





Endovascular theraphy for acute and critical limb ischemia.

Felix Damas De Los Santos. MD. MET. Instituto Nacional de Cardiología "Ignacio Chávez" Mexico City.









I, (Felix Damas De Los Santos) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.











- Introduction
- Definitions are important
- Objetives of the endovascular therapy
- State of guidelines
- Evidence supporting endovascular treatment
- DEB, DES and more
- Conclusions





Peripheral Arterial Disease 10-year-survival (ABI stratification)



McKenna M. Atherosclerosis 1991; 87: 119-28

ACC.



Coexistent vascular disease







Ness J et al. J Am Geriatr Soc. 1999;47:1255-1256



Atherosclerosis and more





Adapted from Stary HC et al. Circulation. 1995;92:1355-1374 and Fuster V. Vasc Med. 1998;3:231-239.





FINNVASC Risk stratification and CLI

Risk Factor	Points
Diabetes mellitus	1
Coronary artery disease	1
Foot gangrene	1
Urgent operation	1





JVasc Surg 2010;51:230-241



ACCESS REGISTRY Subgroup:







Andreas Gruentzig





Gruentzig et al. Die Erfhrung mit der perkutanen rekanalisation chronischer arteriellerverschülsse nach Dotter. Sweiz Med Wschr 1976, 106:422-424.





- Bypass surgery is a limb-preserving standard treatment modality for patients with critical limb ischemia (CLI).
- Recent technical advances have made endovascular treatment (EVT) an alternative first-line treatment for CLI.
- Heterogeneity in intervention indications, location of diseased vessels, clinical characteristics, procedural endpoints and EVT techniques.
- ALI: Embolism, graft oclusion, arteriovenous fistula oclussion



Critical limb ischemia

Defined as the presence of ischemic rest pain, and ischemic lesions, organ gangrene objectively attributable to arterial occlusive disease.



Acute limb ischemia



The sudden onset or worsening of ischemic manifestations within the lower extremities due to arterial thrombosis or embolism.











Table 1 Definition of Endpoint Measures for the Critical Limb Ischemia Objective Performance Goals

Outcomes	Definition		
MALE	Major adverse limb event: above-ankle amputation of the index limb or major reintervention (new bypass graft, jump/ interposition graft revision, or thrombectomy/thrombolysis)		
nd primae	erv patency secondary paten		
restenos	sis rate etc And more		
Amputation	Above ankle amoutation of the index limb		
Anputation	Amputation-free survival: above-ankle		
AIU	amputation of the index limb or death (any cause)		
RAO	amputation of the index limb or death (any cause) Any reintervention or above-ankle amputation of the index limb		
RAO	amputation of the index limb or death (any cause) Any reintervention or above-ankle amputation of the index limb Any reintervention, above-ankle amputation of the index limb, or stenosis		



Α



Consistency of endpoints







Criteria for a complete evaluation of



- **a revascularization technique.** High Feasibility: evaluated in a series of consecutive patients.
- Effectiveness: getting direct flow to the foot or significant rising in TcPO2 value.
- Clinical result: limb salvage in the large majority of cases.
- Repeatability: easy treatment of recurrences.
- Patient's acceptance .
- Low risk.



Affordable cost .





Catheterization and Cardiovascular Interventions 75: 433-443(2010)

Treiman GS, Copland S, McNamara RM, et al. Factors influencing ulcer healing in patients with combined arterial and venous insufficiency. J Vasc Surg. 2001;33(6):1158-1164.





SFA-popliteal artery: a complex segment





Two different aspects of a disease





Intermittent claudication

Critical limb ischemia



How to optimize the acute result of Proposed balloon inflation (>180 sec).

- Gradual high-pressure balloon dilatation.
- Dilatation using a correct balloon size.
- Use of stent (specific cases).
- Use of atherectomy devices (specific cases).





Circulation, 1994, Vol. 89, 1118-1125; Am J. Cardiol. 1996 May 15;77(12); 1062-6; Am Heart J. 1998 Apr;135(4):709-13; J.Vasc Interv Kadio 2002, 18355 359; P.Vasc Interv Radiol. 2002 Apr; 3(4):86(9); I.Cather Cardiovasc Diagn. 1993 Jul;29(3):199-202; Z.Kardiol, 1996 Apr;85(4): 273-80; Circulation. 1989, Vol. 80, 1029-1040; J.Am Coll Cardiol. 1989 Apr;13(5):1094-100; Am Heart J. 1996 May;131(5): Control Control Control Cardiol. 1989 Apr;13(5):1094-100; Am Heart J. 1996 May;131(5):



Goals of stent implantation



Imporve an inssufficient primary result .

 \star Residual stenosis.

*Extensive recoil

*Flow-limit dissection

- Improve long term Patency
- Avoid stent in bending areas and in segments situables as a landing zone (Bypass).

ESC guidelines on the diagnosis and treatment of peripheral artery diseases. European heart journal 2011.



The role of stent fractures













A variety of possible indications for revascularization for CLI.

- Risk of Amputation To reduce the level.
- Pain at Rest (present only in about 50% of ischemic ulcers).
 J Diabetes Complications. 1998;12:96-102.
- Ulcerations (often at the onset!), even healed.
- Symptomatic Claudication (often absent → Neuropathy !)
 Diabetes Care. 2001; 24:78-83.
- Decreased Transcutaneous Oxygen Tension (TcPO2 < 30-50mmHg)
 J Vasc Surg 31, 1, 2000.



State of guidelines ACCF/AHA

2005 Recommendations

Class I

S AN A DECK

For individuals with combined inflow and outflow disease with critical limb lschemia, inflow lesions should be addressed first. (Level of Evidence: C)

For individuals with combined inflow and outflow disease in whom symptoms of critical limb ischemia or infection persist after inflow revascularization, an outflow revascularization procedure should be performed (53). (Level of Evidence: B)

If it is unclear whether hemodynamically significant inflow disease exists, intra-arterial pressure measurements across suprainguinal lesions should be measured before and after the administration of a vasodilator. (Level of Evidence: C)

2011 Focused Update Recommendations

Class IIa

- For patients with limb-threatening lower extremity ischemia and an estimated life expectancy of 2 years or less or in patients in whom an autogenous vein conduit is not available, balloon angioplasty is reasonable to perform when possible as the initial procedure to improve distal blood flow (54). (Level of Evidence: B)
- For patients with limb-threatening ischemia and an estimated life expectancy of more than 2 years, bypass surgery, when possible and when an autogenous vein conduit is available, is reasonable to perform as the initial treatment to improve distal blood flow (54). (Level of Evidence: B)

Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, Golzarian J, Gornik HL, Halperin JL, Jaff MR, Moneta GL, Olin JW, Stanley JC, White CJ, White JV, Zierler RE. 2011 ACCF/AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011;58:2020–45



State of guidelines ESC CLI



Recommendations for the management of critical limb ischaemia

Recommendations	Class ^a	Level ^b	Ref ^c
For limb salvage, revascularization is indicated whenever technically feasible.	ŕ	A	302, 331, 336
When technically feasible, endovascular therapy may be considered as the first-line option.	Шb	B	302, <mark>3</mark> 31
If revascularization is impossible, prostanoids may be considered.	lib	B	338, 339

*Class of recommendation.

^bLevel of evidence.

"References







State of guidelines ESC ALI



0	
Ċ.	
Za	
al	
n	
Ū	
JS	
Ð	

Grade	Category	Sensory loss	Motor deficit	Prognosis
I.	Viable	None	None	No immediate threat
IIA	Marginally threatened	None or minimal (toes)	None	Salvageable if promptly treated
IIB	Immediately threatened	More than toes	Mild/ moderate	Salvageable if promptly revascularized
₩ ▲	Irreversible	Profound, anaesthetic	Profound, paralysis (rigor)	Major tissue loss Amputation. Permanent nerve damage inevitable

Amputation

Recommendations	Class ^a	Levelb
Urgent revascularization is indicated for ALI with threatened viability (stage II).	Ŀ	A
In the case of urgent endovascular therapy, catheter-based thrombolysis in combination with mechanical clot removal is indicated to decrease the time to reperfusion.	Ë	8
Surgery is indicated in ALI patients with motor or severe sensory deficit (stage IIB).	Ţ	B
In all patients with ALI, heparin treatment should be instituted as soon as possible.	Ŀ	C
Endovascular therapy should be considered for ALI patients with symptom onset <14 days without motor deficit (stage IIA).	Ila	A

ESC guidelines on the diagnosis and treatment of peripheral artery diseases. European heart journal 2011.

ALUS EST EN 101

Patency rate of bypass grafting in CLI



Adam DJ, Bradbury AW. TASCII document on the management of peripheral arterial disease. Eur J Vasc Endovasc Surg. 2007;33(1):1-2.

ACC.13









J Vasc Surg;54:100-8, 2011





BASIL: Intention to treat







BASIL: BTR Amputation free survival





JVasc Surg 2010;51:18S-31S



BASIL: Angiographic score and survival model predictors

Table I. Bollinger scoring matrix^a

Ser		Severity			
Occlusion	Stenosis >50%	Stenosis 25-49%	Plaques <25%	Extent of disease	
	4	2	1	Single lesion	
13	5	3	2	Multiple lesions affecting less than half the segment	
15	6	4	3	Multiple lesions affecting more than half the segment	J Vasc Surg 2010;51:32S-42

	Use menus or enter values	in blue cells to de	scribe the case of	interest
Notes	Patient characteristics		Results	
	Tissue loss	Yes	Time from decision	Proportion
	BMI	20-25	6 months	71%
	Creatinine	low	1 year	57%
	Lower Bollinger Score	5 or over	2 years	40%
Enter 40 if below 40 and 95 if over 95	Age	79		
	Smoking	Ex smoker		
	Any history of MI/angina	hist of mi		
	Any history of stroke/TIA	no history of stroke/TIA		
Ankle pressure measurements attempted at Dorsal pedis or Posterior tibial and perforating peroneal	Number of ankle pressures measured*	0		
Enter 0 if no ankle pressures obtained	Ankle Pressure (highest obtained in mmHg)	0		



J Vasc Surg 2010;51:52S-68S

13















OLIVE Registry Baseline characteristics -3



Lower limb characteristics	mean ±SD(n)	n (%)
Prior history of intermittent		150(48%)
claudication		130(40%)
Rutherford classification		
R4/R5/R6		38(12%)/228(73%)/46(15%)
Tissue loss		274(88%)
Location of wound		
Digit		177(57%)
Dorsal surface		30(10%)
Plantar surface		86(28%)
Calcaneal		39(13%)
Multiple ischemic wounds		62 (20%)
Wound infection		48(15%)
Ankle brachial index(ABI)	0.70±0.22(263)	
ABI >=0.9 / ABI <0.4		51(19%)/16(6%)
Skin perfusion pressure (SPP)		11 AM 40 -
Dorsal surface	26±12(285)	
Plantar surface	30±16(282)	
Activities of Daily Living (ADL) before	revascularization	
Ambulatory/Wheel ch Bedridden	air/	37(12%)/188(63%)/74(25%)

Circ Cardiovasc Interv. 2013;6:00-00 Ahead of print



OLIVE Registry



TASC classification for lesions



Circ Cardiovasc Interv. 2013;6:00-00 Ahead of print



OLIVE Registry





Freedom from major amputation







Freedom from reintervention



Freedom from major amputation or reintervention

Circ Cardiovasc Interv. 2013;6:00-00 Ahead of print



Multivariate Analysis

	HR (95%CI)	p-value
AFS	HR (95%CI)	p-value
BMI<18.5	2.22 (1.23-4.01)	0.008*
Statin administration	0.59 (0.30-1.13)	0.11
Anemia	1.80 (0.97-3.32)	0.06
Heat failure	1.73 (1.02-2.91)	0.04*
Wound infection	1.89 (1.07-3.32)	0.02=
MALE		
Hernodialysis	1.98 (1.23-3.20)	0.005*
Heart failure	1.69 (1.08-2.66)	0.02*
Rutherford classification 6	2.25 (1.36-3.74)	0.002*
One straight line to foot	0.55 (0.23-1.28)	0.16
Fime to wound healing		
BMI<18.5	0.54 (0.31-0.96)	0.03*
Hemodialysis	0.79 (0.58-1.09)	0.15
Wound infection	0.60 (0.36-0.98)	0.04*



OLIVE Registry

*Statistically significant Post-EVT AFS



Assigned to one of three risk groups based on the number of risk factors; Low [0]; Moderate [1]; High [2-3].

Circ Cardiovasc Interv. 2013;6:00-00 Ahead of print

SOLA



30 day morbidity differences: A=Endovascular. B=Surgical.



Study name	Time point	Statistics for each study			
		Odds ratio	Lower limit	Upper limit	p-Value
Scali	2011	13,514	4,641	39,348	0,000
Lepantalo	2009	0,957	0,284	3,227	0,944
Chong	2009	5,116	2,642	9,907	0,000
Dosluoglu	2008	3,525	0,674	18,445	0,136
Kedora	2006	0,628	0,132	2,991	0,559
BASIL trial	2005	1,414	0,974	2,053	0,069
BASIC trial	2004	5,714	0,596	54,824	0,131
Blair	1989	11,214	0,605	208,012	0,105
		2,926	1,336	6,410	0,007

Odds ratio and 95% Cl



Meta Analysis

а



JVasc Surg 2013; 57:242-53.



Biondi-Zoccai G, et al, Drug-eluting balloons for peripheral artery disease: A metaanalysis of 7 randomized clinical trials and 643 patients, Int J Cardiol (2013), <u>http://dx.doi.org/10.1016/j.ijcard.2013.01.247</u>

DEB in PAD Amputations

Biondi-Zoccai G, et al, Drug-eluting balloons for peripheral artery disease: A metaanalysis of 7 randomized clinical trials and 643 patients, Int J Cardiol (2013), <u>http://dx.doi.org/10.1016/j.ijcard.2013.01.247</u>

DES: Destiny Trial

Acute limb ischemia

The multivariable model for primary patency loss.

Measure	Level	Hazard ratio (95% CI)	P value vs reference	P value overall
Dialysis	Yes	3.66 (2.35, 5.71)	<.001	<.001
Graft thrombus	Yes	2.57 (1.24, 5.33)	.012	.012
Location ^a	Fempop	2.63(1.13, 6.12)	.025	.024
	Tibial	2.80 (1.09, 7.21)	.033	1400.04000
	Multilevel	1.03 (0.38, 2.80)	.95	
Technical success	Yes	0.25 (0.11, 0.56)	<.001	<.001

J Vasc Surg 2011;53:340-6.

Acute limb ischemia

V. vanWeel,R.B. vanTongeren,V.W.M. van Hinsbergh, J.H.vanBockel ,and P.H .A.Quax. Vascular Growth in Ischemic Limbs: A Review of Mechanisms and Possible Therapeutic Stimulation Ann Vasc Surg 2008;22:582-597

Reference	Thase	Tatiers:	#	Tactor	Delivery	Beneficial	Parameter(s)
With cont	rol group				4		
132	νn	сц	45	BMC	IM	Yes	ABL TcO2, pain-free walking time, angiography on 27 of 45 patients
134	μn	сц	14+14	G-CSF mobilized PBMC	IM	Yes	Ulter healing, limb salvage, Alit, laser Doppler flow, angiography
135	νn	си	14+15	BMC	IM	No	No improvement in ABI, TeO ₂ , angiography; marginally improved ulter healing and timb salvage
136	1/11	1C	13+12	EMC	Combined IM + 1A	Yes	ABI, pain-fmr walking distance, capillary-venous oxygen saturation, venous plethysmography
Without o	ontrol gro	up					
137	μn	CIJ and IC	8	BMC	IM	Varying	Rest pain, ulcer healing, skin temperature, Allf, andography
138	1/11	CLI	7	BMC	IM	Yes	ABL, TcO2, pain-free walking time
133	ν n	сц	12	BMC	IM	Yes	ABI, pain-free walking time, VAS, *****Tc-TF perfusion scintigraphy
139	3/11	CLI and IC	8	BMC	IM	Varying	ABL TOO2
140	1/11	CU	7	G-CSF mobilized PBMC	IA	Yes	ABL TcO ₅ , pain-free walking distance, pain score
341	1/11	CII and IC	152	G-CSF mobilized PBMC	IM	Varying	Ulter healing, limb salvage, ABL TcO2
142	νп	CII and IC	29	G-CSF mobilized PBMC	IM	Varying	Ulter healing, limb salvage, pain score, ABI, walking distance
143	1/11	CII and IC	8	BMC	Combined IM + IA	Yes	ABI, pain-free walking distance, capillary-venous oxygen saturation
144	1/11	cu	26	BMC	IM	Yes	Ulter healing, ABI, VAS, peak walking time, quality of life, angiography
145	1/11	CU	8	BMC	IM	Varying	Ulter healing, ABL VAS, angiography
146	π	CII and IC	92	G-CSF mobilized PBMC	IM	Varying	Limb salvage, thermography, plethysmography, CT anglography
147	1/11	CLI	7	BMC (6) PBMC (1)	IM	Varying	ABL TOOD, VAS
148	1/11	CLI	14	BMC	IM	Yes	Ulcer healing, pain score

Table III. Overview of cell-based clinical trials in patients with peripheral arterial disease

CONCLUSION

- Two entities with very different forms of treatment.
- ALI: Endovascular treatment with thrombolysis and thrombectomy devices as first line of treatment. <48 Hrs and <14 days.
- CLI: Advances in technology will made the endovascular therapy the first option of treatment
- Keep in mind DEB and DES

CONCLUSION

- Criotherapy ?
- Spinal cord stimulation?
- Prostanoids?
- Gene and cell therapy?
- Still there is too much to do

THANK YOU

