

Minicorso GISE:
Interventistica per gli arti inferiori
e per il piede diabetico

**Follow-up Clinico e Trattamento Post-
Rivascolarizzazione Percutanea**

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DISCLOSURE

- **Consultant:** Boston Scientific, Cordis, Mediolanum Cardio Research
- **Lecture fees:** Bristol-Myers Squibb



LEARNING GOALS

- Goals of post-PTA management
- Pharmacologic strategies
- Non-pharmacologic strategies



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- Pharmacologic strategies
- Non-pharmacologic strategies



SURGERY WITHOUT ARTERIAL REVASCULARIZATION IS NOT ENOUGH...





...BUT REVASCULARIZATION ALONE IS OFTEN NOT ENOUGH





ARE YOU SATISFIED WITH CURRENT RX?

Balloon angioplasty of popliteal and crural arteries in elderly with critical chronic limb ischemia

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Abstract

Objective: Elderly patients with extensive infrainguinal peripheral vascular disease and critical chronic limb ischemia (CCLI) are poor surgical candidates. Our purpose was to evaluate angiographic and clinical results of popliteal, infrapopliteal, and multi-level disease percutaneous transluminal angioplasty (PTA) in such patients. *Design:* Retrospective study of angiographic and clinical files in selected group. *Materials and methods:* Between 1996 and 2002, 38 elderly patients aged 80–94 years old (mean age 83.3) with critical leg ischemia were treated with PTA. All patients were at high surgical risk. 31/38 (81.5%) patients had chronic non-healing wounds, and 14/38 (37%) had multi-level disease of superficial femoral, popliteal and crural arteries. One hundred and two lesions were treated by angioplasty. Immediate angiographic and 1 year clinical results were retrospectively analyzed. *Results:* The overall procedural success rate was 32/38 (84.2%). There were three major complications (7.9%), but no deaths, and three technical failures, all were of infrapopliteal lesions. After 1 year, 27 patients could be followed, five patients died during the first year of unrelated causes. Twenty-three patients (85.2%), were clinically re-occluded within 1 year but complete and partial wound healing was achieved in 80% (16/20) and rest pain improvement in 57% (4/7), so that overall limb salvage was 74% (20/27). *Conclusions:* Elderly patients with multi-level CCLI have a short patency term following angioplasty of 14.8% after 1 year. Nevertheless, this temporary vascular patency enables wound healing or improvement in 74% of these patients, thus such endovascular interventions are recommended in this age group.

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Risk Factors Leading To Arterial Occlusion Following Diagnostic Arteriography*

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Objectives: *Arteriography may precipitate occlusive complications in stenotic vessels by a toxic effect on the vascular endothelium, leading to intra-arterial thrombosis. The aim of this retrospective study was to determine the incidence of arterial occlusion following arteriography,*

Methods: *We studied 101 consecutive patients (71 male, 30 female; median age 72 years) undergoing percutaneous transluminal angioplasty (PTA) of stenotic lesions, which had been identified on diagnostic arteriograms performed a median of 109 days (range 6–519) previously. One hundred and thirty-one arterial stenoses suitable for PTA were identified in the patient cohort.*

Results: *Seventeen patients (17%) progressed to occlusion in the period between diagnostic arteriography and PTA. Stenoses in the femoro-popliteal segment (21%) progressed to occlusion more frequently than lesions of the iliac arteries (3%). Independent risk factors were analysed to determine the risk factors predisposing to arterial occlusion following diagnostic arteriography. Both groups were well matched for age and sex. The mode of presentation, the presence of ischaemic heart disease, hypertension, diabetes or current smoking habits did not predict progression of disease to arterial occlusion. However, the rate of occlusion appeared to be influenced by the proportion of patients taking anti-platelet medication (51% in non-occluders as compared to 11% in patients who occluded, 95% CI 0.1 to 10), and to the length of time between arteriography and PTA (median of 92 days in non-occluders as compared to 125 days in patients who occluded, 95% CI 21 to 57).*

Conclusions: *These data demonstrate that occlusion of pre-existing arterial stenoses following diagnostic arteriography is significantly more frequent in patients not taking anti-platelet medication and when the time interval between arteriography and PTA exceeds 92 days. To minimise thrombotic arterial occlusion both diagnostic and therapeutic procedures should be performed simultaneously, but if a delay is unavoidable, patients should be treated with anti-platelet medication, which reduces the incidence of arterial occlusion.*



LEARNING GOALS

- Goals of post-PTA management
- **Pharmacologic strategies**
- Non-pharmacologic strategies



MEDICAL THERAPY: PIVOTAL EVEN AFTER SURGERY

EFFECT OF TICLOPIDINE ON THE LONG-TERM PATENCY OF SAPHENOUS-VEIN BYPASS GRAFTS IN THE LEGS

JEAN-PIERRE BECQUEMIN, M.D., FOR THE ETUDE DE LA TICLOPIDINE APRES PONTAGE FEMORO-POPLITE
AND THE ASSOCIATION UNIVERSITAIRE DE RECHERCHE EN CHIRURGIE*

NEJM
1997

ABSTRACT

Background Optimal therapy to prevent late occlusion of arterial bypass grafts in the legs has not been determined. We assessed the effect of ticlopidine, an inhibitor of platelet aggregation, on the long-term patency of saphenous-vein bypass grafts for the treatment of peripheral vascular disease.

Methods A total of 243 patients with femoropopliteal or femorotibial saphenous-vein bypass grafts were randomly assigned to receive either ticlopidine (250 mg twice a day) or matching placebo for two years. The primary end point was graft patency at two years, as assessed by physical examination, measurement of the ankle brachial index, and duplex ultrasonography or arteriography. The incidence of death and major ischemic events was also analyzed in the two groups.

Results After two years, 66.4 percent of the patients were alive with a patent graft in the ticlopidine group, as compared with 51.2 percent in the placebo group (95 percent confidence interval for the difference between the two groups, 2.9 to 27.4 percent; $P=0.02$). The two-year cumulative patency rate was 82 percent in the ticlopidine group and 63 percent in the placebo group ($P=0.002$). There was no significant difference between groups in overall mortality or major ischemic events.

Conclusions Ticlopidine significantly improved the long-term patency of saphenous-vein bypass grafts in the legs. Since the drug was well tolerated, its use can be recommended after peripheral-vein bypass surgery. (N Engl J Med 1997;337:1726-31.)

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or to deterioration of the graft itself. Stenosis is generally due to the development of fibrous intimal hyperplasia, which thickens the vessel wall, reducing the effective size and compliance of the lumen,² or to the progression of atherosclerosis. The mechanisms of endothelial hyperplasia are complex and not fully understood, but the adhesion of platelets to the damaged endothelial cell layer and their subsequent activities may play a part. Treatment with platelet-inhibiting drugs, especially aspirin, has been investigated as a way of improving the patency of saphenous-vein grafts. Multicenter randomized trials have shown that aspirin with or without dipyridamole increased the immediate and long-term patency of aortocoronary saphenous-vein grafts.³⁻⁶ However, clinical studies have failed to establish the efficacy of aspirin, with or without dipyridamole, or of oral anticoagulation in femoropopliteal bypass with autologous-vein grafts.⁷⁻¹¹ Therapy with ticlopidine, an inhibitor of platelet aggregation, increases the distance that patients are able to walk¹²; reduces the rate of death, myocardial infarction, and stroke; and reduces the need for reconstructive arterial surgery of the leg in patients with intermittent claudication.¹³⁻¹⁶ Moreover, as compared with placebo, ticlopidine increases the immediate and one-year patency of aortocoronary bypass grafts.^{17,18} We undertook the present study to determine whether ticlopidine could reduce the rate of late occlusion of saphenous-vein grafts below the knee.



IMPROVING PATENCY AFTER PTA

Background

Peripheral arterial disease (PAD) is frequently treated by balloon angioplasty. Restenosis/reocclusion of the dilated segments occurs often depending on length of occlusion, lower leg outflow, stage of disease and presence of cardiovascular risk factors. To prevent reocclusion, patients are treated with antithrombotic agents.

Objectives

To determine whether any antithrombotic drug is more effective in preventing reocclusion after peripheral endovascular treatment, compared to another antithrombotic drug, no treatment, placebo, or other vasoactive drugs.

Search strategy

We searched the Cochrane Peripheral Vascular Diseases Group's trials register (last searched April 2004), the Cochrane Central Register of Controlled trials (CENTRAL Issue 2, 2004), MEDLINE and EMBASE (last searched June 2004).

Selection criteria

Randomised trials were categorised as A (double or single blinded) or B (not blinded). Participants included patients with symptomatic PAD treated by endovascular revascularisation of the pelvic or femoropopliteal arteries. Interventions were anticoagulant, antiplatelet or other vasoactive drug therapy compared with no treatment, placebo, or any other vasoactive drug. Clinical endpoints were re-obstruction, amputation, death, myocardial infarction, stroke and major bleeding.

Data collection and analysis

Details of the number of randomised patients, treatment, study design, study category, allocation concealment and patient characteristics were extracted. Analysis was based on intention-to-treat data. To examine the effects of binary outcomes such as amputation and major bleeding, odds ratios were computed using a fixed effect model. The 95% confidence intervals of the effect sizes were calculated.

Main results

A 60% reduction of recurrent obstruction was found with aspirin (ASA) 330 mg combined with dipyridamol (DIP) as compared to placebo at 12 months follow-up. At six months following endovascular treatment, a positive effect on patency was found with 50 to 100 mg ASA combined with DIP (n = 356). However, this was not significant. ASA/DIP tended towards showing a superior effect on patency after femoropopliteal angioplasty compared with VKA at three, six, and twelve months. Periinterventional treatment with LMWH in femoropopliteal obstructions resulted in significantly lower restenosis/reocclusion rates than with unfractionated heparin.



MEDICAL THERAPY

Therapy	Frequency	Benefit
Supervised exercise program (116)	30–45 min 3 × /week	Comparable to cilostazol
Cilostazol (phosphodiesterase inhibitor); mechanism of benefit unknown (117)	100 mg BID	Improves walking distance: 40%–60%
Pentoxifylline (lowers blood viscosity by modifying red blood cell conformability); mechanism of benefit unclear (116,118)	400 mg TID	Improves walking distance: 20%–25%
Antiplatelet agents (118,119):		Decreases risk of MI, stroke and vascular death
Aspirin	75–325 mg QD	
Clopidogrel (aspirin-intolerant)	75 mg QD	
Risk factor modification (116,118,120):	Goals:	Decreases risk of MI, stroke, vascular death, and microvascular ischemic events
Blood pressure	BP <130/80 mm Hg	
Diabetes	HbA _{1c} <7%	
Lipids	LDL cholesterol <100 mg/dl	
Smoking	Cessation	

BID = twice a day; BP = blood pressure; HbA_{1c} = glycosylated hemoglobin; LDL = low-density lipoprotein; MI = myocardial infarction; QD = once daily; TID = three times a day.



MEDICAL TREATMENT OF PERIPHERAL ARTERIAL DISEASE

Table 2. Medical Treatment of Peripheral Arterial Disease

Indication	Intervention	Method/Comment
→ Improving leg symptoms	Smoking cessation ^{36,37}	Physician advice Nicotine replacement therapy Bupropion
	Exercise ^{41,42}	Consider structured exercise program
	Statin drugs ⁴⁴⁻⁴⁶	Benefit appears to be related to non-cholesterol-lowering properties of statins
	Blood pressure-lowering drugs ⁴⁹⁻⁵²	Angiotensin-converting enzyme inhibitors
	Cilostazol ⁵³	Contraindicated in patients with heart failure
→ Preventing systemic complications	Smoking cessation ^{37*}	
	Weight loss ^{77,78†}	Consider in overweight patients with peripheral arterial disease
	Lowering blood pressure ^{66,67}	Effect determined by magnitude of blood pressure lowering
	Angiotensin-converting enzyme inhibitors ^{66,67}	Possible benefits beyond blood pressure-lowering effect
	Lowering blood cholesterol level ⁷⁰	
Antiplatelet therapy ⁷⁹⁻⁸⁶	Aspirin, with clopidogrel as suitable alternative	

*No randomized evidence but based on convincing observational data.
†Efficacy unproven in randomized trials, but observational data are compelling.



EVIDENCE-BASED TREATMENTS

Table 3. Effects of Treatments for Improving Walking Ability in Patients with Claudication*

Claudication Treatments (Reference)	Number of Trials	No. of Patients		Change in Maximal Walking Time or Maximal Walking Distance		Difference in Maximal Walking Time or Maximal Walking Distance, Change between Treated and Control Patients (%)
		Control	Treated	Control	Treated	
Exercise rehabilitation						
Leng et al. (27)	6	56	64	5.8 min	12.3 min	6.5 min (112)
Girolami et al. (28)	5	55	58	338.2 m	599.6 m	261.4 m (77)
Pentoxifylline						
Girolami et al. (28)	7	279	288	264.4 m	370.6 m	106.2 m (40)
Hood et al. (29)	8	258	253	311.9 m	456.0 m	144.1 m (46)
Cilostazol						
Regensteiner and Hiatt (30)	6	730	740	50.0 m	100.0 m	50.0 m (100)
Graded Constant load				27.0 m	76.0 m	49.0 m (181)

Graded = treadmill protocol that increases in grade over time; constant load = treadmill protocol that maintains the same work load throughout the test.

* All trials included are positive meta-analyses in peripheral arterial disease, and include levels of evidence 1 or 2, or both. Pharmacologic treatments are included only if approved for use in the United States.



EVIDENCE-BASED TREATMENTS

Table 2. Effects of Treatments on Systemic Cardiovascular Morbidity and Mortality in Peripheral Arterial Disease

Therapy	Trial (Reference)	Primary Endpoint	Controls	Treated Patients	Relative Risk or Odds Ratio, with 95% Confidence Interval	Absolute Risk Reduction (%)	Number Needed to Treat
			n events/n subjects (%)				
Antiplatelet therapy							
Aspirin* [†]	ATC (patients with claudication) (19)	Composite endpoint of death, nonfatal MI, and stroke	195/1649 (11.8)	160/1646 (9.7)	OR = 0.78 (0.50–1.10) [‡]	2.1	48
Ticlopidine [§]	STIMS (20)	Composite endpoint of fatal or nonfatal MI, or stroke, and TIA	99/341 (29.0)	89/346 (25.7)	RR = 0.66 (0.45–0.96)	3.3	30
Ticlopidine [§]	EMATAP (21)	Cluster of outcome events: sudden death, fatal or nonfatal MI or stroke, and cardiovascular intervention	20/311 (6.4)	5/304 (1.6)	RR = 0.26 (0.10–0.67)	4.8	21
Clopidogrel [§]	CAPRIE (peripheral arterial disease subgroup only) (22)	Composite endpoint of MI, stroke, and vascular death	277/3229 (8.6)	215/3223 (6.7)	RR = 0.24 (0.09–0.36)	1.9	53
ACE inhibitor therapy							
Ramipril [§]	HOPE (23)	Composite endpoint of MI, stroke, and cardiovascular death	459/2085 (22)	316/1966 (16) [‡]	RR = 0.73 (0.61–0.86) [‡]	6.0	17
Lipid-lowering therapy							
Lipid lowering [†]	(25)	Mortality	8/268 (2.9)	2/269 (0.7)	OR = 0.21 (0.03–1.17)	2.2	45

* Similar nonsignificant results observed for peripheral angioplasty or peripheral grafts.

[†] Meta-analysis.

[‡] Data estimated from information in article.

[§] Positive trial in peripheral arterial disease.

^{||} Aspirin used as a control.

ATC = Antiplatelet Trialists' Collaboration; CAPRIE = Clopidogrel versus Aspirin in Patients At Risk of Ischemic Events; EMATAP = Estudio Multicéntrico Argentino de la Ticlopidine en las Arteriopatías Periféricas; HOPE = Heart Outcomes Prevention Evaluation; MI = myocardial infarction; OR = odds ratio; RR = relative risk; STIMS = Swedish Ticlopidine Multicentre Study; TIA = transient ischemic attack.



LACK OF BENEFITS FROM PROSTANOIDS

Recommendation 28. Use of prostanoids in critical limb ischemia (CLI)

- Previous studies with prostanoids in CLI suggested improved healing of ischemic ulcers and reduction in amputations [A].
- However, recent trials do not support the benefit of prostanoids in promoting amputation-free survival [A].
- There are no other pharmacotherapies that can be recommended for the treatment of CLI [B].



WAVE GOOD-BYE TO WARFARIN

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Oral Anticoagulant and Antiplatelet Therapy and Peripheral Arterial Disease

The Warfarin Antiplatelet Vascular Evaluation Trial Investigators*

ABSTRACT

BACKGROUND

Atherosclerotic peripheral arterial disease is associated with an increased risk of myocardial infarction, stroke, and death from cardiovascular causes. Antiplatelet drugs reduce this risk, but the role of oral anticoagulant agents in the prevention of cardiovascular complications in patients with peripheral arterial disease is unclear.

METHODS

We assigned patients with peripheral arterial disease to combination therapy with an antiplatelet agent and an oral anticoagulant agent (target international normalized ratio [INR], 2.0 to 3.0) or to antiplatelet therapy alone. The first coprimary outcome was myocardial infarction, stroke, or death from cardiovascular causes; the second coprimary outcome was myocardial infarction, stroke, severe ischemia of the peripheral or coronary arteries leading to urgent intervention, or death from cardiovascular causes.

RESULTS

A total of 2161 patients were randomly assigned to therapy. The mean follow-up time was 35 months. Myocardial infarction, stroke, or death from cardiovascular causes occurred in 132 of 1080 patients receiving combination therapy (12.2%) and in 144 of 1081 patients receiving antiplatelet therapy alone (13.3%) (relative risk, 0.92; 95% confidence interval [CI], 0.73 to 1.16; $P=0.48$). Myocardial infarction, stroke, severe ischemia, or death from cardiovascular causes occurred in 172 patients receiving combination therapy (15.9%) as compared with 188 patients receiving antiplatelet therapy alone (17.4%) (relative risk, 0.91; 95% CI, 0.74 to 1.12; $P=0.37$). Life-threatening bleeding occurred in 43 patients receiving combination therapy (4.0%) as compared with 13 patients receiving antiplatelet therapy alone (1.2%) (relative risk, 3.41; 95% CI, 1.84 to 6.35; $P<0.001$).

CONCLUSIONS

In patients with peripheral arterial disease, the combination of an oral anticoagulant and antiplatelet therapy was not more effective than antiplatelet therapy alone in preventing major cardiovascular complications and was associated with an increase in life-threatening bleeding. (ClinicalTrials.gov number, NCT00125671.)

The members of the writing group (Sonia Anand, M.D., Ph.D., F.R.C.P., Salim Yusuf, D.Phil., Changchun Xie, Ph.D., Janice Pogue, M.Sc., and John Eikelboom, M.B., B.S., McMaster University, Hamilton, ON, Canada; Andrzej Budaj, M.D., Ph.D., Grochowski Hospital, Warsaw, Poland; Bruce Sussex, M.D., M.B., B.S., Memorial University of Newfoundland, St. John's, Canada; Lisheng Liu, M.D., National Center of Cardiovascular Disease, Beijing; Randy Guzman, M.D., F.R.C.S., University of Manitoba, Winnipeg, Canada; Claudio Cina, M.D., Sp.Chir.It., F.R.C.S., Hamilton Health Sciences and St. Joseph's Hospital, Hamilton, ON, Canada; Richard Crowell, M.D., F.R.C.P., Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; Matyas Keltai, M.D., Ph.D., Hungarian Institute of Cardiology, Semmelweis University, Budapest, Hungary; and Gilbert Gosselin, M.D., Montreal Heart Institute, Montreal) assume responsibility for the overall content and integrity of the article. Address reprint requests to Dr. Anand at Hamilton General Hospital, Hamilton Health Sciences, 237 Barton St. East, Hamilton, ON L8L 2X2, Canada, or at anands@mcmaster.ca.

*The Warfarin Antiplatelet Vascular Evaluation (WAVE) trial investigators are listed in the Appendix.

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INTENSIVE DIABETES CONTROL

- Intensive diabetes control reduces the development of several complications including neuropathy
- Severe hyperglycaemia is associated with a higher risk for DFU



TREATMENT GOALS

Table 1. Risk Factors and Treatment Goals for Patients With Diabetes and PAD

Risk Factor	Relative Risk Increase for PAD	Treatment Goal
Smoking	2.5	Cessation
Diabetes	4.0	Glycosylated hemoglobin <7%
Dyslipidemia	1.1 (per 10 mg/dl increase)	Low-density lipoprotein <100 mg/dl*
Hypertension	1.5	Blood pressure <130/80 mmHg

*Consider <70 mg/dl.

PAD = peripheral arterial disease.



MANAGEMENT OF CVD/ PAD RISK FACTORS

A.

Antiplatelet agents: Aspirin +/- Clopidogrel
ACE-inhibitors (or ARB if ACE-I not tolerated)
Anti-coagulant therapy in selected individuals

B.

Blood pressure control of $<130/85$ mm Hg ($<130/80$ in DM)
Beta-blockers (Especially post-MI or with low LVEF)

C.

Cholesterol management (LDL <100 mg/dl, TG <150 mg/dl)
Cigarette smoking cessation

D.

Improved Diabetes/glycemic control
Improved Dietary habits and weight

E.

Exercise and education



ACC/AHA PAD GUIDELINES: ANTI-HYPERTENSIVE



- Beta-adrenergic blocking drugs are effective anti-hypertensive agents and are not contraindicated in patients with PAD *(Class I, Level of evidence A)*
- The use of ACE-inhibitors is reasonable for symptomatic patients with lower extremity PAD to reduce the risk of adverse cardiovascular events *(Class IIa, Level of evidence B)*



ACC/AHA PAD GUIDELINES: LIPID-LOWERING

- Treatment with a HMG-CoA reductase inhibitor (Statin) medication is indicated for all patients with PAD to achieve a target **LDL < 100 mg/dl** (*Class I, Level of evidence B*)
- Treatment with a HMG-CoA reductase inhibitor (Statin) medication to achieve a target **LDL < 70 mg/dl** is reasonable for patients with L.E. PAD at very high risk of ischemic events (*Class IIa, Level of evidence B*)
- Treatment with a fibric acid derivative can be useful for patients with PAD and low HDL, normal LDL, and elevated triglycerides (*Class IIa, Level of evidence C*)



ACC/AHA PAD GUIDELINES: ANTI-PLATELETS

- Antiplatelet therapy is indicated to reduce the risk of MI, stroke, or vascular death in individuals with atherosclerotic L.E. PAD *(Class I, Level of evidence A)*
- Aspirin, in daily dose of 75-325 mg, is recommended as safe and effective antiplatelet therapy to reduce the risk of MI, stroke, or vascular death in individuals with atherosclerotic L.E. PAD *(Class I, Level of evidence A)*
- Clopidogrel (75 mg per day) is recommended as an effective alternative antiplatelet therapy to aspirin to reduce the risk of MI, stroke, or vascular death in individuals with atherosclerotic L.E. PAD *(Class I, Level of evidence B)*



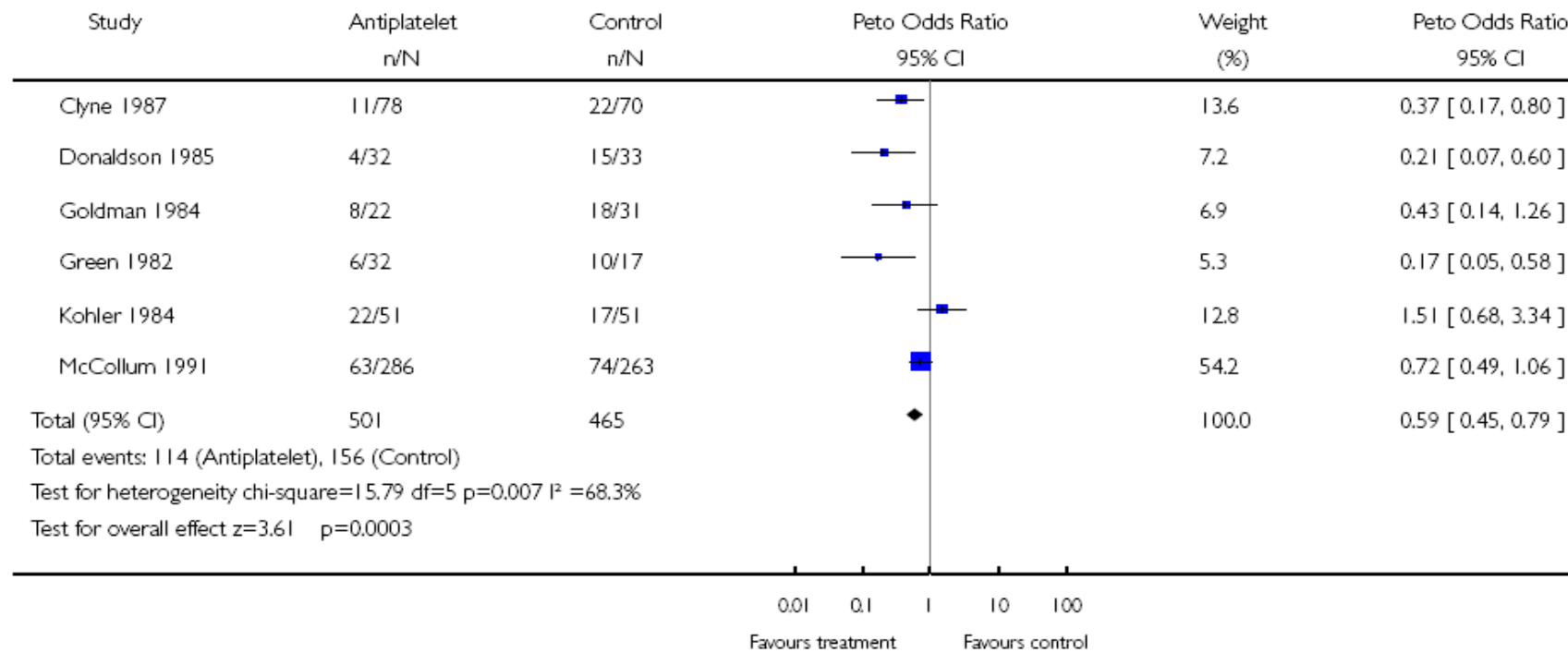
ANTIPLATELET THERAPY

Analysis 01.01. Comparison 01 ASA or ASA/DIP vs nothing, all grafts, Outcome 01 Primary graft patency at 12 months

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 01 ASA or ASA/DIP vs nothing, all grafts

Outcome: 01 Primary graft patency at 12 months





ACC/AHA PAD GUIDELINES: CILOSTAZOL

- Cilostazol (100 mg p.o. bid) is indicated as an effective therapy to improve symptoms and increase walking distance in patients with L.E. PAD and intermittent claudication (in the absence of heart failure) *(Class I, Level of evidence A)*
- Pentoxifylline (400 mg tid) may be considered as second-line alternative therapy to cilostazol to improve walking distance in patients with intermittent claudication *(Class IIb, Level of evidence A)*
- The clinical effectiveness of pentoxifylline as therapy for claudication is marginal and not well established *(Class IIb, Level of evidence C)*



LEARNING GOALS

- Goals of post-PTA management
- Pharmacologic strategies
- **Non-pharmacologic strategies**



SUPERVISED EXERCISE

Background

Although exercise therapy is considered to be of significant benefit to people with leg pain (intermittent claudication), almost half of those affected do not undertake any exercise therapy.

Objectives

To evaluate the effects of supervised versus non-supervised exercise therapy on the maximal walking time or distance for people with intermittent claudication.

Search strategy

The Cochrane Peripheral Vascular Diseases Group searched their Specialized Register (last searched November 2005) and the Cochrane Central Register of Controlled Trials (CENTRAL) database in *The Cochrane Library* (last searched Issue 4, 2005).

In addition, we handsearched the reference lists of relevant articles for additional trials. There was no restriction on language of publication.

Selection criteria

Randomized and controlled clinical trials comparing supervised exercise programs with non-supervised exercise programs for people with intermittent claudication.

Data collection and analysis

Two authors (BB and EMW) independently selected trials and extracted data. One author (BB) assessed trial quality and this was confirmed by a second author (MP). For all continuous outcomes we extracted the number of participants, the mean differences, and the standard deviation. If data were available, the standardized mean difference was calculated using a fixed-effect model.

Main results

We identified twenty-seven trials, of which 19 had to be excluded because the control group received no exercise therapy at all. The remaining eight trials involved a total of 319 male and female participants with intermittent claudication. The follow up ranged from 12 weeks to 12 months. In general, the supervised exercise regimens consisted of three exercise sessions per week. All trials used a treadmill walking test as one of the outcome measures. The overall quality of the included trials was good, though the trials were all small with respect to the number of participants, ranging from 20 to 59.

Supervised exercise therapy showed statistically significant and clinically relevant differences in improvement of maximal treadmill walking distance compared with non-supervised exercise therapy regimens, with an overall effect size of 0.58 (95% confidence interval 0.31 to 0.85) at three months. This translates to a difference of approximately 150 meters increase in walking distance in favor of the supervised group.



HOW TO EXERCISE FOR MAXIMAL BENEFIT?

- 21 studies included in meta-analysis
- Greatest improvement in pain distances occurred with:
 1. Exercise to near maximal pain
 2. At least 3 times per week
 3. Duration of at least 6 months
 4. Walking as exercise mode



FOOT INSPECTION

SHOES
and
SOCKS

take 'em off!



IF YOU HAVE DIABETES

Have your doctor check your feet.



AVOID FOOT TRAUMA





Preventive Tips for Patients

- Daily self-inspection:
 - Top, bottom, back, sides
 - Between toes!
- Keep feet clean and dry
- Cut or file toenails with shape of the toe, smooth all sharp edges
- For dry feet, moisturize with good topical product
- Avoid foot injury; see specialist if corns, calluses, ingrown toenails
- AVOID OTC products with keratolytics, other irritating compounds; avoid vasoconstricting agents





Preventive Tips for Patients

- Wear socks that are padded and “breath”; avoid thick seams; best material is acrylic and cotton or wool blend
- Wear shoes that fit well
- NEVER GO BAREFOOT!
- Check shoes daily for pebbles, cracks, etc.
- Surgical repair of structural problems
- If smoking, STOP!!!



COMPREHENSIVE MANAGEMENT

Sommario sul trattamento dell'ulcera del piede

<i>Obiettivi</i>	<i>Strategia</i>
• Migliorare la circolazione	Tecniche vascolari non invasive Angioplastica percutanea transluminale (PTA) Chirurgia vascolare
• Trattare l'edema	
• Controllo del dolore	Analgesici Alleviare l'ansia
• Trattamento dell'infezione	Antibiotici - Orale - Parenterale Cultura, biopsia Radiografia, TAC, Scintigrafia ossea, RMN
• Migliorare il controllo metabolico	
• Riduzione del carico	Calzature curative Plantari/ortesi Gessi a contatto totale/ stivaletti in resine polimeriche Stampelle Sedia a rotelle/riposo a letto
• Trattamento topico	Detersione Medicazione Agenti topici Trapianto di pelle
• Chirurgia del piede	Incisione/drenaggio Chirurgia correttiva Amputazione
• Condizioni generali	Trattamento cardiovascolare Trattamento della retinopatia/nefropatia Trattamento della malnutrizione Cessare di fumare
• Ambiente	Educazione paziente/staff Adesione Assistenza/follow-up Multidisciplinarietà



FOOT PRECAUTIONS

Ispezionare e lavare ogni giorno i piedi

Controllare la temperatura dell'acqua col gomito o col termometro

Asciugare bene ma delicatamente, eventualmente con phon

Usare calze che non stringano e cambiarle ogni giorno

Idratare il piede se secco con creme specifiche

Non usare callifughi o strumenti taglienti per le callosità

Tagliare le unghie con forbice a punte smusse, arrotondare con lima di cartone

Non camminare a piedi scalzi

Non usare fonti di calore dirette (borse d'acqua calda, calorifero, camino, etc)

Usare scarpe comode con punta rotonda e tacco non superiore a 4 cm

Quando si calzano scarpe nuove, controllare il piede dopo pochi minuti di cammino



POST-PTA FOOT/ANKLE MANAGEMENT

Sistema di classificazione del rischio

Classe	Descrizione del rischio	Frequenza del check-up
0	neuropatia sensitiva assente	una volta l'anno
1	neuropatia sensitiva	una volta ogni 6 mesi
2	neuropatia sensitiva e segni di vasculopatia periferica e/o deformità del piede	una volta ogni 3 mesi
3	pregressa ulcera	una volta ogni 1–3 mesi



HISTORY OR PHYSICAL EXAMINATION ARE UNRELIABLE

Does the Clinical Examination Predict Lower Extremity Peripheral Arterial Disease?

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CLINICAL SCENARIOS

In the following cases, the clinician would like to know if the patient has peripheral arterial disease (PAD).

Case 1

A 65-year-old man with a history of a myocardial infarction (MI) is referred for problems of deep calf pain in his right leg. This pain occurs when he walks farther than 1 city block and is relieved by rest in less than 10 minutes. On examination, you hear a bruit over his right common femoral artery.

Case 2

A 55-year-old female smoker is admitted to the hospital for a chronic obstructive airways disease exacerbation. Other than her respiratory problem, she has no other complaints. On physical examination, you cannot feel her left dorsalis pedis or posterior tibial pulse.

WHY IS THIS AN IMPORTANT QUESTION TO ANSWER WITH

Context Lower extremity peripheral arterial disease (PAD) is common and associated with significant increases in morbidity and mortality. Physicians typically depend on the clinical examination to identify patients who need further diagnostic testing.

Objective To systematically review the accuracy and precision of the clinical examination for PAD.

Data Sources, Study Selection, and Data Extraction MEDLINE (January 1966 to March 2005) and Cochrane databases were searched for articles on the diagnosis of PAD based on physical examination published in the English language. Included studies compared an element of the history or physical examination with a reference standard of ankle-brachial index, duplex sonography, or angiogram. Seventeen of the 51 potential articles identified met inclusion criteria. Two of the authors independently extracted data, performed quality review, and used consensus to resolve any discrepancies.

Data Synthesis For asymptomatic patients, the most useful clinical findings to diagnose PAD are the presence of claudication (likelihood ratio [LR], 3.30; 95% confidence interval [CI], 2.30-4.80), femoral bruit (LR, 4.80; 95% CI, 2.40-9.50), or any pulse abnormality (LR, 3.10; 95% CI, 1.40-6.60). While none of the clinical examination features help to lower the likelihood of any degree of PAD, the absence of claudication or the presence of normal pulses decreases the likelihood of moderate to severe disease. When considering patients who are symptomatic with leg complaints, the most useful clinical findings are the presence of cool skin (LR, 5.90; 95% CI, 4.10-8.60), the presence of at least 1 bruit (LR, 5.60; 95% CI, 4.70-6.70), or any palpable pulse abnormality (LR, 4.70; 95% CI, 2.20-9.90). The absence of any bruits (iliac, femoral, or popliteal) (LR, 0.39; 95% CI, 0.34-0.45) or pulse abnormality (LR, 0.38; 95% CI, 0.23-0.64) reduces the likelihood of PAD. Combinations of physical examination findings do not increase the likelihood of PAD beyond that of individual clinical findings. However, when combinations of clinical findings are all normal, the likelihood of disease is lower than when individual symptoms or signs are normal. A PAD scoring system, which includes auscultation of arterial components by handheld Doppler, provides greater diagnostic accuracy.

Conclusions Clinical examination findings must be used in the context of the pre-test probability because they are not independently sufficient to include or exclude a diagnosis of PAD with certainty. The PAD screening score using the hand-held Doppler has the greatest diagnostic accuracy.

JAMA. 2006;295:536-546

www.jama.com



POST-PTA SURVEILLANCE

Table 12. Surveillance Program for Aortoiliac and Infrainguinal Transluminal Angioplasty

Patients undergoing aortoiliac and infrainguinal transluminal angioplasty for lower extremity revascularization should be entered into a surveillance program, which consists of:

- Interval history (new symptoms)
- Vascular examination of the leg with palpation of proximal and outflow vessel pulses
- Resting and, if possible, postexercise ABI recording

Surveillance programs should be performed in the immediate post-PTA period and at intervals for at least 2 years

ABI indicates ankle-brachial index; PAD, peripheral arterial disease; and PTA, percutaneous transluminal angioplasty.

Adapted from J Vasc Surg, 31, Dormandy JA, Rutherford RB, for the TransAtlantic Inter-Society Consensus (TASC) Working Group, Management of peripheral arterial disease (PAD), S1-S296, Copyright 2000, with permission from Elsevier (1).



POST-PROCEDURE SURVEILLANCE

- **CLAUDICATION:**
 - Periodic Hx and PE
 - ABI, and Doppler echography at 3-6 months, and then every 6-12 months
- **CRITICAL LIMB ISCHEMIA:**
 - Periodic Hx and PE, with thorough foot inspection
 - ABI and TcPO₂ at discharge
 - ABI, TcPO₂, and Doppler echography at 2-3, 6, and 12 months, and then at least every 6-12 months

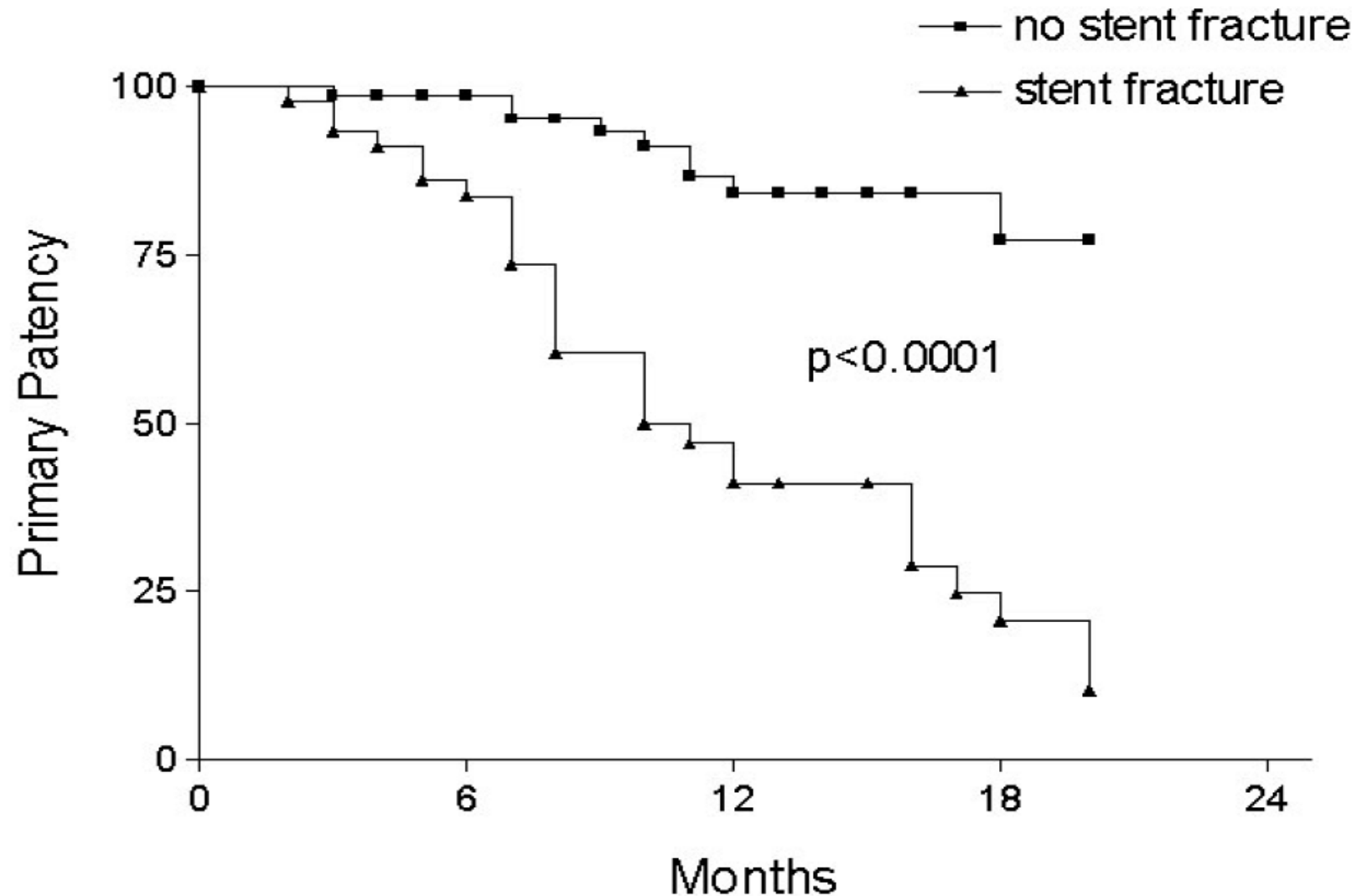


STANDARDS OF CARE

- Annual comprehensive foot exam
 - Assessment of protective sensation: Monofilament test
 - Foot structure and biomechanics
 - Vascular status: Pedal pulses (dorsalis pedis, posterior tibial)
 - Skin integrity; nails
 - Patients can be categorized by risk, low vs. high
- Visual foot inspection at each office visit for people with neuropathy



STENT FRACTURES



Scheinert et al, JACC 2005



FAST TRIAL

Interventional Cardiology

Nitinol Stent Implantation Versus Percutaneous Transluminal Angioplasty in Superficial Femoral Artery Lesions up to 10 cm in Length The Femoral Artery Stenting Trial (FAST)

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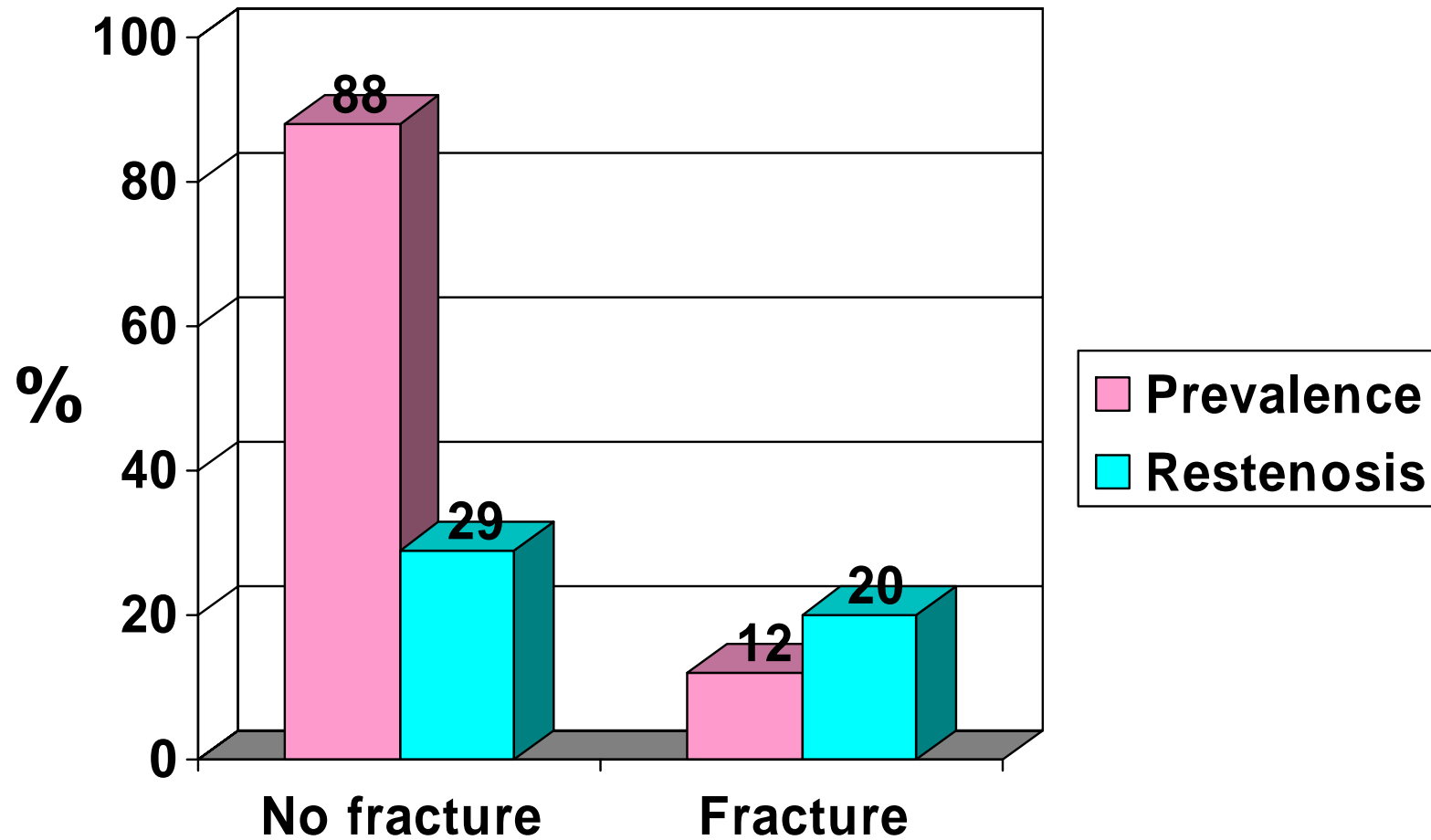
Background—Endoluminal treatment of superficial femoral artery lesions is a matter of controversy. The present study was designed to investigate the impact of nitinol stenting of superficial femoral artery lesions with a maximum length of 10 cm on restenosis and clinical outcomes at 1 year.

Methods and Results—Two hundred forty-four patients (168 men; 66 ± 9 years) with a single superficial femoral artery lesion and chronic limb ischemia were randomized to implantation of a single Bard Luminexx 3 stent (123 patients) or stand-alone percutaneous transluminal angioplasty (PTA) (121 patients). Mean lesion length was 45 mm. Technical success (residual stenosis $<50\%$ for PTA, $<30\%$ for stenting) was achieved in 96 patients assigned to PTA (79%) and 117 patients assigned to stenting (95%); 13 PTA group patients (11%) “crossed over” to stenting. At 1 year, the primary end point of ultrasound-assessed binary restenosis was reached in 39 of 101 PTA group patients (38.6%) and 32 of 101 stent group patients (31.7%; absolute treatment difference, -6.9% ; 95% CI, -19.7% to 6.2% ; $P=0.377$). Target lesion revascularization rates at 1 year were 18.3% and 14.9%, respectively (absolute treatment difference, -3.3% ; 95% CI, -13.0% to 6.4% ; $P=0.595$). No statistically significant difference between treatment groups was observed at 12 months in the improvement by at least 1 Rutherford category of peripheral arterial disease.

Conclusions—In the present study of patients with short superficial femoral artery lesions, the hypothesized absolute difference of 20% in binary restenosis at 1 year between the implantation of a single Luminexx nitinol stent and stand-alone PTA could not be demonstrated. A smaller difference requiring a larger trial might have been missed. (*Circulation*. 2007;116:285-292.)



STENT FRACTURES IN FAST



Krankenberga et al, Circ 2007



STENT FRACTURE IN THE NITINOL STENT ERA

Among the patients who received a stent, stent fractures were observed in 2 percent at both 6 and 12 months

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Balloon Angioplasty versus Implantation of Nitinol Stents in the Superficial Femoral Artery

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ABSTRACT

BACKGROUND

Because stent implantation for disease of the superficial femoral artery has been associated with high rates of late clinical failure, percutaneous transluminal angioplasty is preferred for endovascular treatment, and stenting is recommended only in the event of suboptimal technical results. We evaluated whether primary implantation of a self-expanding nitinol (nickel–titanium) stent yielded anatomical and clinical benefits superior to those afforded by percutaneous transluminal angioplasty with optional secondary stenting.

METHODS

We randomly assigned 104 patients who had severe claudication or chronic limb ischemia due to stenosis or occlusion of the superficial femoral artery to undergo primary stent implantation (51 patients) or angioplasty (53 patients). Restenosis and clinical outcomes were assessed at 6 and 12 months.

RESULTS

The mean (\pm SD) length of the treated segment was 132 \pm 71 mm in the stent group and 127 \pm 55 mm in the angioplasty group. Secondary stenting was performed in 17 of 53 patients (32 percent) in the angioplasty group, in most cases because of a suboptimal result after angioplasty. At 6 months, the rate of restenosis on angiography was 24 percent in the stent group and 43 percent in the angioplasty group ($P=0.05$); at 12 months the rates on duplex ultrasonography were 37 percent and 63 percent, respectively ($P=0.01$). Patients in the stent group were able to walk significantly farther on a treadmill at 6 and 12 months than those in the angioplasty group.

CONCLUSIONS

In the intermediate term, treatment of superficial-femoral-artery disease by primary implantation of a self-expanding nitinol stent yielded results that were superior to those with the currently recommended approach of balloon angioplasty with optional secondary stenting.

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FAILED PTA -> SURGERY IS STILL FEASIBLE

Is Infrainguinal Bypass Grafting Successful Following Failed Angioplasty?

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Objectives. Angioplasty is often used in the management of lower limb ischaemia and can reduce the need for infrainguinal bypass in some patients. There is an associated failure rate with this technique and bypass surgery is often used in this situation as a secondary limb salvage procedure. We aimed to evaluate the outcome of infrainguinal bypass grafting following failed attempt at angioplasty.

Methods. All cases of infrainguinal bypass at a single centre over a seven year period were identified and notes reviewed. Cases were divided into four groups according to their indication for surgery; acute ischaemia, chronic critical ischaemia, failed angioplasty and an 'other' group including aneurysmal disease and claudicants. The failed angioplasty group was compared with the other three groups. Survival analysis was performed using Kaplan Meier curves and groups compared in terms of long term patency and survival.

Results. Primary patency was 61.2% in the failed angioplasty group at 12 months compared with 60.6% in the other groups ($P=1.11$). There was also no significant difference in primary patency at 60 months (50% vs 40.6%, $P=0.26$). Survival at 12 months was also comparable between the groups (failed angioplasty group 74.2% compared with 77.3% in the other groups, $P=0.662$) as was 60 months survival (33.3% and 35.4% respectively, $P=0.166$).

Discussion. In this study, outcome of infrainguinal bypass following failed angioplasty was comparable to outcome of surgery performed for another indication. This paper supports the use of distal bypass surgery for limb salvage in cases where minimal access techniques have failed.



QUESTIONS?



TAKE HOME MESSAGES

- Comprehensive patient management before and after PTA is pivotal to maximize success rates and long-term clinical benefits
- Evidence-based treatments should be systematically used in these very high risk cardiovascular patients
- Systematic post-PTA surveillance is mandatory, especially in patients with CLI who are at high risk of asymptomatic recurrences