Is Duplex Surveillance of Value After Leg Vein Bypass Grafting?

Principal Results of the Vein Graft Surveillance Randomised Trial (VGST)

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on Behalf of the VGST Participants

Background—The purpose of this study was to assess the benefits of duplex compared with clinical vein graft surveillance in terms of amputation rates, quality of life, and healthcare costs in patients after femoropopliteal and femorocrural vein bypass grafts.

Methods and Results—This was a multicenter, prospective, randomized, controlled trial. A total of 594 patients with a patent vein graft at 30 days after surgery were randomized to either a clinical or duplex follow-up program at 6 weeks, then 3, 6, 9, 12, and 18 months postoperatively. The clinical and duplex surveillance groups had similar amputation rates (7% for each group) and vascular mortality rates (3% versus 4%) over 18 months. More patients in the clinical group had vein graft stenosis at 18 months (19% versus 12%, \( P < 0.04 \)), but primary patency, primary assisted patency, and secondary patency rates, respectively, were similar in the clinical group (69%, 76%, and 80%) and the duplex group (67%, 76%, and 79%). There were no apparent differences in health-related quality of life, but the average health service costs incurred by the duplex surveillance program were greater by £495 (95% CI £183 to £807) per patient.

Conclusions—Intensive surveillance with duplex scanning did not show any additional benefit in terms of limb salvage rates for patients undergoing vein bypass graft operations, but it did incur additional costs. (Circulation. 2005;112:1985-1991.)

Key Words: imaging • stenosis • amputation • grafting • occlusion

Infrainguinal vein bypass graft procedures are performed routinely on patients with lower-limb peripheral arterial disease; however, vein grafts are prone to develop lesions or stenoses, which reduce blood flow and can precipitate thrombosis.1,2 Such stenoses are identifiable in 25% to 30% of vein bypass grafts within the first year.3,4 Duplex ultrasound scanning is currently the best method for detecting stenotic lesions that threaten graft patency during follow-up.5 The correction of such lesions may improve graft patency and limb salvage rates.6,7 However, to date, evidence to support this has been based largely on the findings of smaller-scale observational studies,8–11 in the absence of a large multicenter, randomized, controlled trial (RCT).

A major consideration within the current healthcare environment is that procedures must be cost-effective.12,13 Duplex surveillance programs are expensive to establish and maintain, not only with regard to the initial outlay for the machine but also with regard to the employment of a trained vascular technologist, as well as funding for the additional interventions performed. Grigg et al13 estimated that if Duplex surveillance of all vein grafts prevented 5% of patients from needing an amputation, then the savings would be great enough to justify the expense of establishing a surveillance program.

Although amputation is the most clinically relevant measure of graft failure, graft occlusion does not necessarily result in amputation.12 Unfortunately, the few reports that have been published10,11,13–15 tend to argue in favor of duplex surveillance on the basis of patency alone, with no measurement of limb salvage. Golledge et al5 undertook a summation analysis of infrainguinal vein graft outcomes on those studies that provided occlusion rates, comparing 2680 duplex surveillance patients with 3969 nonsurveillance patients. The levels of distal anastomosis and presence of critical ischemia were found to be similar in both groups. However, only 6 of 17 studies reported amputation rates; only 2 of these were RCTs, and both of these were small.

In one randomized trial, Lundell et al16 studied both vein (n=106) and synthetic (n=50) grafts randomized to either
“intensive” surveillance of clinical examination, ankle-brachial pressure index (ABPI), and duplex scans or “routine” surveillance of clinical examination and ABPI only. Their results at 3 years after operation showed that there was an advantage of duplex scanning when patency rates were compared but not when amputation rates were compared. Ilhberg et al.\(^\text{20}\) could not demonstrate any difference in limb salvage between duplex surveillance and clinical assessment in a second randomized trial of 185 consecutive vein grafts; however, they had difficulty obtaining complete follow-up data on patients.\(^\text{18}\) Both groups concluded that there was a need for a large RCT.\(^\text{16–18}\)

Here, we report on the results of a large-scale RCT of 594 infrapelvic vein graft reconstructions.

Methods
The design of the Vein Graft Surveillance Trial has been reported previously.\(^\text{19}\) Patients undergoing femoropopliteal or femorocrural vein bypasses were recruited between April 1998 and December 2001 from 22 centers within the United Kingdom and 7 from Europe. Indications for surgical correction included critical ischemia, claudication, or symptomatic popliteal aneurysm. Patients receiving synthetic grafts such as polytetrafluoroethylene (PTFE) grafts were excluded from the study. Each center received ethical approval.

Randomization and Follow-Up
Patients from participating centers whose vein graft was patent at 30 days after surgery were randomized at \(\approx 6\) weeks (range 4 to 10 weeks) to either the clinical group (clinical examination with ABPI measurements) or the duplex group (same as clinical plus a routine duplex scan). The allocation of patients was performed by a central computer–based randomization service at the University of York. This used randomly sized allocation blocks of sizes 4 and 6 (plus a small number of odd-sized blocks), stratified by center and presenting symptoms (claudication or critical ischemia). Patients then underwent a surveillance program with follow-up appointments at the time of recruitment (6 weeks) and then subsequently at 3, 6, 9, 12, and 18 months. All patients received a duplex scan at 18 months; this was performed in the clinical arm of the trial solely to identify the incidence of stenoses.

The rationale for scheduling the follow-up to finish at 18 months was that the majority of stenoses and graft failures occur within the first year.\(^\text{3,4,20,21}\) There are 3 time periods of graft failure: early (within 30 days), which is attributed to technical failure; intermediate (30 days to 1 year), usually attributed to graft stenosis; and late failure, usually attributed to progression of disease. Early graft failures were excluded because an entry criterion for the trial was a patent graft at 30 days. The length of follow-up in such programs is controversial; both Idu et al.\(^\text{20}\) and Mills et al.\(^\text{21}\) suggest that as stenoses occur, early surveillance need only be performed for the first 6 months, whereas others recommend a longer follow-up.\(^\text{22}\) The Transatlantic Consensus states that the optimum length and frequency of follow-up are unknown.\(^\text{23}\)

Duplex Surveillance
The duplex group was scanned along the graft, including the distal and proximal anastomoses. The inflow and outflow vessels were scanned for specific structural abnormalities or exceptional flow characteristics in color-flow images. Graft flow velocity and blood flow patterns were evaluated at multiple sites along the bypass graft. A graft at risk of failure was defined as having a slow peak systolic flow velocity of less than 45 cm/s\(^\text{24}\) or a ratio of V2 (peak systolic velocity at the site of the stenosis) to V1 (peak systolic velocity at any other point within 2 cm at the normal adjacent graft) of \(>2.5\). At 18 months, an abnormal V2/V1 ratio was used to define the presence of a stenosis. Any other irregularities, such as inflow/outflow problems, graft dilatation, or arteriovenous fistula, were also noted.

Intervention criteria included clinical signs of a failing graft, such as onset of disabling claudication, ischemic pain, or ischemic ulcers, and a decrease in ABPI of \(\approx 0.1.\)\(^\text{25}\)

Outcomes Assessed
The primary outcomes were time to amputation (above knee, below knee, or through knee) and time to vascular mortality (death due to myocardial infarction, heart failure, arrhythmia, or cerebrovascular accident). Patency, cost, and quality of life were regarded as secondary outcome measures. We used the recommended definitions of patency,\(^\text{25}\) subdividing primary patency (patency without intervention) from primary assisted patency (patency without intervention plus patency after intervention for graft stenosis) and secondary patency (patency without intervention plus patency after intervention for graft stenosis plus patency after intervention for graft occlusion).

Health-related quality-of-life data were collected at 6 and 18 months with the SF-36 (36-item short-form health survey) and EuroQol questionnaires.\(^\text{26–28}\) The SF-36 data were summarized with the physical and mental subscales and the EuroQol with the derived EuroQol 5 dimensions (EQ5D) utility measure. Healthcare costs were obtained for each patient by applying health resource group costs for the financial year 2002/2003\(^\text{29}\) to the duplex scans, angiograms, angioplasties, thrombolysis, and surgical interventions performed.

Statistical Methods
On the basis of anticipated 18-month amputation rates of \(\approx 10\%\), the sample size of 600 patients yields a standard error for the difference in amputation rates between groups of \(\approx 2.5\%\). The original plan was to recruit 1200 patients,\(^\text{19}\) but this proved impossible in the time available because of the increased use of percutaneous endovascular treatments; the standard error based on 1200 patients would have been \(1.7\%\). The statistical analysis was conducted according to a prespecified plan, drawn up before the outcome data were examined, which used the intention-to-treat principle. The main outcomes of time to amputation and vascular death were analyzed with Cox regression; planned adjustment of the resulting hazard ratios for age, sex, smoking, and diabetes made no material difference, so only the unadjusted results are presented. Kaplan-Meier estimates of cumulative amputation rates were drawn, with censoring for deaths and withdrawals. Patency rates over time were estimated with life-table methods and compared with the log rank test. Quality-of-life scores were compared between groups with a Mann-Whitney test, whereas average costs were compared with a t test.\(^\text{30}\)

Results
Of the 594 patients recruited, 290 were randomized to clinical follow-up and 304 to duplex surveillance. Their baseline data are shown in Table 1. Preoperative characteristics were similar in the 2 randomized groups (median age 70 years, 72% male, and median ABPI 0.48). The majority of the operations were from the common femoral (proximal anastomosis) to the above-knee or below-knee popliteal (distal anastomosis) and were performed with ipsilateral reversed leg vein. The most common indication for surgery was critical ischemia.

The progress of patients throughout the trial is shown in Figure 1. Apart from deaths, the withdrawal from follow-up was 12% overall (11% and 13% in the clinical and duplex groups, respectively). Of the withdrawals, 45% were due to amputation. Among patients remaining in the trial, the proportion of follow-up appointments attended was 89% in the clinical group and 90% in the duplex group. At 18 months, 91% of all patients due for follow-up had a duplex scan. The response rate to the quality-of-life questionnaires was slightly lower at \(\approx 80\%\).
Some patients had additional radiological or surgical interventions (Table 2). The median time to first intervention was 20 weeks from randomization in the clinical arm and 15 weeks in the duplex arm. Twenty-seven percent of the clinical group had a duplex scan at some time during the 18-month follow-up period (owing to a suspicion of a clinical problem from either history or a fall in ABPI); only 7% of the duplex group had additional duplex scans beyond those in the planned schedule. Angiograms, angioplasty, thrombolysis, and surgery were each slightly more common in the duplex group, as might be expected, but none to a very marked extent. The reported interventional success rate was similar in the clinical group and duplex group at 90%.

Table 2 indicates the methodology that first raised the suspicion that a graft was at risk. It does not include the asymptomatic lesions identified by the 18-month duplex scan in the clinical arm, because this was used solely to calculate the incidence of stenoses. Even in the duplex arm of the trial, 49% of patients were deemed to be potentially at risk by history alone.

The major outcomes in the trial are shown in Table 4. Amputations, vascular mortality, and overall mortality were equally distributed between the 2 groups, so the hazard ratios were close to unity. On the duplex scan at 18 months, the proportion of patients with a stenosis in the graft (defined in the protocol as a V2/V1 ratio > 0.2) was greater in the clinical group.

The cumulative incidence of amputation is shown in Figure 2; there was no difference between the 2 groups. Graft patency at each follow-up occasion is shown in Figure 3. Patency diminished over time, primary patency being re-
placed by primary-assisted patency and secondary patency as expected, but to a similar degree in both groups. The Kaplan-Meier estimates at 18 months of the proportions with primary, primary assisted, and secondary patency were 69%, 76%, and 80%, respectively, in the clinical group, and 67%, 76%, and 79%, respectively, in the duplex group. The median ABPI showed no evidence of a difference between groups over time.

Results from the quality-of-life assessments (Table 5) gave no clear indication of a difference between randomized groups at either 6 or 18 months. However, the average health service cost per patient was higher in the duplex than in the clinical follow-up group (mean difference £495, 95% CI £183 to £807) because of the cost of duplex scans and the slightly increased rates of intervention in the duplex group.

Discussion

The need for a further, larger RCT was demonstrated by the results of the 2 small trials16–18 and reflected in the Transatlantic Consensus Statement.23 The present study is the largest multicenter trial to examine the potential benefits of duplex surveillance in terms of amputation and graft patency.

Overall, the trial has provided conclusive evidence of the suspicions raised by the summation analysis of Golledge et al5 and the combined results of the 2 small RCTs that limb salvage is not improved by duplex surveillance.31 The combined results of the previous small RCTs suggested that overall patency was worse in patients in the clinical follow-up arm rather than the duplex group; this trial has shown no statistically or clinically significant improvement in patency.

Table 6 compares patency rates and limb salvage from the previous RCTs and the present trial. The 12-month point was
was no difference in terms of patency. Mattos et al33 have also showed that in a cohort of patients who did not receive treatment for a stenosis or inflow or outflow problems, there was no difference in terms of patency,17 although the latter acknowledges a degree of difficulty with respect to the number of patients lost to follow-up.18 The amputation rate in the present study is comparable to that found in the summation analysis and other studies. Similarly, the patency rates are comparable to these other studies. However, the 18-month data with respect to the incidence of vein graft stenoses are different. These results are in line with the findings of the Bristol group,32 who showed that in a cohort of patients who did not receive treatment for a stenosis or inflow or outflow problems, there was no difference in terms of patency. Mattos et al33 have also previously concluded that the majority of stenoses stay patent whether treated or not. Furthermore, it is well accepted that the 1-year incidence of stenosis can be as high as 30%. The present trial has shown a lower prevalence at 18 months because this figure does not include patients who have had a previous stenosis corrected.

One of the complicating factors in this area is the indication for determining that a graft is at risk. It is accepted that duplex scanning is the noninvasive investigation of choice for identifying an abnormality in a vein graft.6 The following are the common noninvasive criteria for identifying an at-risk graft: ABPI fall >0.2, peak systolic velocity <45 cm/s, increase in peak systolic velocity at the site of the stenosis to >150 cm/s, and peak systolic velocity ratio across a stenosis >2.0.6 However, we used an ABPI fall of 0.1 because this is the figure used by the 1997 standards recommendation of Rutherford et al.25 Controversy exists as to when one should intervene; for example, in one series of 46 patients with a peak systolic velocity ratio >3.0, only 14 grafts were revised, and only 3 occluded during follow-up.34 Other factors that may be deemed to be important are graft diameter, outflow, and location of the distal anastomosis. In devising the present trial, it was thought to be important to adopt a pragmatic approach, so that determining exactly when to intervene should follow local policy. Furthermore, in certain situations, the exact type of intervention required may be controversial, for example, whether to perform an endovascular procedure (angioplasty) or an open revision (such as vein patch angioplasty or interposition graft). Hence, each center was given the freedom to determine the type of intervention required for a patient.19

Another issue is the length of follow-up programs. The highest incidence of developing stenosis is within the first year, after which there is a very low incidence. Despite this, the Leicester group22 advocates life-long surveillance, whereas others suggest that the majority of patients may only require surveillance for the first 6 months.20,21 The present trial confirms that the majority of interventions occur within the first year after implantation.

Patency and limb salvage rates are not the only outcomes that need consideration: The effect on quality of life and cost are important. To date, neither has been reported in an RCT. Improvements in quality of life after bypass surgery have been well established previously,19 and the data from the

### TABLE 5. Quality-of-Life Assessments at 6 and 18 Months* and Health Service Costs Over 18 Months

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Clinical Follow-Up</th>
<th>Duplex Follow-Up</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 physical score</td>
<td>447</td>
<td>47 ± 27</td>
<td>50 ± 30</td>
</tr>
<tr>
<td>SF-36 mental score</td>
<td>439</td>
<td>71 ± 20</td>
<td>71 ± 21</td>
</tr>
<tr>
<td>EQ5D utility score</td>
<td>443</td>
<td>0.59 ± 0.30</td>
<td>0.63 ± 0.30</td>
</tr>
</tbody>
</table>

*Higher SF-36 and lower EQ5D scores each represent worse perceived health.
†P values from Mann-Whitney test for quality-of-life scores and from t test for costs.

### TABLE 6. Twelve-Month Comparative Data on Patency and Limb Salvage From 3 Randomized Trials

<table>
<thead>
<tr>
<th></th>
<th>Clinical Follow-Up</th>
<th>Duplex Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>PP, %</td>
</tr>
<tr>
<td>Ilhberg et al17</td>
<td>90</td>
<td>68</td>
</tr>
<tr>
<td>Lundell et al16</td>
<td>50</td>
<td>NA</td>
</tr>
<tr>
<td>Davies et al</td>
<td>290</td>
<td>73</td>
</tr>
</tbody>
</table>

n indicates No. in each group; PP, primary patency; PAP, primary assisted patency; SP, secondary patency; LS, limb salvage; and NA, not available.
The present trial show no evidence of a difference in overall quality-of-life scores between the 2 types of follow-up used.

Evidence suggests that there is no difference in outcome between reversed and nonreversed long saphenous vein grafts37 and that comparable patency can be obtained with arm vein.38 Because arm vein grafts are often used in difficult repeat surgery, there may be a mistaken impression of poorer outcomes. In the present study, the number of arm veins used was very small, and so no subgroup analysis was performed.

The cost of duplex surveillance is considerable; previous estimates have suggested that at least a 5% per annum improvement in limb salvages rates is required to justify a surveillance program.13 13 Because primary amputation is more expensive than successful reconstruction,39 it is tempting to extrapolate these figures and suggest that interventions to maintain patency are mandatory. However, not all stenoses inevitably lead to critical leg ischemia.33 The present study has confirmed this; however, with the higher incidence of asymptomatic stenoses in the clinical arm at 18 months, it is possible that they may have a longer-term impact. Interestingly, an economic study in the United States showed that the mean costs of reconstruction and a 5-year surveillance program were the same as for primary amputation.40 40 With the fact that limbs would be lost irrespective of the surveillance strategy, the direct comparison with primary amputation is difficult. In the present study, there was no evidence of a difference in amputation rates, although there was a higher intervention rate in the duplex group (some of which therefore could be deemed as unnecessary interventions).

In conclusion, this large RCT has shown no clinical benefit or quality-of-life improvement in patients participating in a duplex surveillance program after distal reconstruction despite increased financial costs. Hence, we can no longer recommend the widespread use of duplex vein graft surveillance in the presence of close clinical follow-up.

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