

Factors Influencing Infrainguinal Reverse Vein Bypass Patency at Universitas Academic Hospital

A Retrospective Review

Submitted in fulfilment of the requirements in respect of the Master's Degree MMed in the Department of General Surgery in the Faculty of Health Sciences at the University of the Free State.

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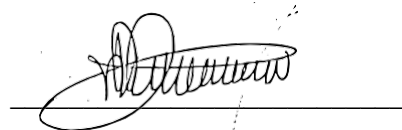
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DECLARATION OF AUTHORSHIP

I declare that the coursework Master's Degree mini-dissertation and interrelated publishable article that I herewith submit for the degree in M.Med (Surgery) at the University of the Free State is my own independent work and that I have not previously submitted it for a qualification at another institution of higher education. Where help was sought, it has been acknowledged.

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I hereby declare that all royalties in relation to intellectual property that was developed during the course of and/or in connection with the study at the University of the Free State will accrue to the University.



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ABSTRACT

Introduction and Aim: Peripheral arterial disease is a serious global healthcare concern with a subgroup of patients requiring revascularisation for chronic limb-threatening ischaemia. Open bypass surgery remain a valuable tool in the armamentarium of revascularisation options and several factors are known to affect the patency of a bypass procedure. Literature in this regard is, however, lacking in the South African population.

Methods: This was a retrospective cohort analytic study of infrainguinal reverse vein bypasses performed at a central academic hospital in South Africa between January 2012 and December 2016 for the indication of chronic limb-threatening ischaemia. 211 patients with a total of 219 bypass procedures were included. Patency data was assessed for 138 bypasses with 79 patients (36.1%) lost to follow-up and 2 patients (0.9%) who demised.

Results: 156 (73.9%) were males and 55 (26.1%) were females. The median age was 61 years. The majority of the patients (78.2%) had hypertension and were known smokers (83.4%), whereas only 32.2% had diabetes mellitus and 11.4% had renal impairment. The human immunodeficiency virus status was unknown in the majority (70.6%) of patients. 83.1% of bypasses were performed for the indication of tissue loss in addition to rest pain. The proximal anastomosis was performed from the common femoral artery in 47.9% of cases and the distal anastomosis to the tibialis posterior artery in 27.9% of cases. Most patients (26.9%) had a single vessel runoff. The median diameter of greater saphenous vein utilised was 2.7mm. 26.1% of grafts demonstrated early graft failure within 30 days compared to 45.7% demonstrating patency beyond 12 months. Age, race, hypertension, diabetes, renal failure, the presence of tissue loss, level of the proximal and distal anastomoses and number of runoff vessels had no significant effect on graft patency. Female gender, a small greater saphenous diameter as well as a single anterior tibial vessel runoff, however, proved to be statistically significant indicators of early graft failure. Smoking, on the other hand, was associated with a longer graft patency beyond 12 months.

Conclusions: Female gender, small vein diameter and a single anterior tibial runoff vessel are independent predictors of early graft failure. Smoking, on the other hand, is associated with prolonged patency beyond 12 months which is in contrast to the majority of existing literature.

KEYWORDS

Bypass, chronic limb-threatening ischaemia, critical limb ischaemia, infrainguinal, patency, revascularisation, vein

LIST OF ABBREVIATIONS

ABPI	Ankle-brachial pressure index
ACC	American College of Cardiology
AHA	American Heart Association
AK POP	Above-knee popliteal
BASIL	Bypass versus Angioplasty in Severe Ischemia of the Leg
BK POP	Below-knee popliteal
CFA	Common femoral artery
CI	Confidence interval
CLTI	Chronic limb-threatening ischaemia
DP	Dorsalis pedis
GSV	Greater saphenous vein
HIV	Human immunodeficiency virus
NSQIP	National Surgical Quality Improvement Program
PAD	Peripheral arterial disease
Per	Peroneal artery
PFA	Deep femoral artery
PREVENT	Project Ex Vivo graft Engineering via Transfection
PTFE	Polytetrafluoroethylene
SFA	Superficial femoral artery
TA	Anterior tibial artery
TP	Posterior tibial artery
TPT	Tibioperoneal trunk
VA	Veterans Affairs

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- A. Health Sciences Research Ethics Committee (HSREC) letter of approval
- B. Free State Department of Health (FSDOH) letter of approval
- C. Head of Department (HOD) of Surgery letter of approval
- D. Biostatistics letter of approval
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CHAPTER 1

Peripheral arterial disease (PAD) poses a major global healthcare problem with a disease prevalence of 3 to 10% in the general population, increasing to 15 to 20% in persons over the age of 70 years. It is associated with a worse prognosis than the general population as it is considered a manifestation of a systemic disease. ¹

Chronic limb-threatening ischaemia (CLTI) refers to the most severe manifestation of PAD in which patients present with chronic ischaemic rest pain or ischaemic skin lesions, often manifesting as ulcers or even gangrene, in the presence of one or more abnormal haemodynamic parameter. ² It is most commonly caused by atherosclerosis, however, several other causes have been identified of which human immunodeficiency virus (HIV) plays an important role in Southern Africa. ³ Despite developments in the field, effective revascularisation still remains the cornerstone of limb salvage in CLTI with large surveys suggesting that approximately half the patients with CLTI will undergo some type of revascularisation in order to prevent limb loss. ¹

Several open surgical and endovascular revascularisation methods exist and include, amongst others, surgical bypass, endarterectomy, profundaplasty, angioplasty with or without stenting, or a combination of these. ¹ The type of intervention chosen depends on several factors, including the patient's periprocedural risk estimation, life expectancy, the severity of disease and the anatomic pattern of disease distribution. ²

Based upon the findings of the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial, the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend that for patients with a life expectancy of more than two years, and who have an available autologous vein conduit, bypass surgery is reasonable to perform as the initial treatment. ^{4,5}

This recommendation is supported by a review of studies published since 1981, which found that primary above-knee femoropopliteal graft patency is 84% and 69% at one and four years when reverse saphenous vein is the conduit compared to 79% and 60% at one and four years when polytetrafluoroethylene (PTFE) is used. With below-knee grafts, explicitly performed for limb salvage, cumulative primary patency with reversed saphenous vein or PTFE is approximately 90% and 75% at one and four years, respectively. Secondary patency for PTFE grafts in the below-knee position for all indications is 68% and 40% at one and four years. Based upon these numbers, prosthetic material is avoided whenever possible for below-knee bypass. ⁶

Despite the good outcome from autologous vein grafts, graft failure still remains a significant challenge for vascular surgeons. Graft failures have traditionally been divided into either early failure (within 30 days) or late failure (beyond six months). Early failure is generally considered to be due to either technical factors (usually fails within 72 hours) or an inadequate inflow, runoff or conduit. Late failures, on the other hand, can be attributed to progression of the underlying disease or neointimal hyperplasia at the anastomotic sites.^{7,8}

A vast number of studies have been dedicated to an attempt to determine those factors which influence graft patency. These factors, however, do not appear to be consistent throughout the literature, and conflicting data is commonplace.

In one of the largest studies to date, Singh et al analysed the Veterans Affairs (VA) National Surgical Quality Improvement Program's (NSQIP) sizeable clinical database to investigate which factors, other than technical, were associated with a higher incidence of early graft failure in infrainguinal bypass. The NSQIP database identified 14 788 patients who underwent infrainguinal lower extremity arterial bypass during the study period, and 723 acute graft failures (4.9%) occurred. On multivariate analysis, patients aged less than 60 years, African American race as well as a lower haematocrit level, were all associated with early graft failure. Diabetes mellitus, on the other hand, had a negative association with early graft failure.⁷

The PREVENT III (Project Ex Vivo Graft Engineering via Transfection) trial was a prospective, randomised, double-blinded, placebo-controlled, multicentre trial that evaluated the effect of edifoligide on vein graft patency. Although a negative study with regards to the primary outcome, the PREVENT III investigators, through statistical analysis and propensity scores, evaluated the association of race and gender on outcomes of vein bypass for CLTI. The authors concluded that African-American race was at increased risk for early graft failure with a hazard ratio of 2.5.⁹

Alpagut et al, at the Department of Cardiovascular Surgery, Istanbul University in Turkey, performed a retrospective analysis to evaluate the impact of gender on patency of infrainguinal bypass grafts. A total of 575 patients, 375 males and 200 females, underwent infrainguinal bypass for femoropopliteal and or distal arterial occlusive disease over a period of approximately nine years. The majority of cases underwent autologous vein bypass (65%), of which the reversed configuration was most commonly employed (59%). PTFE grafts were only utilised if no autologous options were available. Even though 30-day mortality appeared similar between males and females (2%), early graft thrombosis was more common in females, although this was not considered statistically significant. On the other hand, primary patency was significantly worse in females (60%, 52%, and 40% at 1, 3, and 5 years) compared to males

(78%, 70%, and 62% at 1, 3, and 5 years). This was again emphasised with a significantly decreased secondary patency for females compared to males (68% and 61% vs 83% and 80% at 1 and 3 years). The researchers of this study concluded that female patients with infrainguinal arterial reconstruction have a significantly worse outcome compared to their male counterparts which was attributed to smaller distal runoff arteries compared to their male counterparts as well as smaller vein graft diameter.¹⁰

In one of the earlier studies conducted on this topic, Rutherford et al analysed the outcome of 249 infrainguinal bypasses. Autologous vein was utilised in 48% of cases, of which the majority (59%) was in the in situ configuration. PTFE and human umbilical vein were utilised in 24% and 28% of cases, respectively. The authors concluded that the graft type and level of anastomosis were the two factors that had the most significant influence on infrainguinal bypass patency. This was especially pronounced whenever the anastomosis was below the knee – a clear advantage was seen with the use of autologous vein over PTFE and/or human umbilical vein, which was already apparent at 1 year. On the other hand, there was no significant difference in outcome between reversed or in situ vein configurations. In addition, the authors found that tobacco use was associated with a significantly decreased patency (51% vs 68% at 3 years) whereas diabetes appeared to be protective with an improved overall 3-year primary patency (60% vs 42%). The runoff status, pre- and postoperative ankle-brachial index (ABI), clinical classification, and use of antiplatelet therapy was, on the other hand, were not associated with a significant difference in primary or secondary patency.¹¹

In an attempt to determine the causes of reversed vein bypass occlusion that could be addressed in the postoperative period, Gissel et al from the Oregon Health & Science University and Portland Veterans Affairs Medical Center, evaluated 55 patients who developed graft occlusion after a lower limb bypass. Dialysis therapy, a known hypercoagulable state, as well as persistent smoking were found to be independent predictors of graft occlusion. Smoking, being a modifiable risk factor, is of particular concern with a hazard ratio of 4.72 for graft failure in this study.¹²

Ray et al performed a retrospective study of 150 patients with femoropopliteal bypass grafts where a detailed analysis of the factors that contributed to the graft patency was performed. The factors analysed in this study were clinical indication, runoff, placement of the proximal and distal anastomosis, the diameter of the saphenous vein graft, and the patient's age. The clinical indications for bypass were intermittent claudication, rest pain and gangrene. The best results were found in patients with intermittent claudication showing a 90% long term patency. Very little difference was shown in patients with rest pain and gangrene, with patency rates of 81.8% and 80.7%, respectively. The runoff segments were classified into three groups according to the patency of the popliteal, anterior tibial, and posterior tibial arteries.

Although the patency rate drops from 92.6% in patients with a three-vessel runoff to 65% in patients with only a single vessel runoff, this study showed that an isolated popliteal segment or single tibial vessel is often adequate to sustain function with autologous vein grafts. This study also showed that patients with saphenous vein graft diameter of 3-4mm and 5-6mm had 75.6% and 85.1% patency rates, respectively, compared to 19% patency for 7mm or more.¹³

Budd et al at the Department of Surgery and Community Medicine, University of Leicester, United Kingdom, performed a retrospective study to evaluate factors determining late graft patency for infrainguinal bypass surgeries. The single centre results of 373 infrainguinal bypass grafts between 1980 and 1988 were reviewed. 130 in situ saphenous vein, 47 reversed saphenous vein, 118 PTFE and 78 human umbilical vein grafts were used. The indications for surgery were disabling claudication in 25% of patients and limb salvage in 75%. In 36% of the operations, the distal anastomosis was above the knee, and 64% was below the knee. Overall, 5-year patency and limb salvage rates were 41% and 69% for in situ saphenous vein, 62% and 90% for reversed saphenous vein, 31% and 67% for PTFE and 29% and 59% for human umbilical vein. There was no significant difference in patency among these grafts at the above knee level, but significant differences between vein and prosthetic grafts were evident below the knee ($p < 0.001$). Using a proportional hazard model, the three factors that consistently correlated with late graft patency were graft type, site of distal anastomosis and distal runoff.¹⁴

In a retrospective study done by Cheshmedzhiev et al at St Marina University Hospital in Bulgaria, the clinical significance of venous graft size and runoff segment for peripheral bypass patency was assessed. The study aimed to analyse the one-year patency of infrainguinal arterial reconstructions in relation to venous graft diameter and length. Results were worse in venous grafts less than 3.5mm and the length over 40cm.¹⁵

Wengerter et al at Montefiore Medical Centre in New York performed a retrospective study to evaluate the influence of the vein size diameter on the infrapopliteal reversed vein graft patency. They reviewed 239 infrapopliteal reversed greater saphenous vein bypasses performed for critical limb ischaemia over a 7-year period in order to determine the influence of vein diameter on graft patency and limb salvage. A pattern of increasing graft patency and limb salvage was noted as the minimum diameter increased from <3.0mm to >4.0mm. When compared to the larger grafts > 4.0mm, primary graft patency was significantly lower both for < 3.0mm grafts (0% for < 3.0mm vs 65% for >4.0mm at 3 years, $p < 0.001$). The author concluded that long 3.0mm and all reversed saphenous vein grafts <3mm should be considered at high risk for failure.¹⁶

Hertzer et al from the Department of Vascular Surgery, Cleveland Clinic Foundation, in the United States, performed a retrospective analysis to evaluate the impact of diabetes mellitus and other factors on the outcome of infrainguinal bypasses. Six hundred fifty patients were included in the study. Bypasses were performed for critical limb ischaemia in 85% of cases and autologous vein was utilised in 60% of cases. The operative mortality was 4.8%. 12% of grafts occluded and 7.5% of patients underwent an amputation during the index admission. Autologous grafts had a significantly improved primary patency compared to prosthetic grafts. Diabetes did not appear to affect graft patency. The number of graft revisions, on the other hand, was an important predictor of graft failure and risk for amputation.¹⁷

Frangos et al at Yale University School of Medicine, New York, performed a retrospective analysis to assess the influence of gender on patient selection and outcome in patients requiring infrainguinal vein bypass graft procedures. They reviewed 217 infrainguinal vein bypass grafts performed over an 8-year period. Gender and multiple covariables affecting patient survival were analysed as well as postoperative complications and graft patencies. The results showed no statistical differences between men and women for age, diabetes, cardiac disease, tobacco use, hypertension, stroke, renal disease, or prior contralateral bypass or major amputation. The study concluded that gender does not affect graft patency, limb salvage, or survival rates.¹⁸

In London, Slim et al at King's College Hospital, performed a retrospective study to assess the difference in patency rate and amputation-free survival in infrainguinal bypass grafts with vein diameter more or less than 3mm in patients with critical limb ischaemia. A total of 157 patients and 171 bypasses were included in the study. The majority of bypasses were performed for tissue loss (54%) and was of a femorodistal configuration (78%). Reversed autologous greater saphenous vein was utilised in all cases. Only 18% of cases had a vein diameter < 3mm. The study concluded that primary and assisted primary patency at 1 year was not significantly influenced by a vein diameter <3mm. The secondary patency, on the other hand, was significantly increased in bypasses performed with a vein diameter > 3mm (95% vs 83%). The amputation-free survival, however, was comparable between the two groups.¹⁹

Davies at the University of Bristol performed a prospective study to assess vein factors that affect the outcome of femorodistal bypass. One hundred femoropopliteal or infrapopliteal bypasses were performed on 95 patients (31 female and 64 males) with a mean age of 67 years. Graft stenosis occurred in up to 30% of the grafts, the etiology of which was poorly understood. The mean diameter of those veins that developed stenosis was 3.7mm compared with 4.7mm in those which did not develop a stenosis ($p = 0.006$).²⁰

A critical assessment of infrainguinal reverse vein bypasses was performed by Golledge et al. They found that, despite a secondary graft patency of 82% at 12 months, only 22% of patients had an ideal outcome. At one year, 44 (19%) patients died, 93 (39%) required further ipsilateral intervention and 39 (17%) contralateral intervention, and a total of 108 (46%) were readmitted. An ideal outcome was more likely in patients receiving calcium channel blockers, principally because of improved primary patency, and less likely in those with cardiac failure requiring furosemide, principally because of worse survival in these patients. ²¹

Chew et al from the Division of Vascular and Endovascular Surgery at Harvard Medical School performed a retrospective analysis of graft patency and limb salvage in patients who underwent autologous infrainguinal bypasses. The majority of bypasses were performed utilising autologous greater saphenous vein with the distal anastomosis situated at the tibial or pedal level. Overall morbidity and 30-day mortality did not appear to be affected by race, however, graft failure at 30-days was significantly greater in the African American cohort compared to Caucasians (12% vs 5%). Furthermore, the overall 5-year primary patency as well as 5-year limb salvage rate was also significantly decreased in the African American cohort. In addition, other factors that were identified to be a significant risk for primary graft failure included age younger than 65 years, female gender, graft revisions, tibial bypasses as well as critical limb ischaemia as the indication for the bypass. ²²

In a separate analysis of the patients included in the Dutch BOA (Bypass, Oral anticoagulants or Aspirin) Study by Tangelder et al, risk factor for infrainguinal bypass failure were identified. In evaluation of 2650 patients that were included, female gender, critical ischaemia, femoro-distal bypass as well as the use of a non-venous conduit were independent risk factors for graft failure. In this study they randomly assigned patients that had undergone infrainguinal bypass to either oral anticoagulants (target international normalised ratio 3-4.5, n =1339) or aspirin (80mg daily=1351). They concluded that oral anticoagulation was better for prevention of infrainguinal vein graft occlusion and lowering the rate of ischaemic events. Aspirin was found to be better for the prevention of non-venous graft occlusion and was associated with fewer bleeding episodes. ²³

Several studies have evaluated bypass conduit type, diameter, length, single-segment versus spliced vein, veins other than greater saphenous and graft configuration as potential influential factors on bypass patency. ^{19, 24-28} As previously stated, Slim et al found a statistically significant effect of secondary patency if vein grafts < 3mm were utilised. ¹⁹ Oresanya et al also confirmed vein graft diameter < 3mm to be an independent predictor for graft occlusion in a retrospective analysis of the subjects included in the PREVENT III trial that suffered primary graft occlusion. ²⁴ In general, the aforementioned studies mostly

reflect the correlation between vein calibre and patency outcomes with small veins being inferior. Schanzer et al reemphasised this finding in a critical analysis of the vein-related factors in the PREVENT III. They found an increased risk for early graft failure with vein size < 3.5mm as well as the use of a composite vein graft. Analysis at one year demonstrated a persistent significant influence of a vein graft < 3.5mm, but in addition, the use of veins other than the greater saphenous as well as vein length > 50cm were considered important contributors to graft failure.²⁷ This is, however, in contrast to a study that evaluated the outcomes of long vein bypasses (from the femoral artery to the ankle), in which the authors concluded these bypasses to be a durable procedure resulting in excellent long term patency and limb salvage rates.²⁸

The unit for Vascular Surgery at Universitas Academic Hospital in Bloemfontein, South Africa, is a referral centre responsible for addressing vascular surgical pathology in all the public sector patients in the provinces of the Free State, Northern Cape as well as Lesotho. The unit, therefore, undertakes revascularisation for CLTI in a relative number of patients. Currently, data regarding graft patency rates on patients operated at Universitas Academic Hospital is lacking. A retrospective record review of patients with CLTI who underwent an infrainguinal reverse vein bypass at Universitas Academic Hospital over the past 5 years was therefore conducted to investigate factors influencing graft patency. In addition, the 1-year patency for infrainguinal reverse vein bypasses performed at Universitas Academic Hospital was assessed.

Literature has established that the most important factors that influence long term infrainguinal graft patency are graft material, vein diameter, level of the distal anastomosis and the condition of the distal runoff arteries. Evaluating these and other factors might assist in identifying those patient groups who are unlikely to benefit from bypass surgery or patients in whom early graft failure should be anticipated.

References

1. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FGR, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg.* 2007; 45 (1): S5A-S67A
2. Conte MC, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, et al. Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischaemia. *Eur J Vasc Endovasc Surg.* 2019; 58(1): S1-S109
3. Van Marle J, Mistry PP, Botes K. HIV-occlusive vascular disease. *S Afr J Surg,* 2009; 47(2): 36-42
4. BASIL Trial Participants. Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL): Multicenter, Randomized Controlled Trial. *Lancet.* 2005; 366(9501): 1925-1934
5. 2011 Writing Group Members, 2005 Writing Committee Members, ACCF/AHA Task Force Members. 2011 ACCF/AHA Focused Update of the Guideline for the Management of patients with peripheral artery disease (Updating the 2005 Guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation.* 2011; 124(18): 2020
6. Dalman RL, Taylor LM. Basic Data Related to Infrainguinal Revascularization Procedures. *Ann Vasc Surg.* 1990; 4(3): 309-3012
7. Singh N, Sidawy AN, DeZee KJ, Neville RF, Akbari C, Henderson W. Factors Associated with Early Failure of Infrainguinal Lower Extremity Arterial Bypass. *J Vasc Surg.* 2008; 47(3): 556-561
8. Stept LL, Flinn WR, McCarthy WJ, Bartlett ST, Bergan JJ, Yao JST. Technical Defects as a Cause of Early Graft Failure After Femorodistal Bypass. *Arch Surg.* 1987; 122: 599-604
9. Conte MS, Bandyk DF, Clowes AW, Moneta GL, Seely L, Lorenz TJ, et al. Results of PREVENT III: a multicenter, randomized trial of edifoligide for the prevention of vein graft failure in lower extremity bypass surgery. *J Vasc Surg.* 2006; 43:742-751
10. Alpagut U, Ugurlucan M, Banach M, Mikhailidis DP et al. Does gender influence the patency of infrainguinal bypass grafts? *Angiology.* 2008. 59(3),278-282.
11. Rutherford RB, Jones DN, Bergentz SE, Bergqvist D, Comerota AJ, Dardik H, et al. Factors Affecting the Patency of Infrainguinal Bypass. *J Vasc Surg.* 1988; 8: 236-246

12. Giswold ME, Landry GJ, Sexton GJ, Yeager RA, Edwards JM, Taylor LM, et al. Modifiable Patient Factors are Associated with Reverse Vein Graft Occlusion in the Era of Duplex Scan Surveillance. *J Vasc Surg.* 2003; 34: 47-53
13. Ray FS, Lape CP, Lutes CA, Dillihunt RC. Femoropopliteal Saphenous Vein Bypass Grafts: Analysis of 150 Cases. *Am J Surg.* 1970; 119(4): 385-391
14. Budd JS, Brennan J, Beard JD, Warren H, Burton PR, Bell PRF. Infrainguinal Bypass Surgery: Factors Determining Late Graft Patency. *Br J Surg.* 1990; 77(12):1382-1387
15. Cheshmedzhiev M, Jordanov E, Yordanov M, K. Clinical Significance of Venous Graft Size and Run Off Segment for Peripheral Bypass Patency. *J Vasc Med Surg.* 2015; 3(2)
16. Wengerter KR, Veith FJ, Gupta SK, Ascer E, Rivers SP. Influence of Vein Size (Diameter) on Infrapopliteal Reversed Vein Graft Patency. *J Vasc Surg.* 1990; 11(4): 525-531
17. Hertzner NR, Bena JF, Karafa MT. A Personal Experience with the Influence of Diabetes and Other Factors on the Outcome of Infrainguinal Bypass Grafts for Occlusive Disease. *J Vasc Surg.* 2007; 46(2): 271-279
18. Frangos SG, Karimi S, Kerstein MD, Harpavat M, Sumpio B, Roberts AB, et al. Gender does not impact infrainguinal vein bypass graft outcome. *Surgery.* 2000; 127(6): 679-686
19. Slim H, Tiwari A, Ritter JC, Rashid H. Outcome of Infra-inguinal Bypass Graft Using Vein Conduit With Less Than 3 Millimetres Diameter in Critical Leg Ischemia. *J Vasc Surg.* 2011; 53: 421-425
20. Davies, AH. Vein factors that affect the outcome of femorodistal bypass. *Ann R Coll Surg Engl.* 1995; 77(1): 63-66
21. Golledge J, Iannos J, Walsh JA, Burnett JR, Foreman RK. Critical Assessment of the Outcome of Infrainguinal Vein Bypass. *Ann Surg.* 2001; 234(5): 697-701
22. Chew DK, Owens CD, Belkin M, Donaldson MC, Whittemore AD, Mannich JA, et al. Bypass in the absence of ipsilateral greater saphenous vein: safety and superiority of the contralateral greater saphenous vein. *J Vasc Surg.* 2002; 35:1085-1092
23. Tangelder MJD, Algra A, Lawson JA, Eikelboom BC. Risk Factors for Occlusion of Infrainguinal Bypass Grafts. *Eur J Vasc Endovasc Surg.* 2000; 20: 118-124
24. Oresanya L, Makam AN, Belkin M, Moneta GL, Conte MS. Factors Associated with Primary Vein Graft Occlusion in a Multicenter trial with Mandated Ultrasound Surveillance. *J Vasc Surg.* 2014; 56: 996-1002

25. Ballotta E, Renon L, De Rossi A, Barbon B, Terranova O, Da Giau G. Prospective randomized study on reversed saphenous vein infrapopliteal bypass to treat limb-threatening ischemia: common femoral artery versus superficial femoral or popliteal and tibial arteries as inflow. *J Vasc Surg.* 2004; 40:732-740
26. Wengerter KR, Veith FJ, Gupta SK, Goldsmith RN, Farrell E, Harris PL, et al. Prospective randomized multicenter comparison of in situ and reversed vein infrapopliteal bypasses. *J Vasc Surg.* 1991; 13:189-197
27. Schanzer A, Hevelone N, Owens CD, Clowes AW, Moneta GL, Conte MD. Technical factors affecting autogenous vein graft failure: observations from a large multicenter trial. *J Vasc Surg.* 2007; 46(6):1180-1190
28. Shah DM, Darling C, Chang BB, Kaufman JL, Fitzgerald KM, Leather RP. Is Long Vein Bypass from Groin to Ankle a Durable Procedure? An Analysis of a Ten-year Experience. *J Vasc Surg.* 1992; 15: 402-408

CHAPTER 2

Factors Influencing Infrainguinal Reverse Vein Bypass Patency at a South African Tertiary Academic Hospital

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Abstract

Introduction and Aim: Peripheral arterial disease is a serious global healthcare concern with a subgroup of patients requiring revascularisation for chronic limb-threatening ischaemia. Open bypass surgery remain a valuable tool in the armamentarium of revascularisation options and several factors are known to affect the patency of a bypass procedure. Literature in this regard is, however, lacking in the South African population.

Methods: This was a retrospective cohort analytic study of infrainguinal reverse vein bypasses performed at a central academic hospital in South Africa between January 2012 and December 2016 for the indication of chronic limb-threatening ischaemia. 211 patients with a total of 219 bypass procedures were included. Patency data was assessed for 138 bypasses with 79 patients (36.1%) lost to follow-up and 2 patients (0.9%) who demised.

Results: 156 (73.9%) were males and 55 (26.1%) were females. The median age was 61 years. The majority of the patients (78.2%) had hypertension and were known smokers (83.4%), whereas only 32.2% had diabetes mellitus and 11.4% had renal impairment. The human immunodeficiency virus status was unknown in the majority (70.6%) of patients. 83.1% of bypasses were performed for the indication of tissue loss in addition to rest pain. The proximal anastomosis was performed from the common femoral artery in 47.9% of cases and the distal anastomosis to the tibialis posterior artery in 27.9% of cases. Most patients (26.9%) had a single vessel runoff. The median diameter of greater saphenous vein utilised was 2.7mm. 26.1% of grafts demonstrated early graft failure within 30 days compared to 45.7% demonstrating patency beyond 12 months. Age, race, hypertension, diabetes, renal failure, the presence of tissue loss, level of the proximal and distal anastomoses and number of runoff vessels had no significant effect on graft patency. Female gender, a small greater saphenous diameter as well as a single anterior tibial vessel runoff, however, proved to be statistically significant indicators of early graft failure. Smoking, on the other hand, was associated with a longer graft patency beyond 12 months.

Conclusions: Female gender, small vein diameter and a single anterior tibial runoff vessel are independent predictors of early graft failure. Smoking, on the other hand, is associated with prolonged patency beyond 12 months which is in contrast to the majority of existing literature.

Introduction

Peripheral arterial disease (PAD) is a serious global healthcare problem with the incidence increasing, especially in the elderly population ¹. Chronic limb-threatening ischaemia (CLTI) refers to a manifestation of PAD in which patients present with chronic ischaemic rest pain or ischaemic skin lesions (ulcers or gangrene) in the presence of one or more abnormal haemodynamic parameter i.e. a decreased ankle-brachial index (ABI). ² Effective revascularisation still remains the cornerstone of limb salvage in CLTI with large surveys suggesting that approximately half the patients with CLTI will undergo some type of revascularisation in order to prevent limb loss. ¹

Several open surgical and endovascular revascularisation methods exist and include, amongst others surgical bypass, endarterectomy, profundaplasty, angioplasty with or without stenting, or a combination of these. ¹ Despite the advent of endovascular intervention for CLTI, bypass surgery still remains an integral part of the armamentarium of revascularisation. The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend bypass surgery as an initial treatment for patients with a life expectancy of more than two years, and who have an available autologous vein conduit based upon the findings of the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial. ^{3,4}

The abovementioned recommendation is supported by a review of studies published since 1981 which found that above-knee femoropopliteal reverse saphenous vein graft patency has a primary patency of 84% and 69% at one and four years, respectively. With below-knee grafts, explicitly performed for limb salvage, cumulative primary patency with reverse saphenous vein is approximately 90% and 75% at one and four years, respectively. ⁵

Despite bypass surgery still being considered the “gold standard” by many vascular surgeons, several factors have been identified that are associated with failure of a bypass procedure such as the diameter of the vein graft, the distal runoff segment, the site of distal anastomosis and the race of the patient. ¹

A retrospective study done by Singh et al analysed the Veterans Affairs (VA) National Surgical Quality Improvement Program's (NSQIP) large clinical database to investigate which factors, other than technical, were associated with a higher incidence of early graft failure in infrainguinal bypass. A multivariate analysis demonstrated that patients aged younger than 60 years as well as African American race was associated with early graft failure. Diabetes mellitus, on the other hand, had a negative association with early graft failure. ⁶

Ray et al performed a retrospective study of 150 patients that had femoropopliteal bypass grafts where a detailed analysis of the factors that contributed to the graft patency were performed. The best results were found in patients with intermittent claudication demonstrating a 90% long term patency. Very little difference was shown in patients with rest pain and gangrene with patency rates of 81.8% and 80.7% respectively. Although the patency rate drops from 92.6% in patients with a three-vessel run off to 65% in patients with only a one vessel run off, the study showed that an isolated popliteal segment or single tibial vessel is often adequate to sustain function with autologous vein grafts. They also found that a saphenous vein graft diameter of 3-4mm and 5-6mm had a 75.6% and 85.1% patency rates, respectively, compared to 19% patency for those of 7mm or more. ⁷

Budd et al at the University of Leicester, United Kingdom, performed a retrospective analysis to evaluate factors determining late graft patency for infrainguinal bypass surgeries. Single centre results of 373 infrainguinal bypass grafts between 1980 and 1988 were reviewed. Overall, 5-year patency and limb salvage rates were 41% and 69% for in situ saphenous vein, 62% and 90% for reversed saphenous vein, 31% and 67% for PTFE and 29% and 59% for human umbilical vein. There was no significant difference in patency among these grafts at the above knee level, but significant differences between vein and prosthetic grafts were evident below the knee ($P < 0.001$). Using a proportional hazard model, the three factors that consistently correlated with late graft patency were graft type, site of distal anastomosis and distal run-off. ⁸

Wengerter et al at Montefiore Medical Centre in New York, reviewed 239 infrapopliteal reversed greater saphenous vein bypasses performed for critical limb ischaemia over a 7-year period and concluded that long 3.0mm diameter, and all reversed saphenous vein grafts with a diameter less than 3mm, should be considered at high risk for failure. ⁹

Frangos et al at Yale University School of Medicine, New York, performed a retrospective study to assess the influence of gender on patient selection and outcome in patients requiring infrainguinal vein bypass graft procedures. They reviewed 217 infrainguinal vein bypass grafts performed over an 8-year period. The results showed no statistical differences between men and women for age, diabetes, cardiac disease, tobacco use, hypertension, stroke, renal disease, or prior contralateral bypass or major amputation. The conclusion from this study was that gender does not affect graft patency, limb salvage, or survival rates. ¹⁰

Methods

This was a retrospective cohort analytic study of infrainguinal reverse vein bypasses performed at a central academic hospital in South Africa from January 2012 till December 2016 for the indication of CLTI. Prior to initiation of the study, ethics approval was obtained from the Health Sciences Research Ethics Committee of the University of the Free State (UFS-HSD 2017/1264) and Free State Department of Health (FS_2017_007). Patients who underwent infrainguinal bypasses for indications other than CLTI e.g. acute limb ischaemia or popliteal artery aneurysm, were excluded from the analysis. Different vascular surgeons performed the bypass procedures without a standardise protocol.

Patient demographics and perioperative data for each patient was obtained from a combination of electronic patient records, departmental statistics and files stored at the Vascular Laboratory at the Universitas Academic Hospital. All patient identification was kept confidential.

Where applicable, preoperative marked vein diameter was indicated as the smallest vein diameter measured.

Graft patency was evaluated as a clinically documented distal pulse or flow observed on duplex ultrasound graft surveillance. Due to the retrospective nature of the analysis, no differentiation was made between primary, primary assisted or secondary patency. A standardised graft surveillance protocol was also not utilised.

The study's primary objective was to identify factors affecting infrainguinal reverse vein bypass patency in patients operated for CLTI at Universitas Academic Hospital from January 2012 till December 2016, a five-year period. In addition, the 1-year infrainguinal reverse vein bypass patency was also to be determined. A secondary aim was to attempt to identify a subgroup of patients who are unlikely to benefit from bypass surgery or in whom early graft failure should be anticipated.

Results

During the period under review, 211 patients met the study's inclusion criteria with a total of 219 bypasses performed. 8 patients received bilateral bypasses. 2 patients (0.9%) demised and 79 of the 219 (36.1%) of bypasses were eventually excluded from the patency evaluation due to loss to follow-up. Patient characteristics are demonstrated in Table 1 and will be discussed in more detail.

Demographics

156 patients (73.9%) were males, and 55 (26.1%) were females. The median age was 61 years, with the ages ranging from 23 years to 88 years. The majority of patients were of black race (56.9%, n=120) followed by white (30.3%, n=64) and coloured (12.8%, n=27) patients.

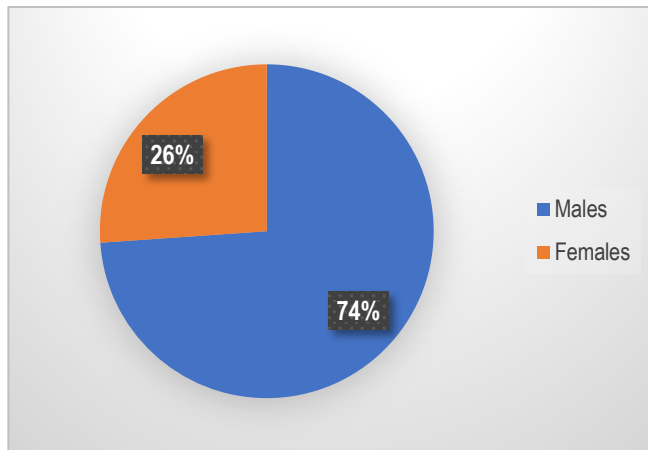


Figure 1: Gender distribution

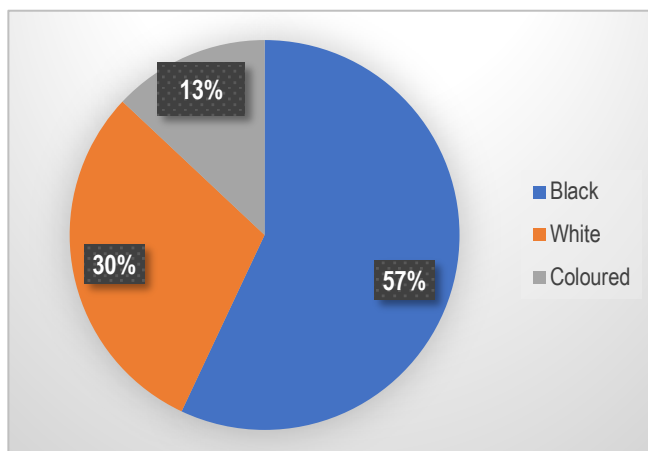


Figure 2: Race distribution

Comorbidities

The majority of patients had hypertension (78.2%, n=165) and were known smokers (83.4%, n=176). On the other hand, only 32.2% (n=68) of patients were diabetics, and only 11.4% (n=24) of patients had renal impairment.

Table 1: Patient Characteristics	
Variable	
<i>Age (years)</i>	
Median	61.0
<i>Gender</i>	
Males	156 (73.9%)
Female	55 (26.0%)
<i>Race</i>	
Black	120 (56.9%)
White	64 (30.3%)
Coloured	27 (12.8%)
<i>Comorbidities</i>	
Hypertension	165 (78.2%)
Diabetes mellitus	68 (32.2%)
Smoker	176 (83.4%)
Renal failure	24 (11.4%)
HIV	
Positive	25 (11.9%)
Unknown	149 (70.7%)
<i>Severity of ischaemia</i>	
Tissue loss	182 (83.1%)
<i>GSV diameter (mm)</i>	
Median	2.7
<i>Proximal anastomosis</i>	
CFA	105 (48.0%)
SFA	88 (40.1%)
AK POP	9 (4.1%)
PFA	8 (3.65%)
BK POP	8 (3.65%)
<i>Distal anastomosis</i>	
TP	61 (27.9%)
BK POP	49 (22.4%)
TA	42 (19.2%)
AK POP	41 (18.7%)
DP	10 (4.6%)
TPT	9 (4.1%)
Peroneal	6 (2.7%)
<i>Number of runoff vessels</i>	
1	59 (26.8%)
3	48 (21.8%)
4	35 (15.9%)
2	31 (14.1%)
5	20 (9.1%)
6	14 (6.4%)
0	13 (5.9%)

The human immunodeficiency virus (HIV) status was unknown in the majority of patients (70.6%, n=149), with only 11.8% (n=25) of patients known to be HIV positive. 72.0% of HIV positive patients (n=18/25) were on antiretroviral therapy at the time of admission.

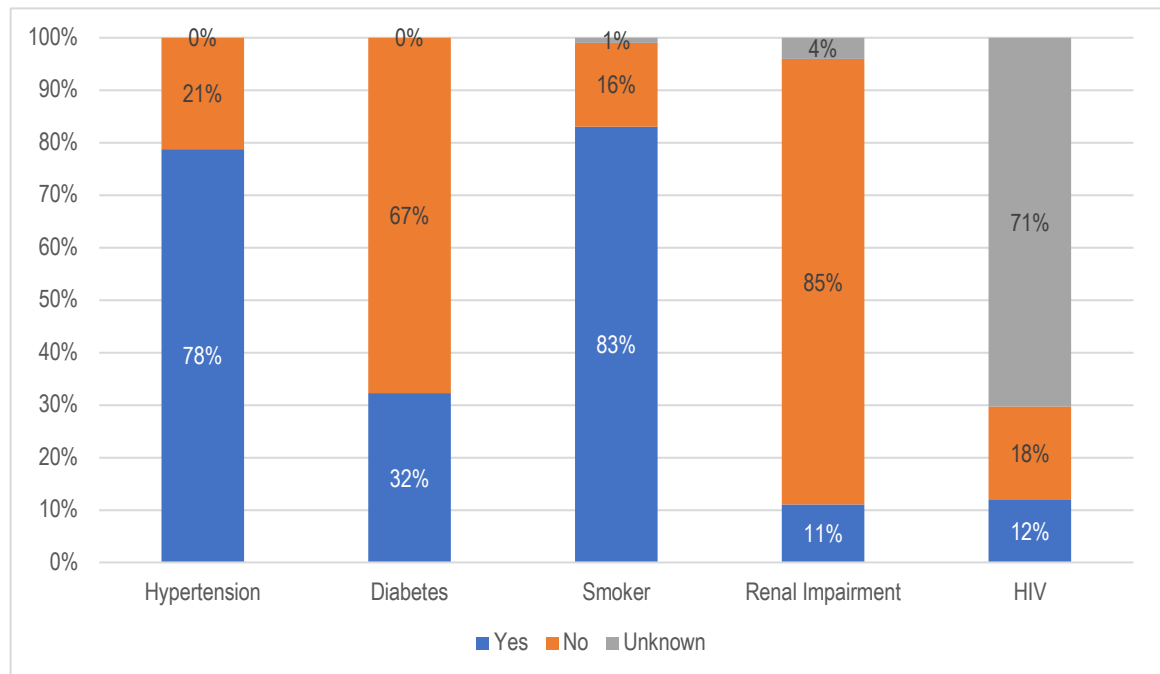


Figure 3: Comorbidities

Severity of Ischaemia

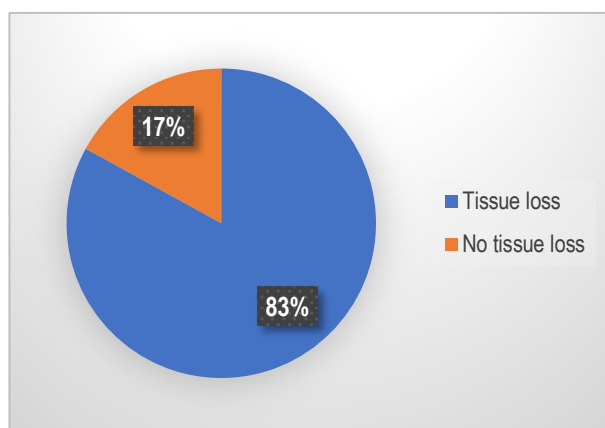


Figure 4: Severity of Ischaemia

All 219 bypasses were performed for the indication of chronic limb-threatening ischaemia. All patients (100.0%) reported the presence of rest pain (Rutherford 4). In addition to rest pain, tissue loss characterised by a non-healing ulcer and or gangrene on the affected limb, was present in 83.1% (n=182/219) of limbs prior to bypass surgery. Only 16.9% (n=37) had no tissue loss. The amount of tissue loss was not specified, therefore, Rutherford 5 or 6 could not be differentiated.

Surgical Factors

Proximal Anastomosis

The majority of bypasses (47.9%, n=105/219) had the proximal anastomosis performed at the level of the common femoral artery (CFA), followed by the superficial femoral artery (SFA) (40.2%, n=88), the above knee popliteal artery (AK POP) (4.1%, n=9), the below knee popliteal artery (BK POP) (3.7%, n=8) and the deep femoral artery (PFA) (3.7%, n=8). The level of proximal anastomosis was unknown in one patient.

Distal Anastomosis

The distal anastomosis was performed at the level of the posterior tibial artery (TP) in the majority of patients (27.9%, n=61). This was followed by the BK POP (22.4%,n=49), the anterior tibial artery (TA) (19.2%, n=42), the AK POP (18.7%,n=41), the dorsalis pedis artery (DP) (4.6%,n=10), the tibioperoneal trunk (TPT) (4.1%,n=9) and the peroneal artery (Per) (2.7%,n=6). The level of the distal anastomosis was unknown in one patient.

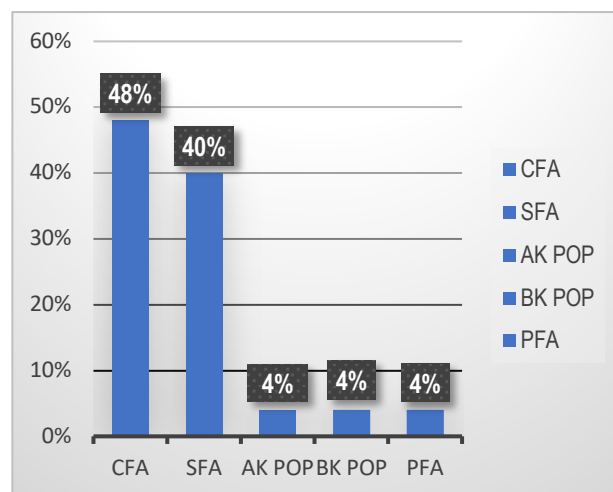


Figure 6: Level of Proximal Anastomosis

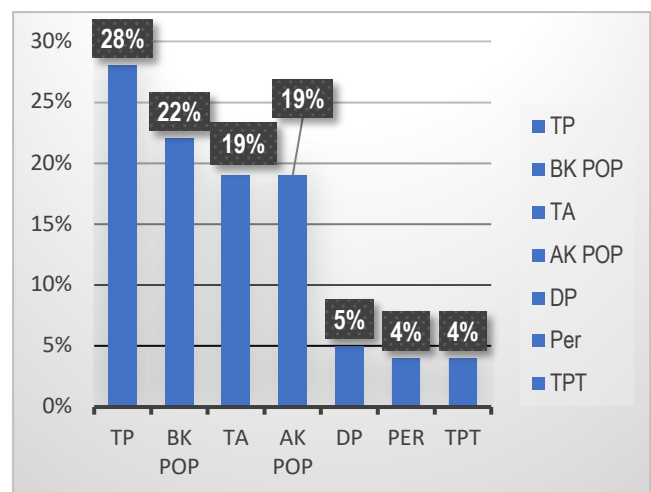


Figure 5: Level of Distal Anastomosis

Vein Diameter

One hundred ninety-six patients had preoperative vein marking data available. The median vein diameter was 2.7mm, ranging from 1.7mm to 5mm. Only 35.2% (n=69) of patients had an adequate vein diameter of 3mm or more. The majority of patients (61.2%, n=120) in fact, had a vein diameter of 2-3mm. No

differentiation was made between ipsilateral, contralateral greater saphenous veins, small saphenous veins or arm veins.

Number of Runoff Vessels

The patency of the runoff vessels were determined by evaluation of the preoperative imaging reports. The following vessels were assessed for patency to determine the number of patent runoff vessels: popliteal artery, anterior tibial artery, tibioperoneal trunk, posterior tibial artery, peroneal artery and the dorsalis pedis artery. The majority of patients (26.9%, n=59) only had a single runoff vessel. A 3-vessel runoff followed this in 21.9% (n=48) of patients with only 6.4% (n=14) of patients presenting with a 6-vessel runoff.

Graft Patency

Graft patency was evaluated as a clinically documented distal pulse or flow observed on duplex ultrasound graft surveillance. Due to the retrospective nature of the analysis, no differentiation was made between primary, primary assisted or secondary patency. As there was no dedicated graft surveillance protocol, 36.1% (n=79) of patients were lost to follow-up and subsequently excluded from the patency analysis.

Patency periods were divided into 3 groups: < 30 days (early graft failure), 1-12 months and > 12 months (late graft patency). 26.1% (n=36/138) of grafts demonstrated early failure within 30 days, whereas 45.7% (n=63/138) of grafts had late patency > 12 months. 28.3% (n=39) of grafts failed within 1 year.

In order to determine factors contributing to early graft failure or late graft patency, a subgroup analysis was performed of all bypasses with graft patency < 30 days as well as graft patency > 12 months. A comparative table between the patency groups can be found in *Table 2*.

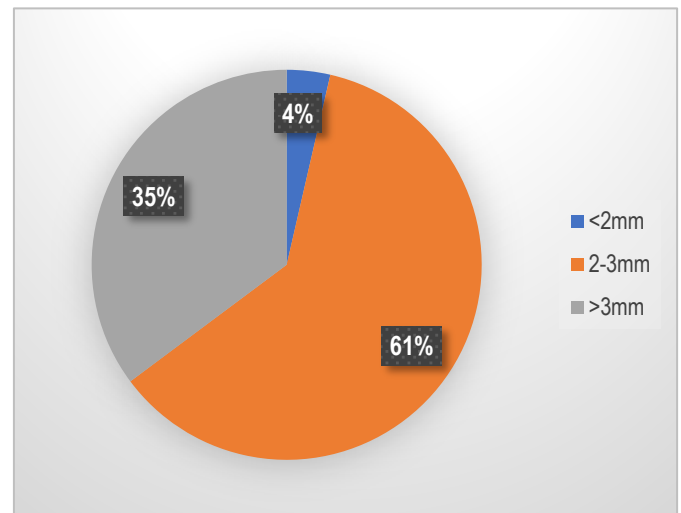


Figure 7: Distribution of Vein Diameter

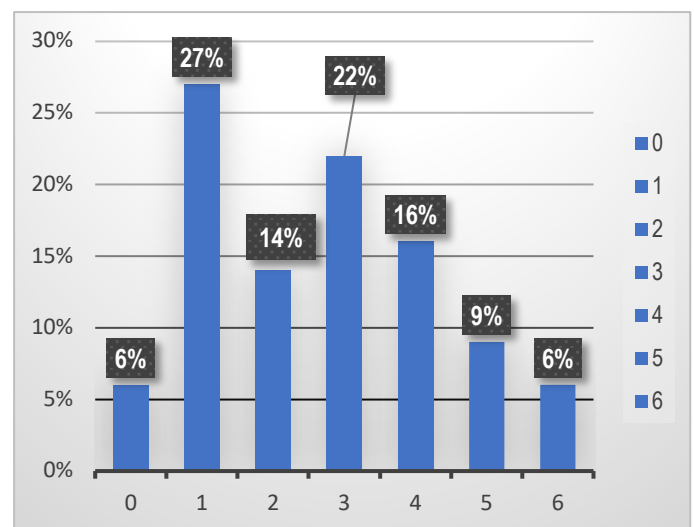


Figure 8: Number of Runoff Vessels

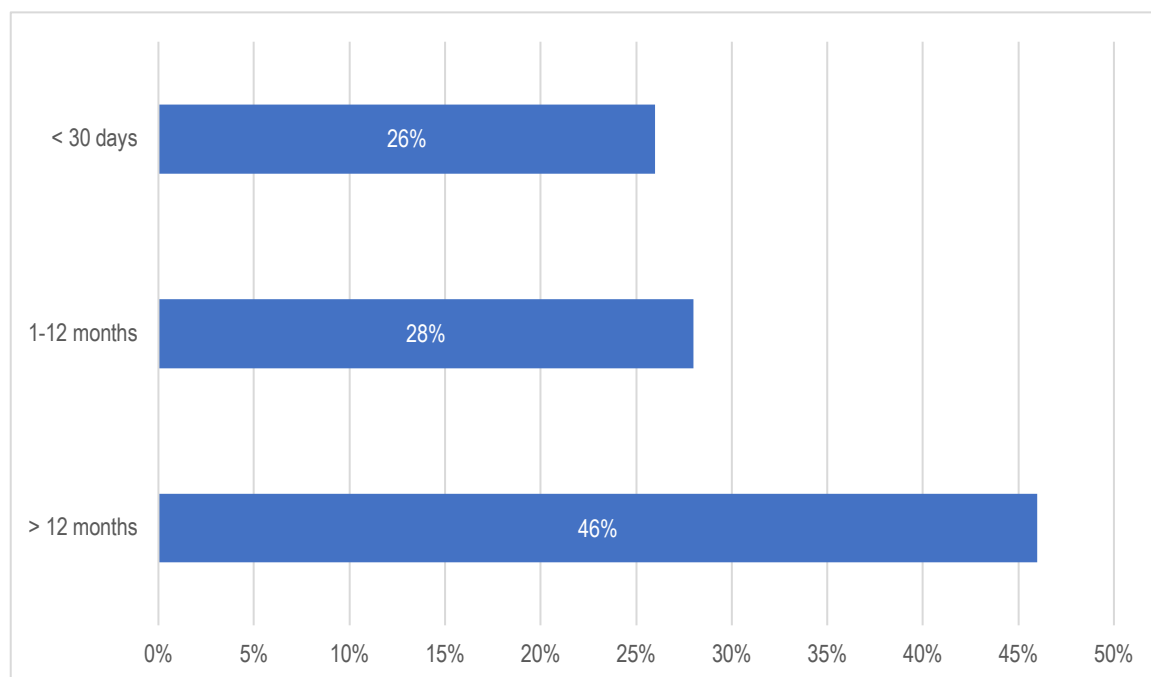


Figure 9: Distribution of Graft Patency

Gender

Female gender demonstrated a statistically significant increased risk for early graft failure (p-value 0.01) with a relative risk of 2.45 (95% CI [1.2;4.9]). Females demonstrated a 1-year patency of 28.6% compared to 51.5% for males.

Age

The median age of patients who suffered early graft failure was 59.5 years compared to 63 years for patients with late patency. Age was, however, not a statistically significant predictor of either early graft failure or late graft patency.

Table 2: Patency Analysis			
	< 30 days	> 12 months	P-value
Age (years)	59.5	63	
Gender			
Male	22 (23.4%)	53 (51.5%)	0.0102
Female	14 (40.0%)	10 (28.6%)	
Race			
Black	27 (32.6%)	34 (41.0%)	
White	7 (16.3%)	24 (55.8%)	
Coloured	2 (16.7%)	5 (41.7%)	
Comorbidities			
Hypertension	30 (28.0%)	52 (48.6%)	0.0031
Diabetes	16 (36.4%)	16 (36.4%)	
Smoker	24 (21.6%)	57 (51.4%)	
Renal failure	5 (41.7%)	5 (41.7%)	
HIV	5 (25.0%)	9 (45.0%)	
Severity of ischaemia			
Tissue loss	30 (27.3%)	50 (45.5%)	
GSV diameter (mm)			
Median	2.15	2.8	0.0007
Number of runoff vessels			
Median	2.5	3.0	

Race

Race was not found to affect graft patency significantly. Grafts demonstrated a 1-year patency of 55.8%, 41.7%, and 41.0% for white, coloured and black patients, respectively.

Comorbidities

The presence of hypertension, diabetes, HIV, and renal impairment had no significant effect on graft patency. On the other hand, smoking had a statistically significant protective effect on graft patency (p-value <0.01). Smokers demonstrated a 1-year patency of 51.4% compared to 22.3% for non-smokers.

Severity of Ischaemia

There was no significant difference in graft patency between patients who presented with rest pain only and those with associated tissue loss. As this was a retrospective analysis, patients could not be classified according to the extent of tissue loss as this was not always indicated. Patients who presented with tissue loss demonstrated a 1-year patency of 45.5% compared to 46.0% for patients who presented with rest pain only.

Vein Diameter

The median vein diameter among the grafts that suffered early graft failure was 2.15mm. This was in comparison to 2.8mm for the grafts that demonstrated late patency. Vein diameter proved to be an independent predictor for both early graft failure (p-value < 0.01) as well as late patency (p-value < 0.01) with a linear relationship between vein diameter and patency. Patients with a vein diameter <3mm demonstrated a 1-year patency of 40.4% compared to 57.2% for patients with a vein diameter ≥ 3mm.

Quality of Runoff

The number of patent runoff vessels had no significant impact on graft patency. The median number of runoff vessels were 2.5 for the grafts that occluded within 30 days compared to 3 for the grafts that remained patent beyond 12 months. Patients with a 6-vessel runoff demonstrated a 1-year patency of 50.4% compared to 48.7% with a single vessel runoff. The presence, however, of a single anterior tibial artery runoff proved to be a statistically significant risk for early graft failure (p-value 0.02) with a relative risk of 1.5 (95% CI [1.1;2.2])

Level of Proximal and Distal Anastomoses

Neither the level of the proximal nor distal anastomosis had any significant impact on graft patency. 1-year patency for the proximal anastomosis on the BK POP was 60% compared to 47%, 46%, 38%, and 20% for the SFA, CFA, AK POP and PFA, respectively. 1-year patency for the distal anastomosis on the peroneal and TPT was 67% and 60%. This was compared to 55%, 48%, 44%, 32% and 20% for the TP, AK POP, BK POP, TA, and DP, respectively. The cumulative 1-year patency of bypasses to the infrapopliteal vessels was 46% compared to 45% when the popliteal artery was selected as the target vessel.

Discussion

This study aimed to identify factors that influence infrainguinal reverse vein bypass patency among patients operated for CLTI at a tertiary academic hospital in central South Africa. It was postulated that knowledge of these factors would allow a critical analysis of bypass patency and outcome data as well as potentially identify a subgroup of patients who are unlikely to benefit from bypass surgery. This is essential in a resource-constrained environment like the government healthcare sector of South Africa.

The majority of patients (74%) included in this study were males, which correlates with other studies on this topic.^{6, 11-16} This may be due to the underrepresentation of the female gender in these studies, as pointed out by Hoel et al in the examination of the balance of enrolment with respect to gender and race in several randomised controlled trials conducted in the United States from 1983 till 2007. The author concluded that both minorities and women were underrepresented disproportionately in these trials on different vascular pathology compared to the actual incidence in the population.¹⁷

Even though the majority of patients included were of black race (57%, n=120) followed by white (30%, n=64) and coloured (13%, n=27) patients, this does not accurately reflect the composition of the South African demographic. The 2011 Census published by Statistics South Africa indicated that 80% of South Africans are of black race, followed by 8.8% coloured and 8.4% white.¹⁸ This may, however, indicate the demographic of the patients presenting to the state health sector in central South Africa.

The median age of included patients was 61 years. This is on average 5 to 9 years younger than the age quoted in other studies, which might indicate a younger population requiring peripheral bypass grafting in South Africa.^{6, 11, 12, 14, 16}

While the majority of patients had hypertension (78%) and were known smokers (83%), only a limited number of patients had renal failure (11%). The aforementioned is in keeping with findings in other studies on this topic, however, the majority (64%) of patients included in the PREVENT III trial, as well as the studies by Wengerter et al (87%) and Slim et al (76%), had diabetes, compared to only 32% in this study. ^{6, 11, 12, 14, 16} Wengerter et al and Slim et al also reported that only 44% and 15% of included patients were known smokers, respectively. ^{14, 15}

With South Africa having one of the fastest-growing HIV epidemics globally, it is concerning that only 29% of patients' HIV status were known. ¹⁹ HIV is well documented risk factor for occlusive vascular disease and appears to play a role in outcome with poor overall limb salvage rates of 31.6%. ²⁰⁻²² Knowledge of a patient's HIV status is, therefore, of paramount importance to predict success of revascularisation.

83% of patients included in this study had evidence of tissue loss indicating a more advanced level of ischaemia which correlates with results of the PREVENT III trial (75%) as well as the study by Wengerter et al (71%). ^{11, 15} This is considerably higher than other studies by Ray et al and Slim et al including only 38% and 54% of patients with tissue loss, respectively. ^{7, 14}

The majority of patients (27%) in this study had only a single runoff vessel. This is in contrast to findings in other studies. Ray et al reported a single vessel runoff in only 13% of patients with the majority (55%) of patients having a 3-vessel runoff. ⁷

66% of patients in this study had a vein diameter which is considered inadequate (<3mm) for lower limb bypass surgery. This is in contrast to other studies demonstrating that the majority of patients had a vein diameter of at least 3-4mm. ^{7, 11, 14, 15} In fact, in the PREVENT III trial, as well as the study by Wengerter et al, only 6% and 6.5% of patients had a vein diameter < 3mm, respectively. ^{11, 15}

As with the PREVENT III trial (49%), the majority of bypasses (48%) utilised the CFA for the proximal anastomosis. ¹¹ 40% of proximal anastomoses were performed on the SFA which is considerably more than the 25% in the PREVENT III trial. ¹¹ The popliteal artery, however, was utilised as the proximal anastomotic site in 18% of cases in the PREVENT III trial compared to only 8% in this study. ¹¹

The majority (59%) of infrainguinal bypasses included in this study were performed on infrapopliteal target vessels with the posterior tibial artery (28%) being the most commonly chosen target vessel. This correlated with the PREVENT III trial findings in which 65% of bypasses were performed to infrapopliteal vessels. ¹¹

Factors Affecting Patency

The PREVENT III Trial demonstrated an overall 1-year primary patency of 61% compared to 71% primary patency shown by Wengertner et al.^{11, 15} This study, on the other hand, demonstrated a 1-year patency of only 46%. No differentiation was made between primary, primary-assisted and secondary patency, however.

Gender

This study demonstrated that female gender is an independent predictor (p-value 0.01) of early graft failure with a relative risk of 2.45 (95% CI [1.2;4.9]). This contrast with the findings of Frangos et al which failed to show a significant impact of gender on graft patency.¹⁰ A study by Tangelder et al, however, had a similar conclusion and identified female gender as an independent risk factor for graft failure.¹⁴

Age

This study did not demonstrate any significant influence of age on graft patency. This finding is similar to that of Ray et al, which demonstrated lack of impact of age on femoropopliteal bypass success rate.⁷ Singh et al, on the other showed that age > 70 years, as well as < 50 years and between 51 and 60 years, were significantly associated with early graft failure. A similar association was not, however, found for ages 61 to 70 years.⁶

Race

This study also did not identify any significant impact of race on graft patency. This is again in contrast to the findings of Singh et al, which demonstrated African American race as a predictor of early graft failure. In this large VA evaluation of the NSQIP, compared to all other races, African Americans demonstrated an odds ratio of 1.4 for early graft failure.⁶

In another multivariable analysis by Chew et al, African Americans also revealed an adjusted hazard ratio for loss of primary graft patency of 1.74 compared to Caucasians.²³

In addition, the PREVENT III investigators also concluded that African American patients appeared to be at increased risk for early graft failure (30 days) with a hazard ratio. This finding was apparent even when patients with high-risk conduits were excluded. They also determined that specifically African American women were at highest risk for loss of both primary-assisted patency and secondary patency as well as amputation at 1 year.¹¹

Comorbidities

The majority of associated comorbidities had no significant impact on graft patency in this study. Studies by Rutherford et al and Singh et al, however, demonstrated a protective effect of diabetes on graft patency with better overall 3-year primary patency (60% for diabetics versus 42% for non-diabetics) and a negative association with early graft failure, respectively.^{6, 12} A study performed by Wengertner et al, however, failed to show any significant effect of diabetes on graft patency.¹⁶

Overall, the outcomes of bypass grafts in patients with diabetes and renal disease are less favourable. Their independent contributions to actual graft failure, however, remain to be established. According to multiple reports, renal failure and diabetes increased the risk of amputation and mortality, but do not appear to directly influence vein graft patency.²⁴⁻²⁷

Most series have also failed to establish an association with hyperlipidaemia or hypertension on vein bypass patency.²⁷ If these risk factors, in fact, contribute to decreased patency, the size of this effect is likely minimal and thus difficult to detect in small series'.

Interestingly, analysis of the impact of smoking on graft patency in this study showed that smoking appeared to be protective in nature with a statistically significant difference (p value 0.003) between graft patency of smokers compared to non-smokers. In general, the negative effect of smoking on the patency of vein bypass grafting is well-known.²⁸ In the study by Singh et al, patients with a history of smoking had an early graft failure rate of 5.4% compared to 4.4 % in non-smokers.⁶ Univariate analysis, however, indicated the difference was statistically significant. In a study by Rutherford et al, tobacco use was associated with a significantly reduced patency (51% at three years for smokers vs 68% for non-smokers).¹²

On the other hand, the study by Wengertner et al. failed to show any significant effect of smoking on graft patency.¹⁵ Even more remarkably, one study concluded that smoking ten or more cigarettes per day is associated with improved patency following an endovascular intervention. The authors of this study postulated that carbon monoxide was the most important contributing factor, in view of its potent anti-inflammatory and anti-proliferative properties.²⁹

This study showed no statistically significant difference in the graft patency of patients who are HIV positive compared to HIV negative. Due to the lack of known HIV status the study sample was very small. Studies regarding the outcomes of lower limb bypasses in the HIV-positive population are lacking, however, Botes et al indicated a dismal limb salvage rate of 31.6% for patients with HIV-associated occlusive disease.²²

Severity of ischaemia

Compared to rest pain alone as the indication for surgery, the presence of tissue loss was found to have no significant impact on graft patency. This finding is reflected in a study done by Ray et al which found that there was very little difference in graft patency of patients with rest pain as compared to those with gangrene (81.8% vs 80.7%).⁷ This, however, differs from the findings of Schanzer et al which demonstrated that in the setting of tissue loss, patients undergoing bypass surgery had lower patency rates than those who underwent a bypass for rest pain only.³⁰

Vein diameter

This study demonstrated a statistically significant difference (p-value 0.0007) between graft patency of patients with a larger versus smaller vein diameter. This is consistent with the findings demonstrated by several other studies. Wengertner et al, showed that the infrapopliteal reverse vein bypass graft patency and limb salvage increase proportional to the vein diameter.³⁰ In another study by Ray et al, the success rate of saphenous vein graft decreased from 85.1% in cases in which the vein graft was between 5 and 6mm to 75% when the vein was less than 5mm in diameter.⁷ Cheshmedzhiev et al showed that venous grafts less than 3.5mm had 46% failure rate compared to 30% failure rate for venous grafts with a diameter over 3.5mm.³¹

These findings were also reinforced in an evaluation of the vein-related factors in the PREVENT III database. Schanzer et al demonstrated a linear increase in the risk for loss of primary and secondary patency as vein diameter decreased from > 3.5mm to < 3mm.³⁰

The vein diameter appears to play such a prominent role that, as a matter of fact, in a study by Wengertner et al, none of the vein grafts with a diameter < 3mm remained patent beyond 2 years.⁹

Only a single study by Slim et al had contradictory findings.¹⁴ In this study, they evaluated the outcomes of infrainguinal bypass grafts using vein conduits <3mm for CLTI and found that primary and assisted primary patency rates in small veins were not significantly different at 1 year.

Level of anastomosis

This study demonstrated that neither proximal nor distal anastomosis level had any significant impact on graft patency. This finding is in contrast to a study by Ray et al, where utilisation of the superficial femoral artery for the proximal anastomosis appeared to convey a lower patency rate.⁷

Quality of Runoff

In this study, the number of patent runoff vessels had no significant impact on graft patency. This is consistent with Rutherford et al, who showed that neither primary nor secondary patency was significantly affected by runoff status or clinical classification.¹² The study by Ray et al, on the other hand, demonstrated that the patency rate drops from 92.6% in patients with a 3-vessel (popliteal and both tibial arteries) to 65% in patients with only a single vessel run-off.⁷

Limitations of the Study

The retrospective nature of the study posed several challenges. 36% of patients had to be excluded from the patency analysis due to loss to follow-up. In view of the lack of a dedicated graft surveillance protocol as well as a lack of definition of patency according to accepted reporting standards, primary, primary-assisted and secondary patency could not be differentiated.

Even though tissue loss was classified separately from rest pain (Rutherford 4), the extent of tissue loss was not defined and could therefore not be further categorised into Rutherford 5 or 6. Even though all the bypass procedures included were of reverse vein configuration, bypass procedures were also performed by different vascular surgeons without a standardised protocol. All of the above could potentially affect the patency outcome and accuracy of data included. This would, however, be addressed by a prospectively designed research protocol with standardisation of surgical methods and follow-up surveillance.

Conclusion

In this retrospective review, female gender, small greater saphenous vein diameter as well as a single anterior tibial vessel runoff were identified as independent predictors of early (< 30 days) infrainguinal reverse bypass failure. On the other hand, smoking appears to be predictive of graft patency beyond 12 months.

This study's 1-year patency of 46% for infrainguinal reverse vein bypasses is considerably lower than that quoted in other studies. This could potentially be a reflection of several factors. The most important factor appears to be the small vein diameter of patients included in this study with 66% of patients demonstrating a vein diameter considered insufficient for lower limb bypass surgery. Other possible contributors include a considerable number of patients with tissue loss, limited runoff vessels as well as infrapopliteal bypasses being the majority. These factors were, however, not found to be predictors of early graft failure in this study.

In conclusion, several factors appear to affect the patency of infrainguinal reverse vein bypass. These factors should be noted as potential predictors of graft failure, however, they should not be used to exclude patients from potential limb-saving surgery as they have not been prospectively validated in the South African context.

Author Contributions

LM Khambule was the principal investigator. A Malan was the supervisor for this research project. Both authors worked together on the protocol and analysed the data. LM Khambule wrote the first draft manuscript, both authors modified and approved the final version.

Conflict of Interest

None

Author Funding Sources

Self-funded

References

1. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FGR, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *JVS*. 2007; 45 (1): S5A-S67A
2. Conte MC, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, et al. Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischaemia. *EJVES*. 2019; 58(1): S1-S109
3. BASIL Trial Participants. Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL): Multicenter, Randomized Controlled Trial. *Lancet*. 2005; 366(9501): 1925-1934
4. 2011 Writing Group Members, 2005 Writing Committee Members, ACCF/AHA Task Force Members. 2011 ACCF/AHA Focused Update of the Guideline for the Management of patients with peripheral artery disease (Updating the 2005 Guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2011; 124(18): 2020
5. Dalman RL, Taylor LM. Basic Data Related to Infrainguinal Revascularization Procedures. *Ann Vasc Surg*. 1990; 4(3): 309-3012
6. Singh N, Sidawy AN, DeZee KJ, Neville RF, Akbari C, Henderson W. Factors Associated with Early Failure of Infrainguinal Lower Extremity Arterial Bypass. *JVS*. 2008; 47(3): 556-561
7. Ray FS, Lape CP, Lutes CA, Dillihunt RC. Femoropopliteal Saphenous Vein Bypass Grafts: Analysis of 150 Cases. *Am J Surg*. 1970; 119(4): 385-391
8. Budd JS, Brennan J, Beard JD, Warren H, Burton PR, Bell PRF. Infrainguinal Bypass Surgery: Factors Determining Late Graft Patency. *BJS*. 1990; 77(12):1382-1387
9. Wengerter KR, Veith FJ, Gupta SK, Ascer E, Rivers SP. Influence of Vein Size (Diameter) on Infrapopliteal Reversed Vein Graft Patency. *JVS*. 1990; 11(4): 525-531
10. Frangos SG, Karimi S, Kerstein MD, Harpavat M, Sumpio B, Roberts AB, et al. Gender does not impact infrainguinal vein bypass graft outcome. *Surgery*. 2000; 127(6): 679-686
11. Conte MS, Bandyk DF, Clowes AW, et al. Result of PREVENT III: a multicenter, randomized trial of edifoligide for the prevention of vein graft failure in lower extremity bypass surgery. *J Vasc Surg*. 2006; 43: 742-751
12. Rutherford RB, Jones DN, Bergentz SE, Bergqvist D, Comerota AJ, Dardik H, et al. Factors Affecting the Patency of Infrainguinal Bypass. *J Vasc Surg*. 1988;8:236-246

13. Tangelder MJD, Algra A, Lawson JA, Eikelboom BC. Risk Factors for Occlusion of Infrainguinal Bypass Graft. *Eur J Vasc Endovasc Surg*. 2000; 20: 118-124
14. Slim H, Tiwari A, Ritter JC, Rashid H. Outcome of infra-inguinal bypass grafts using vein conduit with less than 3 millimeters diameter in critical leg ischemia. *J Vasc Surg*. 2011;53: 421-425
15. Wengerter KR, Veith FJ, Gupta SK, et al. Prospective randomized multicenter comparison of in situ and reversed vein infrapopliteal bypasses. *J Vasc Surg*. 1991; 13: 189-197
16. Oresanya L, Makam AN, Belkin M, Moneta GL, Conte MS. Factors Associated with Primary Vein Graft Occlusion in a Multicenter Trial with Mandated Ultrasound Surveillance. *J Vasc Surg*. 2014;59: 996-1002
17. Hoel A. Under-representation of women and ethnic minorities in vascular surgery randomized control trials. *Society for Clinical Vascular Surgery*. 2008. Las Vegas, NV.
18. Statistical release (Revised). 2012. Available from:
<https://www.statssa.gov.za/publications/P03014/P030142011.pdf>
19. UNAIDS. 2020. Available from:
<https://www.unaids.org/en/regionscountries/countries/southafrica>
20. Van Marle J, Mistry PP, Botes K. HIV-occlusive vascular disease. *SAJS*, 2009; 47(2): 36-42
21. Pillay B, Ramdial P, Naidoo DP. HIV-associated large-vessel vasculopathy: a review of the current and emerging clinicopathological spectrum in vascular surgical practice. *Cardiovasc J Afr*. 2015; 26: 70-81
22. Botes K, Van Marle J. Surgical Intervention for HIV Related Vascular Disease. *Eur J Vasc Endovasc Surg*. 2007; 34: 390-396
23. Chew DK, Nguyen LL, Owens CD, et al. Refinement of survival prediction in patients undergoing lower extremity bypass grafts in African Americans and Caucasians: the association of race with graft function and limb salvage. *J Vasc Surg*. 2005; 42: 695-701
24. Conte MS, Belkin M, Upchurch GR, Mannick JA, Whittemore AD, Donaldson MC. Impact of increasing comorbidity on infrainguinal reconstruction: a 20-year perspective. *Ann Surg*. 2001; 233: 445-452
25. Panneton JM, Glovaczki P, Bower TC, Rhodes JM, Conton LG toomey BJ. Pedal bypass for limb salvage: impact of diabetes on long-term outcome. *Ann Vasc Surg*. 2000; 14: 640-647
26. Hertzner NR, Bena JF, Karafa MT. A personal experience with the influence of diabetes and other factors on the outcome of infrainguinal bypass grafts for occlusive disease. *J Vasc Surg*. 2007; 46: 271-279

27. Pomposelli FB, Kansal N, Hamdan AD, et al. A decade of experience with dorsalis pedis artery bypass: analysis of outcome in more than 1000 cases. *J Vasc Surg.* 2003; 37: 307-315
28. Willigendael EM, Teijink JA, Bartelink ML, Peters RJ, Buller HR, Prins MH. Smoking and the patency of lower extremity bypass grafts: a meta-analysis. *J Vasc Surg.* 2005; 42: 67-74
29. Schillenger M, Exner M, Mlekusch W, et al. Effect of smoking on restenosis during the 1st year after lower-limb endovascular interventions. *Radiology.* 2004; 231: 831-838
30. Schanzer A, Hevelone N, Owens CD, et al. Technical factors affecting autogenous vein graft failure: observations from a large multicenter trial. *J Vasc Surg.* 2007; 46: 1180-1190
31. Cheshmedzhiev M, Jordanov E, Yordanov M, K. Clinical Significance of Venous Graft Size and Run Off Segment for Peripheral Bypass Patency. *J Vasc Med Surg.* 2015; 3(2)

APPENDICES

Appendix A – HSREC Letter of Approval

UNIVERSITY OF THE
FREE STATE
UNIVERSITEIT VAN DIE
VRYSTAAT
YUNIVESITHI YA
FREISTATA



UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

12-Nov-2018

Dear **Dr Lucky Khambule**

Ethics Clearance: **Factors Influencing Infrainguinal Reverse Vein Bypass Patency at Universitas Academic Hospital.**

Principal Investigator: **Dr Lucky Khambule**

Department: **Surgery Department (Bloemfontein Campus)**

APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is: **UFS-HSD2017/1264**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite), Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

Dr. SM Le Grange

Chair : Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee

Office of the Dean: Health Sciences

T: +27 (0)51 401 7795/7794 | E: ethicsfhs@ufs.ac.za

IRB 00006240; REC 230408-011; IORG0005187; FWA00012784

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Appendix B – FSDOH Letter of Approval



health

Department of
Health
FREE STATE PROVINCE

17 November 2017

Dr LM Khambule
Dept. of Surgery
Faculty of Health Science
UFS

Dear Dr LM Khambule

Subject: Factors Influencing Infrainguinal Reverse Vein Bypass Patency at Universitas Academic Hospital.

- Please ensure that you read the whole document, Permission is hereby granted for the above – mentioned research on the following conditions:
- Serious adverse events to be reported.
- Ascertain that your data collection exercise neither interferes with the day to day running of Universitas Hospital nor the performance of duties by the respondents or health care workers.
- Confidentiality of information must be ensured.
- Research results and a complete report should be made available to the Free State Department of Health on completion of the study (a hard copy plus a soft copy).
- Progress report must be presented not later than one year after approval of the project to the Ethics Committee of the University of Free State and to Free State Department of Health.
- Any amendments, extension or other modifications to the protocol or investigators must be submitted to the Ethics Committee of the University of Free State and to Free State Department of Health.
- **Conditions stated in your Ethical Approval letter should be adhered to and a final copy of the Ethics Clearance Certificate should be submitted to sebelats@fshealth.gov.za before you commence with the study**
- No financial liability will be placed on the Free State Department of Health
- Please discuss your study with the institution managers/CEOs on commencement for logistical arrangements
- Department of Health to be fully indemnified from any harm that participants and staff experiences in the study
- Researchers will be required to enter in to a formal agreement with the Free State department of health regulating and formalizing the research relationship (document will follow)
- You are encouraged to present your study findings/results at the Free State Provincial health research day
- Future research will only be granted permission if correct procedures are followed see <http://nhrd.fst.org.za>

Trust you find the above in order.

Kind Regards,

Dr D Motau

HEAD: HEALTH

Date: 11/12/17

Head : Health
PO Box 227, Bloemfontein, 9300
4th Floor, Executive Suite, Bophele House, cnr Maitland and, Harvey Road, Bloemfontein
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Appendix C – HOD Surgery Letter of Approval

12 September 2017

Head of Department: Surgery
Faculty of Health Sciences
University of the Free State
Bloemfontein

Dear Dr le Grange

RE: PERMISSION TO CONDUCT RESEARCH IN THE DEPARTMENT OF SURGERY

I would like to have your permission to conduct the research for my M.Med.-project on the topic: "Factors influencing infra-inguinal reverse vein bypass patency at Universitas Academic Hospital".


My supervisor is Dr AF Malan. We will submit the protocol to the Health Research Ethics Committee for approval this month.

Thank you very much for your kind attention in this matter.

Yours faithfully


LM KHAMBULE (DR)
REGISTRAR: SURGERY

I, Dr SM le Grange grant permission to Dr Khambule to conduct his research in the Dept of Surgery.


SM LE GRANGE (DR)
ACTING HoD: SURGERY

14 September 2017

Appendix D – Biostatistics Letter of Approval

28 August 2017

For attention: Health Sciences Research Ethics Committee
Faculty of Health Sciences

Title of project:

FACTORS INFLUENCING INFRAINGUINAL REVERSE VEIN BYPASS PATENCY
AT UNIVERSITAS ACADEMIC HOSPITAL.

Researcher:

Dr LM Khambule

I have given input regarding the above mentioned project's protocol on the following aspects of the protocol, namely the study design, sample, measurement, measuring instrument and statistical analysis.

The input will be implemented under supervision of the study leader Dr AF Malan.

Yours faithfully

M. Mel



Appendix E – Data Collection Sheet

DATA COLLECTION SHEET					
Patient Identifier					
<input type="text"/>					
Patient Demographics					
Age	<input type="text"/>				
Gender	Male <input type="checkbox"/>	Female <input type="checkbox"/>			
Race	Black <input type="checkbox"/>	White <input type="checkbox"/>	Coloured <input type="checkbox"/>	Indian <input type="checkbox"/>	Asian <input type="checkbox"/>
	Other <input type="checkbox"/>				
Province	FS <input type="checkbox"/>	NC <input type="checkbox"/>	Gau <input type="checkbox"/>	Les <input type="checkbox"/>	EC <input type="checkbox"/>
	Lim <input type="checkbox"/>	Mpu <input type="checkbox"/>	WC <input type="checkbox"/>	KZN <input type="checkbox"/>	NW <input type="checkbox"/>
Clinical Characteristics					
Hypertension	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="checkbox"/>		
Diabetes mellitus	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="checkbox"/>		
Smoker	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="checkbox"/>		
Renal impairment (eGFR < 60 ml/min)	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="checkbox"/>		
HIV	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="checkbox"/>		
On treatment at time of admission			Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="checkbox"/>
Indication for Surgery					
Rest pain	Yes <input type="checkbox"/>	No <input type="checkbox"/>			
Tissue loss	Yes <input type="checkbox"/>	No <input type="checkbox"/>			
Surgical Factors					
Minimum GSV diameter	<input type="text"/> mm				
Available run-off vessels	Pop <input type="checkbox"/>	TP trunk <input type="checkbox"/>	TP <input type="checkbox"/>	TA <input type="checkbox"/>	Peroneal <input type="checkbox"/>
	DP <input type="checkbox"/>				
Proximal anastomosis	CFA <input type="checkbox"/>	SFA <input type="checkbox"/>	PFA <input type="checkbox"/>	AK Pop <input type="checkbox"/>	BK Pop <input type="checkbox"/>
Distal anastomosis	AK Pop <input type="checkbox"/>	BK Pop <input type="checkbox"/>	TP trunk <input type="checkbox"/>	TP <input type="checkbox"/>	TA <input type="checkbox"/>
	Peroneal <input type="checkbox"/>	DP <input type="checkbox"/>			
Graft Patency Period	< 30 d <input type="checkbox"/>	1-3 mths <input type="checkbox"/>	3-6 mths <input type="checkbox"/>	6-9 mths <input type="checkbox"/>	9-12 mths <input type="checkbox"/>
	> 12 mths <input type="checkbox"/>				

Factors Influencing Infrainguinal Reverse Vein Bypass Patency at Universitas Academic Hospital

A Retrospective Review

*A research protocol submitted in partial fulfillment of the requirements for the degree of Masters in
Medicine in General Surgery, School of Medicine, University of the Free State*

Dr. L.M. Khambule

Supervisor: Dr. A.F. Malan

September 2017

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Summary

Peripheral arterial disease is a serious global healthcare problem with the incidence increasing, especially in the elderly population. This has subsequently resulted in a rise in the subset of patients that require revascularisation for the manifestation of critical limb ischaemia.

Despite the advent of endovascular intervention for critical limb ischaemia, bypass surgery still remains an integral part of the armamentarium of revascularisation. Several factors have been identified that are associated with either success or failure of a bypass procedure. The literature, however, is somewhat contradictory.

This retrospective study, therefore, aims to assess factors influencing infrainguinal reverse vein bypass patency on patients operated at Universitas Academic Hospital over a period of 5 years. The study will be utilised to identify areas for improvement as well as, potentially, a subgroup of patients who might not benefit from bypass surgery or in whom early graft failure should be anticipated

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INTRODUCTION

Literature Review

Peripheral arterial disease (PAD) poses a major healthcare burden with total disease prevalence in the region of 3 to 10 percent in the general population and increasing to 15 to 20 percent in persons over the age of 70 years. ⁽¹⁾

Critical limb ischaemia (CLI) refers to a manifestation of PAD in which patients present with chronic ischaemic rest pain or ischaemic skin lesions (ulcers or gangrene). The presence of CLI is an accepted indication for revascularisation with large surveys suggesting that approximately half the patients with CLI will undergo some type of revascularisation in order to prevent limb loss. ⁽¹⁾

Options for revascularisation include ⁽¹⁾

- Surgical bypass
- Endarterectomy
- Profundaplasty
- Angioplasty with or without stenting

or a combination of any of the above.

The type of intervention chosen depends on several factors including: ⁽¹⁾

- Comorbid condition
- Transatlantic Inter-Society Consensus (TASC) classification of the arterial lesion/s
- Available suitable autologous conduit
- Life-expectancy
- Amount of tissue loss

Based upon the findings of the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial ⁽²⁾, the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines ⁽³⁾ recommend that for patients with a life expectancy of more than 2 years, and who have an available autologous vein conduit, bypass surgery is reasonable to perform as the initial treatment.

This recommendation is supported by a review of studies published since 1981 ⁽⁴⁾ which found that primary above-knee femoropopliteal graft patency is 84 and 69 percent at one and four years when reverse saphenous vein is the conduit compared to 79 and 60 percent at one and four years when polytetrafluoroethylene (PTFE) is used. With below-knee grafts, performed specifically for limb salvage, cumulative primary patency with reverse saphenous vein or PTFE is approximately 90 and 75 percent at one and four years. Secondary patency for PTFE grafts in the below-knee position for all indications is 68 and 40 percent at one and four years. Based upon these numbers, prosthetic material is avoided whenever possible for below-knee bypass.

Despite the good outcome from autologous vein grafts, graft patency is affected by several factors.

A retrospective study done by Singh et al ⁽⁵⁾ analysed the Veterans Affairs(VA) National Surgical Quality Improvement Program's (NSQIP) large clinical database to investigate which factors, other than technical, were associated with a higher incidence of early graft failure in infrainguinal bypass. The NSQIP database identified 14 788 patients who underwent infrainguinal lower extremity arterial bypass during the study period, and 723 acute graft failures (4.9 percent) occurred. On multivariate analysis patients aged <50 and 51 to 60 years as well as African American race were

associated with early graft failure. Diabetes mellitus, on the other hand, had a negative association with early graft failure.

Ray et al ⁽⁶⁾ did a retrospective study of 150 patients that had femoropopliteal bypass grafts where detailed analysis of the factors that contributed to the graft patency were analysed. The factors that were analysed in this study were clinical indication, run-off, placement of the proximal and distal anastomosis, the diameter of the saphenous vein graft and the age of the patient. The clinical indications for bypass were intermittent claudication, rest pain and gangrene. The best results were found in patients with intermittent claudication showing a 90 percent long term success rate. Very little difference was shown in patients with rest pain and gangrene with success rates of 81.8 and 80.7 percent respectively. The run off segments were classified in three groups according to the patency of the popliteal, anterior, and posterior tibial arteries. Although the success rate drops from 92.6 percent in patients with a three-vessel run off to 65 percent in patients with only a one vessel run off, this study showed that an isolated popliteal segment or single tibial vessel is often adequate to sustain function with autogenous vein grafts. This study also showed that patient with saphenous vein graft diameter of 3-4mm and 5-6mm had 75.6 percent and 85.1 percent patency rates, respectively, compared to 19 percent patency for those of 7mm or more.

Budd et al ⁽⁷⁾ at Department of Surgery and Community Medicine, University of Leicester, UK did a retrospective study to check factors determining late graft patency for infrainguinal bypass surgeries. The results of 373 infrainguinal bypass grafts in a single centre between 1980 and 1988 were reviewed. One hundred and thirty in situ vein (ISV), 47 reversed saphenous vein (RSV), 118 polytetrafluoroethylene (PTFE) and 78 human umbilical vein (HUV) grafts were used. The indications for surgery were disabling claudication in 25 percent of patients and limb salvage in 75 percent. In 36 percent of the operations the distal anastomosis was above the knee and the 64 percent was below the knee. Overall 5-year patency rates and limb salvage rates respectively were, for ISV 41 percent and 69 percent, RSV 62 percent and 90 percent, PTFE 31 percent and 67 percent and HUV 29 percent and 59 percent. There was no significant difference in patency among these grafts at the above knee level, but significant differences between vein and prosthetic grafts were evident below the knee ($P < 0.001$). Using a proportional hazard model, the three factors that consistently correlated with late graft patency were graft type, site of distal anastomosis and distal run off.

In a retrospective study done by Cheshmedzhiev et al ⁽⁸⁾ at St Marina University Hospital in Bulgaria they looked at the clinical significance of venous graft size and run off segment for peripheral bypass patency. The aim of the study was to analyse the one year patency of infrainguinal arterial reconstructions in relation to venous graft diameter and length. Results were worse in venous grafts less than 3.5mm and the length over 40cm.

Wengerter et al ⁽⁹⁾ at Montefiore Medical Centre in New York, did a retrospective study to check the influence of the vein size diameter on the infrapopliteal reversed vein graft patency. They reviewed 239 infrapopliteal reversed greater saphenous vein bypasses performed for critical limb ischaemia over 7-year period to determine the influence of vein diameter on graft patency and limb salvage. A pattern of increasing graft patency and limb salvage was noted as the minimum external diameter increased from $>3.0\text{mm}$ to $<4.0\text{mm}$. When compared to the larger grafts $>4.0\text{mm}$, primary graft patency was significantly lower both for $<3.0\text{mm}$ grafts (0 percent for $<3.0\text{mm}$ vs 65 percent for $>4.0\text{mm}$ at 3 years, $p < 0.001$) and long ($>45\text{cm}$) 3.0mm grafts (38 percent for long 3.0mm vs 75 percent for $>4.0\text{mm}$ at 3 years, $p < 0.005$). All 3.5mm and short ($<45\text{cm}$) 3.0mm grafts had patency rates similar to $>4.0\text{mm}$ veins. Thus long 3.0mm and all less than 3.0mm reversed saphenous vein grafts should be considered at high risk for failure.

Frangos et al ⁽¹⁰⁾ at Yale University School of Medicine, New York did a retrospective study to assess the influence of gender on patient selection and outcome in patients requiring infrainguinal vein bypass graft procedures. They reviewed 217 infrainguinal vein bypass grafts performed over an 8-year period. Gender and multiple covariables affecting patient survival were analysed as well as postoperative complications and graft patencies. The results showed that no statistical differences existed between men and women for age, diabetes, cardiac disease, tobacco use, hypertension, stroke,

renal disease, or prior contralateral bypass or major amputation. The conclusion from this study was that gender does not affect graft patency, limb salvage, or survival rates.

Davies ⁽¹¹⁾ at University of Bristol did a prospective study to assess vein factors that affect the outcome of femorodistal bypass. One hundred femoropopliteal or infrapopliteal bypasses were performed on 95 patients (31 female and 64 males) with a mean age of 67 years (range 47-91). Graft stenosis occurred in up to 30 percent of the grafts, the aetiology of which was poorly understood. The mean internal diameter of those veins that developed stenosis was 3.7mm (range 3.1- 4.2 mm) compared with 4.7mm (range 4.4 – 5.0 mm) in those which did not develop a stenosis (P= 0.006, Mann-Whitney U test).

Golledge et al ⁽¹²⁾ from the Department of Vascular Surgery, The Repatriation General Hospital, Daw Park, Adelaide, South Australia did a critical assessment of the outcome of infrainguinal vein bypass. During a 6-year period 236 patients undergoing primary vein grafts were entered into the study. An ideal outcome required the patient to have survived 12 months with a patent graft on duplex scanning, no perioperative complication and no further related open or endovascular surgery or admission. At 12 months, the secondary graft patency rate was 82 percent, however, only 22 percent of patients had an ideal outcome. At 1 year, 44 (19 percent) patients died, 93 (39 percent) required further ipsilateral and 39 (17 percent) contralateral intervention, and a total of 108 (46 percent) were readmitted. An ideal outcome was more likely in patients receiving calcium channel blockers, principally because of improved primary patency, and less likely in those with cardiac failure requiring furosemide, principally because of worse survival in these patients.

Motivation for Study

The Department of Vascular Surgery at Universitas Academic Hospital performs lots of infrainguinal reverse vein bypass surgeries on an annual basis. Currently, data regarding graft patency rates on our patient population is lacking. We, therefore, opted to perform a retrospective review of patients with critical limb ischaemia who underwent a infrainguinal reverse vein bypass at Universitas Academic Hospital during the course of the past 5 years in order to evaluate factors influencing graft patency.

Literature has shown that the three most important factors that influence long term infrainguinal graft patency are graft material, level of the distal anastomosis and the condition of the distal run off arteries. Evaluating these and other factors might assist in identifying patients groups who are unlikely to benefit from bypass surgery or patients in whom early graft failure should be anticipated.

Study Questions and Aims

Primary Objective

- To identify factors affecting infrainguinal reverse vein bypass patency in patients operated for critical limb ischaemia at Universitas Academic Hospital from January 2012 to December 2016

Secondary Objectives

- To determine the 1 year infrainguinal reverse vein bypass patency rates in patients operated for critical limb ischaemia at Universitas Academic Hospital from January 2012 to December 2016
- To identify a subgroup of patients who are unlikely to benefit from bypass surgery or in whom early graft failure should be anticipated
- To identify any association between patient demographics and surgical factors

METHODOLOGY

Definitions

Infrainguinal

Infrainguinal bypass is a major arterial reconstruction using a bypass conduit (whether autogenous or prosthetic) that originates at or below the inguinal ligament ⁽¹³⁾

Reverse vein bypass

Bypass with harvested autologous great saphenous vein and placed in reverse orientation ⁽¹⁴⁾

Critical limb ischaemia

Presence of chronic (more than 2 weeks) ischaemic rest pain, ulceration or gangrene attributable to objectively proven arterial occlusive disease ⁽¹⁾

Study Design

Retrospective cohort analytical study

Sample Population

This study will include all patients, approximately 50 per year, who had infrainguinal reverse vein bypasses for critical limb ischaemia at Universitas Academic Hospital between November 2011 and October 2016.

The following patients will be excluded from the study:

- Patient that did not have pre-operative greater saphenous vein marking
- Patients who underwent infrainguinal reverse vein bypasses for indications other than critical limb ischaemia i.e. acute limb ischaemia, popliteal artery aneurysmal disease

Measurement

Patients who underwent infrainguinal bypass surgeries at Universitas Academic Hospital from November 2011 till October 2016 will be identified through the following methods:

- All bypass surgeries performed as per the theatre register
- All infrainguinal bypass surgeries performed as per the departmental statistics
- All bypass surgeries performed as per the Meditech CPT4 coding

Data for each patient will be obtained from a combination of Meditech notes, departmental statistics and files stored at the Vascular Laboratory by the researcher.

All patients included in the study will be assigned a unique study identifier in order to ensure confidentiality.

Measurement Errors

The following allows potential for measurement and methodological errors in this study. Measures to limit these errors are mentioned where applicable.

Drop-out

Patients that have not returned for follow-up will be excluded from the study. This might exclude a population that are on the one hand more likely to have graft failure due to associated comorbidities as well as successful bypasses as asymptomatic patients do not see the sense in returning for a follow-up.

The data sheet will allow for follow-up results at different intervals to include more patients

Pilot Study

As soon as approval is obtained from the local ethics committee, a pilot study will be conducted. The aim of the pilot study is:

- To determine the feasibility of the study
- The detect flaws in the study protocol

The pilot study will include the first 10 patient files. During this period, all the logistical aspects of the study will be scrutinised and the methodology tested and refined.

The following aspects of the proposed study will be evaluated by the pilot study:

- Executability of the study
- Organisation of the study
- Efficiency of the data collection form

If any amendments are made to the study protocol, it will be resubmitted to the ethics committee for approval.

The patients included in the pilot study will be included in the final study sample.

DATA MANAGEMENT AND ANALYSIS

The data collection form will allow for collection of the following data on each patient:

- **Patient demographics**
 - Age
 - Gender
 - Race
 - Province
- **Clinical characteristics**
 - Hypertension
 - Diabetes mellitus
 - Smoking history
 - Renal impairment (estimated glomerular filtration rate < 60 ml/min)
 - HIV status and whether on treatment at time of admission

- **Indication for surgery**
 - Rest pain
 - Tissue loss (none healing ulcer or gangrene)
- **Surgical Factors**
 - Minimum greater saphenous vein diameter as marked pre-operatively
 - Available run-off vessel/s
 - Popliteal (Pop)
 - Tibioperoneal trunk (TP trunk)
 - Tibialis posterior (TP)
 - Tibialis anterior (TA)
 - Peroneal
 - Placement of proximal anastomosis
 - Common femoral (CFA)
 - Superficial femoral (SFA)
 - Deep femoral (PFA)
 - Above knee popliteal (AK Pop)
 - Below knee popliteal (BK Pop)
 - Placement of the distal anastomosis
 - Above knee popliteal (AK Pop)
 - Below knee popliteal (BK Pop)
 - Tibioperoneal trunk (TP trunk)
 - Tibialis posterior (TP)
 - Tibialis anterior (TA)
 - Peroneal
 - Dorsalis pedis (DP)
- **Graft patency period**
 - 0-31 days
 - 1-3 months
 - 3 -6 months
 - 6-9 months
 - 9-12 months
 - > 12 months

The researcher will enter the data into an Excel spreadsheet for analysis by the Department of Biostatistics. Results will be summarised by frequencies and percentages (categorical variables) and means, standard deviations or percentiles (numerical variables). Associations between variables and outcome will be investigated using contingency tables with relative risks and appropriate hypothesis testing. Logistic regression will be performed to find independent significant predictors of outcome.

IMPLEMENTATION OF FINDINGS

The Vascular Surgery Unit at Universitas Academic Hospital performs a significant amount of infrainguinal bypass surgeries annually. At this stage no audit exists of the outcomes of these operations.

This retrospective review will aim to enable us to perform a critical analysis of the results and outcomes and assist us in identifying possible risk factors for graft failure as well as identify those patients who might not benefit from bypass surgery.

LOGISTICS AND TIME SCHEDULE

Responsibilities of Personnel

Planning

Responsibilities of the researcher/s

- Refinement of the research idea.
- Submission of the research idea to the Department of Surgery for approval.
- Performance of comprehensive literature research.
- Compilation of the research protocol.
- Design of data collection sheet.
- Obtain research approval from the relevant hospital managers and departmental heads.
- Completion of ethics committee submission form.
- Submission of research protocol for ethics approval.
- Manage and respond to concerns from the ethics committee.

Execution

Responsibilities of researcher/s

- Execution of pilot study.
- Amendments to protocol if required and resubmission to ethics committee.
- Collection of data.

Data Analysis

Responsibilities of researcher/s

- Compilation of research report comprising of, amongst others, shortcomings in current literature and suggestions for the future research.

Time Schedule

PHASE	TIME PERIOD
Literature study	1 April 2017 – 30 April 2017
Planning and drafting of research protocol	1 May 2017 – 30 June 2017
Finalisation of research protocol	1 July 2017 – 31 August 2017
Ethics committee submission	September
Pilot study	1 November 2017 – 30 November 2017
Data collection and verification	1 December 2017 – 30 September 2018
Statistical analysis	October – November 2018
Compilation of research report	December 2018
Completion of project	January 2019
TOTAL TIMESPAN OF STUDY	± 20 months

BUDGET

Funding for the study will be provided by the principal researcher.

BUDGET			
Forms			R180.00
	Data collection sheets (300 @ R0.60/form)	R180.00	
TOTAL EXPENSES			R180.00

ETHICAL ASPECTS

The study will be conducted in accordance with the ethical standards as laid down in the 1974 Declaration of Helsinki.

Prior to initiation of the study Prior to initiation of the study, the following will be obtained:

- Prior to initiation of the study the following will be obtained:
 - Approval from the Health Sciences Research Ethics Committee of the University of the Free State
 - Permission from the Free State Department of Health
- There are no interventions to be performed on the patients, so the care of patients will not be altered at all
- Patient identification will be kept confidential, only the primary researcher will have access to the patients' names
- Data analysis will be conducted separate from patient identifiers
- The project is not funded by any industry or organisation
- The study will remain faithful to the study protocol and will respect the opinions, beliefs, and traditions of all the participants and their respective families
- Patients are not chosen to participate in the study based on their ethnicity, age, religion or social class so no discrimination will, therefore, be of concern.
- There are no conflicts of interest that require declaration

REFERENCES

1. Norgren, L et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Journal of Vascular Surgery*. 2007; 45 (1): S5A
2. Adam, DJ et al. Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL): Multicenter, Randomized Controlled Trial. *Lancet*. 2005; 366(9501): 1925-1934
3. 2011 Writing Group Members, 2005 Writing Committee Members, ACCF/AHA Task Force Members. 2011 ACCF/AHA Focused Update of the Guideline for the Management of patients with peripheral artery disease (Updating the 2005 Guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2011; 124(18): 2020
4. Dalman, RL; Taylor, LM Jr. Infringuinal revascularization procedures. In: Basic Data Underlying Clinical Decision Making in Vascular Surgery, Porter, JM, Taylor, LM, Jr (Eds), Quality Medical Publishing, St. Louis 1994. p.141.
5. Singh, N et al. Factors Associated with Early Failure of Infringuinal Lower Extremity Arterial Bypass. *Journal of Vascular Surgery*. 2008; 47(3): 556-561
6. Ray, FS et al. Femoropopliteal Saphenous Vein Bypass Grafts. *American Journal of Surgery*. 1970; 119(4): 385-391
7. Budd JS et al. Infringuinal Bypass Surgery: Factors Determining Late Graft Patency. *British Journal of Surgery*. 1990; 77: 1382-1387
8. Cheshmedzhiev, M et al. Clinical Significance of Venous Graft Size and Run Off Segment for Peripheral Bypass Patency. *Journal of IMAB*. 2013; 19(1): 396-398
9. Wengerter, KR et al. Influence of Vein Size (diameter) on Infrapopliteal Reversed Vein Graft Patency. *Journal of Vascular Surgery*. 1990; 11:525-31
10. Frangos, SG et al. Gender does not impact infringuinal vein bypass graft outcome. *Surgery*. 2000; 127(6): 679-686
11. Davies, AH. Vein factors that affect the outcome of femorodistal bypass. *Annals of the Royal College of Surgeons of England*. 1995; 77: 63-66
12. Golledge, J et al. Critical Assessment of the Outcome of Infringuinal Vein Bypass. *Annals of Surgery*. 2001; 234(5): 697-701
13. Pennywell DJ, Tan TW, Zhang WW. Optimal Management of Infringuinal Arterial Occlusive Disease. *Vasc Health Risk Manag*. 2014; 10: 599-608
14. Dalman RL, Taylor LM, Porter JM. Technique of Reversed Vein Bypass to Distal Leg Arteries. In: Chang, JB, ed. *Modern Vascular Surgery*. New York: Springer-Verlag, 1992: 371-391

DATA COLLECTION SHEET

DATA COLLECTION SHEET					
Patient Identifier					
<input type="text"/>					
Patient Demographics					
Age	<input type="text"/>				
Gender	Male <input type="checkbox"/>	Female <input type="checkbox"/>			
Race	Black <input type="checkbox"/>	White <input type="checkbox"/>	Coloured <input type="checkbox"/>	Indian <input type="checkbox"/>	Asian <input type="checkbox"/>
	Other <input type="text"/>				
Province	FS <input type="checkbox"/>	NC <input type="checkbox"/>	Gau <input type="checkbox"/>	Les <input type="checkbox"/>	EC <input type="checkbox"/>
	Lim <input type="checkbox"/>	Mpu <input type="checkbox"/>	WC <input type="checkbox"/>	KZN <input type="checkbox"/>	NW <input type="checkbox"/>
Clinical Characteristics					
Hypertension	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="text"/>		
Diabetes mellitus	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="text"/>		
Smoker	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="text"/>		
Renal impairment (eGFR < 60 ml/min)	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="text"/>		
HIV	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="text"/>		
On treatment at time of admission			Yes <input type="checkbox"/>	No <input type="checkbox"/>	Unknown <input type="text"/>
Indication for Surgery					
Rest pain	Yes <input type="checkbox"/>	No <input type="checkbox"/>			
Tissue loss	Yes <input type="checkbox"/>	No <input type="checkbox"/>			
Surgical Factors					
Minimum GSV diameter	<input type="text"/> mm				
Available run-off vessels	Pop <input type="checkbox"/>	TP trunk <input type="checkbox"/>	TP <input type="checkbox"/>	TA <input type="checkbox"/>	Peroneal <input type="checkbox"/>
	DP <input type="checkbox"/>				
Proximal anastomosis	CFA <input type="checkbox"/>	SFA <input type="checkbox"/>	PFA <input type="checkbox"/>	AK Pop <input type="checkbox"/>	BK Pop <input type="checkbox"/>
Distal anastomosis	AK Pop <input type="checkbox"/>	BK Pop <input type="checkbox"/>	TP trunk <input type="checkbox"/>	TP <input type="checkbox"/>	TA <input type="checkbox"/>
	Peroneal <input type="checkbox"/>	DP <input type="checkbox"/>			
Graft Patency Period	< 30 d <input type="checkbox"/>	1-3 mths <input type="checkbox"/>	3-6 mths <input type="checkbox"/>	6-9 mths <input type="checkbox"/>	9-12 mths <input type="checkbox"/>
	> 12 mths <input type="text"/>				

Appendix G – SAJS Author Guidelines

SOUTH AFRICAN JOURNAL OF SURGERY

Author Guidelines

Submitted manuscripts that are not in the correct format and without the required supporting documentation specified in these guidelines will be returned to the author(s) for correction and will delay publication.

AUTHORSHIP

Named authors must consent to publication by signing a covering letter which should be submitted as a supplementary file. Authorship should be based on substantial contribution to:

- (i) conception, design, analysis and interpretation of data;
- (ii) drafting or critical revision for important intellectual content; and
- (iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org); and
- (iv) exact contribution of each author must be stated.

DECLARATION OF CONFLICT OF INTEREST

Authors must declare all sources of support for the research and any association with a product or subject that may constitute a conflict of interest. If there is no conflict of interest to declare please include the following statement: The authors declare no conflict of interest.

FUNDING SOURCE

All sources of funding should be declared. Also define the involvement of study sponsors in the study design, collection, analysis and interpretation of data; the writing of the manuscript; the decision to submit the manuscript for publication. If the study sponsors had no such involvement, this should be stated as follows: No funding source to be declared.

RESEARCH ETHICS COMMITTEE APPROVAL

The submitting author must provide written confirmation of Research Ethics Committee approval for all studies including case reports. The ethics committee as well as the approval number should be included.

STATISTICAL ANALYSIS

Authors are advised to involve medical statisticians at the protocol stage of their research project: to plan sample size, and the selection of appropriate statistical tests for analysis and presentation.

PROTECTION OF PATIENT'S RIGHTS TO PRIVACY

Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives informed written consent for publication. The patient should be shown the manuscript to be published. Refer to www.icmje.org.

ETHNIC CLASSIFICATION

The rationale for analysis based on racio-ethnic-cultural categorisation should be indicated.

CATEGORIES OF SUBMISSIONS

Shorter items are more likely to be accepted for publication, owing to space constraints and reader preferences.

Original articles

Original articles on research relevant to surgery should not exceed 3 000 words, no more than 30 references, with up to 6 tables or figures. A structured abstract under the following headings, Background, Methods, Results, and Conclusions is a requirement and should not exceed 250 words.

Scientific letters/short reports

Short reports should not exceed 1 500 words with a maximum of 10 references. Only one table or illustration is permissible. A structured abstract under the following headings, Background, Methods, Results, and Conclusions, is a requirement and should not exceed 250 words.

Case reports

Case reports should not exceed 1 500 words with no more than 10 references. Figures are limited to 2 figures and may include images or photographs. The case report should have three headings: Summary (not exceeding 100 words), Case report (with no introduction) and Discussion. Case reports will be published online only. The summary and the URL will appear in the printed version.

Video case reports (SAJS-VIDEO)

Video case reports should not exceed 1 500 words with 10 references and 6 figures. Headings should include Summary (not exceeding 100 words) and Case description (with three subheadings: Introduction, Case presentation and Discussion). The video file format must be only MP4 or MOV and should not exceed 300 MB and 8 minutes. Video case reports will be published online only. The summary and the URL will appear in the printed version.

Editorials and Opinions

Editorials and Opinions should not exceed 1 000 words and are welcome, but unless invited, will be subjected to the SAJSpeer review process.

Review articles

Review articles relevant to surgery should not exceed 5 000 words, with a maximum of 50 references and no more than 6 tables or figures. A summary of 250 words or less is required.

Letters to the editor

Letters to the editor should be 400 words or less with only one image or table.

Obituaries

Obituaries should be 900 words or less and should be accompanied by a photograph.

MANUSCRIPT PREPARATION

Refer to articles in recent issues for the presentation of headings and subheadings. If in doubt, refer to 'uniform requirements' - www.icmje.org. Manuscripts must be provided in UK English.

Qualification, affiliation and contact details

This information must be provided for ALL authors and must be submitted as a supplementary file.

Email addresses of all author must be provided.

ORCID number of ALL authors must be provided – if authors do not have ORCID, please register at <https://orcid.org/>

Abbreviations

All abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

Scientific measurements

Scientific measurements must be expressed in SI units except blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres). Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and <) should also be preceded by a space e.g. > 20 years. No spaces should precede \pm and $^{\circ}$, i.e. '35 \pm 6' and '19 $^{\circ}$ C'.

Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160...

Quotes should be placed in single quotation marks: i.e. The respondent stated: '...' Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

General formatting

The manuscript must be in Microsoft Word document format. Text must be 1,5-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, except for Tables). The manuscript must be free of track changes.

Disclaimers should follow the Conclusion and it should be in the following order: Acknowledgements, Declaration of conflict of interest, Funding source, Ethics declaration and ORCID.

ILLUSTRATIONS AND TABLES

If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

Tables may be embedded in the manuscript file and provided as 'supplementary files'. They must be numbered in Arabic numerals (1,2,3...) and referred to consecutively in the text (e.g. 'Table 1'). Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged. Tables must be cell-based (i.e. not constructed with text boxes, tabs or enters) and accompanied by a concise title and column headings. Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Figures must be numbered in Arabic numerals and referred to in the text, e.g. '(Figure 1)'. Figure legends: Figure 1: 'Title...'. All illustrations/figures/graphs must be of high resolution/quality: 300 dpi or more is preferable, but images must not be resized to increase resolution. Unformatted and uncompressed images must be attached as 'supplementary files' upon submission (not embedded in the accompanying manuscript). TIFF and PNG formats are preferable; JPEG and PDF formats are accepted, but authors must be wary of image compression. Illustrations and graphs prepared in Microsoft PowerPoint or Excel must be accompanied by the original workbook.

REFERENCES

Authors must verify references from the original sources. Only complete, correctly formatted reference lists will be accepted. Reference lists may be generated with the use of reference manager software, but the final document must be delinked from the reference database or otherwise generated manually. Citations should be inserted in the text as superscript, e.g. These regulations are endorsed by the World Health Organization,² and others.^{3,4-6} The superscript reference number should come after the punctuation mark and should not be in brackets.

All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order). Approved abbreviations of journal titles must be used; see the List of Journals in Index

Medicus. Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al. First and last page, volume and issue numbers should be given. Wherever possible, references must be accompanied by a digital object identifier (DOI) link and PubMed ID (PMID)/PubMed Central ID (PMCID). Authors are encouraged to use the DOI lookup service offered by [CrossRef](#). Crossref DOIs should always be displayed as a full URL link in the form <https://doi.org/10.xxxx/xxxxx>

Journal references: Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. *Stat Med* 1998;289(1):350-355. [<http://dx.doi.org/10.1000/hgjr.182>] [PMID: 2764753]

Book references: Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101. Chapter/section in a book: Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA jun, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.

Internet references: World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: World Health Organization, 2002. <http://www.who.int/whr/2002> (accessed 16 January 2010).

Other references (e.g. reports) should follow the same format: Author(s). Title. Publisher place: publisher name, year; pages. Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'. Unpublished observations and personal communications in the text must not appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

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A covering letter to the editor is mandatory and must include statements that the manuscript has not been published previously and is not under review elsewhere. It should state details of any prior publication of the research in abstract form or in Congress proceedings. The letter must declare if any of the authors have a conflict of interest and that the requirements for submission, including ethics approval and patient permission for case reports have been fulfilled. All authors must sign the covering letter.

Please provide the names and email addresses of three possible reviewers for this manuscript.

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Factors Influencing Infrainguinal Reverse Vein Bypass Patency at a South African Tertiary Academic Hospital

by Lucky Khambule

Submission date: 28-Mar-2021 03:21PM (UTC+0200)

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Introduction

Peripheral arterial disease (PAD) is a serious global healthcare problem with the incidence increasing, especially in the elderly population.¹ Chronic limb-threatening ischaemia (CLTI) refers to a manifestation of PAD in which patients present with chronic ischaemic rest pain or ischaemic skin lesions (ulcers or gangrene) in the presence of one or more abnormal haemodynamic parameter i.e. a decreased ankle-brachial index (ABI).² Effective revascularisation still remains the cornerstone of limb salvage in CLTI with large surveys suggesting that approximately half the patients with CLTI will undergo some type of revascularisation in order to prevent limb loss.¹

Several open surgical and endovascular revascularisation methods exist and include, amongst others surgical bypass, endarterectomy, profundaplasty, angioplasty with or without stenting, or a combination of these.¹ Despite the advent of endovascular intervention for CLTI, bypass surgery still remains an integral part of the armamentarium of revascularisation. The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend bypass surgery as an initial treatment for patients with a life expectancy of more than two years, and who have an available autologous vein conduit based upon the findings of the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial.^{3,4}

The abovementioned recommendation is supported by a review of studies published since 1981 which found that above-knee femoropopliteal reverse saphenous vein graft patency has a primary patency of 84% and 69% at one and four years, respectively. With below-knee grafts, explicitly performed for limb salvage, cumulative primary patency with reverse saphenous vein is approximately 90% and 75% at one and four years, respectively.⁵

Despite bypass surgery still being considered the "gold standard" by many vascular surgeons, several factors have been identified that are associated with failure of a bypass procedure such as the diameter of the vein graft, the distal runoff segment, the site of distal anastomosis and the race of the patient.¹

A retrospective study done by Singh et al analysed the Veterans Affairs (VA) National Surgical Quality Improvement Program's (NSQIP) large clinical database to investigate which factors, other than technical, were associated with a higher incidence of early graft failure in infrainguinal bypass. A multivariate analysis demonstrated that patients aged younger than 60 years as well as African American race was associated with early graft failure. Diabetes mellitus, on the other hand, had a negative association with early graft failure.⁶

Ray et al performed a retrospective study of 150 patients that had femoropopliteal bypass grafts where a detailed analysis of the factors that contributed to the graft patency were performed. The best results were found in patients with intermittent claudication demonstrating a 90% long term patency. Very little difference was shown in patients with rest pain and gangrene with patency rates of 81.8% and 80.7% respectively. Although the patency rate drops from 92.6% in patients with a three-vessel run off to 65% in patients with only a one vessel run off, the study showed that an isolated popliteal segment or single tibial vessel is often adequate to sustain function with autologous vein grafts. They also found that a saphenous vein graft diameter of 3-4mm and 5-6mm had a 75.6% and 85.1% patency rates, respectively, compared to 19% patency for those of 7mm or more. ⁷

Budd et al at the University of Leicester, United Kingdom, performed a retrospective analysis to evaluate factors determining late graft patency for infrainguinal bypass surgeries. Single centre results of 373 infrainguinal bypass grafts between 1980 and 1988 were reviewed. Overall, 5-year patency and limb salvage rates were 41% and 69% for in situ saphenous vein, 62% and 90% for reversed saphenous vein, 31% and 67% for PTFE and 29% and 59% for human umbilical vein. There was no significant difference in patency among these grafts at the above knee level, but significant differences between vein and prosthetic grafts were evident below the knee ($P < 0.001$). Using a proportional hazard model, the three factors that consistently correlated with late graft patency were graft type, site of distal anastomosis and distal run-off. ⁸

Wengerter et al at Montefiore Medical Centre in New York, reviewed 239 infrapopliteal reversed greater saphenous vein bypasses performed for critical limb ischaemia over a 7-year period and concluded that long 3.0mm diameter, and all reversed saphenous vein grafts with a diameter less than 3mm, should be considered at high risk for failure. ⁹

Frangos et al at Yale University School of Medicine, New York, performed a retrospective study to assess the influence of gender on patient selection and outcome in patients requiring infrainguinal vein bypass graft procedures. They reviewed 217 infrainguinal vein bypass grafts performed over an 8-year period. The results showed no statistical differences between men and women for age, diabetes, cardiac disease, tobacco use, hypertension, stroke, renal disease, or prior contralateral bypass or major amputation. The conclusion from this study was that gender does not affect graft patency, limb salvage, or survival rates. ¹⁰

Methods

This was a retrospective cohort analytic study of infrainguinal reverse vein bypasses performed at a central academic hospital in South Africa from January 2012 till December 2016 for the indication of CLTI. Patients who underwent infrainguinal bypasses for indications other than CLTI e.g. acute limb ischaemia or popliteal artery aneurysm, were excluded from the analysis. Different vascular surgeons performed the bypass procedures without a standardise protocol.

Patient demographics and perioperative data for each patient was obtained from a combination of electronic patient records, departmental statistics and files stored at the Vascular Laboratory at the Universitas Academic Hospital. All patient identification was kept confidential.

Where applicable, preoperative marked vein diameter was indicated as the smallest vein diameter measured.

Graft patency was evaluated as a clinically documented distal pulse or flow observed on duplex ultrasound graft surveillance. Due to the retrospective nature of the analysis, no differentiation was made between primary, primary assisted or secondary patency. A standardised graft surveillance protocol was also not utilised.

The study's primary objective was to identify factors affecting infrainguinal reverse vein bypass patency in patients operated for CLTI at Universitas Academic Hospital from January 2012 till December 2016, a five-year period. In addition, the 1-year infrainguinal reverse vein bypass patency was also to be determined. A secondary aim was to attempt to identify a subgroup of patients who are unlikely to benefit from bypass surgery or in whom early graft failure should be anticipated.

Results

During the period under review, 211 patients met the study's inclusion criteria with a total of 219 bypasses performed. 8 patients received bilateral bypasses. 2 patients (0.9%) demised and 79 of the 219 (36.1%) of bypasses were eventually excluded from the patency evaluation due to loss to follow-up. Patient characteristics are demonstrated in Table 1 and will be discussed in more detail.

Demographics

156 patients (73.9%) were males, and 55 (26.1%) were females. The median age was 61 years, with the ages ranging from 23 years to 88 years. The majority of patients were of black race (56.9%, n=120) followed by white (30.3%, n=64) and coloured (12.8%, n=27) patients.

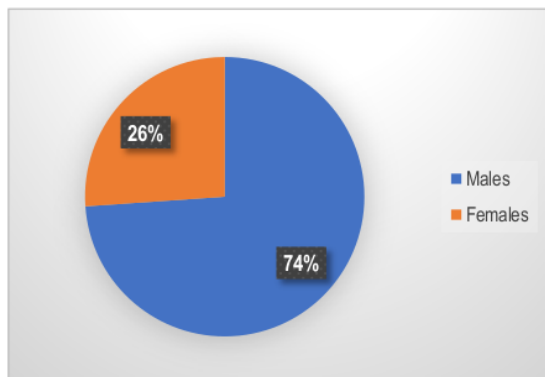


Figure 1: Gender distribution

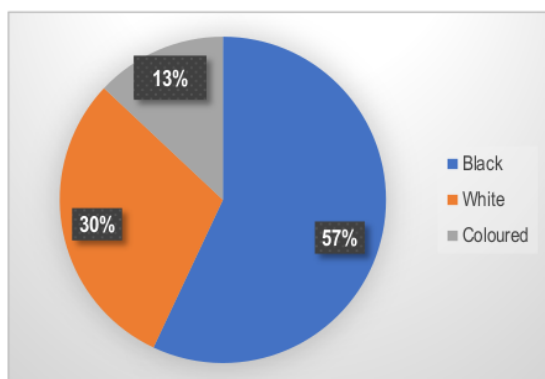


Figure 2: Race distribution

Comorbidities

The majority of patients had hypertension (78.2%, n=165) and were known smokers (83.4%, n=176). On the other hand, only 32.2% (n=68) of patients were diabetics, and only 11.4% (n=24) of patients had renal impairment.

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Table 1: Patient Characteristics

Variable	
Age (years)	
Median	61.0
Gender	
Males	156 (73.9%)
Female	55 (26.0%)
Race	
Black	120 (56.9%)
White	64 (30.3%)
Coloured	27 (12.8%)
Comorbidities	
Hypertension	165 (78.2%)
Diabetes mellitus	68 (32.2%)
Smoker	176 (83.4%)
Renal failure	24 (11.4%)
HIV	
Positive	25 (11.9%)
Unknown	149 (70.7%)
Severity of ischaemia	
Tissue loss	182 (83.1%)
GSV diameter (mm)	
Median	2.7
Proximal anastomosis	
CFA	105 (48.0%)
SFA	88 (40.1%)
AK POP	9 (4.1%)
PFA	8 (3.65%)
BK POP	8 (3.65%)
Distal anastomosis	
TP	61 (27.9%)
BK POP	49 (22.4%)
TA	42 (19.2%)
AK POP	41 (18.7%)
DP	10 (4.6%)
TPT	9 (4.1%)
Peroneal	6 (2.7%)
Number of runoff vessels	
1	59 (26.8%)
3	48 (21.8%)
4	35 (15.9%)
2	31 (14.1%)
5	20 (9.1%)
6	14 (6.4%)
0	13 (5.9%)

The human immunodeficiency virus (HIV) status was unknown in the majority of patients (70.6%, n=149), with only 11.8% (n=25) of patients known to be HIV positive. 72.0% of HIV positive patients (n=18/25) were on antiretroviral therapy at the time of admission.

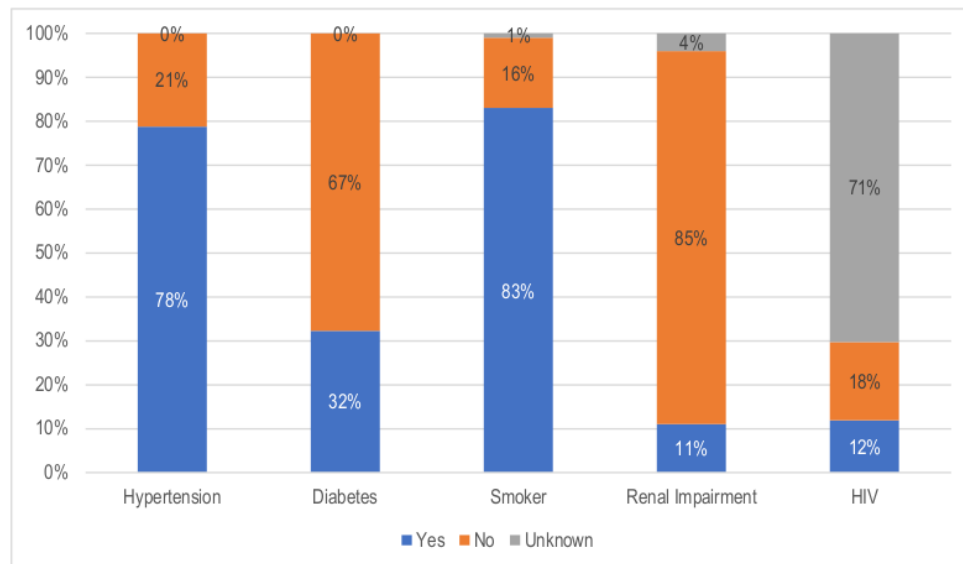


Figure 3: Comorbidities

Severity of Ischaemia

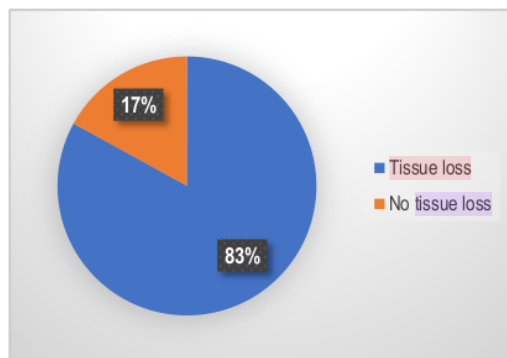


Figure 4: Severity of Ischaemia

All 219 bypasses were performed for the indication of chronic limb-threatening ischaemia. All patients (100.0%) reported the presence of rest pain (Rutherford 4). In addition to rest pain, tissue loss characterised by a non-healing ulcer and or gangrene on the affected limb, was present in 83.1% (n=182/219) of limbs prior to bypass surgery. Only 16.9% (n=37) had no tissue loss. The amount of tissue loss was not specified, therefore, Rutherford 5 or 6 could not be differentiated.

Surgical Factors

Proximal Anastomosis

The majority of bypasses (47.9%, n=105/219) had the proximal anastomosis performed at the level of the common femoral artery (CFA), followed by the superficial femoral artery (SFA) (40.2%, n=88), the above knee popliteal artery (AK POP) (4.1%, n=9), the below knee popliteal artery (BK POP) (3.7%, n=8) and the deep femoral artery (PFA) (3.7%, n=8). The level of proximal anastomosis was unknown in one patient.

Distal Anastomosis

The distal anastomosis was performed at the level of the posterior tibial artery (TP) in the majority of patients (27.9%, n=61). This was followed by the BK POP (22.4%, n=49), the anterior tibial artery (TA) (19.2%, n=42), the AK POP (18.7%, n=41), the dorsalis pedis artery (DP) (4.6%, n=10), the tibioperoneal trunk (TPT) (4.1%, n=9) and the peroneal artery (Per) (2.7%, n=6). The level of the distal anastomosis was unknown in one patient.

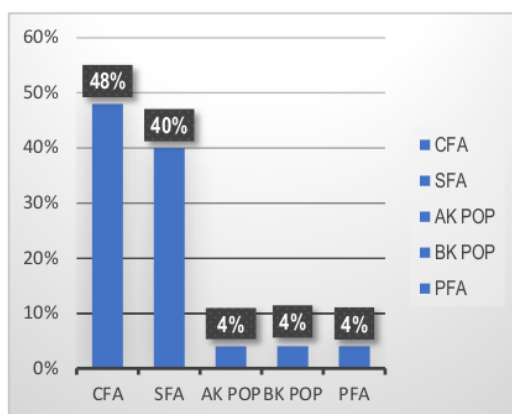


Figure 6: Level of Proximal Anastomosis

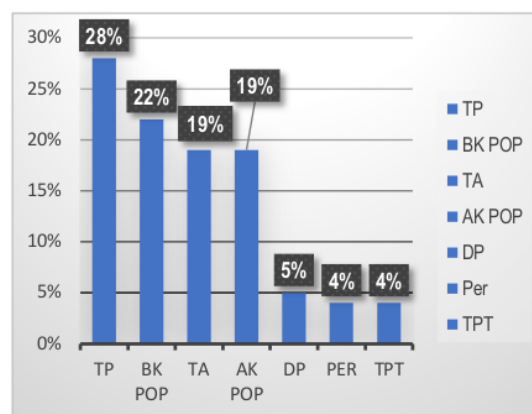


Figure 5: Level of Distal Anastomosis

Vein Diameter

One hundred ninety-six patients had preoperative vein marking data available. The median vein diameter was 2.7mm, ranging from 1.7mm to 5mm. Only 35.2% (n=69) of patients had an adequate vein diameter of 3mm or more. The majority of patients (61.2%, n=120) in fact, had a vein diameter of 2-3mm. No

differentiation was made between ipsilateral, contralateral greater saphenous veins, small saphenous veins or arm veins.

Number of Runoff Vessels

The patency of the runoff vessels were determined by evaluation of the preoperative imaging reports. The following vessels were assessed for patency to determine the number of patent runoff vessels: **popliteal artery, anterior tibial artery, tibioperoneal trunk, posterior tibial artery, peroneal artery and the dorsalis pedis artery.** The majority of patients (26.9%, n=59) only had a single runoff vessel. A 3-vessel runoff followed this in 21.9% (n=48) of patients with only 6.4% (n=14) of patients presenting with a 6-vessel runoff.

Graft Patency

Graft patency was evaluated as a clinically documented distal pulse or flow observed on duplex ultrasound graft surveillance. Due to the retrospective nature of the analysis, no differentiation was made between primary, primary assisted or secondary patency. As there was no dedicated graft surveillance protocol, 36.1% (n=79) of patients were lost to follow-up and subsequently excluded from the patency analysis.

Patency periods were divided into 3 groups: < 30 days (early graft failure), 1-12 months and > 12 months (late graft patency). 26.1% (n=36/138) of grafts demonstrated early failure within 30 days, whereas 45.7% (n=63/138) of grafts had late patency > 12 months. 28.3% (n=39) of grafts failed within 1 year.

In order to determine factors contributing to early graft failure or late graft patency, a subgroup analysis was performed of all bypasses with graft patency < 30 days as well as graft patency > 12 months. A comparative table between the patency groups can be found in *Table 2*.

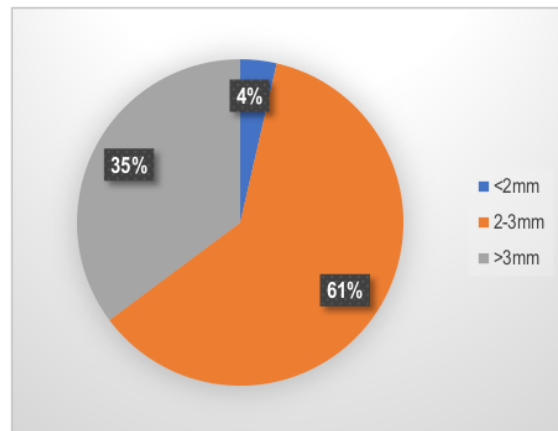


Figure 7: Distribution of Vein Diameter

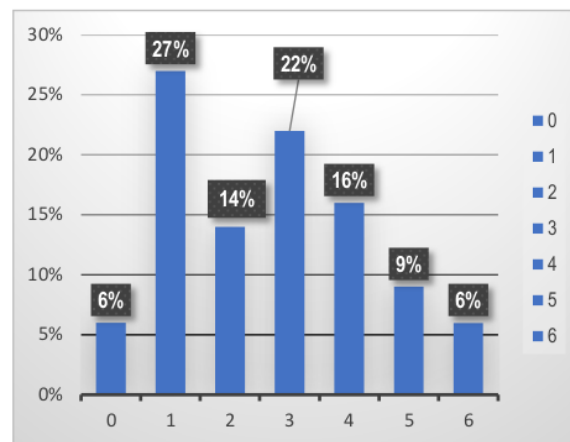


Figure 8: Number of Runoff Vessels

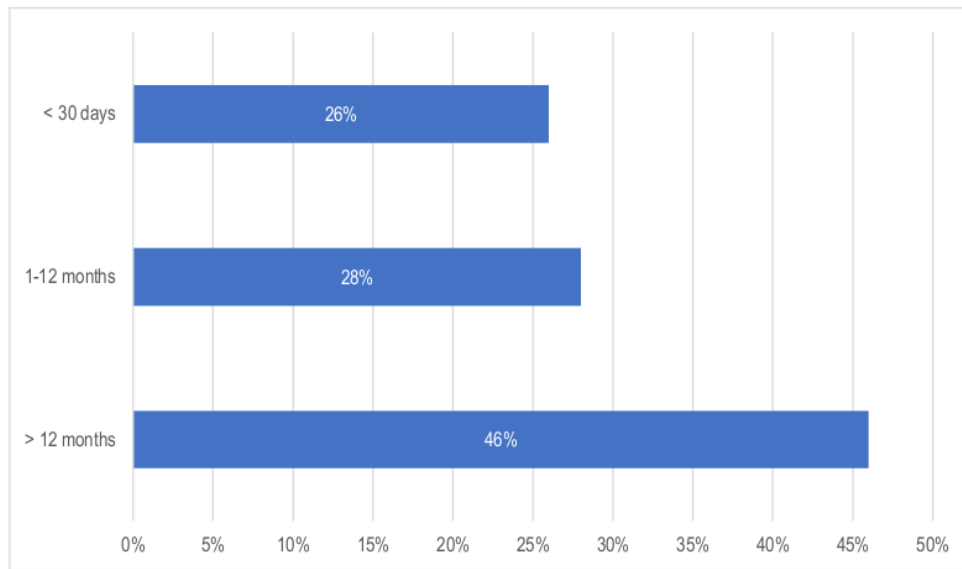


Figure 9: Distribution of Graft Patency

Gender

Female gender demonstrated a statistically significant increased risk for early graft failure (p-value 0.01) with a relative risk of 2.45 (95% CI [1.2;4.9]). Females demonstrated a 1-year patency of 28.6% compared to 51.5% for males.

Age

The median age of patients who suffered early graft failure was 59.5 years compared to 63 years for patients with late patency. Age was, however, not a statistically significant predictor of either early graft failure or late graft patency.

Table 2: Patency Analysis			
	< 30 days	> 12 months	P-value
Age (years)	59.5	63	
Gender			
Male	22 (23.4%)	53 (51.5%)	0.0102
Female	14 (40.0%)	10 (28.6%)	
Race			
Black	27 (32.6%)	34 (41.0%)	
White	7 (16.3%)	24 (55.8%)	
Coloured	2 (16.7%)	5 (41.7%)	
Comorbidities			
Hypertension	30 (28.0%)	52 (48.6%)	0.0031
Diabetes	16 (36.4%)	16 (36.4%)	
Smoker	24 (21.6%)	57 (51.4%)	
Renal failure	5 (41.7%)	5 (41.7%)	
HIV	5 (25.0%)	9 (45.0%)	
Severity of ischaemia			
Tissue loss	30 (27.3%)	50 (45.5%)	
GSV diameter (mm)			
Median	2.15	2.8	0.0007
Number of runoff vessels			
Median	2.5	3.0	

Race

Race was not found to affect graft patency significantly. Grafts demonstrated a 1-year patency of 55.8%, 41.7%, and 41.0% for white, coloured and black patients, respectively.

Comorbidities

The presence of hypertension, diabetes, HIV, and renal impairment had no significant effect on graft patency. On the other hand, smoking had a statistically significant protective effect on graft patency (p-value <0.01). Smokers demonstrated a 1-year patency of 51.4% compared to 22.3% for non-smokers.

Severity of Ischaemia

There was no significant difference in graft patency between patients who presented with rest pain only and those with associated tissue loss. As this was a retrospective analysis, patients could not be classified according to the extent of tissue loss as this was not always indicated. Patients who presented with tissue loss demonstrated a 1-year patency of 45.5% compared to 46.0% for patients who presented with rest pain only.

Vein Diameter

The median vein diameter among the grafts that suffered early graft failure was 2.15mm. This was in comparison to 2.8mm for the grafts that demonstrated late patency. Vein diameter proved to be an independent predictor for both early graft failure (p-value < 0.01) as well as late patency (p-value < 0.01) with a linear relationship between vein diameter and patency. Patients with a vein diameter <3mm demonstrated a 1-year patency of 40.4% compared to 57.2% for patients with a vein diameter ≥ 3mm.

Quality of Runoff

The number of patent runoff vessels had no significant impact on graft patency. The median number of runoff vessels were 2.5 for the grafts that occluded within 30 days compared to 3 for the grafts that remained patent beyond 12 months. Patients with a 6-vessel runoff demonstrated a 1-year patency of 50.4% compared to 48.7% with a single vessel runoff. The presence, however, of a single anterior tibial artery runoff proved to be a statistically significant risk for early graft failure (p-value 0.02) with a relative risk of 1.5 (95% CI [1.1;2.2])

4 Level of Proximal and Distal Anastomoses

Neither the level of the proximal nor distal anastomosis had any significant impact on graft patency. 1-year patency for the proximal anastomosis on the BK POP was 60% compared to 47%, 46%, 38%, and 20% for the SFA, CFA, AK POP and PFA, respectively. 1-year patency for the distal anastomosis on the peroneal and TPT was 67% and 60%. This was compared to 55%, 48%, 44%, 32% and 20% for the TP, AK POP, BK POP, TA, and DP, respectively. The cumulative 1-year patency of bypasses to the infrapopliteal vessels was 46% compared to 45% when the popliteal artery was selected as the target vessel.

Discussion

This study aimed to identify factors that influence infrainguinal reverse vein bypass patency among patients operated for CLTI at a tertiary academic hospital in central South Africa. It was postulated that knowledge of these factors would allow a critical analysis of bypass patency and outcome data as well as potentially identify a subgroup of patients who are unlikely to benefit from bypass surgery. This is essential in a resource-constrained environment like the government healthcare sector of South Africa.

The majority of patients (74%) included in this study were males, which correlates with other studies on this topic.^{6, 11-16} This may be due to the underrepresentation of the female gender in these studies, as pointed out by Hoel et al in the examination of the balance of enrolment with respect to gender and race in several randomised controlled trials conducted in the United States from 1983 till 2007. The author concluded that both minorities and women were underrepresented disproportionately in these trials on different vascular pathology compared to the actual incidence in the population.¹⁷

Even though the majority of patients included were of black race (57%, n=120) followed by white (30%, n=64) and coloured (13%, n=27) patients, this does not accurately reflect the composition of the South African demographic. The 2011 Census published by Statistics South Africa indicated that 80% of South Africans are of black race, followed by 8.8% coloured and 8.4% white.¹⁸ This may, however, indicate the demographic of the patients presenting to the state health sector in central South Africa.

16
The median age of included patients was 61 years. This is on average 5 to 9 years younger than the age quoted in other studies, which might indicate a younger population requiring peripheral bypass grafting in South Africa.^{6, 11, 12, 14, 16}

While the majority of patients had hypertension (78%) and were known smokers (83%), only a limited number of patients had renal failure (11%). The aforementioned is in keeping with findings in other studies on this topic, however, the majority (64%) of patients included in the PREVENT III trial, as well as the studies by Wengerter et al (87%) and Slim et al (76%), had diabetes, compared to only 32% in this study.^{6, 11, 12, 14, 16} Wengerter et al and Slim et al also reported that only 44% and 15% of included patients were known smokers, respectively.^{14, 15}

¹⁴ With South Africa having one of the fastest-growing HIV epidemics globally, it is concerning that only 29% of patients' HIV status were known.¹⁹ HIV is well documented risk factor for occlusive vascular disease and appears to play a role in outcome with poor overall limb salvage rates of 31.6%.²⁰⁻²² Knowledge of a patient's HIV status is, therefore, of paramount importance to predict success of revascularisation.

83% of patients included in this study had evidence of tissue loss indicating a more advanced level of ischaemia which correlates with results of the PREVENT III trial (75%) as well as the study by Wengerter et al (71%).^{11, 15} This is considerably higher than other studies by Ray et al and Slim et al including only 38% and 54% of patients with tissue loss, respectively.^{7, 14}

The majority of patients (27%) in this study had only a single runoff vessel. This is in contrast to findings in other studies. Ray et al reported a single vessel runoff in only 13% of patients with the majority (55%) of patients having a 3-vessel runoff.⁷

66% of patients in this study had a vein diameter which is considered inadequate (<3mm) for lower limb bypass surgery. This is in contrast to other studies demonstrating that the majority of patients had a vein diameter of at least 3-4mm.^{7, 11, 14, 15} In fact, in the PREVENT III trial, as well as the study by Wengerter et al, only 6% and 6.5% of patients had a vein diameter < 3mm, respectively.^{11, 15}

As with the PREVENT III trial (49%), the majority of bypasses (48%) utilised the CFA for the proximal anastomosis.¹¹ 40% of proximal anastomoses were performed on the SFA which is considerably more than the 25% in the PREVENT III trial.¹¹ The popliteal artery, however, was utilised as the proximal anastomotic site in 18% of cases in the PREVENT III trial compared to only 8% in this study.¹¹

The majority (59%) of infrainguinal bypasses included in this study were performed on infrapopliteal target vessels with the posterior tibial artery (28%) being the most commonly chosen target vessel. This correlated with the PREVENT III trial findings in which 65% of bypasses were performed to infrapopliteal vessels.¹¹

Factors Affecting Patency

The PREVENT III Trial ¹ demonstrated an overall 1-year primary patency of 61% compared to 71% primary patency shown by Wengertner et al. ^{11, 15} This study, on the other hand, demonstrated a 1-year patency of only 46%. No differentiation was made between primary, primary-assisted and secondary patency, however.

Gender

This study demonstrated that female gender is an independent predictor (p-value 0.01) of early graft failure with a relative risk of 2.45 (95% CI [1.2;4.9]). This contrast with the findings of Frangos et al which failed to show a significant impact of gender on graft patency. ¹⁰ A study by Tangelder et al, however, had a similar conclusion and identified female gender as an independent risk factor for graft failure. ¹⁴

Age

This study did not demonstrate any significant influence of age on graft patency. This finding is similar to that of Ray et al, which demonstrated lack of impact of age on femoropopliteal bypass success rate. ⁷ Singh et al, on the other showed that age > 70 years, as well as < 50 years and between 51 and 60 years, were significantly associated with early graft failure. A similar association was not, however, found for ages 61 to 70 years. ⁶

Race

This study also did not identify any significant impact of race on graft patency. This is again in contrast to the findings of Singh et al, which demonstrated African American race as a predictor of early graft failure. In this large VA evaluation of the NSQIP, compared to all other races, African Americans demonstrated an odds ratio of 1.4 for early graft failure. ⁶

In another multivariable analysis by Chew et al, African Americans also revealed an adjusted hazard ratio for loss of primary graft patency of 1.74 compared to Caucasians. ²³

In addition, the PREVENT III investigators also concluded that African American patients appeared to be at increased risk for early graft failure (30 days) with a hazard ratio. This finding was apparent even when patients with high-risk conduits were excluded. They also determined that specifically African American women were at highest risk for loss of both primary-assisted patency and secondary patency as well as amputation at 1 year. ¹¹

Comorbidities

The majority of associated comorbidities had no significant impact on graft patency in this study. ⁴ Studies by Rutherford et al and Singh et al, however, demonstrated a protective effect of diabetes on graft patency with better overall 3-year primary patency (60% for diabetics versus 42% for non-diabetics) and a negative association with early graft failure, respectively. ^{6, 12} A study performed by Wengertner et al, however, failed to show any significant effect of diabetes on graft patency. ¹⁶

¹ Overall, the outcomes of bypass grafts in patients with diabetes and renal disease are less favourable. Their independent contributions to actual graft failure, however, remain to be established. According to multiple reports, renal failure and diabetes increased the risk of amputation and mortality, but do not appear to directly influence vein graft patency. ²⁴⁻²⁷

¹ Most series have also failed to establish an association with hyperlipidaemia or hypertension on vein bypass patency. ²⁷ If these risk factors, in fact, contribute to decreased patency, the size of this effect is likely minimal and thus difficult to detect in small series'.

Interestingly, analysis of the impact of smoking on graft patency in this study showed that smoking appeared to be protective in nature with a statistically significant difference (p value 0.003) between graft patency of smokers compared to non-smokers. In general, the negative effect of smoking on the patency of vein bypass grafting is well-known. ²⁸ In the study by Singh et al, patients with a history of smoking had an early graft failure rate of 5.4% compared to 4.4 % in non-smokers. ⁶ Univariate analysis, however, indicated the difference was statistically significant. In a study by Rutherford et al, tobacco use was associated with a significantly reduced patency (51% at three years for smokers vs 68% for non-smokers). ¹²

On the other hand, the study by Wengertner et al. failed to show any significant effect of smoking on graft patency. ¹⁵ Even more remarkably, one study concluded that smoking ten or more cigarettes per day is associated with improved patency following an endovascular intervention. The authors of this study postulated that carbon monoxide was the most important contributing factor, in view of its potent anti-inflammatory and anti-proliferative properties. ²⁹

This study showed no statistically significant difference in the graft patency of patients who are HIV positive compared to HIV negative. Due to the lack of known HIV status the study sample was very small. Studies regarding the outcomes of lower limb bypasses in the HIV-positive population are lacking, however, Botes et al indicated a dismal limb salvage rate of 31.6% for patients with HIV-associated occlusive disease.²²

Severity of ischaemia

Compared to rest pain alone as the indication for surgery, the presence of tissue loss was found to have no significant impact on graft patency. This finding is reflected in a study done by Ray et al which found that there was very little difference in graft patency of patients with rest pain as compared to those with gangrene (81.8% vs 80.7%).⁷ This, however, differs from the findings of Schanzer et al which demonstrated that in the setting of tissue loss, patients undergoing bypass surgery had lower patency rates than those who underwent a bypass for rest pain only.³⁰

Vein diameter

This study demonstrated a statistically significant difference (p-value 0.0007) between graft patency of patients with a larger versus smaller vein diameter. This is consistent with the findings demonstrated by several other studies. Wengertner et al, showed that the infrapopliteal reverse vein bypass graft patency and limb salvage increase proportional to the vein diameter.³⁰ In another study by Ray et al, the success rate of saphenous vein graft decreased from 85.1% in cases in which the vein graft was between 5 and 6mm to 75% when the vein was less than 5mm in diameter.⁷ Cheshmedzhiev et al showed that venous grafts less than 3.5mm had 46% failure rate compared to 30% failure rate for venous grafts with a diameter over 3.5mm.³¹

These findings were also reinforced in an evaluation of the vein-related factors in the PREVENT III database. Schanzer et al demonstrated a linear increase in the risk for loss of primary and secondary patency as vein diameter decreased from > 3.5mm to < 3mm.³⁰

The vein diameter appears to play such a prominent role that, as a matter of fact, in a study by Wengertner et al, none of the vein grafts with a diameter < 3mm remained patent beyond 2 years.⁹

Only a single study by Slim et al had contradictory findings.¹⁴ In this study, they evaluated the outcomes of infrainguinal bypass grafts using vein conduits <3mm for CLTI and found that primary and assisted primary patency rates in small veins were not significantly different at 1 year.

Level of anastomosis

This study demonstrated that neither proximal nor distal anastomosis level had any significant impact on graft patency. This finding is in contrast to a study by Ray et al, where utilisation of the superficial femoral artery for the proximal anastomosis appeared to convey a lower patency rate.⁷

Quality of Runoff

In this study, the number of patent runoff vessels had no significant impact on graft patency. This is consistent with Rutherford et al, who showed that neither primary nor secondary patency was significantly affected by runoff status or clinical classification.¹² The study by Ray et al, on the other hand, demonstrated that the patency rate drops from 92.6% in patients with a 3-vessel (popliteal and both tibial arteries) to 65% in patients with only a single vessel run-off.⁷

Limitations of the Study

The retrospective nature of the study posed several challenges. 36% of patients had to be excluded from the patency analysis due to loss to follow-up. In view of the lack of a dedicated graft surveillance protocol as well as a lack of definition of patency according to accepted reporting standards, primary, primary-assisted and secondary patency could not be differentiated.

Even though tissue loss was classified separately from rest pain (Rutherford 4), the extent of tissue loss was not defined and could therefore not be further categorised into Rutherford 5 or 6. Even though all the bypass procedures included were of reverse vein configuration, bypass procedures were also performed by different vascular surgeons without a standardised protocol. All of the above could potentially affect the patency outcome and accuracy of data included. This would, however, be addressed by a prospectively designed research protocol with standardisation of surgical methods and follow-up surveillance.

Conclusion

In this retrospective review, female gender, small greater saphenous vein diameter as well as a single anterior tibial vessel runoff were identified as independent predictors of early (< 30 days) infrainguinal reverse bypass failure. On the other hand, smoking appears to be predictive of graft patency beyond 12 months.

This study's 1-year patency of 46% for infrainguinal reverse vein bypasses is considerably lower than that quoted in other studies. This could potentially be a reflection of several factors. The most important factor appears to be the small vein diameter of patients included in this study with 66% of patients demonstrating a vein diameter considered insufficient for lower limb bypass surgery. Other possible contributors include a considerable number of patients with tissue loss, limited runoff vessels as well as infrapopliteal bypasses being the majority. These factors were, however, not found to be predictors of early graft failure in this study.

In conclusion, several factors appear to affect the patency of infrainguinal reverse vein bypass. These factors should be noted as potential predictors of graft failure, however, they should not be used to exclude patients from potential limb-saving surgery as they have not been prospectively validated in the South African context.

Author Contributions

L.M Khambule was the principal investigator. A Malan was the supervisor for this research project. Both authors worked together on the protocol and analysed the data. L.M Khambule wrote the first draft manuscript, both authors modified and approved the final version.

Conflict of Interest

None

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Factors Influencing Infrainguinal Reverse Vein Bypass Patency at a South African Tertiary Academic Hospital

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J. S. Budd, J. Brennan, J. D. Beard, H. Warren, P. R. Burton, P. R. F. Bell. "Infrainguinal bypass surgery: Factors determining late graft patency", British Journal of Surgery, 1990

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"Surgery", Springer Science and Business Media LLC, 2008

Publication

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5	Robert B. Rutherford, Darrell N. Jones, Sven-Erik Bergentz, David Bergqvist et al. "Factors affecting the patency of infrainguinal bypass", <i>Journal of Vascular Surgery</i> , 1988 Publication	1%
6	Niten Singh, Anton N. Sidawy, Kent J. DeZee, Richard F. Neville, Cameron Akbari, William Henderson. "Factors associated with early failure of infrainguinal lower extremity arterial bypass", <i>Journal of Vascular Surgery</i> , 2008 Publication	1%
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11	Spiros G. Frangos, Suzanne Karimi, Morris D. Kerstein, Mona Harpavat, Bauer Sumpio, Andrew B. Roberts, Vivian Gahtan. "Gender	<1%

does not impact infrainguinal vein bypass graft outcome", Surgery, 2000

Publication

12

textarchive.ru

Internet Source

<1 %

13

Wen Wen Ni, Sum Leong, Farah Irani, Ankur Patel et al. "“Angioplasty-First” Approach for Limb Salvage in Asian Patients with Critical Limb Ischemia: Outcomes from 3,303 Angioplasties on 2,402 Limbs in a Single Tertiary Hospital", Journal of Vascular and Interventional Radiology, 2020

Publication

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14

K. Botes, J. Van Marle. "Surgical Intervention for HIV Related Vascular Disease", European Journal of Vascular and Endovascular Surgery, 2007

Publication

<1 %

15

link.springer.com

Internet Source

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16

"Abstracts", Journal of Thoracic Oncology, 2009

Publication

<1 %

17

www.science.gov

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18

Monahan, T.S.. "Risk Factors for Lower-Extremity Vein Graft Failure", Seminars in

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Vascular Surgery, 200912

Publication

19

[insights.ovid.com](https://www.insights.ovid.com)

Internet Source

<1 %

20

Submitted to King's College

Student Paper

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Igor J. Rychlik, Philip Davey, Jamie Murphy, Mark E. O'Donnell. "A meta-analysis to compare Dacron versus polytetrafluoroethylene grafts for above-knee femoropopliteal artery bypass", Journal of Vascular Surgery, 2014

Publication

<1 %

22

www.statpearls.com

Internet Source

<1 %

23

M.K. Nasr, R.J. McCarthy, J.S. Budd, M. Horrocks. "Infrainguinal Bypass Graft Patency and Limb Salvage Rates in Critical Limb Ischemia: Influence of the Mode of Presentation", Annals of Vascular Surgery, 2003

Publication

<1 %

24

Michael S. Conte, Andrew W. Bradbury, Philippe Kolh, John V. White et al. "Global vascular guidelines on the management of chronic limb-threatening ischemia", Journal of Vascular Surgery, 2019

Publication

<1 %

25

www.ajronline.org

Internet Source

<1 %

26

Allen, B.T.. "Femoropopliteal Bypass for Claudication: Vein vs. PTFE", Annals of Vascular Surgery, 199603

Publication

<1 %

27

Andrew Bradbury, Teun Wilmink, Amanda J Lee, Jocelyn Bell, Robin Prescott, Ian Gillespie, Gerry Stansby, F.Gerry R Fowkes. "Bypass versus angioplasty to treat severe limb ischemia: factors that affect treatment preferences of UK surgeons and interventional radiologists", Journal of Vascular Surgery, 2004

Publication

<1 %

28

Guth, A.A.. "Influence of gender on surgical outcomes: Does gender really matter?", Journal of the American College of Surgeons, 200503

Publication

<1 %

29

en.wikipedia.org

Internet Source

<1 %

30

Harris, R.. "Preoperative Prediction of Graft Patency for Infrapopliteal Arterial Bypass using Pulse-generated Runoff", European Journal of Vascular & Endovascular Surgery, 199905

Publication

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31

inba.info

<1 %

32

research-information.bris.ac.uk

Internet Source

<1 %

33

www.termedia.pl

Internet Source

<1 %

34

"Noninvasive Vascular Diagnosis", Springer
Science and Business Media LLC, 2013

Publication

<1 %

35

"Surgery", Springer Nature, 2008

Publication

<1 %

36

Thomas Whayne. "A Review of the Role of
Anticoagulation in the Treatment of Peripheral
Arterial Disease", International Journal of
Angiology, 2012

Publication

<1 %

37

www.ncbi.nlm.nih.gov

Internet Source

<1 %

38

P. A. Stonebridge. "Continued smoking and the
results of vascular reconstruction", British
Journal of Surgery, 01/1994

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Introduction

Peripheral arterial disease (PAD) is a serious global healthcare problem with the incidence increasing, especially in the elderly population.¹ Chronic limb-threatening ischaemia (CLTI) refers to a manifestation of PAD in which patients present with chronic ischaemic rest pain or ischaemic skin lesions (ulcers or gangrene) in the presence of one or more abnormal haemodynamic parameter i.e. a decreased ankle-brachial index (ABI).² Effective revascularisation still remains the cornerstone of limb salvage in CLTI with large surveys suggesting that approximately half the patients with CLTI will undergo some type of revascularisation in order to prevent limb loss.¹

Several open surgical and endovascular revascularisation methods exist and include, amongst others surgical bypass, endarterectomy, profundaplasty, angioplasty with or without stenting, or a combination of these.¹ Despite the advent of endovascular intervention for CLTI, bypass surgery still remains an integral part of the armamentarium of revascularisation. The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend bypass surgery as an initial treatment for patients with a life expectancy of more than two years, and who have an available autologous vein conduit based upon the findings of the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial.^{3,4}

The abovementioned recommendation is supported by a review of studies published since 1981 which found that above-knee femoropopliteal reverse saphenous vein graft patency has a primary patency of 84% and 69% at one and four years, respectively. With below-knee grafts, explicitly performed for limb salvage, cumulative primary patency with reverse saphenous vein is approximately 90% and 75% at one and four years, respectively.⁵

Despite bypass surgery still being considered the 'gold standard' by many vascular surgeons, several factors have been identified that are associated with failure of a bypass procedure such as the diameter of the vein graft, the distal runoff segment, the site of distal anastomosis and the race of the patient.¹

A retrospective study done by Singh et al analysed the Veterans Affairs (VA) National Surgical Quality Improvement Program's (NSQIP) large clinical database to investigate which factors, other than technical, were associated with a higher incidence of early graft failure in infrainguinal bypass. A multivariate analysis demonstrated that patients aged younger than 60 years as well as African American race was associated with early graft failure. Diabetes mellitus, on the other hand, had a negative association with early graft failure.⁶

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