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A Comparison of Clinical Outcomes Between Primary Bypass and Secondary Bypass After Failed Plain Balloon Angioplasty in the Bypass versus Angioplasty for Severe Ischaemia of the Limb (BASIL) Trial

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WHAT THIS PAPER ADDS

Angioplasty has been seen as a "free shot" at revascularisation of chronic limb threatening ischaemia. This work suggests that patients requiring secondary bypass after failed initial angioplasty do significantly worse than those who undergo primary bypass surgery.

Objective: Chronic limb threatening ischaemia (CLTI) is a growing global health problem. The UK NIHR HTA funded BASIL trial is still the only randomised controlled trial to have compared a "bypass surgery first" with a "plain balloon angioplasty (PBA) first" strategy for the management of CLTI. In patients who were likely to survive for 2 years and had a suitable vein, primary bypass (PB) was associated with better clinical outcomes. Furthermore, PBA was associated with a high technical and clinical failure rate and many went on to have secondary bypass (SB). This study aimed at comparing clinical outcomes following PB and SB in the BASIL trial.
Methods: Demographic, procedural, and outcome data were obtained from the BASIL case report forms. Outcomes were amputation free survival (AFS), limb salvage (LS), overall survival (OS), and freedom from revascularisation (FFR). The SB cohort comprises patients whose first trial intervention was PBA and who subsequently underwent bypass during follow up. The PB cohort comprises those patients whose first trial intervention was bypass.
Results: The 190 PB and 49 SB patients were well matched except that the SB patients were more likely to be current smokers. At a median of 7 years, PB was associated with better AFS (PB 60% vs. SB 40%; HR 1.58, $p = .04$), LS (PB 85% vs. SB 73%, $p = .06$), and OS (PB 68% vs. 51%, $p = .06$). FFR was equivalent (PB 53% vs. 53%, $p = .3$).
Conclusion: In the BASIL trial, clinical outcomes following PB were significantly better than in patients undergoing SB after failed PBA. Prior to treating patients with CLTI with primary PBA, clinicians should consider that if this should fail, the outcome of attempted subsequent bypass is likely to be significantly worse than if PB were attempted.

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INTRODUCTION

Although chronic limb threatening ischaemia (CLTI) is a growing global health problem,[1,2] the evidence underpinning the choice of revascularisation strategy remains poor. The UK NIHR HTA funded Bypass versus Angioplasty for Severe Ischaemia of the Limb (BASIL) trial remains the only randomised controlled trial (RCT) to have compared a "bypass surgery first" with a "plain balloon angioplasty (PBA) first" strategy for CLTI resulting from infra-inguinal disease.[3] An intention to treat analysis (ITT) of BASIL outcome data showed that, in patients who were likely to survive for at least 2 years and who had a suitable vein, primary bypass (PB) led to better clinical outcomes than primary PBA. Furthermore, primary PBA was associated with a high technical and clinical failure rate such that many of the patients went on to have secondary bypass (SB). Despite this 'level 1' evidence in support of surgical bypass as the preferred revascularisation strategy for patients with a suitable vein, enthusiasm for an endovascular first approach to most, perhaps even all, patients with CLTI continues to grow.[4] As a result, vein bypass is increasingly being viewed as a secondary, salvage procedure to be performed when all endovascular revascularisation options have been exhausted.[5,6] There are surprisingly few published reports of outcomes following SB for failed

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endovascular revascularisation. Furthermore, in the few studies that are available, patient numbers are often small, patients were not randomised, and patients with intermittent claudication and CLTI are often conflated.[7–9] This topic was briefly reported in the analysis by treatment received, only SB within 8 weeks of primary PTA were included and only AFS was reported but no further in depth analyses were performed.[10] The aim of this study, therefore, was to compare clinical outcomes following PB, and all SB after failed primary PBA in the BASIL trial.

METHOD

The BASIL trial methodology has been published previously.[3] Ethical approval was obtained from the Multi-Centre Research Ethics Committee for Scotland. Briefly, patients with CLTI resulting from infra-inguinal disease were randomised to either a PB or primary PBA revascularisation strategy between 1999 and 2004. Patients were followed up until death or the censor date of July 1, 2007. This provided all surviving patients with a minimum of 3 years follow up (median 51, range 0–92 months).

BASIL trial case report forms (CRF) were interrogated to obtain demographic, procedural, and outcome data including amputation free survival (AFS), limb salvage (LS), overall survival (OS), and freedom from re-intervention (FFR) defined as any further revascularisation of the index limb. The SB cohort comprised patients whose first trial intervention was PBA and who subsequently underwent SB (with any conduit) at any point during trial follow up. The PB cohort comprised those patients whose first trial intervention was PB with any conduit. Time to event analyses are presented over a 7 year period using Kaplan-Meier plots. Hazard ratios were used to detect statistically important differences in outcomes using 95% CI. Differences between the cohorts were compared using *t* test, chi-squared and Wilcoxon Rank Sum tests according to distribution of data. Statistical analysis was performed using SAS v 9.4.

RESULTS

There were 238 attempted primary PBA in the BASIL trial; of these, 69 patients went on to have a secondary intervention, 17 had a tertiary intervention, and seven had a fourth intervention. Twenty-five (36.2%) of the secondary interventions were PBA; of these, three (12%) subsequently underwent SB. The remaining 46 SBs were performed after failed primary PBA. In BASIL, 190 patients underwent PB.

The 190 PB and the 49 SB patients were well matched at the time of randomisation in terms of baseline demographics except that the SB patients were more likely to be current smokers (Table 1). Medical management was also similar (Table 2). Of those who went on to have SB, 49% (24/49) had a technically successful primary PBA. Tissue loss was present in most patients in both groups (ulcer 62% vs. 69%, $p = .3$, gangrene 34% vs. 29% $p = .5$). The median time interval between primary PBA and SB was 0 months (range 0–20 months). Of those who underwent PB, 9.5% (18/190) underwent secondary PTA, 94.4% (17/18) of these were for vein graft stenosis and 100% survived with their limb at the end of trial follow up.

At a median of 7 years, PB was associated with significantly better AFS (PB 60% vs. SB 40%; HR 1.58, 95% CI 1.03–2.44, $p = .04$). Although LS and OS did not reach statistical significance there was a trend to better outcomes in the PB group (LS; PB 85% vs. SB 73%; HR 1.86, 95% CI 0.97–3.58, $p = .06$, and OS; PB 68% vs. 51%; HR 1.57, 95% CI 0.97–2.54, $p = .06$). FFR was the same in both groups (PB 53% vs. 53%; HR 1.43, 95% CI 0.74–2.74, $p = .3$) except that, of course, by definition, those patients undergoing SB were all undergoing a re-intervention (Figs. 1–4).

Procedural data were available for all patients who underwent SB (Table 3). All SB were deemed technically successful at the end of the procedure. Four (8%) SB were prosthetic compared with 22% (41/190) PB ($p = .03$). The absolute amputation rate to the end of follow up was 15.3% vs. 26.5% ($p = .06$). The distal anastomosis was not statistically different between PB and SB with 68% (130/190) versus 64% (31/49) being to the popliteal artery ($p = .4$). There was no significant difference between PB and SB in terms of 30 day morbidity and mortality (Table 4).

DISCUSSION

In the BASIL trial, 190 patients underwent PB and, of the 238 patients who underwent an attempt at primary PBA, 49 (21%) went on to require a SB at some point during the trial follow up. The key finding of the present study is that PB was associated with statistically significantly better AFS and a strong trend ($p = .06$) towards better LS and OS. It is accepted that the SB group are a group of failures, which suggests they are different to the PB group, the challenge for this analysis is to identify why. It is also accepted that the BASIL trial was not powered to investigate this relationship, nevertheless it is an important relationship that is poorly understood. The two cohorts were well matched in terms of baseline demographics and medical therapy at randomization, PB patients were more likely to be current smokers and have a history of TIA; however, it is noted that this group was observed to have better clinical outcomes. This suggests that the observed differences are not related to the patient's medical characteristics. The anatomical burden of disease is certainly influential in type of revascularisation required and outcome of said intervention. Bollinger analysis of these groups suggests that there is no difference in burden or distribution of disease between these groups (Table 5).

The appropriateness of the observed trend in recent years towards an endovascular first strategy for most, perhaps even all, CLTI is now being challenged.[11–13] However, although several groups have reported outcomes following PB and primary endovascular revascularisation, few have analysed the effect of failed endovascular intervention on the success of SB. But, these reports, taken with the data from the BASIL trial presented here, indicate that primary endovascular intervention is not the "free shot" that it has so often been claimed to be.

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