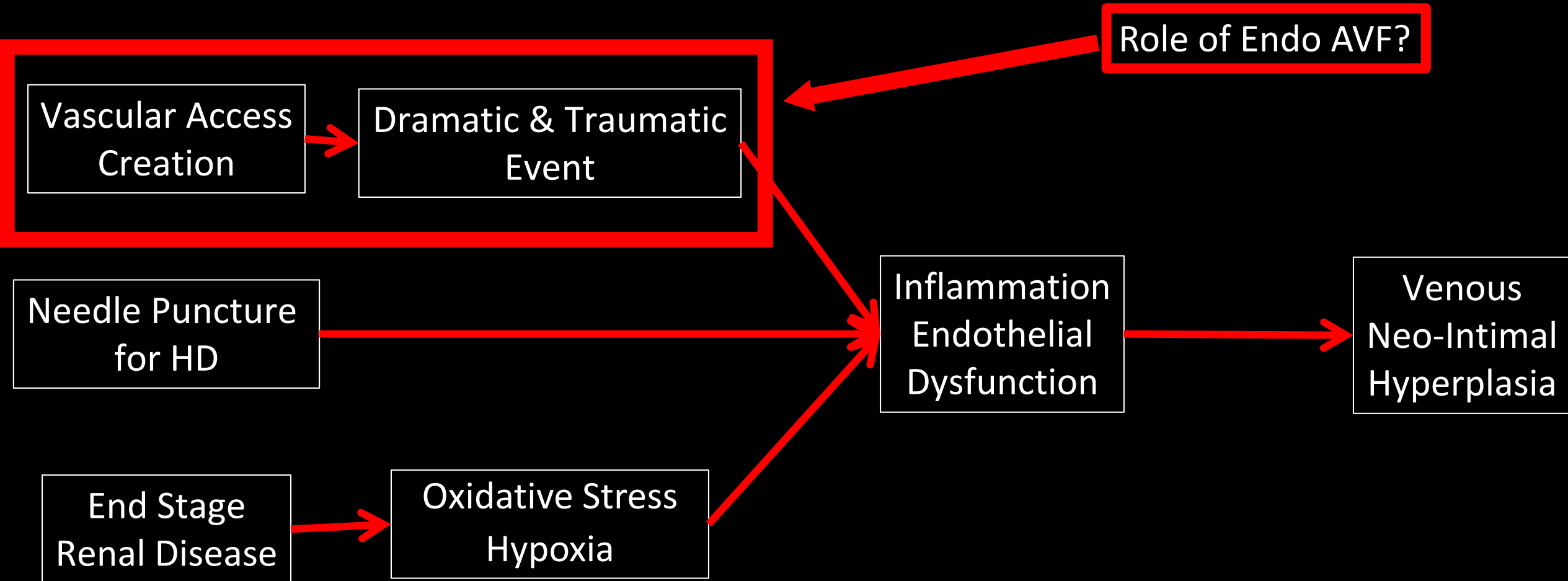


DCB 4 AV

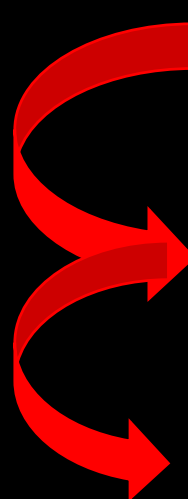
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Why do we get
Stenosis in AV access?

Characteristics of AV access stenosis



Characteristics of AV access stenosis

- 
- Myofibroblasts and differentiated contractile SMCs
 - Extensive extracellular matrix formation and accumulation
 - Fibromuscular thickening of the vascular wall

Venous Neo-Intimal Hyperplasia

Roy-Chaudhury P, et al. Neointimal hyperplasia in early arteriovenous fistula failure. Am J Kidney Dis 2007;50:782-790.

Roy-Chaudhury P et al. Future directions for vascular access for hemodialysis. Semin Dial 2015;28(2):107-113

Roy-Chaudhury P et al. Hemodialysis vascular access dysfunction: a cellular and molecular viewpoint. J Am Soc Nephrol 2006;17(4):1112-1127

Skartsis N, Manning E, Wei Y, et al. Origin of neointimal cells in arteriovenous fistulae: bone marrow, artery, or the vein itself? Semin Dial 2011;24(2):242-248

Drug-Coated Balloons (DCBs)

Paclitaxel: Cytotoxic Chemotherapeutic Drug that exerts its toxicity by inhibiting the disassembly of microtubules in M phase of cell cycle

Excipient: Substance facilitating drug transfer and apposition to the vascular wall. Different substances are used as excipients in different DCBs

Drug Dosage: Paclitaxel dose varies between devices from 2 to $>3.5\mu\text{g}/\text{mm}^2$

Treatment Approach for AV stenosis

DCB use in AV access transformed the treatment into a 2-step procedure

Step 1: Mechanical Treatment of Stenosis (Immediate Lumen Gain)

Step 2: Inhibition of Restenosis Process (Future Pharmaceutical Gain)

Tips & Tricks: How I do it

Vessel Preparation: High Pressure Balloon (HPB) Angioplasty to “beat” the fibrotic stenosis

Geographic Miss: DCB is 5mm longer from each side compared to the initial HPB

Balloon Diameter: DCB diameter is the same or 1mm higher than HPB

Inflation Pressure: 2atm greater than nominal pressure

Inflation Time: A minimum of 2minutes of DCB inflation is needed

Data Analysis

Available published data so far (July 2018)

Study Design - based	# of Studies	# of Patients with DCB
Multi-center RCT	1	141
Single-center RCT	5	156
Single-arm Prospective Studies	4	105
Retrospective Analysis	6	181

Device – based	# of Studies	# of Patients with DCB
Lutonix (Becton Dickinson)	4	223
In.Pact (Medtronic)	8	271
SeQuent Please (B Braun)	1	10
Elutax-SV (Aachen Resonance)	1	15
Freeway 035 (Eurocor, Germany)	1	26
Mixed	1	38

16	583
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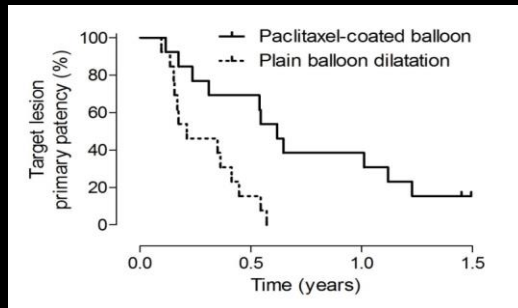
Author (year)	Type	Group	Device Category	Pts	VA	F-up	Primary Endpoint	Results	Sig.	Device Type	Comments
Zheng et al. (2018)	PS	SG	PCB+SB	23	AVF AVG	12	TLPP	45%	n.a.	Lutonix 035, BARD PV	+Scoring Balloon
Irani et al. (2018)	RCT	SG	PCB	63	AVF AVG	12	TLPP	51%	s.s.	IN.PACT, Medtronic	Randomization after lesion crossing
		CG	PTA	62				34%		Reef HP, Medtronic	
Trerotola et al. (2018)	RCT	SG	PCB	141	AVF	6	TLPP	71%	n.s.	Lutonix 035, BARD PV	Multicenter
		CG	PTA	144				63%		High Pressure Balloon	
Maleux et al. (2018)	RCT	SG	PCB	33	AVF	12	TLPP	42%	n.s.	IN.PACT, Medtronic	Low Pressure balloon Angioplasty
		CG	PTA	31				39%		Admiral Extreme, Medtronic	
Kitrou et al. (2017)	RCT	SG	PCB	20	AVF AVG	6	IFP	179d	s.s.	Lutonix 035, BARD PV	Central Venous Stenosis
		CG	PTA	20				124.5d			
Troisi et al. (2017)	RA	SG	PCB	38	AVF AVG	14.3	TLPP	7.9m	s.s.	Freeway Eurocor - IN.PACT Medtronic - Ranger Boston	Longitudinal Comparison of treatments
		CG	PTA					6.4m			
Lucev et al. (2017)	PS	SG	PCB	31	AVF	24	TLPP	45%	s.s.	IN.PACT, Medtronic	Study compared with historical group
		CG	PTA	31				16%		Reef HP, Medtronic	
Çıldag˘ et al. (2016)	RA	SG	PCB	26	AVF	12	TLPP	65%	s.s.	Freeway 035 (Eurocor, Germany)	Sizing of 1mm higher than actual vessel diameter
		CG	PTA	26				34.6%		n.a.	
Kitrou et al. (2016)	RA	SG	PCB	39	AVF AVG	6	TLPP	75%	n.a.	Lutonix 035, BARD PV	Comparison between 1 st & 2 nd treatment
Verbeeck et al. (2016)	PS	SG	PCB	41	AVF	12	TLPP	60%	n.a.	IN.PACT, Medtronic	Venous Stenosis
Swinnen et al. (2015)	RA	SG	PCB	37	AVF	12	RFP	69%	s.s.	IN.PACT, Medtronic	In-stent Restenosis
		CG	PTA	37				19%		n.a.	
Massmann et al. (2015)	RA	SG	PCB	10	AVF	n.a.	RI	9m	s.s.	Elutax-SV, Aachen Resonance	CVS Included, CB+HPB used if needed
		CG	PTA	15				18.4		4m	
Lai te al. (2014)	PS	SG	PCB	10	AVF	12	TLPP	20%	n.s.	SeQuent Please, B Braun	Concomitant lesions in same patient.
		CG	PTA	10				0%		FoxPlus, Abbott Invatec, Medtronic	
Patane et al. (2014)	RA	SG	PCB	26	AVF	24	TLPP	57.8%	n.a.	IN.PACT, Medtronic	Anastomotic Stenosis
Kitrou et al. (2014)	RCT	SG	PCB	20	AVF	12	MS	308d	s.s.	IN.PACT, Medtronic	No pre-dilation
		CG	HPB	20				161d		OJ HPB	
Kitrou et al. (2014)	RCT	SG	PCB	20	AVF AVG	12	TLPP	35%	s.s.	IN.PACT, Medtronic	No Pre-dilation
		CG	HPB	20				5%		OJ HPB	

Kitrou et al. 2014

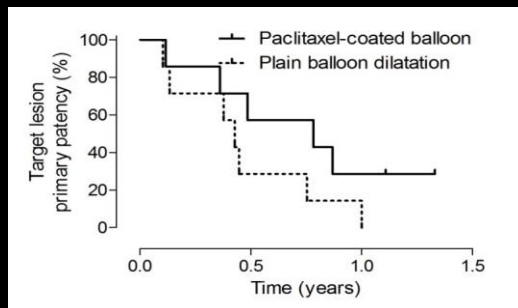
RCT that included **both AVGs and AVFs** (40 pts in total)

At that time max DCB diameter was 7mm (Post dilation with a bigger balloon in 55% of cases)

Cost-effectiveness analysis was performed



AVG: 13/20



AVF: 7/20



There was, overall, statistical significance in favor of DCB @ 1 year (**25% vs. 5%; p<0.001**)

However, when subgroup analysis was performed, difference did not reach significance in case of AVFs

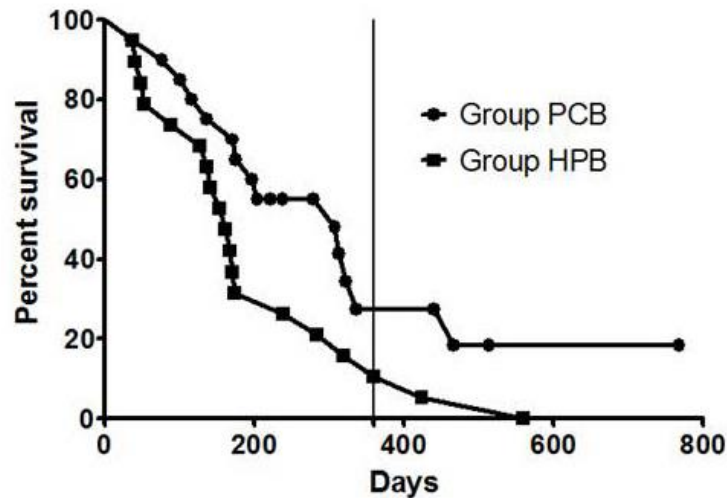
Kitrou PM et al. Drug-eluting versus plain balloon angioplasty for the treatment of failing dialysis access: final results and cost-effectiveness analysis from a prospective randomized controlled trial (NCT01174472). Eur J Radiol. 2015 Mar;84(3):418-423. doi: 10.1016/j.ejrad.2014.11.037

Kitrou et al. 2014

First RCT that included **only AVFs** (40 pts in total)

Study performed following subgroup analysis of the previous study

Post dilation was needed in **65% of the cases** (again DCB max D:7mm)



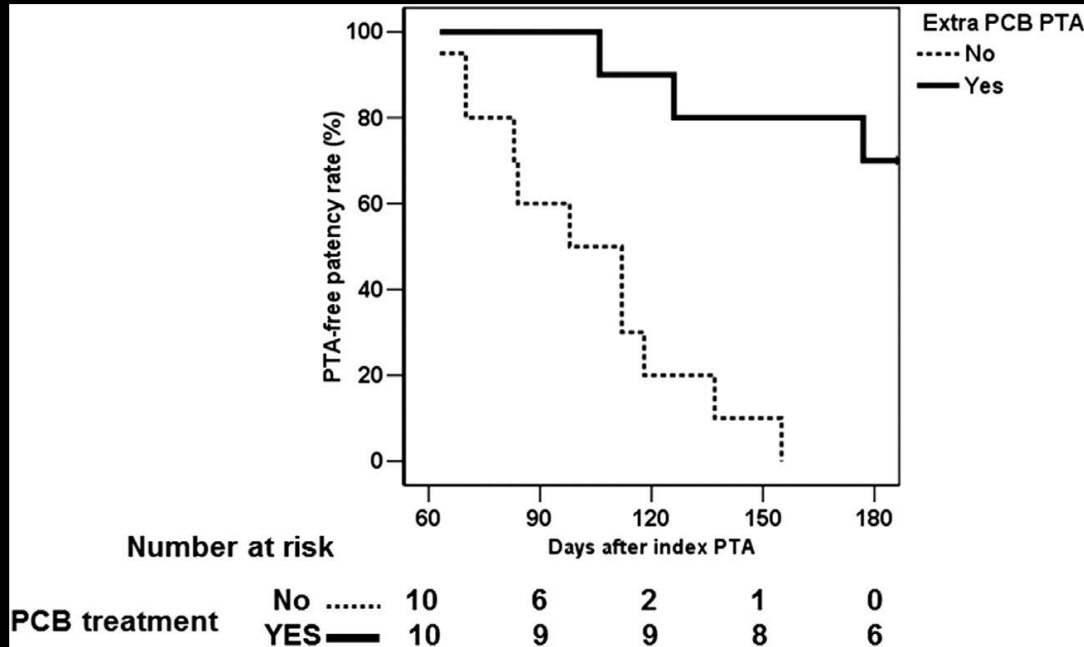
Group HPB	20	12	5	1	1	Subjects at risk
Group PCB	20	6	2	0	0	

There was statistical significance in favor of DCBs over PTA both in target lesion and access circuit primary patency (**270 days vs. 161 days; p=0.04**)

Lai et al. 2014

10 pts with 20 concomitant lesions in AVFs

One lesion treated with and the other without DCB



TLR-free duration in DCB Group was significantly longer (251.2d vs 103.2d; $P < .01$).

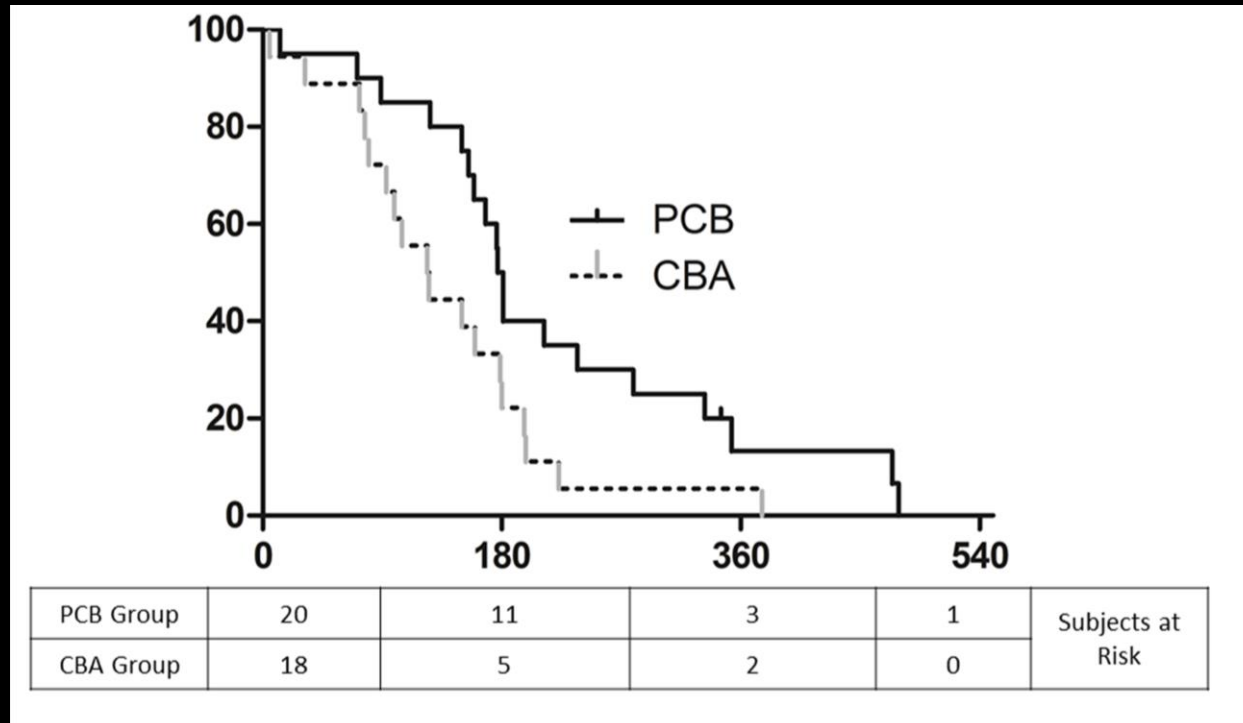
TLPP was significantly higher at 6 months (70% vs 0%; $P < .01$)

but not at 12 months (20% vs 0%; $P > .05$).

Kitrou et al. 2017

First RCT on DCB use for **Symptomatic Central Venous Stenosis**

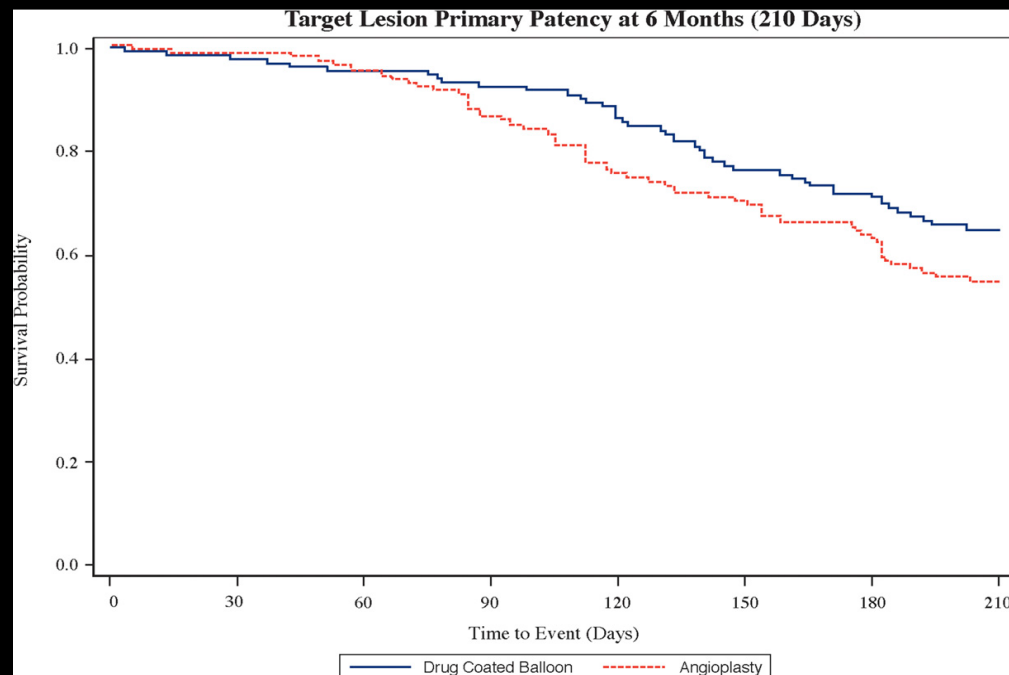
40pts recruited in total



Median Intervention free period was significantly better in PCB group (PCB group: 179 days, vs CBA group: 124.5 days, $P = .026$).

Trerotola et al. 2018

Multicenter IDE RCT held in the US. **285 pts in 25 centers** with a dysfunctional AVF.

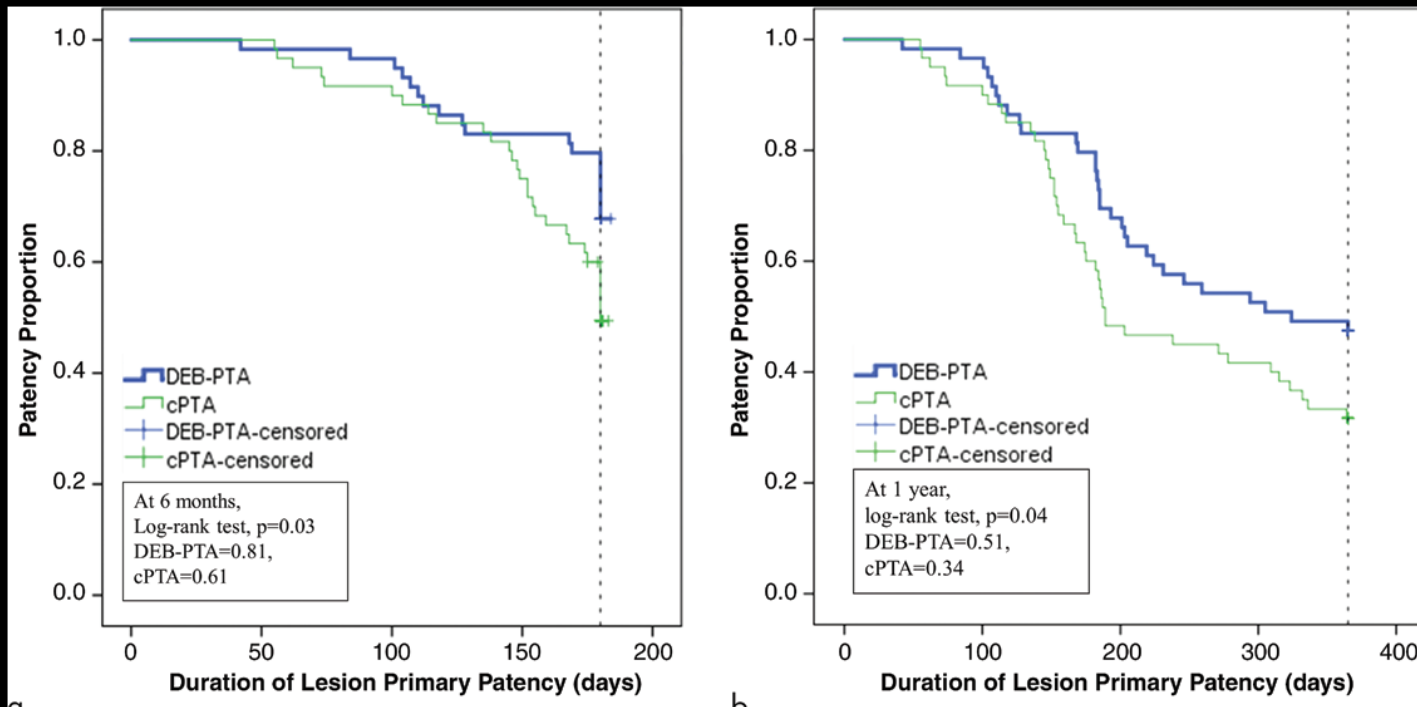


Target lesion primary patency
71% for DCB and 63% for control; P=0.06
 Significant difference was not reached
 @ 6 months but @ 8 months

Irani et al. 2018

Biggest Single-Center RCT with 119 subjects

AVFs: 98, AVGs: 21



Target lesion primary patency @ 6 months:

81% for DCB, 61% for control;
 $P=0.03$

@ 12 months:

51% for DCB, 34% for control;
 $P=0.04$

Ongoing Trials

Lutonix Global AV Registry

PI: Prof. Dimitrios Karnabatidis

INPACT AV Access IDE Study

PI: Prof. Andrew Holden

Lutonix AV PAS

PI: Prof. Scott Trerotola, Prof. Deeraj Rajan

PAVE Study

PI: Cons. N. Karunanithy

Synopsis

DCB use in AV is **Safe** (in a 30-day post-procedural period)

They are used as **Drug Delivery Devices**

A proper **Vessel Preparation** is a prerequisite to ensure immediate successful mechanical result (**wide heterogeneity between studies**)

50.9% of patients are enrolled in RCTs

84.7% of patients were included in studies using either In.Pact or Lutonix DCB

They have been tested both in **AVF & AVG**

They have been used in **Symptomatic Central Venous Stenosis** although device diameter up to date is limited to 12-14mm

There is wide **Procedural Heterogeneity** among studies

In the vast majority of cases, there is consistency of data regarding

TLPP @ 6 months of 70-75% with fluctuating patencies in the control group

More data is needed for adequate subgroup analysis with regard to focused lesion type and lesion site effectiveness

DCB 4 AV

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