

Life and limb: bypass versus angioplasty in the ischaemic limb



In today's *Lancet*, the BASIL trial investigators report the results of their exploration of the role of bypass surgery and balloon angioplasty in the management of patients with severe leg ischaemia.¹ Before now, attempts have been made to find out if one approach surpasses the other, and although one previous study² reached similar conclusions to the BASIL trial, previous studies were generally underpowered^{3,4} or done in low-risk patients.² In BASIL, as in previous trials, the number of patients eligible for randomisation only represents 30% of those with severe limb ischaemia¹ and 2% of those with peripheral vascular disease.⁵ Despite this, the data convincingly show the similar ability of bypass surgery and balloon angioplasty in preserving both life and limb. Thus for the first time, percutaneous angioplasty is formally validated as an acceptable option for patients with severe leg ischaemia.

These results emphasise the need for physicians (surgeons and interventionalists) to work as a team rather than compete. In addition, the results confirm that patients with critical limb ischaemia are a high-risk subset of those with atherothrombosis, regardless of the initial revascularisation option. The advanced age and multiple comorbidities of the patients in BASIL explain the high overall mortality (37%), which is far greater than in most randomised trials in, for example, patients with coronary disease. Given the important difference in early morbidity, it seems clear that angioplasty, when technically feasible, should be attempted first. At the other end of the spectrum, as the authors of BASIL rightly remind us, primary amputation is probably the best option for some patients. Efforts should be made to differentiate these patients early to avoid useless, costly, and potentially dangerous procedures.

The BASIL data are reminiscent of the earlier randomised trials that compared coronary balloon angioplasty or bare-metal stenting with coronary artery bypass surgery.^{6,7} The studies all found no difference in mortality at 1 year and no differences in other endpoints, such as myocardial infarction or stroke. But the studies showed that surgery reduced the need for repeat revascularisation procedures. In some of these trials, there was also a late survival benefit for diabetic patients treated with surgery,⁸ and in both groups of BASIL the prevalence of diabetes was an impressive 42%. This finding should be kept in mind when considering the post-hoc analysis suggesting

a possible late-survival advantage (beyond 2 years) of those patients treated surgically in BASIL.

Recruitment of patients in BASIL took place between 1999 and 2004, and stents were not used. Despite the accepted view that bare-metal stents are associated with disappointing results when placed distal to the iliac arteries, there are encouraging early data in small series treated with drug-eluting stents in the superficial femoral arteries.⁹ It is possible that medium-term and long-term results will improve, and the need for further revascularisation will be reduced after stent-based peripheral percutaneous intervention.

As mentioned by the BASIL investigators, management of severe peripheral vascular disease remains a considerable challenge. This is because most of these patients have severe comorbidities, such as diabetes, renal failure, coronary artery disease, carotid obstruction, or previous strokes. In these patients the ischaemic limb is only the tip of an iceberg. The ischaemic limb is an acute problem that must be addressed with the goal of saving the leg and relieving pain; in parallel a multifactorial medical approach is required to treat the underlying risk factors and improve the patient's outlook. In BASIL, at the time of enrolment, a high number of patients were cigarette smokers, almost 40% were not receiving antiplatelet therapy, and both statins and antihypertensive

Published online
November 25, 2005
DOI:10.1016/S0140-6736(05)
67705-7

See [Articles](#) page 1925

**Rights were not granted to include
this image in electronic media. Please
refer to the printed journal.**

Science Photo Library

Balloon angioplasty procedure

agents were much underused. No information on diabetic control was given (HbA_{1c} would have been of interest). The medical management in BASIL is therefore insufficient relative to current standards and guidelines, which should serve as a reminder that patients with peripheral arterial disease require comprehensive medical management at least as much as the best available technical procedure.

*Jean-Jacques Goy, Philip Urban

Cardiology Service, Clinique Cecil, 1003 Lausanne, Switzerland
jgoy@goyman.com

JJG declares that he has no conflict of interest. PU has consulted for Cordis, Johnson and Johnson, Terumo, Boston Scientific, and Medtronic.

- 1 BASIL trial investigators. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. *Lancet* 2005; **366**: 1925–34.

- 2 Wilson SE, Wolf GL, Cross AP. Percutaneous transluminal angioplasty versus operation for peripheral arteriosclerosis: report of a prospective randomized trial in a selected group of patients. *J Vasc Surg* 1989; **9**: 1–9.
- 3 Angioplasty or bypass for superficial femoral artery disease? A randomised controlled trial. *Eur J Vasc Endovasc Surg* 2004; **28**: 132–37.
- 4 Holm J, Arfvidsson B, Jivegard L, et al. Chronic lower limb ischaemia: a prospective randomised controlled study comparing the 1-year results of vascular surgery and percutaneous transluminal angioplasty (PTA). *Eur J Vasc Surg* 1991; **5**: 517–22.
- 5 Burns P, Gough S, Bradbury A. Management of peripheral arterial disease in primary care. *BMJ* 2003; **326**: 584–88.
- 6 Pocock SJ, Henderson RA, Rickards AF, et al. Meta-analysis of randomised trials comparing coronary angioplasty with bypass surgery. *Lancet* 1995; **346**: 1184–89.
- 7 Mercado N, Wijns W, Serruys PW, et al. One-year outcome of coronary artery bypass graft surgery versus percutaneous coronary intervention with multiple stenting for multisystem disease: a meta-analysis of individual patient data from randomized clinical trials. *J Thorac Cardiovasc Surg* 2005; **130**: 512–19.
- 8 King SB III. Is surgery preferred for the diabetic with multivessel disease? *Circulation* 2005; **112**: 1500–07.
- 9 Duda SH, Pusich B, Richter G, et al. Sirolimus-eluting stents for the treatment of obstructive superficial femoral artery disease—six-month results. *Circulation* 2002; **106**: 1505–10.

Nature’s randomised trials

See [Articles](#) page 1954

A randomised trial without an intervention is difficult to envisage. In today’s *Lancet*, however, Nic Timpson and colleagues¹ take advantage of natural genetic randomisation during sexual reproduction—that of alleles bearing single nucleotide polymorphisms (SNPs) governing the abundance of C-reactive protein (CRP)—to assess whether associations between CRP and components of the metabolic syndrome are causal.

In prospective observational studies, CRP concentration has consistently been linked with cardiovascular events² as well as with high-risk vascular phenotypes including high blood pressure, diabetes, and the metabolic syndrome.^{3,4} This fits with the prevailing view that inflammation is critical to atherogenesis. Whilst the similar and well-known associations of blood pressure and cholesterol levels with cardiovascular events are considered causal—because reducing blood pressure or cholesterol reduces cardiovascular risk in randomised trials—the same might not be true for CRP. Associations between CRP and disease could be explained by confounding, because of CRP’s associations with other risk factors such as low birthweight, lower sociodemographic position, lack of physical activity, smoking, and abdominal obesity.^{5,6} Reverse causation might also be at work, whereby inflammatory cytokines from atheroma or adipose tissue raise CRP (figure 1). While statistical adjustment can reduce confounding, not all confounding

factors are known, or accurately measured. Moreover, adjustment requires a judgment about mechanism. For example, if blood pressure or diabetes mediate rather than confound the association between CRP and cardiovascular events, adjusting for these factors would lead to underestimation of the causal association.

How might we get better insight into causation? Mechanistic studies in vitro have yielded conflicting results. Potentially proatherogenic and blood pressure-raising effects of CRP on vascular cells and tissues⁷ might have been mediated by proinflammatory bacterial peptides or sodium azide present in commercial CRP preparations.^{8,9} The increased atheroma formation in apolipoprotein-E-deficient mice that overexpress human CRP was not reproducible.¹⁰ A randomised trial of a selective CRP-lowering therapy is required, because randomisation would ensure that measured and unmeasured confounders were evenly distributed between placebo and intervention groups (figure 2).

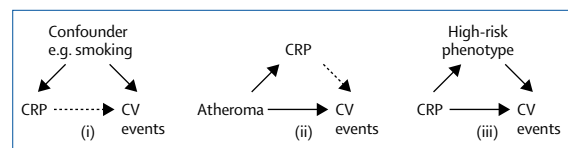


Figure 1: CRP and cardiovascular disease (CVD)
Association between CRP and CVD might arise by confounding (i), reverse causation (ii), or because of true causal link (iii), perhaps via a high-risk phenotype such as the metabolic syndrome.