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Fairway

**Below the knee interventions, BMS,
balloon or DES?**

Mohamad Ashraf Ahmad, MD
Lecturer of Cardiology - Assiut University

AGENDA

- Introduction
- Use of plain balloon angioplasty
- Use of BMS
- Use of DES
- Use of drug coated balloon
- Take home message



Introduction

- The accepted indication for BTK endovascular interventions remains primarily the treatment of critical limb ischemia.
- Acute or chronic CLI is defined as the lack of sufficient perfusion to maintain the metabolic needs of the skin and other tissues, even under resting conditions.
- Only 1.4% of patients with PVD develop ischemic rest pain or tissue loss, it is more frequent in diabetics and smokers.



Critical limb ischemia

- CLI is diagnosed when ≥ 2 weeks of rest pain, ulcer or tissue loss associated with
 - Ankle brachial index ≤ 0.4
 - Ankle systolic pressure ≤ 50 mmHg
 - Toe systolic pressure ≤ 30 mmHg.
- Symptoms of ischemic rest pain (Rutherford grade 4), ischemic tissue ulceration (Rutherford grade 5) and gangrene (Rutherford grade 6) are used to further categorize patients according to disease severity.
- The prognosis for untreated CLI is poor, with upwards of 70% of patients requiring amputation.





UP TO **30%**
Amputation Rate
By 1 year post-diagnosis

UP TO **25%**
Mortality Rate

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BTK Intervention

- The primary goal BTK intervention, either in isolation or with synchronous treatment of more proximal disease, is to produce or preserve straight-line blood flow to the foot to allow for wound healing, decreased pain and limb/mobility preservation.

BTK revascularization



Surgical bypass versus angioplasty

Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial (Lancet 2005).

- Randomly assigned 452 patients with CLI.
- The trial ran for 5.5 years.
- Endpoints (amputation of trial leg above the ankle or death)
- **Conclusion**
- In patients presenting with CLI due to infra-inguinal disease and who are suitable for surgery and angioplasty, a bypass-surgery-first and a balloon-angioplasty-first strategy are associated with broadly similar outcomes in terms of amputation-free survival.



Endovascular techniques have the advantages of:

- Avoiding the trauma of open surgery and the need for Autologous conduits.
- Avoiding incision through ischemic tissue beds.
- Options for recanalization of multiple tibial arteries.
- Options for targeted recanalization to angiosomes specifically supplying ischemic areas.



Recommendations for revascularization in patients with infrapopliteal lesions

Recommendations	Class ^a	Level ^b
When revascularization in the infrapopliteal segment is indicated, the endovascular-first strategy should be considered.	IIa	C

^aClass of recommendation.

^bLevel of evidence.

PTA = percutaneous transluminal angioplasty.



9.1.1. Endovascular Revascularization for CLI: Recommendations

Recommendations for Endovascular Revascularization for CLI		
COR	LOE	Recommendations
I	B-R	Endovascular procedures are recommended to establish in-line blood flow to the foot in patients with nonhealing wounds or gangrene (292, 293).

Gerhard-Herman MD, et al. 2016 AHA/ACC Lower Extremity PAD Guideline



POBA in BTK intervention



Is balloon angioplasty sufficient for BTK CLI?

- There is agreement that stand-alone balloon angioplasty is frequently suboptimal in virtually every arterial bed studied.
- This is true especially in the case of BTK angioplasty, in which the lesions tend to be complex.
- Risk factors predicting poor PTA outcomes include small vessel diameter, lesion length, patient gender, chronic kidney disease, diabetes, or poor runoff



BTK Restenosis and TLR rates post-PTA *Insufficient Durability*



Recommendations for revascularization in patients with infrapopliteal lesions

Recommendations	Class ^a	Level ^b
When revascularization in the infrapopliteal segment is indicated, the endovascular-first strategy should be considered.	IIa	C
For infrapopliteal lesions, angioplasty is the preferred technique, and stent implantation should be considered only in the case of insufficient PTA.	IIa	C

^aClass of recommendation.

^bLevel of evidence.

PTA = percutaneous transluminal angioplasty.



Original Studies

SCAI Expert Consensus Statement for Infrapopliteal Arterial Intervention Appropriate Use

Bruce H. Gray,^{1*} DO, Larry J. Diaz-Sandoval,² MD, Robert S. Dieter,³ MD, Michael R. Jaff,⁴ DO, and Christopher J. White,⁵ MD

- Bailout bare metal and drug eluting stents in the tibial arteries should be considered for failures of balloon angioplasty.
- Balloon angioplasty should remain the initial endovascular therapy for most IP disease.

Catheterization and Cardiovascular Interventions 84:539-545 (2014)



BMS in BTK intervention



- The advent of stents resulted in a quantum improvement in the procedural safety and technical success of vascular intervention.
- The same conceptual paradigm suggests that stents placed in the tibial arteries should behave in a fashion similar to coronary stents
- Feiring et al 2004, investigated the safety and efficacy of using coronary BMS as a primary mode of treating patients with severe tibial claudication and CLI. This study showed that BMS were highly effective in stabilizing the initial intervention.



- From Rand et al 2006, six months patency is **83.7%** using Carbostent (Sorin) versus **61.1%** plain old balloon angioplasty. Overall limb salvage at six months is 98%.
- Another study with the InPeria Carbostent (Sorin, Milan, Italy) reported a six-month angiographic patency of **61.1%** with plain old balloon angioplasty and **83.7%** with stent.



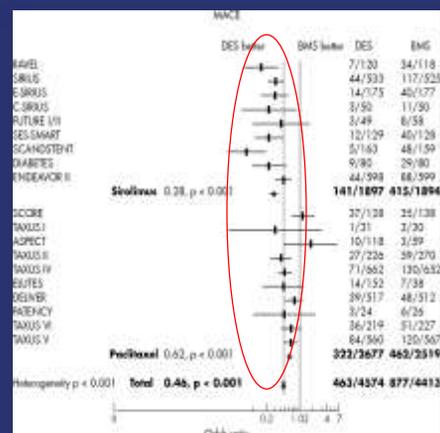
Are BMS as effective as DES for treating CLI?

- Level A data show that BTK interventions with DES are superior to BMS.
- Whereas technical success rates are equally as high for both devices, the binary restenosis and TLR were substantially higher for BMS.



Are BMS as effective as DES for treating CLI?

- The benefit of DESs over BMSs has been studied extensively in the coronary arteries. A meta-analysis of 38 studies showed that the use of DESs associated with significantly Lower TLR when compared with BMS.



- The similarities between infrapopliteal and coronary vessel (regarding diameter, behavior to balloon angioplasty and response to nitroglycerine) make the use of DES in the BK vascular bed an intuitive application.
- The positive results of DES in coronaries have led to excitement about the use of DESs in the infrapopliteal vessels and many single-center studies have been done.



- Feiring and colleagues 2004 were the first to demonstrate the safety and utility of using coronary DES in the BK vessel and paved the way for a more widespread application of DES for treating BK vessel.

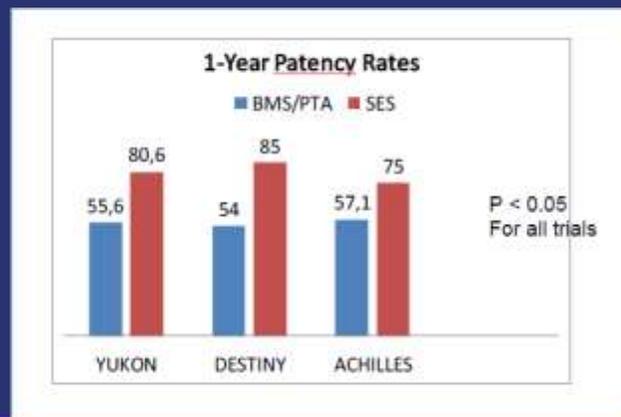


Randomized controlled trials of BTK DES

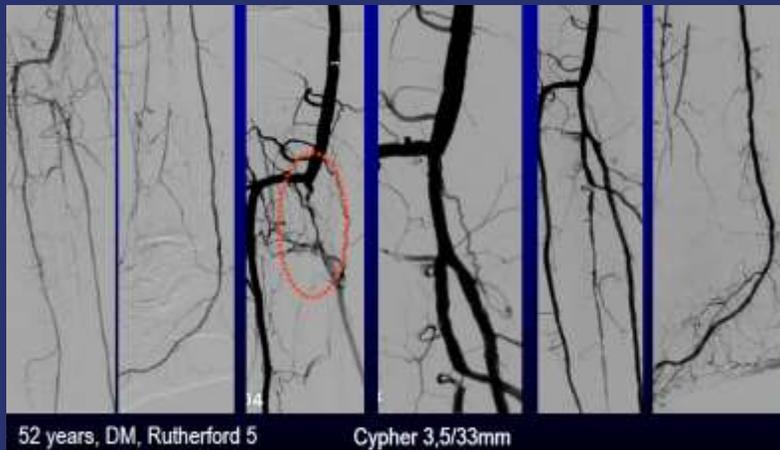
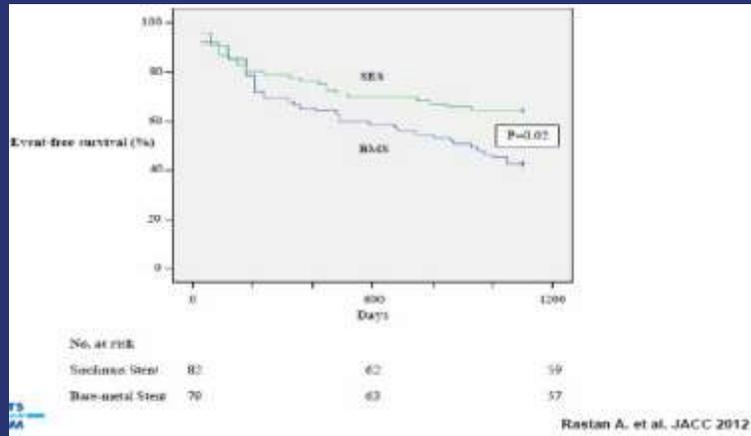
Trials	Stent/Drug	Finish	No. of Patients	Lesion Length	Endpoints
ACHILLES ¹⁵	Cypher vs PTA (sirolimus)	2010	200	≤ 120 mm	Binary restenosis 19% vs 49% at 1 y
DESTINY ¹⁶	Xience (everolimus) vs MultiLink Vision	2010	140	≤ 40 mm	Primary patency 85% vs 54% at 1 y; TLR 34% vs 9% at 1 y
YUKON-BTK ¹⁷	Yukon DES (sirolimus) vs Yukon BMS	2010	177	≤ 45 mm	Primary patency 81% vs 56% at 1 y
Total			517		



YUKON / DESTINY / ACHILLES 12-month primary patency

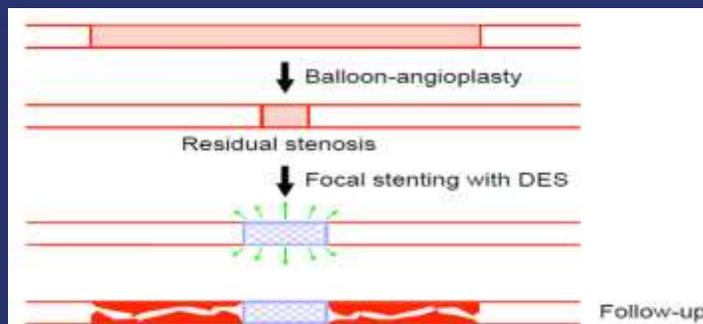
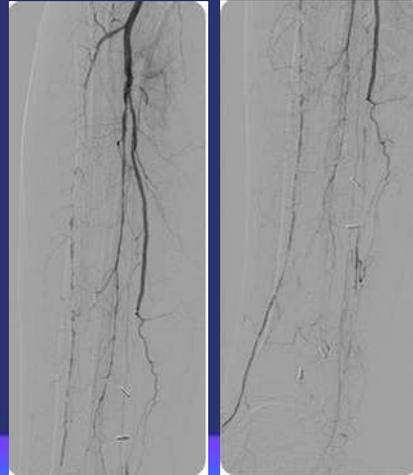


YUKON-BTK Trial: Event-free Survival at 24 months



DES in BTK vessels

- The results were Excellent
- BUT most of the study were selected short lesions
- Average lesion length was 15.9 mm
- Not like the usual cases of BTK disease



- Long term vessel patency is limited by patency rate of segment treated with PTA only



DISTENY 2 study

This study was designed to evaluate the immediate and long-term (up to 12 months) outcome of Xience Prime™ Everolimus-Eluting Stent (Abbott) in a controlled, prospective, multi-center investigation for long lesions up to 10 cm.

Conclusion:

The use of everolimus-eluting stents in longer infrapopliteal lesions in the treatment of CLI is safe and effective with a comparable primary patency, freedom from target lesion revascularization and amputation free survival as in short lesions. *Bosier et al., J Cardiovasc Surg (Torino). 2017 Feb.*



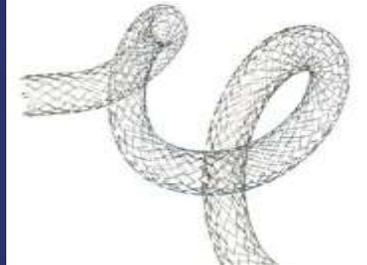
Limitations of balloon expandable stents in BTKI

- Include:
 - Lack of significant flexibility.
 - The potential for fracture or compression from external trauma (particularly in the distal anterior and posterior tibial artery).
 - High-cost expense (particularly when using multiple stents for long lesions).



Self expandable stents

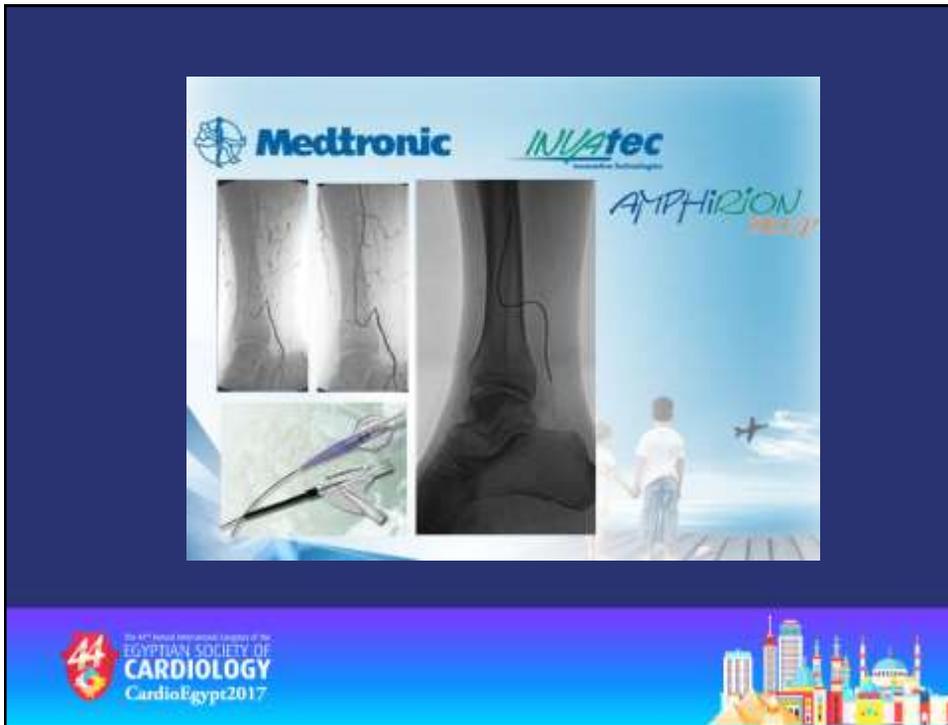
- Self-expanding stents have got some advantages in comparison to coronary stents: longer length, more conformability.
- The use of dedicated Nitinol stent (Xpert) for BTK – CLI, have showed limb salvage rate comparable to or even better than the published reports of surgical revascularization. *Bosiers et al 2009*



Drug-Eluting Balloons

- The concept of using a balloon catheter to deliver an anti-proliferative drug directly at the site of injury has gained interest during the last years.





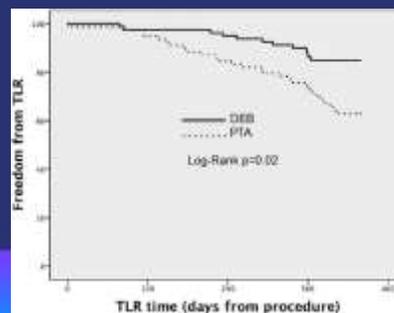
Interventional Cardiology

Drug-Eluting Balloon in Peripheral Intervention for Below the Knee Angioplasty Evaluation (DEBATE-BTK)

A Randomized Trial in Diabetic Patients With Critical Limb Ischemia

Francesco Liistro, MD; Italo Porto, MD PhD; Paolo Angioli, MD; Simone Grotti, MD; Lucia Ricci, MD; Kenneth Ducci, MD; Giovanni Falsini, MD; Giorgio Ventruzzo, MD; Filippo Turini, MD; Guido Bellandi, MD; Leonardo Bolognese, MD

- DEB compared with PTA strikingly reduce 1-year restenosis, TLR, and target vessel occlusion in the treatment of BTK lesions in diabetic patients with CLI.



(Circulation. 2013;128:615-621.

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Drug-Eluting Balloon Versus Standard Balloon Angioplasty for Infrapopliteal Arterial Revascularization in Critical Limb Ischemia

12-Month Results From the IN.PACT DEEP Randomized Trial

Thomas Zeller, MD,¹ Iris Baumgartner, MD,¹ Dierk Scheinert, MD,¹ Marianne Brodmann, MD,¹ Marc Bosiers, MD,¹ Antonio Micari, MD, PhD,² Patrick Poeterens, MD, PhD,³ Frank Vermeulen, MD, PhD,⁴ Mario Landini, MSc,¹ David B. Sneed, PhD,¹ K. Craig Kent, MD,¹ Krishna J. Rocha-Singh, MD,¹ IN.PACT DEEP Trial Investigators

• CONCLUSIONS

This first multicenter, RCT of DEB versus PTA in CLI patients with infrapopliteal disease demonstrated that:

- IA-DEB did not provide a significant reduction in either LLL or CD-TLR revascularization compared to PTA.
- IA-DEB was associated with a trend toward an increased rate of major amputations through 1 year post-procedure

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DEB-BTK - Negative Evidence: IN.PACT DEEP Failure to meet Primary Efficacy Endpoint

Primary IN.PACT DEEP Outcomes

Primary Efficacy	DEB	PTA	p
12-month LLL (mm) ^[2]	0.61 ± 0.78	0.62 ± 0.78	0.950
12-month CD-TLR ^[2]	9.2% (18/196)	13.1% (14/107)	0.291

Primary Safety	DEB	PTA	p
6-month Death, Major Amputation or CD TLR	17.7% (41/232)	15.8% (18/114)	0.021 (non-inferiority) 0.662 (superiority)

1. Angio Cohort, Corvita adjudicated. Angiographic imaging 12-month FU compliance = 79.9% (DEB) vs. 71.4% (PTA)

2. Clinically driven TLR of the target lesion in the (non-) amputation free surviving subjects at 12 months. *Clinically driven TLR defined as any TLR of the target lesion associated with: a) deterioration of IFC and / or b) increase in size of pre-existing wounds and / or c) occurrence of a new wound(s), with b) and c) adjudicated by the Wound Healing Core lab

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DEB-BTK - Negative Evidence: IN.PACT DEEP Trend towards higher Major Amp. Rate in DEB arm T.

Secondary Safety Outcomes

12-month Safety	DEB	PTA	p
Major Amputation	8.8% (20/227)	3.6% (4/111)	0.080
All-Cause Mortality	10.1% (23/227)	8.1% (9/111)	0.551
Death and Amputations ¹⁾	35.2% (80/227)	25.2% (28/111)	0.064
Death, Major Amp, CD TLR ²⁾	26.9% (61/227)	23.4% (26/111)	0.496
Amputation Free Survival	81.1% (184/227)	89.2% (99/111)	0.057
Wound Healing (site reported)	73.8% (121/164)	76.9% (70/91)	0.579

1. Death of any Cause, Major or Minor Amputation of target limb (MAE per protocol)
2. Death of any Cause, target limb Major Amputation and clinically driven TLR

FDA APPROVES 6-MONTH PRIMARY ENDPOINT FOR THE LUTONIX BTK -COATED BALLOON

- September 19, 2016
- The Lutonix® 014 device is currently the only DCB in an investigational device exemption (IDE) clinical trial in the U.S. for treatment of arteries below the knee (BTK).

- NO DEB Class Effect.
- IN.PACT DEEP failure applies to IN.PACT Amphirion only.
- Each DEB stands on the merits of its own data
- On going RCT with 480-patient using Lutonix DCB vs. PTA in BTK-CLI.



DEB in the Foot arteries

DEB at ankle and foot seem to have lower patency than for the proximal and mid-tibial arteries.

- This may be due to :
 - Small caliber of the arteries,.
 - Significant drug loss upstream due the friction between vessel wall and balloon surface.
 - Also may be due to a mechanical effect (external forces, impingement, and constant movement).
- In these cases, DEB may not enhance much the results of POBA.



Take home message

- **DES in BTK** are associated with significantly lower rates of restenosis, TLR, and amputations and improved wound healing compared with plain BA and BMS.
- Use of **DEB in BTK** intervention still under investigations. Improvement of its materials and profiles may enhance its efficacy.
- In Foot artery PTA, neither DEB nor DES showed better outcome and still the use of small profile plain hydrophilic balloons is the best option.



THANK YOU

