Technologies Targeting Acute Limb Ischemia in Cardiogenic Shock

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Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Nature of Financial Relationship	Ineligible Company
Grant/Research Support	Abiomed/JNJ-MedTech
Consultant Fees/Honoraria	Abiomed/JNJ-MedTech; Myo1
Individual Stock(s)/Stock Options	None
Royalties/Patent Beneficiary	None
Executive Role/Ownership Interest	Co-Founder, Tulyp Inc
Other Financial Benefit	None

All Relevant Financial Relationships have been mitigated.
Faculty disclosure information can be found on the app

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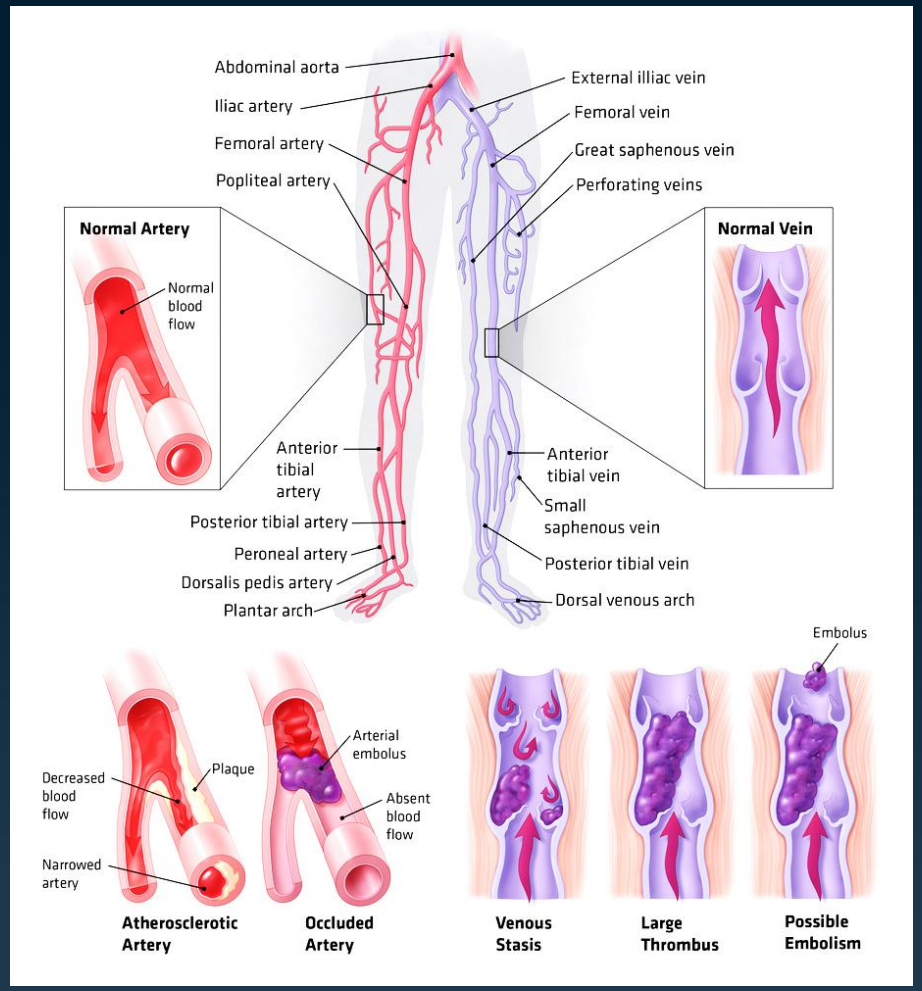
Delays to Reperfusion Increase Limb Loss and Mortality
Irreversible Damage Occurs after 6 hours of Acute Limb Ischemia (ALI)



ALI is a highly morbid condition with 1-year mortality and amputation rates ranging between 16-42% and 11-37%, respectively.

Paradis et al AM J Physiol Cell Physiol 2016

Delays to Reperfusion Increase Limb Loss and Mortality
Irreversible Damage Occurs after 6 hours of Acute Limb Ischemia (ALI)

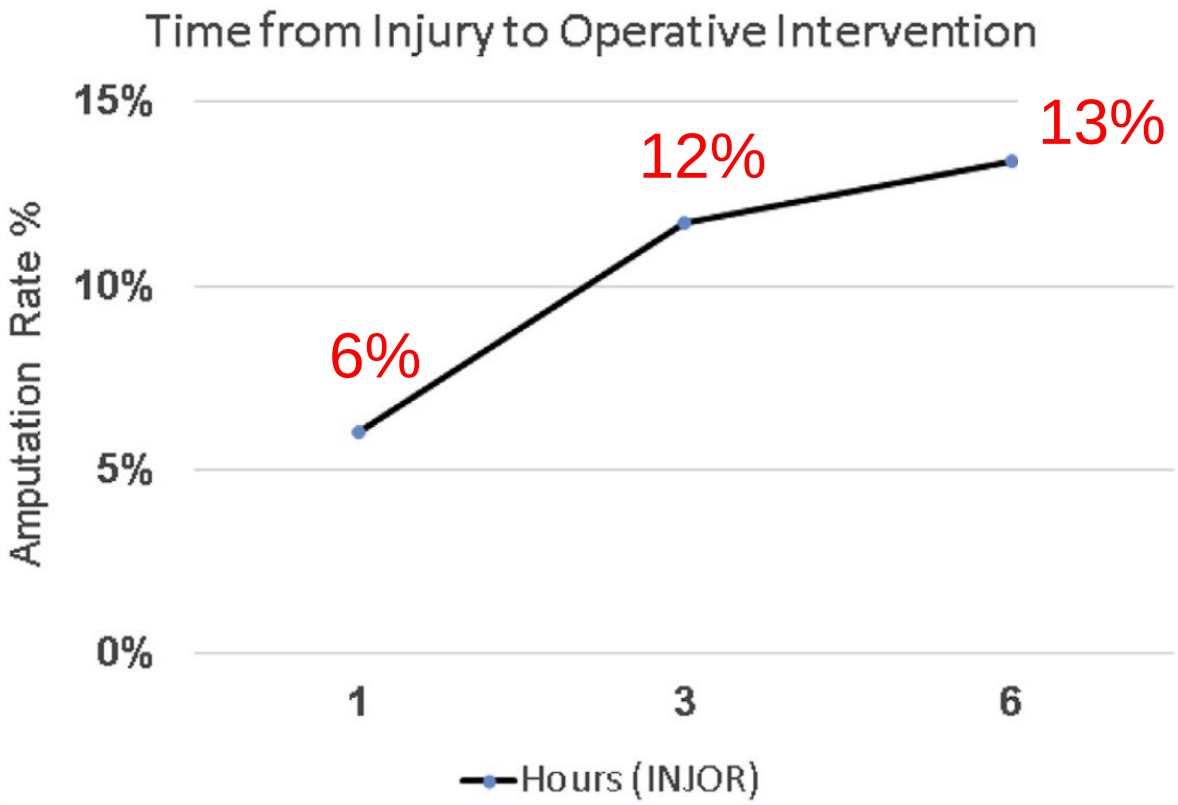


Fig. Relationship between injury to operating room (*INJOR*) times and amputation rates.

Table. Patients with shorter injury to operating room (*INJOR*) times had decreased amputation rates

INJOR time	Amputation rates
≤60 minutes	6.0% (33/554)
61-180 minutes	11.7% (255/2186)
181-360 minutes	13.4% (171/1275)

$P < .01$.

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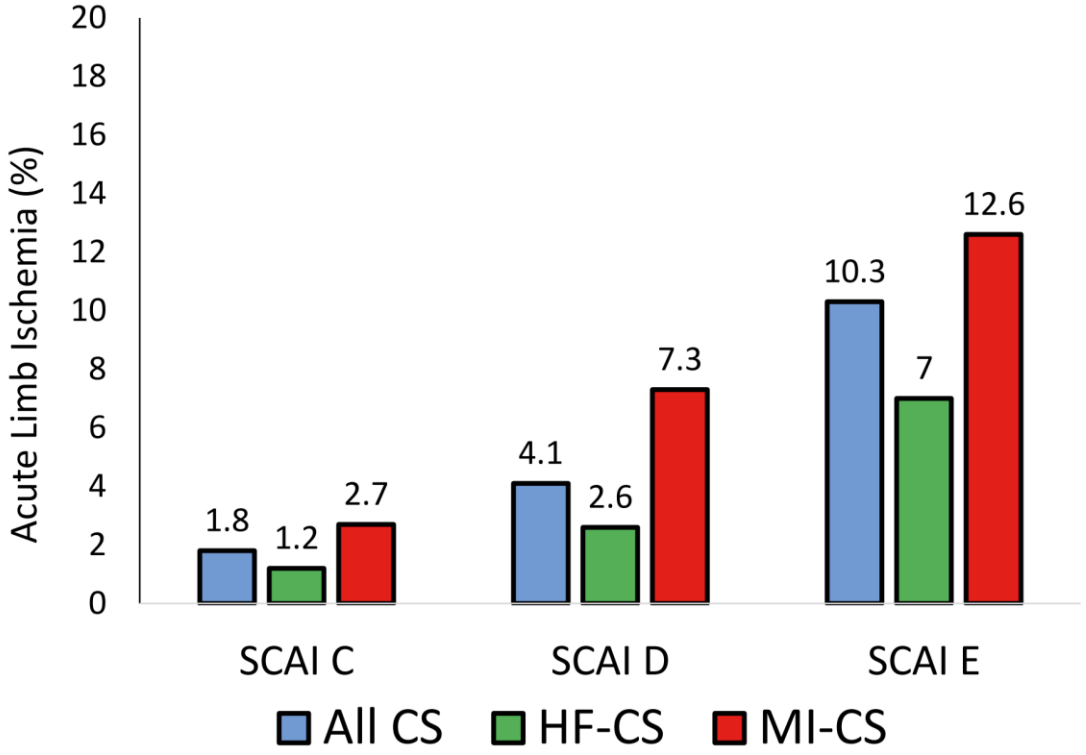
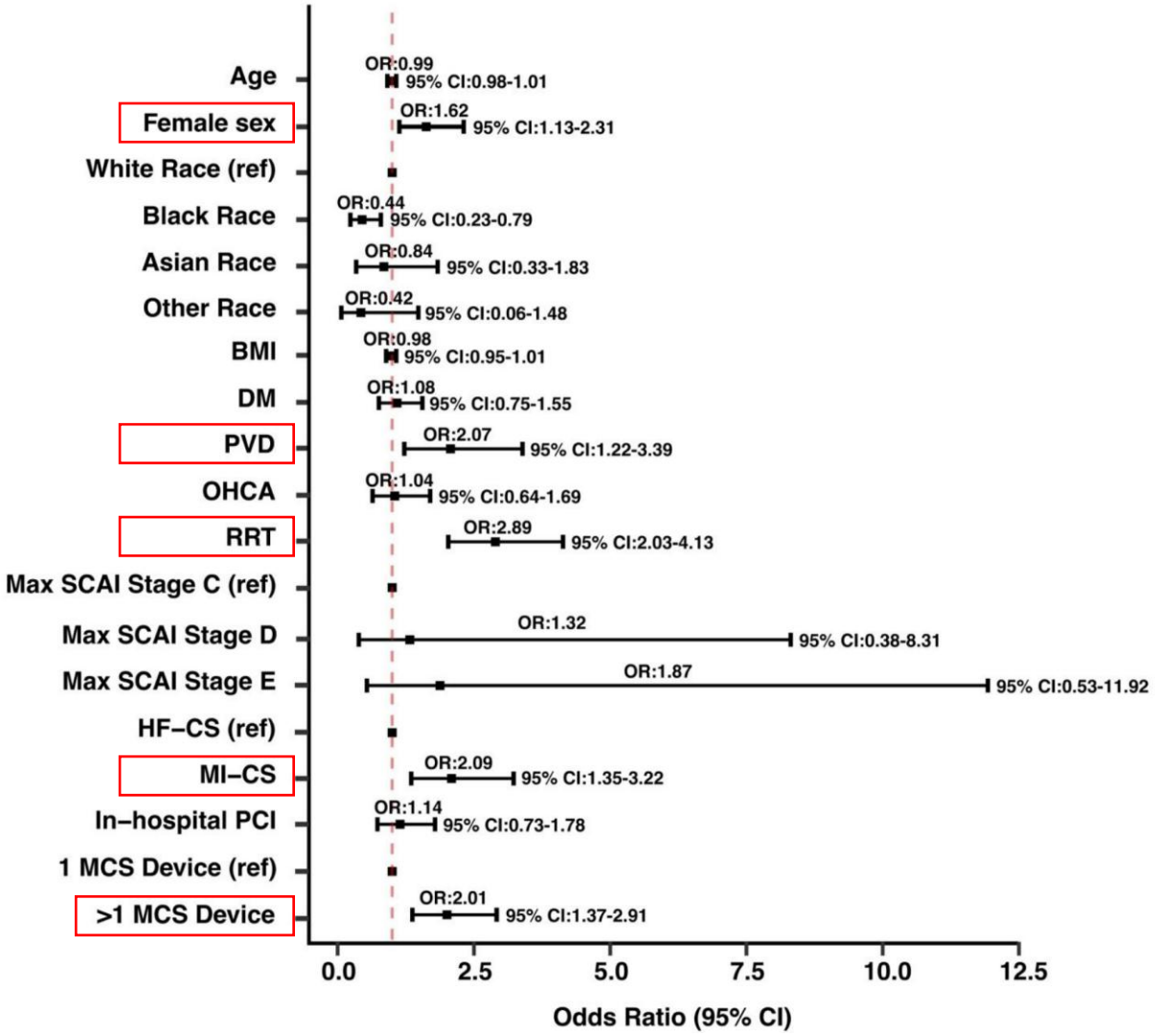
Alarhayem et al J Vasc Surgery 2019

Acute Limb Ischemia: A Growing and Deadly Problem

Factors Contributing to Risk of ALI in CS: Female, PVD, RRT, MI-CS and MCS





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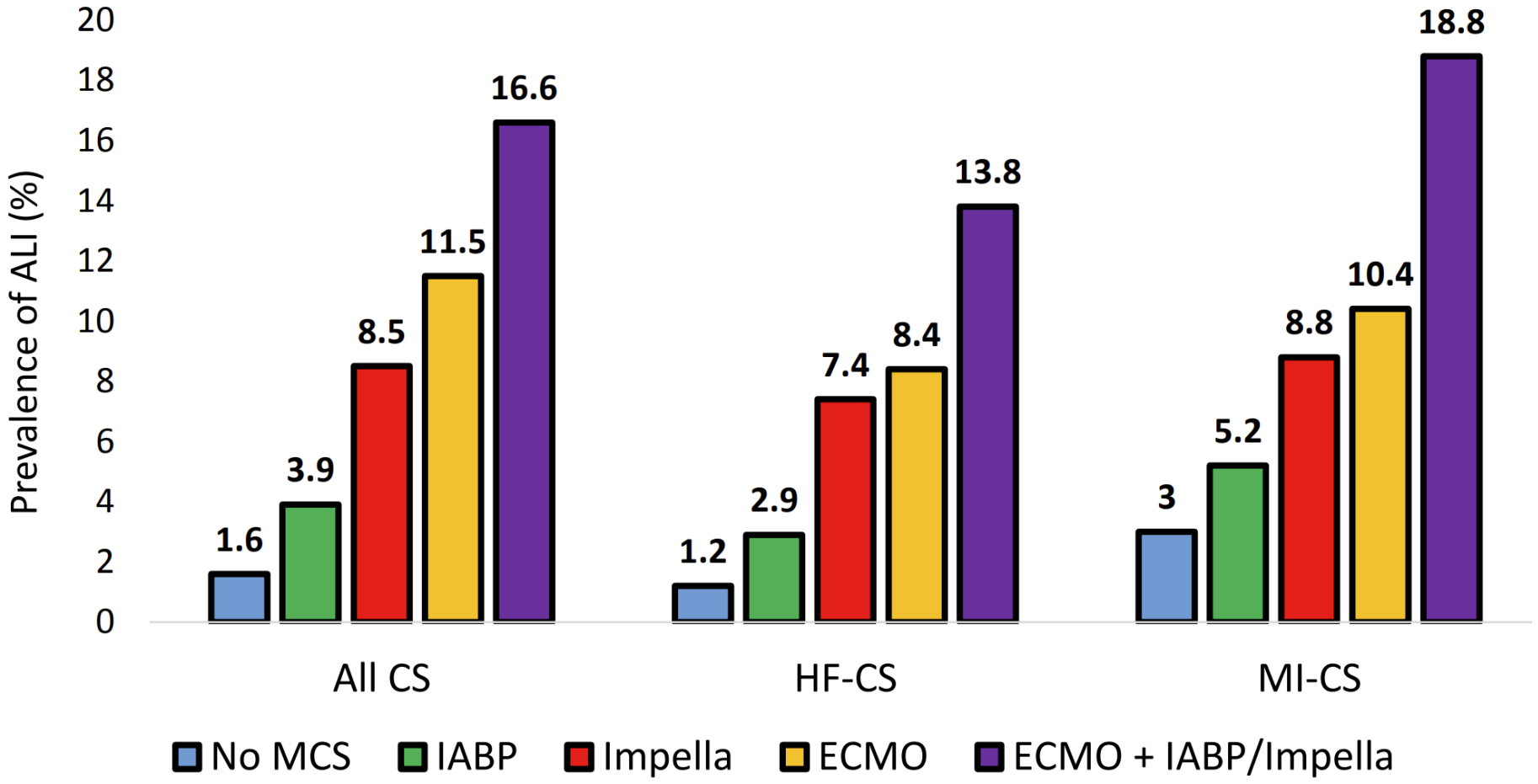
Kochar and Kapur (CSWG) et al JHLT 2024

Acute Limb Ischemia: A Growing and Deadly Problem

All CS patients are at risk of ALI especially with need for higher capacity Acute MCS



Kochar and Kapur (CSWG) et al JHLT 2024

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Acute Limb Ischemia: Impacts Length of Stay and Hospital Costs

	Limb Ischemia (N=392)	No Limb Ischemia (N=6,551)	
Bleeding	57.4% (225)	22.1% (1,446)	< 0.01
Hemolysis	21.9% (86)	9.1% (594)	<0.01
Hospital Length of Stay	37.3±42.9 (132)	24.7±33.8 (2,509)	<0.01
Mortality	57.4% (225)	30% (1,966)	<0.01

Table II. In-hospital outcomes and resource utilization in patients with and without acute limb ischemia (*ALI*)

In-hospital outcomes	No ALI	ALI	Total	*P* value
Death	27,924 (33.53)	510 (39.20)	28,434 (33.62)	<.0001
Total charges, $	260,738 ± 314873	540,617 ± 612,308	107,981 ± 136,834	
Length of stay, days	9.81 ± 11.50	17.96 ± 18.51	4.71 ± 5.84	<.0001
30-Day readmission	1272 (1.53%)	18 (1.38%)	1290 (1.52%)	<.0001

Values are number (%) or mean ± standard deviation.
Comparing the in-hospital procedural outcomes, death rates, hospital expenses, length of stay and 30-day readmission rate of patients with and without ALI.

Kochar and Kapur (CSWG) JHLT 2024
Bashir et al J Vasc Surgery 2023

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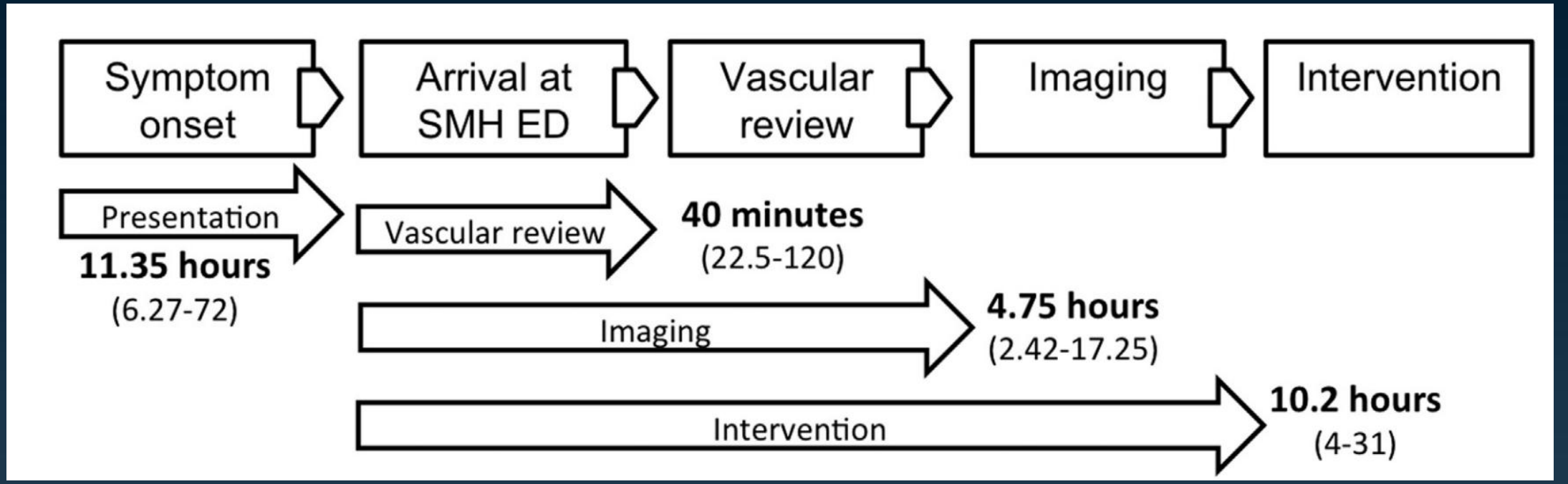
Delays to Reperfusion Increase Limb Loss and Mortality (Goal: <6 hours)
LimbSave Can Reduce Time to Reperfusion in Acute Limb Ischemia

In the Field | **In the ER** | **In the Hospital** | **In the Cath Lab/OR**



Innovation Needed: Prevention, Detection, Therapeutics

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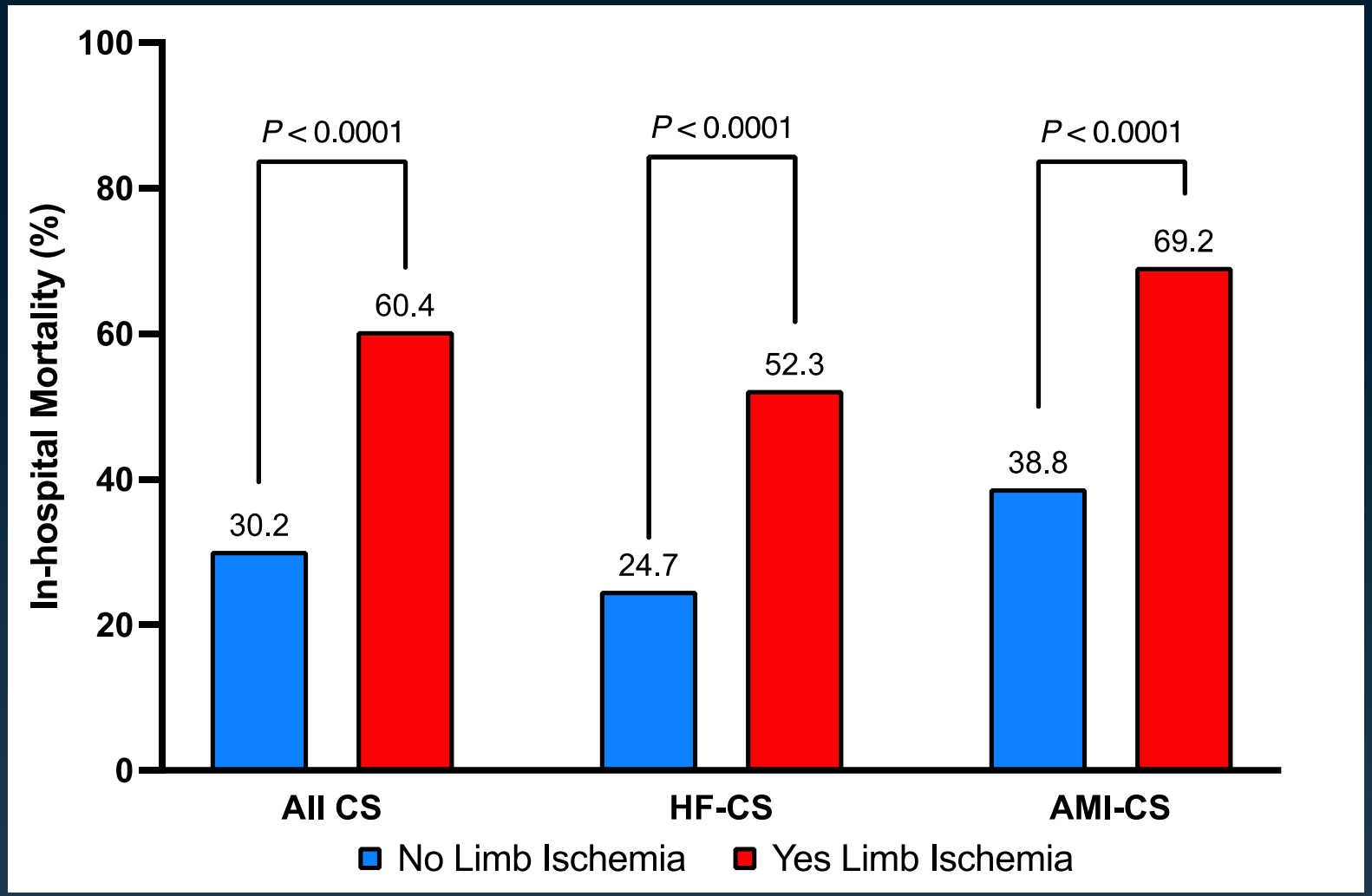
Normahani et al Ann Vasc Surg 2017

Acute Limb Ischemia: Doubles Mortality in Cardiogenic Shock



Kochar and Kapur et al JHLT 2024

Acute Limb Ischemia : A Dark Horse Driving Poor Outcomes in Shock

IABP SHOCK II: Peripheral Ischemic Vascular Complications Warranting Intervention

4.3% IABP vs 3.4% Control: Relative Risk 1.29 (0.58-2.90)

DanGer Shock: Peripheral Ischemic Vascular Complications Warranting Intervention

5.6% Impella CP vs 1.1% Control: Relative Risk 5.15 (1.11 to 23.84)

ECLS Shock: Peripheral Ischemic Vascular Complications Warranting Intervention

11% ECMO vs 3.8% Control: Relative Risk 2.86 (1.31 to 6.25)

Emerging Technologies for ALI Detection: MYO1

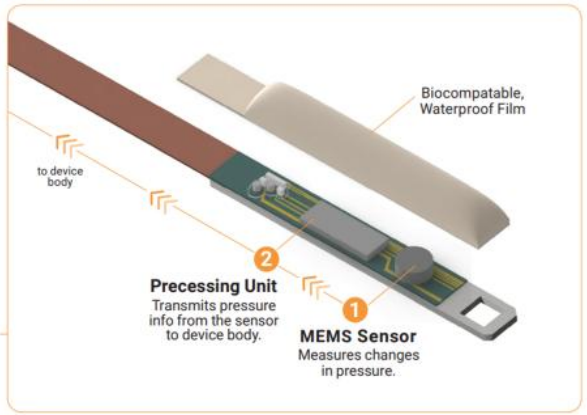
MY01 Continuous Compartmental Pressure Monitor and Mobile Application

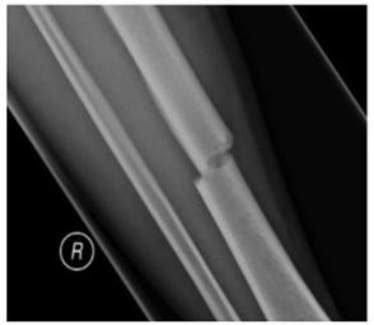
Advantages for Pressure Sensing

6x more accurate

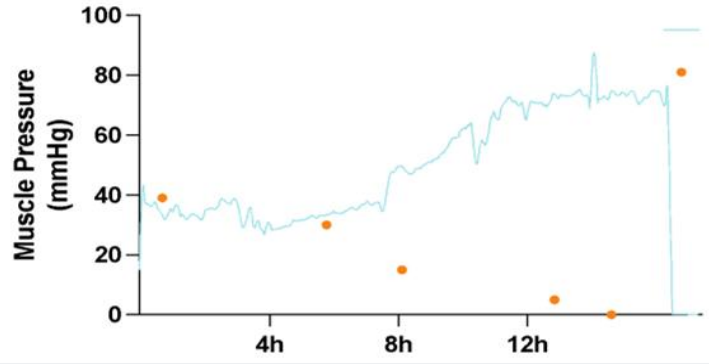
Through the use of MEMS technology, the MY01 device is proven to be six times more accurate than fluid-based pressure monitors.[1]

MY01 Use





Age: 21
Sex: Male
Injury: (OTA:42A3)
MY01 Usage: Pre-Op



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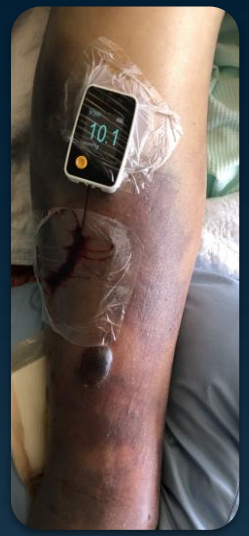
MYO1: Continuous Pressure Monitoring Applications

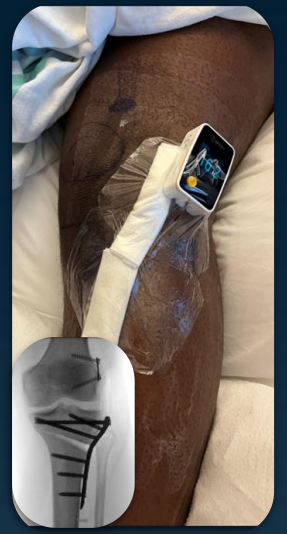


Tibia Pre-Op

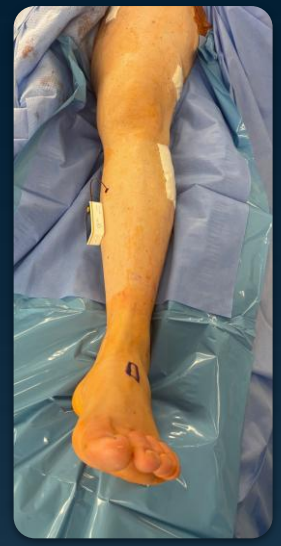
Forearm Pre-Op

Tibia Post-Op

Tibia Post-Op + Nerve Block



Osteotomy Post-Op + Nerve Block



Vascular Reperfusion Post-Op

ECMO Post-Op

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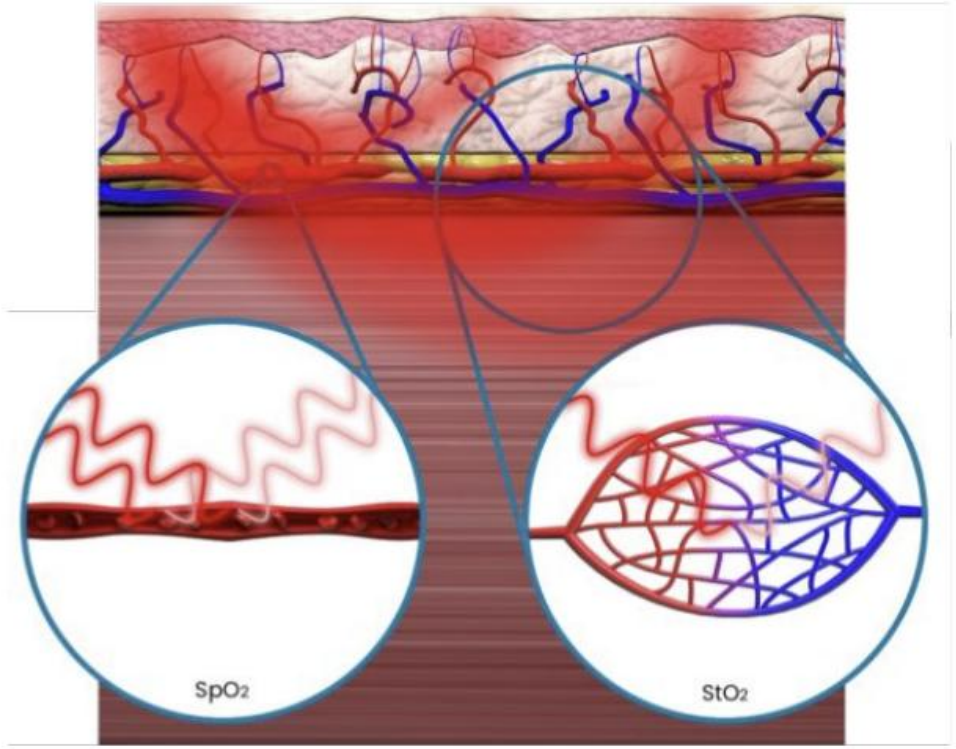
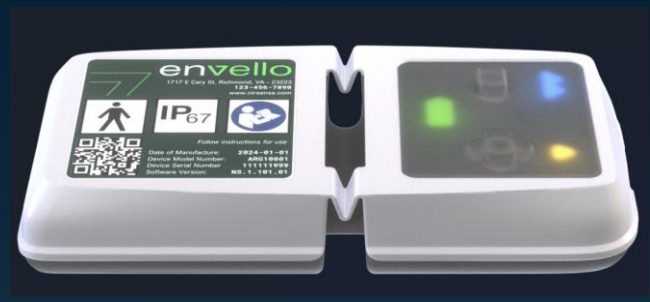
Emerging Technologies for ALI Detection: NIRSense

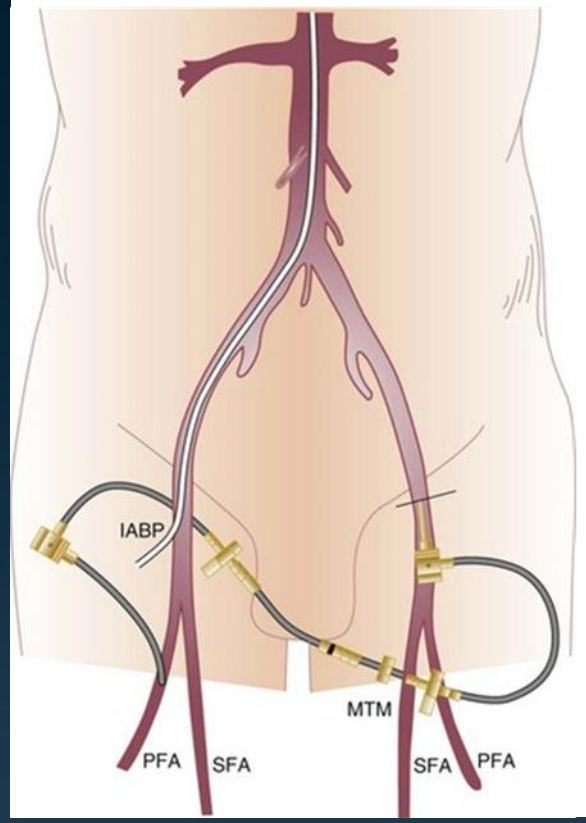


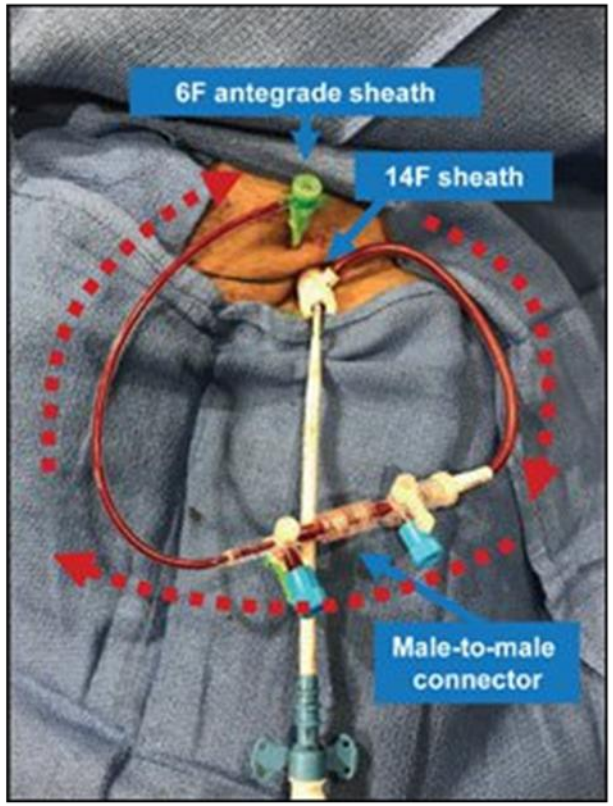


Current Approaches to Manage ALI in Cardiogenic Shock with MCS

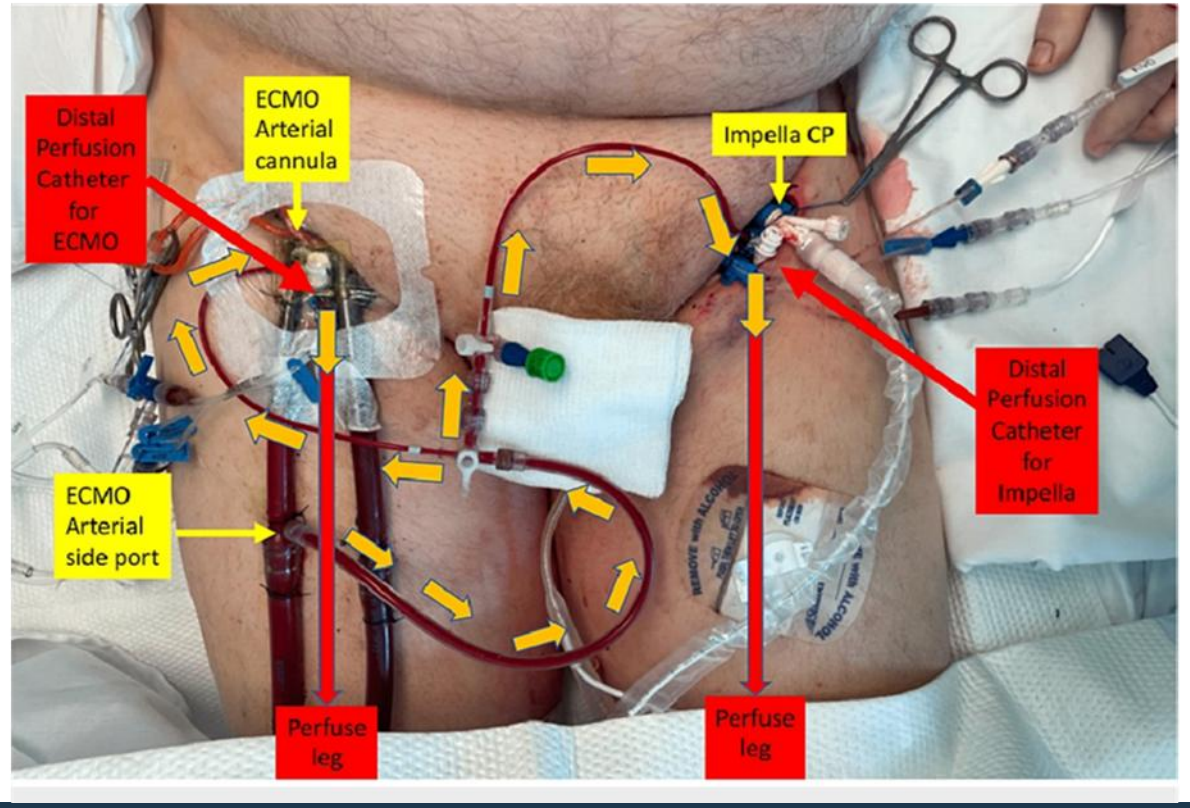
Percutaneous Femoral-to-Femoral Bypass via a Distal Perfusion Catheter (DPC)

Passive Bypass (Require Native Blood Pressure)





Active Bypass (Requires an External ECMO Circuit)



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The Clinical Moment… Asked to Put a Woman on ECMO for Her Legs…

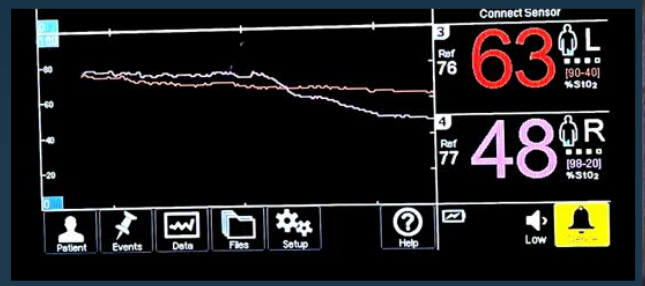
Bilateral Calf NIRS (R and L Legs)

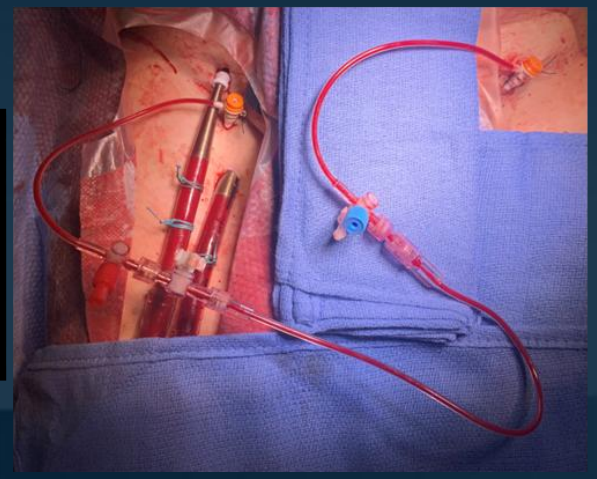
Bilateral Acute Limb Ischemia: Thrombo-emboli due to IABP
Clinical Team Considering Bilateral Leg Amputations

Baseline Condition

Right sided Arterial
ECMO Cannula Placed

No change in NIRS
with Passive Fem to
Fem Arterial Bypass





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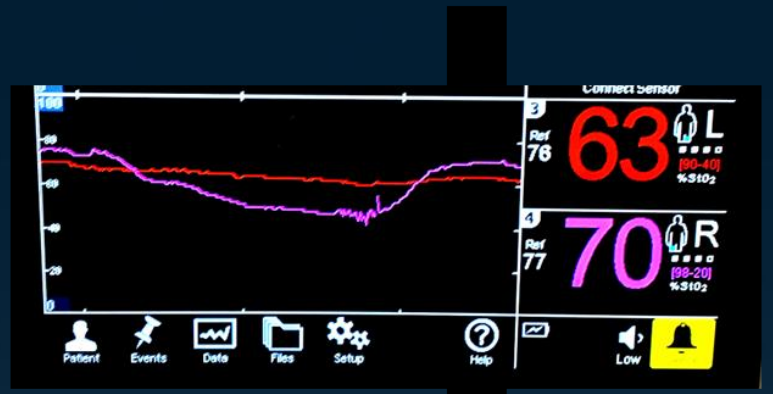
The Clinical Moment… Asked to Put a Woman on ECMO for Her Legs…

Antegrade Right Leg ECMO Perfusion *Normalized* NIRS and Improved Foot Perfusion

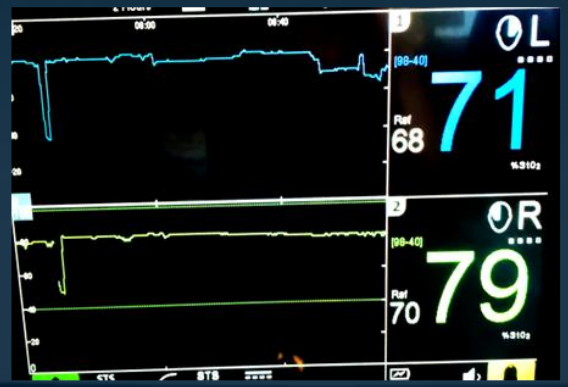
Bilateral Calf NIRS (R and L Legs)



Resolving Acute Limb Ischemia
No Amputations Required

Within 12 hours bilateral antegrade perfusion showed normalization of NIRS and improved bilateral foot perfusion

Bilateral Toe NIRS (R and L Legs)



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Operating and Innovating… Another ECMO Associated Limb Ischemia

Transfer from another hospital with no flow in either leg despite ECMO

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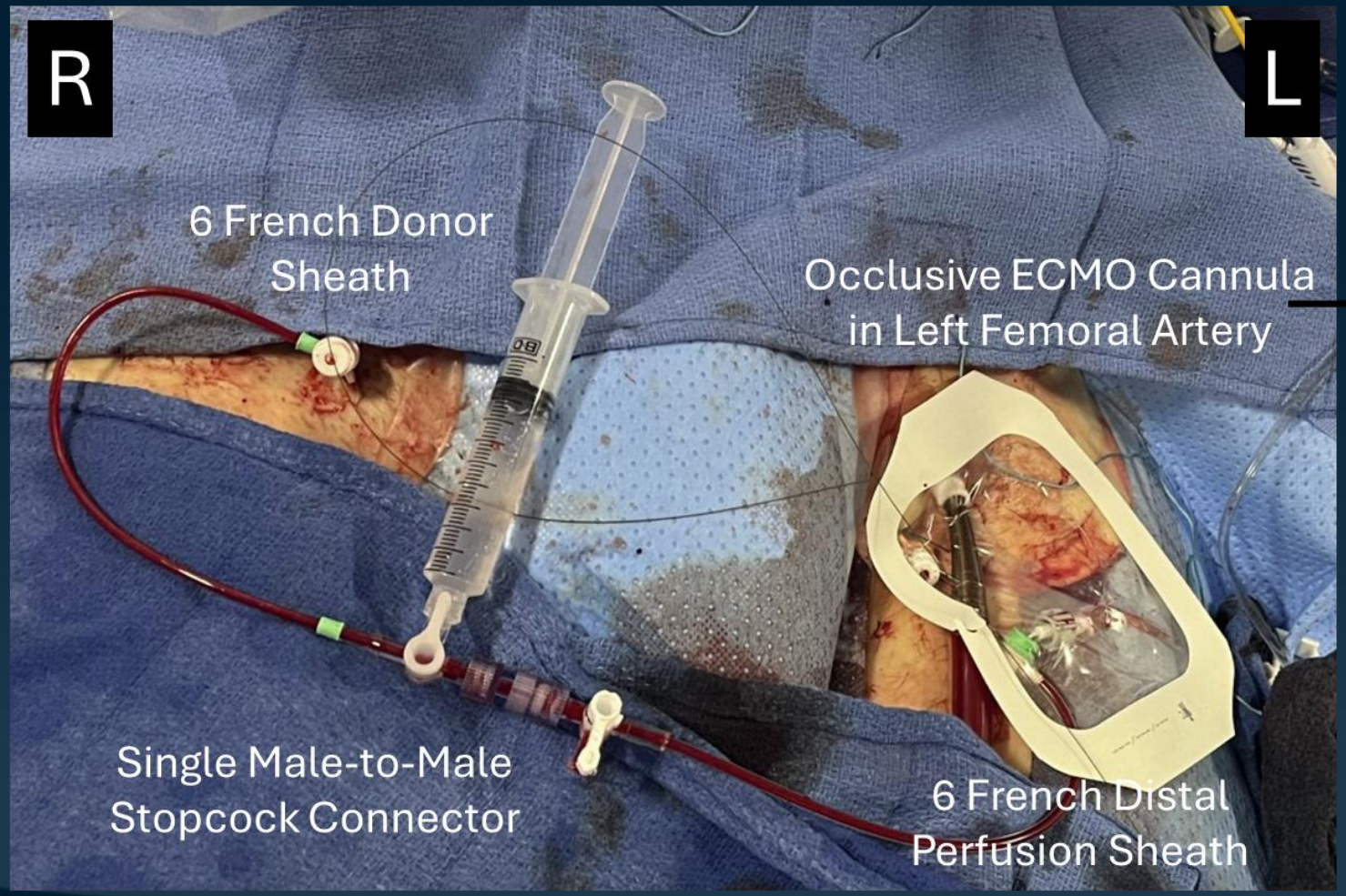
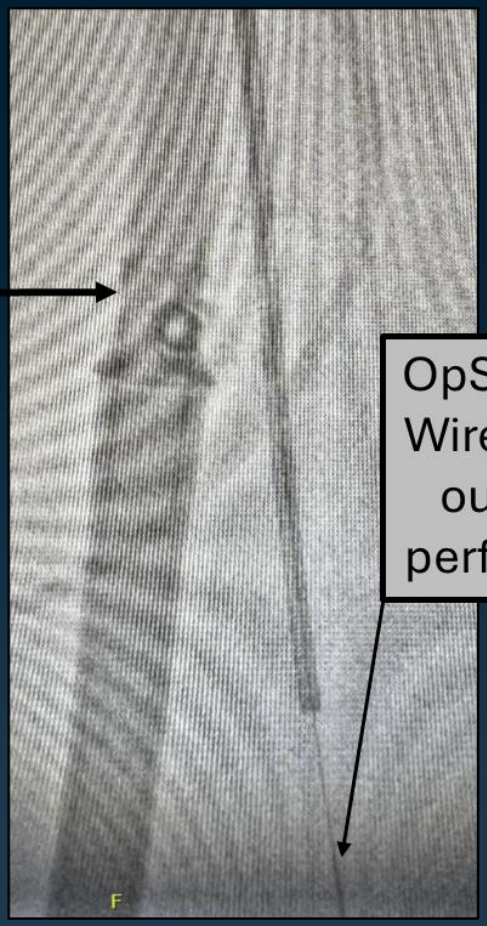
Assessment of the Distal Limb Pressure Index (DLPI)

Patient with Cardiogenic Shock on 4 Vasopressor Drugs Referred for VA-ECMO
Testing the Utility of Passive vs Active Bypass





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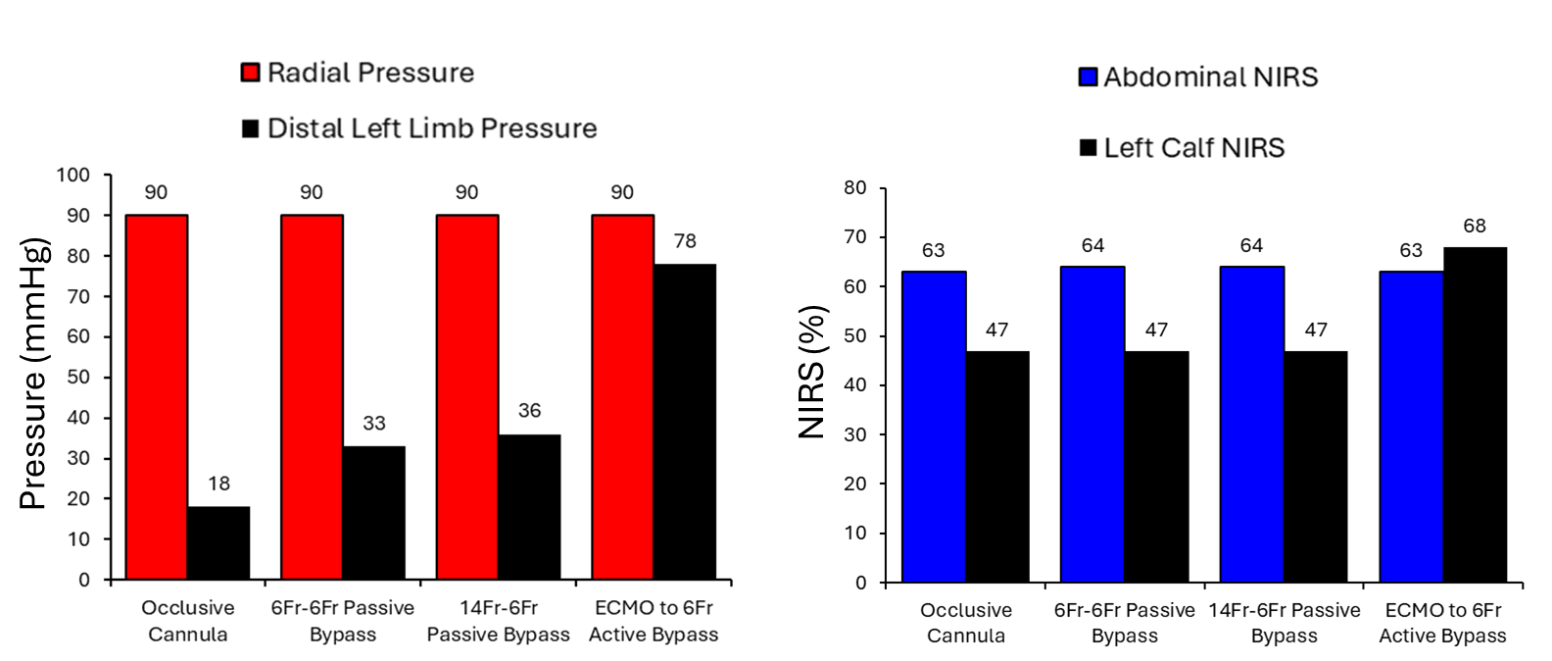
Kapur Lab: Peter Natov MD

Pressurized Perfusion Is Necessary & Sufficient to Reduce Limb Ischemia

	Baseline Occlusive Cannula	Condition 1 6Fr-6Fr Passive Bypass	Condition 2 14Fr-6Fr Passive Bypass	Condition 3 ECMO to 6Fr Active Bypass
Radial Pressure	90	90	90	90
Distal Limb Pressure	18	33	36	78
Abdominal NIRS	63	64	64	63
Left Calf NIRS	47	47	47	68



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Kapur Lab: Peter Natov MD

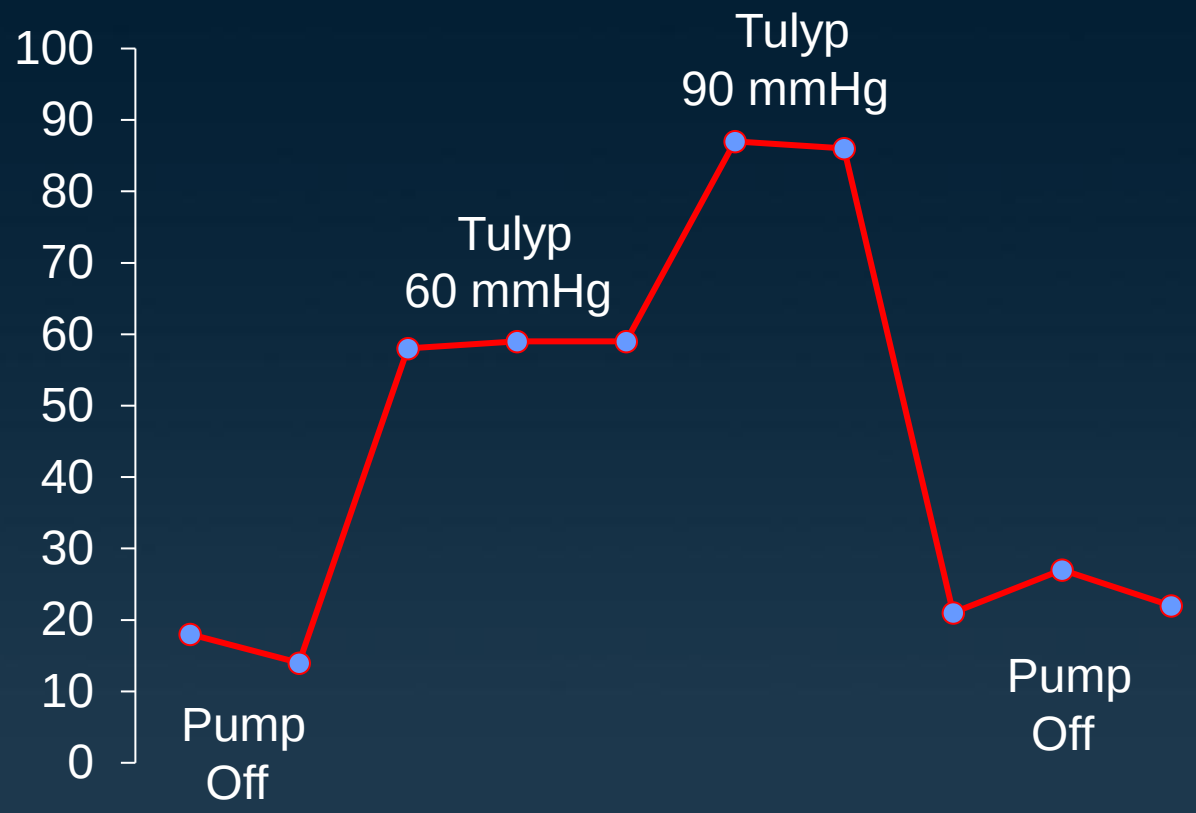
Delivering Pressurized Regional Perfusion to an Ischemic Limb

Tulyp Medical

Intelligent Pressure-Controlled Perfusion

Pressure-Controlled Rotary Flow Pump Designed to Autonomously Regulate Intravascular Pressure and Flow to Optimize Muscle Perfusion and RECOVERY

Distal Limb Pressure: Occluded Femoral Artery



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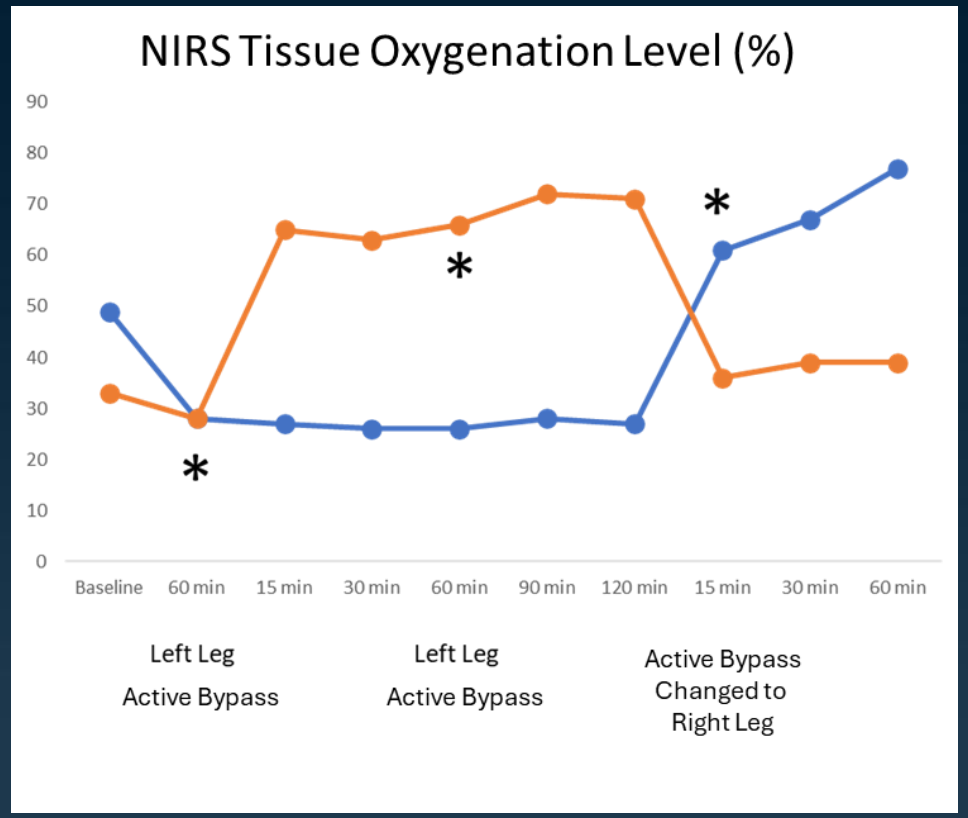
Pressure-Controlled System: Rotary pump with intravascular pressure sensor

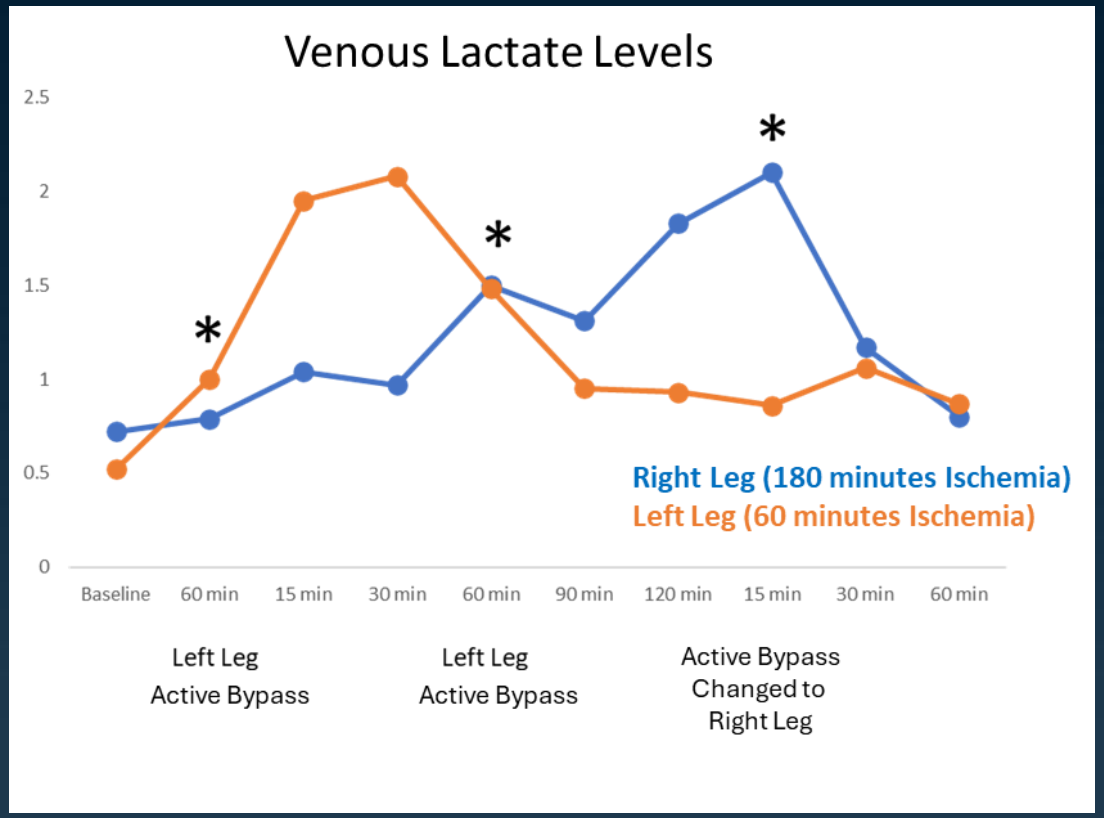
System will intelligently augment blood flow to the limb in patients with compromised flow:

- ✓ **Rotary pump:** designed for low flow applications
- ✓ **Inlet and Outlet Pressure Monitoring:** critical safety management
- ✓ **Flow-controlled or Pressure-controlled:** important optionality for users
- ✓ **Micropuncture kits and sheaths:** reduced access site risk

Active Bypass Promotes Tissue Perfusion and Decreases Lactate Production (Ischemia)

60 min Aortic Occlusion	Left Limb Tulyp Activation	Right Limb Tulyp Activation





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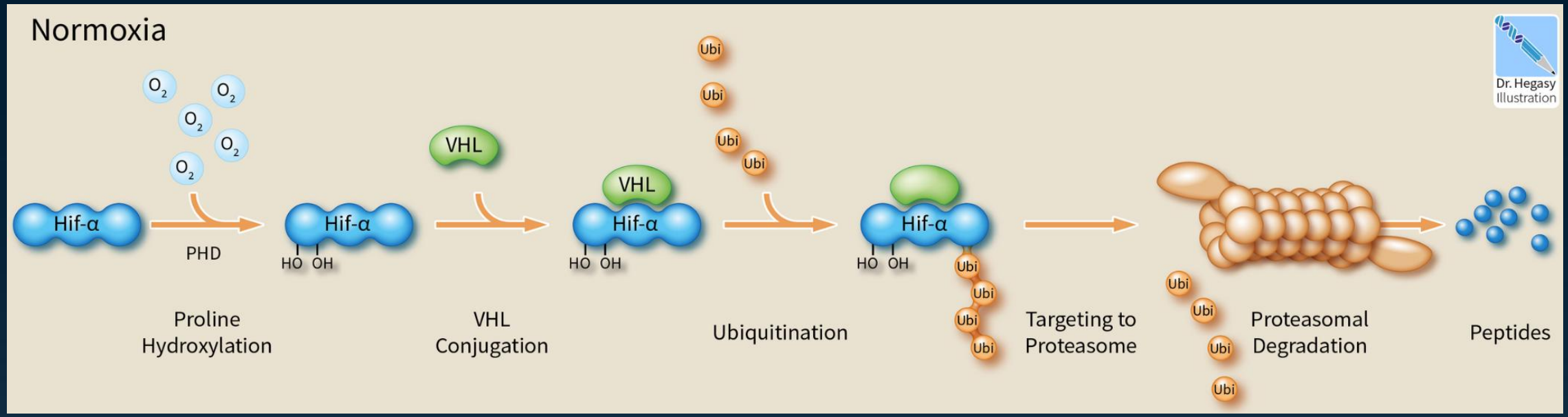
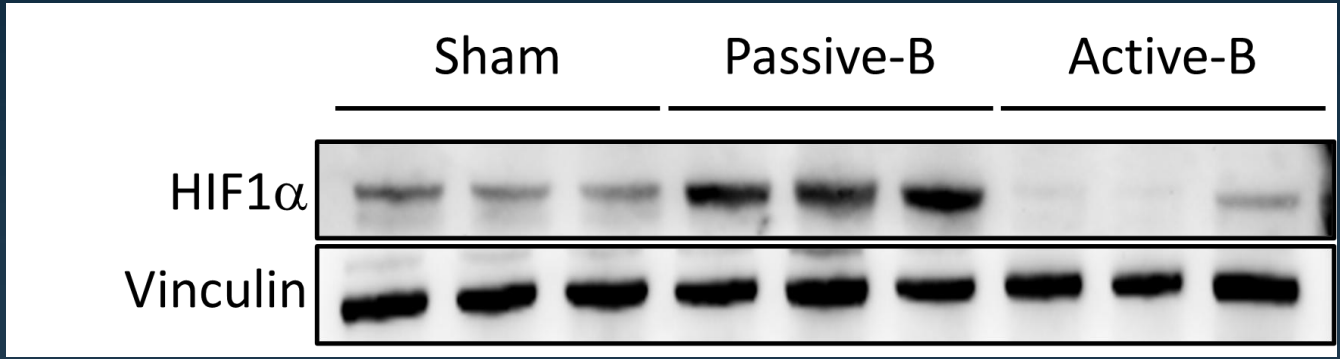
Active, not Passive, Bypass Reduces Expression of Hypoxia Inducible Factor 1a A Tissue Marker of Ischemia in Skeletal Muscle





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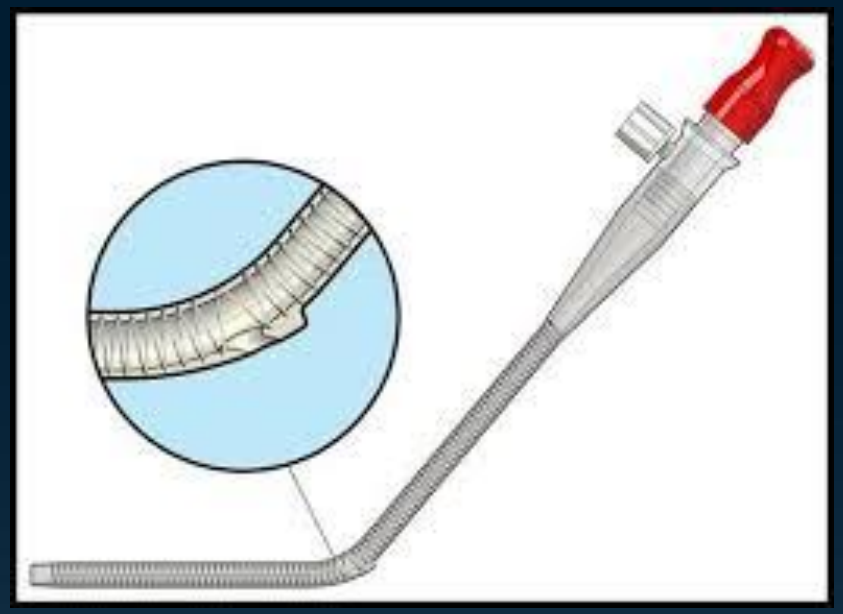
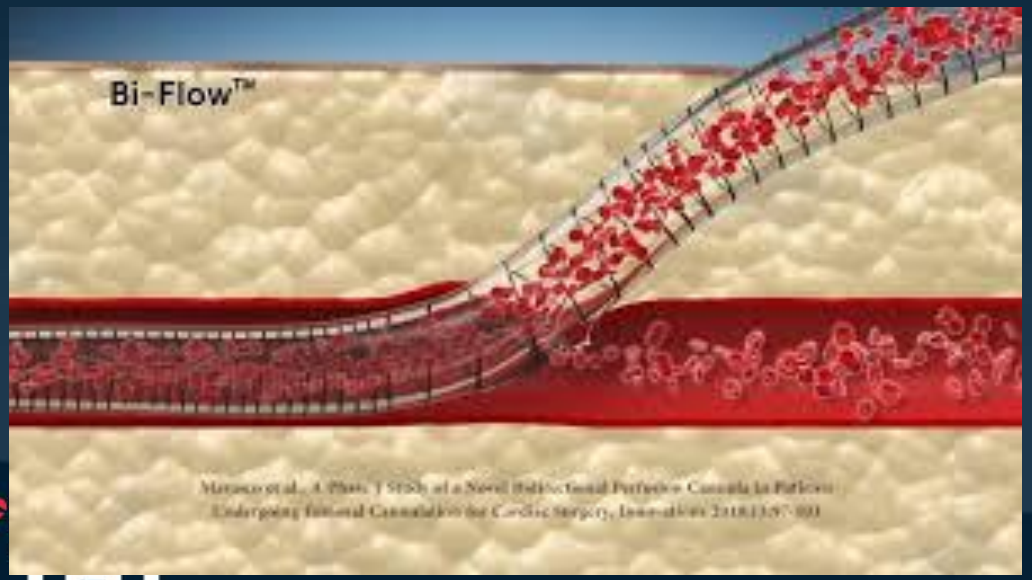
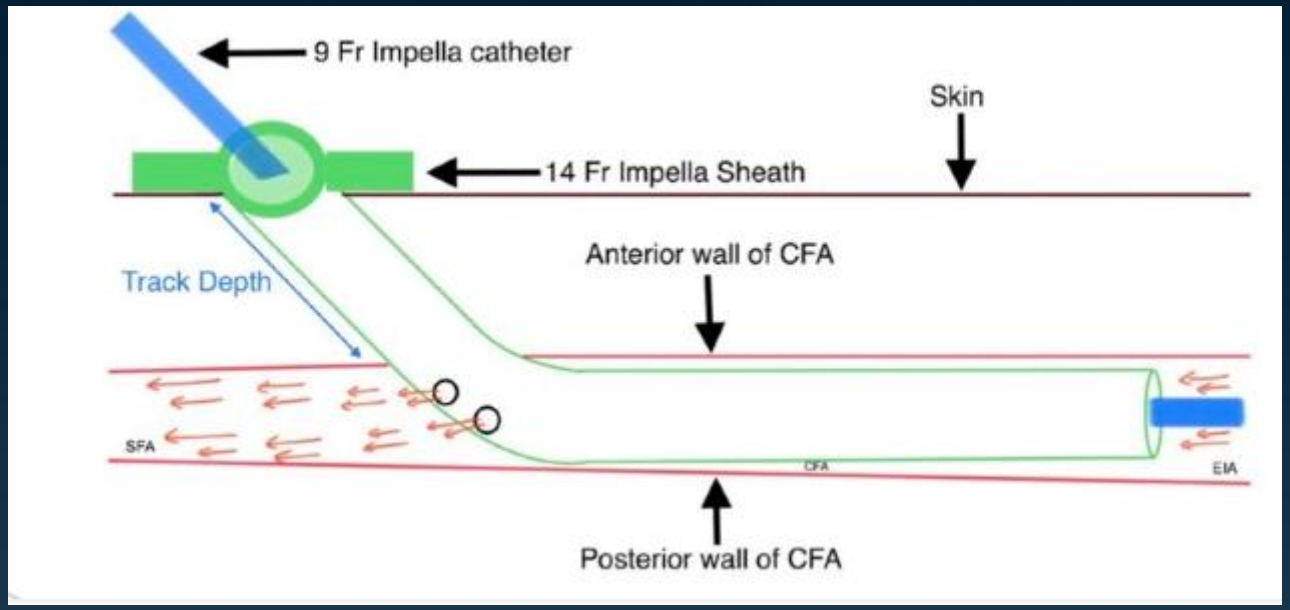
Swain and Natov et al (Kapur Lab)

Mitigating Acute Limb Ischemia: Bi-Directional Flow Cannulas and Sheaths

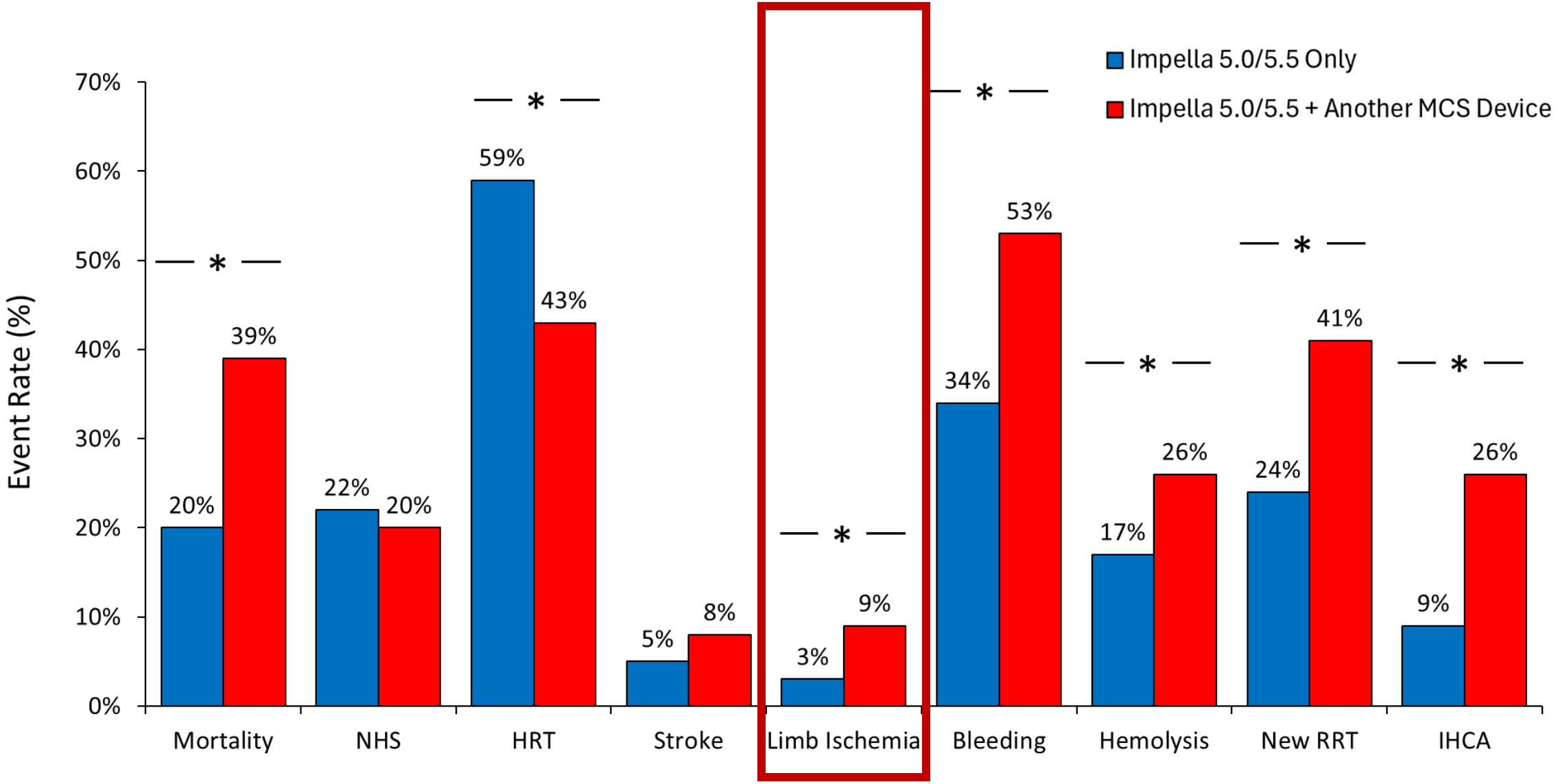






LivaNova; ASAIO 2021

Get Out of the Groin : Escalation to 5.5 for Acute Limb Ischemia



Farr, Fried and Kapur et al (CSWG) ISHLT 2024

Take Home Messages

- Acute Limb Ischemia is a Complication of Shock with High Morbidity, Mortality, and Cost
- Time to Therapy for Limb Salvage is <6 Hours: Prevention, Diagnosis, and Treatment
- Endovascular MCS is Associated with an Increased Risk of Acute Limb Ischemia
- Early Diagnosis with Novel Sensors is Critical for Hypo-Perfusion and No-Perfusion
- Pressurized Perfusion with Active Bypass is Necessary and Sufficient to Perfuse Skeletal Muscle and Limits Muscle Necrosis

Technologies Targeting Acute Limb Ischemia in Cardiogenic Shock

Thank you

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