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Effect of Optimal Medical Therapy: BEST-CLI Trial

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DISCLOSURES

NO FINANCIAL DISCLOSURES

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Surgery or Endovascular Therapy for Chronic Limb-Threatening Ischemia

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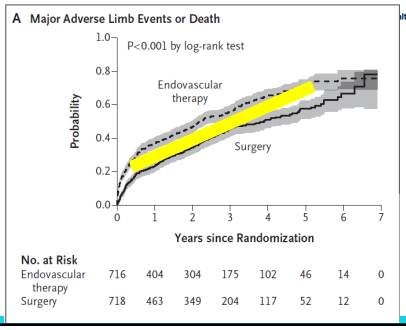
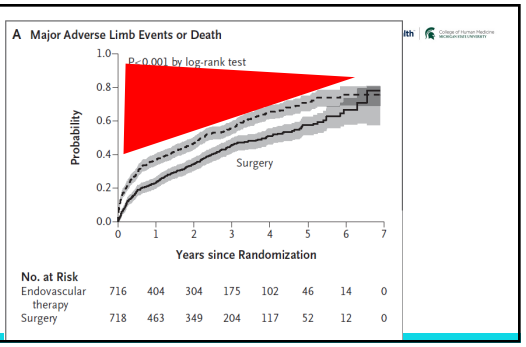
Background and Objectives

- The use of guideline-directed optimal medical therapy (OMT) is considered a cornerstone of treatment in patients with chronic limb threatening ischemia (CLTI).
- The Best Endovascular vs Best Surgical Therapy in Patients with CLTI (BEST-CLI) compared revascularization strategies in patients with CLTI.
- In this pre-specified analysis, we studied the effect of OMT intensity on the outcomes of patients with CLTI.





Methods

- A multispecialty committee defined OMT criteria during the trial design.
- OMT included metrics that each received 1 point: hypertension management, lipid-lowering and anti-platelet medication use, and tobacco cessation.
- Patients were stratified by OMT scores from 0 to 4.
- OMT scores were assessed for the duration of the trial.
- The association of Major Adverse Limb Events (MALE), Major Adverse Cardiovascular Events (MACE), and death were examined.

OMT scoring

OMT Criteria	Points
Controlled blood pressure – <150/90 mmHg in patients aged >=60 – <140/90 in those aged <60 years	1
Not currently smoking	1
On at least 1 lipid lowering medication	1
On at least 1 antiplatelet agent	1
Controlled diabetes mellitus as evidenced by HbA1c < 7	*

*not used in further analyses due to missing values

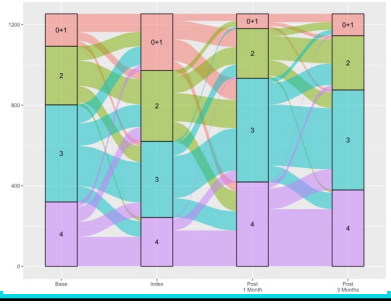
Results—Baseline Characteristics Stratified by OMT Score

Characteristics (Overall N = 1782)	Score 0 & 1 (N = 227)	Score 2 (N = 436)	Score 3 (N = 673)	Score 4 (N = 446)	P-Value
Demographic					
Age (Yrs)					
Mean ± SD	64.1±9.8 (227)	66.0±10.0 (436)	67.4±9.5 (673)	69.6±9.1 (446)	<.001
Median (Q1, Q3)	63.4 (58.5,70.7)	65.5 (59.6,72.8)	67.1 (60.9,74.0)	69.8 (63.9,75.2)	
(Min, Max)	(27.9,88.9)	(28.7,91.1)	(42.6,91.8)	(35.2,94.1)	
Gender					0.260
Male	68.3% (155/227)	69.5% (303/436)	72.1% (485/673)	74.4% (332/446)	
Female	31.7% (72/227)	30.5% (133/436)	27.9% (188/673)	25.6% (114/446)	
Medical History					
BMI (kg/m^2)					
Mean ± SD	26.4±5.7 (222)	27.8±6.0 (425)	28.0±6.0 (658)	28.8±5.9 (435)	<.001
Median (Q1, Q3)	25.5 (22.1,29.4)	26.9 (23.4,31.1)	27.3 (23.6,31.7)	28.0 (24.4,32.0)	
(Min, Max)	(16.4,46.8)	(14.4,49.5)	(15.8,51.9)	(14.3,52.5)	
Hypertension	75.3% (171/227)	84.2% (367/436)	89.7% (604/673)	92.8% (414/446)	<.001
Hyperlipidemia	38.8% (88/227)	67.0% (292/436)	81.0% (545/673)	87.7% (391/446)	<.001
Diabetes	51.5% (117/227)	68.6% (299/436)	71.6% (482/673)	76.2% (340/446)	<.001
Current smoking	74.4% (169/227)	54.8% (239/436)	33.7% (227/673)	0.0% (0/446)	<.001
Coronary artery disease	21.1% (48/227)	35.6% (155/436)	47.3% (318/673)	64.1% (286/446)	<.001
Congestive heart failure	3.5% (8/227)	3.2% (14/436)	6.2% (42/673)	9.2% (41/444)	<.001
Stroke	10.6% (24/227)	10.8% (47/436)	15.3% (103/673)	15.9% (71/446)	0.040
Chronic obstructive pulmonary disease	14.5% (33/227)	15.6% (68/436)	17.5% (118/673)	11.2% (50/446)	0.037
End-stage kidney disease	6.6% (15/227)	10.8% (47/436)	11.3% (76/673)	12.4% (55/445)	0.144

Multivariable Cox regression Models

Covariate (Effect) at baseline	MALE HR (95% CI), p-value	Major Reinterventions	MACE	Survival
Age (additional 10 years)	0.89(0.79,0.99),p=0.032	0.91(0.80,1.05),p=0.192	1.23(1.12,1.35),p<0.001	1.07(0.99,1.16),p=0.098
CHF	1.43(0.97,2.12),p=0.072	1.36(0.83,2.21),p=0.219	1.71(1.27,2.31),p<0.001	1.60(1.22,2.11),p=0.001
ESRD	1.44(1.05,1.98),p=0.023	0.91(0.58,1.43),p=0.686	3.21(2.55,4.04),p<0.001	1.96(1.57,2.44),p<0.001
Female Sex	0.83(0.65,1.06),p=0.133	0.87(0.65,1.16),p=0.337	0.96(0.79,1.17),p=0.708	0.86(0.73,1.03),p=0.100
Infrapopliteal Disease	1.11(0.88,1.40),p=0.365	0.88(0.68,1.16),p=0.369	1.12(0.93,1.36),p=0.230	1.14(0.96,1.35),p=0.127
Prior Infrainguinal Revascularization	1.07(0.70,1.63),p=0.765	1.13(0.68,1.87),p=0.646	1.19(0.85,1.66),p=0.321	1.19(0.89,1.59),p=0.241
Randomized to Open Surgery	0.52(0.42,0.65),p<0.001	0.41(0.31,0.54),p<0.001	0.91(0.77,1.08),p=0.298	0.70(0.60,0.82),p<0.001
OMT Score (3/4 vs 0/1)	0.74(0.57,0.96),p=0.023	0.73(0.54,1.00),p=0.051	0.92(0.73,1.16),p=0.471	0.82(0.67,1.01),p=0.063

OMT Score Migration—Alluvial Graph



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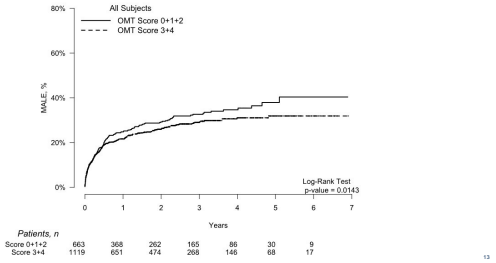
Kaplan-Meier curve of MALE in patients stratified by OMT Score 3/4 vs. OMT Score 0-2



13

Forest plot of MALE using time varying analysis

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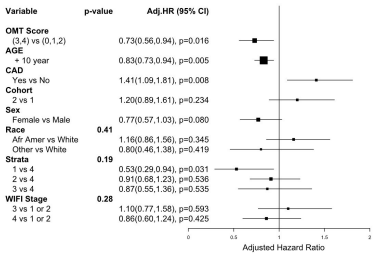

14

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Conclusions

- In a clinical trial setting of patients with chronic limb threatening ischemia, medical therapy use improved modestly early in a trial environment but was highly variable through the trial follow up.
- Higher OMT scores were associated with reduced risk of MALE and major reintervention in patients undergoing revascularization for CLTI.
- More intensive medical therapy was not associated with lower risk of MACE, including death.