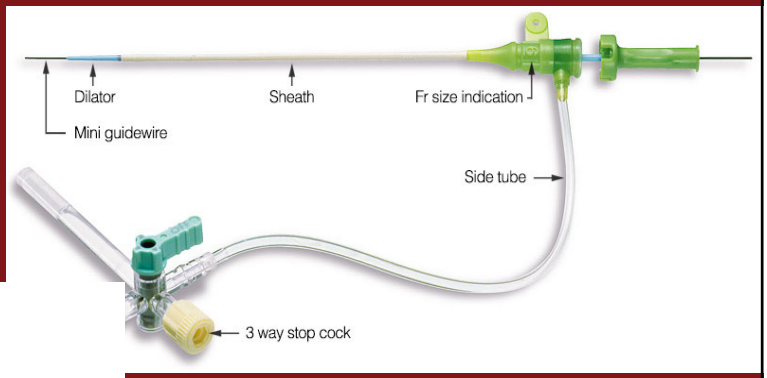


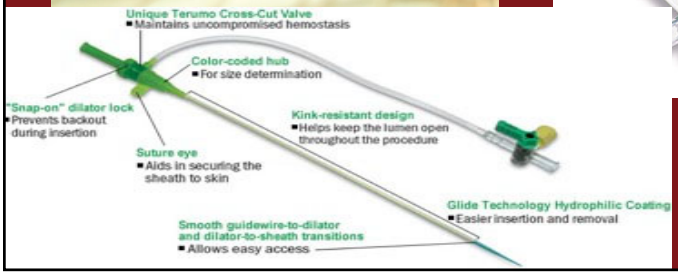


Closure Device



Sheaths





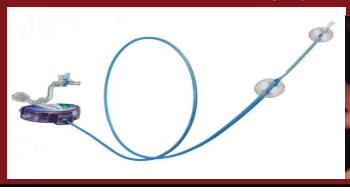
Stents

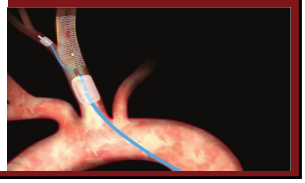
Supera

Viabahn

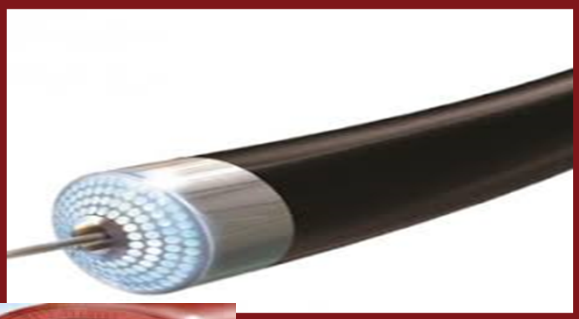
iCast

Mo.Ma





Turbo-Elite Spectronitecs Laser Catheter

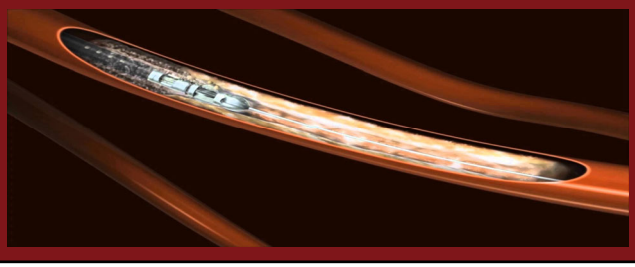


- Utilizes the power of ultraviolet light to provide a atherectomy
- Able to open above and bellow the knee stenoses and occlusions with precision and control

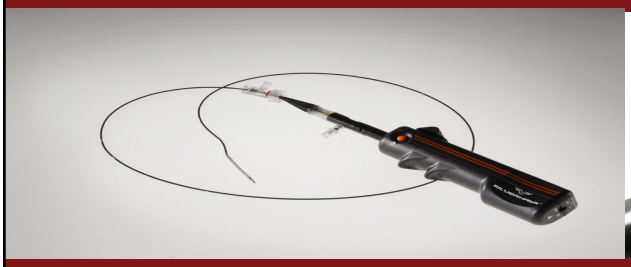
OTW Peripheral Over-the-Wire Catheters

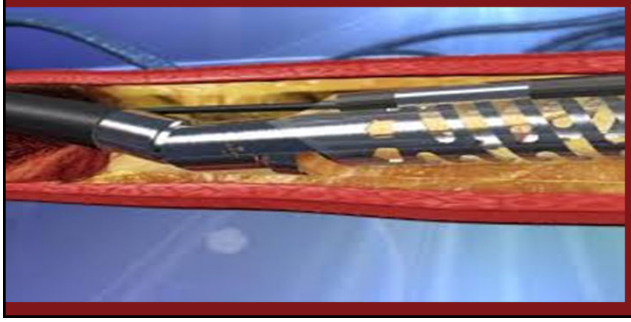
Catheter Diameter	0.9mm	1.4mm	1.7mm	2.0mm	2.3mm	2.5mm	2.3mm	2.5mm
Model Number	410-152	414-151	417-152	420-006	423-001	425-011	423-135	425-135
Vessel Diameter	≥1.4mm	≥2.1mm	≥2.6mm	≥3.0mm	≥3.5mm	≥3.8mm	≥3.5mm	≥3.8mm
Max Guidewire Compatibility	0.014″	0.014″	0.018″	0.018″	0.018″	0.018″	0.035″	0.035″
Sheath Compatibility	4F	5F	5F	6F	7F	8F	7F	8F
Max Tip Outer Diameter	0.038″	0.055″	0.068″	0.080″	0.091″	0.101″	0.091″	0.101″
Max Shaft Outer Diameter	0.047″	0.056″	0.069″	0.081″	0.091″	0.102″	0.091″	0.102″
Working Length	150cm	150cm	150cm	150cm	120cm	110cm	125cm	112cm
Fluence (mJ/mm2)	30-80	30-60	30-60	30-60	30-60	30-45	30-60	30-60
Repetition Rate (Hz)	25-80	25-80	25-80	25-80	25-80	25-80	25-80	25-80

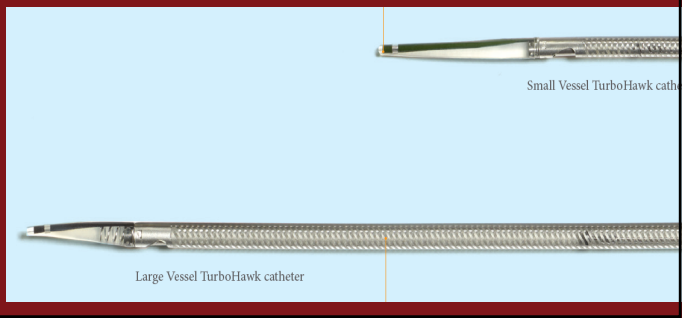
CSI Catheter
Rotational Atherectomy



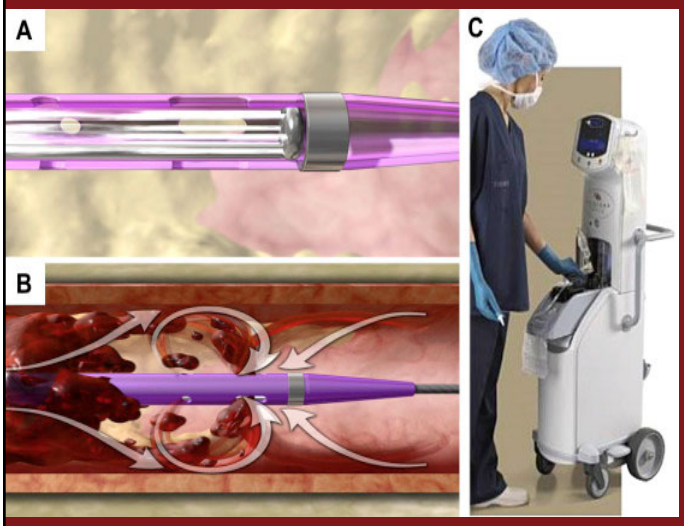
Turbohawk – Medtronic
Directional Atherectomy



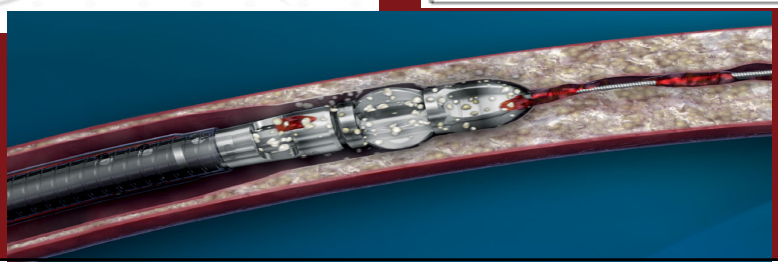




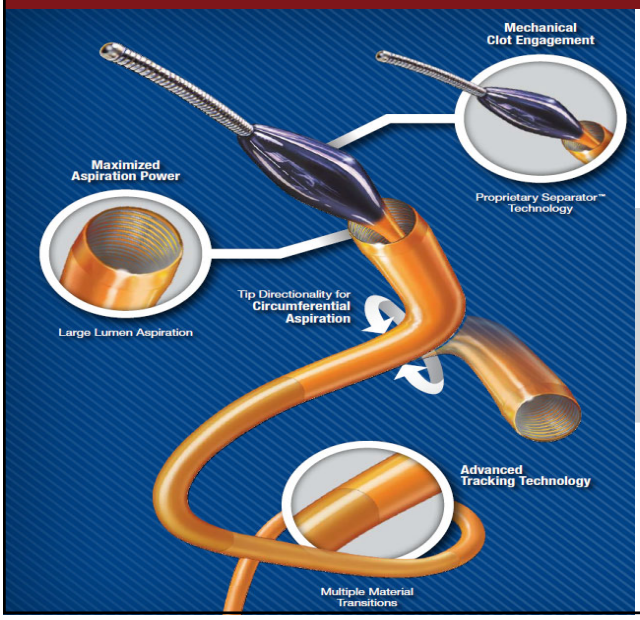
AnigoJet – Thrombectomy System

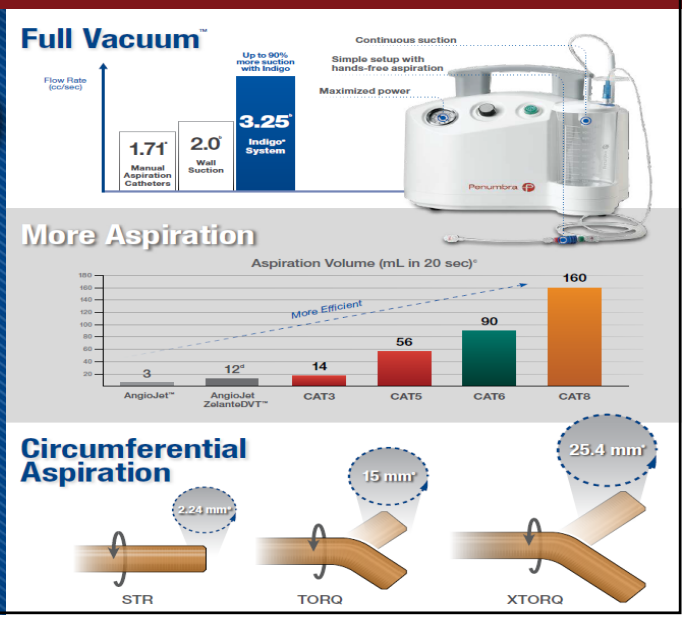


JetStream – Atherectomy catheters

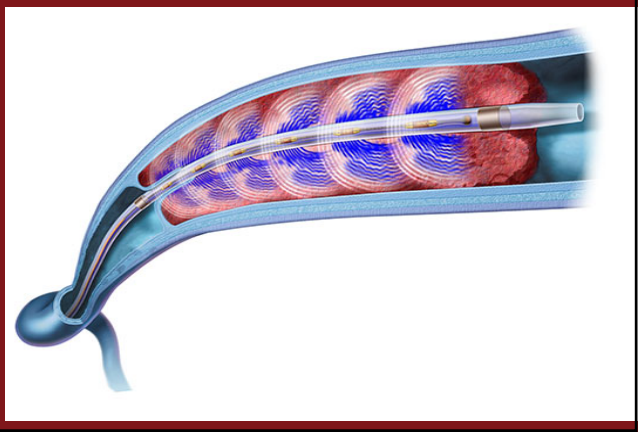


Penumbra - Catheter

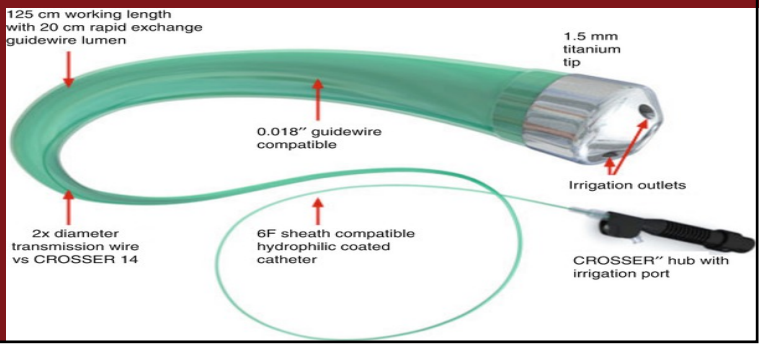




EKOS – Acoustic Pulse Thrombolysis



Crosser Catheter

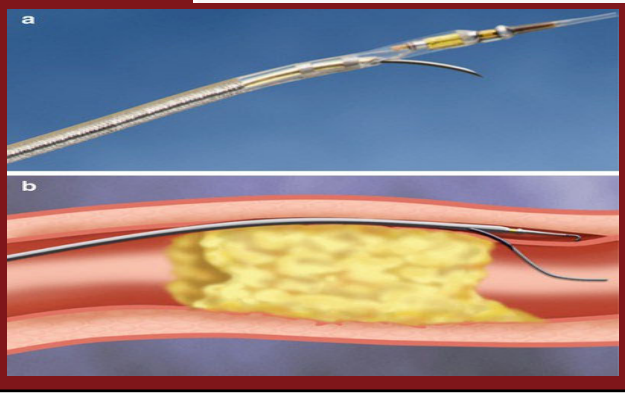


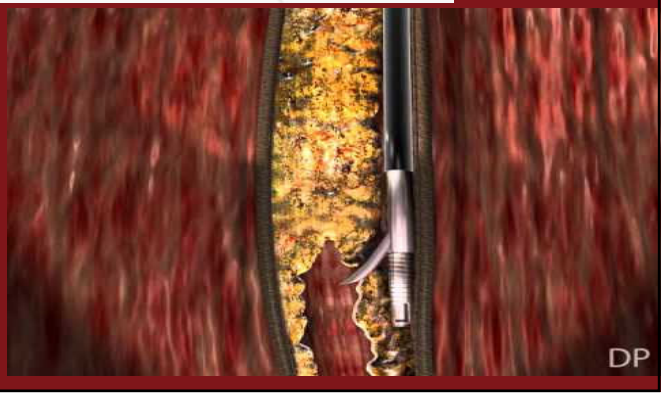
Drug Coating Balloon

Medtronic

In.Pact Balloon

Viance Crossing Catheter





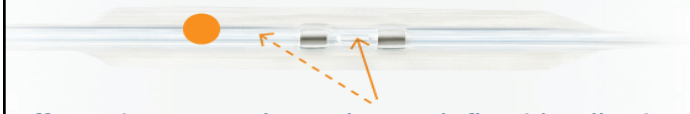
Multi-wire coiled shaft delivers 1:1 torque

Handle enables fast-spin techinque

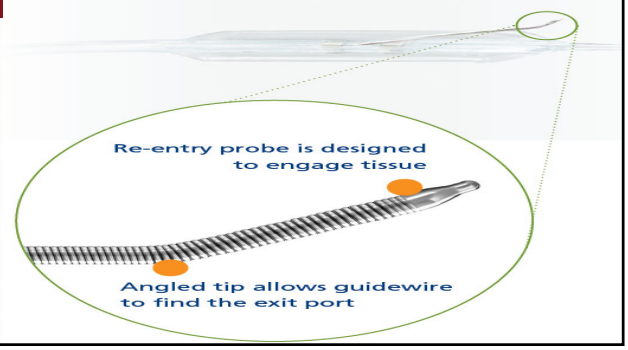
Ratchet limits torque output if too much resistance is built up

Description	Working length (cm)	Guidewire Compatibility (in)	Crossing Profile (max. in)	Sheath Compatibility (F)
Flexible	150	0.014	0.038	5
Standard	150	0.014	0.038	5

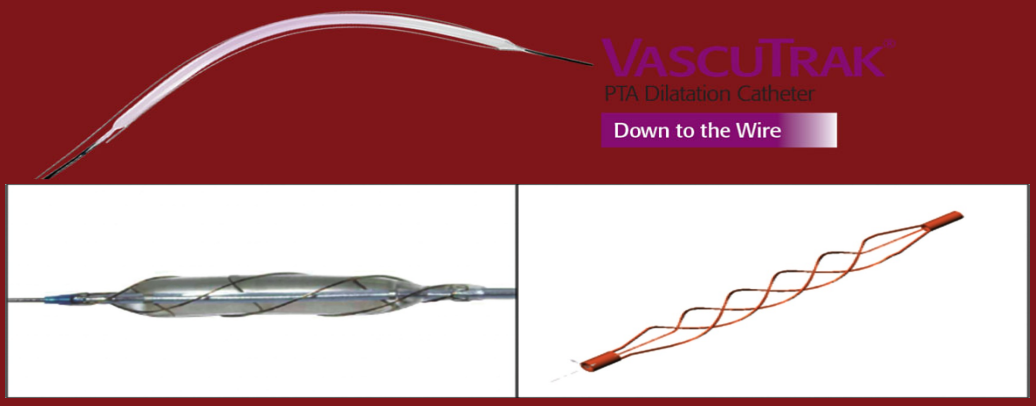
One flat side of the device orients to the true lumen when inflated



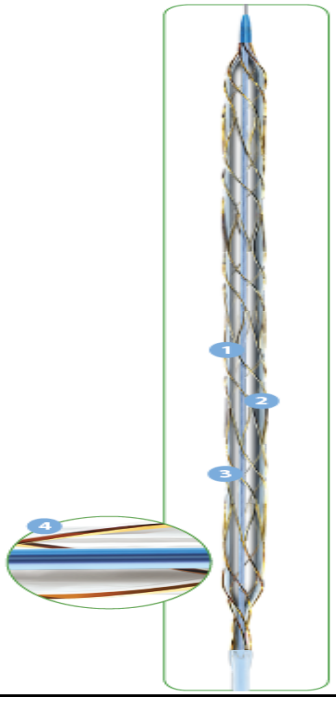
Offset exit ports are located on each flat side, allowing you to steer the guidewire through the correct port to re-enter the true lumen



Vascutrak PTA Dilation Catheter
Low pressure dilation

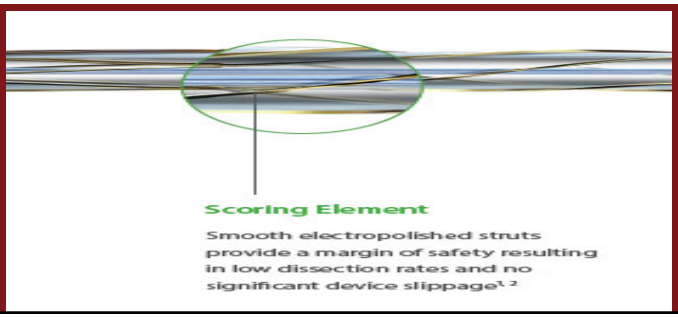


- Two external wires deliver Focused Force along the the length of the balloon, for dilation at low pressures
- Focused Force is applied in the two parallel planes and dual wire system, unlike the others



Angiosculpt

1. Large working range (2–up to 20 atm) allows physician to tailor device to vessel size*
2. Nitinol-enhanced balloon deflation for excellent rewrap and recross capabilities
3. Electropolished, helical scoring element safely scores lesion circumferentially[4]
4. Rectangular edges provide a predictable dilatation resulting in low dissection rates and minimal device slippage[1]



Case Presentation

- 52 years old female with past medical history of Takayasu's arteritis, left subclavian occlusion who presents with both legs pain with chronic non-healing ulcer on left foot for a month.

Physical examination:

V/S BP 137/60 mmHg, HR 88 per min , RR 18 per min

Left leg : Loss of hair, unable to palpate dorsalis pedis pulse but Dopplerable, 3x3 cm black eschar below left knee, purplish toes

Right leg : dopplerable pulse on DP and PT, mild pitting edema

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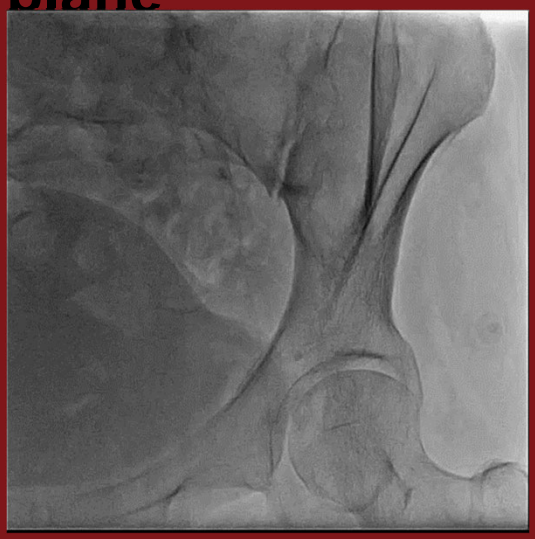
Left groin access: Wire went into dissected plane



Video 1 Left groin access

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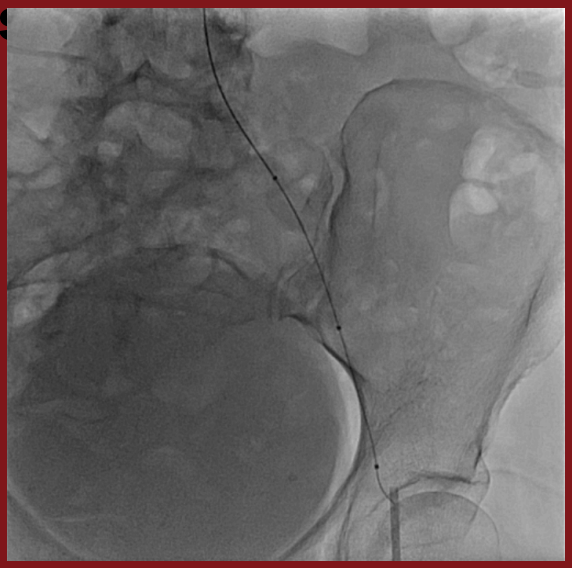
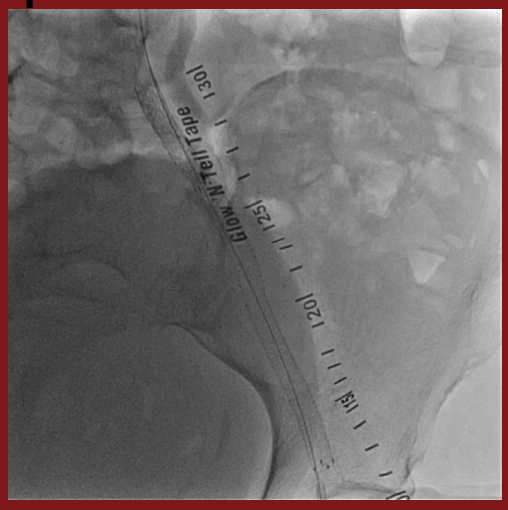
Right Brachial Access

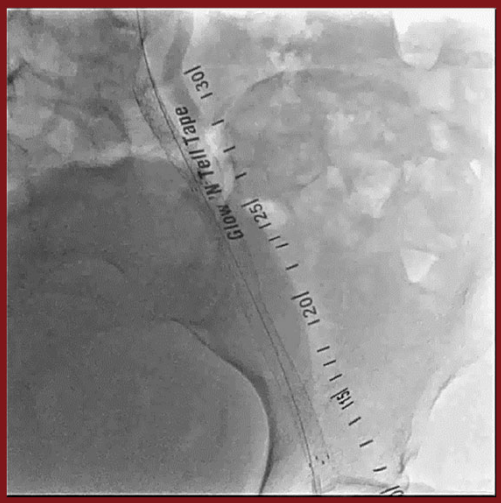
- 6 Fr vascular sheath >> 6F 90 cm sheath
- Pigtail advance for angiogram
- V18 carefully advanced to left common femoral artery with the help of QuickCross catheter



A 7x100 mm Gore Viabahn covered stent and deployed distal left CIA and EIA and 7x38 mm ICast stents deployed at proximal left CIA due to residual proximal lesion

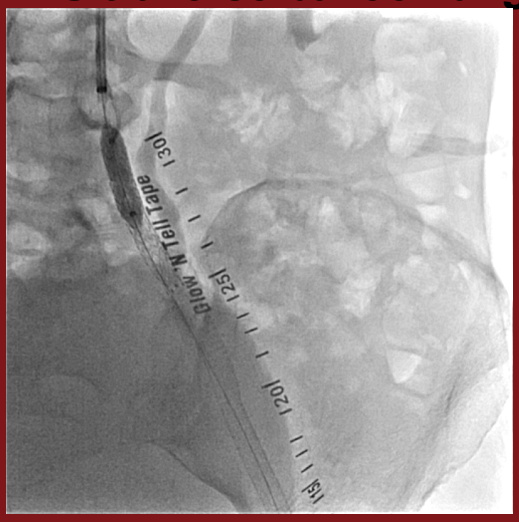


The stent deployed at left CIA and EIA

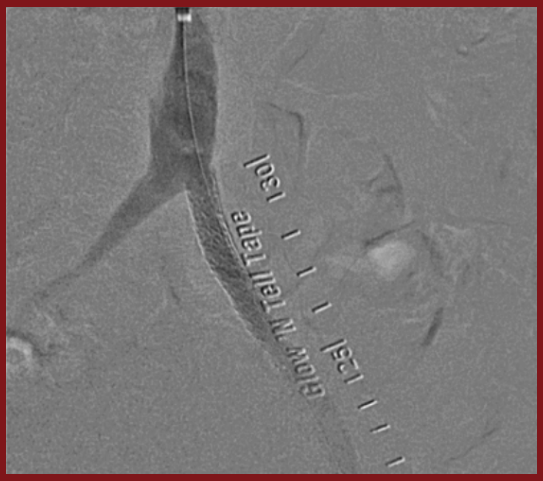


Video 3 Angiography post-stent deployed->residual proximal lesion

7x22 mm Icast was deployed at residual ostial to proximal residual lesion>>multiple 7x 120 mm Ultraverse balloon angioplasty

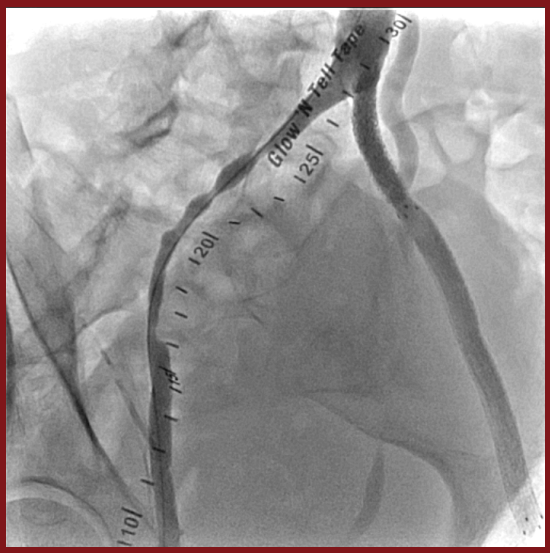


The stent deployed at proximal LCIA

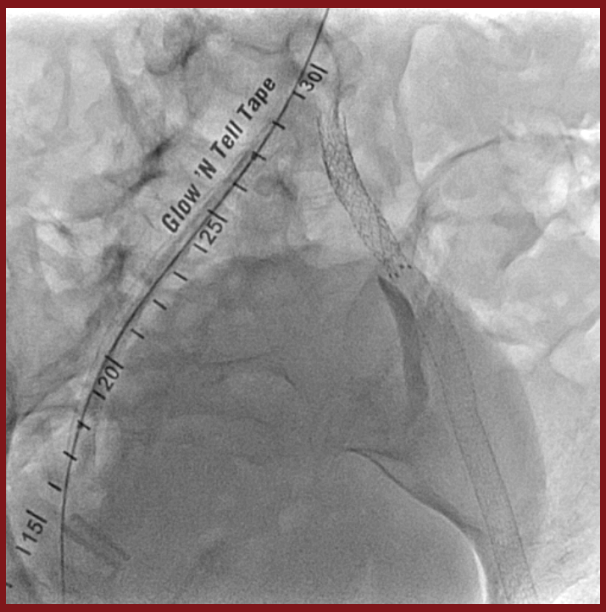


Angiography post-stent deployed

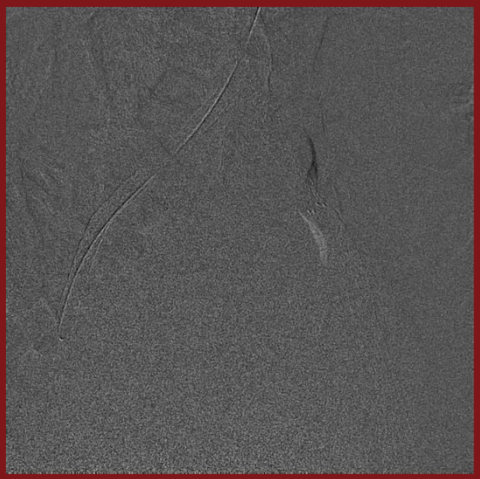
Redirect V18 wire to right FA



- 7x100 mm Stent was advanced into target lesion at right CIA and EIA
- 7x80 mm EverCross balloon was advanced over the wire into the right iliac stent for post-stent dilatation



Final result



Video 4 Angiography post-intervention

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Special technique used:

- Brachial access
- Tunnelling the wire
- Externalizing the wire
- Flossing the wire
- Covered stent placement
- Tech-mix administration –during the procedure!

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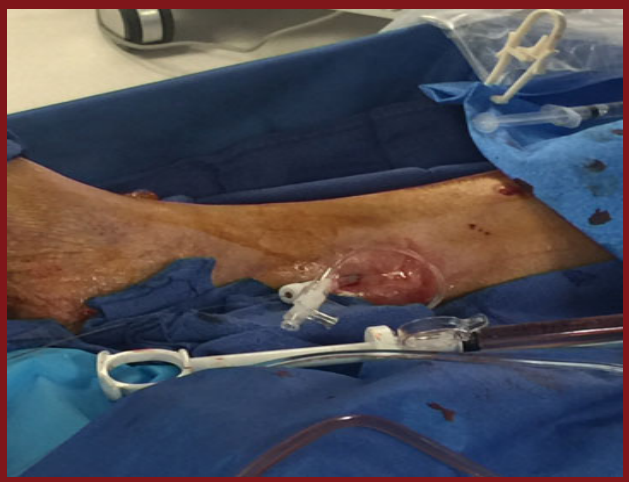


The Efficacy Of Trans Radial Access For Peripheral Interventions In Patients With Complex Trans Femoral Access

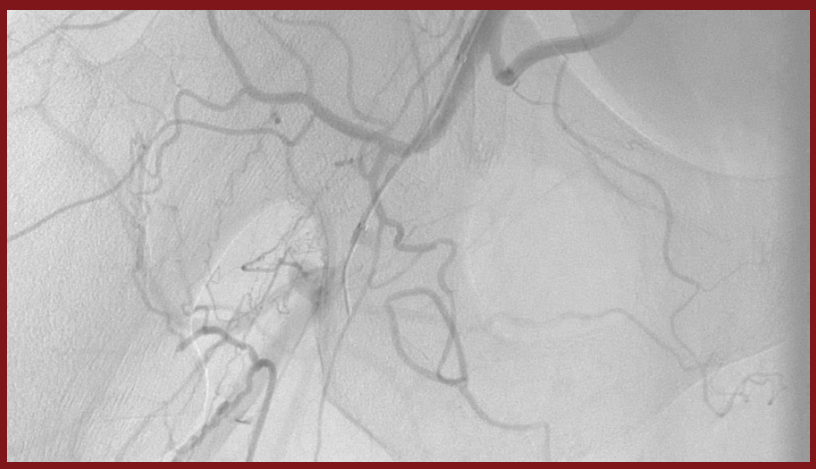
Conclusion:

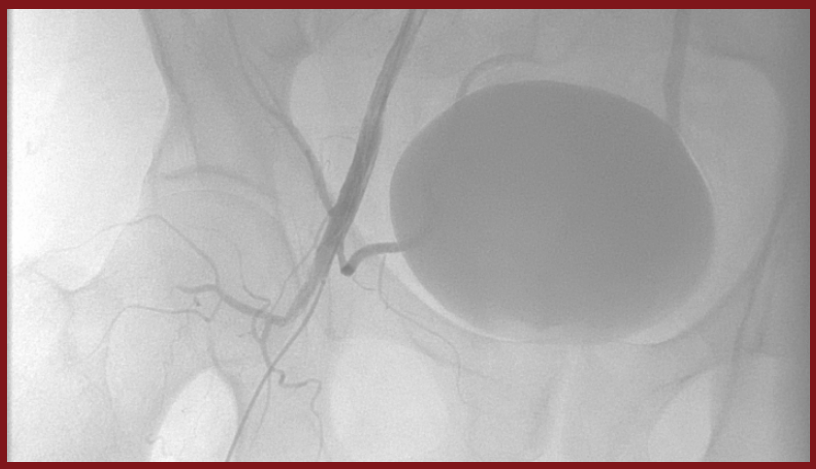
- Our experience has emphasized the utility, efficacy, and safety in approaching peripheral interventions through distal radial access
- In obese patients with difficult, unfavorable trans-femoral access and this allowed same-day discharge, which has also appeared to beeconomically feasible in comparison.

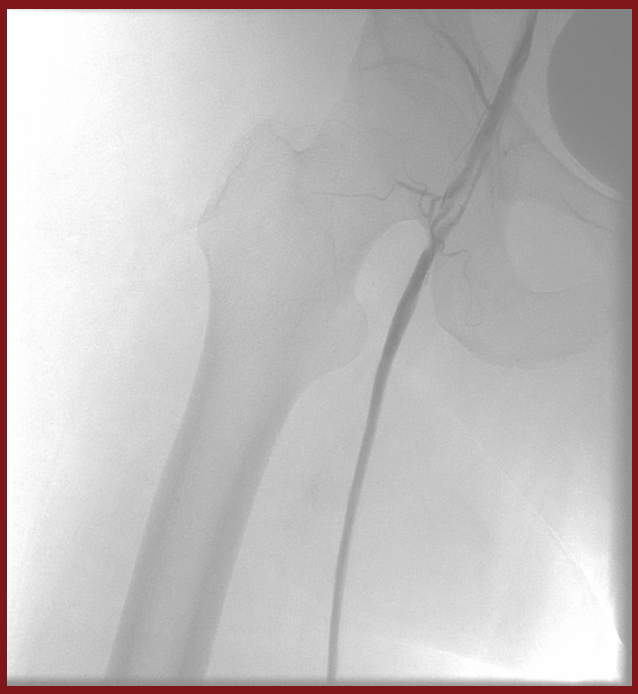
- Contrast used?
- Radiation Time?

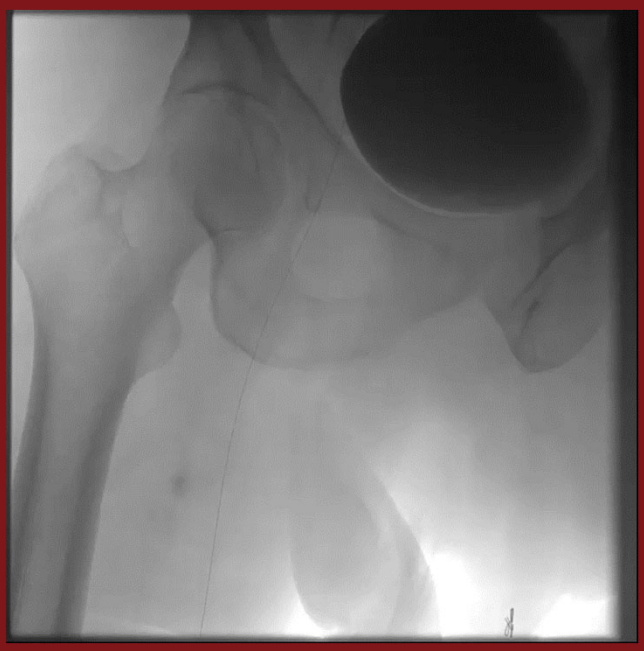
Case 1

- 58 y/o man with right lower extremity non-healing wound
- PMH: Active smoker, HTN, HLD, CAD, PAD
- CFA and SFA CTO



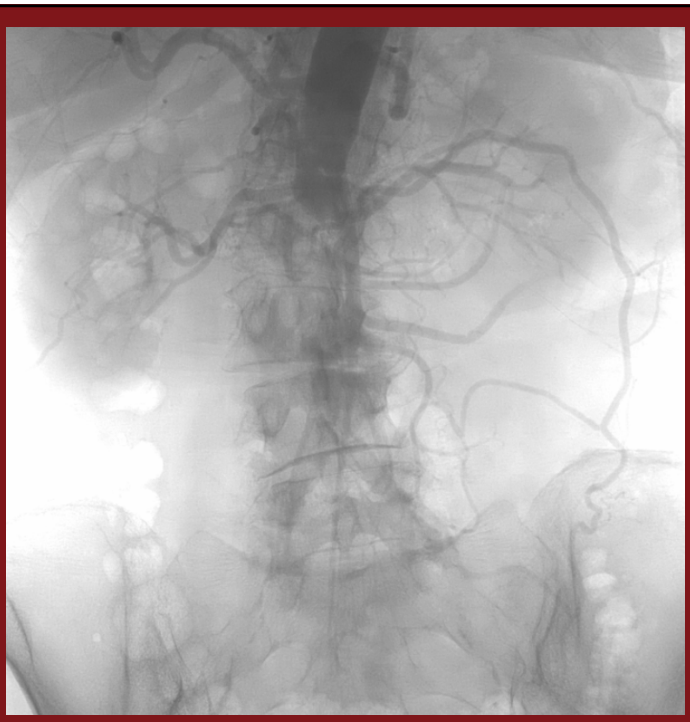


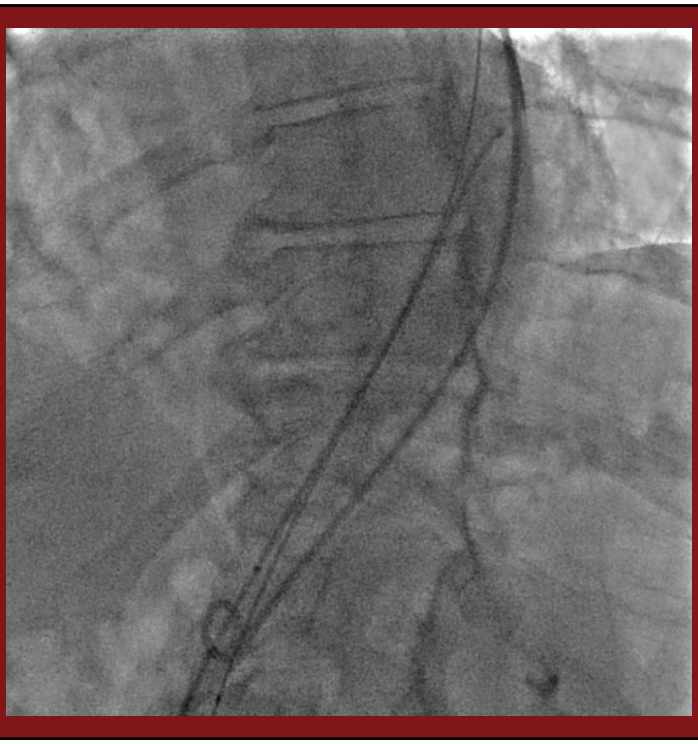


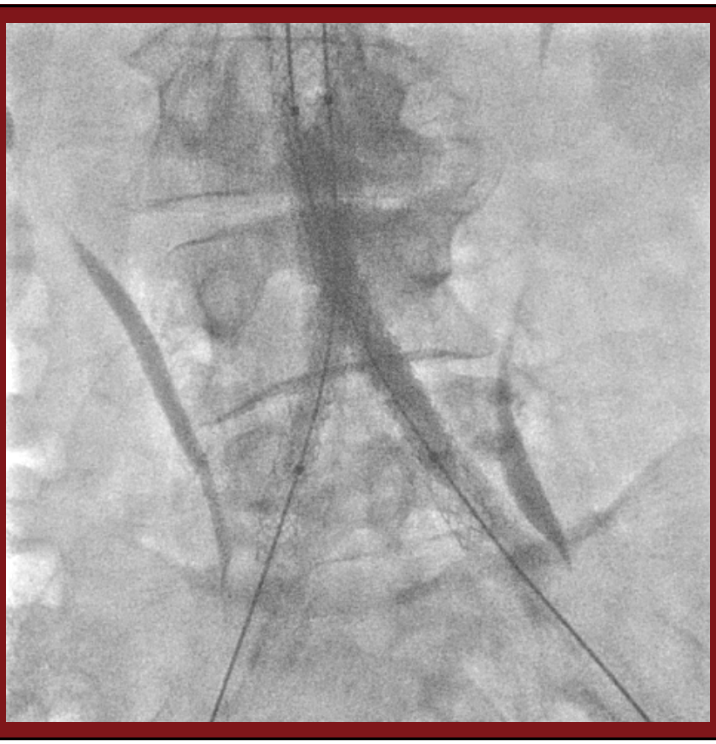


Case 2

- 72 y/o female Aorto-iliac Occlusive Disease and Distal toe gangrene
- PMHx: EtOH abuse, HTN, HLD, PAD, CAD, Alcohol Abuse, Former Tobacco Abuse
- Deemed poor surgical candidate and was referred for peripheral angiogram and intervention

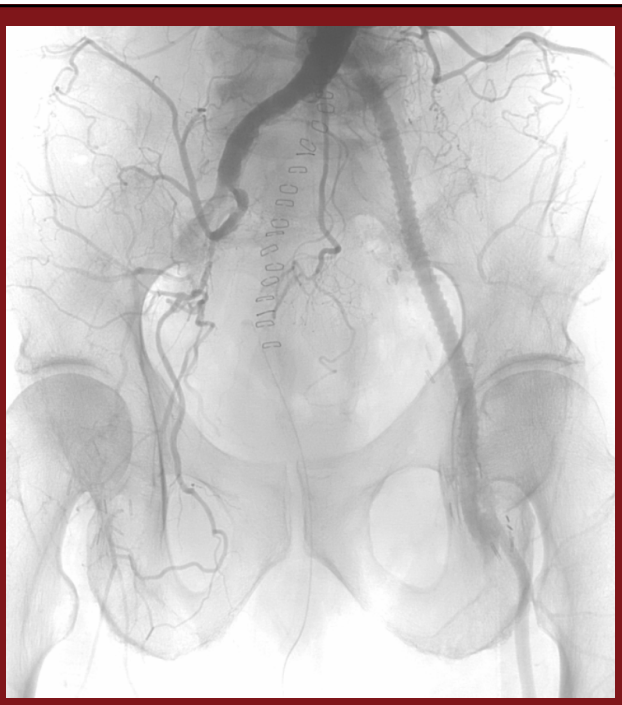


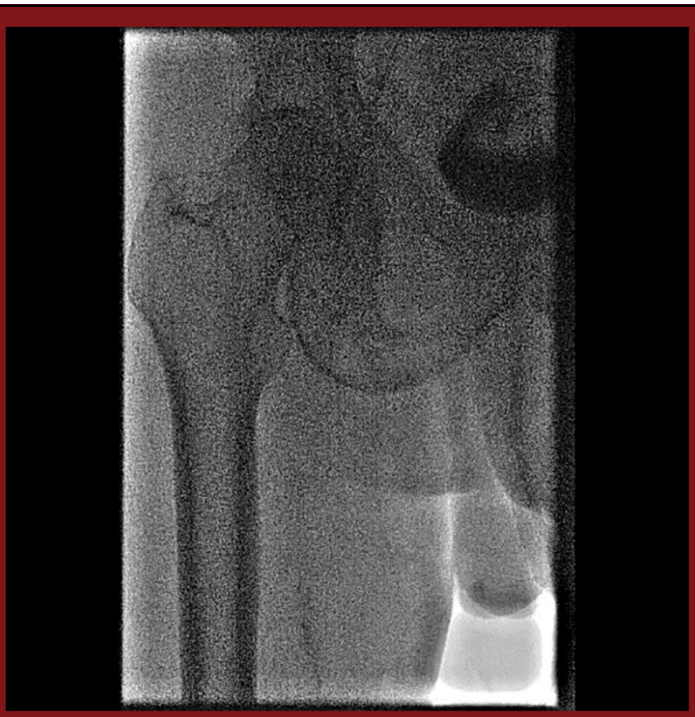


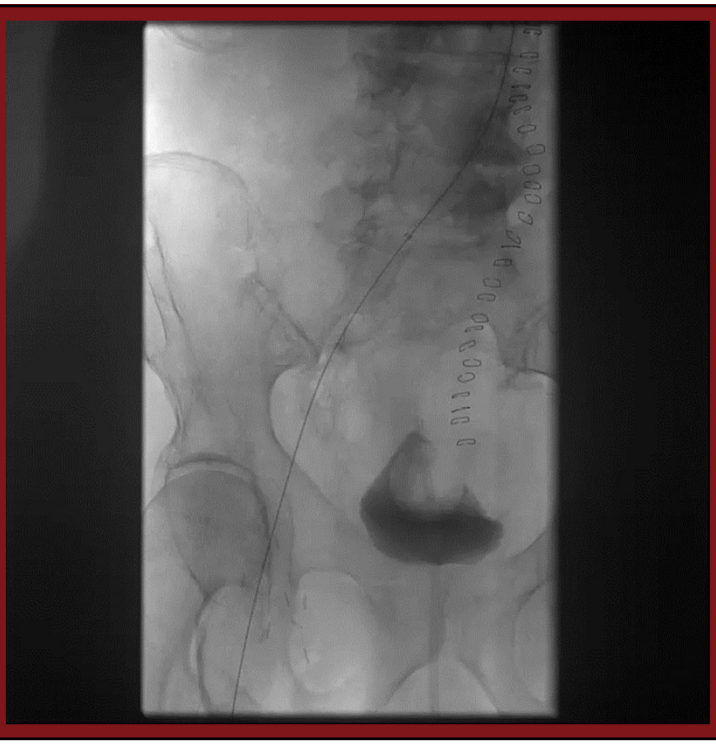


Case 3

- 68 y/o male presented with right leg pan after undergoing bilateral aorto-femoral bypass and right femoro-popliteal bypass surgery
- PMHx: Chronic tobacco smoker, PAD
- Arterial Doppler of right lower extremity revealed acute limb ischemia

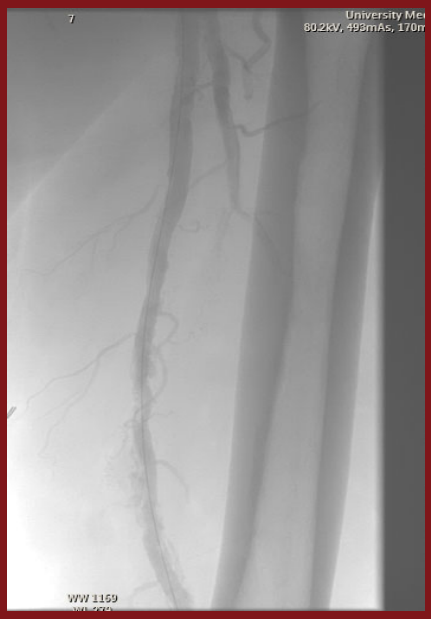


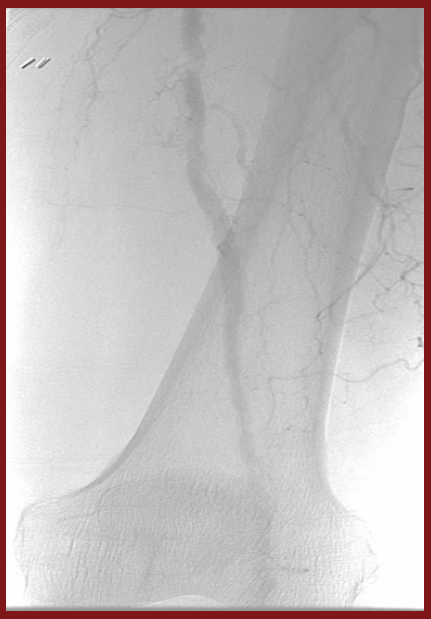


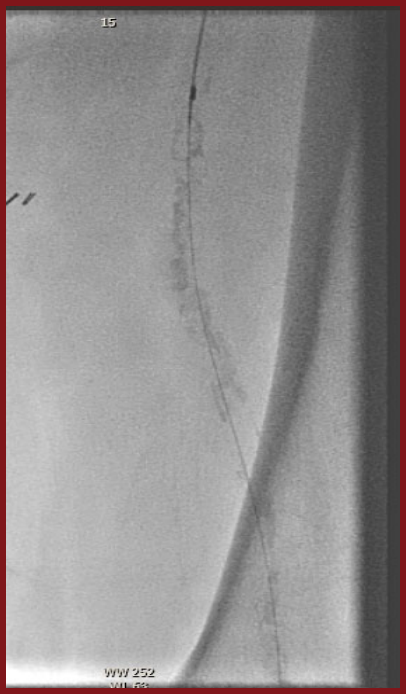


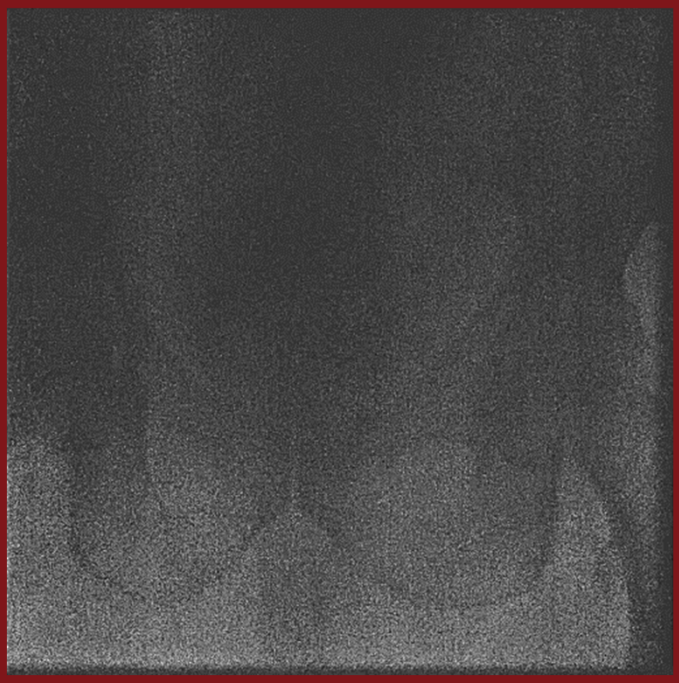
Case 4

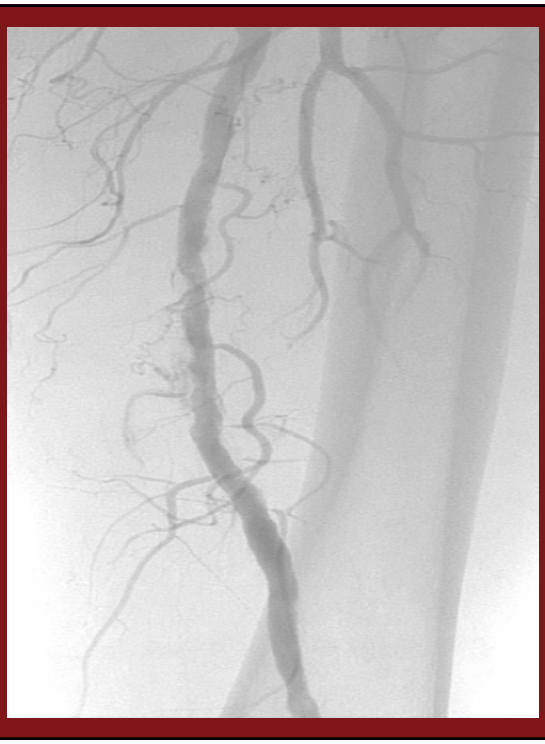
- 75 y/o man presented with bilateral LE pain
- PMHx: CAD s/p CABG, ischemic cardiomyopathy s/p ICD placement, DM, HTN, PAD
- Left common and SFA


7
WW 1169



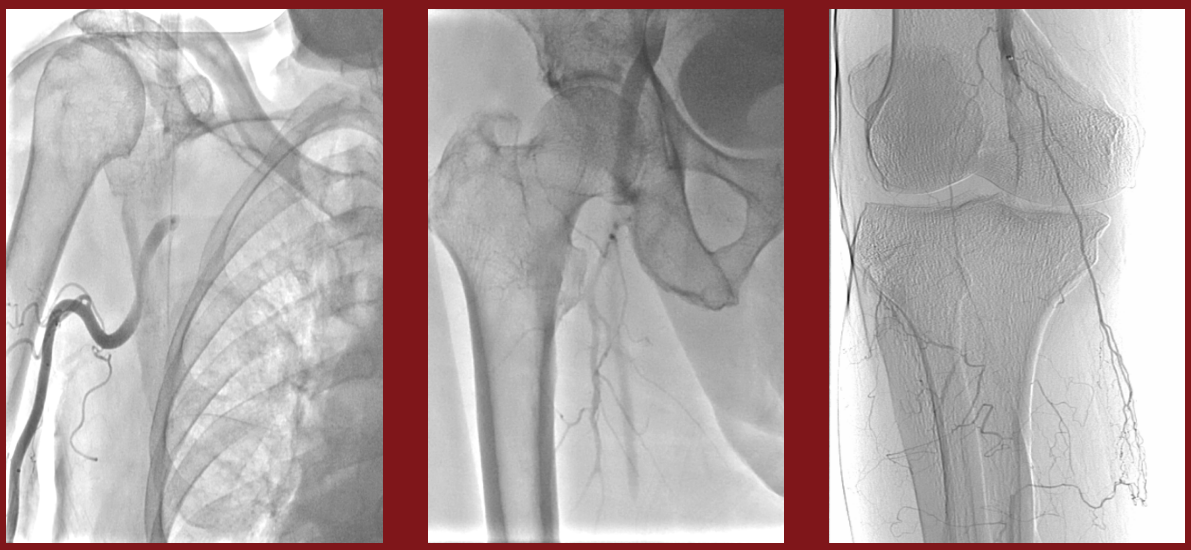

15
WW 252

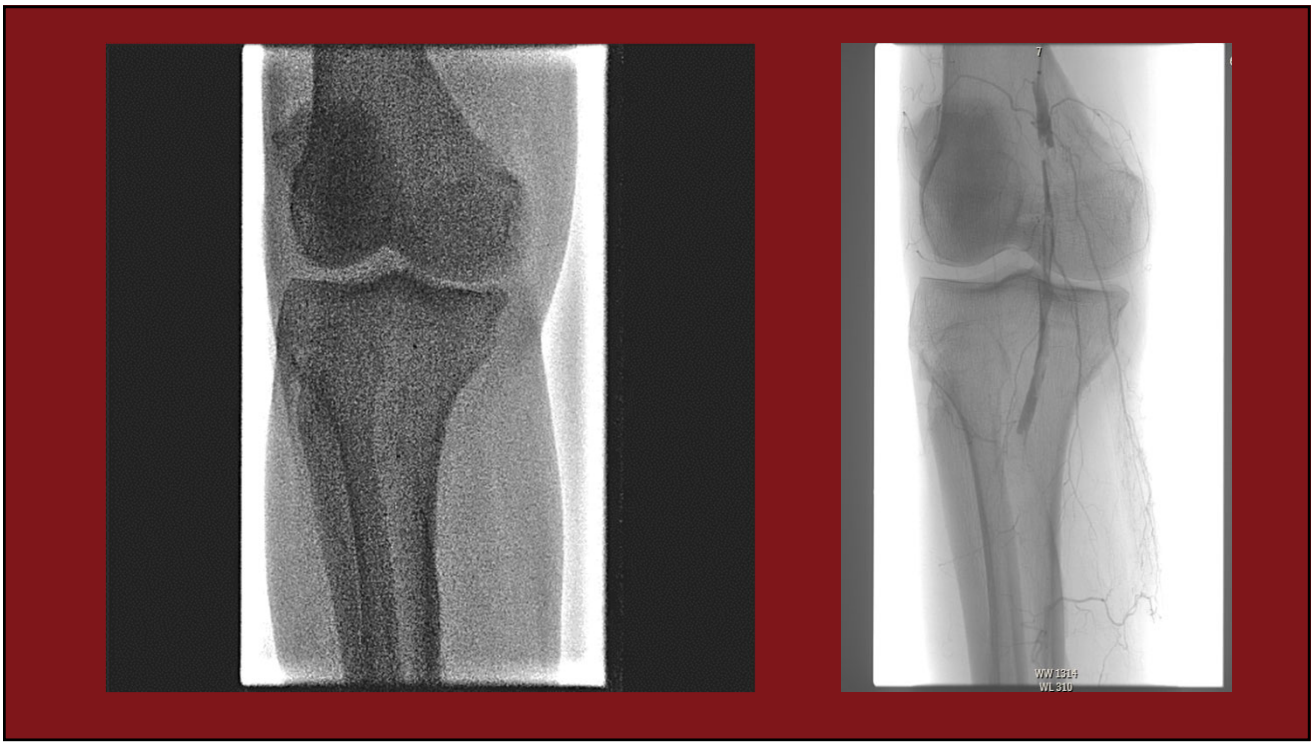


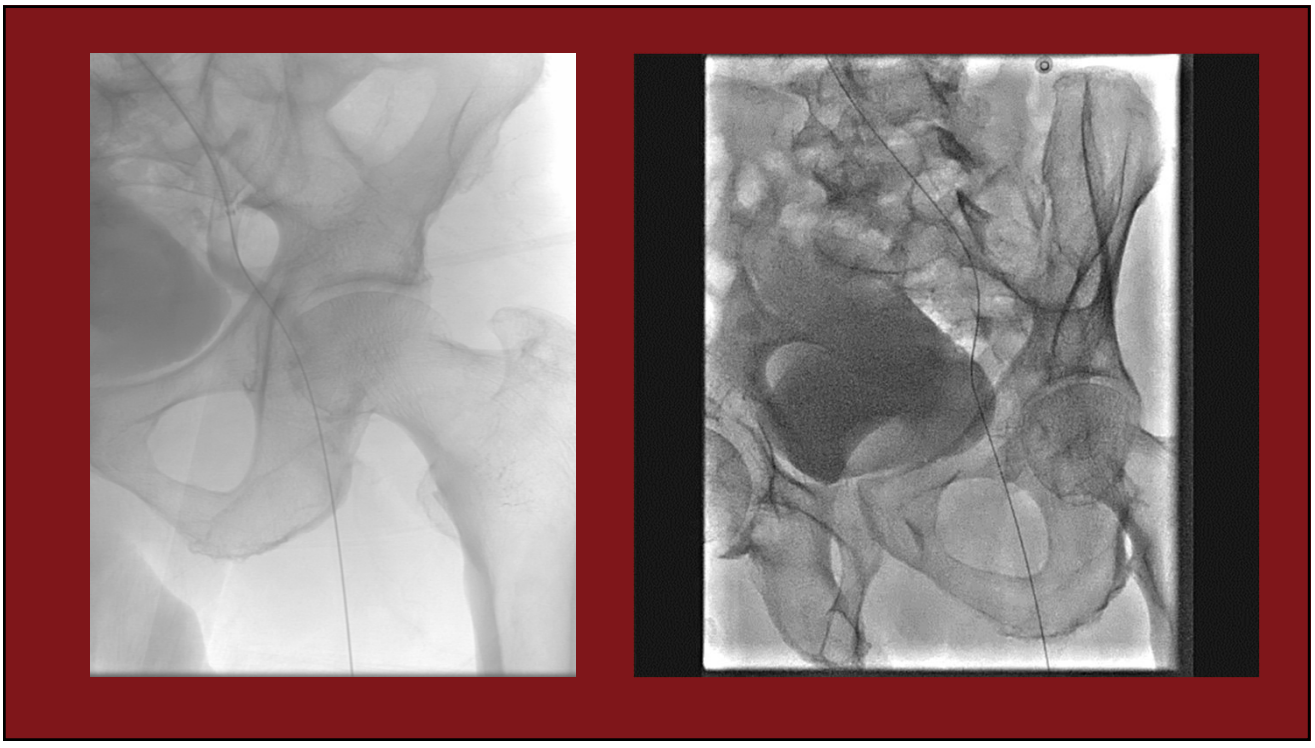


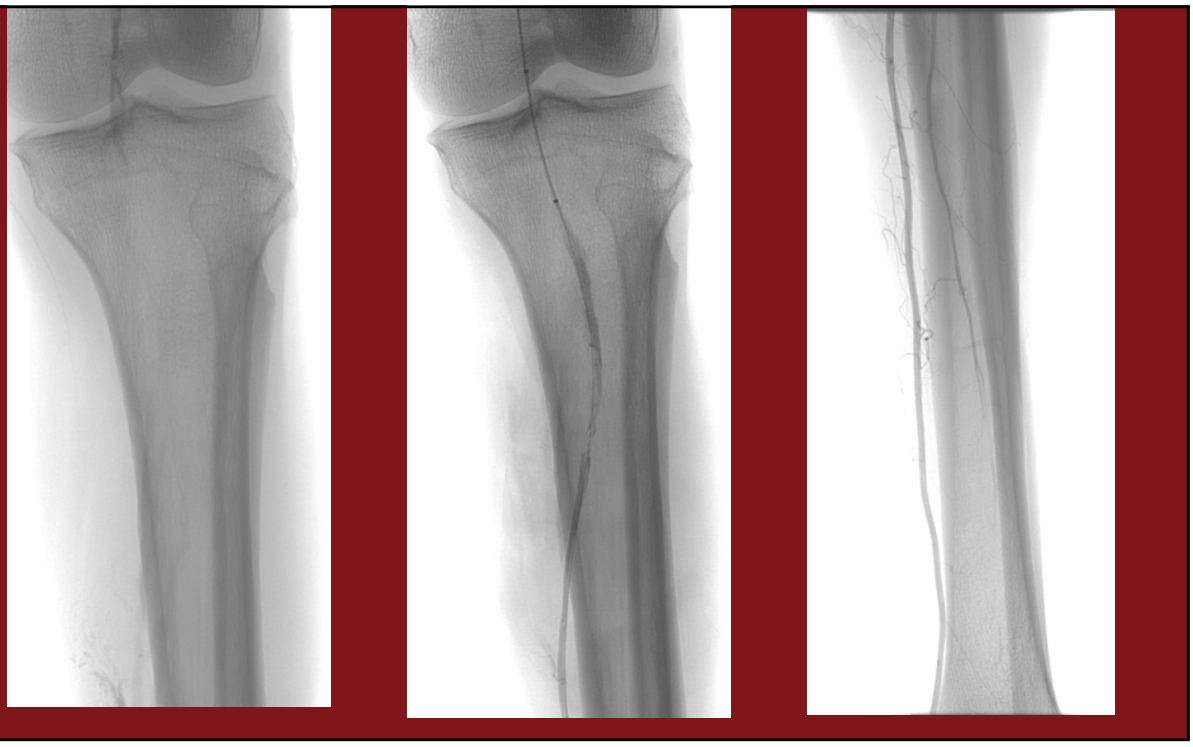
Case 5

- 85 y/o man presented with abdominal pain, generalized weakness, with lower extremity weakness and numbness
- Doppler showed bilateral acute limb ischemia as, intra-cavitary LV thrombus.



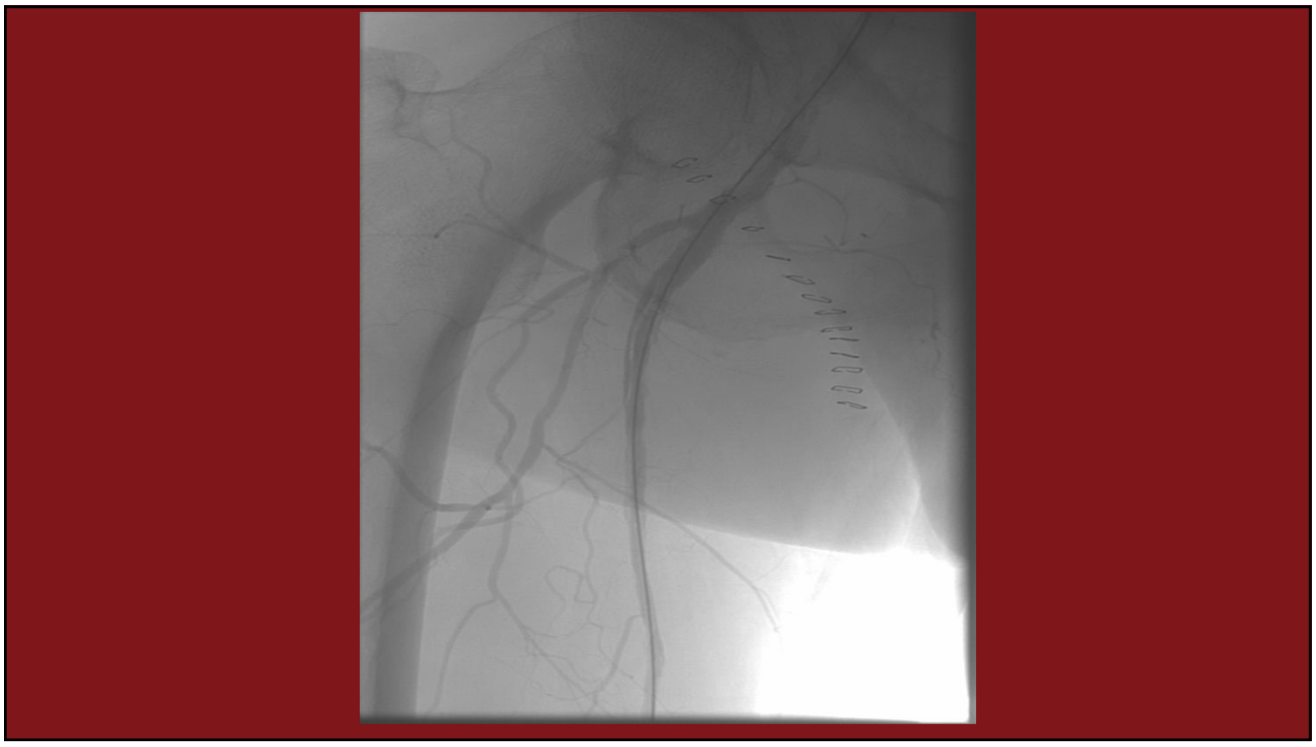

WW 1314
WL 510

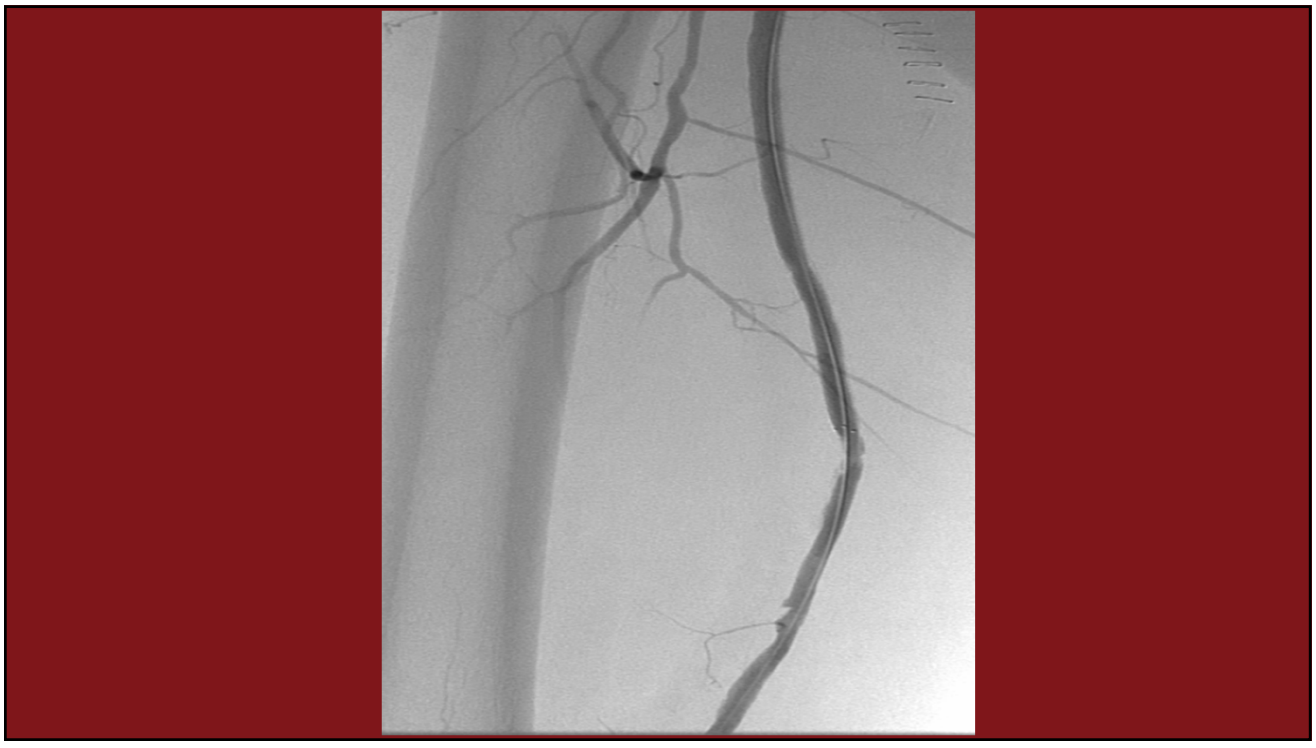


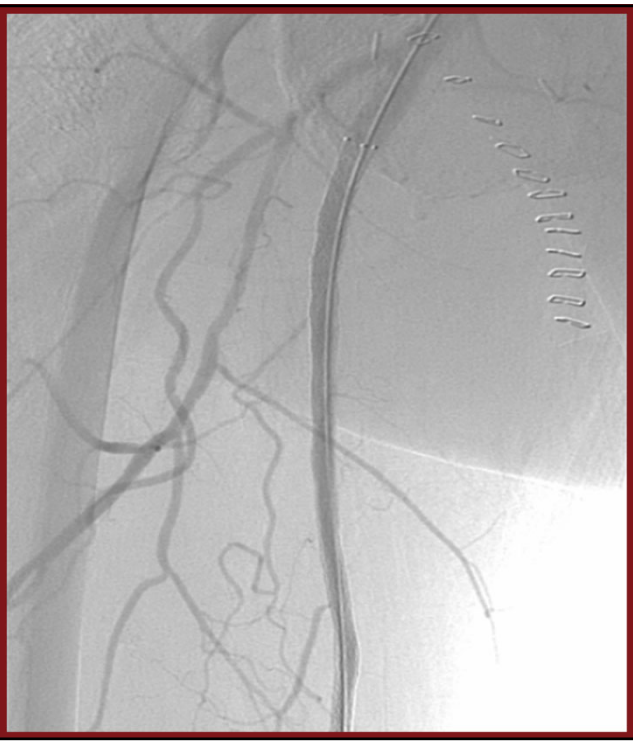


Case 6

- 73 y/o man admitted due to acute limb ischemia to bilateral lower extremities.
- Persistent bilateral lower extremity signs of hypo-perfusion.
- PMHx: Active Smoker, PAD, HTN, HLD, CAD, COPD, CKD

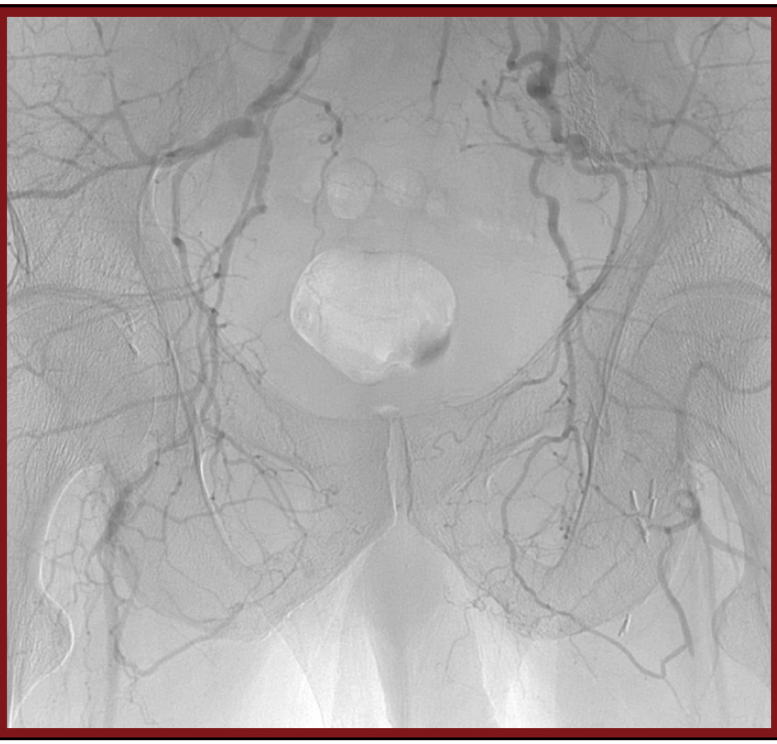


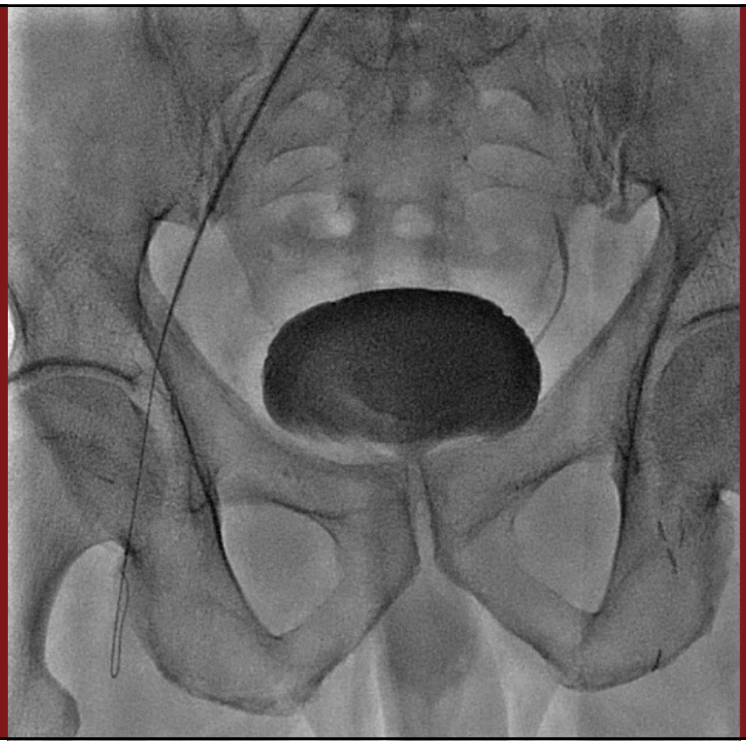


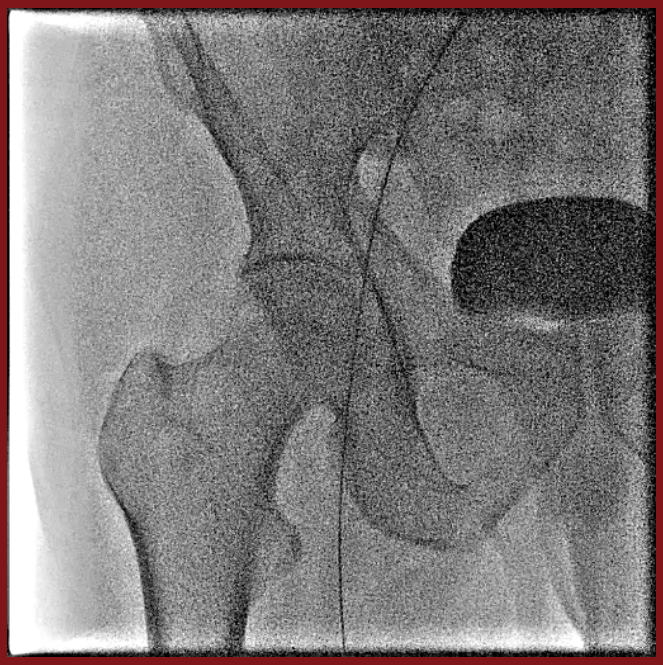


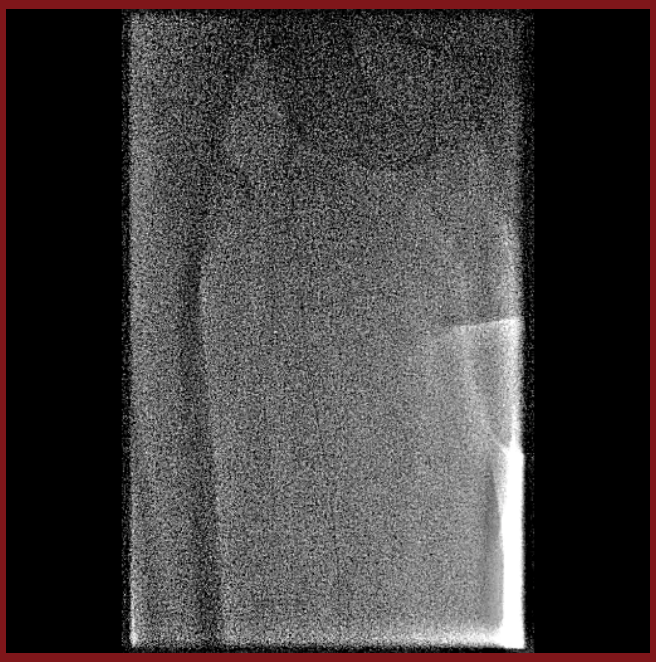
Case 7

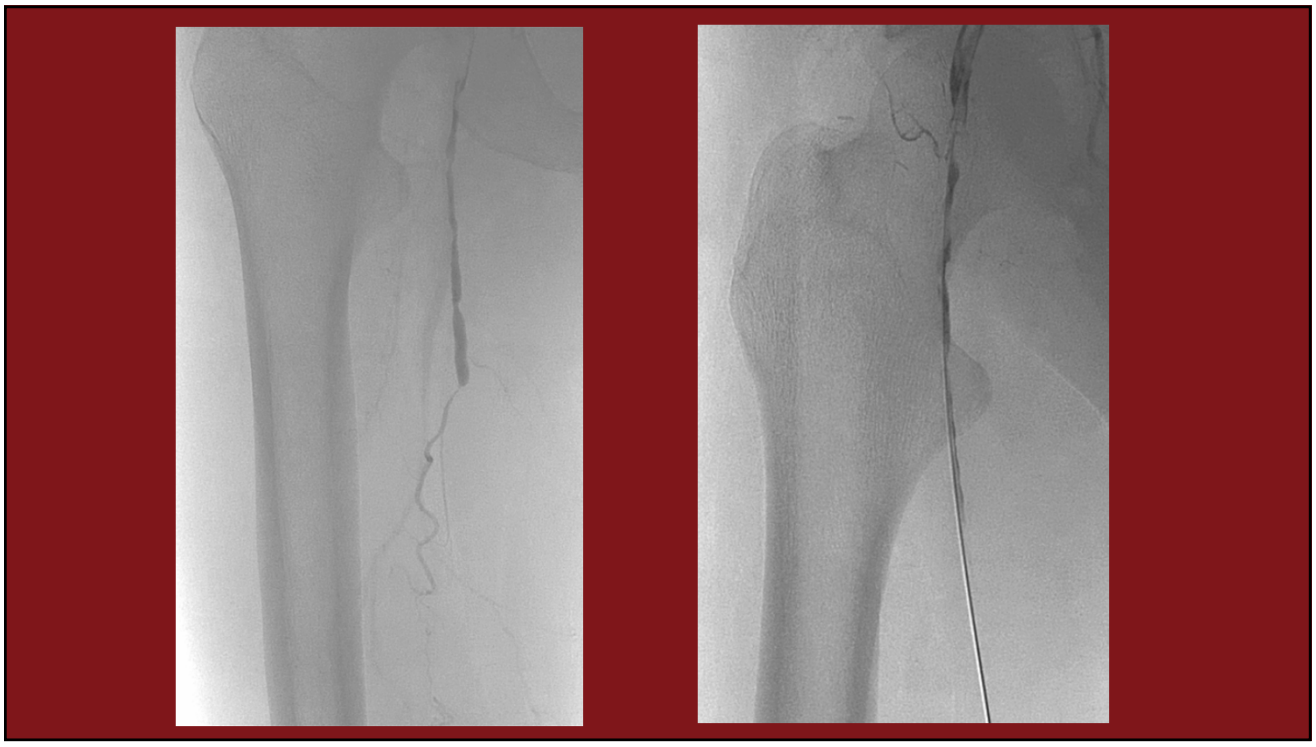
- 66 y/o male presented to hospital for acute on chronic right lower extremity pain
- PMH of CAD, PAD s/p R Fem-pop bypass, left common iliac stenting and left external iliac stenting and prior left below the knee PVI, former smoker
- After thrombectomy ; Misago stent placement at distal SFA and proximal popliteal junction

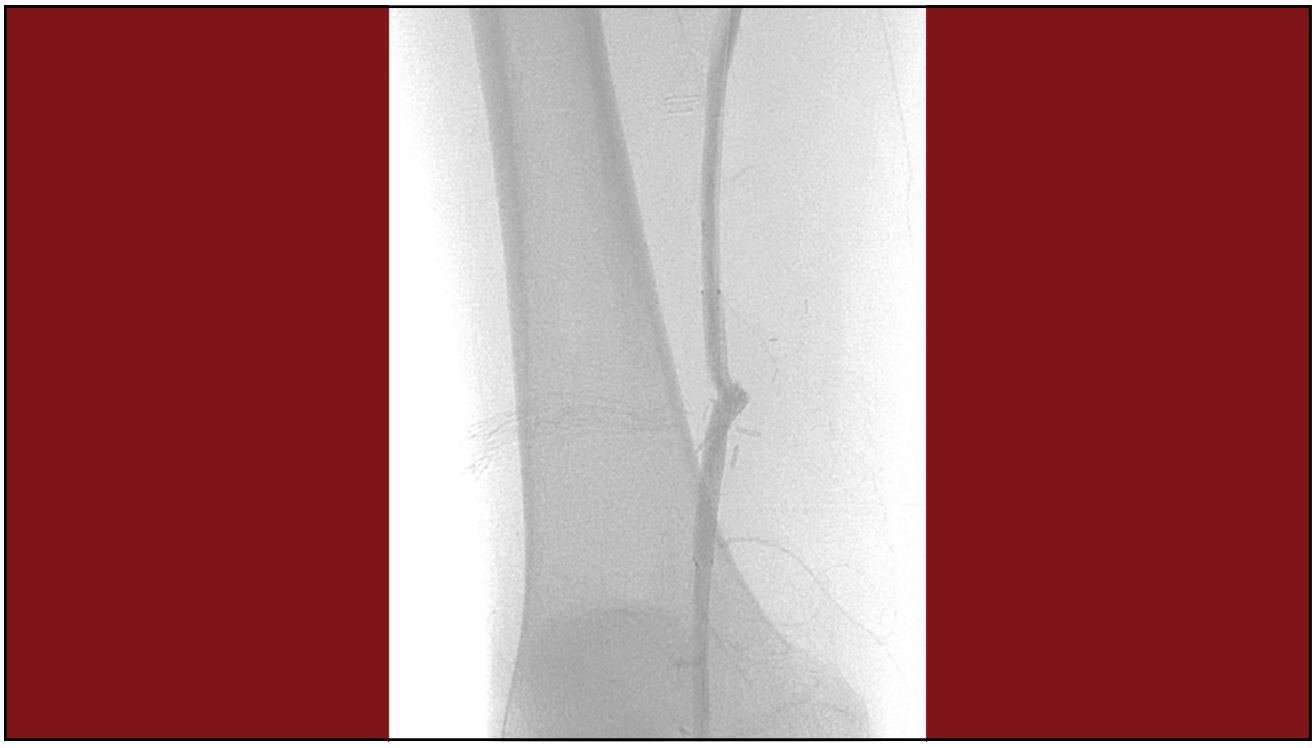






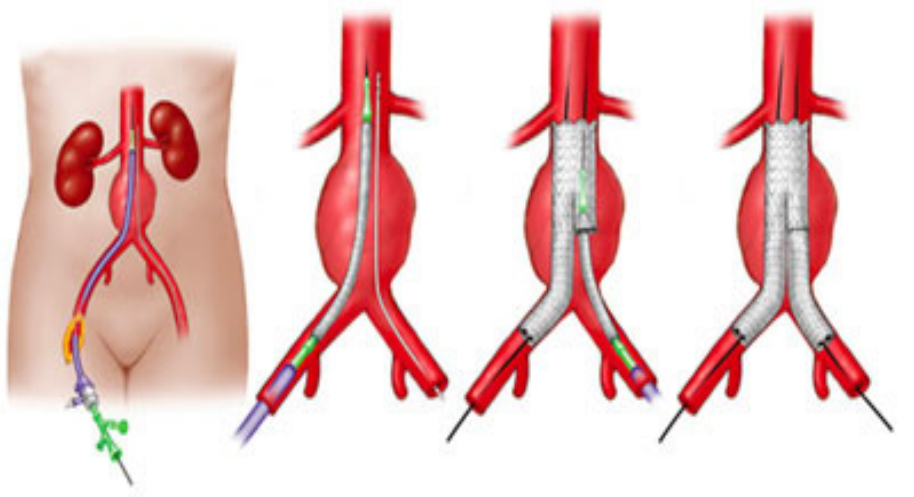


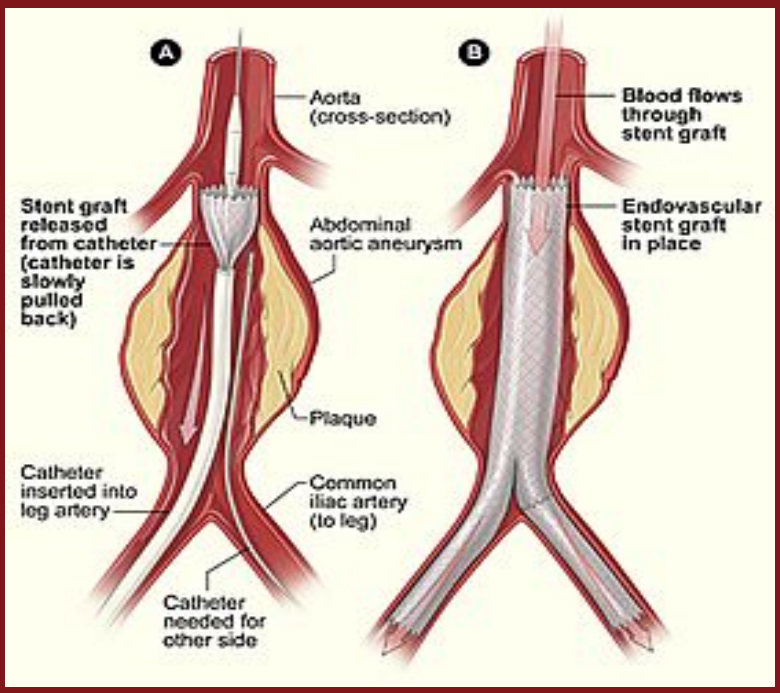


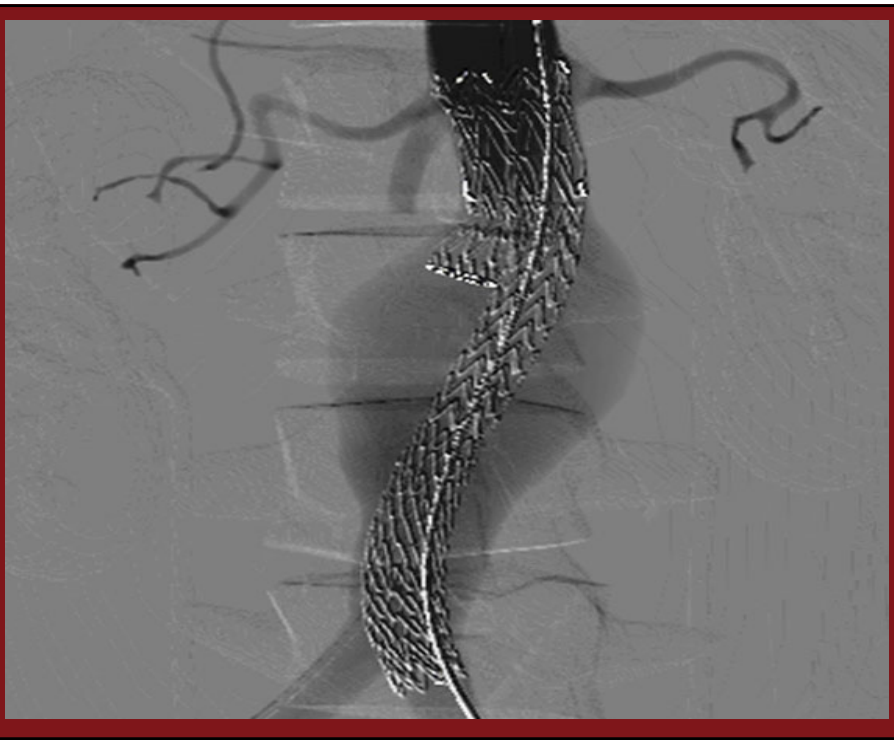


Endovascular Repair of Aortic Aneurysm

Open repair of abdominal aortic aneurysm (AAA) was first introduced by Dubost in 1951
In the 1990s, the less invasive endovascular aneurysm repair (EVAR) was introduced
Indicated for elective or emergent repair of abdominal aortic aneurysm ≥ 5 cm
Currently 4 RCT's comparing elective AAA repair




A
B
Aorta
(cross-section)
Blood flows
through
stent graft
Stent graft
released
from catheter
(catheter is
slowly
pulled
back)
Abdominal
aortic aneurysm
Endovascular
stent graft
in place
Plaque
Catheter
inserted into
leg artery
Common
iliac artery
(to leg)
Catheter
needed for
other side



Mission: TTUHSC PAD Center Of Excellence

The Center of Excellence in Peripheral Arterial Disease Treatment is a Texas Tech University Health Sciences Center initiative focused on providing successful screening, treatment, and education on Peripheral Artery Disease/Critical Limb Ischemia through the collaborative efforts of multidisciplinary clinicians, providers, and students at TTUHSC. Our mission is to coordinate a multispecialty treatment approach for patients diagnosed with PAD while obtaining optimal care of comorbidities, with end goal of quality care in an effort to prevent limb amputation. Save a limb, save a life.

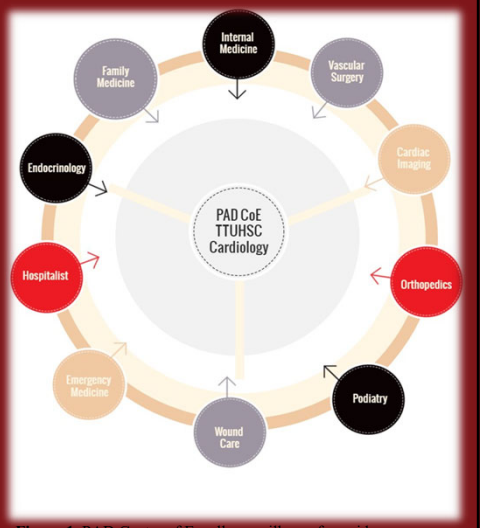
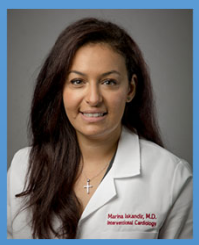


Figure 1. PAD Center of Excellence village of providers

Mac Ansari, MD
Director
Structural and Interventional Cardiologist



Marina Iskandir, MD
Interventional Cardiologist

Scott Shurmur, MD
Patron

Victoria Acosta
Clinical Research Associate

Steven Daley
Clinical Research Associate

Mary Amador
Head Nurse-Center for Cardiovascular Health

Braden Cook
Manager-Center for Cardiovascular Health

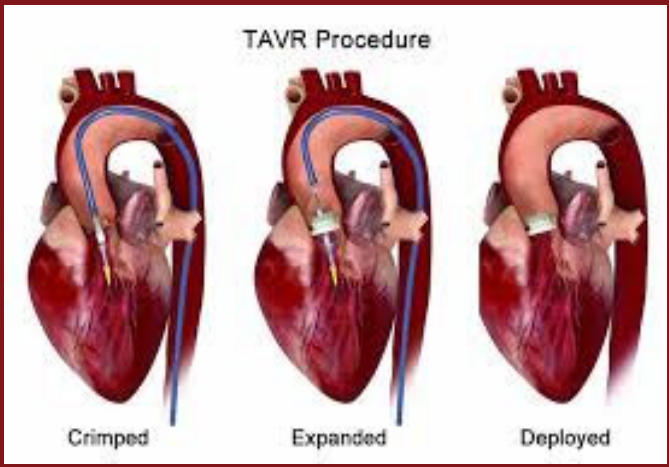
Aliakbar Arvandi, MD
Director of Imaging

Maxim Yeremenko
Clinical Research Associate

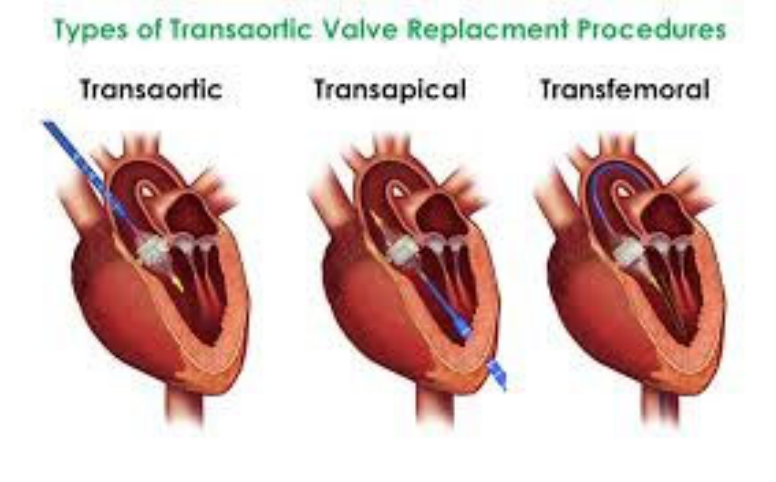
Theresa Condez
Manager of Clinical Research

Objectives
Percutaneous aortic valve replacement
Percutaneous mitral valve replacement
MitraClip
Left atrial appendage closure – Watchman device
Percutaneous pulmonary valve replacement
Endovascular repair of AAA
High-risk PCI and TamdemHeart
Paravalvular leak closure
ECMO
Pecutaneous PFO closure
Percutaneous ASD closure
Percutaneous VSD closure

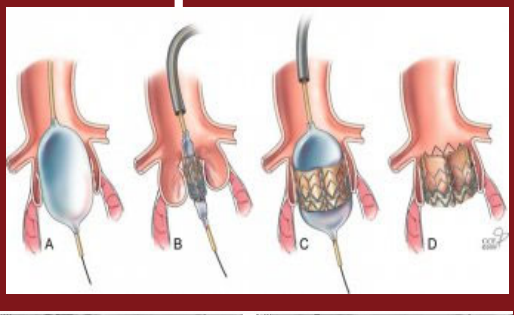
Transcatheter Valve Replacement (TAVR)

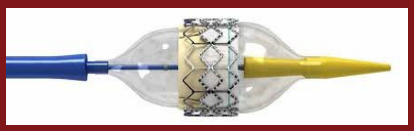


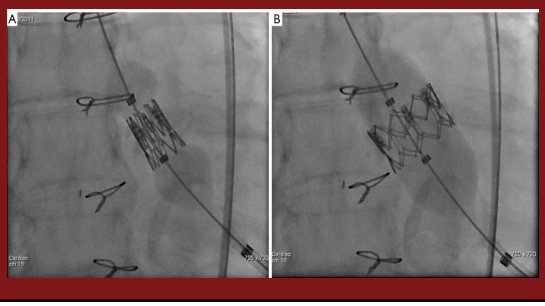
TAVR

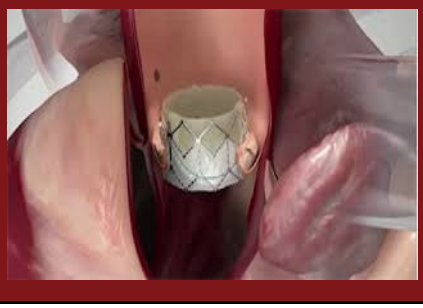


Edward Sapiens

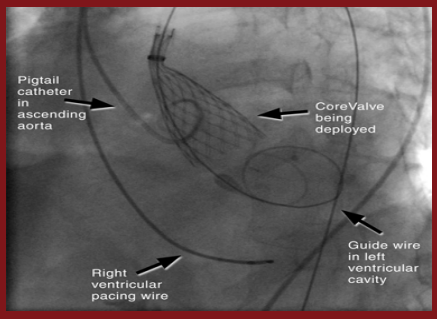


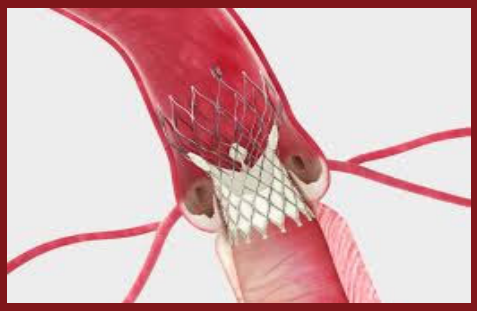


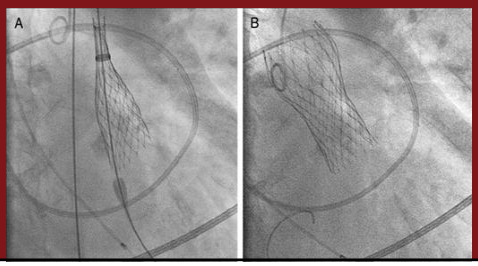




Core Valve







TAVR

Author/Study	
Leon/Partner 2.2015	In intermediate risk patients, TAVR and SAVR similar for death/disabling stroke (19 vs 21%). In transfemoral cohort, TAVR had less death/disabling stroke versus SAVR (17 vs 20%; P = 0.05)
Thourani.2015	Intermediate risk patients treated with TAVR compared to SAVR group in PARTNER 2. TAVR was superior for the composite endpoint of death, stroke, and moderate/severe AR
Deeb.2015	In high-risk patients, all-cause death or stroke was lower with TAVR versus SAVR (37 vs 47%, P = 0.006). Individual adverse events were also lower with TAVR
Reardon.2015	In high-risk patients with STS < 7%, 2-year all-cause death was lower with TAVR vs. SAVR 15% versus 26% (log rank P = 0.01), while stroke rate was similar (11% vs 15%)
Sondegard (Notion).2015	In all-comers (mostly low-risk) TAVR similar to SAVR for 2-year all-cause death (8.0% vs 9.8%), CV death (6.5% vs 9.1%), and composite of death, stroke, or MI (16% vs 19%)
Kapadia (SENTINEL).2015	Cerebral embolic protection during TAVR captured debris, reduced volume of cerebral MRI lesions, but did not improve neurocognitive function or 30-day stroke rates
Yoon (Bicuspid TAVR).2015	TAVR is safe in patients with Bicuspid Aortic stenosis. New-generation devices (Sapien 3 or Lotus) were associated with less PVL than early-generation (Sapien XT or Core Valve) devices
Chakravarty (TAVR-LM).2015	1-year mortality similar in TAVR plus LM PCI patients and those without LM disease. Unplanned LM PCI (for TAVR related complication) increased 30-day and 1-year death
D'Errigo.2015	TAVR with conscious sedation vs. GA in low-intermediate risk patients was associated with shorter intensive care stay and similar mortality at 30-days and 3-years, and similar risk of PVL
Rampat, Meredith.2015	Initial experience with the Lotus Valve and Direct Flow Medical Valve demonstrated good outcomes, and significant reductions in PVL compared to earlier valve systems

TAVR : Low risk population STS score < 4%
The NOTION randomized trial (Europe) showed clinical equivalence of TAVR to SAVR in a predominantly low-risk population (11.4% vs 4.9%)
OBSERVANT: propensity-matched analysis of 355 pairs of low-risk patients showed better outcomes at 3 years with SAVR, including survival (83% vs 72%) and freedom from major adverse cardiac and cerebrovascular events (81% vs 67%)
Partner 3: ongoing in the USA

Circ Cardiovasc Interv.2016

Transcatheter Aortic Valve Replacement (TAVR)

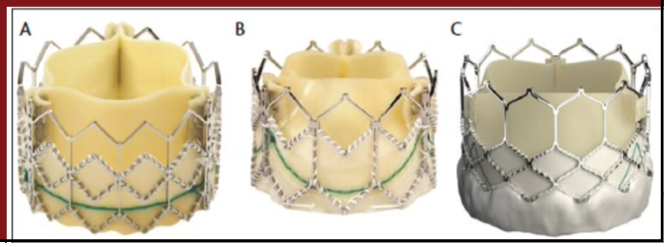
- ***Aortic stenosis*:**
  - In recent population-based echocardiographic studies, 1% to 2% of persons aged 65 or older and 12% of persons 75 or older had calcific aortic stenosis.
  - **The most common presentation is** gradual decrease in exercise tolerance, fatigue, or dyspnea on exertion **due to** LV diastolic dysfunction, with an excessive rise in end-diastolic pressure leading to pulmonary congestion.
  - **E**xertional symptoms may be a result of the limited ability to increase cardiac output with exercise.

History

- The idea of implanting a prosthetic valve to prevent restenosis after balloon valvuloplasty is credited to Henning Andersen, a Danish cardiologist who fashioned a stent from stainless steel surgical wires and mounted a bioprosthetic valve inside the stent.
- His initial animal experiments demonstrating feasibility were presented at the European Society of Cardiology in 1992.
- The ensuing decade led to improvements in valve and stent design along with development of a delivery system, culminating in the first successful human implantation by Cribier in 2002.
- The development of the *retrograde transfemoral* arterial route by Webb and colleagues and the *antegrade transapical* approach by Walther and associates allowed expansion of the procedure to other operators and centers.

Two main types of stent design are used for TAVR:

- The Edwards Sapien Valve (Edwards Lifesciences, Irvine, California) is a cobalt chromium balloon-expandable valve with the valve leaflets made of treated bovine pericardium.
  - A: Sap**ien valve**
  - B: Sapien XT valve
  - **C: Sapien 3**
- CoreValve (Medtronic, Minneapolis, Minnesota) is the most common self-expanding valve, now in its third generation as the Evolut-PRO valve.



SAPIEN VALVE (FIRST GENERATION)

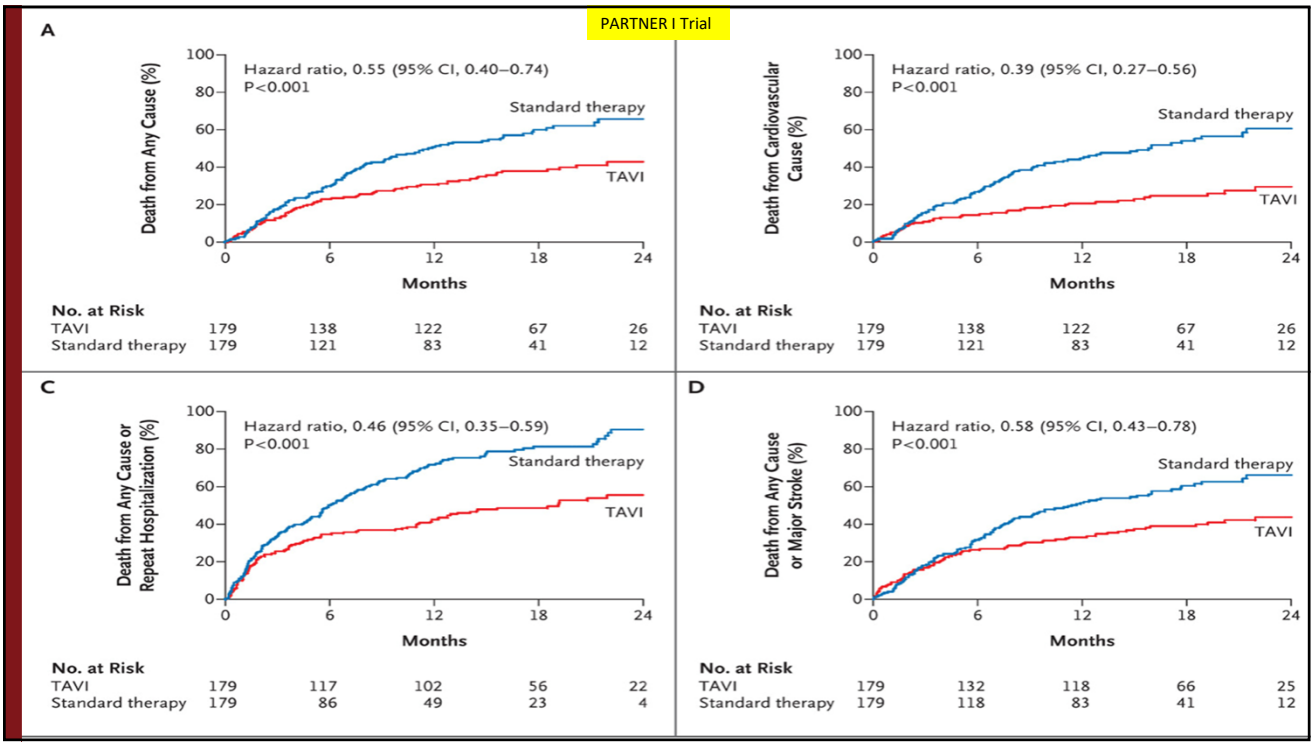
- Sapien valve is a trileaflet bioprosthesis made of bovine pericardium that is mounted on a balloon-expandable stainless steel stent.
- The stent frame has an inner polyethylene terephthalate (PET) fabric skirt placed on the ventricular side covering half of the frame, limiting stent expansion and decreasing paravalvular insufficiency.
- It is available in two sizes:
  - 23-mm valve with a 14.5-mm stent height
  - 26-mm valve with a 16-mm stent height.
- In benchtop testing, its durability has been shown for more than 10 years.

PARTNER IB Trial (Sapien valve)

- In patients with severe aortic stenosis who were not suitable candidates for surgery, TAVI, as compared with standard therapy, significantly reduced the rates of death from any cause, the composite end point of death from any cause or repeat hospitalization, and cardiac symptoms, despite the higher incidence of major strokes and major vascular events.

- **In PARTNER IA Trial TAVR=SAVR.**

PARTNER I Trial

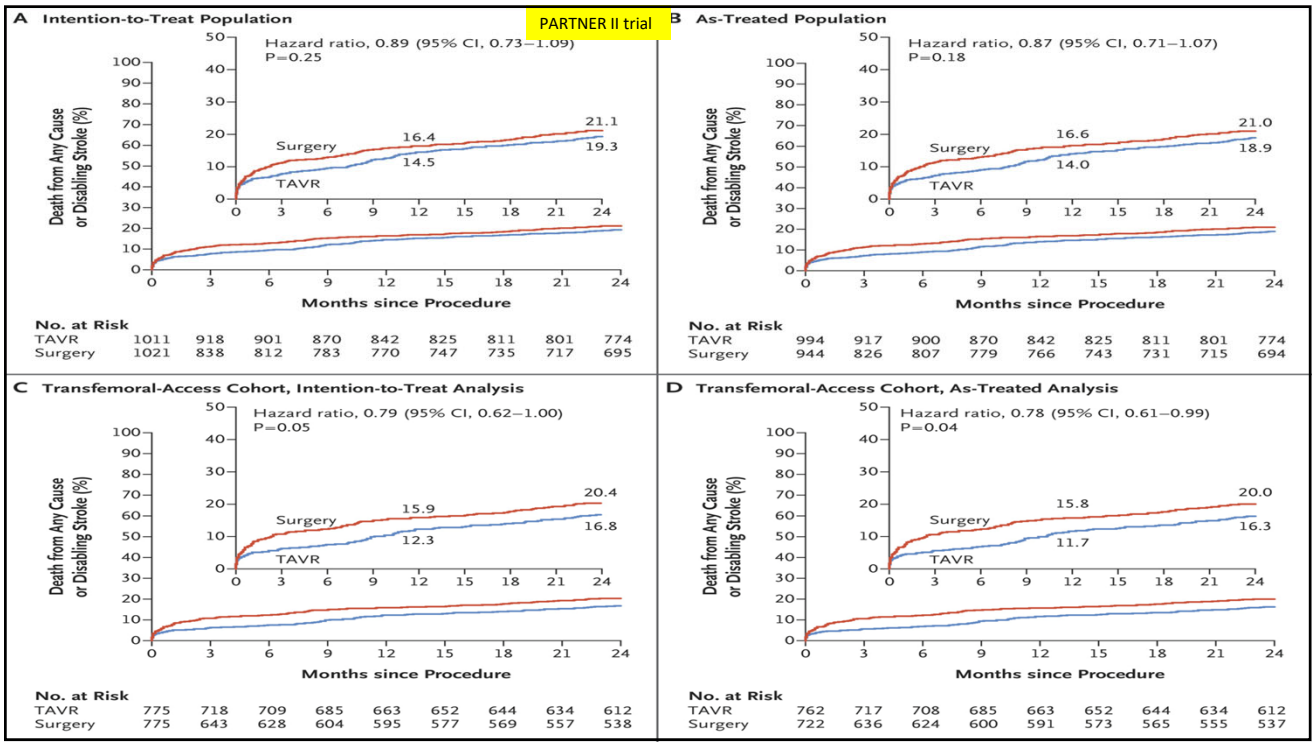


SAPIEN XT VALVE (SECOND GENERATION)

- Changes in the stent material and design, as well as the ability to mount the valve on the deployment balloon inside the abdominal aorta, allowed for a smaller delivery system.
- Trans-femoral valve implantation utilizes the NovaFlex catheter, which allows safe passage around the aortic arch with its deflectable nose cone and utilizes an expandable sheath (e-sheath) that minimizes the arteriotomy size.
- Transapical and transaortic delivery is possible by the Ascendra+ delivery system, which is optimized for a single operator.
- The Sapien XT prosthesis is available in three valve sizes: 23, 26, and 29 mm, allowing the treatment of patients with aortic annuli ranging from 18 to 27 mm

Partner II trial (Sapien XT)

- In intermediate-risk patients, TAVR was similar to surgical aortic-valve replacement with respect to the primary end point of death or disabling stroke for up to 2 years and resulted in a similar degree of lessening of cardiac symptoms.



SAPIEN 3 VALVE

- The Sapien 3 valve is the newest iteration of the Sapien family of valves designed to minimize aortic insufficiency and reduce the diameter of the delivery system.
- The inflow portion of the valve has a PET fabric cuff in addition to an internal skirt to minimize paravalvular leak. It has a smaller crimped profile and a longer stent frame compared to the first- and second-generation Sapien valves.
- The longer length of the frame prevents native leaflet prolapse and better positioning during deployment. It has a cobalt chromium frame with wide strut angles providing a low delivery profile and an enhanced frame geometry for greater radial strength.
- It is available in four sizes (20, 23, 26, and 29 mm), thus widening the range of patients eligible for TAVR. The 20-, 23-, and 26-mm devices are delivered using a 14-F e-sheath, and the 29-mm device is delivered by a 16-F e-sheath.

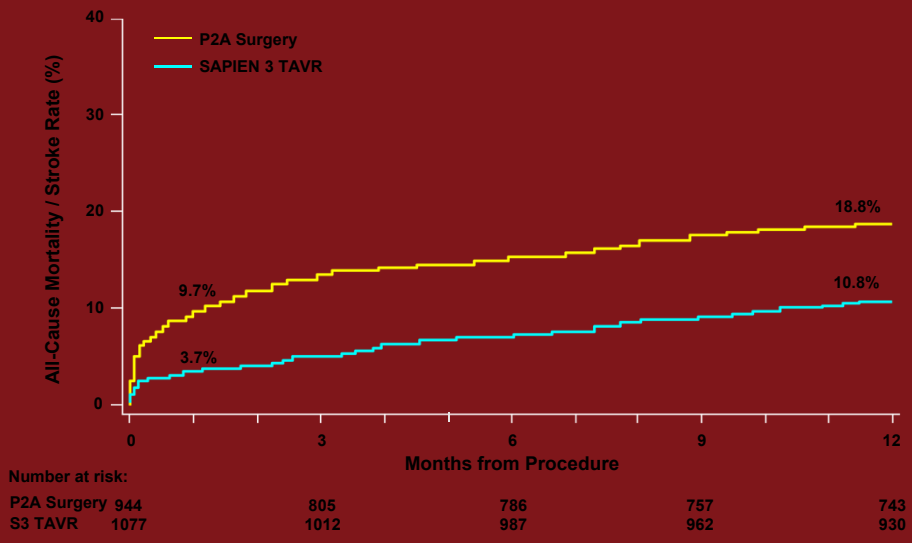
SAPIEN 3 VALVE

- The delivery system for the TF route (Commander) is more flexible than NovaFlex+ and has a distal flex point that allows more coaxial alignment of the valve, especially in horizontal aortic root.
- The balloon has a central marker that is positioned at the annular plane during deployment.
- The new Certitude system for the transaortic and TA approach is more ergonomically designed for single-operator use and better control during valve deployment.
- It uses an 18-F sheath for the 23- and 26-mm valves and a 21-F sheath for the 29-mm valve

PARTNER II S3I

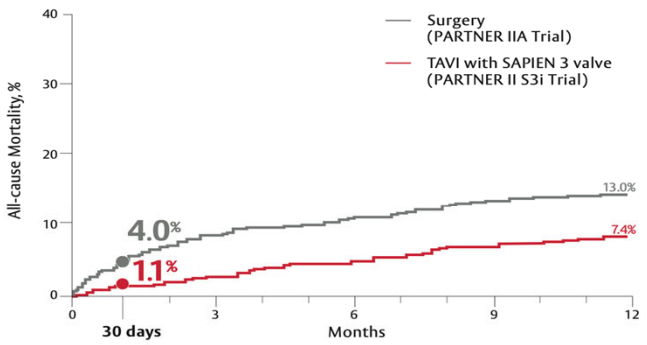
- Among patients at intermediate surgical risk with severe aortic stenosis, S3-TAVR resulted in improved QoL at both 1 month and 1 year compared with both XT-TAVR and SAVR.

Unadjusted Time-to-Event Analysis
All-Cause Mortality and All Stroke (AT)



TAVI with the SAPIEN 3 valve demonstrated 75% lower rates of 30-day all-cause mortality and disabling stroke compared to surgery†

All-cause Mortality‡



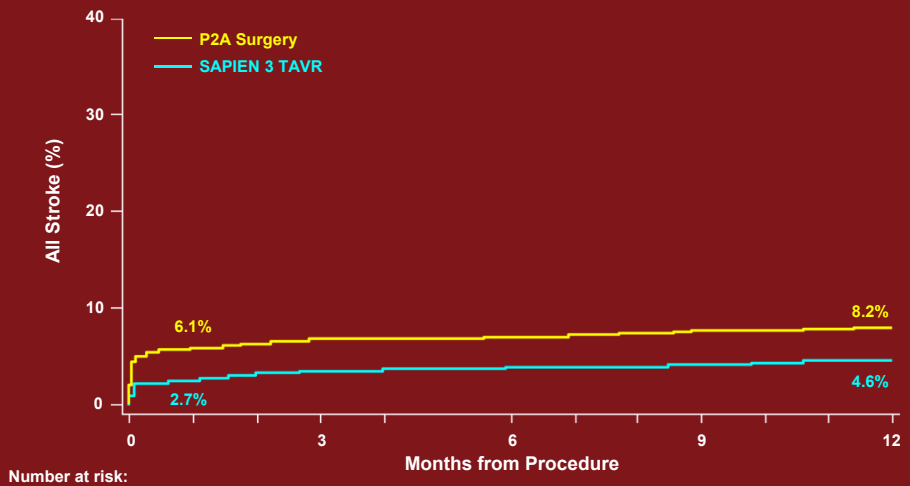
No. at risk:					
Surgery	944	859	836	808	795
SAPIEN 3 TAVI	1,077	1,043	1,017	991	963

Thourani V., et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: A propensity score analysis. *Lancet*. 2016;387: 2218-25.

† The PARTNER II Trial intermediate-risk cohort 30-day unadjusted clinical event rates for TAVI with the SAPIEN 3 valve, AT population (n=1,077).

‡ The PARTNER II Trial intermediate-risk cohort unadjusted clinical event rates, AT population.

Unadjusted Time-to-Event Analysis
All Stroke (AT)



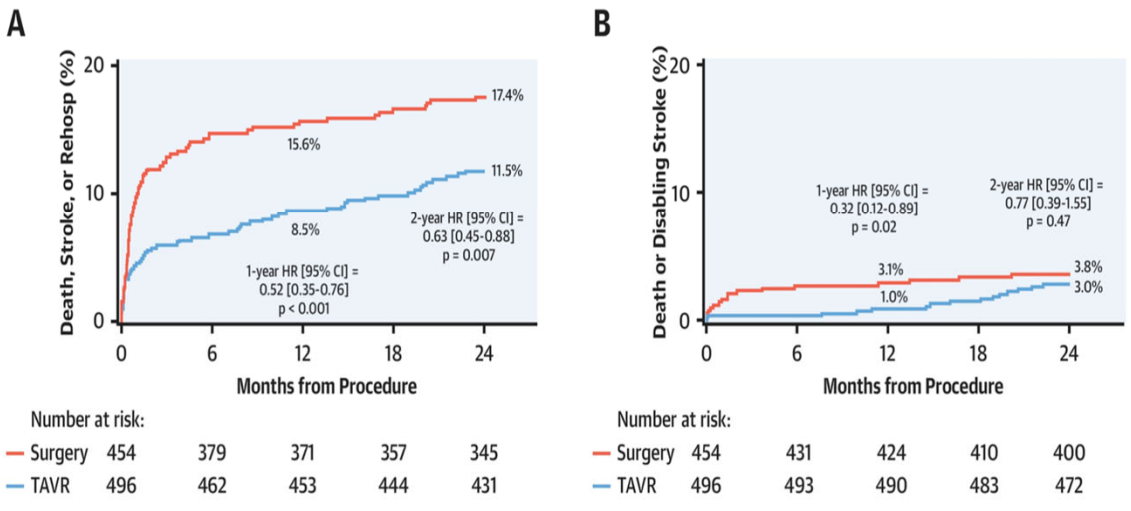
Number at risk:					
P2A Surgery	944	805	786	757	743
S3 TAVR	1077	1012	987	962	930

PARTNER III (TAVR in low-risk patients)

- In low surgical risk patients with symptomatic severe aortic stenosis, the PARTNER 3 (Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low-Risk Patients With Aortic Stenosis) trial demonstrated superiority of transcatheter aortic valve replacement (TAVR) versus surgery for the primary endpoint of death, stroke, or re-hospitalization at 1 year.

- At 2 years, the primary endpoint remained significantly lower with TAVR versus surgery, but initial differences in death and stroke favoring TAVR were diminished and patients who underwent TAVR had increased valve thrombosis.

CENTRAL ILLUSTRATION: Time-to-Event Curves and Disease-Specific Health Status in TAVR Versus Surgery Through 2 Years

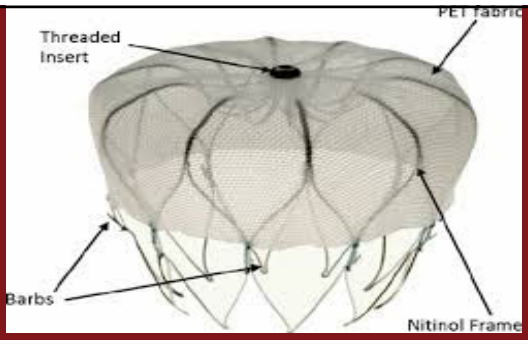


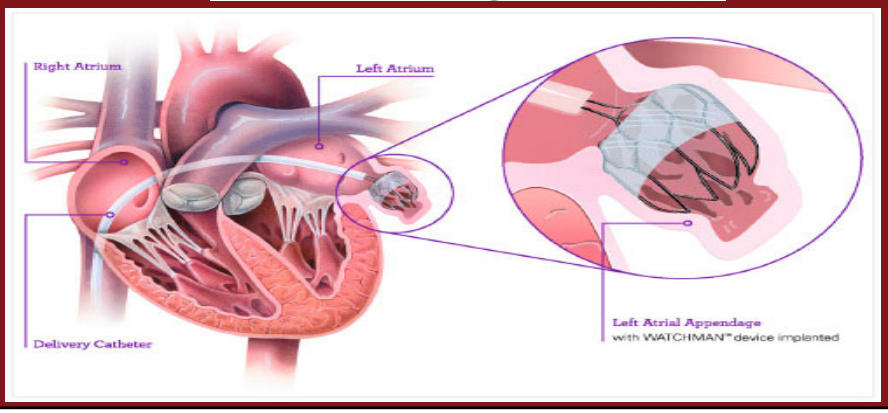
Evolute low risk trial

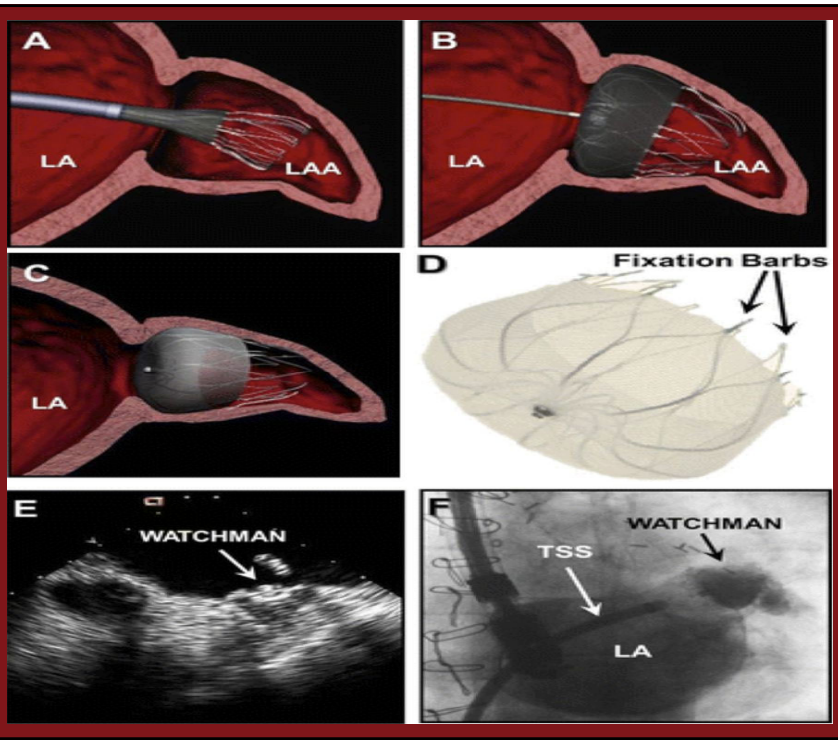
In patients with severe aortic stenosis who were at low surgical risk, TAVR with a self-expanding supra-annular bioprosthesis was noninferior to surgery with respect to the composite end point of death or disabling stroke at 24 months.

LAA closure devices

- AF is common, affecting 9% of patients aged 65 years or older in the United States and the prevalence is increasing.
- AF causes > 20% of all strokes and leads to more disabling symptoms, with higher mortality and higher health care costs compared to other causes of stroke.
- The mechanism of stroke in AF is most commonly related to embolism of thrombus formed in the left atrial appendage(LAA) , 91% Of left atrial thrombi resides in the LAA.
- Therefore, targeted local LAA mechanical therapy to remove the source of thromboembolism has been explored for decades.


Threaded
Insert
PET fabric
Barbs
Nitinol Frame


Right Atrium
Left Atrium
Delivery Catheter
Left Atrial Appendage
with WATCHMAN™ device implanted


A
LA
LAA
B
LA
LAA
C
LA
D
Fixation Barbs
E
WATCHMAN
F
WATCHMAN
TSS
LA

LAA closure devices

- The first percutaneous device (PLAATO, Appriva Medical Inc.) was implanted in 2001, however Safety concerns were raised, with two deaths and six cases of pericardial tamponade, and the device was later taken off the market for financial reasons.
- The first, and only, device registered for use in the United States is the Watchman device (Boston Scientific Corporation).
- The Watchman 2.5 device received FDA approval in 2015 based on the results of two randomized trials, PROTECT AF and PREVAIL, and their extended follow-up registries.

Left Atrial appendage percutaneous closure

- 5-year outcomes of PREVAIL, and the combined 5-year outcomes of PREVAIL and PROTECT AF, demonstrate that LAAC with **Watchman** provides stroke prevention in nonvalvular AF patients to a similar degree as warfarin.
- Because it minimizes major bleeding and stroke, LAAC results in less disability or death than warfarin.

EWOULTION trial

(Evaluating real-life clinical outcomes in atrial fibrillation patients receiving the **WATCHMAN** left atrial appendage closure technology)

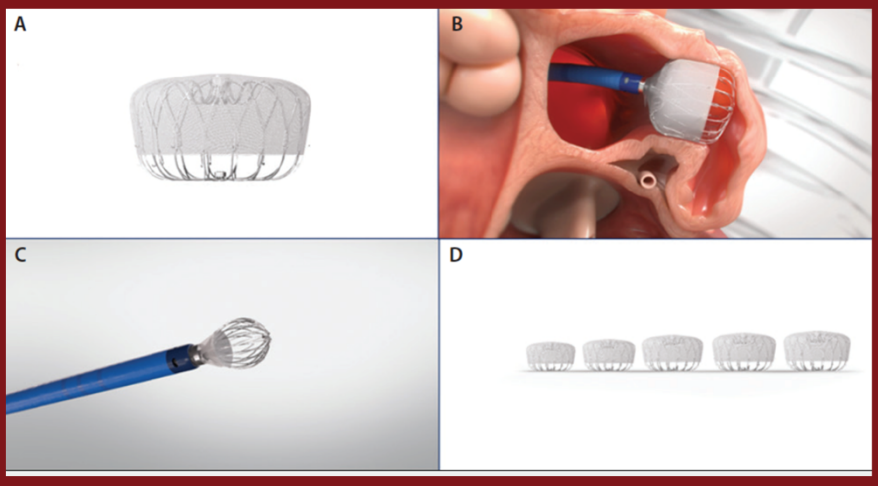
- **O**ver 2 years of follow-up in this first study to report longer-term outcomes after **WATCHMAN** implantation, patients had consistently low rates of stroke and nonprocedural bleeding, compared to historic rates.

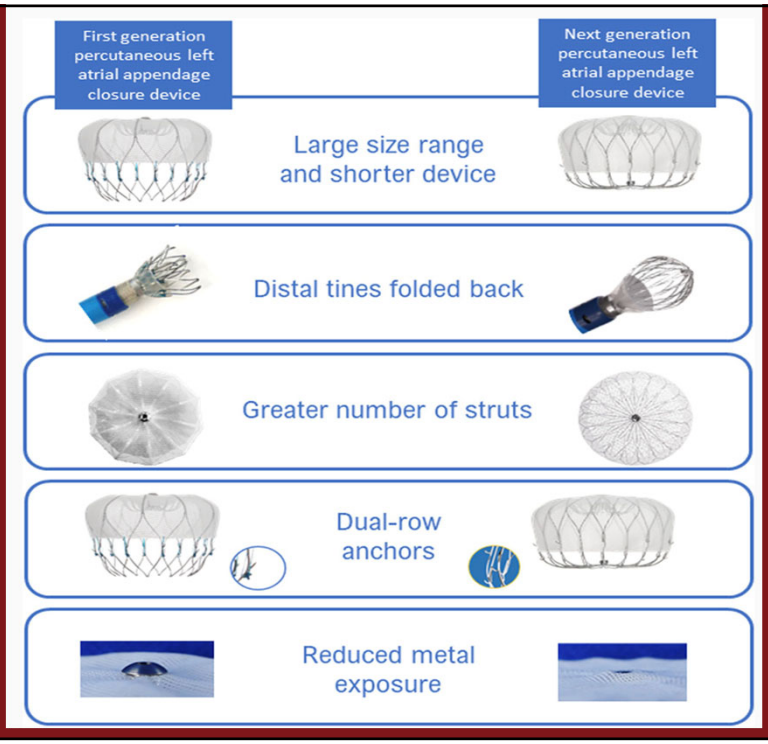
Watchman FLX

- The Watchman FLX (Boston Scientific Corporation) is the latest iteration of the Watchman device.
- Compared to Watchman 2.5, the FLX has a closed distal end to lessen the likelihood of perforation and is fully recapturable.
- It covers a greater size range (five device sizes ranging from 20-35 mm) as well as more overlap between sizes, allowing for deployment in LAA ostia ranging from 14 to 31.5 mm.
- The FLX has 50% more anchors, which are now J-shaped rather than straight, resulting in three times greater holding strength according to the manufacturer.
- The new FLX is less tapered, allowing greater apposition with the LAA wall, and also has reduced metal exposure that may potentially reduce risk of device related thrombosis.

The PINNACLE FLX Trial

- LAA closure with this next-generation LAA closure device was associated with a low incidence of adverse events and a high incidence of anatomic closure.





Amplatzer Amulet Left Atrial Appendage Occluder (LAAO)

Approved by FDA 8/2021

AMULET IDE trial

- The Amulet occluder was noninferior for safety and effectiveness of stroke prevention for nonvalvular atrial fibrillation compared with the Watchman device and superior for LAA occlusion.
- Procedure-related complications were higher with the Amulet occluder and decreased with operator experience.

- The growing evidence for both the Watchman and Amplatzer devices resulted in societal guidelines giving a class IIb recommendation for LAAC in patients with contraindication to anticoagulation.

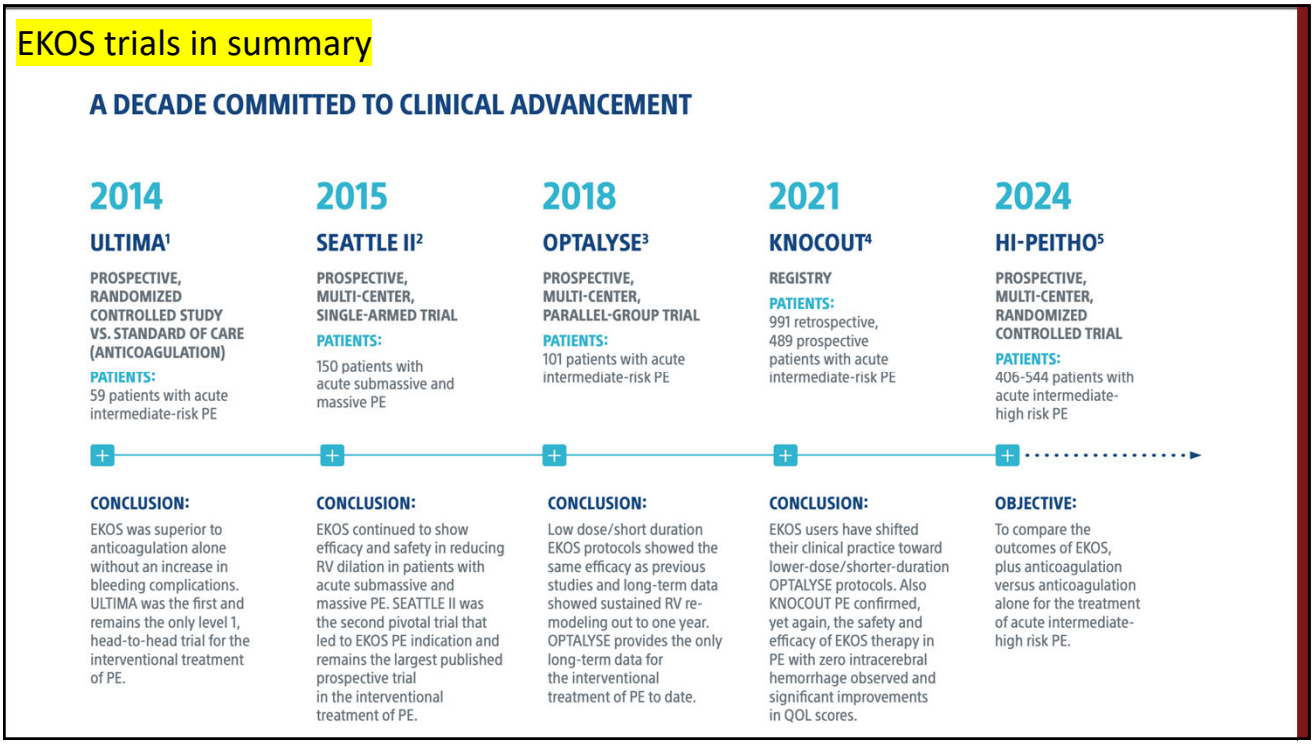
Pulmonary Embolism

- The incidence of VTE in North America and Europe is approximately 1.5 cases per 1000 person-years. About two thirds of cases are DVT, and the rest are PE with or without DVT. The incidence increases with age in both men and women.
- Patients with massive PE or high-risk submassive PE (with both right ventricular dysfunction and troponin elevation due to right ventricular injury) generally warrant advanced therapy.
  - systemic anticoagulation
  - systemic thrombolysis
  - catheter-directed thrombolysis
  - mechanical thrombectomy

Catheter Directed therapy

- The typical dose of tissue plasminogen activator in a pharmacomechanical catheter–based procedure, for example, is 24 mg or less compared with 100 mg for systemic administration.
- Low-intensity ultrasound–facilitated fibrinolysis is a novel approach. Ultrasound disaggregates fibrin strands, increases clot permeability, and disperses infused fibrinolytic drug into the clot through acoustic microstreaming effects.
- The SEATTLE II Trial studied 150 patients with massive or submassive PE to evaluate the safety and efficacy of ultrasound-facilitated, catheter-directed fibrinolysis using 24 mg of tissue plasminogen activator.
- No patient suffered intracranial hemorrhage.
- This procedure decreased right ventricular dilation, reduced pulmonary hypertension, and decreased the anatomic thrombus burden

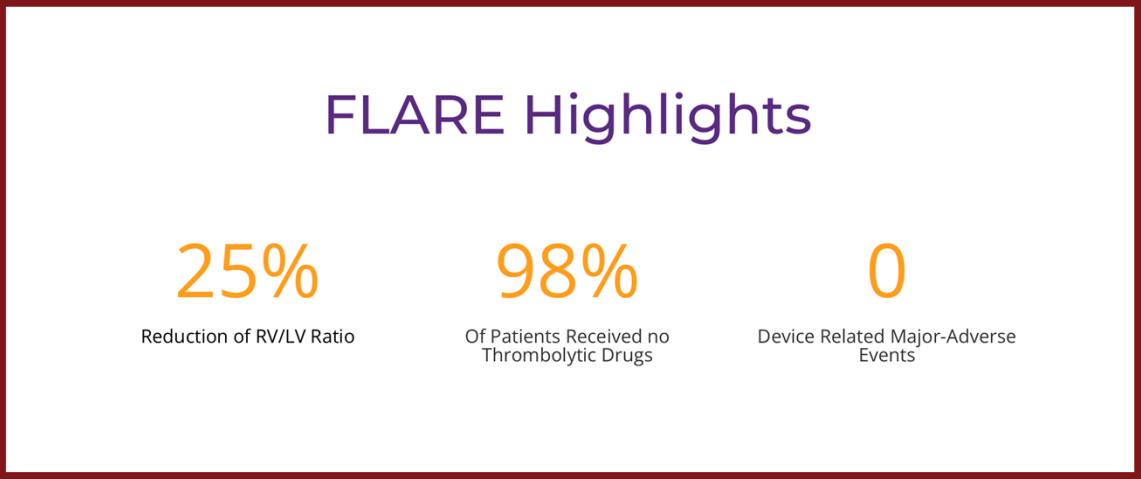
EKOS trials in summary



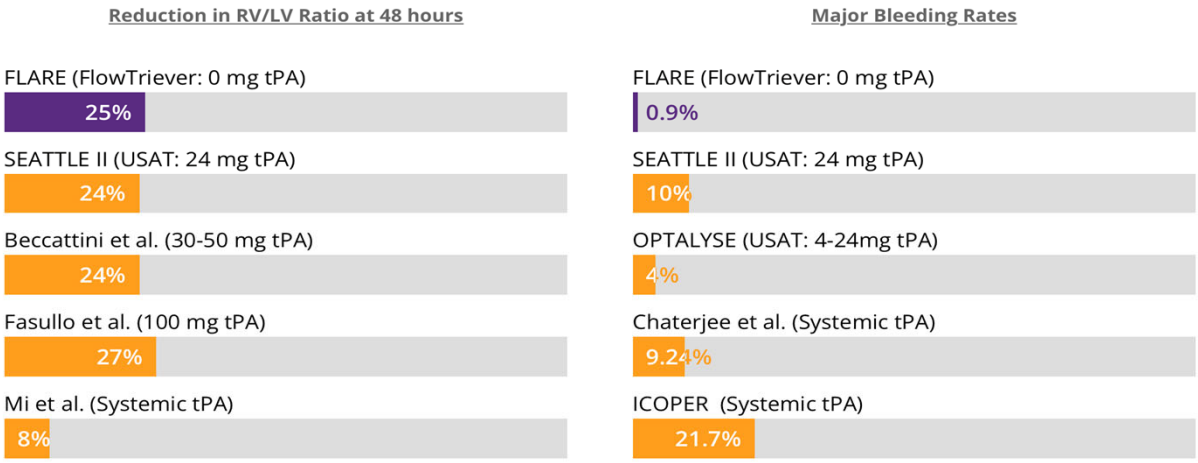
FlowTriever (INARI-Medical)

- Mechanical thrombectomy with the FlowTriever System appears safe and effective for treatment of patients with acute intermediate-risk PE, with significant acute improvement in RV function and minimal bleeding complications.
- Further studies are needed to comparatively evaluate this therapy against other catheter-directed and pharmacological approaches.

FALRE study

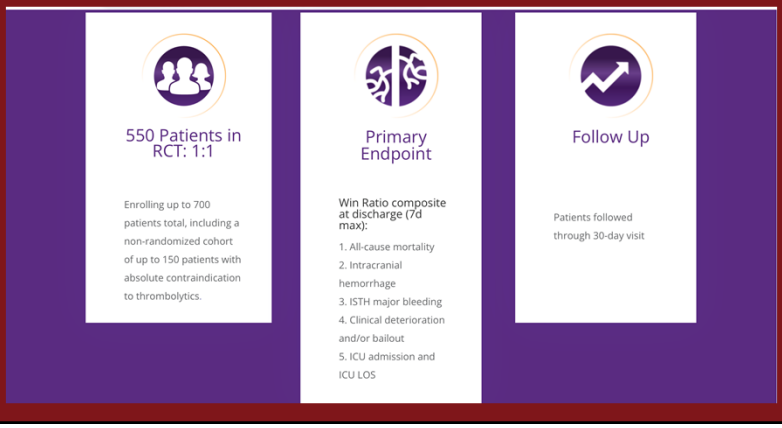


FLARE in Context[1]



PEERLESS trial ongoing trial (started 2/2022)

- Prospective, multicenter, randomized controlled trial of the FlowTriever System compared to Catheter-Directed Thrombolysis (CDT) for acute intermediate-high-risk pulmonary embolism (PE), and includes a non-randomized cohort of up to 150 subjects with an absolute contraindication to thrombolytics.

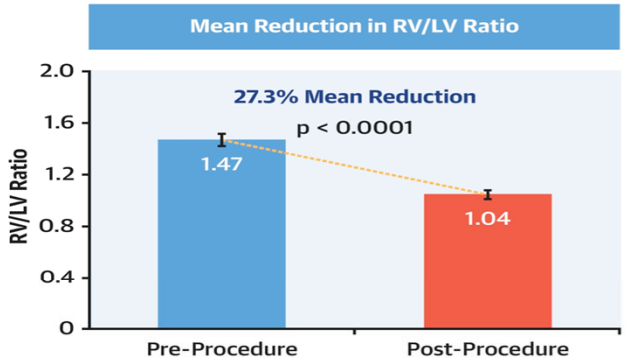


Pneumbra (Indigo aspiration system)

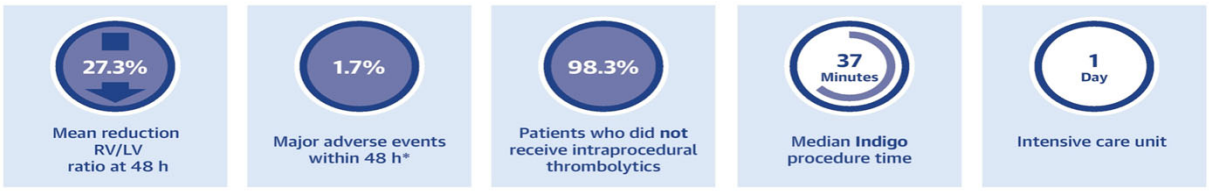
EXTRACT-PE (Evaluating the Safety and Efficacy of the Indigo Aspiration System in Acute Pulmonary Embolism) trial.

- EXTRACT-PE (Evaluating the Safety and Efficacy of the Indigo Aspiration System in Acute Pulmonary Embolism) trial.
- This single-arm study in 119 patients with submassive PE showed significantly reduced right ventricular-to-left ventricular ratios at 48 hours (0.43 ratio reduction; 95% CI, 0.38–0.47; *P* <0.0001).

CENTRAL ILLUSTRATION: Primary Efficacy and Safety Endpoint Results of the EXTRACT-PE Trial



Primary Safety Endpoint Analysis	All Patients (N = 119)	95% CI
Major adverse events within 48 h Clinical Events Committee, a composite of:	1.7% (2/119)	0.0%–4.0%
Device-related death within 48 h	0.8% (1/119)	0.0%–2.5%
Major bleeding within 48 h	1.7% (2/119)	0.0%–4.0%
Device-related serious adverse events within 48 h Clinical Events Committee, a composite of:	0.8% (1/119)	0.0%–2.5%
Clinical deterioration within 48 h	0.8% (1/119)	0.0%–2.5%
Pulmonary vascular injury within 48 h	0.8% (1/119)	0.0%–2.5%
Cardiac injury within 48 h	0.0%	N/A

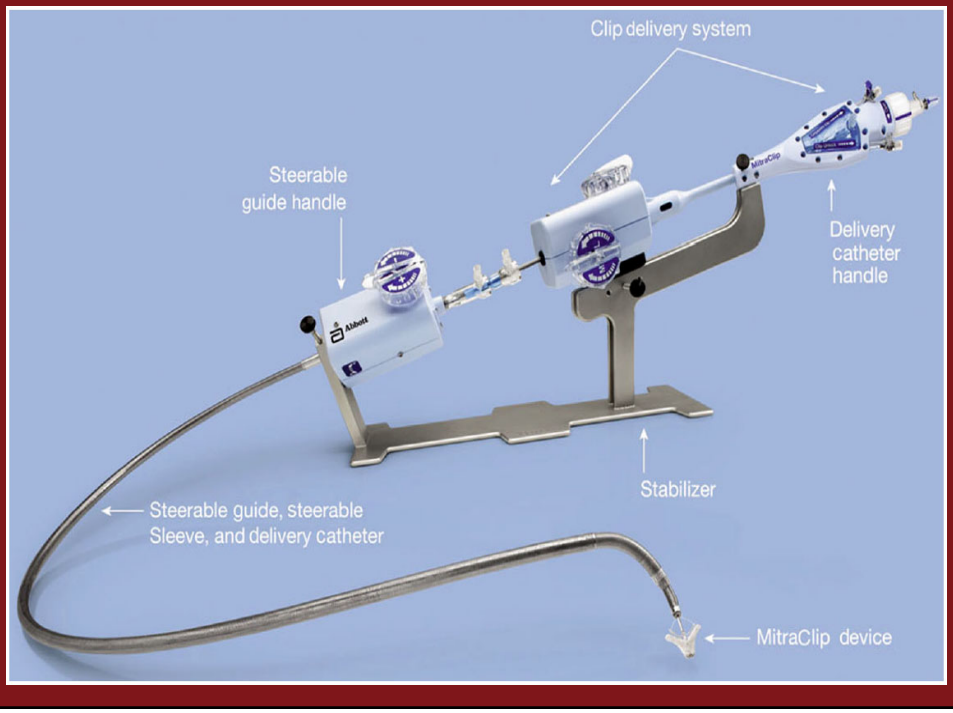


Sista, A.K. et al. J Am Coll Cardiol Intv. 2021;14(3):319–29.

- In the United States, this trial led to the designation of PE as an indication for use of the Indigo CAT 8 system and later the Lightning 8 and Lightning 12 Intelligent Aspiration systems (Penumbra).

MitraClip

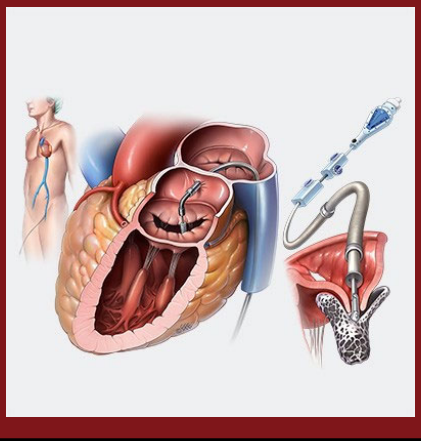
Similar to Alfieri technique: connects the middle scallops of anterior and posterior leaflets
Percutaneous edge-to-edge reconstruction
Patients with severe mitral regurgitation who are deemed at high risk for surgery
FDA approved in October 2013

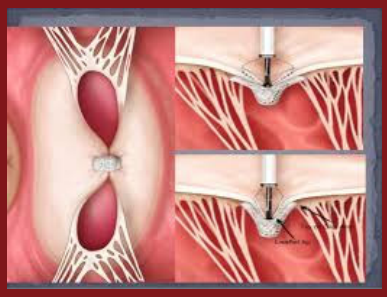


Mitral Regurgitation

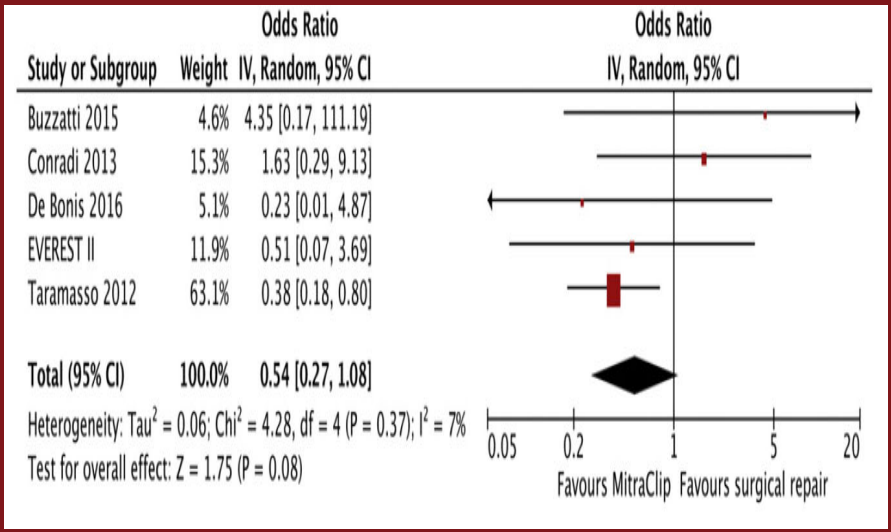
- Patients with chronic heart failure (HF) with reduced ejection fraction and symptomatic secondary mitral regurgitation have a poor prognosis.
- There are no proven therapies for secondary MR in HF, but registry data suggest that the transcatheter mitral valve repair (TMVR) with the **MitraClip** device is safe and may provide symptomatic benefit in these patients.

Mitra





Early Mortality (30 days)



Takagi et al. Int J Cardiol 2017

Percutaneous mitral valve repair using mitral clip device (transcatheter edge-to-edge repair)

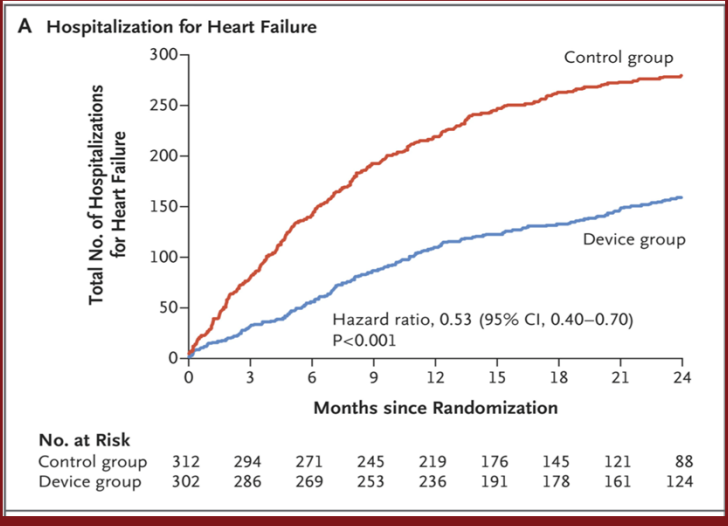
- **MitraClip** (Abbott Vascular) was the first transcatheter mitral valve repair technology to receive CE (Conformité Européenne) Mark approval (European Union).
- **Indications:**
  - Severe Primary MR with prohibitive risk for surgery (FDA approved 2013)
  - **Severe Secondary MR who failed GDMT with the following* (FDA approved 2019)**
    - NYHA II-IV
    - **Suitable anatomy**
    - LVEF 20-50%
    - **LVESD ≤ 70 mm**
    - PASP ≤ 70 mmHg

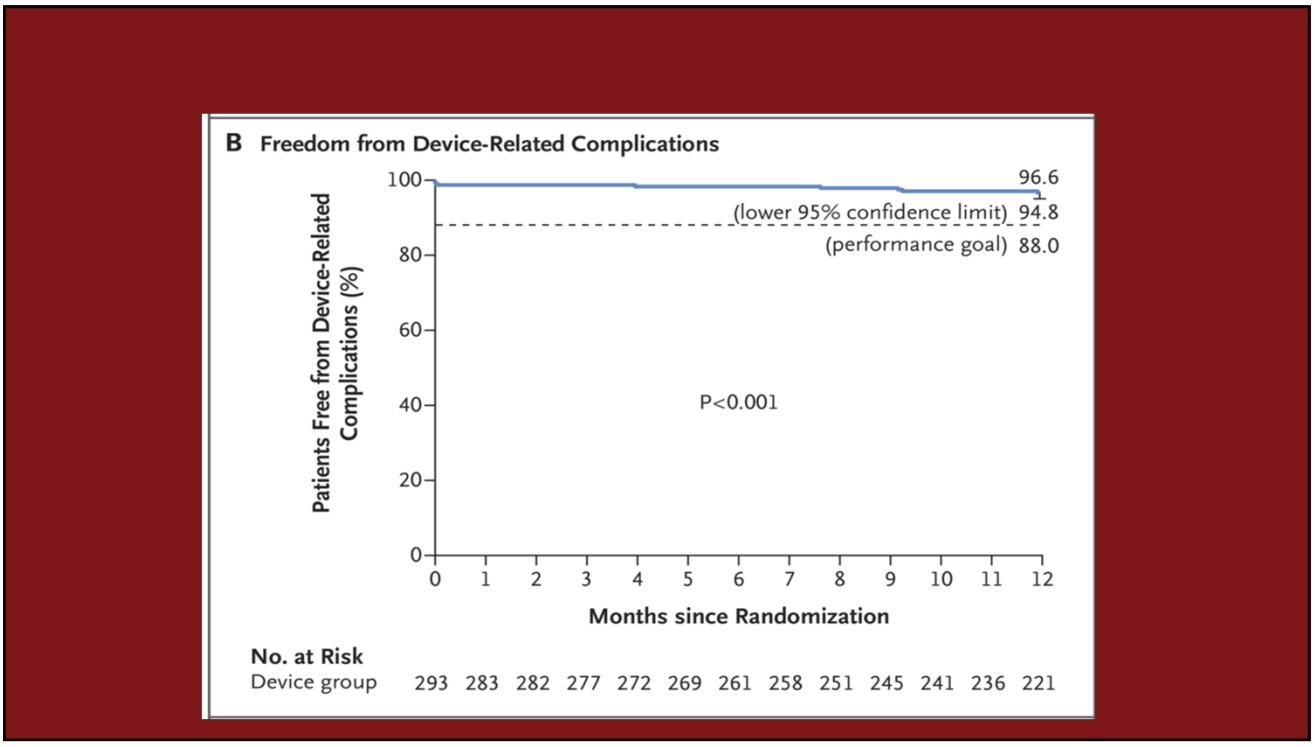
***strengthened to a class IIa in 2022 Guidelines for heart failure treatment**

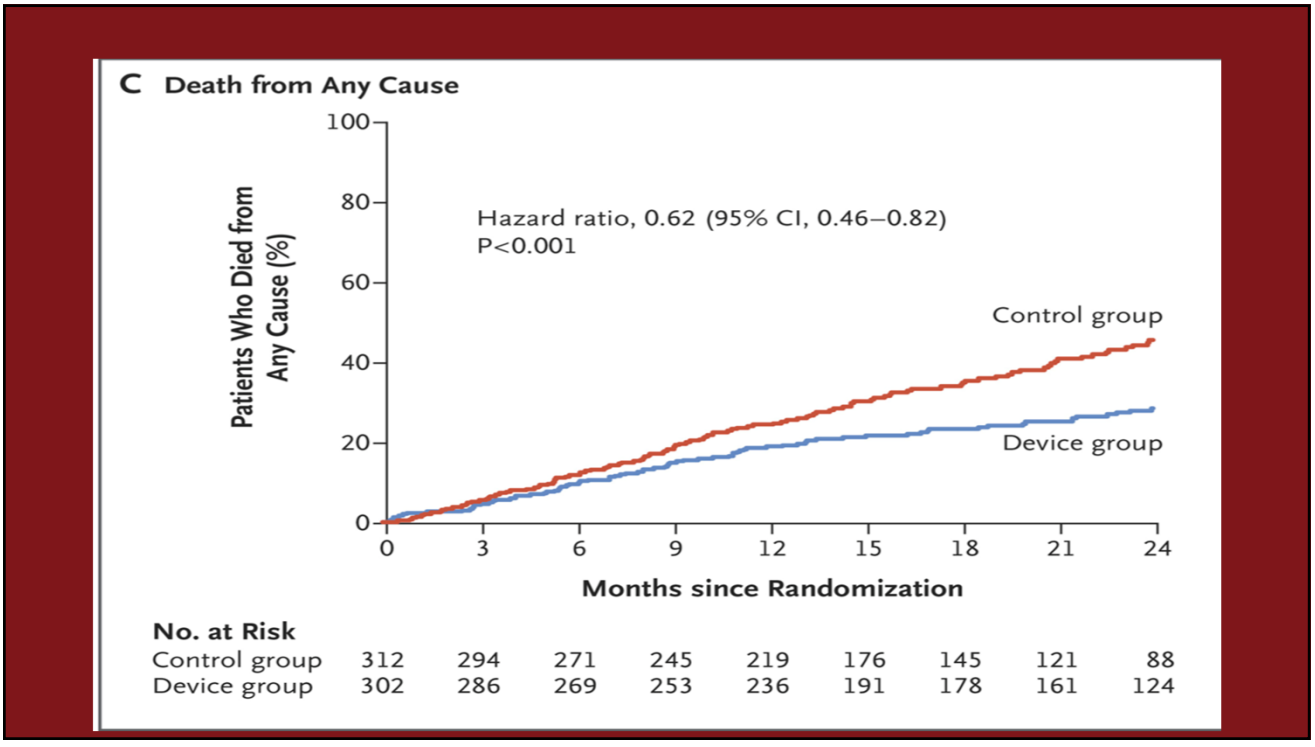
Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) trial

- Patients were randomly assigned to transcatheter mitral-valve repair plus medical therapy (device group) or medical therapy alone (control group). The primary effectiveness end point was all hospitalizations for heart failure within 24 months of follow-up. The primary safety end point was freedom from device-related complications at 12 months; the rate for this end point was compared with a prespecified objective performance goal of 88.0%.

COAPT




B Freedom from Device-Related Complications
Patients Free from Device-Related Complications (%)
100
80
60
40
20
0
96.6
(lower 95% confidence limit) 94.8
(performance goal) 88.0
P<0.001
0 1 2 3 4 5 6 7 8 9 10 11 12
Months since Randomization
No. at Risk
Device group 293 283 282 277 272 269 261 258 251 245 241 236 221

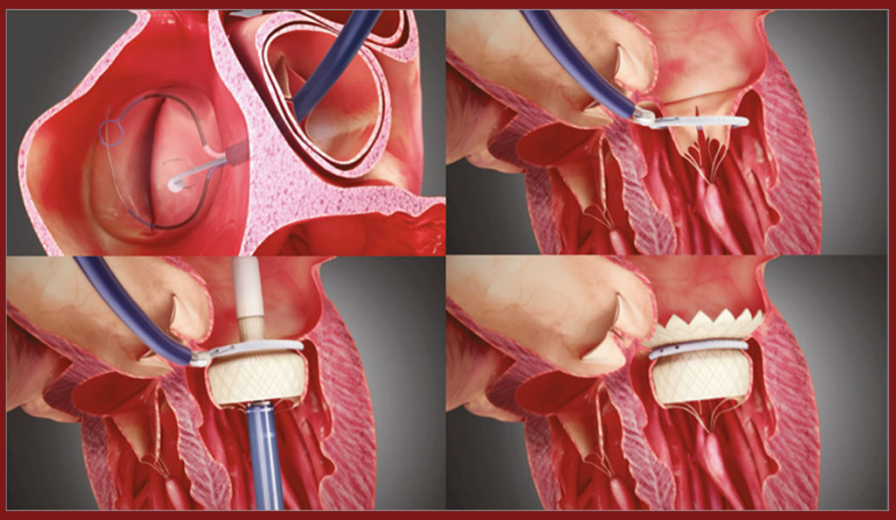

C Death from Any Cause
Patients Who Died from Any Cause (%)
100
80
60
40
20
0
Hazard ratio, 0.62 (95% CI, 0.46–0.82)
P<0.001
Control group
Device group
0 3 6 9 12 15 18 21 24
Months since Randomization
No. at Risk
Control group 312 294 271 245 219 176 145 121 88
Device group 302 286 269 253 236 191 178 161 124

COAPT

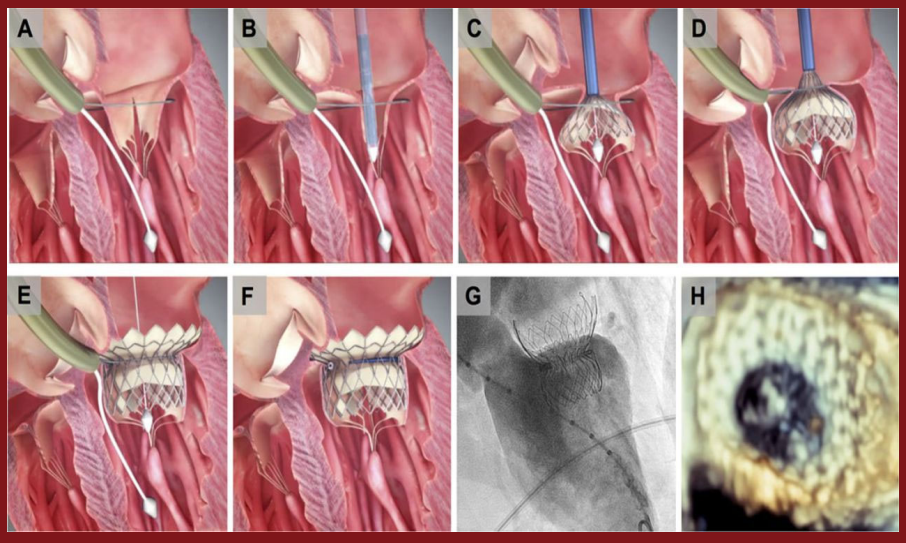
Among patients with heart failure and moderate-to-severe or severe secondary mitral regurgitation who remained symptomatic despite the use of maximal doses of guideline-directed medical therapy, transcatheter mitral-valve repair resulted in a lower rate of hospitalization for heart failure, lower mortality, and better quality of life and functional capacity within 24 months of follow-up than medical therapy alone, and the prespecified goal for freedom from device-related complications was met.

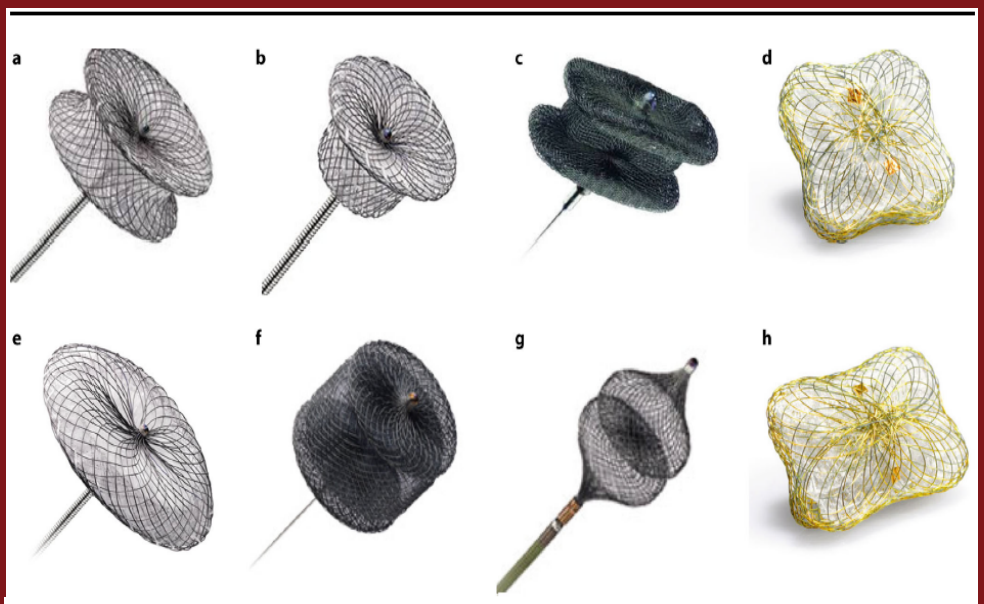
Mitral Valve Implantation
Endovalve (Micro Interventional Devices,Inc, Newtown, Pennsylvania)
CardiAQ (CardiAQ valve Technologies Inc,Irvine, California)
Edwards FORTIS (Edwards Lifesciences)
MitrAssist (MitrAssist Ltd., Misgav, Israel)
Neovasc Tiara (Neovasc Inc,Richmond,Canada)

Percutaneous Valve Replacement



Percutaneous Valve Replacement





PVL closure devices. a Amplatzer Muscular VSD Occluder. b Amplatzer Duct Occluder. c Amplatzer Vascular Plug III. d Occlutech PLD (square-shaped design). e Amplatzer Septal Occluder. f Amplatzer Vascular Plug II. g Amplatzer Vascular Plug IV. h Occlutech PLD (rectangular-shaped design)

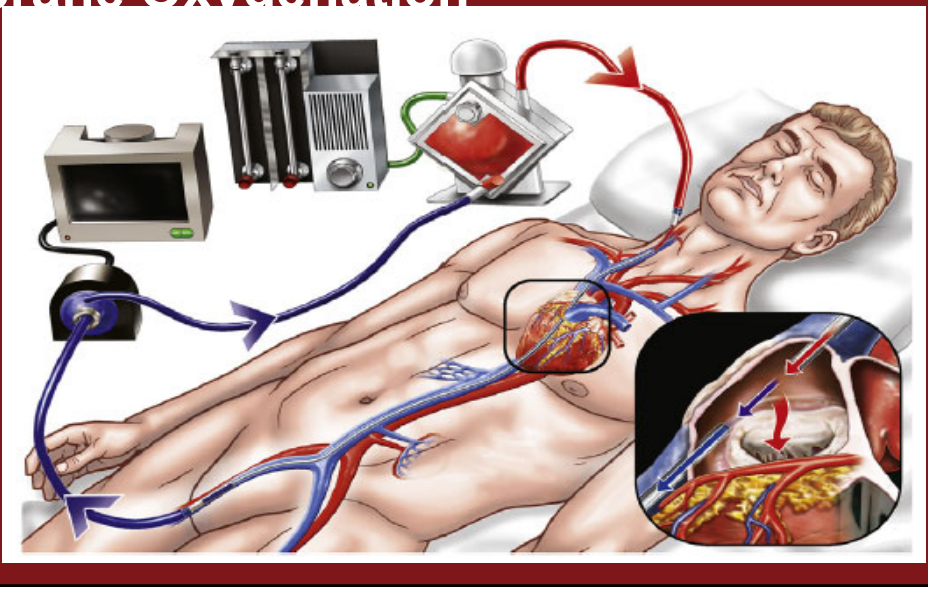
High-risk PCI and LV Assist Device

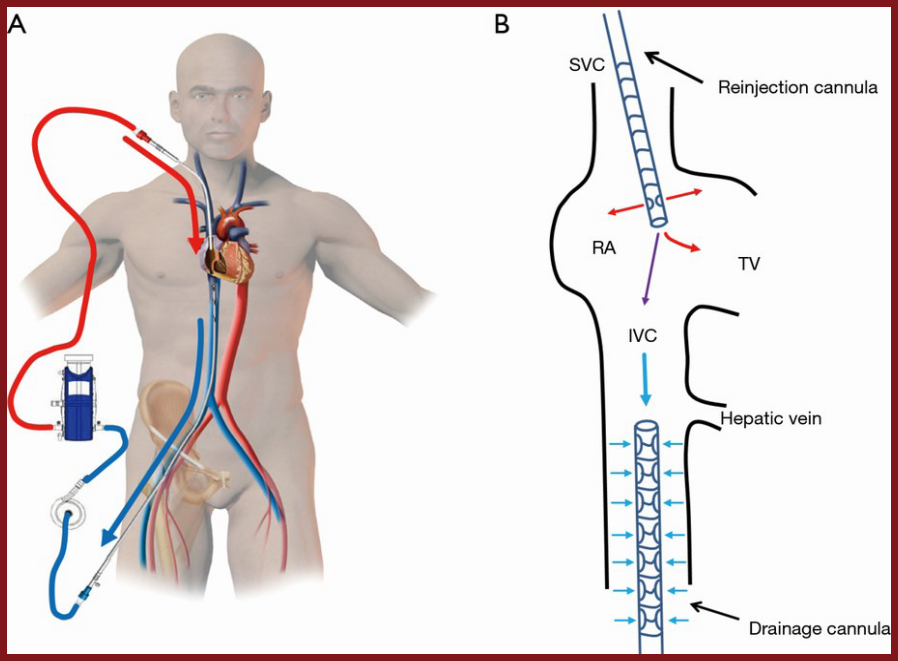
High risk patients: Left ventricular (LV) dysfunction and /or hemodynamic instability
High risk coronary intervention : complex coronary artery disease (CAD) such as multivessel, bypass graft, or left main CAD
This population is at increased risk of periprocedural hemodynamic compromise and cardiovascular complications
Intra-aortic balloon pump (IABP) is the most commonly used mechanical support device
It only provides modest hemodynamic support, and its use is not associated with survival benefit in the setting of high-risk PCI or cardiogenic shock
Provide partial or complete hemodynamic support during high-risk PCI by reducing LV volumes, wall stress, and myocardial oxygen consumption and augmenting cardiac output and coronary perfusion

Briasoulis et al. Am J Cardiol 2016

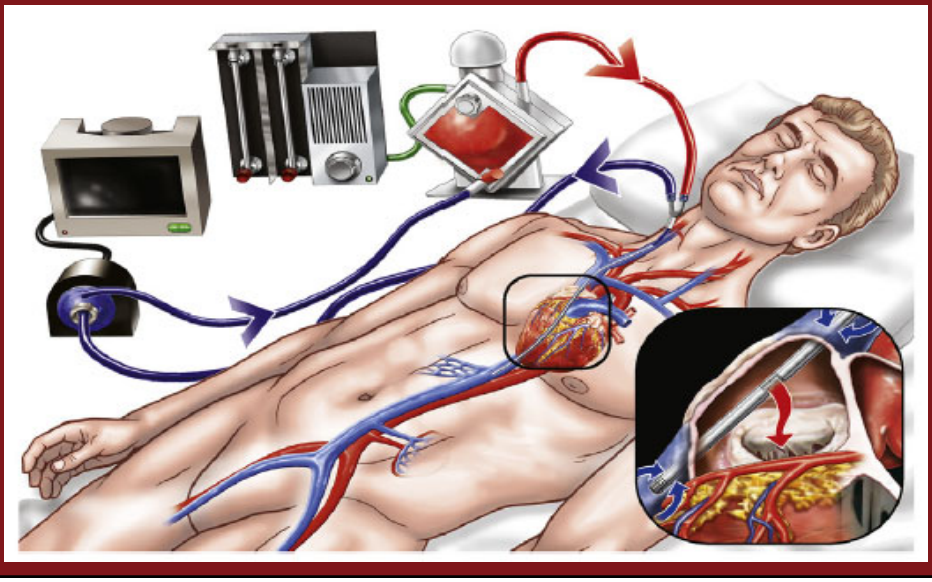
Extracorporeal membrane oxygenation (ECMO)
Directly oxygenates and removes carbon dioxide from the blood using an oxygenator
Venovenous ECMO: •Hypercapnic respiratory failure •Eliminate carbon dioxide in primarily hypoxemic respiratory failure
Arteriovenous ECMO: •Carbon dioxide removal •Femoral cannulation •Limits patient mobility and rehab

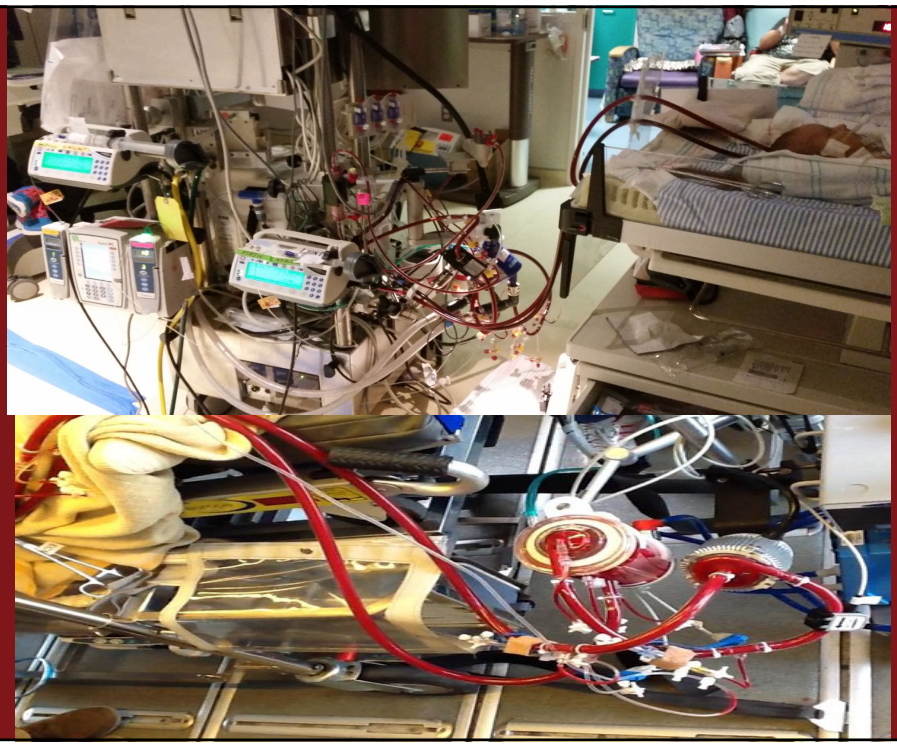
Two-site Venovenous Extracorporeal Membrane Oxygenation





Single-Site Venovenous ECMO

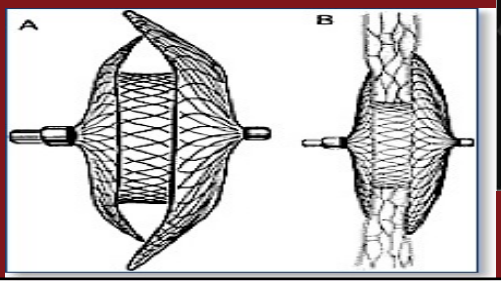


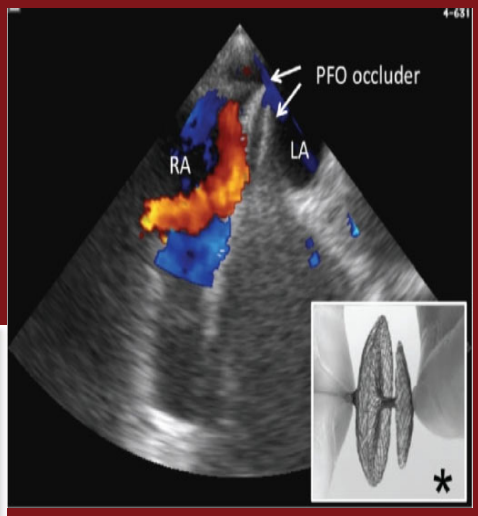


Percutaneous PFO Closure

Current AHA/ASA guidelines do not support the use of PFO closure among patients with PFO and cryptogenic stroke
This recommendation was based on the null results of the 3 trials included in this pooled analysis.
Meta-analysis of the 3 main trials was able to suggest evidence that closure can prevent stroke recurrence in some patients with cryptogenic stroke found to have a PFO
However, AF is increased with closure, though less strongly with the occluder device
The annualized rate of ischemic stroke, if treated medically, is approximately 1%
Device closure decreases this rate by half.

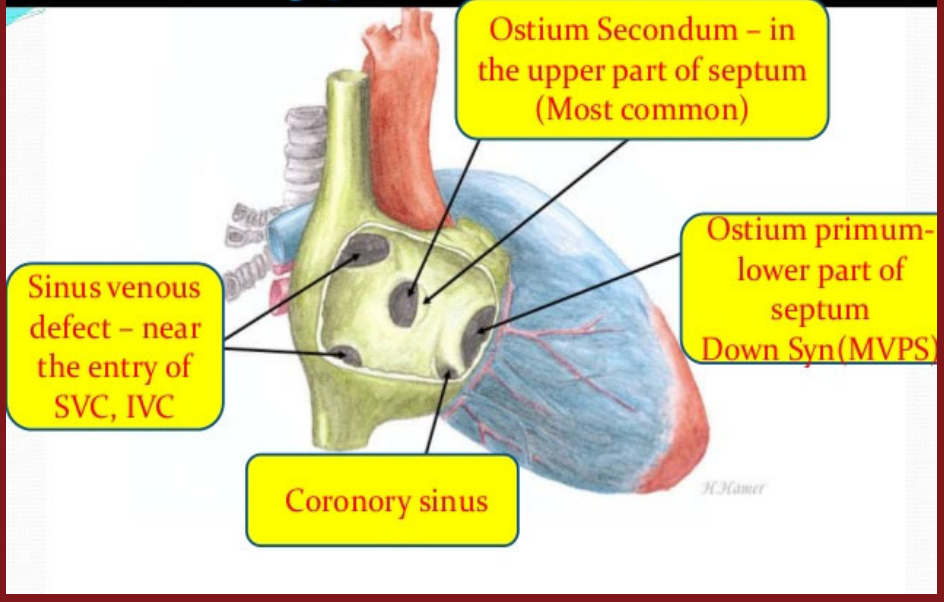
AMPLATZ PFO Closure Device





RCT's for PFO closure device
The CLOSURE I Trial: 909 patients randomized to STARFlex septal closure system (NMT Medical, Inc., Boston, Massachusetts) or medical therapy. Device group: After closure, all device patients received an antiplatelet regimen of clopidogrel 75 mg daily for 6 months and aspirin 81 or 325 mg daily for 2 years. Medical therapy group: warfarin with a target international normalized ratio of 2.0 to 3.0; aspirin 325 mg daily
The RESPECT Trial:980 patients randomized to Amplatzer PFO Occluder (AGA Medical/St. Jude Medical, St. Paul, Minnesota) and medical therapy. Device group: 81 to 325 mg of aspirin and clopidogrel for 1 month after device placement, followed by aspirin monotherapy for 5 months Medical therapy group: 1 of 4 permissible medical regimens: aspirin; warfarin; clopidogrel; or aspirin/extended-release dipyridamole.
The PC Trial: 414 patients randomized to Amplatzer PFO Occluder and medical therapy. Device group: Aspirin (100 to 325 mg/day) for at least 5 to 6 months, plus ticlopidine (250 to 500 mg/day) or clopidogrel (75 to 150 mg/day) for 1 to 6 months. Medical group: antiplatelet or anticoagulation therapy upon physician discretion.

Types of ASD



Percutaneous ASD Closure

Confers the advantage of avoidance of cardiopulmonary bypass, sternotomy scar, shorter mechanical ventilation and intensive care unit hospitalization duration

•The most commonly used and US FDA-approved devices are the Amplatzer Septal Occluder (ASO) (St. Jude Medical, St. Paul, MN) and the Gore HELEX (WL Gore & Associates, Flagstaff, AZ)
•The ASO is the most studied device in the literature

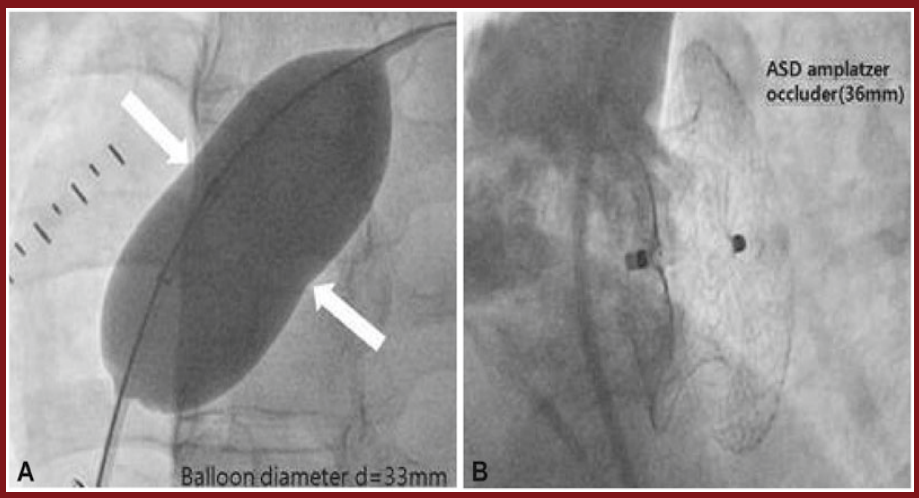
Short-term device-related mortality rates is 0.01% and long-term 0.1%, as reported in a meta-analysis of 28,142 patients from 203

Rate of device thrombosis was 1.0% (95% [CI], 0.8%-1.0%) after ASD closure

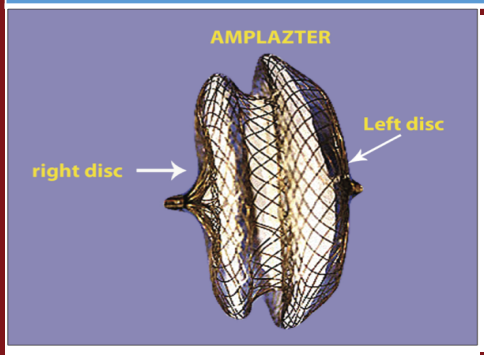
ACC/AHA 2008 guidelines recommend closure:
•right atrial and ventricular enlargement with or without symptoms
•ASD minimum diameter bwtween 5mm and 40 mm
•Paradoxical embolization (cryptogenic stroke) and/or orthodeoxia-platypnea

Abaci et al. CCI 2013
Wames et al JACC 2008

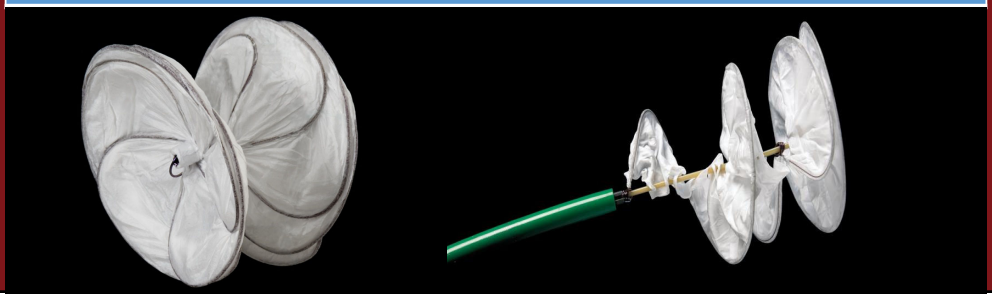
Pre-balloon measure of the orifice size

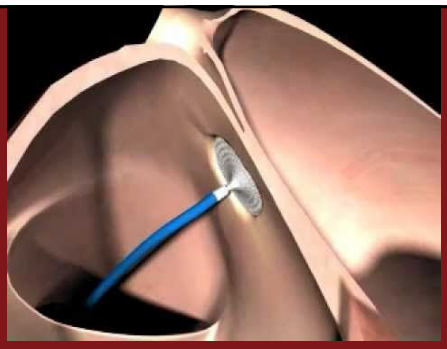


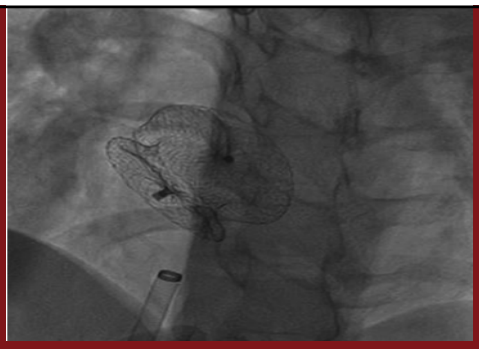
Amplatzer Septal Occluder (ASO)

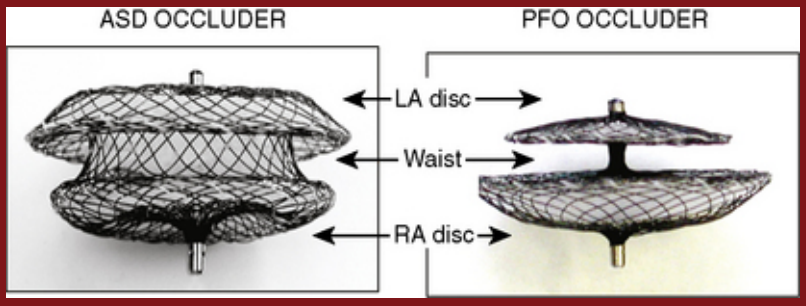


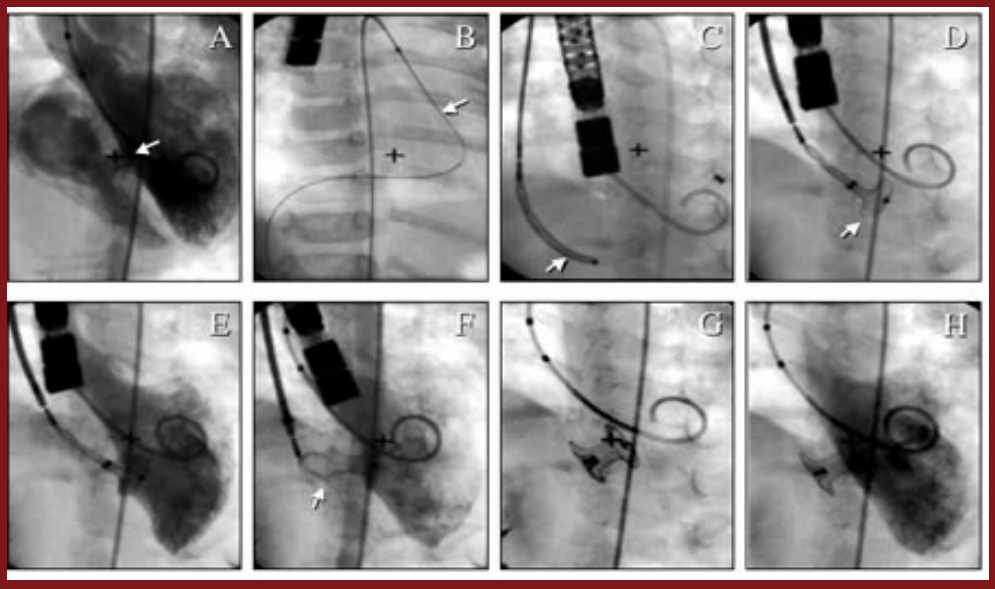
Gore HELEX








ASD OCCLUDER
PFO OCCLUDER
LA disc
Waist
RA disc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Research Trials

- Future
- Innovation
- 3 New Trials at TTUHSC-UMC
- No one needs to go to Dallas- Houston or Canada!

Teams!

- Cardiology;
- -CHF
- -Cardiac EP
- -Cardiac Imaging
- -Cardiac Vascular Service
- -Interventional and Structural Cardiology
- -Preventive Cardiology


THANK YOU
ANY QUESTION?