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# How to best treat heavy calcified infrainguinal lesions BMS, DES, Scoring, Cutting Balloons, Atherectomy, Laser, etc.?

Jos C. van den Berg MD PhD

# SFA-challenges

- Complex lesions i.e. high disease burden and presence of clinical and anatomic co-factors (lesion length, plaque burden and calcium) continue to present a challenge for endovascular modalities
- Vascular calcium presents a significant challenge to percutaneous interventions and results in:
  - Acute procedural failure (improper balloon/stent expansion)
  - Recoil, dissections and increased embolic risk
  - Diminished effectiveness of DCBs by impeding drug uptake
  - Increased post procedural stent use

Fanelli, F: Cardiovasc Intervent Radiol 2014; 37:898–907 2.
Rocha-Singh K et al. Catheter Cardiovasc Interv 2014; 83(6): E212–E220
Okuno S, et al. JET 2016;23:731-737

# SFA-challenges

- Inconsistent definitions of calcium severity across clinical trials due to lack of a uniform validated calcium scoring system
- How do we manage severe calcium for optimized outcomes?


Fanelli, F: Cardiovasc Intervent Radiol 2014; 37:898–907 2.
Rocha-Singh K et al. Catheter Cardiovasc Interv 2014; 83(6): E212–E220
Okuno S, et al. JET 2016;23:731-737

# Dilemma

- What is ‘heavy’ calcification?
- What about lesion length and lesion type (total occlusion vs. stenosis)?
- RCT’s typically do not include severely calcified lesions

# Definition of calcification severity

- Beth Israel classification
- Synvacor classification
- PACCS classification
- PARC classification

# Definition of calcification severity

**Beth Israel**

**Severe calcification:**

- radiopacities noted on both sides of the arterial wall and extending more than <u>1 cm</u> of length prior to contrast injection or digital subtraction

**SynvaCor**

**Severe calcification:**

- calcium visible along both sides of the arterial wall
- covers <u>2 cm</u> or greater of the target lesion area
- encompasses greater than 50% of the total target lesion treatment area by visual estimate and/or the calcium is circumferential (360°) in nature
    - on both sides of the vessel lumen extending 2cm or greater on a single AP view

      **OR**
    - classified as exophytic calcification, significantly impedes blood flow in the vessel.

**Brodmann, M. AMP 2017. Krishnan, P., et al. (2017). Circulation. Schroeder, H., et al. (2017). Circulation. Zeller, T. LINC 2017 .Krishnan, P. NCVH 2016**

**Rocha-Singh, K. LINC 2017; Patency, lesion lengths, and calcification: Tepe, G., et al. (2015). Circulation 131(5): 495-502; Jaff, M. VIVA 2016.; IN.PACT™ Admiral™ IFU, Rev 1F**

# Definition of calcification severity

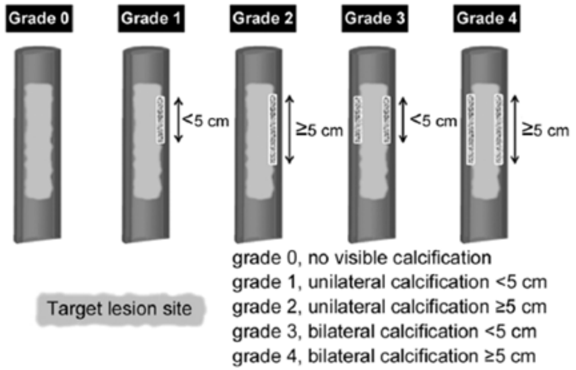
**PACSS (Peripheral Arterial Calcium Scoring Scale)**

**Grading System:**

Grade 0: no visible calcium at the target lesion site
Grade 1: unilateral calcification < 5cm
Grade 2: unilateral calcification ≥ 5cm
Grade 3: bilateral calcification < 5cm
Grade 4: bilateral calcification ≥ 5cm

For grade 1-4 subdivision

a) intimal calcification
b) medical calcification
c) mixed type




**PARC (Peripheral Arterial Research Consortium )**

**Focal:** <180$^0$ (**one side of vessel**) and less than half the total lesion length

**Mild:** <180$^0$ and greater than half the total lesion length

**Moderate**: ≥180$^0$ (**both sides of vessel at the same location** ) and less that half the total lesion length

**Severe**: >180$^0$ (**both sides of the vessel at the same location** ) and greater than half the total lesion length

**Rocha-Singh et al., Cath Cardiovasc Interv. 2014**

**Patel MR et al JACC 2015/Dattilo R et al JIC 2014**

# Definition of calcification severity

| Fanelli et al[1] | 1a | 1b | 2a | 2b | 3a | 3b | 4a | 4b |
|---|---|---|---|---|---|---|---|---|
| Circumferential burden | 0-90° | 0-90° | 90-180° | 90-180° | 180 - 270° | 180 - 270° | 270-360° | 270-360° |
| Length | <3cm | >3cm | <3cm | >3cm | <3cm | >3cm | <3cm | >3cm |

| Compliance 360[2] | 0 | 1 | 2 | 3 | 4/Severe |
|---|---|---|---|---|---|
| Circumferential burden | None | <180° (1 side of vessel) | <180° (1 side of vessel) | ≥180° (both sides of vessel) | ≥180° (both sides of vessel) |
| Length | NA | <50% of lesion length | ≥50% of lesion length | <50% of lesion length | ≥50% of lesion length |

| PACSS[3] | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| Circumferential burden | None | unilateral | unilateral | bilateral | bilateral |
| Length | NA | <5cm | ≥5cm | <5cm | ≥5cm |

| PARC[4] | Focal | Mild | Moderate | Severe |
|---|---|---|---|---|
| Circumferential burden | <180° (1 side of vessel) | <180° (1 side of vessel) | ≥180° (both sides of vessel) | ≥180° (both sides of vessel) |
| Length | <1/2 lesion length | >1/2 lesion length | <1/2 lesion length | >1/2 lesion length |

| SynvaCore[5] | | | Severe |
|---|---|---|---|
| Circumferential burden | | | Both sides of the arterial wall |
| Length | | | ≥2cm |

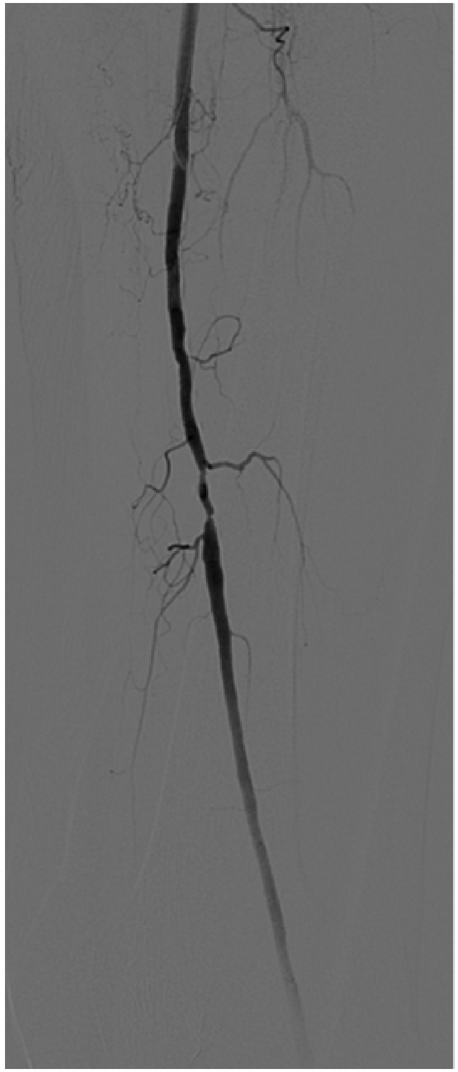
| Beth Israel[6] | | | Severe |
|---|---|---|---|
| Circumferential burden | | | Both sides of the arterial wall |
| Length | | | ≥1cm |

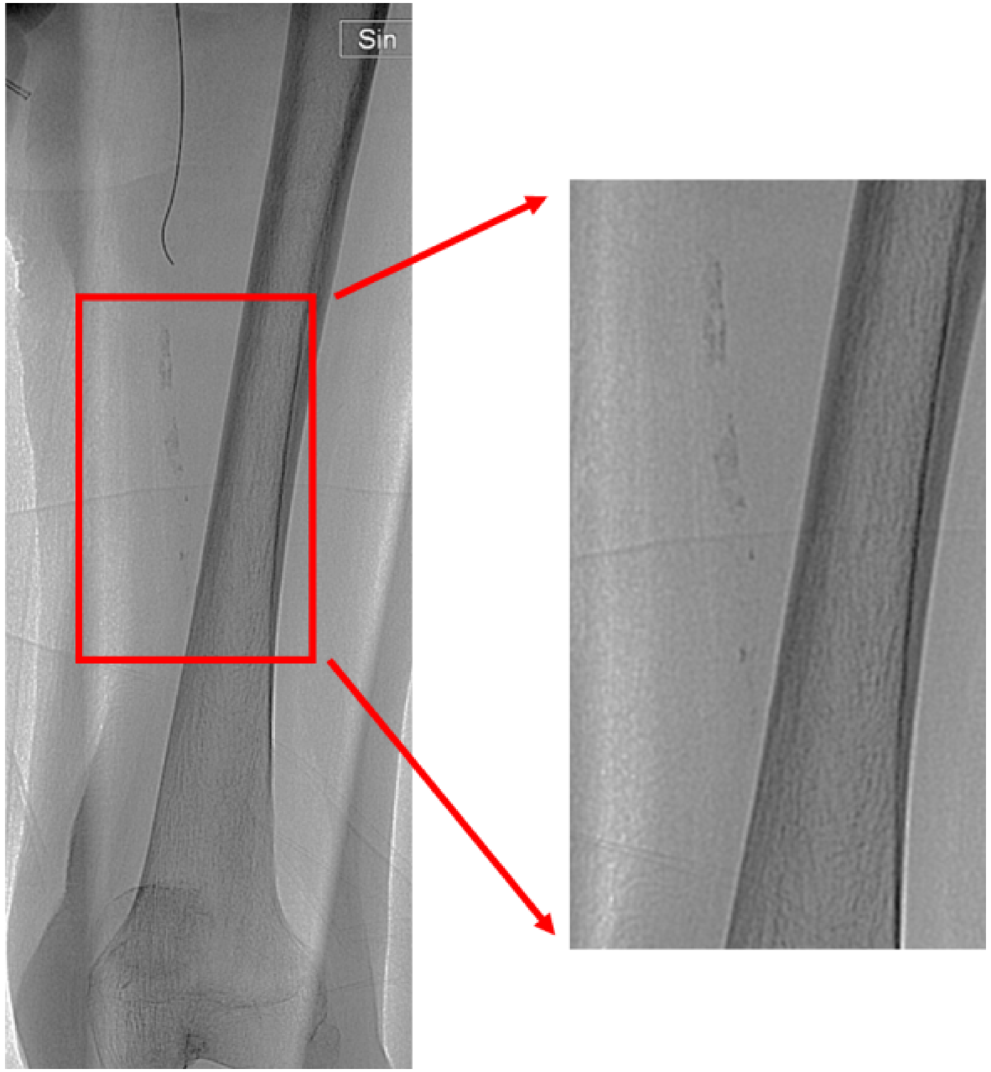

1. Fanelli F et al. Cardiovasc Intervent Radiol. 2014 Aug;37(4):898-907.
2. Dattilo R et al. J Invasive Cardiol. 2014 Aug;26(8):355-60.
3. Rocha-Singh KJ et al. Catheter CardiovascInterv. 2014 May 1;83(6):E212-20.
4. Patel MR et al. J Am Coll Cardiol. 2015 Mar 10;65(9):931-41. doi: 10.1016/j.jacc.2014.12.036. Erratum in: J Am Coll Cardiol. 2015 Jun 16;65(23):2578-9.
5. Rosenfield, K. et al. N Engl J Med 2015;373:145-153.
6. Schroe, H. et al. Catheter Cardiovasc Interv 2017;91:497-504.

# Severe calcification?


Definitely yes!

# Severe calcification?






Maybe not

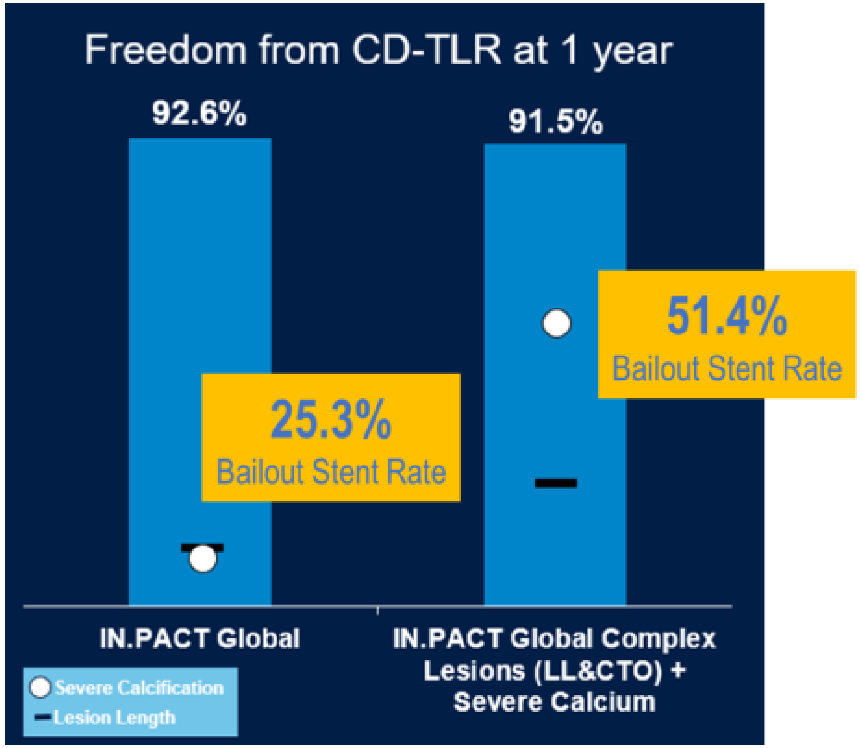
# Problem of lesion length

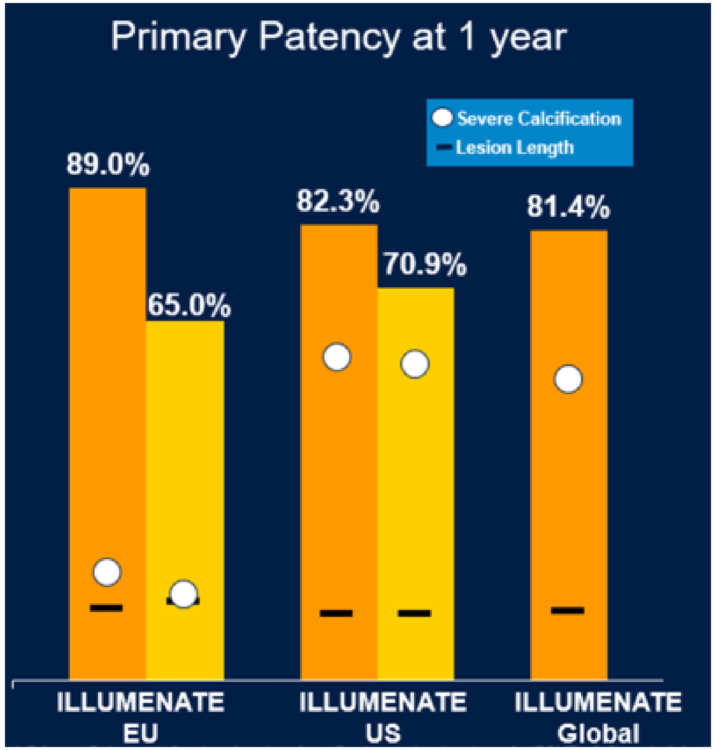
- 2/3 of lesions longer than 10 cm
- Primary patency of longer lesions poor

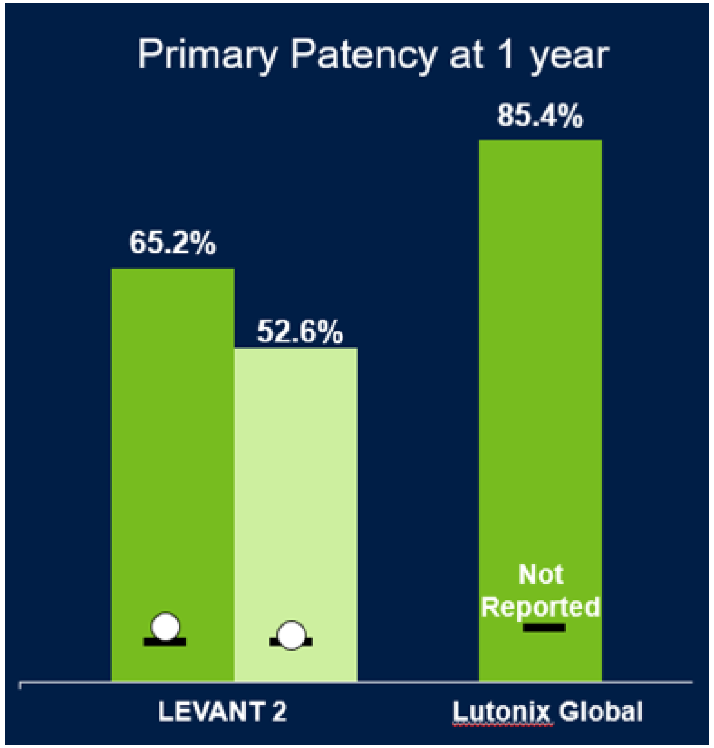
| | # patients | 12 months | 24 months | 36 months |
|---|---|---|---|---|
| TASC A/B | 46/82 | 79% | 67% | 57% |
| TASC C/D | 38/35 | 53% | 36% | 19% |

**Dearing DD et al, JVS 2009;50:542-548**

# Calcified lesions and DCB




Synvacor

Beth Israel

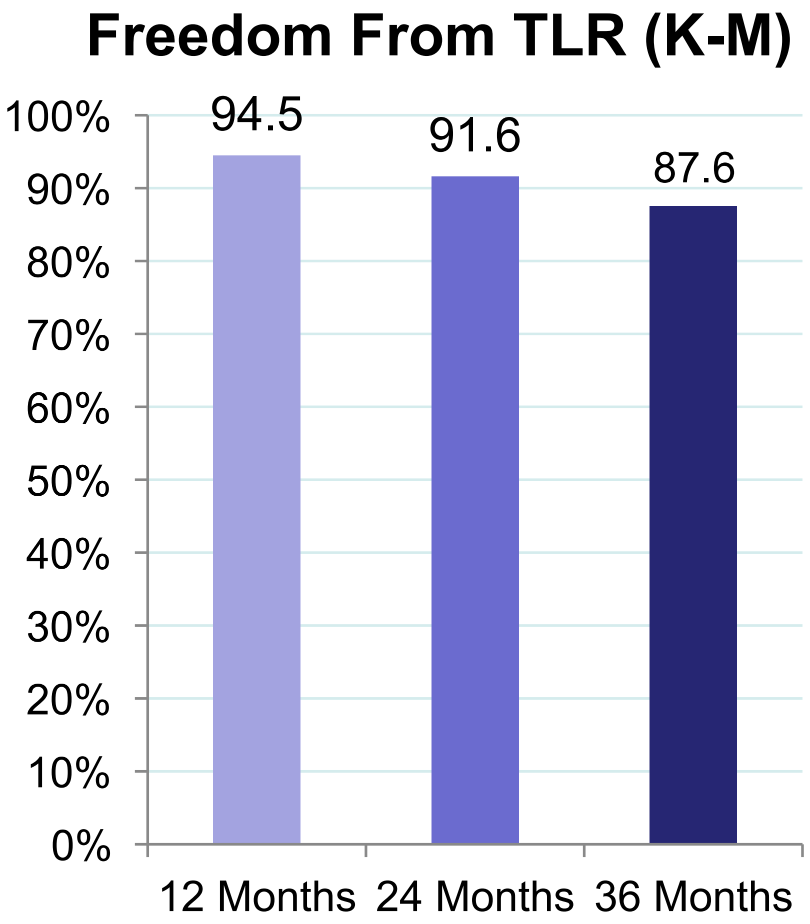
Not specified

# Calcified lesions and stents (interwoven nitinol)

- No RCT data
- Registry data (SUPERB)
- 45% ‘severe calcification’
- No influence lesion length
- Influence of quality of stent deployment

**Garcia L et al Circ Cardiovasc Interv. 2015;8:e000937**
**Garcia L et al Cath Cardiovasc Interv 2017;89:1259–1267**

# Calcified lesions and stents (interwoven nitinol)

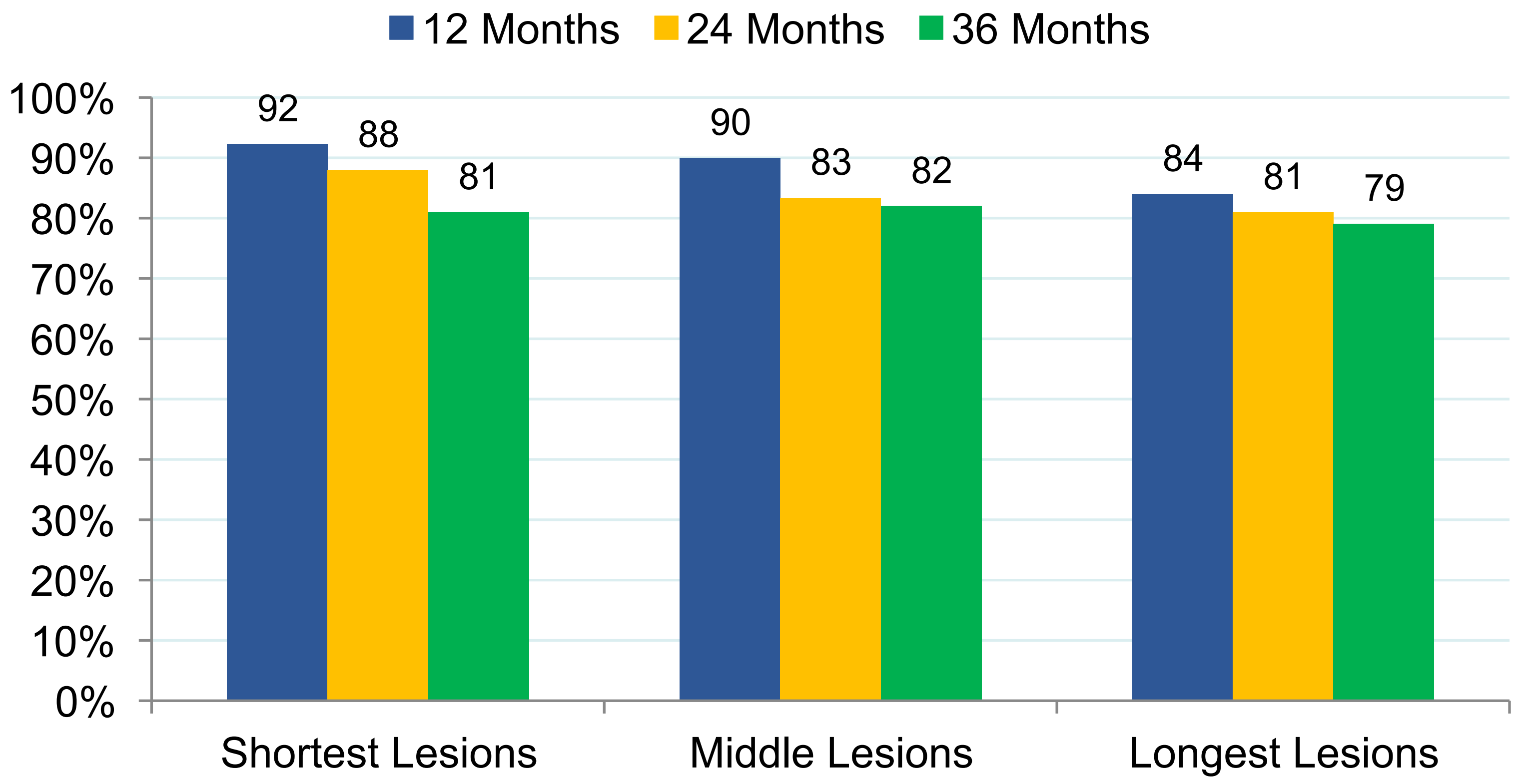



| Superb Severe Calcification Subset | |
|---|---|
| Severe calcification | 45% |
| Patency (VIVA) | 89% |

Severe Ca++ Beth Israel grading

Garcia L et al Circ Cardiovasc Interv. 2015;8:e000937
Garcia L et al Cath Cardiovasc Interv 2017;89:1259–1267

# Calcified lesions and stents (interwoven nitinol)




| | Shortest Lesions | Middle Lesions | Longest Lesions |
|---|---|---|---|
| Mean Lesion Length | 35.4 mm | 73.5mm | 126.1 mm |
| Min, Max Lesion Length | 8.5, 55.0 mm | 55.5, 91.5 mm | 96.1, 236.4 mm |

**Garcia L et al Circ Cardiovasc Interv. 2015;8:e000937**
**Garcia L et al Cath Cardiovasc Interv 2017;89:1259–1267**

# Calcified lesions and directional atherectomy

- DEFINITIVE AR DAART vs. DCB
- No statistically significant differences between arms
- Clinical opportunities for DAART
  - Added benefit of DA in lesions < 30% residual stenosis (RCT) vs. >30%
    - DUS patency: 84.2% vs. 77.8% (KM)
    - Angiographic patency: 88.2%  vs. 68.8%
  - In the randomized DA+DCB arm, no stents were required

**Zeller T et al, Circ Cardiovasc Interv 2017**

# Calcified lesions and IVL

- RCT IVL plus DCB vs. DCB (DISRUPT PAD III)
- 306 patients with moderately-to-severely calcified femoropopliteal arteries IVL (n=153) or PTA (n =153) prior to DCB treatment or stenting (PARC grading)
- Powered secondary effectiveness endpoint: primary patency at 1 year, defined as freedom from clinically driven target lesion revascularization plus freedom from restenosis determined by duplex ultrasound
- Acute PTA failure requiring stent placement during the index procedure considered loss of primary patency

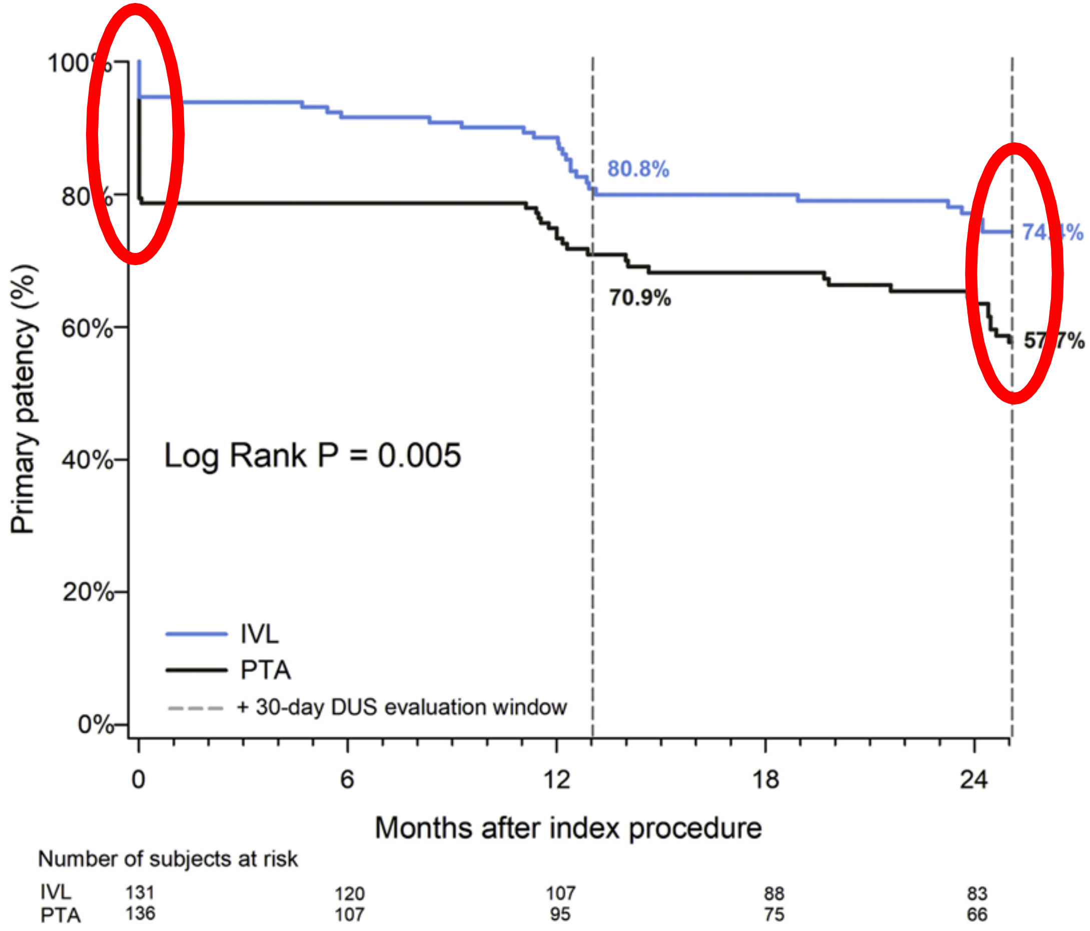
**Tepe G et al JSCAI 2022;in press**

# Calcified lesions and IVL

- Primary patency at 1 year was significantly greater in the IVL arm (80.5% vs 68.0%, P = .017)
- Provisional stenting significantly lower in the IVL group (4.6% vs 18.3%, P < .0001)
- Freedom from cdTLR (IVL: 95.7% vs PTA: 98.3%, P = .94) and restenosis rates (IVL: 90.0% vs PTA: 88.8%, P = .48) were similar between the 2 groups at 1 year
- At 2 years, primary patency remained significantly greater in the IVL arm (70.3% vs 51.3%, P=.003)
- Post hoc Kaplan-Meier analysis of primary patency modeled without defining provisional stenting as a failure demonstrated similar 2-year primary patency rates between the 2 groups (IVL: 79.2% vs PTA: 75.6%, P =.70)
- Post hoc Kaplan-Meier analysis of non-stented patients demonstrated similar 2-year primary patency rates between the 2 groups (IVL: 78.6% vs PTA: 72.7%, P = .48)

**Tepe G et al JSCAI 2022;in press**

# Calcified lesions and IVL




**Tepe G et al JSCAI 2022;in press**

# Network meta-analysis

*Meta-analysis*

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A SAGE Publication

Journal of Endovascular Therapy
2020, Vol. 27(1) 42–59

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www.jevt.org
SAGE

## Comparative Effectiveness of Endovascular Treatment Modalities for De Novo Femoropopliteal Lesions: A Network Meta-analysis of Randomized Controlled Trials

**Yang Zhou, MM[1], Zhihui Zhang, MD[1], Shaomang Lin, MB[1], Jianbin Xiao, MM[1], Wenjia Ai, MD[1], Junwei Wang, MM[1], Yangyong Li, MM[1], and Qiang Li, MM[1]**

**Zhou Y et al, JET 2020;27:42-59**

# Network meta-analysis

- Comparison of 14 treatments (atherectomy, brachytherapy, cryoplasty, cutting balloons, drug-coated balloons, bare nitinol stents, drug-eluting stents, covered stents, and combinations)
- 53 articles reporting on 45 studies (91 study arms; 5565 patients)

**Zhou Y et al, JET 2020;27:42-59**

# Network meta-analysis

- Technical success
  - Stent technology most effective treatment and atherectomy the least effective treatment
  - Stent  technology had significantly higher technical success rates than balloon angioplasty and atherectomy
  - Combination of balloon and atherectomy more effective treatment than either as a single treatment

**Zhou Y et al, JET 2020;27:42-59**

# Network meta-analysis

- Binary restenosis
  - Most effective treatments were DES, BNS-DCB, and CS at 6-, 12- and 24-month follow-up
  - DES most effective single treatment at the 12-month follow-up
  - Both DES and CS had significantly lower binary restenosis rates than the majority of other single treatments, including BA, CB, CR, DA, and BNS during all follow-up periods
  - CS had a lower 24-month binary restenosis rate than DES
  - DA-DCB was better than DA, BNS-DCB was better than BNS (12 months); combination therapies were more effective treatments than any of the single treatments

**Zhou Y et al, JET 2020;27:42-59**

# Network meta-analysis

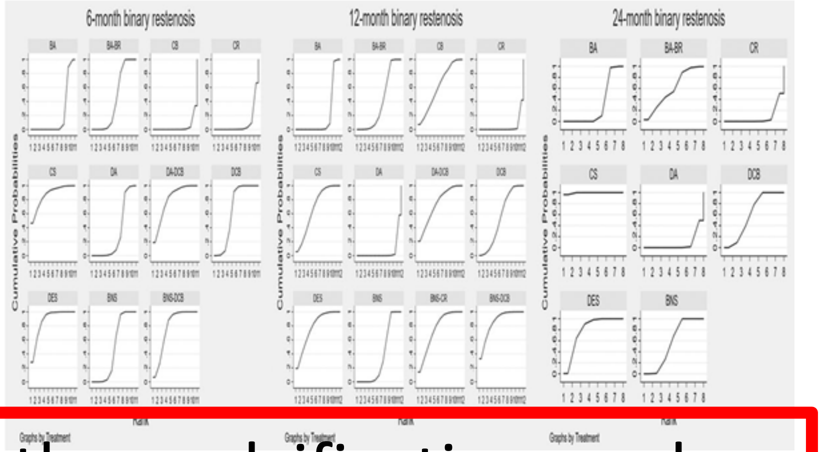
- Target lesion revascularization
  - BNS-DCB was the most effective treatment in 6- and 24-month follow-up, DES was the second effective single treatment at 6-month follow-up and most effective single treatment in the 12-month period
  - CS was the most effective single treatment at the 24-month follow-up
  - Both DES and CS had significantly lower TLR rates than the majority of other single treatments
  - BNS-DCB was better than BNS and DCB with regard to 24-month TLR

**Zhou Y et al, JET 2020;27:42-59**

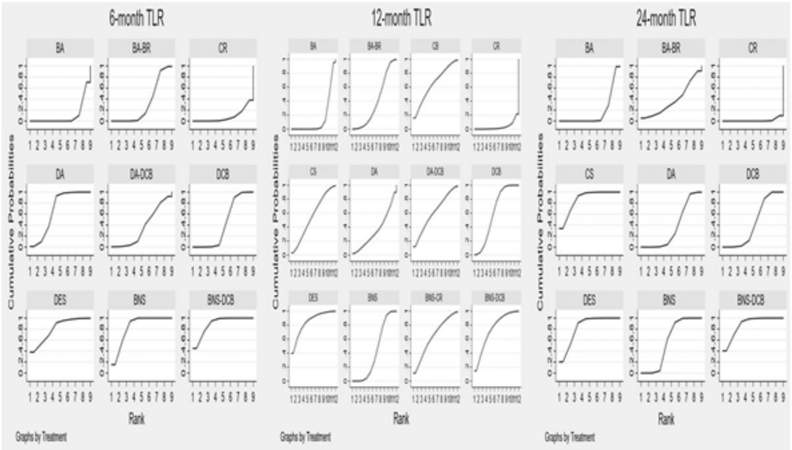
# Network meta-analysis

**Table 1.** Characteristics of the Eligible Studies Included in the Network Meta-analysis.

| Study | Follow-up, mo | Treatment Arms | Patients | Men, % | Age, y | Lesion Length, mm | Occlusion, % | CLTI, % |
|---|---|---|---|---|---|---|---|---|
| Vroegindeweij 1995 | 24 | BA vs DA | 35 vs 38 | 75.3 | 64.0 | n/a | 4.1 | 0.0 |
| Shammas 2011 | 12 | BA vs DA | 29 vs 29 | 63.8 | 69.2 | 88.1 | n/a | 20.7 |
| Nakamura 1995 | 6 | BA vs RA | 13 vs 26 | 97.4 | 65.0 | 194.0 | 100.0 | 0.0 |
| Dattilo 2014 | 6 | BA vs OA | 27 vs 38 | 32.0 | 69.7 | 68.9 | 20.0 | n/a |
| Zeller 2017 | 12 | DCB vs DA-DCB | 54 vs 48 | 66.7 | 69.5 | 104.0 | 29.4 | 2.0 |
| Krankenberg 2007 | 12 | BA vs BNS | 121 vs 123 | 68.9 | 66.5 | 44.9 | 30.7 | 3.0 |
| Laird 2010 (RESILIENT) | 36 | BA vs BNS | 72 vs 134 | 69.4 | 67.3 | 68.3 | 17.5 | 0.5 |
| Schillinger 2006 and 2007 | 12 / 24 | BA vs BNS | 53 vs 51 | 52.9 | 66.5 | 96.4 | 34.6 | 12.5 |
| Dick 2009 | 12 | BA vs BNS | 39 vs 34 | 68.5 | 69.0 | 72.9 | 38.4 | 5.5 |
| Zdanowski 1999 | 12 | BA vs BNS | 17 vs 15 | 43.8 | 71.5 | 72.4 | 100.0 | 84.4 |
| Chalmers 2012 (SUPER) | 12 | BA vs BNS | 76 vs 74 | 82.0 | 67.9 | 119.9 | 93.3 | 18.0 |
| Rastan 2013 and 2015 | 12 / 24 | BA vs BNS | 127 vs 119 | 64.3 | 72.5 | 42.3 | 33.0 | 20.7 |
| Krueger 2004 | 24 | BA vs BA-BR | 15 vs 15 | 76.7 | 60.9 | 30.0 | 3.3 | n/a |
| Gallino 2004 (PAB) | 6 | BA vs BA-BR | 84 vs 81 | 61.5 | 72.0 | 51.0 | 26.6 | 0.0 |
| Waksman 2003 (PARIS II) | 12 | BA vs BA-BR | 40 vs 35 | n/a | n/a | n/a | n/a | n/a |
| Zehnder 2003 (Swiss) | 12 | BA vs BA-BR | 49 vs 51 | 58.0 | 70.8 | 46.6 | 10.0 | 8.0 |
| van Tongeren 2005 (VARA) | 12 | BA vs BA-BR | 33 vs 27 | 66.7 | 64.0 | 35.2 | 31.7 | 13.3 |
| Minar 20[illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| Pokrajac [illegible]005 (Vienna3) | 24 | BA vs BA-BR | 67 vs 67 | 64.6 | n/a | 91.0 | 29.2 | 19.8 |
| Poncyljus 201[illegible] | 12 | BA vs CB | 30 vs 30 | 55.0 | 63.[illegible] | 33.[illegible] | [illegible] | 13.3 |
| Amighi 2[illegible]8 | [illegible] | BA vs [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | 18.6 |
| Fossacec[illegible] 2011 | 12 | BA vs CR | [illegible] vs 24 | 56.3 | 70.0 | n/a | n/a | n/a |
| Shamma[illegible] 2012 | 6 | BA vs CR | 20 vs 20 | 47.5 | 67.1 | 90.4 | n/a | 15.0 |
| Spiliopoulos 2010 | 36 | BA vs CR | 26 vs 24 | 82.0 | 67.9 | 119.5 | 18.5 | 40.0 |
| Lammer 2013 and 2015 (VIASTAR) | 12 / 24 | BNS vs CS | 69 vs 72 | 70.9 | 69.1 | 181.7 | 72.3 | 15.6 |
| Saxon 2003 and 2008 | 12 / 24 | BA vs CS | 100 vs 97 | 76.1 | 67.0 | 70.0 | 24.9 | 10.7 |
| Jia 2016 (Acotec) | 12 | BA vs DCB | 100 vs 100 | 73.5 | 65.8 | 149.5 | 54.5 | 42.0 |
| Scheinert 2015 (BIOLUX PI) | 12 | BA vs DCB | 30 vs 30 | 57.0 | 70.8 | 60.0 | n/a | 16.7 |
| Liistro 2013 (DEBATE SFA) | 12 | BNS vs BNS-DCB | 51 vs 53 | 69.1 | 75.0 | 95.0 | 61.9 | 74.0 |
| Tepe 2017 and Albrecht 2018 (CONSEQUENT) | 12 / 24 | BA vs DCB | 75 vs 78 | 68.0 | 68.1 | 131.6 | 26.1 | 0.0 |
| Werk 2013 (Fempac) | 24 | BA vs DCB | 42 vs 45 | 60.0 | 68.7 | 43.4 | 15.9 | 5.8 |
| Tepe 2015 and Laird 2015 (IN.PACT SFA) | 12 / 24 | BA vs DCB | 111 vs 220 | 66.0 | 67.7 | 88.7 | 24.7 | 5.4 |
| Werk 2012 (Pacifier) | 12 | BA vs DCB | 44 vs 41 | 61.6 | 71.0 | 67.9 | 30.8 | 4.4 |
| Tepe 2008 (Thunder) | 24 | BA vs DCB | 54 vs 48 | 63.9 | 68.5 | 74.5 | 26.5 | 12.8 |
| Krishnan 2017 (ILLUMENATE) | 12 | BA vs DCB | 100 vs 200 | 58.7 | 68.8 | 83.0 | 18.7 | 4.3 |
| Schroeder 2017 (ILLUMENATE EU) | 12 | BA vs DCB | 72 vs 222 | 71.1 | 67.5 | 71.8 | 19.0 | 1.7 |
| Bausback 2017 and Steiner 2018 (RANGER) | 6 / 12 | BA vs DCB | 34 vs 71 | 72.4 | 67.7 | 65.4 | 34.0 | 2.9 |
| Scheinert 2014 (LEVANT1) | 24 | BA vs DCB | 52 vs 49 | 63.3 | 68.5 | 80.5 | 41.5 | 6.9 |
| Rosenfield 2015 (LEVANT2) | 12 | BA vs DCB | 160 vs 316 | 63.0 | 68.2 | 63.0 | 21.3 | 8.0 |
| Duda 2002 | 6 | BNS vs DES | 18 vs 18 | 75.0 | 65.5 | 85.8 | 57.6 | n/a |
| Duda 2005 | 6 | BNS vs DES | 28 vs 29 | 70.2 | 66.7 | 81.5 | 66.7 | n/a |
| Duda 2006 | 24 | BNS vs DES | 46 vs 47 | 72.0 | 66.1 | 83.0 | 61.3 | n/a |
| Dake 2011 and 2013 | 12 / 24 | BNS vs DES | 59 vs 61 | 64.8 | 67.8 | 64.7 | 27.1 | n/a |
| Banerjee 2012 (Cobra) | 12 | BNS vs BNS-CR | 29 vs 29 | 84.5 | 64.4 | 106.7 | 41.4 | 13.5 |
| Ott 2017 | 24 | BNS-DCB vs BNS vs DA | 48 vs 52 vs 55 | 71.6 | 69.2 | 65.8 | 56.1 | 5.8 |




**No subgroup analysis for lesion length or calcification grade**




Zhou Y et al, JET 2020;27:42-59

# Summary

- Presence of calcium in the vasculature still poses a significant challenge to current endovascular device strategies
- Results from contemporary studies show promising outcomes when treating calcified lesions, however comparisons across these trials are futile given differences in calcium definitions and differences in adjudication

# Conclusion

- As to what is the best treatment for heavily calcified lesions in the infra-inguinal segment the jury is still out
- Even network meta-analyses consider only highly selected patient groups, not taking into considering degree of calcification or lesion length
- More data is needed to answer the question “How to best treat heavy calcified infrainguinal lesions BMS, DES, Scoring, Cutting Balloons, Atherectomy, Laser, etc.?”

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Jos C. van den Berg MD PhD