Drug eluting stents and balloons in peripheral arterial disease

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Drug eluting stents and balloons

- Endovascular treatment now becoming more popular for treatment of superficial femoral artery
- Late clinical failure due to restenosis, neo-intimal hyperplasia, and stent fracture still major problem
- Angioplasty and or stenting preferred because of shorter hospital stay less wound infection and peri-op mortality compared with open surgery[1,2]

1.Amighi J et al Radiology 2008 ;247(1):267-272

2.Pietzsch JB et al Catheter Cardiac Interv 2014;84(4):546-554

Angioplasty

- Plain balloon angioplasty is considered first line treatment for femoro-popliteal disease and stenting only for poor outcome – high rate of re-stenosis despite initial technical success rate of 95% even with stenting 1 year restenosis rates have varied between 20-50% depending on an increasing with length of lesion.
- Balloon angioplasty for shorter lesions(<4cm) and primary stenting in longer lesions and secondary stenting if residual stenosis/dissection
- Bypass surgery still gold standard but recent advances in stent design, drug coated balloons, drug eluting stents and Endograft are challenging this gold standard

Drug coated balloons

- Deliver sufficient drug at target lesion to intervene at the level of the smooth muscle cells inhibiting cell proliferation and hence reducing intimal hyperplasia and decreasing incidence of re-stenosis

- Paclitaxel is the drug used stops cellular cycle in the M phase leading to cell apoptosis.

- Optimal delivery dose is 3ug/mm^2 of Paclitaxel and at least 180 seconds inflation time excipients such as polyethylene glycol to improve release of drug also used
- Pre-dilation with plain balloon essential to achieve release of drug

- Sirolimus, Everolimus and Rapamycin also used.

Drug coated balloons (DCB) trials

- THUNDER[1]
- LEVANT 1[2] and 11[3]
- PACIFIER[4]
- IN.PACT SFA[5,6]

1.Tepe G et al JACC Cardiovasc Interv 2015;8:102-108

2.Scheinert M et al JACC Cardiovasc Interv 2014;7(1):9-10

3.Rosenfield K et al NEJM 2015;373(2):145-53

4.Werk M et al Circ Cardiovasc Interv 2012;5(6):831-840

5.Tepe G et al Circulation2015;131(5):495-502

6.Laird JR et al J Am Coll Cardiology 2015;66(21):2329-38

Table 1 DCB Trials

Study	Year	Study Size	Location	Outcome(s)	Follow-up Time	Results			
						Outcome	POBA	DCB	P Value
THUNDER	2008	154	Germany	LLL and TLR	6 Months	LLL	1.7mm	0.4mm	<0.001
						TLR	37%	4%	<0.001
Werk *et al*	2008	87	Germany	LLL and TLR	6 Months	LLL	0.8mm	0.3mm	0.031
						TLR	50%	13%	0.001
LEVANT I	2014	101	Primarily Germany and Belgium	LLL	6 Months	LLL	1.09mm	0.46mm	0.016
LEVANT II	2015	476	US and Europe	PP and TLR	12 Months	PP	52.6%	65.2%	0.02
						TLR	16.8%	12.3%	0.21
						PP (US)	56.5%	69.9%	not given
						PP (Non-US)	46%	69.1%	not given
PACIFIER	2015	85	Germany	LLL and TLR	12 Months	LLL	0.65mm	0.1mm	0.001
						TLR	27.90%	7.10%	0.02
IN.PACT SFA	2015	331	US and Europe	PP and CD-TLR	24 Months	PP	50.10%	78.9%	<0.001
						CD-TLR	28.30%	9.10%	<0.001

POBA: Plain old balloon angioplasty; **DCB:** Drug-coated balloon; **LLL:** Late lumen loss; **TLR:** Target lesion revascularisation; **CD-TLR:** Clinically driven target lesion revascularisation; **PP:** Primary patency

Drug coated balloon trials

- Thunder trial --- 6/12 follow-up – late lumen loss less at 5 years TLR
  21% VS 56%
- Levant 11 trial – primary patency 73.5% vs 56.8% at 1 year
- IN.PACT SFA trial –primary patency 89.8% vs 66.8% at 1 year
  2 years primary patency 78.9% vs 50.1%

Drug coated balloons

- Summary

Multiple large European and USA trials --- benefit for drug coated balloons in the femoro-popliteal segments however industry driven and short term follow-up

Drug coated balloons infra-popliteal lesions

- IDEAS RCT DCB vs DES in infra-popliteal disease

  Binary stenosis (more than 50%)angiographic stenosis in DES 28% vs DCB 57.9% at 6 months

- IN.PACT DEEP Trial – DEB comparable efficacy to standard balloon trend towards higher amputation rate in DEB. **Balloon withdrawn**

- Siablis D et al JACC INTV 2014 ;7(9);1048-1056

Drug eluting stents (DES)

- ZILVER PTX trial [1]– comparing DES to BMS -- largest randomized trial with 5 year follow-up
- 1 year primary patency 84.4%
- 4 year primary patency 75% vs 57.9%
- 5 year primary patency 72.4% vs 53%

SIROCCO[2] Trial 1 and11

Sirolimus stent- no reduction in restenosis and no difference in any of the end points

STRIDES [3]TRIAL – Everolimus – 3month drug release– primary patency 94% at 6/12 and 68% at 12/12.

1 Dake MD et al Circulation 2016

2 Duda SH et al J Vasc Interv Radiol 2005 ;16:331-338

3 Lemmer J et al JVS 2011 ;54(2):394-401

Drug eluting stents in infra-popliteal disease

- Meta-analysis of drug eluting stents for infra-popliteal disease– 5 trials with 611 patients
- DES vs angioplasty/BMS
- At a median follow-up at 12 months DES **reduced** target vessel revascularization, restenosis, and amputation

Fusaro M et al JACC INTV 2013;6(12):1284-1293

Consider when to use drug elution

- DES and DEB have been shown to be superior to bare counterparts
- A significant SFA lesions require stenting
- DCB and BMS not shown superiority to DES results
- DCB for calcified lesions ?
- Will still need long term results.

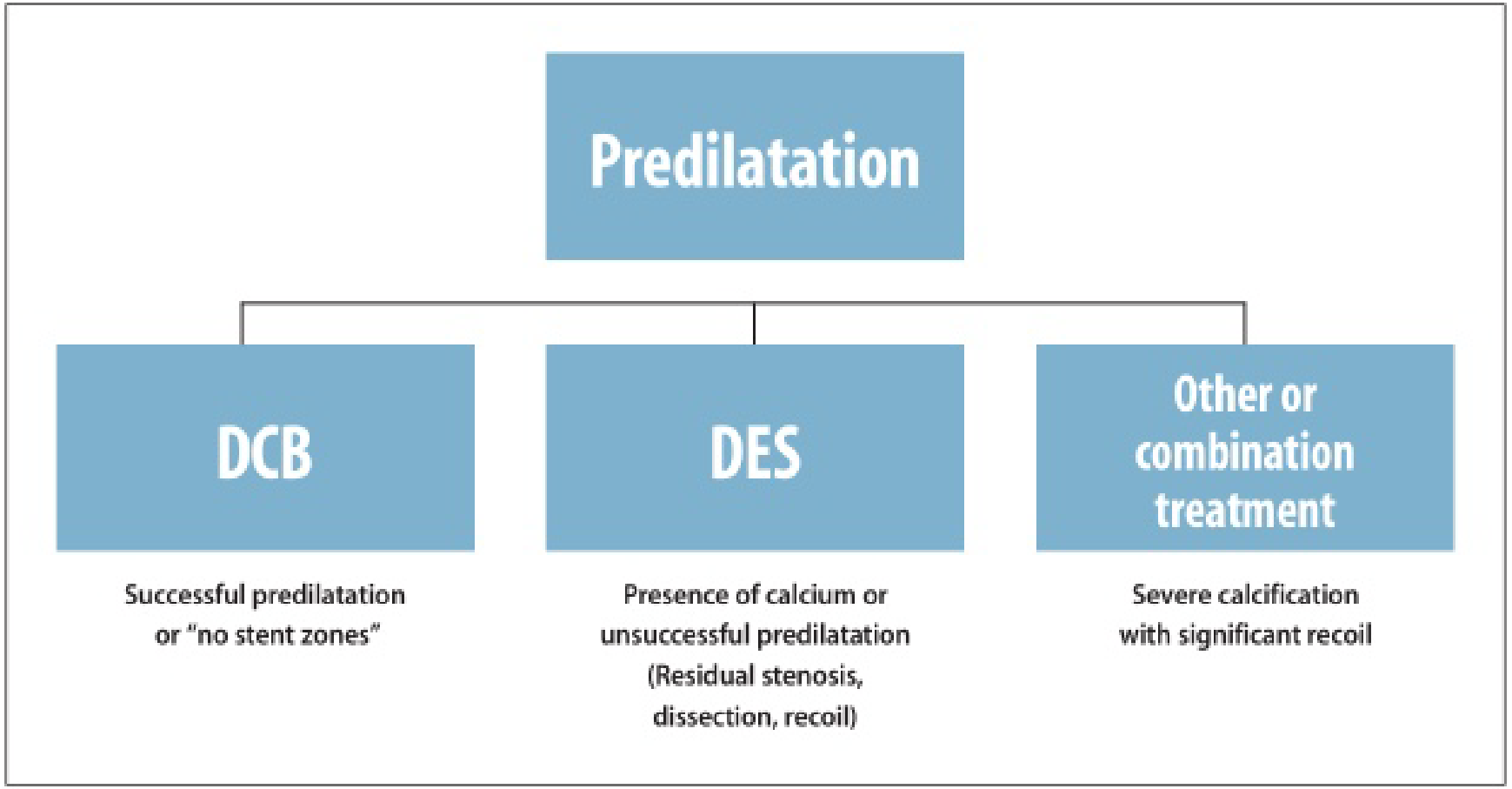

Figure 1. Choosing a drug-eluting modality for SFA lesions.

Ansel G, Phillips JA 2014 suppl Endovascular Today

Conclusions

- Drug coated balloons and stents have superior results as compared to plain balloon angioplasty and bare metal stents
- Early results are encouraging
- They are expensive
- We need longer data and more specific indications