Intravascular Lithotripsy of Peripheral Arteries – Interim Analysis of a Randomized Bicentric Study

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Czech Cardiovascular Research and Innovation Days, November 4, 2024

Randomized Bicentric Study (Dept. Cardiology Prague, Dept. Radiology Kladno)

Main hypothesis: Arterial calcification may reduce an effect of drug-coated balloons (DCB) causing a mechanical barrier to drug penetration*

Main question: Could lithotripsy improve long-term results of DCB angioplasty in calcified femoropopliteal stenoses by disrupting this barrier?

If yes, long-term patency in lithotripsy + subsequent DCB dilatation should be superior over

- the combination of lithotripsy + plain balloon dilatation
- the solely DCB angioplasty (= control group)

* *Fanelli F, et al. Calcium Burden Assessment and Impact on Drug-Eluting Balloons in Peripheral Arterial Disease. Cardiovasc Intervent Radiol (2014) 37:898-907*

Patient Enrollment

Both clinical and angiographic criteria must be present:

Clinical: Symptomatic peripheral artery disease

Angiographic: Significant (> 50%) calcified stenosis of

- common femoral artery and/or
- superficial femoral artery and/or
- deep femoral artery and/or
- popliteal artery

+ A minimum of one vessel run-off

No stent implantation could be performed

Study Design

Patients were randomized 1:1 into two groups:

1) DCB plus Group (DCB+): **treated with lithotripsy + subsequent DCB dilatation**

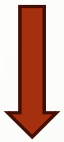
2) DCB minus Group (DCB-): **treated with lithotripsy or if necessary with subsequent plain balloon dilatation**

3) Control Group: **created retrospectively from the database of an angiology outpatient office. It consists of patients managed with DCB without previous lithotripsy. The inclusion and exclusion criteria were the same.**

Patient Follow-up

Two-year follow–up

- Both clinical and duplex ultrasonography examination in six-month intervals is completed



- Significant restenosis (>50%) is defined as the intrastenotic / prestenotic peak systolic velocity ratio (PSVR) > 2,0

Endpoints

	Efficacy	Safety
Primary Endpoints	Long-term patency, comparison among study groups (Patency = freedom from ≥50% restenosis)	Surgical revascularization and/or major amputation within 30 days after procedure
Secondary Endpoints	Acute procedural success – comparison between lithotripsy managed groups Improvement in Rutherford classification during follow-up	Surgical revascularization and/or major amputation within 24 months after procedure

Patient Population				
	DCB+	DCB-	Control	Statistics (95 % confidence Interval)
dures = 61)	22	23	16	
gender	73 % (16/22)	83 % (19/23)	56 % (9/16)	p = 0.195
± SD e	69.82 ± 9.57 47 – 87	73.87 ± 6.24 61 – 85	73.51 ± 9.85 53 – 88	p = 0.287

Risk Factors				
	DCB+	DCB-	Control	S
Hypertension	90.9 % (20/22)	82.6 % (19/23)	100 % (16/16)	p
Current or former smoker	81.8 % (18/22)	91.3 % (21/23)	87.5 % (14/16)	p
Dyslipidemia	72.7 % (16/22)	78.3 % (18/23)	93.8 % (15/16)	p
Diabetes mellitus	54.5 % (12/22)	52.2 % (12/23)	37.5 % (6/16)	p

Clinical Classification Before Procedure – Rutherford Categories			
	DCB+	**DCB-**	**Control**
Category 2	27.3 % (6/22)	30.4 % (7/23)	18.8 % (3/16)
Category 3	**54.5 % (12/22)**	**52.2 % (12/23)**	**50 % (8/16)**
Category 4	9.1 % (2/22)	4.3 % (1/23)	12.5 % (2/16)
Category 5	9.1 % (2/22)	13 % (3/23)	18.8 % (3/16)

p = 0.92

Intervened Arterial Segments

	DCB+	DCB-	Control
non femoral artery	4.5 % (1/22)	-	12.5 % (2/16)
non femoral artery, icial femoral artery	22.7 % (5/22)	4.3 % (1/23)	6.3 % (1/16)
non fermoral artery, femoral artery	4.5 % (1/22)	4.3 % (1/23)	-
non femoral artery, icial fermoral artery, eal artery	9.1 % (2/22)	8.7 % (2/23)	-
icial femoral artery	**40.9 % (9/22)**	30.4 % (7/23)	31.3 % (5/16)
icial fermoral artery, eal artery	9.1 % (2/22)	**39.1 % (9/23)**	**37.5 % (6/16)**
eal artery	9.1 % (2/22)	13 % (3/23)	12.5 % (2/16)

p = 0.305

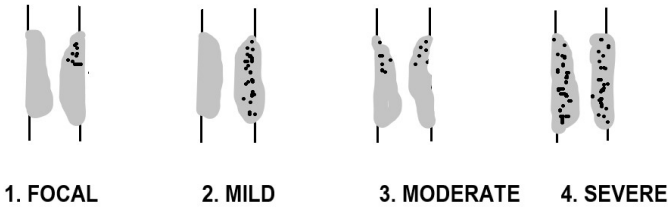
Procedural Characteristics

	DCB+	DCB-	Control	Sta
De novo procedures	90.9 % (20/22)	78.3 % (18/23)	-	p =
Repeated procedures	9.1 % (2/22)	21.7 % (5/23)	-	
Lesion length, mean ± SD **Range**	8.54 ± 10.27 cm 0.5 - 27	8.02 ± 6.13 cm 0.5 - 38	9.56 ± 8.95 cm 0.5 - 24	p =
Lithotripsy pulses, mean ± SD **Range**	225.59 ± 82.61 60 - 300	240.22 ±98.99 90 - 300	-	p =
Predilatation	4.5 % (1/22)	17.4 % (4/23)	-	p =
Residual stenosis after lithotripsy, mean ± SD **Range**	21.87 ± 19.87 % 0 - 50 %	21.81 ± 15,31%) 0 – 83 %	-	p =
Final residual stenosis, mean ± SD **Range**	9.77 ± 9.93 % 0 - 40 %	17.69 ± 16.45 % 0 – 72 %	-	p =

Calcification – Highest Degree in Each Patient

	DCB+	DCB-	Control
1.Focal One side of the vessel + less than one-half of the lesion length	4.5 % (1/22)	-	18.8 % (3/16)
2. Mild One side of the vessel + greater than one-half of the lesion length	13.6 % (3/22)	4.3 % (1/23)	12.5 % (2/16)
3. Moderate Both sides of the vessel + less than one-half of the lesion length	9.1 % (2/22)	8.7 % (2/23)	-
4. Severe Both sides of the vessel + greater than one-half of the lesion length	**72.7 % (16/22)**	**87 % (20/23)**	**68.8 % (11/16)**
Average degree ± SD	3.51±0.91	3.83±0.49	3.19±1.27

p = 0.099



PARC Consensus – Peripheral Academic Research Consortium, 2015

[3]PATEL MR, CONTE MS, CUTLIP DE, et al. Evaluation and Treatment of Patients with Lower Extremity Peripheral Artery Disease. Journal of the American College of Cardiology 2015; 65(9):931-41. DOI:10.1016/j.jacc.2014.12.036

Results

	DCB+	DCB-	
ngiographic (immediate, primary) success **recanalization of the lesion with residual stenosis ≤ 30%)**	95,5 % (21/22) In 1 pt final residual stenosis > 30 %	91,3 % (21/23) In 2 pts final residual stenosis > 30 %	p= 0.57
Complications	9,1 % (2/22) Femoral pseudoaneurysm in 2 pts	13 % (3/23) 1x peripheral embolization during crossing the stenosis with the guidewire 2x large groin hematoma	p = 0.6
Need for surgical evascularization or major mputation within 30 days after procedure	0	0	

Management of complications

Complication	Management
2x femoral pseudoaneurysm	2x Thrombin injection
2x larger groin hematoma	Conservative
1x peripheral embolization during crossing the stenosis with the guidewire	PAT

A 68-year-old-male patient, former smoker, with diabetes, hypertension, dyslipidemia

PAD RC 3

Randomization in DCB+

Lithotripsy 180 pulses 6x60 mm

DCB 6x100 mm

Long-term Results

- 1 surgical revascularization - femoral endarterectomy - was performed in patient from the group DCB+ more than 30 days after the procedure

- No amputation was necessary during the follow-up

Cumulative Patency Rates for DCB+, DCB-, Controls Using Life-table Analysis

DCB+

Interval (mo)	No. at risk at beginning of interval	No. failed during interval	Withdrawn during interval	Interval failure rate	Cumulative patency rate	Standard error
0-1m	21	1	1	0,049	95,12%	20,66%
1-6 m	19	4	2	0,222	73,98%	16,91%
6-12m	13	1	4	0,091	67,26%	18,59%
12-18m	8	1	0	0,125	58,85%	20,75%
18-24m	7	0	7	0,000	58,85%	22,18%

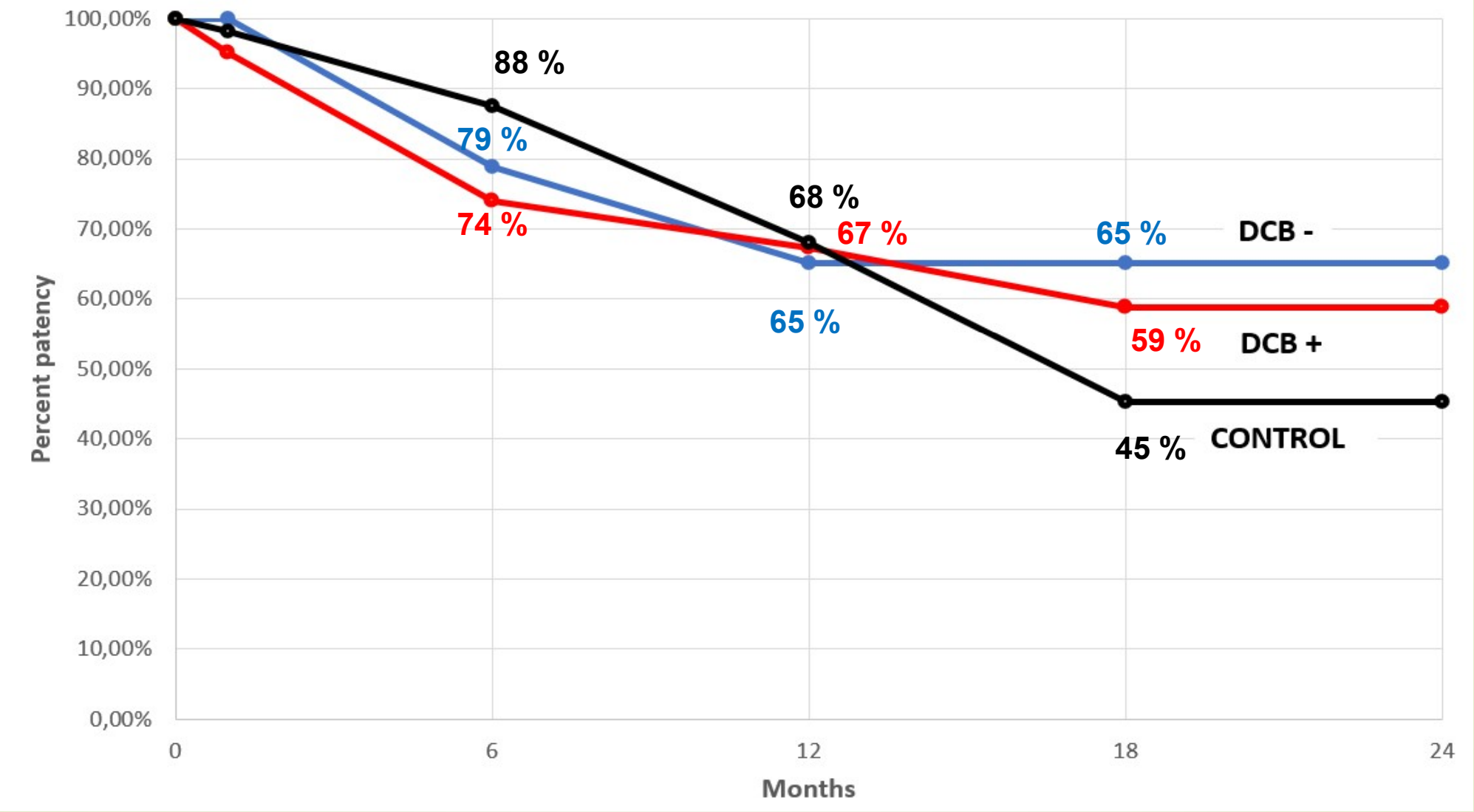
DCB-

Interval (mo)	No. at risk at beginning of interval	No. failed during interval	Withdrawn during interval	Interval failure rate	Cumulative patency rate	Standard error
0-1m	21	0	0	0,000	100,00%	21,71%
1-6 m	21	4	4	0,211	78,95%	17,16%
6-12m	13	2	3	0,174	65,22%	18,03%
12-18m	8	0	1	0,000	65,22%	22,98%
18-24m	7	0	6	0,000	65,22%	24,57%

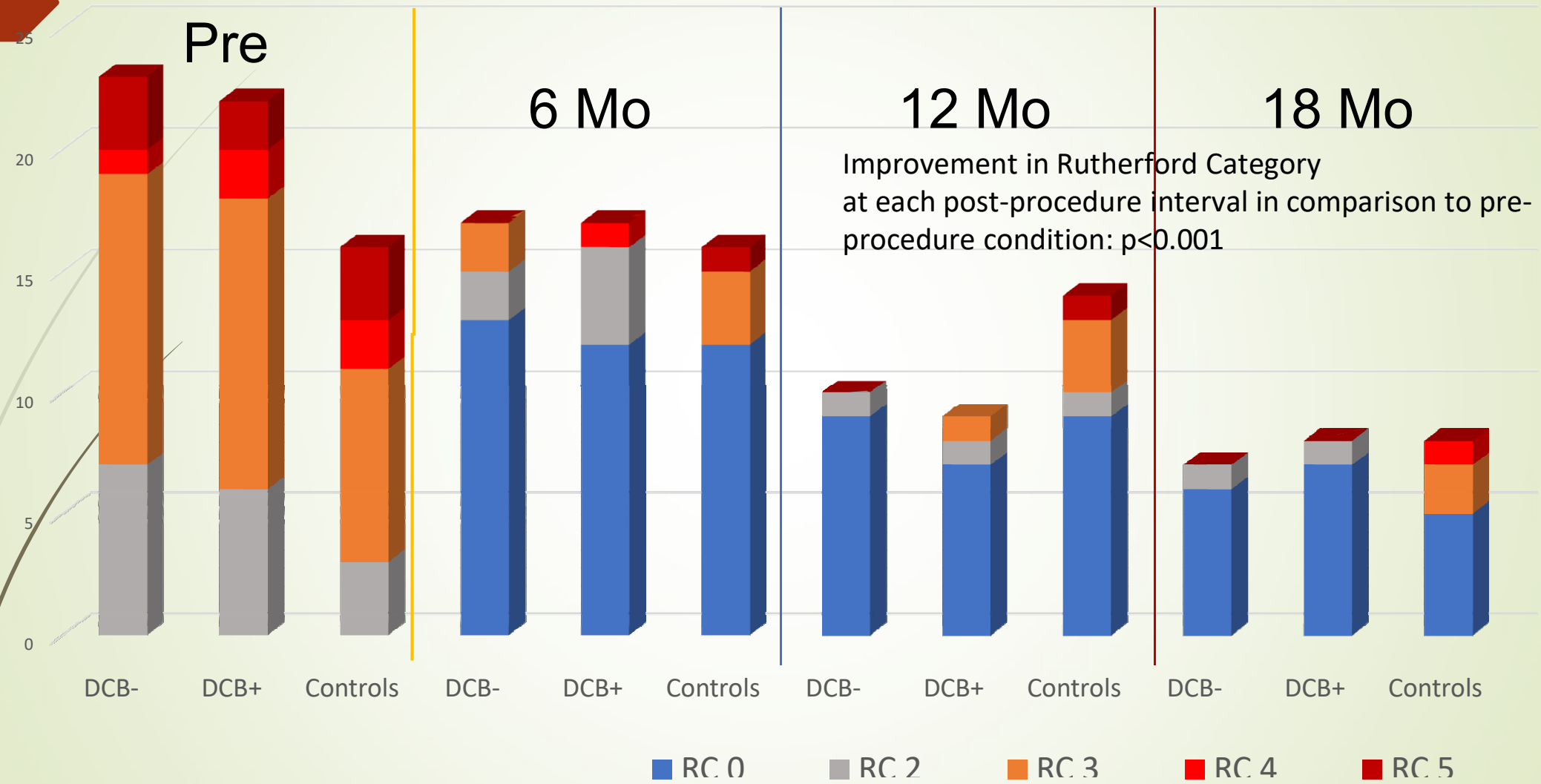
Controls

Interval (mo)	No. at risk at beginning of interval	No. failed during interval	Withdrawn during interval	Interval failure rate	Cumulative patency rate	Standard error
0-6 m	16	2	0	0,125	87,50%	21,78%
6-12m	14	3	1	0,222	68,06%	18,13%
12-18m	10	3	2	0,333	45,37%	14,31%
18-24m	5	0	0	0,000	45,37%	20,24%

Primary Cumulative Patency Rates by Life-table Analysis



Rutherford Category Shift



Preliminary Conclusions

- In calcified femoropliteal lesions, lithotripsy represents a safe and feasible method with favourable immediate outcomes.
- It enables endovascular management of „non stent zones“ – femoral bifurcation, popliteal artery.
- Long-term results: Tendency (no statistical significance) towards better results in patients managed with lithotripsy, howerever there is no evidence of a benefit of the DCB angioplasty over the plain balloon angioplasty after lithotripsy.
- Due to so far inconclusive results, further continuation of the study is needed.