

Transverse View Area Loss (TVAL): An informative angiographic outcome in below- knee lesions

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Disclosure

Speaker name: Mahmood Razavi MD

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I have the following potential conflicts of interest to report:

- Consulting: Abbott, BSC, MDT, Philips, Terumo
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Research support: BD, BSC, Mercator, Philips, NIH

- I do not have any potential conflict of interest

Overview

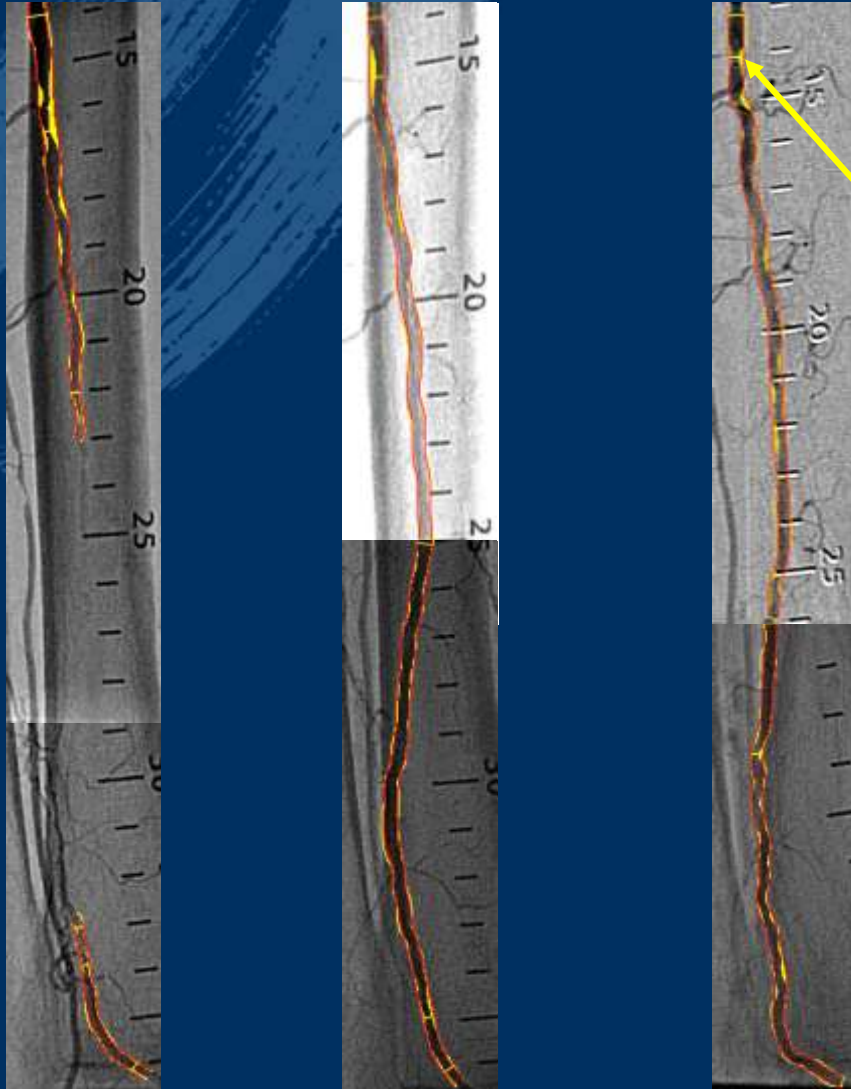
- Improvements in clinical outcome of CLI pts is multifactorial & dependent on multiple variables
- Progress in endovascular revascularization of BTK arteries is incremental
- Sensitive & measurable indicators of incremental therapeutic effects are required
- In long, diffuse lesions, outcomes measures such as LLL or binary “patency” are inadequate to assess treatment success

Measuring Therapy Effect in Long BTK Lesions

Pre:

Post:

6-mo f/u:

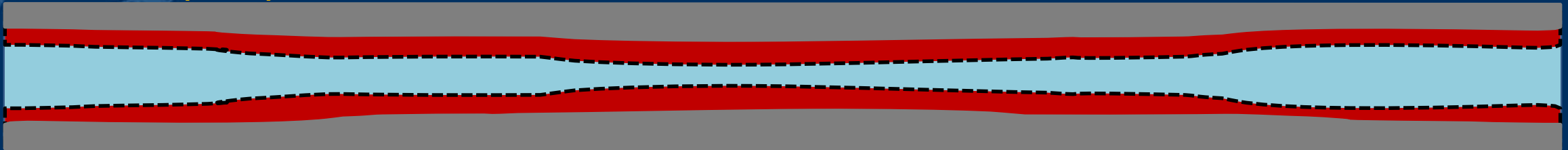


- Total lesion length: 22 cm
- Proximal: diffuse disease
- Distal: 10-cm total occlusion
- Good revascularization result
- Good 6-month outcome
- Slight narrowing at proximal end (in largest part of vessel) results in high LLL: is this a failure?

TVAL: A Proposed Tool for Assessment of Therapeutic Effect in Long Lesions

- Defining Transverse View Area Loss (TVAL)
 - TVAL is the side-view lumen area that is lost from post-revascularization to follow up

TRANSVERSE (SIDE) VIEW:



$$\text{LUMEN AREA} = \text{AREA REMAINING} + \text{AREA LOST}$$

TVAL = AREA LOST as a % of POST REVASC LUMEN AREA (red/initial blue)

TVAL is a 2-dimensional approximation of neointimal volume

Example of TVAL Measurement

PRE
REVASC:



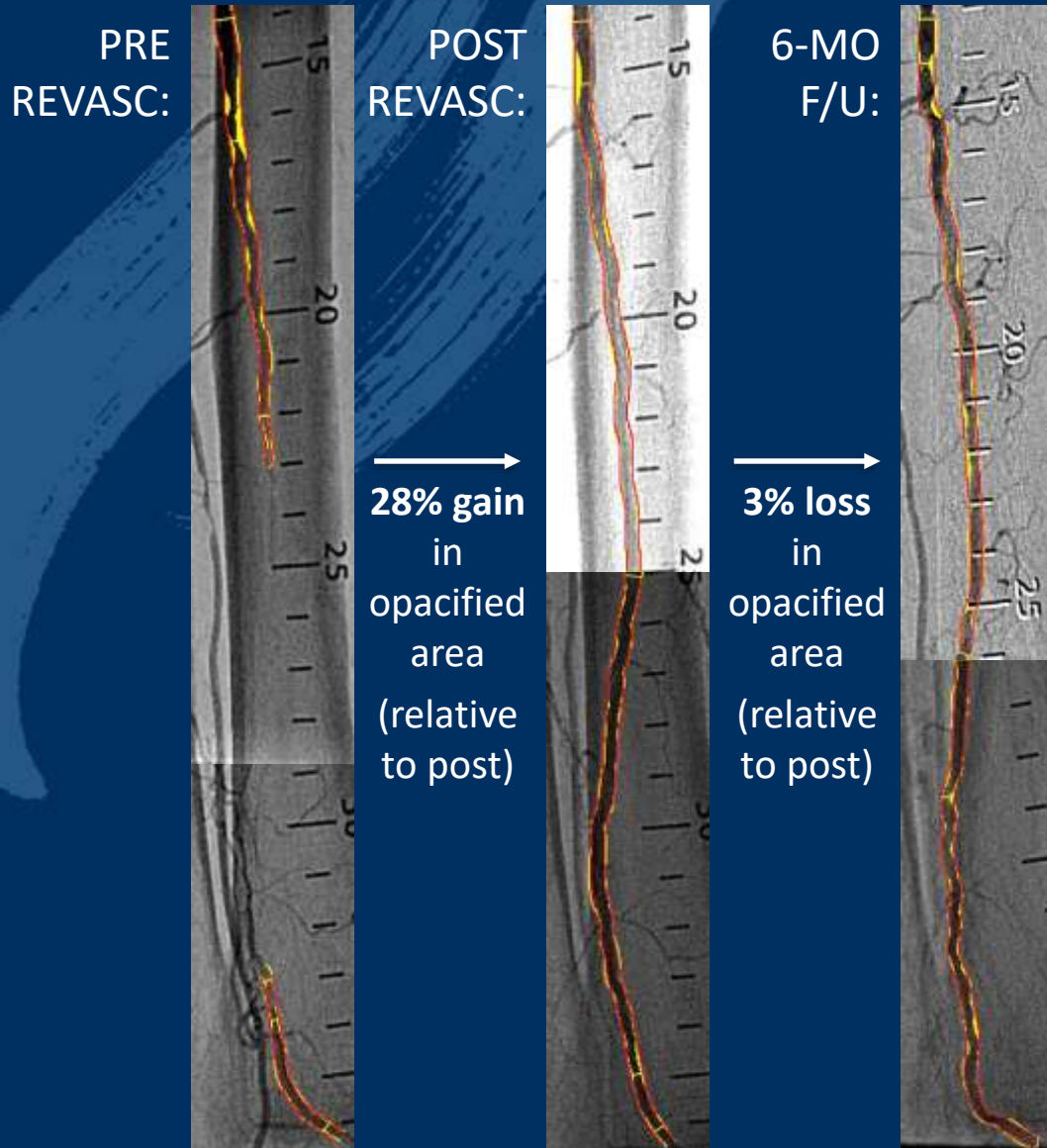
POST
REVASC:



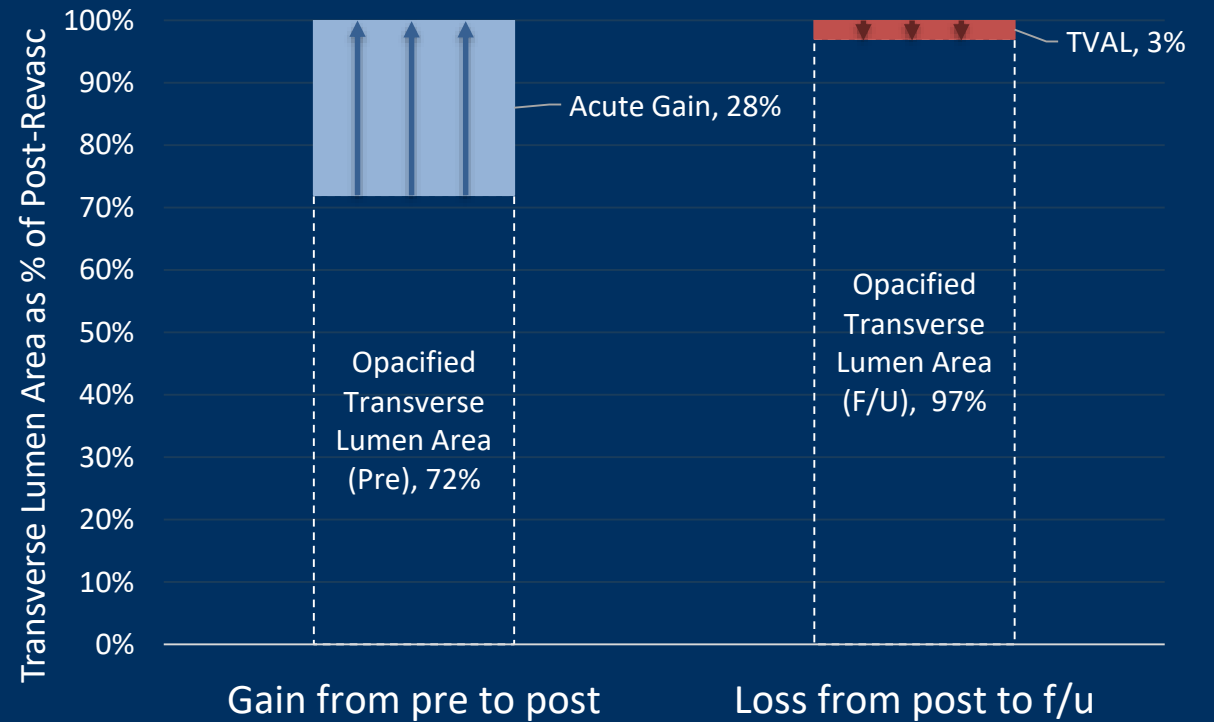
6-MO
F/U:



Example of TVAL Measurement



Example of acute (procedural) transverse lumen area gain and 6-month area loss



Correlation of TVAL to Traditional Endpoints

- LIMBO-ATX
 - 100 subjects randomized 1:1 to treatment (adventitial dexamethasone) or control (no adventitial delivery) after atherectomy with or without PTA
 - Below-the-knee lesions up to 25 cm in length
 - Rutherford 4-5
- TANGO-Low Dose Phase
 - 30 subjects randomized 2:1 to treatment (adventitial temsirolimus) or control (adventitial saline) after atherectomy and/or PTA
 - Below-the-knee lesions up to 25 cm in length
 - Rutherford 3-5
- 6-month follow-up angiographic endpoint in both studies
- Analysis of 6-month TVAL vs. 12-month outcomes pooled all subjects from LIMBO-ATX and TANGO-Low Dose Phase

Endpoints of TANGO & LIMBO-ATX

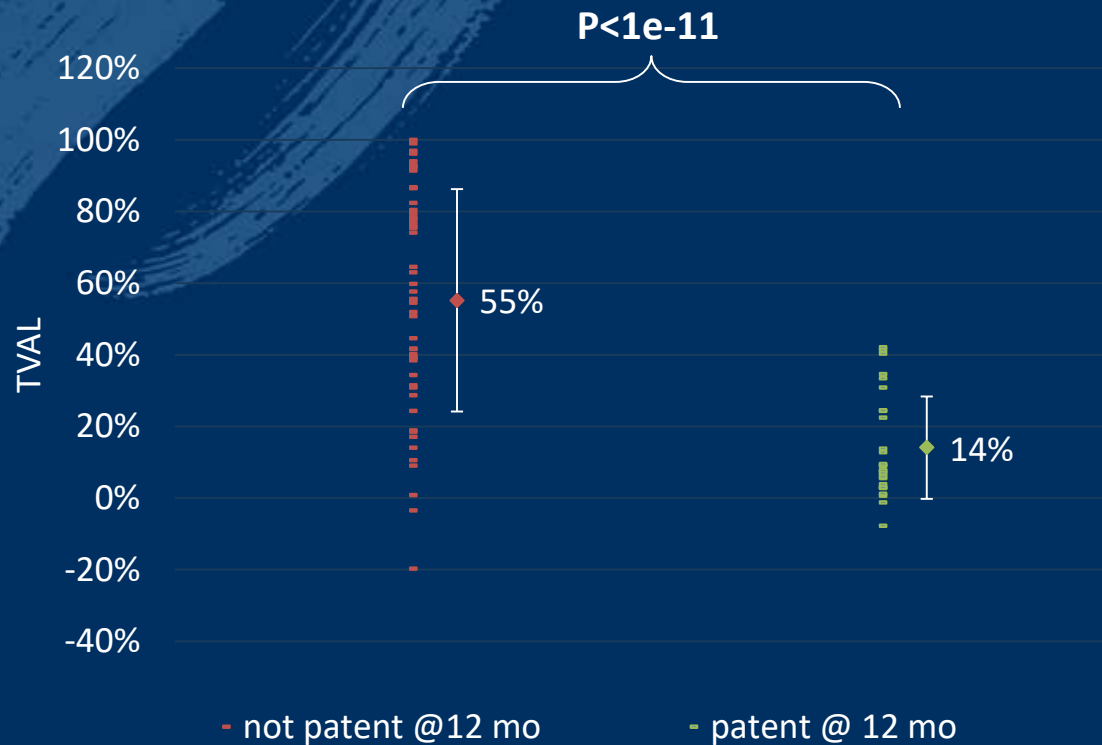
- Primary Patency
 - Freedom from CD-TLR
 - Freedom from DUS occlusion
 - Freedom from angiographic evidence of >95% narrowing
 - Freedom from major amputation due to ischemia
- Sustained Clinical Benefit
 - Sustained improvement of at least one Rutherford Category vs. pre-procedure baseline
 - Freedom from CD-TLR
- TVAL is taken at 6 months or prior to 6-months if during a CD-TLR

Correlation of TVAL to Clinical Endpoints: Subjects

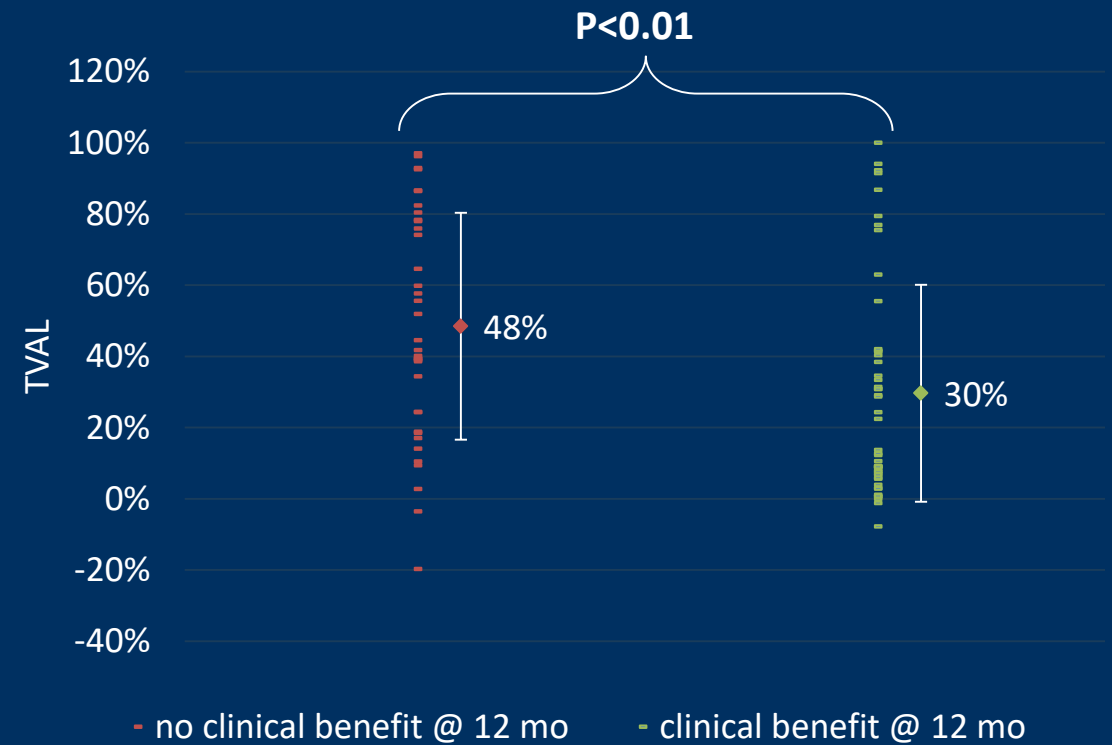
Characteristic	All Subjects	Characteristic	All Subjects
N	130	Rutherford 3	17 (13%)
Age (years)	70.6 ± 9.5	Rutherford 4	53 (41%)
Male	92 (71%)	Rutherford 5	55 (42%)
Black or African Descent	27 (21%)	Rutherford 6	5 (4%)
Caucasian	99 (77%)	ABI	0.84 ± 0.36
Obesity (BMI ≥ 30 kg/m ²)	49 (38%)	Lesion Length (cm)	11.0 ± 7.1
CAD	77 (59%)	TASCII A	36 (28%)
Diabetes Mellitus	87 (67%)	TASCII B	22 (17%)
Hyperlipidemia	113 (87%)	TASCII C	29 (23%)
Hypertension	119 (92%)	TASCII D	41 (32%)
Tobacco Use (Current)	24 (18%)	Severe Calcification	14 (11%)
		Total Occlusion at Baseline	46 (35%)

Correlation of TVAL to Clinical Endpoints

6-month TVAL vs. 12-month Primary Patency in TANGO and LIMBO-ATX

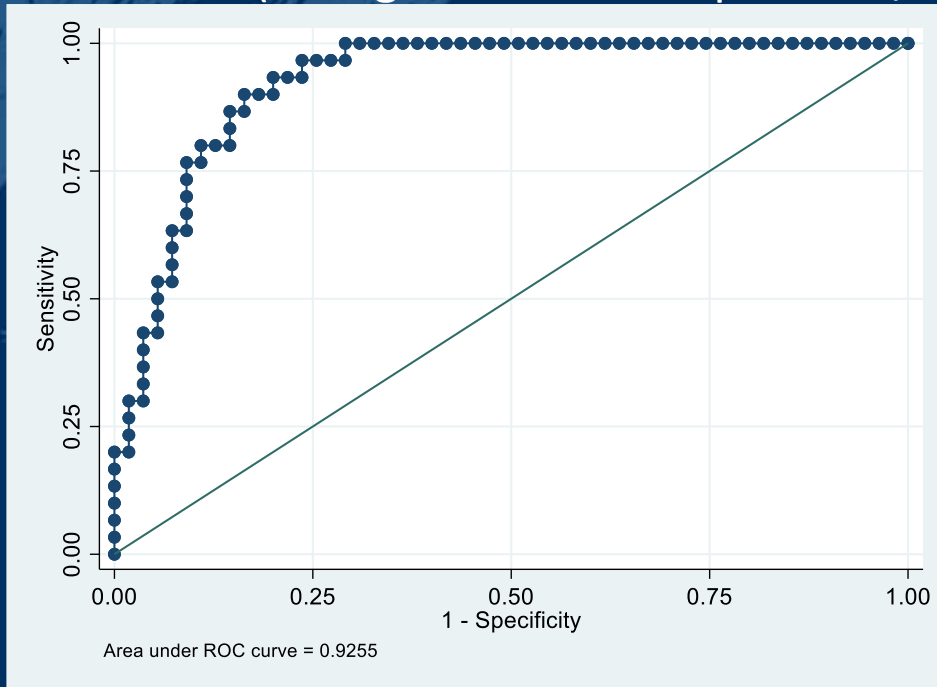


6-month TVAL vs. 12-month Sustained Clinical Benefit in TANGO and LIMBO-ATX



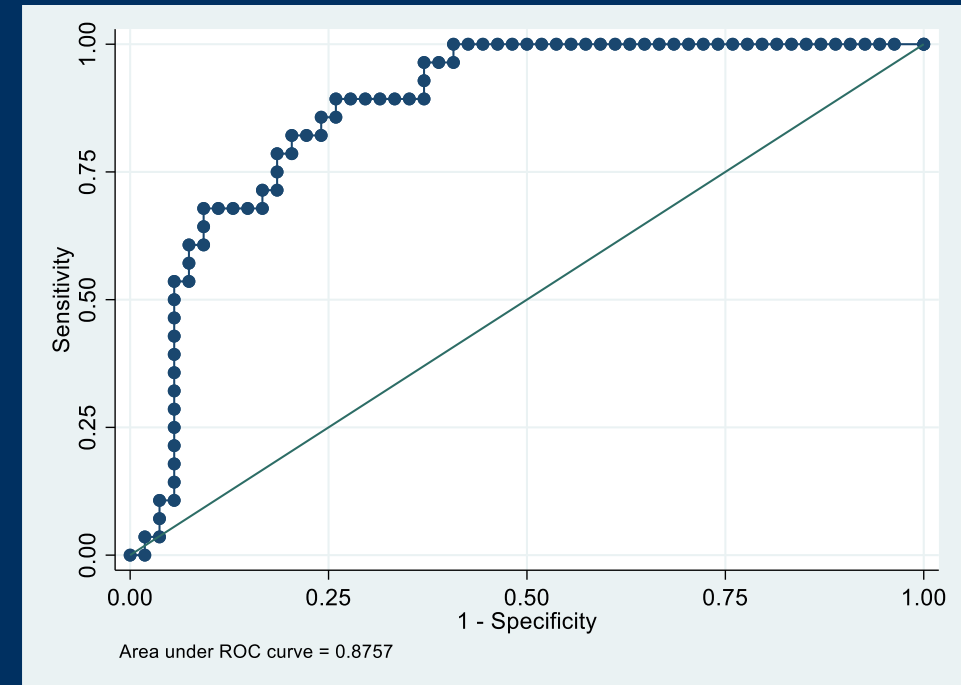
Correlation of 6-mo TVAL to 12-mo Patency

- ROC Curve for Predicting 12-mo Patency Given 6-mo %LLL (change in %DS from post to f/u)



- With an area under ROC curve of 0.9-1.0, change in % diameter stenosis (post-revasc to 6-mo f/u) is an excellent predictor of 12-month patency.
- This result seems obvious, since high %DS indicates loss of patency.

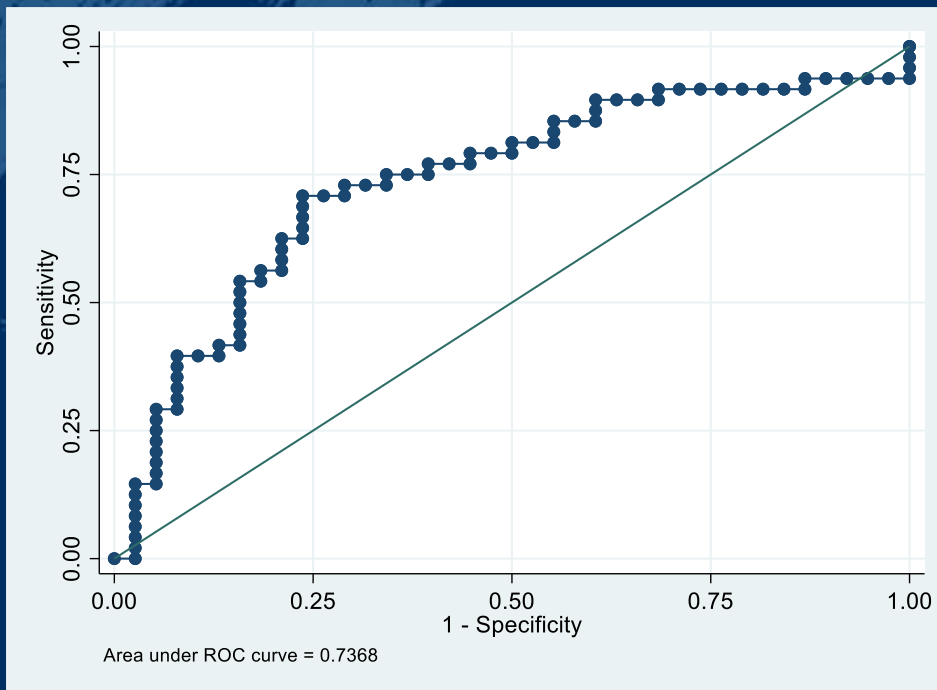
- ROC Curve for Predicting 12-mo Patency Given 6-mo TVAL



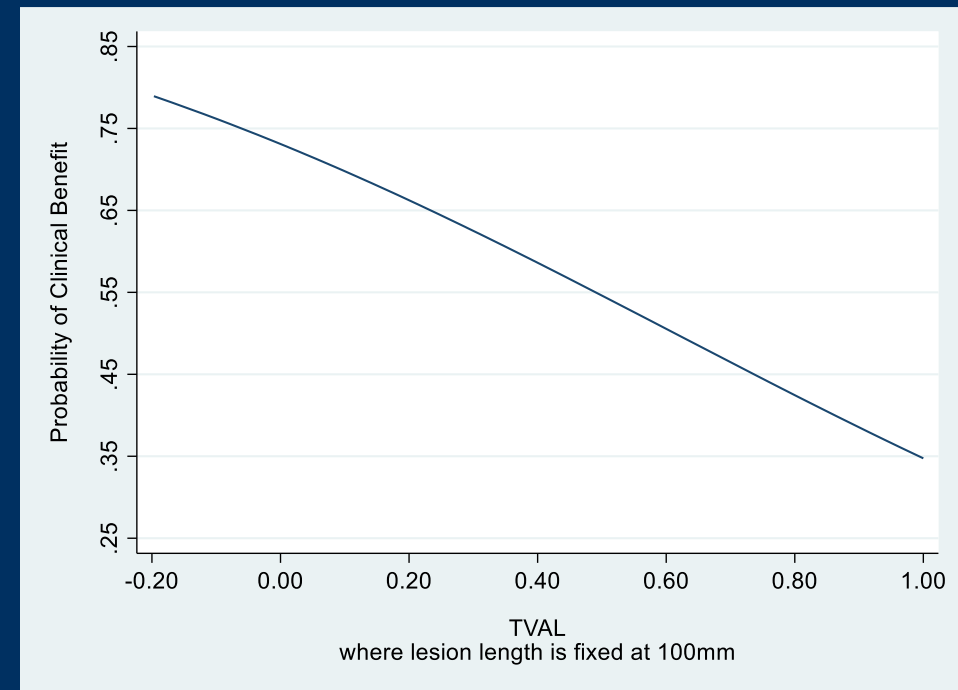
- With area under ROC curve of 0.8-0.9, 6-month TVAL is a good predictor of 12-month patency.
- This result indicates that the average neointimal volume at 6 months predicts long term loss of patency.

Correlation of 6-mo TVAL to 12-mo Clinical Endpoints

ROC Curve for Predicting 12-mo Clinical Benefit Using 6-mo TVAL and Lesion Length



Probability of 12-mo Clinical Benefit versus 6-mo TVAL



- With an area under ROC curve of 0.7-0.8, 6-month TVAL is a fair predictor of 12-month clinical benefit.
- This result indicates the linkage between neointimal hyperplasia and clinical outcomes.

- Measurable changes in 6-month TVAL correlate to meaningful changes in 12-month clinical benefit.

Conclusions

- There are statistically significant correlations between the quantitative vascular angiographic endpoint of 6-month TVAL and the 12-month endpoints of patency and clinical benefit
- Six-month TVAL is a fair predictor of 12-month clinical benefit
- Six-month TVAL is a good predictor of 12-month patency
- 6-month TVAL is a powerful tool to assess the biological response to therapy and can be key in determining programs to advance forward to pivotal studies

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