



COMPARISON OF CONDUIT PATENCY AND ROLE OF ANTICOAGULANTS IN LONGITIVITY OF PROSTHETIC GRAFT VERSUS AUTOLOGOUS SAPHENOUS VEIN FOR BELOW KNEE BYPASS GRAFTING IN CRITICAL LIMB ISCHEMIA

Dr. Nishant Singh Chandel

(m.Ch.) Department Of Cardiovascular And Thoracic Surgery Pt. J.N.M. Medical College And B.R.A.M Hospital ,Raipur (C.G.)

Dr. Krishnakant Sahu*

(m.Ch.) Department Of Cardiovascular And Thoracic Surgery Pt. J.N.M. Medical College And B.R.A.M Hospital ,Raipur (C.G.) *Corresponding Author

ABSTRACT

BACKGROUND: As established fact the autogenous vein is the conduit of choice in below-knee arterial bypasses. However, with availability of newer prosthetic grafts and usage of anti-platelets and anticoagulants, the results of these prosthesis's are also improving, so much so that in case of non availability of good GSV or malnourished patients where wound healing could be a concern prosthetic grafts can be used reasonably well.

We also compared the outcomes of below-knee prosthetic versus autologous vein bypass grafts with different anti-platelets and anti-thrombotic medicines combinations to find out whether the prosthesis performance improves with anticoagulants usage and whether the addition of anticoagulants to anti-platelets is causing more bleeding complications in these patients so much that they are to be used with caution.

METHODS: For this study, we utilised treatment data of Department of Cardiovascular and Thoracic Surgery ,Pt. J.N.M. Medical College Raipur. we studied 70 patients, Single surgeon experience. We included patients who underwent open below knee bypass procedure for critical limb ischemia (claudication/ rest pain/ non healing ulcers/ gangrenous changes) between January 1, 2018 and December 31, 2019. Our analysis was limited to patients whose graft origins were the ipsilateral iliac or femoral arteries and whose targets were the below-knee popliteal or tibial arteries.

We analysed the results by evaluating the Graft Patency at 1 year, major amputation at 1 year, bleeding complications, association of bleeding complications to the combination of anti-platelets + anticoagulation.

we also evaluated the patency at 1 year in relation to the distal anastomotic sites (popliteal or infra popliteal) and amputation in relation to the distal targets for bypass to understand that the disease load has any significance in the patency and limb salvage in patients of lower limb ischemia.

RESULTS : A total of 70 patients who underwent open below knee bypass procedure for critical limb ischemia were analysed; 35 patients (50%) received GSV and 35 patients (50%) received a prosthetic conduit. There was no significant difference in primary patency due to Gender (Male 84.3%, Female 15.7%), Diabetes Mellitus (GSV 20%, Prosthetic 14.3%), Hypertension (GSV 31.4%, Prosthetic 45.7%) & Tobacco addition (GSV 100%, Prosthetic 94.3%). Baseline characteristics were similar among groups with the popliteal artery (54.3%) and infra popliteal arteries. i.e. tibioperoneal trunk (27.1%), Anterior Tibial (4.3%) and posterior tibial (14.3%). We found no significant difference in primary graft patency (77% vs 71%, P=) or major amputation rates (8.5% vs 17%, P=) between GSV and Prosthetic conduit. The prosthetic graft patency was more when the anti platelets were combined with anticoagulants. Saphenous vein graft patients did well even with anti platelets single or combination. Bleeding complications were more common in the prosthetic group with anti platelets with anticoagulants.

CONCLUSIONS: Although limited in size, our study demonstrates that, with appropriate patient selection and anti-thrombotic therapy, 1-year outcomes for below-knee prosthetic bypass graft can be comparable to those for greater saphenous vein conduit. Though the study does not challenge the superiority of vein graft for below knee bypass grafting, but in certain cases where needed prosthetic graft are definitely comparable in performance.

KEYWORDS : Anti-platelets, Anti-thrombotic, Prosthetic Grafts, Gsv Grafts

INTRODUCTION

Type of conduit and the site of below knee distal arterial anastomosis for popliteal and infra popliteal arteries are relevant predictors of infrainguinal bypass patency. Autogenous reversed GSV maintains superior patency compared with prosthetic grafts (e-PTFE or Dacron grafts). Short- segment prosthetic bypasses to above-knee targets can approach the approximately 80% 5-year patency rates as obtained with saphenous vein grafts. But longer prosthetic grafts crossing the joint usually do not perform as well as seen in several retrospective series.

However, many patients with long-segment occlusions lack adequate great saphenous vein, either due to inadequate size, superficial thrombophlebitis or because it has been previously harvested. Adjunctive use of anti-platelets with or without anti-thrombotic therapy has been proposed to improve outcomes. Single anti-platelet therapy (Ecosprin) was associated with a approximately 40% relative risk reduction of venous graft occlusion. For prosthetic grafts that crosses the knee joint, a recently published randomised trial found that the addition of clopidogrel to aspirin contributed an additional 35% to 40% reduction of graft thrombosis. Anticoagulation with warfarin or acitrom may provide a protective effect for below knee prosthetic bypass grafts, especially to infra popliteal targets.

METHODS:

DATABASE AND SUBJECTS

For this study, we utilised data from Department of Cardiovascular and Thoracic Surgery ,Pt. J.N.M. Medical College Raipur. we studied 70 patients, single surgeon experience. Patient-level and operative data were procured Pre Operative, Peri Operative period and at 1-year follow-up.

We included patients who underwent open below knee bypass procedure for critical limb ischemia (claudication/ rest pain/ non healing ulcers/ gangrenous changes) between January 1, 2018 and December 31, 2018. Our analysis was limited to patients whose graft origins were the ipsilateral iliac or femoral arteries and whose targets were the below-knee popliteal or tibial arteries.

Lower extremity bypass grafts that did not cross the knee joint were excluded. To allow comparison of prosthetic conduit to an "ideal" conduit, we studied only patients who underwent surgery with either a single-segment great saphenous vein or prosthetic 25 (71.4%) e-polytetrafluoroethylene and 10 (28.6%) Dacron). We also excluded patients who lacked sufficient follow-up data (4%). Mean follow-up time for the cohort was 400 days.

DEFINITIONS OF ANTI-THROMBOTIC USE

Patients were kept on anti-platelet (single or dual i.e. ecosprin +/- clopidogrel) depending upon tolerance of patients, for vein grafts. where as the prosthetic graft patients were kept on anticoagulation with or without anti-platelets. The anti-thrombotic medication utilised in our study was universal acitrom (nicoumalone). Patients were recorded to be taking these medications preoperatively (ecosprin till the date of surgery, clopidogrel and acitrom stopped 3 days prior to surgery), at hospital discharge after surgery, and till completion of 1-year follow-up.

We studied patients with a venous graft vs prosthetic graft, who were on aspirin alone (n= 23), aspirin plus clopidogrel (n = 19), aspirin plus acitrom (n = 22), and aspirin plus clopidogrel plus acitrom (n = 6). Comparisons between outcomes were performed across these diffe

rent combinations of anti-thrombotic therapy.

MATCHING COHORTS

Decisions regarding conduit type and anti-thrombotic treatment were made by the treating Vascular surgeon. To control for the nonrandom decision to utilise an autologous or prosthetic bypass conduit, we used propensity matching methods to create similar patient cohorts. We matched patients who received a prosthetic conduit to patients with a greater saphenous vein conduit by stratified propensity score . This ensured that our two cohorts were matched equally in terms of age, gender, comorbidity, anticoagulation therapy, indication, and operative details.

DEFINITIONS OF OUTCOME MEASURES

Our main outcome measures were primary graft patency and the incidence of major lower extremity amputation. Primary patency was defined as uninterrupted patency of the bypass graft with no requirement of procedure or intervention of the conduit itself after implantation for 1 year duration of followup. Patency was assessed by physical examination and duplex scan, sometimes CT Angiogram.

Below-knee and above-knee amputations qualified as major leg amputations due to extension of gangrene after surgery. Some cases came with established gangrene but post surgery the gangrene did not extend and thus the level of amputation was lowest possible and thus they were not considered as major amputation.

Secondary outcomes assessed were patient survival and bleeding complications. We defined a bleeding complication as bleeding (overt or occult) requiring blood transfusion of >2 units of packed red blood cells.

STATISTICAL ANALYSIS

When comparing patient demographics, we applied chi-squared analysis, proportion test for categorical variables, depending on the number of groups compared. The chi-squared analysis was used to compare bleeding complication, Primary patency at 1 years follow up & Major Amputation. The 95% confidence intervals (CIs) were reported when appropriate and P < 0.05 was considered as a Significant.

All analyses were performed using Microsoft Excel & SPSS 20.0 version Software.

RESULTS

We studied 70 patients who undergone below knee bypass surgery for critical limb ischemia between Jan. 2018 and Dec. 2019 and met our inclusion criteria. Demographic were similar between the two groups for Age, Sex and there is no statistically significant differences between the two groups. Morbidity wise diabetes was found in 12 (17.1%), Hypertension in 27 (38.6%) (Table 1). Whereas coronary artery disease was found in 3 (4.3%) The incidence of diabetes mellitus was higher in the GSV group but this did not reach statistical significance.

Table No. 1: Patients demographic of the two groups.

Characteristics	GSV	Prosthetic	P Value
Sex (M/F)	29/6	30/5	0.743
Age			
40 - 49	11 (31.4%)	19 (54.3%)	0.181
50 - 59	13 (37.1%)	11 (31.4%)	
60 - 69	10 (28.6%)	4 (1.4%)	
70 - 79	1 (2.8%)	1 (2.8%)	
Tobacco Addiction	35 (100.0%)	33 (94.3%)	0.153
Diabetes Mellitus	7 (20.0%)	5 (14.3%)	0.529
Hypertension	11 (31.4%)	16 (45.7%)	0.219
CAD	2 (5.7%)	1 (2.8%)	0.555

The baseline characteristics and comparisons of the two groups are summarised in table 2. Anti platelets and anti thrombotic procedures were less frequent in the GSV group compared with the Prosthetic group. The prosthetic group had a significantly higher rate of popliteal targets and more frequent use of anticoagulation. Ischemic rest pain was noted in 56 (80%) and tissue loss in 39 (55.7%) patients. Of these, 35 (50%) received greater saphenous vein (GSV) and 35 (50%) received prosthetic conduit.

Table No. 2: Distribution of Operative characteristics of the two groups.

Characteristics	GSV	Prosthetic	P Value
Graft Origin			
External Iliac	6 (17.1%)	9 (25.7%)	0.535
Common Femoral	14 (40%)	15 (42.9%)	
Superficial Femoral	15 (42.9%)	11 (31.4%)	
Graft Recipient			
Below Knee Popliteal	18 (51.4%)	20 (57.1%)	0.473
Tibioperoneal trunk	8 (22.9%)	11 (31.4%)	
Ant. Tibial	2 (5.7%)	1 (2.9%)	
Post Tibial	7 (20%)	3 (8.6%)	
Anti Platelets / Anti thrombotic			
Aspirin	20 (57.1%)	3 (8.6%)	< 0.001
Aspirin + Clopidogrel	11 (31.4%)	8 (22.9%)	
Aspirin + Acitrom	4 (11.4%)	18 (51.4%)	
Aspirin + Clopidogrel + Acitrom	0 (0.0%)	6 (17.1%)	

A comparison of outcomes between the group of patients receiving GSV and the group of patients receiving a prosthetic conduit is shown in table 3. Bleeding complications were more in anti-platelet + anticoagulation group . out of 70 patients , 42 (60%) patients received a anti-platelets (single or dual) and 28 (40%) patients received anti-platelets + anticoagulants. out of anti-platelets group only 3 patients(7%) had significant bleeding complications. whereas 14 patients (32 %) in anti-platelets + anticoagulant group had bleeding complications. Primary graft patency at 1 year was 77% of GSV and 71.4% of Prosthetic group (P = 0.979). Patients with a prosthetic graft were more often treated with acitrom in addition to aspirin (51.4% vs. 11.4% or with acitrom in addition to aspirin and clopidogrel (17% vs. 0%). Conversely, patients with GSV were more commonly treated with aspirin alone 57 % vs. 8.5%) or with aspirin plus clopidogrel (31.4% vs. 22.8%). Major limb amputation occurred in 8.5 % of patients with GSV and 17% of patients with a prosthetic graft .

Table No.3: Comparison of outcomes between GSV & Prosthetic grafts using Anti thrombotic therapy.

Anti Thrombotic Therapy	GSV	Prosthetic	P Value
Bleeding Complications			
Aspirin	0	0	0.999
Aspirin + Clopidogrel	1	2	0.953
Aspirin + Acitrom	3	4	0.979
Aspirin + Clopidogrel + Acitrom	0	7	0.793
Total	4	13	0.825
Primary Patency at 1 Year			
Aspirin	13	0	0.721
Aspirin + Clopidogrel	10	6	0.917
Aspirin + Acitrom	4	14	0.811
Aspirin + Clopidogrel + Acitrom	0	5	0.826
Total	27	25	0.979
Major Amputation at 1 Year			
Aspirin	2	3	0.964
Aspirin + Clopidogrel	0	2	0.886
Aspirin + Acitrom	1	1	0.999
Aspirin + Clopidogrel + Acitrom	0	1	0.919
Total	3	7	0.923

Primary outcomes analysed based on whether patients had their distal anastomosis at the below-knee popliteal artery (or tibioperoneal trunk) vs at a tibial vessel. Those who had a venous conduit to the below-knee popliteal artery maintained 80 % primary graft patency and those grafted at infra popliteal level had 66.7% patency at 1 year . Patients with a prosthetic graft to the same target level had a primary patency rate of 77.4 % at popliteal level and 25% at infra popliteal arteries. The incidence of amputation in patients with venous grafts targeting the popliteal arteries was 7.7% and in prosthetic group was 16% . whereas t in infra popliteal targets amputation rate was 22.6% in GSV, and 50% in prosthetic group.

we could easily see that the bleeding complications were more oftenly seen in dual anti-platelet + anticoagulation group (35%) and single anti-platelet +anti coagulation group (35%) than only anti-platelets

group (15%). this did not have any association to the type of graft, though the prosthetic graft patients were kept on higher anti-platelet+anticoagulation medicines , so this appeared that bleeding is more in prosthetic than GSV group.

we noted a higher amputation rate in the subgroup of patients who were only on aspirin and received a prosthetic versus venous conduit .

DISCUSSION

Since the autogenous saphenous vein was first described as a bypass conduit for femoral arterial disease in 1949, it has remained the conduit of choice. However, many patients with tissue loss and superficial thrombophlebitis due to various reasons autologous saphenous vein remains unavailable for quarter of bypass patients.

These patients often receive a prosthetic bypass conduit as now there are better and improved bypass graft conduits are available ,they can be second option to autologous vein but are definitely satisfactory option, especially in the era of adjunctive anti-platelets and anticoagulants.

In our study, we compared 1-year outcomes of below knee bypass for patients with critical limb ischemia who received a prosthetic conduit with those who received time tested reversed great saphenous vein. Surprisingly, we discovered little difference in primary graft patency, and amputation rates but more bleeding complications within the first year of surgery and only marginal clinical and statistical benefit in terms of limb salvage and survival for those patients who received a saphenous vein bypass.

WE BELIEVE THE POSSIBLE EXPLANATIONS COULD BE

1. Too early to note a difference. Our initiative evaluated patients at 1-year follow-up, which limits our ability to assess long-term outcomes in graft patency and limb salvage. It is highly likely that, in long term the venous grafts outperform the prosthetic grafts but after 1 year, patency rates for prosthetic conduit was almost equally good

Prosthetic graft patients were more commonly on anti-coagulations + anti-platelets .mostly this combination of medicines were responsible for comparable patency of the prosthesis group, resulting in the lack of difference in outcomes by conduit type.

For example, the **CASPAR trial** demonstrated that, in a controlled environment, the addition of a second anti-platelet agent (clopidogrel plus aspirin) provides a greater protective effect for infra geniculate prosthetic bypass grafts when compared with aspirin alone. so this finding led us use higher doses of anti-platelets and anti-coagulations , so that the coagulability of blood was less and so the graft thrombosis.

Brumberg and colleagues reported that therapeutic warfarin use in low-flow below-knee prosthetic grafts is associated with significantly improved patency rates. Further, a single centre randomisation of patients with infrainguinal prosthetic bypass grafts mirrored these findings. **Sarac and colleagues** detailed an improvement in 3-year primary graft patency by 50% in patients who received warfarin in addition to base-fine aspirin.

However, although some studies supported the use of warfarin to preserve graft patency, others have refuted this assumption. A **large multi-centre study in Europe** (Dutch Bypass Oral Anticoagulants or Aspirin Study) demonstrated that oral anticoagulants were not associated with improved graft patency for prosthetic femoropopliteal or femorocrural grafts. Further, in a study from **UCLA**, a 20-year review of infrageniculate bypass surgery with prosthetic conduit showed no association between warfarin use and prosthetic bypass patency.

But in our study we used anticoagulants in view that our region blood hyper-coagulability is common observation, patients are non compliant in abstinence from tobacco, dehydration is common in labourer class, hyper-homocystinemia is endemic in this region.

Nevertheless, study would require stronger evidence than our observational data owing to small sample size and short term followup , could provide. Future work addressing the interaction between conduit types and adjunctive anti-thrombotic regimens, in a controlled setting, will be needed to reach such conclusions. we propose that the patients with this problem can be evaluated with detailed coagulation

profile, if the blood characteristics are towards procoagulant state, adding the anticoagulants will be more justified.

Our study has other limitations. we noticed that the group of patients who were having poor veins and received prosthetic grafts, their atherosclerotic burden was high and had poor runoff vessels. This could have negative effect on the longevity of the conduit. Moreover we did not practice the vein cuff for below knee tibial level prosthetic grafts. We seriously think that when the distal target is any of the tibial arteries , adding a small piece of vein between the prosthetic graft and tibial artery can improve the results of prosthetic graft to tibial level grafting.

Our analysis of bleeding complications was limited to short-term occurrences. We cannot comment on long-term adverse effects that are often associated with chronic anticoagulation, such as hematomas or cerebral bleeds, as our registry does not capture these. Our observation that prosthetic graft group had more bleeding ,owing to anti-platelets + anti-coagulations combinations ,our major deterrent was poor timely followup of patients in PT/INR testing leading to occasional bleeding incidence due to fluctuating INR values causing bleeding issues. Those with acceptable INR values and regular followups were less likely to have bleeding incidences.

In conclusion, our investigation has shown that, within a 1-year period, prosthetic below knee bypass grafts can be equally good conduit as saphenous vein grafts given appropriate patient selection and anti-thrombotic therapy. Further controlled trials, especially those investigating novel anti-thrombotic therapies, are necessary to better delineate the use of protective adjuncts with prosthetic bypass conduits. Nonetheless, given the statistically different limb salvage rates, single-segment GSV, when available, remains the preferred conduit.

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