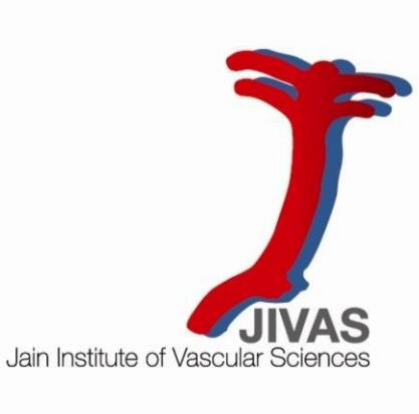
JIVAS
Jain Institute of Vascular Sciences

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled “Comparative study of outcomes between open surgical procedure first versus endovascular first revascularisation in patients with critical limb ischemia having Infra Inguinal disease” is a bonafide and genuine research work carried out by me under the guidance and supervision of Dr. Vivekanand**,** Vascular surgeon, Jain Institute of Vascular Sciences (JIVAS), Bhagwan Mahaveer Jain Hospital, Bengaluru, in partial fulfillment of the requirement of National Board of Examinations regulation for the award of the Degree of DNB in Peripheral Vascular Surgery.

This has not formed the basis for the award of any degree or diploma to me before and I have not submitted this to any other university or board previously.

Date : **Dr.K.Siva krishna**

Place : Bengaluru

CERTIFICATE

This is to certify that the dissertation titled **"**Comparative study of outcomes between open surgical procedure first versus endovascular first revascularisation in patients with critical limb ischemia having Infra Inguinal disease." is a bonafide research work done by **Dr. K.Siva krishna, MBBS, MS(Gen surg)** under my guidance at Jain Institute of Vascular Sciences (JIVAS), a unit of Bhagwan Mahaveer Jain Hospital, Bangalore in partial fulfillment of the requirement of National Board of Examinations regulation for the award of the degree of DNB in super specialty of ***Peripheral Vascular Surgery.***

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Bangalore.

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Bangalore.

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Place : Bengaluru

June 2019 **Dr. K.Siva krishna**

❖ LIST OF ABBREVATIONS:

CLI	Critical Limb Ischemia
PTA	Percutaneous Transluminal Angioplasty
POBA	Plain Balloon
DCB	Drug Coated Balloon
TLR	Target Lesion Revascularization
DES	Drug Eluting Stents
PCB	Paclitaxel-Coated Balloons
BTK	Below The Knee
BMS	Bare Metal Stent
DEB	Drug Eluting Balloon
API	Active Pharmaceutical Ingredient
ISR	In-Stent Restenosis
AVF	ArterioVenous Fistulas
MALE	Major Adverse Limb Events
MACE	Major Adverse Cardiac Events
GLASS	Global Limb Anatomic Staging System
CTO	Chronic Total Occlusion
SFA	Superficial Femoral Artery
DM	Diabetes Mellitus
HTN	Systemic Hypertension
CAD	Coronary Artery Disease
CKD	Chronic Kidney Disease
CVD	Cerebro Vascular Disease
ABI	Ankle Brachial Index
TBI	Toe Brachial Index
PVR	Pulse Volume Recording
TcPO2	Transcutaneous Oximetry
TOF	Time Of Flight
MDRD	Modification of diet in renal disease
MAC	Monitored Anaesthesia Care
ACT	Activated Clotting Time
CRI	Cardiac Risk Index
WIfI	Wound, Ischemia, foot Infection
ESRD	End Stage Renal Disease
GFR	Glomerular Filtration Rate
IC	Iodinated Contrast angiogram
CO2	Carbon dioxide angiogram
ACS	Acute Coronary Syndrome
CIN	Contrast Induced Nephropathy
CVA	Cerebro Vascular Accident(Stroke)
N/C	Non Compressible

Introduction

Peripheral arterial disease (PAD) is growing health problem across and is a steadily increasing global epidemic that affected more than 200 million patients worldwide[1].Peripheral arterial disease of the lower extremity is an important cause of morbidity in terms of limb loss and affects 10 million people in India as shown by Dutta et al[2].The number of people living with limb loss in the country is expected to double by 2050 due to growing rates of diabetes and peripheral arterial disease.

The manifestations of chronic lower extremity ischemia often include pain produced by varying degrees of ischemia, ranging from no symptoms to exertional muscular pain (intermittent claudication)/ ischemic rest pain. Patients may have more than one cause for their extremity pain, making diagnosis and management more difficult.Critical Limb Ischemia(CLI)is the most severe form of peripheral arterial disease and represents approximately 1% of total number of patients with PAD[3] .A significant number of patients with PAD are asymptomatic; however, patients with intermittent claudication usually experience a limb loss rate of <5% over 5 years. Meanwhile, patients with CLI have a 1-year mortality of 25% and major amputation rates of 25%, respectively[4].

Critical limb ischemia (CLI), defined as more than 2 weeks of rest pain, ulcers, or tissue loss attributed to arterial occlusive disease, is associated with great loss of both limb and life[4] .The management of lower extremity peripheral arterial disease is one of the most challenging problems of the vascular specialist. Decisions regarding the management of lower extremity PAD pose a unique challenge because of the complex interplay of factors that must be considered, including the underlying pathology, anatomic defects, degree of ischemia, availability of conduits, co-morbid conditions, functional status, ambulation potential, and suitability of anatomy for successful revascularization. Appropriate management of lower extremity PAD requires a firm understanding of these factors for good decision making.

Patients with CLI who were treated successfully with surgical or endovascular revascularization have better quality of life and longer survival than those treated conservatively or with primary amputation[5,6]. Bypass surgery has traditionally been considered an approach of choice to re-vascularize ischemic limbs with rest pain, non-healing ulcers, or gangrene to avoid major amputation[7].

Transluminal angioplasty, in which the area of occlusion is expanded by a balloon inserted within the artery, is an important treatment for patients with more severe symptoms (short-distance claudication, rest pain, ulcers, and gangrene). Recently, an increasing number

of cases of endovascular revascularizations have reported good limb salvage rates, even in the most challenging target area such as the infrapopliteal segment[8.]

However, nowadays it is still unclear which mode of treatment, angioplasty or bypass surgery, has better benefit/risk ratio. In this study, i intend to compare these two approaches in terms of Amputation-Free Survival(AFS), Wound healing, P atency in terms of PVR(ABI,TBI and TCPO2),and peri operative major adverse cardiac events(MACE).

Review of literature

CLI is a clinical syndrome of chronic, advanced limb ischemia manifested as rest pain, nonhealing ulcerations, and gangrene (necrosis). It is typically associated with markedly impaired perfusion as measured by noninvasive hemodynamic studies (ankle pressure <50 mmHg or toe pressure <30 mmHg). In contrast to IC, the fate of both the patient and the limb with CLI is starkly dissimilar.The **Circulase tria**l, a randomized placebo-controlled pharmacotherapy trial for CLI patients without revascularization options, demonstrated an all-cause mortality of 10% within the first year in both placebo and treatment arms[9.]

Natural history data are not clear as most patients receive some form of therapy. Survey data show ranges of primary amputation ≤40% in some centers, whereas other centers offer revascularization in 90% of cases.Data from prospective trials in CLI suggest that the rate of major adverse limb events, defined as any above ankle amputation or major revascularization, approaches 20% in the first year after an intervention[10].There are no proven options to preserve the limb and relieve ischemic symptoms at this stage of disease other than effective revascularization. Unremitting pain, nonhealing wounds, loss of ambulatory function, and recurrent infections accompany untreated CLI. Therefore, all patients with CLI who have a reasonable life expectancy and functional status should be evaluated for revascularization.

Once it is determined that revascularization is an appropriate treatment option, determination of the optimal strategy is highly individualized.Traditionally, Infrainguinal disease has been treated with open surgery (Endarterectomy/femoro distal bypass) over many decades with favorable patency rates.The emergence of endovascular techniques has changed the landscape of vascular therapy in PAD, but has not fundamentally altered the selection of candidates most likely to benefit from revascularization.Choosing between open versus endovascular approaches takes into consideration a wide variety of factors, including but not limited to the pattern of occlusive disease, anesthetic risk, severity of comorbid conditions, durability of the intervention, extent of tissue loss, previous failed interventions, or other specific anatomic considerations.The principle advantages of endovascular interventions are reduced periprocedural morbidity and shorter hospital stays, whereas the frequent drawback is less hemodynamic gain and inferior long-term durability compared with bypass surgery.

Surgical Revascularization:
Endarterectomy

Endarterectomy is the direct removal of obstructive plaque from an arterial segment and it is best applied for focal lesions in large caliber vessels, particularly at bifurcations . Initially

described by dos Santos[11,]then popularized by Wylie in the 1950s, it takes advantage of a cleavage plane between the plaque and the underlying deep media. Then advantages of endarterectomy are its autogenous nature without need for conduit. Limitations of endarterectomy relate to adequate securing of the end points, thrombogenicity of the resulting surface in low flow environments, and the subsequent healing response of the artery (intimal hyperplasia), which may lead to recurrent stenosis.Femoral endarterectomy remains a common and important procedure in PAD, allowing for durable reconstruction of the common femoral artery (CFA) and the profunda femoris artery, the key source of collateral circulation to the lower leg. It may be performed in an isolated fashion or as part of a hybrid or open bypass revascularization. Femoral endarterectomy is performed most commonly via longitudinal arteriotomy, with removal of the plaque followed by patch closure (prosthetic or biological materials) allowing for a degree of scarring to occur without subsequent lumen compromise.

Bypass

Surgical bypass is a versatile and flexible tool allowing for revascularization across a broad range of disease patterns, from the aorta down to the foot. The principal elements of technical success are unobstructed inflow, good-quality conduit, and adequate outflow. The inflow source should be free of any hemodynamically significant disease, and outflow should be sufficient to resolve the clinical ischemic syndrome and maintain sufficient flow rates through the conduit.small caliber conduits typically required for infrainguinal bypass (≤6 mm) face a more demanding hemodynamic environment for patency. The ideal bypass conduit is an arterial autograft, with its antithrombotic endothelial surface, fidelity to the physiological and mechanical properties of native arterial wall, resistance to infection, and resistance to inflammatory changes that result in stenosis or occlusion.Unfortunately, unlike coronary disease, arterial autografts are not a viable solution for PAD. Superficial extremity veins of appropriate caliber may be readily harvested in relevant lengths and offer a nonthrombogenic, autogenous solution. Venous conduits were first used for surgical reconstructions in the 1940s, initially by Dos Santos as a patch for enterectomy, and later by Kunlin[12] for peripheral bypass. In today's practice, great saphenous vein (GSV) is the dominant conduit for small and medium vessel bypass.Although it is expected that the majority of lower extremity revascularizations can be performed with autogenous vein, there are circumstances where prosthetic grafts may be necessary. Prospective trials have shown a short-term equivalency between prosthetic and vein grafts for femoral to above knee popliteal bypass, with favorable runoff.[13,14]However, the preponderance of evidence suggests that even for above knee bypass, autogenous vein outperforms prosthetic grafts at ≥2 years.[15]When good-quality vein is not

available, a prosthetic is a suitable alternative for bypass to the popliteal level. Some authors have also reported acceptable patency for prosthetic grafts to more distal targets.[16]Other putative advantages of prosthetic are shorter operative times and less surgical dissection. However, a major limitation, in addition to reduced patency, is the life-long risk of prosthetic infection, which can be a life- and limb-threatening complication.Unlike vein grafts, the level of the distal anastomosis has a significant effect on the durability of prosthetic bypasses. Whereas the 5-year patency of prosthetic grafts to the above knee popliteal artery is on the order of 40% to 50%, at the tibioperoneal level, the 5-year patency falls to 15% to 30%.[16] When forced to use prosthetic grafts for infrageniculate bypass, surgical modifications of the distal anastomosis, such as with the Miller cuff, Taylor patch, or St. Mary's boot, may improve patency by altering the compliance at the graft–vessel interface.[17]Recent improvements in prosthetic graft technology, notably heparin-bonding surface technology, may improve on the comparatively lower patency rates reported above.[18]

Endovascular intervention

Current endovascular treatment includes PTA/stenting, cutting PTA, atherectomy, covered stents (stent grafts), drug-coated balloons, drug-coated stents, brachytherapy, and cryoplasty. Most commonly done procedure is angioplasty/stenting. The following is a review of each modality.

Angioplasty/Stenting

The Society of Cardiovascular and Interventional Radiology Transluminal Angioplasty and Revascularization(STAR) registry[17]is a database of patients who underwent conventional angioplasty or other percutaneous intervention for lower extremity PAD performed at seven hospitals over a 3-year period. Patients were followed for 5 years.A total of 219 limbs in 205 patients were analyzed 79% with stenoses and 11% with occlusions were treated and 6% had concurrent stenosis and occlusion. The mean lesion length was 3.8 and 4.7 cm for stenotic lesions and occlusions, respectively. The technical success rate was 95%. The primary patency rates were 87%, 80%, and 69% at 1, 2, and 3 years, respectively. Diabetes and poor runoff scores were associated with decreased patency rates. The type of lesion (stenosis vs. occlusion) or the complexity of the lesion (classifified according to the AHA task force classifification categories 1–4) seemed to have no effect on patency; however, the number of Class 4 lesions was very limited.

A meta-analysis of 19 studies (1993–2000), which included 923 PTAs wherein patients were divided into four categories by combinations of their lesion type

(occlusion vs. stenosis) and symptoms (CLI vs. claudication). The lesion length was <10 cm in all but one study. The combined 3-year primary patency rates were 61% for patients with stenosis and claudication, 48% for occlusion and claudication, 43% for stenosis and CLI, and 30% for occlusion and CLI. These rates were statistically similar to those for primary stenting with regard to patients with claudication and stenosis, but they were inferior with respect to stenting for occlusion/CLI.[18]

Met et al.[19] conducted a systematic review of 23 cohort studies (1966–2007; 1,549 patients) to review outcomes using the subintimal angioplasty technique for infrainguinal occlusive disease. They were unable to perform a meta-analysis because of the heterogeneity between the studies. Technical success ranged from 80% to 90%, with 1-year clinical success rates of 50%–70%. Primary patency rates were approximately 50% at 1 year, and limb salvage rates were 80%–90%. Therefore, the authors concluded that subintimal angioplasty was a useful technique for diffificult lesions, particularly for limb salvage in CLI, and they viewed this technique as a reasonable method of treating patients with CLI and contraindications to surgical treatment.

The use of stents was initially advanced to improve long-term patency rates from PTA, particularly in treating longer segment disease (>10 cm), wherein angioplasty outcomes remained poor. Stenting may improve the initial angiographic outcome, reduce elastic recoil, and provide a scaffold in the setting of dissection. Three major randomized trials comparing primary nitinol stent placement with stent-assisted angioplasty have been reported and showed differing results.The Femoral artery stenting trial analysed outcomes with stand-alone PTA vs. primary stenting with a single self-expanding nitinol stent. Only single short-segment lesions of <10 cm were included, with a mean lesion length of 45 mm for both groups. A total of 123 patients were assigned to primary stenting, and 121 patients were randomized to PTA alone. Technical success was achieved in 79% and 95% of the PTA and stenting groups, respectively. Restenosis rates at 1 year, determined by ultrasound, were not statistically different between the two groups (39% in PTA and 32% in stent). Maximal walking distance was slightly improved in the stenting group, but no difference was found in resting ankle–brachial index or change in Rutherford class.

The RESILIENT trial is a prospective multicenter trial of 234 patients that compared bare nitinol stents (LifeStent, CR Bard, New Jersey, USA) in patients with a mean lesion length of 7.1 cm with PTA patients with a mean lesion length of 6.4 cm. Forty percent of patients with PTA had bailout stent for >30% residual stenosis or dissection. This study suggested a statistical advantage of improved patency with stent over PTA alone in femoral–popliteal lesions. The technical success rate was better with stenting (96% vs. 84%). Freedom from target lesion revascularization in the stent group was

significifically better than that in the PTA group at 6 and 12 months: 94.2% and 81.3% in the stent group, respectively, vs. 47.4% and 36.7% in the PTA group, respectively.The study showed continued advantages of bare metal stents vs. PTA at 3-year follow up. The authors concluded that primary stent placement with a self-expanding nitinol stent is superior to treatment with PTA alone for moderate-length lesions.[19,20]

The ABSOLUTE trial (Balloon Angioplasty vs. Stenting with Nitinol Stents in the SFA) included 104 patients with severe intermittent claudication and/or tissue loss (Rutherford classes 3–5), with lesions longer than 30 mm and at least one patent runoff vessel. Patients were randomized to PTA plus optional stenting or primary stenting with nitinol stents. The mean target lesion length was 112 and 93 mm for the stent and PTA groups, respectively. Restenosis rates were signifificantly lower in the primary stenting group at 2 years (46% vs. 69%). No difference was found between the two groups with respect to Rutherford class upon follow-up, but a trend was found toward improved walking capacity and resting ankle–brachial index in the stent group. Overall, reintervention rates were lower in the primary stent group.[19,20]

With the advances in stent technology, nitinol self-expanding stents have ultimately led to improved results for primary stenting in SFA lesions. The use of newer generation nitinol stents in SFA disease has demonstrated reduced restenosis compared with standard PTA. Schillinger et al. analyzed 104 patients with symptomatic PAD (12% had CLI) and SFA disease. They were randomly assigned to either primary stenting or angioplasty with bailout stenting for suboptimal angioplasty results. At 6months, the angiographic restenosis was 24% and 43% in the stent and angioplasty groups, respectively (p=0.05). This trend became signifificant at 12 months, at which point restenosis by duplex ultrasound was 37% and 63% in the stent and PTA groups, respectively (p=0.01).26) .This study showed statistically superior patency and physical function in 10–12 cm mean lesion lengths with nitinol stents vs. PTA alone.

Montero-Baker et al. analyzed the outcome of endovascular therapy for femoropopliteal disease with the Supera stent. A total of 305 Supera stents were implanted in 147 patients. The mean follow-up was 12.7months. Most patients had CLI with tissue loss (38%) or rest pain (29%). Primary, assisted primary, and secondary patency rates at 12 months by duplex ultrasound imaging were 90%, 91%, and 93%, respectively, with a mean lesion length of 184.5±131.80 mm and a mean stented length of 197.5±113.65 mm. Seventeen patients experienced an event requiring successful reintervention in the stented segment (13 for type I or II restenosis and 4 for type III). Eight major amputations were performed, with five of those having a patent stent at the time of limb sacrifiice. The overall mortality rate was 12% during the study period. No stent fractures were identifified. They

concluded that stenting of the SFA and popliteal arteries using the Supera stent system seem to be safe and effective. The interwoven stent design may better serve areas under extreme mechanical stress.[21]

Cutting Balloon Angioplasty

Cutting balloon angioplasty was originally developed for coronary arteries and used low-pressure balloon catheters mounted with microsurgical blades or microtomes that cut into luminal vessel during inflflation. The cutting balloon by Boston Scientifific (Natick, MA, USA) is equipped with four microsurgical blades that are bonded longitudinally to a balloon. The mechanism of action is controlled disruption of the vessel wall, resulting in more controlled dilatation at lower balloon inflflation pressures. A prospective randomized controlled trial of denovo SFA lesions of 43 patients (19% had CLI) compared cutting balloon angioplasty with conventional angioplasty and showed a restenosis rate of 32% and 62% in the PTA and cutting balloon angioplasty groups, respectively, by duplex ultrasound at 6 months ($p=0.048$).[22] In a comparison of conventional balloon angioplasty and cutting balloon angioplasty in 36 patients with failing infrainguinal bypass grafts, initial success was better for the cutting balloon cohort, but 1-year primary patency did not differ between the two groups.[23] Therefore, cutting balloon angioplasty is not routinely used because of higher costs and inferior results (vs. conventional PTA), but it can be used for in-stent restenosis and diseased arteries in flexion points (common femoral or popliteal artery, stent fracture risk).[22]

Atherectomy

Atherectomy involves debulking or atherosclerotic plaque removal. Current devices for this modality include rotational, directional, orbital, and laser atherectomy. Atherectomy for patients with PAD is currently used as adjunctive/alternative therapy to traditional PTA or stenting. Plaque debulking leads to an immediate increase in lumen size, which should result in reduced stretch injury of the arterial walls.[24,25]

The DEFINITIVE Ca++ study included 133 patients with 168 moderate to severely calcified femoropopliteal lesions treated with the Silverhawk or Turbohawk (Covidien, Plymouth, MN, USA) and distal embolic protection. They reported a 93% freedom from major adverse events, which included clinically signifificant embolization. However, the definitive clinical benefit of atherectomy over PTA was unclear.

The EXCITE (Excimer Laser Atherectomy) trial enrolled patients from 40 United States centers and included patients with a Rutherford class 1–4 target lesion length ≥4 cm and a vessel diameter of 5–7 mm. Patients were randomly divided into excimer laser atherectomy and PTA vs. PTA alone (2 : 1 ratio). The primary effificacy endpoint was target lesion revascularization at 6-month follow-up, and the primary safety

endpoint was a major adverse event (death, amputation, or target lesion revascularization) 30 days postoperatively. The study was stopped at 250 patients due to early effificacy. The mean lesion length was 19.6±12.0 vs. 19.3±11.9 cm. Total occlusion was present in 31% vs. 37% of patients. The Excite laser atherectomy with PTA was superior, with a success rate of 94% vs. 83% (p=0.01). The freedom from target lesion revascularization at 6 months was 74% for the Excite laser atherectomy, with PTA vs. 52% for PTA alone (p<0.005). The 30-day major adverse event rate was 6% vs. 21% (p<0.001). The Excite laser atherectomy with PTA resulted in a 52% reduction in target lesion revascularization.[26]

Drug coated balloon Trials(DCB)

The LEVANT trial (Lutonix Paclitaxel CB [Bard] for Prevention of Femoral–Popliteal Restenosis) randomized 101 patients to Lutonix DCBs or uncoated balloons. A signifificant increase was found in the primary patency rate at 12 months with the Lutonix 0.35 DCB vs. plain balloon angioplasty (74% vs. 57%, p<0.001). At 24 months, major adverse events (death, amputation, target lesion thrombosis/reintervention) were 39% for DCB and 46% for patients with uncoated balloon (p=0.45).[27]Medtronic's IN.PACT SFA trial is a prospective, multicenter, randomized trial wherein 331 patients with intermittent claudication and CLI, secondary to femoral–popliteal PAD, were randomly assigned in a 2 : 1 ratio to treat with DCB (paclitaxel) or PTA. More than 90% of lesions were de novo, with a mean lesion length of ≥8 cm in both groups. A higher primary patency rate at 12 months in the IN.PACT Admiral DCB group was noted, compared with the PTA group (82% vs. 52%, p<0.001). The rate of clinically driven target lesion revascularization was 2.4% and 20.6% in the DCB and PTA groups, respectively (p<0.001). No device/procedure-related death or major amputation occurred.[28]The THUNDER trial followed 154 patients who were treated with DCBs, angioplasty with paclitaxel in contrast medium, or no paclitaxel (control group) for 5 years. Target lesion revascularization was signifificantly lower in the DCB vs. the control group (21% vs. 56%, p=0.0005). DCBs also had lower binary restenosis (17% vs. 54%, p=0.04). DCBs had reduced target lesion revascularization over 5 years. No drug-related local vessel abnormalities were reported.[29]

Drug-Coated Stents

SIROCCO I and II trials

Sirolimus-eluting stents (Cordis Smart nitinol self-expanding stent for the treatment of SFA disease) were compared with bare metal stents. No difference was found in in-stent restenosis at 6 months and 2 years[30,31]

Eluvia DES (Boston Scientifific)

This is a prospective, single-arm, MAJESTIC clinical trial of the treatment of femoral–popliteal lesions up to 110 mm in length (paclitaxel coating). The study enrolled 57 patients, with a mean lesion length of 71±28 mm, in Europe, Australia, and New Zealand. Severe calcifification and occlusion were noted in 65% and 46%, respectively. The freedom from target lesion revascularization at 24 months was 93%. No major amputations and no stent fractures occurred.[32]

Open Surgical vs. Endovascular Treatment

A direct comparison of endovascular therapy and open surgery is generally limited due to variations in vascular anatomy and enrollment in comparative trials is diffificult. Patients treated with endovascular therapy usually present with intermittent claudication, whereas patients who undergo surgery usually have CLI. Patients with CLI have higher periprocedural morbidity and mortality rates, diffuse arterial disease, and worse tibial runoff status. Thus, the outcome for surgery in patients would be signifificantly worse. In a series of 100 potential patients for randomized controlled trials, only 4% were eligible for comparison of PTFE femoropopliteal bypass with endovascular treatment.[33]

A systematic review meta-analysis of observational studies between 1995 and 2012 showed that no difference was found in mortality, amputation, or amputation-free survival at 2 years. Femoropopliteal bypass using vein grafts have been shown to have better patency rate than PTFE grafts.[34]

Randomized Trials of Surgical vs. Endovascular Therapy

Bypass vs. Angioplasty in Severe Ischemia of the Leg (BASIL) trial

This study included 452 patients with CLI that were randomized to surgery or percutaneous transluminal angioplasty (PTA) and followed for up to 5 years. Both ASV (75%) and synthetic grafts were used, with the majority being placed in the femoropopliteal segment. The 30-day mortality rates were 5% and 3% for surgery and PTA, respectively. The morbidity rate was signifificantly higher in the surgery group due to wound complications and myocardial infarctions. A cost analysis also favored the endovascular approach. No differences were found in amputation-free survival or overall survival rates at 1 year; however, late outcomes favored the surgical group. The failed endovascular therapy group requiring surgery had lower amputation-free survival rates. This study had some limitations, including suboptimal medical treatment, lack of revascularization patency endpoints, and limited endovascular techniques (only PTA). This trial concluded that bypass using veins offers a better late outcome. Bypass was the preferred treatment for patients with a 2-year or

longer life expectancy (70% of cohort). Prosthetic bypass was associated with poor results; therefore, angioplasty may be preferred in patients who lack adequate vein conduit. Similar conclusions were made by the American College of Cardiology Foundation/American Heart Association.[35]

BASIL-2 and BASIL-3 trials

The United Kingdom National Institute for Health Research Health Technology Assessment-funded BASIL-2 and BASIL-3 trials, led by Andrew Bradbury at the Birmingham Clinical Trials Unit (BCTU; University of Birmingham, UK) are complementary randomized controlled trials that will provide further Level 1 evidence regarding the surgical and endovascular treatment of severe limb ischemia due to infra- and femoropopliteal diseases, respectively. Since the BASIL-1 report, drug-coated balloons and drug-eluting stents have become widely available, and this has led interventionalists to argue for a "best endovascular treatment" strategy for almost all patients with severe limb ischemia. The National Institute for Health and Care Excellence (NICE) found the results of BASIL-1 more diffificult to interpret with regard to treatment of infrapopliteal disease because only approximately 25% of the cohort of 452 patients had an infrapopliteal bypass or intervention. There remains, therefore, considerable uncertainty as to whether patients presenting with severe limb ischemia due Endovascular vs. Open Bypass for Femoropopliteal Disease Annals of Vascular Diseases Vol. 11, No. 1 (2018) 27 to infrapopliteal disease are best served by endovascular treatment or vein bypass. BASIL-2, which aims to randomize 600 patients with severe limb ischemia secondary to infrapopliteal disease and/or femoropopliteal disease to either the best endovascular treatment first or vein bypass first revascularization strategy. BASIL-3 will randomize 861 patients with severe limb ischemia secondary to femoropopliteal disease and/or infrapopliteal disease, to plain balloon angioplasty and/or bail-out bare metal stent, drug-coated balloon and/or bare metal stent, and drug-eluting stent.

Bypass or Angioplasty in Severe Intermittent Claudication (BASIC) trial

This study was performed between 1995 and 1998 and included 56 patients that were randomized from 18 centers and only seven patients were treated with stents. The 1-year patency rates were 82% and 43% for bypass and angioplasty, respectively.[36]

McQuade trial

This was a randomized trial of 86 patients (100 limbs) that compared synthetic bypass grafts with PTFE nitinolcovered stent grafts. Patient symptoms included both claudication and limb-threatening ischemia. TASC II A (n=18), B (n=56), C (n=11), and D (n=15) lesions were included. The patients were randomized into one or two treatment groups: the

percutaneous treatment group (Group A, n=50) with angioplasty and placement of one or more stent grafts or the surgical treatment group (Group B, n=50) with a femoral to above-knee popliteal artery bypass using a synthetic conduit (Dacron or PTFE). They were followed for 48 months, including clinical assessment, physical examination, ankle–brachial indices, and color flow duplex sonography at 3, 6, 9, 12, 18, 24, 36, and 48 months. The mean total lesion length of the treated arterial segment in the stent graft group was 25.6 cm. The stent graft group demonstrated a primary patency of 72%, 63%, 63%, and 59% with a secondary patency of 83%, 74%, 74%, and 74% at 12, 24, 36, and 48 months, respectively. The surgical femoral–popliteal group showed a primary patency of 76%, 63%, 63%, and 58% with a secondary patency of 86%, 76%, 76%, and 71% at 12, 24, 36, and 48 months, respectively. No statistical difference was found between the two groups with respect to primary (p=0.807) or secondary (p=0.891) patency. They concluded that percutaneous stent grafts exhibit similar primary patency at 4-year follow-up compared with conventional femoral–popliteal artery bypass grafting with synthetic conduit.[37]

PREVENT III and BASIL trials

The Society for Vascular Surgery recently combined data from the BASIL and PREVENT III trials (only vein bypass grafts) to develop objective goals in patients with CLI with a perioperative (30-day) mortality rate of 3%, major adverse cardiovascular event rate of 6%, graft occlusion rate of 5%, and amputation rate of 2%[38] Technical factors were speculated to be critical in the short- and long-term success of bypass surgery, where in vein quality was very important, and single-segment great saphenous veins with a diameter of ≥3.5 mm were optimal conduits for leg bypass. Approximately one half of PREVENT III trial patients had such conduits, which had a 30-day failure rate of 1.7%, with a secondary patency rate of 87%, and a limb salvage rate of 91% at 1 year.The PREVENT III cohort and several large series have found that diabetes mellitus does not adversely affect infrainguinal vein graft patency, in contrast to endovascular treatment.[39,40]

BEST Endovascular vs. Best Surgical Therapy in Patients with Critical Limb Ischemia (BEST-CLI) trial

This randomized trial is currently enrolling patients with CLI who are candidates for both open surgery and endovascular therapy. This study will compare the effectiveness of the best available surgery vs the best available endovascular treatment.[41] This multidisciplinary trial, led by Alik Farber (Boston Medical Center, Boston, USA), Matthew Menard (Brigham and Women’s Hospital, Boston, USA), and Kenneth Rosenfifield (Massachusetts General Hospital, Boston, USA), is currently enrolling patients at 135 sites in the United States and Canada. BEST-CLI both encourages and facilitates specialists who treat CLI at a given trial

site to work together for the benefit of patients. The key to successful engagement in the effort is the ability of participating investigators to set aside their individual treatment biases and acknowledge the absence of reliable scientific evidence to support their impulses. This trial is near the halfway mark.

Nonrandomized Trials

Siracuse et al. reviewed all lower extremity bypass procedures from 2001 to 2009 and all PTA and/or stenting performed from 2005 to 2009 for claudication only. They identifified 113 bypass grafts and 105 PTA and/or stenting of femoral–popliteal lesions without prior intervention. The bypasses were above and below the knee in 62% (45% vein) and 38% (100% vein), respectively. The mean age for bypass and PTA and/or stenting patients was 63 and 69 years, respectively ($p<0.01$). The mean length of hospital stay was 3.9 vs. 1.2 days ($p<0.01$). Bypass grafts were used less for TASC A (17% vs. 40%, $p<0.01$) and more for TASC C (36% vs. 11%, $p<0.01$) and TASC D (13% vs. 3%, $p<0.01$) lesions. No significifant differences were found in the perioperative (2% vs. 0%) or 3-year mortality rate (9% vs. 8%). Wound infection was higher with bypass (16% vs. 0%, $p<0.01$); however, no grafts were involved. Bypass showed improved freedom from restenosis (73% vs. 42% at 3 years; hazard ratio [HR], 0.4), symptom recurrence (70% and 36% at 3 years), and freedom from symptoms at last follow-up (83% vs. 49%; HR, 0.18). No difference was found in freedom from reintervention (77% vs. 66% at 3 years). A multivariable analysis showed that restenosis was predicted by PTA and/or stenting (HR, 2.5) and TASC D (HR, 3.7) lesions. Recurrence of symptoms was similarly predicted by PTA and/or stenting (HR, 3.0) and TASC D lesion (HR, 3.1). Postoperative statin use postoperatively was predictive of patency (HR, 0.6) and freedom from recurrent symptoms (HR, 0.6). They concluded that surgical bypass for the primary treatment of claudication showed improved freedom from restenosis and symptom relief despite treatment of more extensive disease, but it was associated with an increased length of hospital stay and wound infection. Statins improved freedom from restenosis and symptom recurrence overall.[42]

Dosluoglu et al. compared stenting vs. above-the-knee PTFE bypass for TransAtlantic Inter-Society Consensus-II C and D SFA disease. Consecutive patients who underwent above-the-knee femoropopliteal bypass with PTFE or PTA/S for TASC-II C (PTA/S-C) or D (PTA/S-D) SFA lesions between June 2001 and April 2007 were retrospectively analyzed. In 127 patients, 139 limbs were treated (46 above-the-knee femoropopliteal, 49 PTA/S-C, and 44 PTA/S-D).The technical success rate was 84% and 100% in PTA/S-D and other groups, respectively. The mean follow-up was 26.4 months. The 12- and 24-month primary patency was 83%±6% and 80%±7% for PTA/S-C, 54%±8% and 28%±12% for PTA/S-D, and

81%±6% and 75%±7% for above-the-knee femoropopliteal bypass (p<0.001 PTA/S-D vs. PTA/S-C and above-the-knee femoropopliteal bypass).Secondary patency in PTA/S-C was signifificantly better than that in the above the-knee femoropopliteal bypass (p=0.003) and PTA/S-D groups (p<0.001). The difference in above-the-knee femoropopliteal bypass was marginally better than that in PTA/S-D (p=0.064). They concluded that PTA/S-C lesions had a superior midterm patency than above-theknee femoropopliteal bypass using PTFE, and above the-knee femoropopliteal bypass with PTFE has a better primary patency than PTA/S-D[43].

In a study by Caitwin w Hicks et al[44] compared below bypass versus percutaneous interventions interms of 1-year primary patency, major amputation, and mortality Overall, 2566 patients were included (LEB=500, PVI=2066). One-year primary patency was significantly worse following LEB (73% vs 81%; *p*<0.001). One-year major amputation (14% vs 12%; *p*=0.18) and mortality (4% vs 6%; *p*=0.15) were similar regardless of revascularization approach. Multivariable analysis adjusting forbaseline differences between groups confirmed inferior primary patency following LEB versus PVI (HR 0.74; 95% CI, 0.60–0.90; *p*=0.004), but no significant differences in 1-year major amputation (HR 1.06; 95% CI, 0.80–1.40; *p*=0.67) or mortality (HR 0.71; 95% CI, 0.44–1.14; *p*=0.16). Based on these data, they conclude that endovascularrevascularization is a viable treatment approach for critical limb ischemia.

In Soderstom et al[45] the study cohort comprised 1023 patients treated for CLI with 262 endovascular and 761 surgical revascularization procedures to their crural or pedal arteries. A propensity score was used for adjustment in multivariable analysis, for stratification, and for one-to-one match.In the overall series, PTA and bypass surgery achieved similar 5-year leg salvage (75.3% vs 76.0%), survival (47.5% vs 43.3%), and amputation-free survival (37.7% vs 37.3%) rates and similar freedom from any further revascularization (77.3% vs 74.4%), whereas freedom from surgical revascularization was higher after bypass surgery (94.3% vs 86.2%, P < 0.001). In propensity-score-matched pairs, outcomes did not differ, except for freedom from surgical revascularization, which was significantly higher in the bypass surgery group (91.4% vs 85.3% at 5 years, P = 0.045). In a subgroup of patients who underwent isolated infrapopliteal revascularization, PTA was associated with better leg salvage (75.5% vs 68.0%, P = 0.042) and somewhat lower freedom from surgical revascularization (78.8% vs 85.2%, P = 0.17). This significant difference in the leg salvage rate was also observed after adjustment for propensity score (P = 0.044), but not in propensity-score-matched pairs (P = 0.12).This study concluded that when feasible, infrapopliteal PTA as a first-line strategy is

expected to achieve similar long-term results to bypass surgery in CLI when redo surgery is actively utilized.

In Arvela et al [46] study 584 consecutive patients aged at least 80 years treated with either PTA (277) or bypass surgery (307) for CLI are included. After 2 years PTA achieved better results than bypass surgery (leg salvage: 85.4 versus 78.7 per cent, P = 0.039; survival: 57.7 versus 52.3 per cent, P = 0.014; amputation-free survival (AFS): 53.0 versus 44.9 per cent, P = 0.005). Cox regression analysis showed that increased age , decreased estimated glomerular filtration rate , diabetes, coronary artery disease and bypass surgery were associated with decreased AFS. In 95 propensity score-matched pairs, leg salvage at 2 years (88 versus 75 per cent; P = 0.010) and AFS (53 versus 45 per cent; P = 0.033) were significantly better after PTA. Classification and regression tree analysis suggested that PTA was associated with better 1-year AFS, especially in patients with coronary artery disease (63.8 versus 48.9 per cent; P = 0.008).Finally this study concludes when feasible, a strategy of PTA first appears to achieve better results than infrainguinal bypass surgery in patients aged 80 years and older.

In 2004 Vander Zaag et al[36] enrolled 56 patients, all with symptoms related to a 5-15 cm long occlusive lesion of the superficial femoral artery. Thirty-one patients were randomly assigned to percutaneous transluminal angioplasty (PTA); 25 patients to bypass surgery. All patients were followed at 1, 6 and 12 months after the procedure. The primary outcome of our study was re-occlusion of the femoral artery. Thirty patients underwent the allocated PTA and 24 patients underwent bypass surgery. Cumulative 1-year primary patency after PTA was 43 and 82% after bypass surgery. After PTA more than half of the patients had a re-occlusion with an absolute risk reduction of 31% (CI: 6-56%) in favour of bypass surgery. Therefore, they conclude that with respect to patency, for long superficial femoral artery (SFA) stenoses or occlusions, surgery is better than PTA.

Non-randomized registry based study conducted by F. Gentile et al[47] from may 2008 to january 2014 in 549 patients(endo-430 and open-114)showed no differnce in pt demographics, Wound complications requiring treatment within 30 days were more common in patients treated with open procedures (32% vs. 1% for endo; p < .001), as well as stroke and myocardial infarction. Amputation rates were higher at 30 days in the open group (7% vs. 2%; p=.012) but similar at 1 year (10% vs. 7%; p= .206). Mortality was similar at 30 days (p= .400) and 1 year (p= .860). Median survival at the end of the observation period was 43 months for endo and 56 months for open patients (p = .055). Patients with diabetes treated with open procedures had more complications at 30 days and a higher rate of transfemoral amputations at 1 year compared with non-diabetic patients.These findings support the

continued use of both treatments while stressing the importance of minimizing surgical trauma to reduce wound complications.

Khalid Hamid Changal et al[48] conducted a meta-analysis to determine the use of endovascular treatment for CFA Atherosclerotic disease(ASD) and compare it with common femoral endarterectomy in the present era. For comparison, studies were grouped based on the treatment strategy used for CFA-ASD: endovascular treatment with selective stenting (EVT-SS), endovascular treatment with routine stenting (EVT-RS), or common femoral endarterectomy (CFE).Total limbs involved were 2914 (306 in EVT-RS, 678 in EVT-SS, and 1930 in CFE). The pooled Primary patency(PP) at 1 year was 84% for EVT-RS, 78% for EVT-SS, and 93% for CFE. PP at maximum follow-up in EVT-RS was 83.7% and in CFE group was 88.3%. The pooled target lesion revascularization (TLR) rate at one year was 8% for EVT-RS, 19% for EVT-SS, and 4.5% for CFE. The pooled rate of local complications for EVT-RS was 5%, for EVT-SS was 7%, and CFE was 22%. Mortality at maximum follow-up in CFE group was 23.1% and EVT-RS was 5.3% .Hence study concluded that EVT-RS has comparable one-year PP and TLR as CFE. CFE showed an advantage over EVT-SS for one-year PP. The complication rate is lower in EVT RS and EVT SS compared to CFE. At maximum follow-up, CFE and EVT-RS have similar PP but CFE has a higher mortality. These fndings support EVT-RS as a management alternative for CFA-ASD.

Xiaoyang FU et .al[49] performed a meta-analysis on the available clinical trials to compare infra inguinal angioplasty and bypass surgery approaches in terms of mortality, amputation-free survival, 5-year leg salvage, and freedom from surgical re-intervention. The results of this article will provide evidence based information for clinical treatment of CLI. Method-Randomized clinical trials comparing results between angioplasty and bypass surgery in CLI were identified by searching Pubmed (2000-2014) and EMBASE (2000-2014) using the search terms “angioplasty” or “bypass”, “CLI” and “clinical trials”. Primary outcome subjected to meta-analysis was amputation (of trial leg) free survival in 5 years. Secondary outcomes were 30-day mortality; mortality, re-interventions and leg salvage in 1, 3 and 5 years. Results-Seven clinical trials were selected for meta-analysis. No significant difference was found in the primary outcome-amputation free survival, between angioplasty and bypass surgery groups.This study concluded that ,Angioplasty is non-inferior to bypass surgery in regarding the amputation free survival, re-vasculation, leg amputation and overall mortality. However, angioplasty is safer, simple, and less invasive and less cost procedure. It should be considered as the first choice for feasible CLI patients.

Aims and Objectives of the study : To compare the outcomes between open surgical procedure first and endovascular first revascularisation in infra inguinal disease patients in terms of amputation free survival (AFS), wound healing in critical limb ischemia(CLI).

Primary endpoint :

- To compare the amputation free survival(AFS) and wound healing between two groups.

Secondary end point:

- To compare patency in terms PVR(ABI,TBI) and TCPO2.
- To compare peri-operative outcomes in terms of Major adverse cardiac events (MACE) .
-

Materials and Methods

Study Design: Single center,Prospective,non randomised,double arm,interventional,open ended study

Study Period : June 2018 to January 2020 (20 months)

Recruitment period: june 2018 to july 2019

Follow up :at 1st,3month and 6month.

Study Site: Jain institute of Vascular Sciences(JIVAS) a unit of Bhagwan Mahaveer Jain hospital,Bengaluru.

Study population: During this study period, 304 patients were admitted in JIVAS with critical limb ischemia requiring infrainguinal revascularisation. Among these 104 patients underwent hybrid /second time revascularisation .Hence they were excluded from the study.

Sample size calculation: The sample size is calculated based on data from previous similar studies.

Sample size in each group (assumes equal sized groups)

(typically .84 for 80% power).

$$n = \frac{2\sigma^2 (Z_\beta + Z_{\alpha/2})^2}{}$$

Mean of Group 1: 7.8

Mean of Group 2: 9.3

Mean difference: 1.5

Standard Deviation: 2.2

Type I error (α): 0.05

Power of the test (1-β): 0.80

Confidence Level: 0.95

Sample Size required: 35 (for each group)

Minimum sample size required is 35 per group for an 80% power of the study.

Inclusion Criteria :

- Patients having CLI due to infra inguinal disease.
- Patients having adequate inflow(Common Femoral Artery) for performing infra inguinal intervention(with or without correction).

Exclusion criteria :

- Patients who are not willing to give consent.
- Patients with Aorto-iliac disease.
- Patients undergoing Thrombectomy, hybrid procedures.
- Patients presenting with Acute limb ischemia
- Pregnant ladies and ladies who are planning to concieve.

Methodology:

Patient enrolment:

Demographic data of patients were recorded with history and physical examination findings pre operatively in form of chief complaints, personal history of smoking, tobacco if any and previous revascularisation procedure done in the index limb . They were assessed for known medical risk factors delaying ischemic wound healing like diabetes mellitus (DM), hypertension (HTN), coronary artery disease (CAD) and chronic kidney disease (CKD). In all patients general and local examination were carried out with careful documentation of vascular status of both lower limbs along with non invasive vascular lab measurements including ankle brachial index (ABI), toe brachial index (TBI), pulse volume recording (PVR) and transcutaneous oximetry (TcPO2) - supine and foot down. Preoperative imaging was based on clinical findings and was performed in form of arterial Duplex, CT angiography, MR angiography and MR angiography-Time of flight (TOF) sequence. All patients were classified according to GLASS staging as given in global vascular guidelines. The eGFR of all patients were calculated using the Modification of diet in renal disease (MDRD) formula and based on this value the decision to use CO_2 angiogram during the procedure was taken.

All patients were explained preoperatively regarding pros and cons of the interventions i.e endovascular and surgical procedure ,the final decision to proceed with which procedure was in hands of the operating vascular surgeon in concurrence with patients consent.

2. Laboratory analysis:-

Along with routine blood investigations including hematocrit, coagulation profile, renal function tests, serum electrolytes, urine analysis, chest X ray, 2 D Echocardiogram, ECG, glycosylated hemoglobin (HbA1c) and fasting lipid profile was recorded for all patients after enrolment in study.

3. **Medical management**:-

Patients were started on IV hydration with 0.9% NaCl at 1 ml/kg/hr (0.5ml/kg/hr if ejection fraction was <40%) for 12 hours pre- procedure and for a minimum of 12 hours post-procedure based on the urine output. For all endovascular procedures infusion of 150mEq/L sodium bicarbonate as a bolus of 3 mL/kg/hour for 1 hour before the administration of contrast, followed by 1 mL/kg/hour for 6 hours during and after the procedure.. N-acetyl cysteine of 1200mg twice daily was started one day prior to procedure and continued for two days post procedure. All DM patients who were on oral hypoglycemic agents were switched over to regular insulin and strict glycemic control was ensured peri-operatively. All patients were started on

aspirin 150mg once daily preoperatively and if the patient was already on double antiplatelets (aspirin + clopidogrel or aspirin + ticagrelol), they were continued for endovascular interventions but second antiplatelet was stopped prior for surgical interventions. Post operatively all patients in endovascular group were put on dual antiplatelets (aspirin 150mg and clopidogrel 75mg or preoperative combination continued) once daily for a period of 3 months,surgically treated patients were put on only single antiplatelets post operatively. All patients received Statins (atorvastatin 20mg once daily or higher if dyslipidemic) or additional fibrates (based on fasting lipid profile) for 6 months. Non-steroidal anti-inflammatory drugs (NSAIDs) use was restricted for 2 days prior to the procedure. Medication for diabetes, hypertension, cardiac conditions and medical ailments were continued as per physician's advice. The antibiotics and analgesics were prescribed as per patient and procedure requirements.

4. Endovascular intervention:-

Non-ionic contrast media Iohexol 300mg per ml (Omnipaque®) or CO2 angiogram for indicated patients was used for imaging. Most of the procedures were carried out under local anaesthesia with monitored anaesthesia care (MAC) unless patient opted for general anaesthesia. Ultrasound guided femoropopliteal nerve blocks were used as the anaesthetic modality for CO2 angiograms. Angioset CO2 gas delivery system was used for CO2 angiograms. All cases were done by 3 different consultant vascular surgeons with more than 10 years experience in open vascular and endovascular revascularisation. In all patients undergoing a total endovascular approach to the target site was by an ipsilateral antegrade CFA puncture or a contralateral retrograde CFA puncture. Systemic heparinisation was done at 80U/kg body weight and then 1000units IV for every passing hour. standard wire and catheter techniques were used to cross the lesions and the diseased segments were treated with plain balloon angioplasty, inflated to nominal pressure for a period of two minutes. Check angiogram was done to record the result of a plain balloon angioplasty and to rule out reocclusion, residual stenosis, spasm, dissection, recoil and thrombus.In cases with flow limiting dissection,residual stenosis and recoil, bailout stenting was done for femoropopliteal segment.

Surgical revascularization:

Patients enrolled in surgical group were treated with either Femoral endarterectomy or femoral to distal bypass with vein or synthetic graft.For Femoral Endarterctomy common femoral artery(CFA),Superficial femoral artery(SFA),profunda femoris artery(PFA) was exposed using vertical groin incision and looped. endarterectomy is performed via longitudinal arteriotomy of CFA, with removal of the plaque followed by patch closure (prosthetic or vein) allowing for a degree of scarring to occur without subsequent lumen compromise.For patients planned for bypass

vein was used as conduit for below knee popliteal and tibial vessels ,for above popliteal artery bypass vein/prosthetic graft was used depending on quality and availability of vein.Great saphenous vein is used as conduit and pre operatively vein mapping is done and marked.proximal inflow and distal outflow target vessels are exposed and looped. anatomical tunneling is done accordingly with a tunneler and conduit(vein/prothetic material) is placed in the tunnel and anastamosed in end to side fashion proximally and distally and flow is established,and post operatively patients were kept in recovery room for observation and were kept on only single antiplatelet agent.

Post procedure: pulse/doppler signals status was noted and the PVR, ABI/TBI and TcPO2 noted within 48 hours post procedure.

Perioperative- Any other significant perioperative events in form of morbidity (ACS etc) and mortality were also recorded, complications were identified by review of operative reports, discharge summaries, and physician progress notes.

5. **Secondary procedures**:-

Patients with infected ulcers or gangrene underwent wound debridement and toe amputation before or following angioplasty. Depending upon the type of wound, they were either dressed with hydrocolloids, antiseptic spray or vacuum assisted device were used. In follow up period, unplanned toe amputations and debridement done as necessary for wound healing. All patients were counselled about life style modification, daily foot care and appropriate foot wear.

6. Follow up:-

All enrolled patients had thorough clinical examination and PVR, ABI/TBI, TcPO2 (supine and foot down) surveillance done at 1, 3, and 6 months post procedure. Duplex ultrasound examination was performed if there was a worsening in their symptoms with an increase in one category in the Rutherford scale, decrease in ABI >0.15/TBI>0.1/TcPO2>10 from the maximum post procedural level or clinical worsening of tissue loss. Duplex ultrasound examination was performed in an accredited vascular laboratory by experienced sonologist. Revascularisation was then planned if needed.Unplanned toe amputations and debridement were done as necessary for wound healing.

Statistical analysis:-

The following methods of statistical analysis have been used in this study.

The results were averaged (mean $\pm$ standard deviation) for each continuous variable and number and percentage for discrete variables are presented in Table and Figure.

1. Student "t' test.

The student't' test was used to determine whether there was a statistical difference between groups in the parameters measured.

Student's t test is as follows:

. $t=\frac{\bar{x}_1-\bar{x}_2}{s\sqrt{\frac{1}{n_1}+\frac{1}{n_2}}}$ ~~~ $t_{n1+n2-2}$ Where $s^2=\frac{(n_1-1)s_1^{\ 2}+(n_2-1)s_2^{\ 2}}{(n_1+n_2-2)}$

2) Proportions were compared using Chi-square test of significance

Chi-Square (χ^2) test for (r x c tables)

Rows	Columns			Total
	1	2……..	c	
1	a_1	a_2	a_c	t_1
2	b_1	b_2	b_c	t_2
.	.	……	.	.
.	.	……..	.	.
r	h_1	h_2	h_c	t_r
Total	n_1	n_2	n_c	N

a,b…..h are the observed numbers.

N is the Grand Total

$$\chi^2 = N\left[\frac{1}{t_1}\sum_1^c\frac{a_1^2}{n_i}+\frac{1}{t_2}\sum_1^c\frac{b_1^2}{n_i}+\ldots\ldots\ldots\ldots+\frac{1}{t_r}\sum_1^c\frac{h_1^2}{n_i}-1\right]$$

DF=(r-1)*(c-1), where r=rows and c=columns

DF= Degrees of Freedom (Number of observation that are free to vary after certain Restriction have been placed on the data)

3**. Log Rank Test:**

The Log-rank test used to compare the difference in amputed free survival in the open surgery versus endovascular groups. The graph shows KM plots for the data broken out by group.

The null hypothesis for a log-rank test is that the groups have the same survival. The expected number of subjects surviving at each time point in each is adjusted for the number of subjects at risk in the groups at each event time. The log-rank test determines if the observed number of events in each group is significantly different from the expected number. The formal test is based on a chi-squared statistic. When the log-rank statistic is large, it is evidence for a difference in the survival times between the groups.

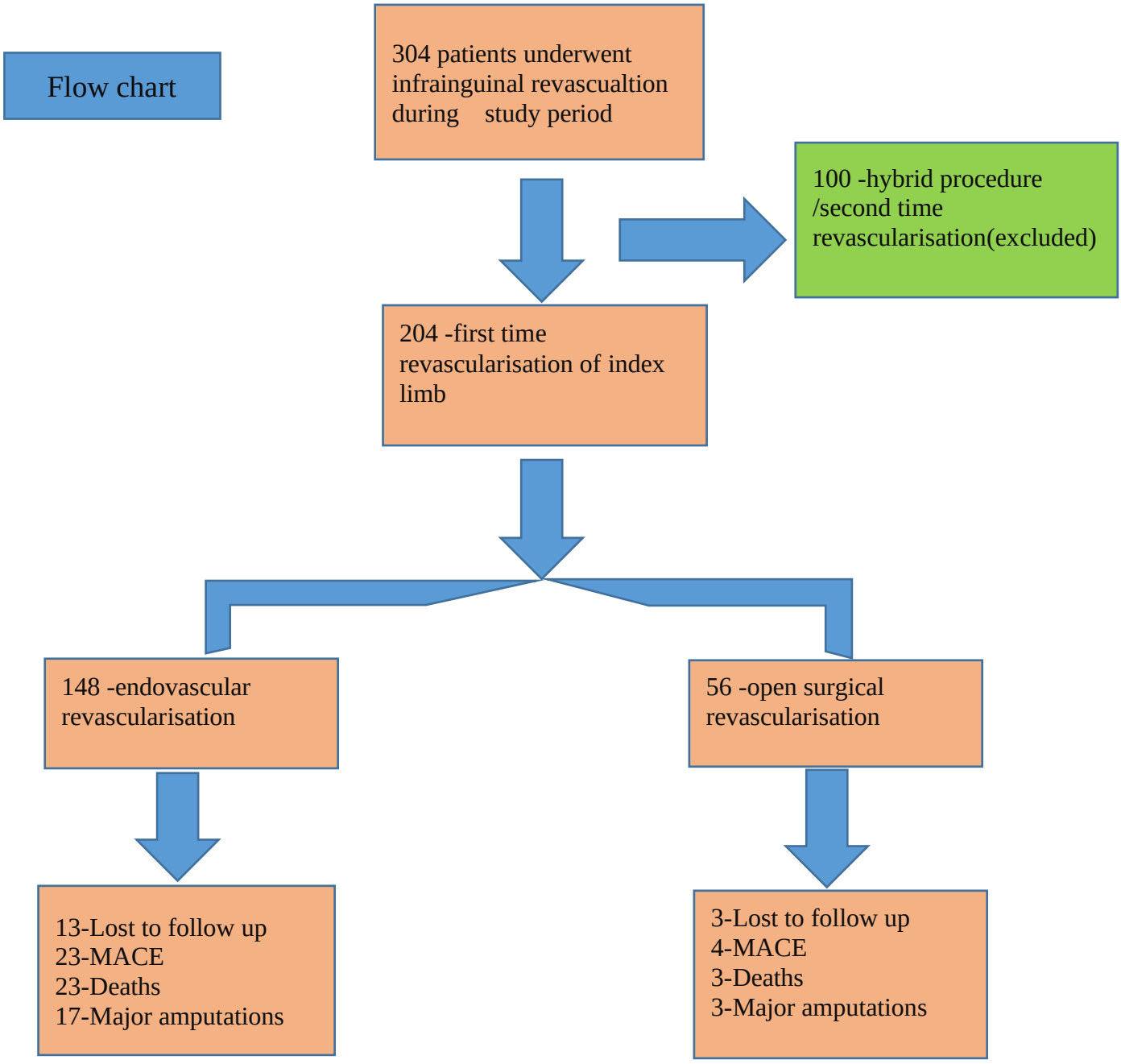
The hazard ratio can be interpreted as the chance of an event occurring in the open surgery divided by the chance of the event occurring in the endovascular group, or vice versa.

In all above test P value less than 0.05 was taken to be statistically significant. The data was analyzed using SPSS package.

8. Ethical and Scientific committee:-

Present study is approved by ethics and scientific committee of Bhagwan Mahaveer Jain Hospital, Bengaluru.

Results



In a period of 14 months (June 1, 2018 to July 31, 2019), 304 patients were admitted in JIVAS with critical limb ischemia requiring infrainguinal revascularisation. Among these, 100 patients include hybrid revascularisation and 2nd time intervention . Hence they were excluded from the study. The rest 204 patients underwent primary infra inguinal revascularisation in the form of open surgical or endovascular intervention with or without inflow correction in the form of open surgical revascularisation or endovascular intervention or hybrid techniques. 148 patients under endovascular intervention and 56 patients underwent open surgical intervention. In the

endovascular group 132 for 1stmonth, 122 for 3rd month and 113 for 6th month and in the open surgical group 54 for 1st month,50 for 3nd and 47for 6th month patients were available for final analysis .At the end of 6 months only 13 patients and 3 patient were lost to follow up in the endovascular and open surgical groups respectively.

Procedures

Open surgical procedure(n=56)	**Endovascular procedure(n=148)**
Bypass with autologous vein (n=34) FEM-ATA BYPASS=8 FEM-PTA BYPASS=12 FEM-POP BYPASS=10 P1-P3 BYPASS=2 P1-ATABYPASS=1 P1-TPT BYPASS=1	Femoral+Popliteal angioplasty(FP)(n=20)
Bypass with prosthetic graft(n=19)	Infrapopliteal segment angioplasty (IP)(n=65)
CFA Endarterctomy+Fem-pop Bypass with graft(n=3)	Both FP+IP (n=63)
	Bare metal stents(n=25)
	Drug Coated Balloon(DCB)(n=2)
	Under Co2 angiogram(n=22)

In open surgical revascularisation bypass with autologous vein(n=34) were done in majority of the people,majority of the vein bypass was done to the tibial vessels and below knee popliteal artery,and great saphenous vein was used as vein conduit for all the patients .bypass with prosthetic graft (Dacron/ePTFE)was done mainly to above knee popliteal artery .In very few patients CFA endarterectomy was done along with bypass procedure .

In endovascular group isolated Femoral and popliteal segment angioplasty was done in 20 patients and only Infrapopliteal segment angioplasty was done in 65 patients ,both segments were angioplasty was done in 63 patients.Bail out stenting for femoro popliteal segment was done with Bare metal stent in 25patients.Drug coated balloon was used in 2patients and Co2 was used as contrast medium for angioplasty for 22 patients .

Age and sex

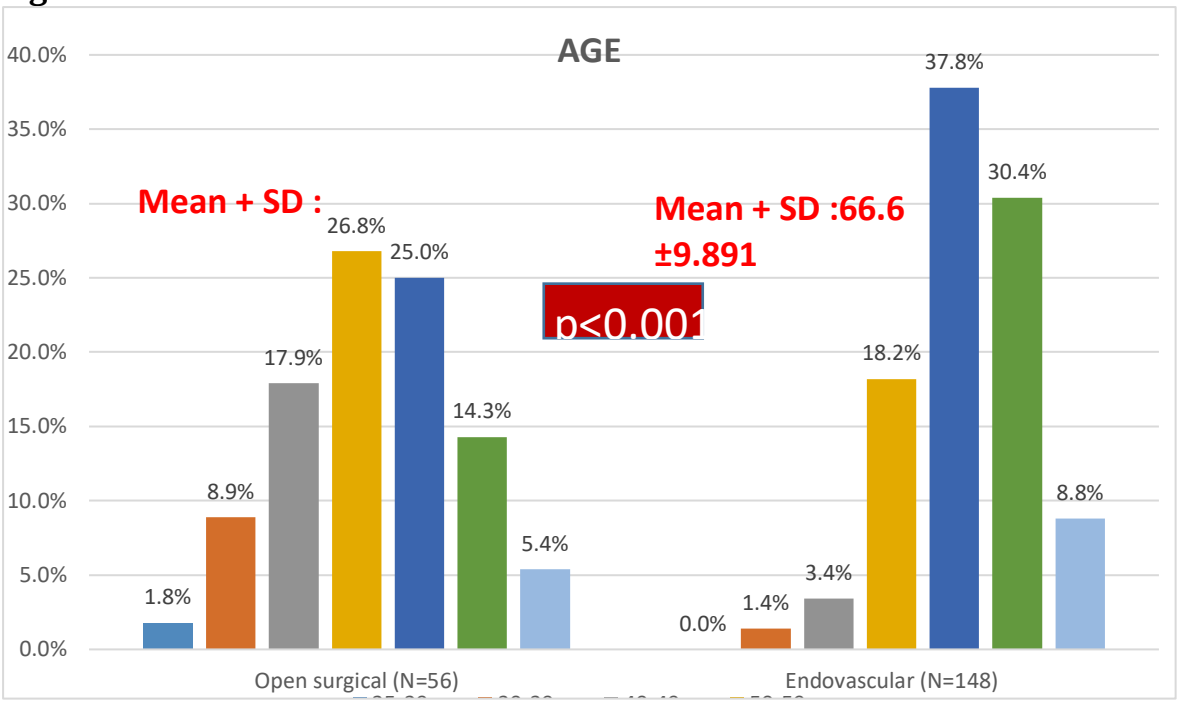


Figure 1: Age distribution

The mean age in the endovascular group was 66.6±9.8 yrs and open surgical group was 57.1±13.17 yrs

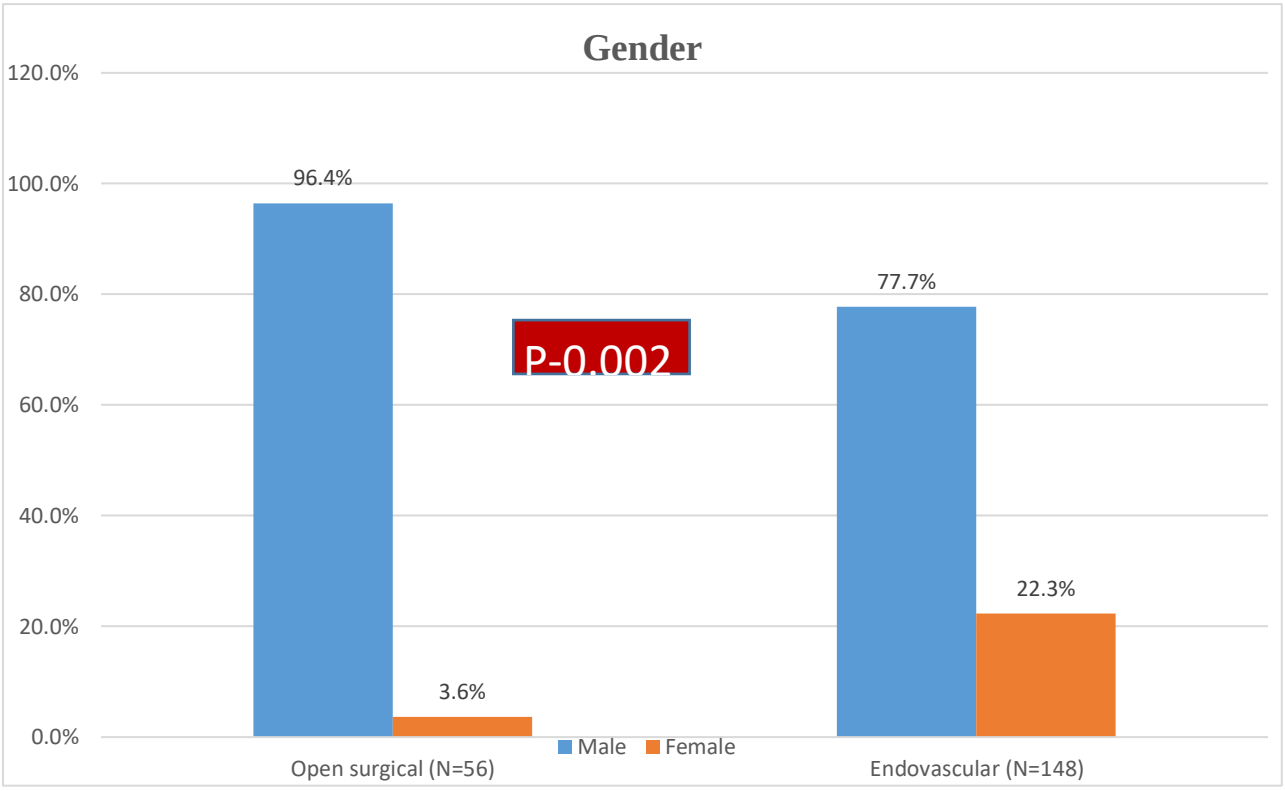


Figure :2 Gender distribution

In both groups the predominant gender was male, 115 of 148 (77.7%) in endovascular and 54 of 56 (96.4%) in open surgical group

Co-morbidities

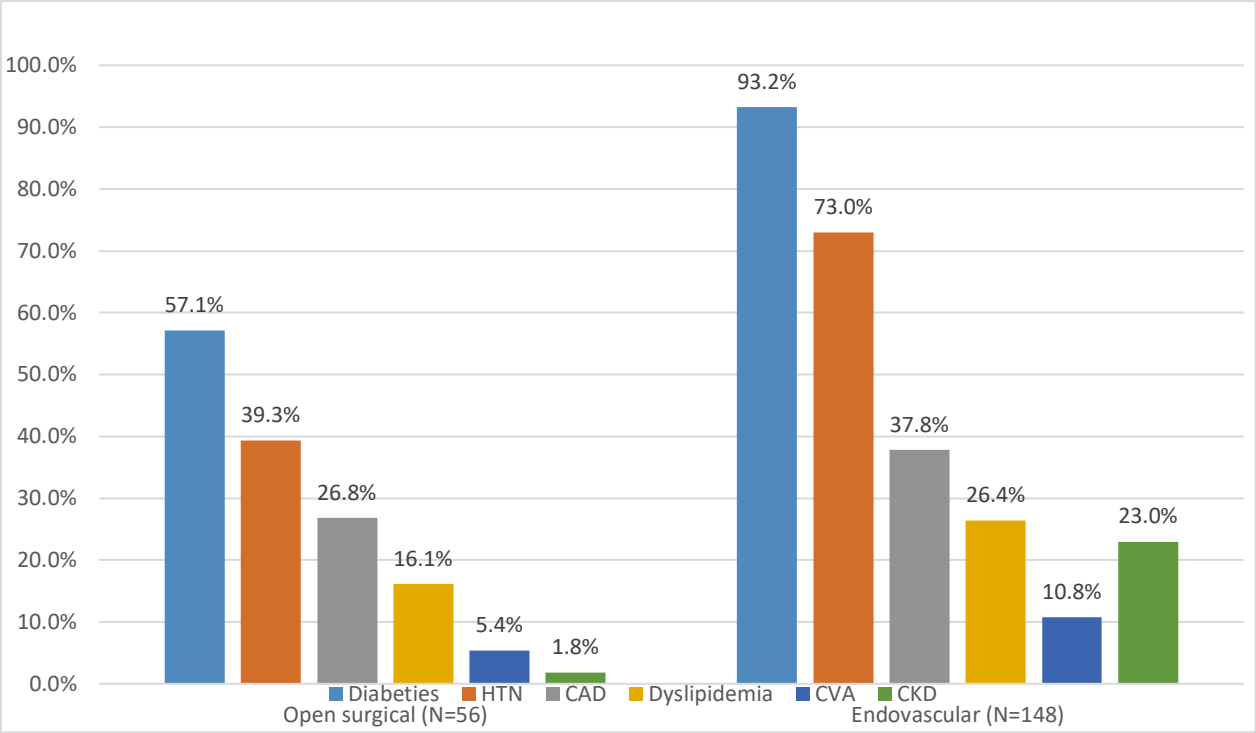


Figure :3 Co-morbidities

On analyzing the pattern of co-morbidities, both groups are not equally matched. Diabetes mellitus was the major co-morbidity in both groups followed by systemic hypertension and ischemic heart disease. Diabetics made up 93% (138/148) in Endovascular group and 57% (35/36) in Open surgical group and the difference is significant with(p value- <0.001).Systemic hypertension was present in 73% (108/148) in Endovascular group and 39% (22/56) in Open surgical group of the patients respectively with significant p value- <0.001. Ischemic heart disease (medically treated or percutaneous coronary stenting done or coronary artery bypass grafting done) was present in37 % (56/148) in Endovascular group and 27.8%(15/56) in Open surgical group of the patients and the difference is not significant (p value- 0.13). History of cerebrovascular disease (ischemic or haemorrhagic stoke) was present in 10.8%(16/148) in endovascular group and 5.4%(3/56) in open surgical group and difference is not significant (p-0.232).Chronic kidney disease was present in 23%% (34/148) in Endovascular group and 1.8% (1 of 56) in Open surgical group of the patients and the difference is significant (p value-0.001). Dyslipidemia was present in 26.4%(39/ 148) in Endovascular group and 16.1% (9/56) Open surgical group of the patients with no significant difference (p value-0.122).

Tobacco use

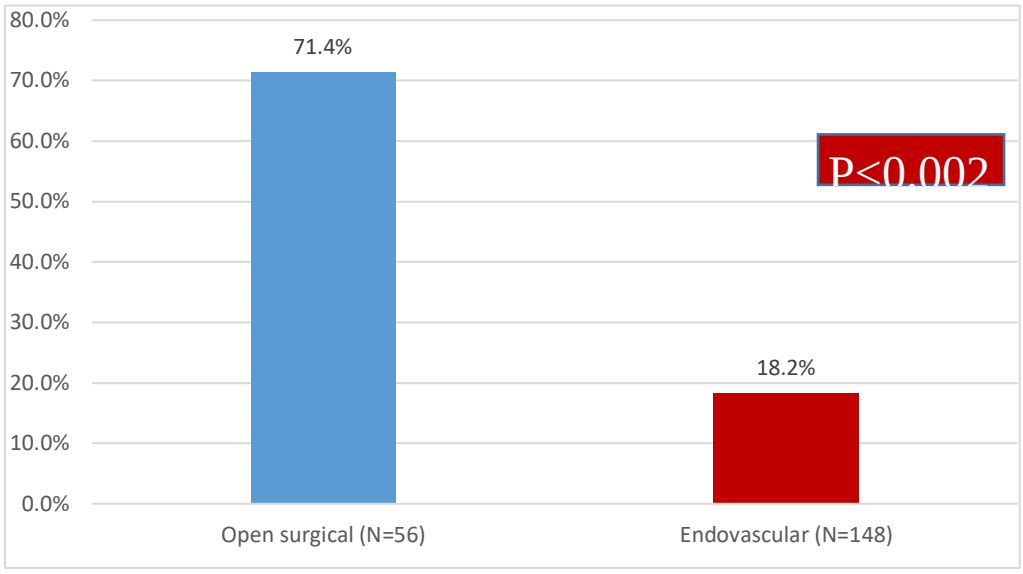


Figure :4 Tobacco use

The use of tobacco was present in 71.4% (40/56) in the open surgical group and 18.2% (27/148) in the Endovasculargroup (p value- 0.001).

WIFI clinical stage

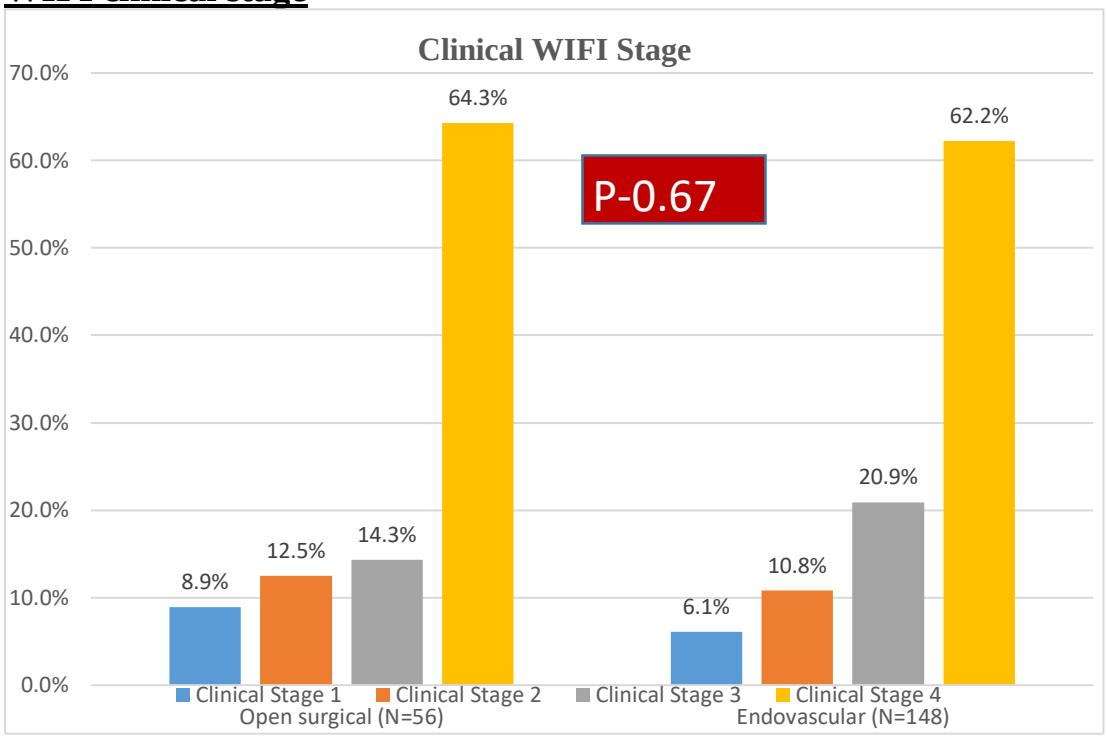
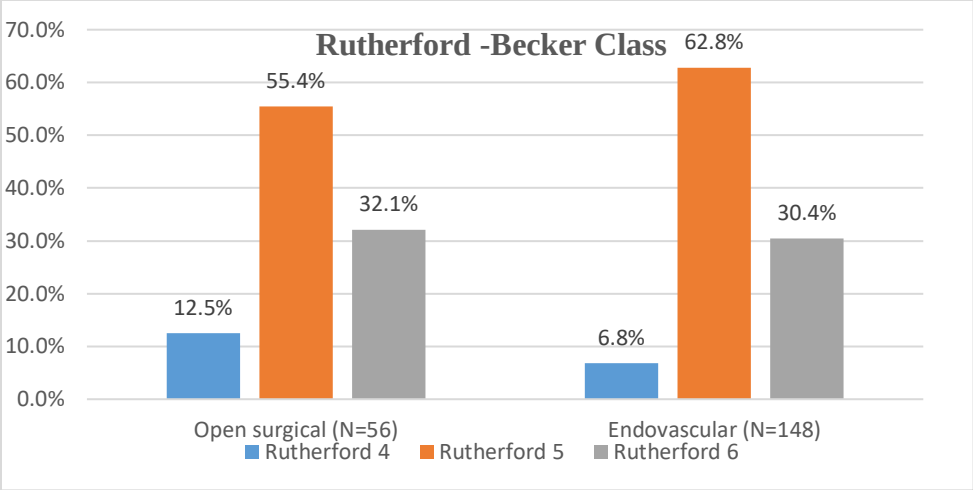


Figure :5 WIFI staging

On categorising patients in both groups into their respective WIfI stages, the distribution is similar (p value- 0.670). Most patients are in Stage 4 which indicates the worst combination of wound, ischemia and foot infection requiring definitive revascularisation and also indicating that higher chance of major amputation is present. endovascular group had 62.2% (92/148) and open surgical group had 64.3%% (36/56) patients in the WIfI stage 4.

Rutherford - Becker class



P-0.36

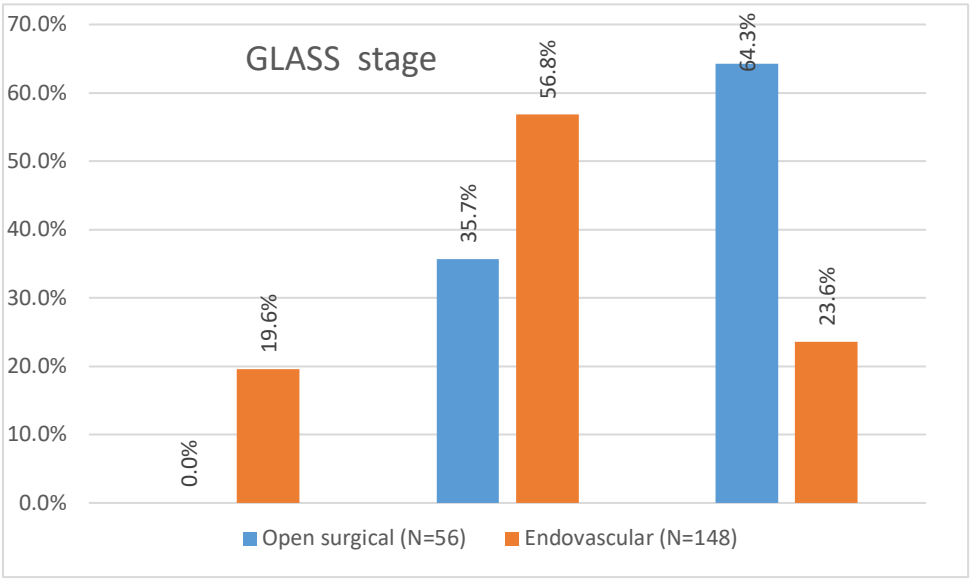
Figure -6 Rutherford Becker class

All patients in the study suffered from critical limb ischemia. Most patients were in Rutherford Becker category 5- 93 patients (62.8%) in the endovascular group and 31(55.4%) in the open surgical group.Rutherford Becker category 6-45patients(30.4%)in endovascular group and 18 patients (32%)in open surgical group.Rutherford- category 4-10 patients(6.8%) in endovascular group and 7patients(12.5%)in open surgical group. There was equal distribution of class of critical ischemia in both groups (p value- 0.364).

GLASS staging

FP Grade	0	1	1.8%	66	44.6%	***<0.001***
	1	0	0.0%	9	6.1%	
	2	0	0.0%	26	17.6%	
	3	21	37.5%	34	23.0%	
	4	34	60.7%	13	8.8%	
TP Grade	0	35	62.5%	19	12.8%	***<0.001***
	1	3	5.4%	7	4.7%	
	2	16	28.6%	57	38.5%	
	3	2	3.6%	49	33.1%	
	4	0	0.0%	16	10.8%	

Table no :1



P<0.001

Figure -7 GLASS stage

On categorising patients in both groups into their respective GLASS stages, the distribution is not similar and difference is significant (p value- <0.001). Most patients are in Stage 2 in endovascular group 84 patients(56.8%) and 20 patients(35.7%).Most patients are in stage3 in open surgical group 36patients(64.3%) and 35patients(23.6%) in endovascular group and no patients in stage 1 in open surgical group while 29 patients (19.6%) in endovascular group.

Amputation Free survival (AFS)

kaplan meier survival curve analysis

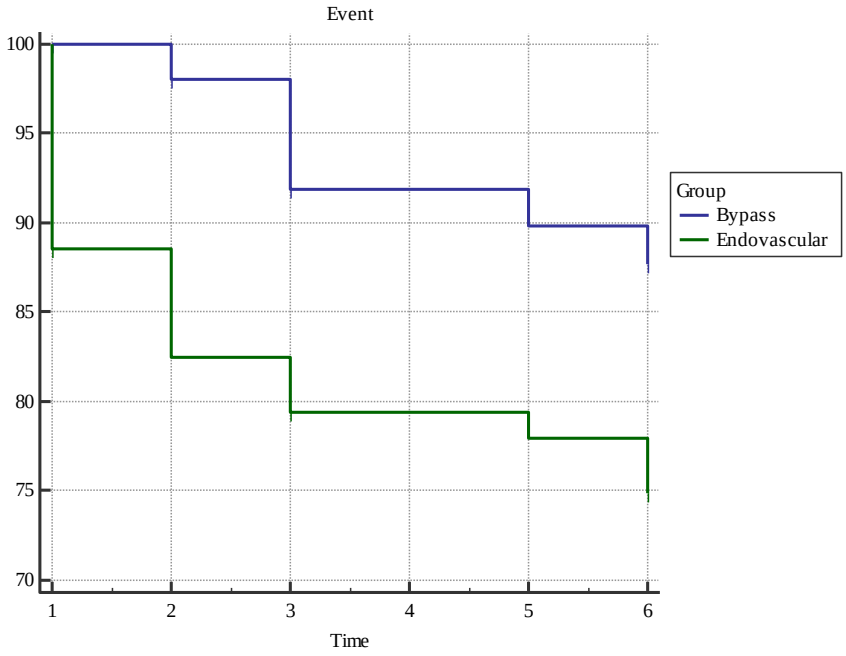


Figure -8 AFS curve

Comparison of survival curves (Logrank test)

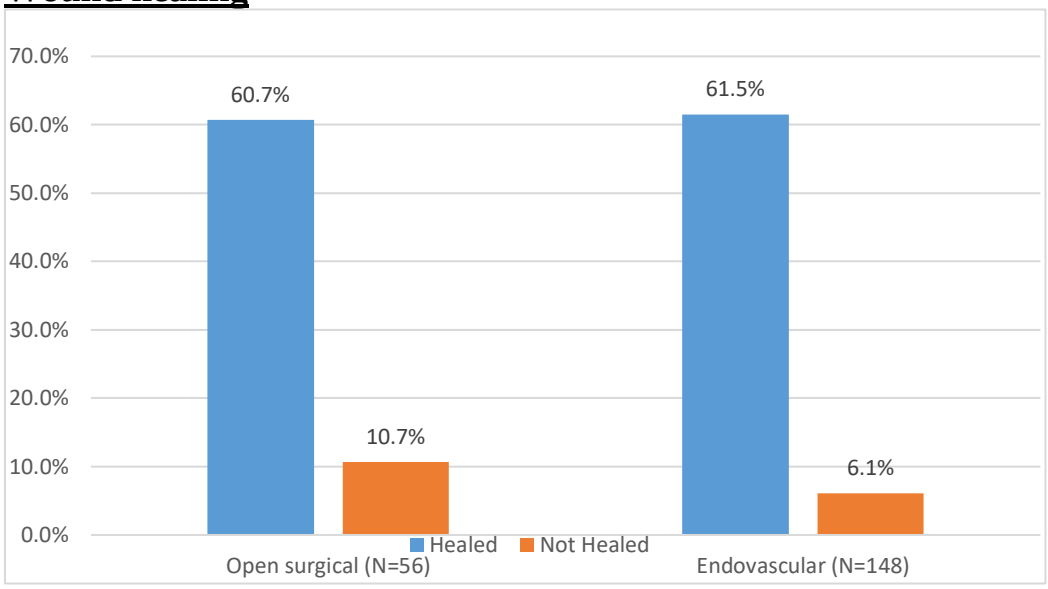
Chi-squared	4.3287
DF	1
Significance	***P = 0.0375***

Hazard ratios[a] with 95% Confidence Interval

Factor	Bypass	Endovascular
Open surgical group	-	2.3787 1.2113 to 4.6710
Endovascular	0.4204 0.2141 to 0.8255	-

Amputation Free survival rate in open surgical group is 88% and endovascular group is 75% logrank test is performed between two groups and is significant (p value -0.0375)

Wound healing

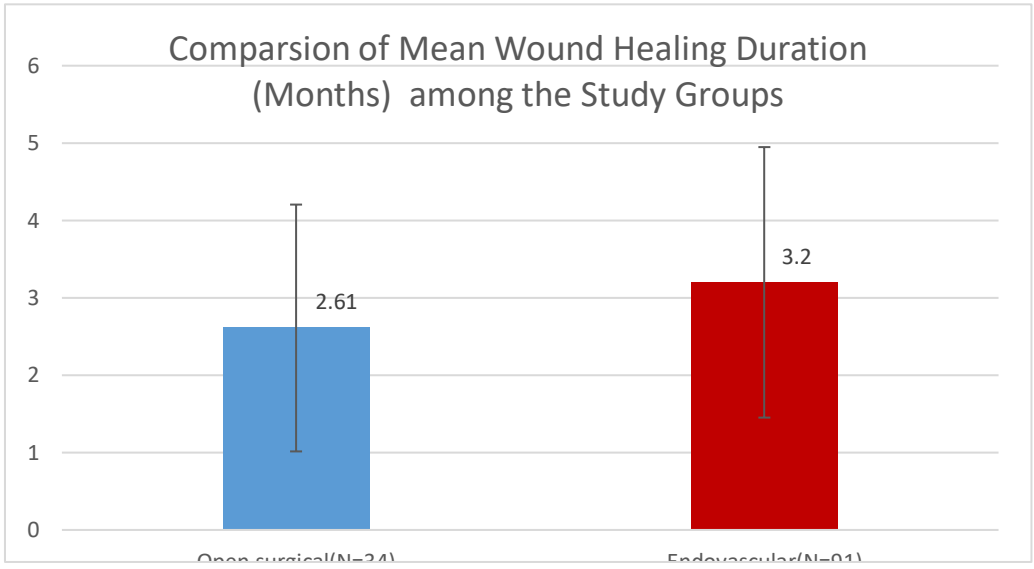


P-0.065

Figure-9 Wound healing status

At the end of 6 months, 10.7% (6/56) and 6.1% (9/148) of the patients in the Open surgical and endovascular group respectively did not have their wound healed. The rest of the patients had healed their wound completely (p value- 0.065).

Wound healing duration



P-0.69

Figure -9 wound healing duration

The mean duration for wound healing in the endovascular group was 3.20±1.74 months and in the open surgical group 2.61±1.59 (p value- 0.065).

Patency

Primary patency in follow up was based on whether the ABI or TBI or TcPO2 was maintained or improved when compared to the post operative measurements. All patients underwent the three measurements in follow up. There is no significance Between two groups.

ABI

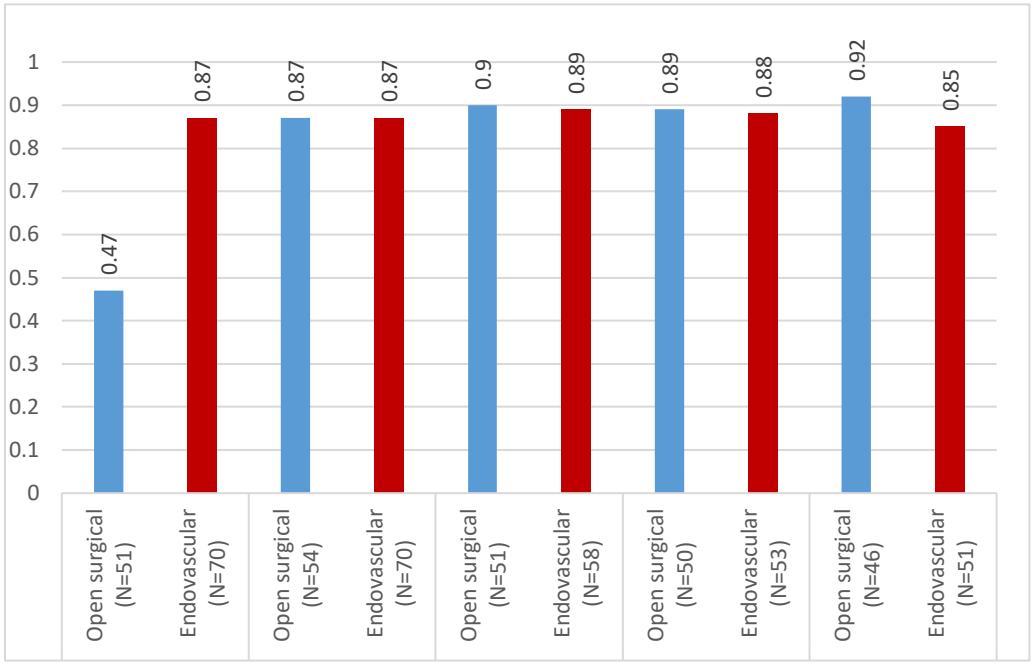


Figure -10 comparision of mean ABI values

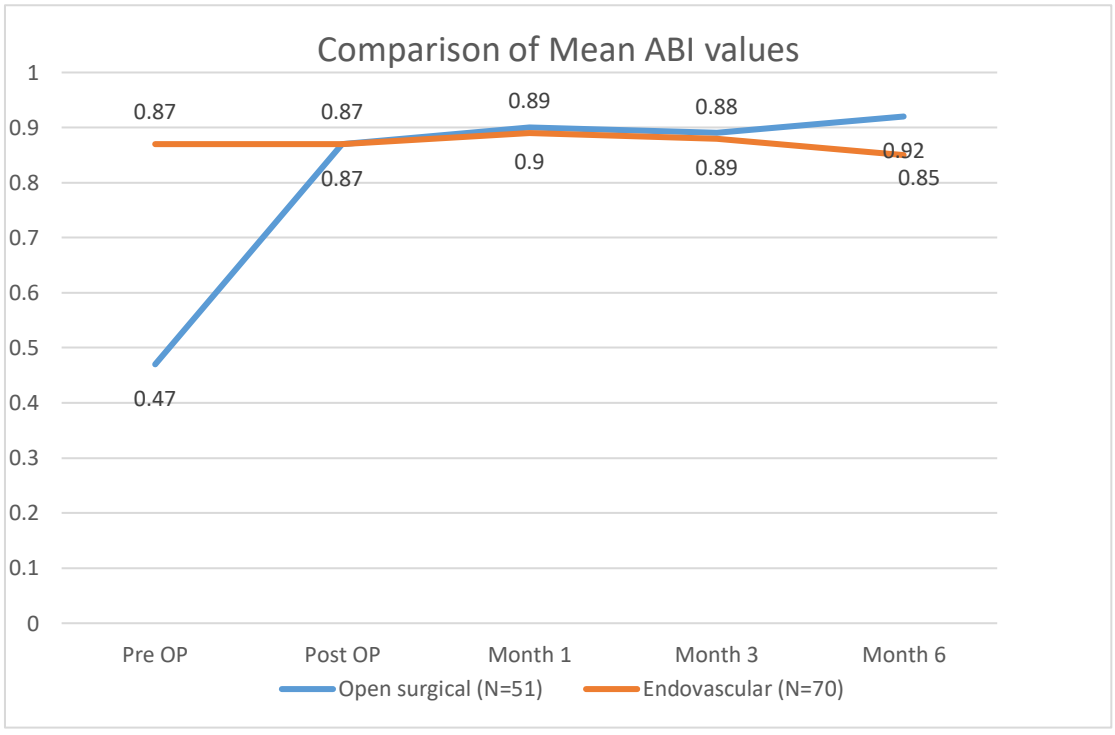


Figure-11 graph showing ABI Trend

In the entire period of follow up there was no difference in the ABI levels between the Endovascular group and open surgical group. ABI was not available when then patient had non compressible vessels (N/C). ABI was available only for 58,53 and 51 patients available for analysis at the 1st,3rd and 6th month follow up in the endovascular group. Similarly in the open surgical group, ABI was available only for 51, 50 and 46 patients at 1st, 3rd and 6th months respectively. There was no statistical differenece in the mean ABI values between both groups in every follow up and P value >0.05

TBI

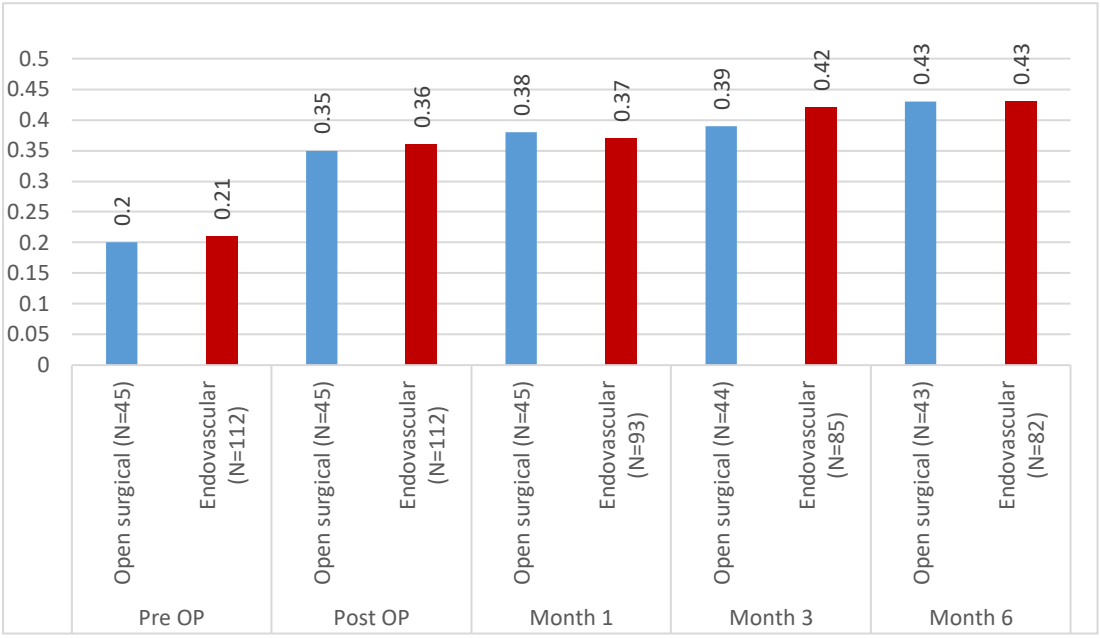


Figure -12 comparision of mean TBI values

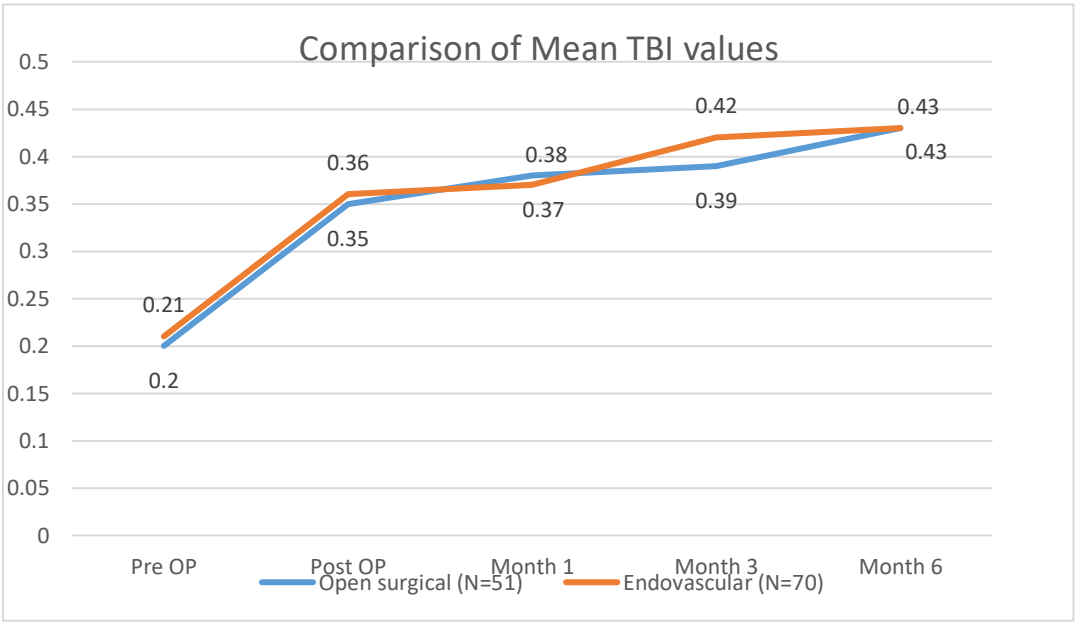


Figure -13 Graph showing TBI Trend in Follow up

In the entire period of follow up there was no significant difference in the TBI levels between the Endovascular and Open surgical groups. TBI was not available when the patient had the 1st or 2nd toes were amputated. TBI was available for only 93, 85 and 82 patients available for analysis in the Endovascular group at the 1st, 3rd and 6th month . In the open surgical group it was available for 45,44 and 43 patients at the 1st, 3rd and 6th month respectively.TBI was maintained in 90% in open surgical group and 74% in Endovascular group at the end of 6months but there is no statistical significance in mean values between the two groups in all the months of follow up.

Foot perfusion based on Tcpo2 values

TcPO2-Down

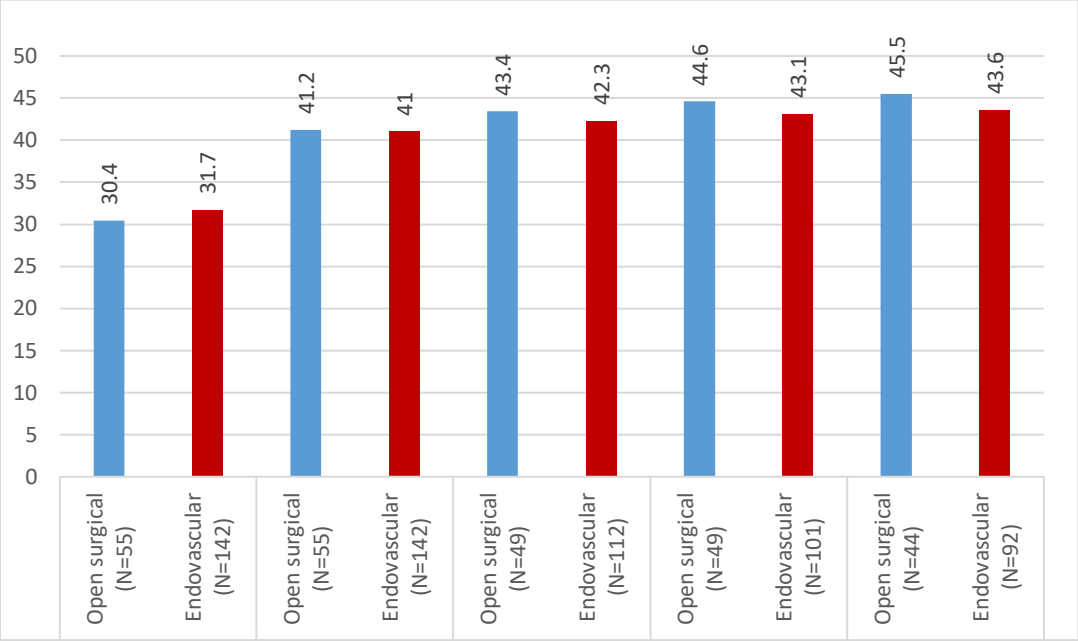


Figure -14 comparision of mean TcPO2 values in Down position

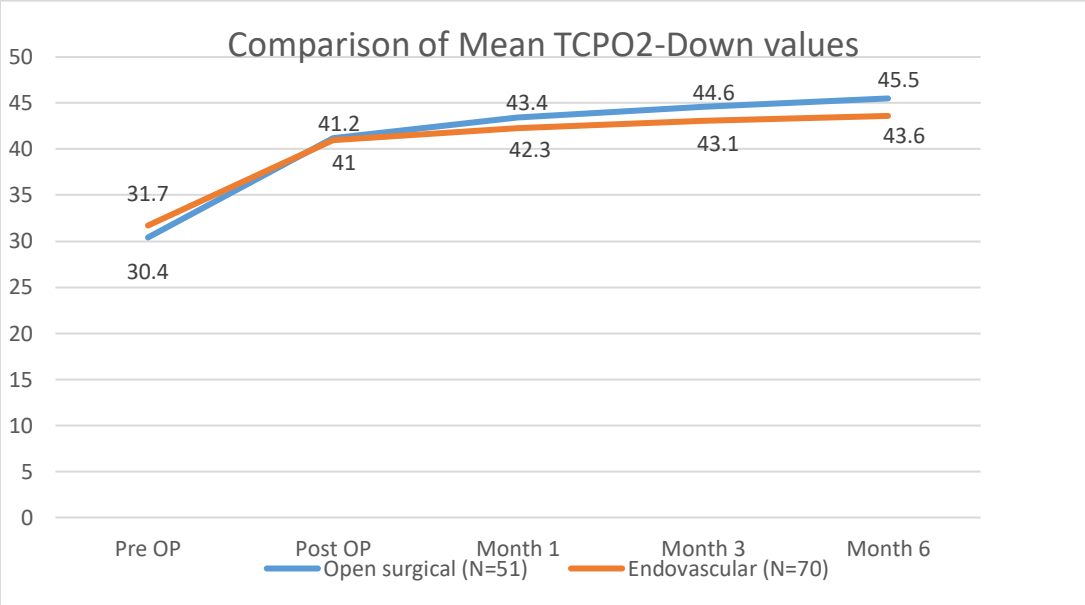


Figure-15 Graph showing TcPO2 trend

TCPO2-Supine

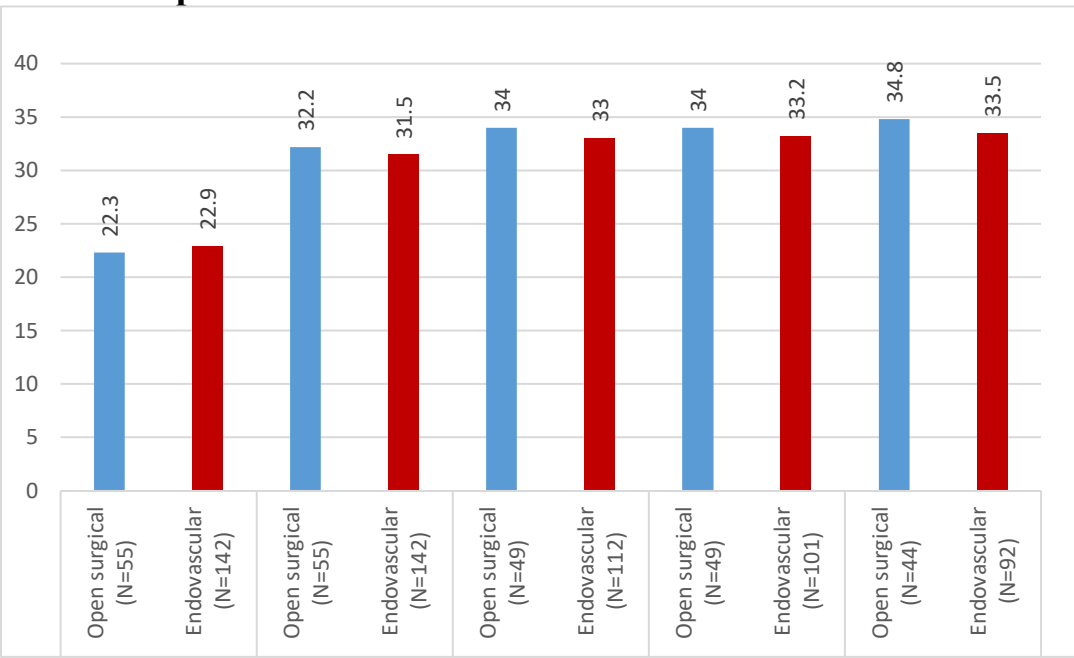


Figure -16 comparision of mean TcPO2 values

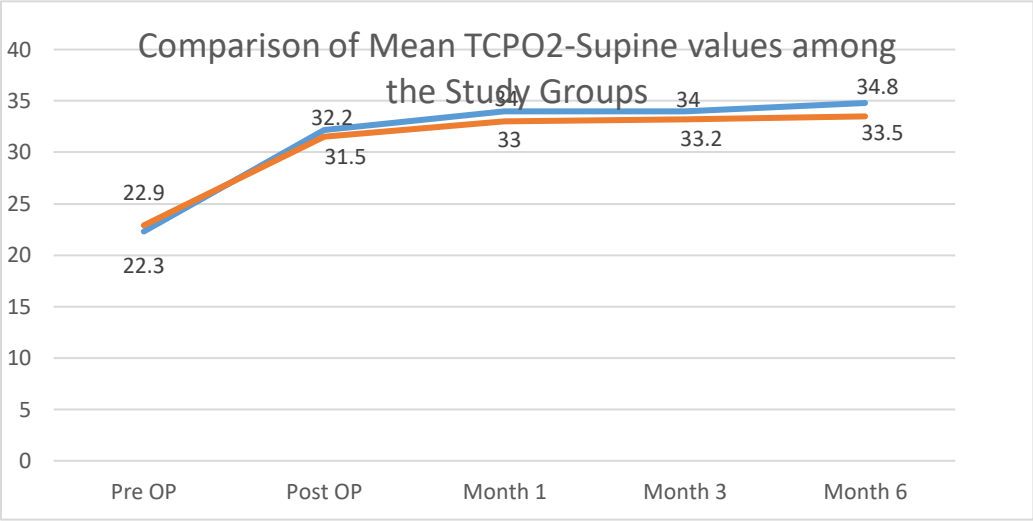
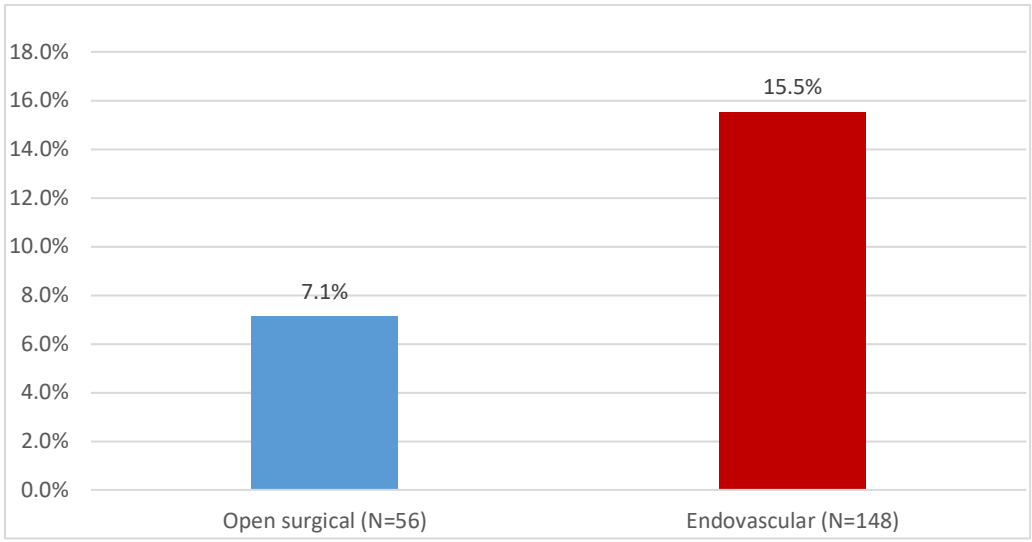


Figure -17 Graph showing TcPO2 trend in supine position

TcPO2 was measured in the supine and in the dependent foot down provocative position. Only for a few patients in both groups, TcPO2 was not available in follow up. Maintenance of foot perfusion by measurement of TcPO2, if taken as a surrogate for primary patency, reveals that there is no significant difference in both the groups at all steps of follow up. Foot perfusion was maintained in 112of 142 patients in 1st month (78.8%), 101 of 112 patients in 3rd month (90%) and 92 of 101 patients in 6th month (90%) in the endovascular group.. In the open surgical group, foot perfusion was maintained in 49 of 55(89%) patients in the 1st month (90%), 46 of 51 patients in the 3rd month (89%) 44 of 49 in 6th months in the open surgical group.

MACE

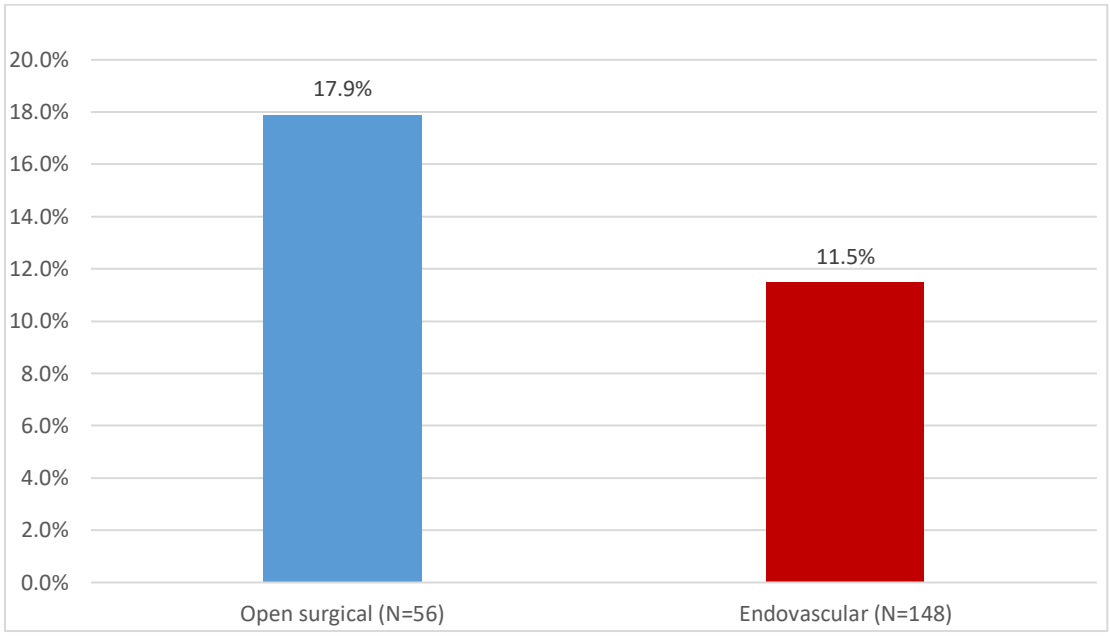


P-0.114

Figure-18 Comparision of MACE

Major adverse cardiac event (MACE) occurred in 15.5% (23 of 148) and 7.1% (4 of 56) of the patients in the endovascular and open surgical groups respectively. The is no significant difference in MACE between two groups (p value- 0.114).

MALE

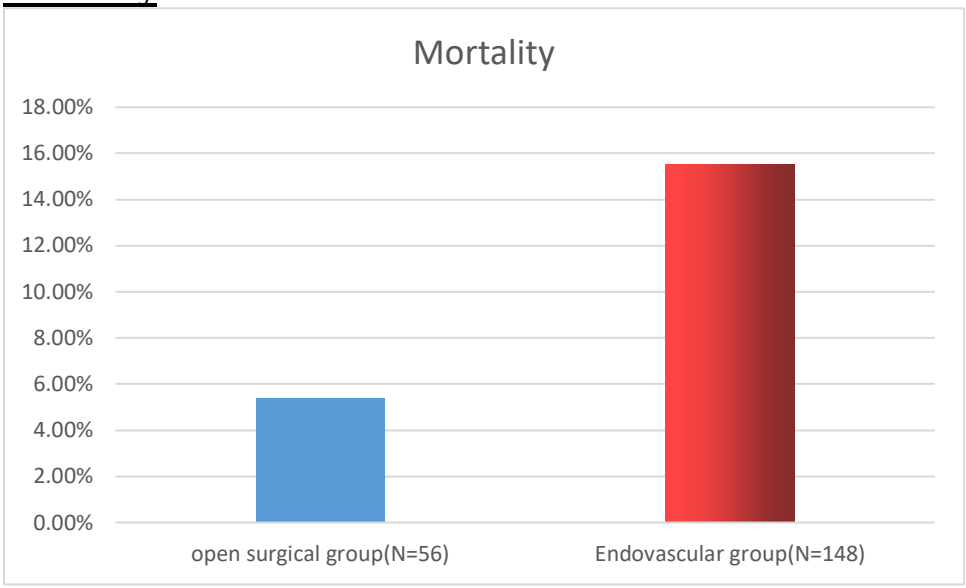


P-0.231

Figure-19 comparision of MALE

Major adverse Limb event (MALE) occurred in 11.5% (17 of 148) and 17.9% (10 of 56) of the patients in the endovascular and open surgical groups respectively. There is no significant difference in MALE between two groups (p value- 0.231).

Mortality



P-0.069

Figure-20 Comparision of Mortality

Overall mortality in open surgical group is 5.4% (3/56) and 15.5% (23/148) in endovascular group .There is no significant difference in both groups (p value -0.069).

Discussion:

In this prospective study we have compared the endovascular revascularisation first Versus open surgical revascularisation first for infra inguinal disease patients. We have analysed the various pre-operative and demographic factors in both . The clinical outcomes like wound healing, Amputation Free Survival, cardiac events (MACE) and Primary Patency which actually matter for the patient were also analysed.

The mean age of patients in the endovascular groupis 66years and the open surgical group is 58years which are comparable to patient groups in previously published randomised trials where the mean age range was from 67 years to 73 years.patients in endovascular group are older than opensurgical group. The proportion of males in our study was 96.4% in open surgical group and 77.7% in endovascular group which is comparable with Bisdas et al[51].proportion of males is higher in both the groups.

Diabetics made up major comorbidity in both the groups which is similar to the study by Bisdas et al[51],Dosluoglu et al[43]and BASIL trial[7].on comparing Diabetis between two groups diabetics are more in endovascular group(93%) than open surgical group(57%). Systemic hypertension(HTN) was present in 73% in Endovascular group and 39.3% in Open surgical group of the patients and there is significant difference between two groups, which is different from other previous studies .In previous studies like Hicks et al[44] ,BASIC trial[36]and Spillerova et al[50] hypertension was the major comorbidity compared to diabetis in both the groups which differs from the present study.

The prevalence of coronary artery disease in our study was 37.8% and 26.8% in the Endovascular group and open surgical groups ,which are comparable with previous studies like Bisdas et al[51] ,Hicks et.al[44], F.Gentile et al[47], and Dosluoglu et.al[43]. Previous cerebrovascular disease was present in 10.8% in Endovascular group and 5.4% in open surgical groups respectively and there is no significant difference,which is comparable with previous studies .

Chronic kidney disease was present in 23% in Endovascular and 1.8%Open surgical groups which is significant differnce between two groups , which differs from the previous studies like Dosluoglu et.al[43],BASIL trial[7] and Spillerova et al[50] and this is fairly low when compared.

Dyslipidemia was present in 26% in the Endovascular group and 16% of the Open surgical group which was not statistically significant of the present study, which similar and

comparable with previous studies like BASIC trial[36], Dosluoglu et.al[43]. Reported range of dyslipidemic patients varies from low values like 32.6% upto 76.9% .

In this study the use of Tobacco was present in 18% in the Endovascular group and 71%in the Open surgical group with a p value-<0.002 implying that two groups are not matched and is significant, open surgical group has more number patients with tobacco usage. This is comparable with previous studies like Dosluoglu et al[43] , in which there is significant difference between two groups and is similar to the present study.The present study included current active smokers with the duration of smoking not taken into consideration. In some previous studies like F.Gentile et.al[47] and Hicks et al[44] they have included both current and ex - smokers which differs from present study.

The level of chronic ischemia was stratified by the Rutherford-Becker class with class 4, 5 and 6 termed as critical ischemia in view of rest pain and tissue loss. Many studies have proven that as the Rutherford class increases the limb salvage decreases, multilevel disease is more, patient is highly morbid, likelihood of cardiovascular events are more and that mortality rates are higher. All patients in our study suffered from critical limb ischemia. Most patients were in Rutherford Becker category 5- 62.8% in the Endovascular group and 55.4% in the Open surgical group. 30.4% patients in Endovascular group and 32% in Open surgical group under category -6.only 6.8% in endovascular group and 12.5% in Open surgical group under rutherford category-4. There was equal distribution of class of critical ischemia in both groups (p value- 0.36). Rutherford 5 was the predominant category in Bisdas et .al[51]which is similar and comparable with the present study.Many studies like Dosluoglu et.al [43],Hicks et.al[44] ,Spillerova et.al [50] patients were not categorised in Rutherford class but all patients in these studies were having critical limb ischemia.previous studies like Vander Zaag et.al[36] , Siracuse et.al[42] were conducted on patients with intermitent claudication.

Perfusion is only one determinant of outcome, Wound extent withpresence and severity of infection also greatly impact the threat to a limb. The Society for Vascular Surgery Lower Extremity Guidelines Committee undertook the task of creating a new classification of the threatened lowerextremity that reflects these important considerations. Risk stratification is based on three major factors that impact amputation risk and clinical management: **Wound, Ischemia, and foot Infection (WIfI)** [52]. To our knowledge the WIfI classification system by Mills et al [52]has not been used for any of the published Endovascular group vs Open surgical studies. The present study has stratified patients in both groups into their respective WIfI stages. Most patients are in Stage 4 which indicates the worst combination of wound, ischemia and foot infection requiring definitive revascularisation and also indicating that higher chance of major amputation is present. Endovascular group had 62.2% and the Open surgical group had

63.4% patients in the WIfI stage 4. The distribution of patients in both groups was similar (p value- 0.67) implying equally matched groups. However the outcomes based on the WIfI stage has not been analysed in the present study.

Global Limb Anatomic Staging System (GLASS),A new anatomic scheme for the threatened limb is proposed. Commonly used anatomic classification schemes for PAD are lesion or segment focused[53] or aim to quantify the overall burden of disease[54,] rather than integrating the complex patterns of disease found in most patients with CLTI.GLASS incorporates two novel and important concepts, the target arterial path (TAP) and estimated limb-based patency (LBP).

Based on appropriate angiographic imaging, the TAP is defined by the treating surgeon or interventionalist as the optimal arterial pathway to restore in-line (pulsatile) flow to the ankle and foot. It may incorporate either the least diseased or an angiosome-preferred path, as chosen by the treating clinician.

LBP is defined as maintenance of in-line flow throughout the TAP, from groin to ankle. LBP allows more direct comparison of anatomic outcomes across revascularization strategies in CLTI. The complexity of disease traversed by the TAP is integrated in the GLASS. Femoropopliteal (FP) and infrapopliteal (IP) arterial segments are individually graded on a scale of 0 to 4. Using a consensusbased matrix, these segmental grades are combined into three overall GLASS (I-III) stages for the limb.To our knowledge till now no study has included GLASS staging. GLASS stages I to III correlate with low-, intermediate-, or highcomplexity infrainguinal disease patterns, with expected correlation to immediate technical success and 1-year LBP for endovascular intervention.

On categorising patients in both groups into their respective GLASS stages, the distribution is not similar and difference is significant (p value- <0.001). Most of the patients are in Stage 2 in endovascular group 84 patients(56.8%) compared to 20 patients(35.7%)in open surgical group.Most patients are in stage3 in open surgical group 36patients(64.3%) compared to 35patients(23.6%) in endovascular group. and no patients in stage 1 in open surgical group while 29 patients (19.6%) in endovascular group.

Our single-center experience of CLI patients with multiple comorbidities and unfavorable anatomy showed that the 6months outcomes are acceptable as a whole, in both endovascular and open surgical groups.

An aggressive use of endovascular interventions in the sicker patients, even in those with unfavorable complex anatomy or unavailable autologous vein for bypass, enabled the more disadvantaged subgroups to have revascularization, rather than a bypass using

nonautologous grafts, or primary amputation, though with poor overall survival. Patients with multilevel disease, long occlusions with a good distal target, good-quality autologous vein, and reasonable medical condition had a good result in six months in terms of early wound healing,patency.Because there is always a strong selection bias for the type of revascularization, which changes not only from center to center but also over time with increased experience, adoption of newer techniques and approaches, it is impossible to make meaningful comparisons between treatment modalities, even when the groups are matched using propensity score analysis.

The BASIL trial[7] favored the bypass group for survival and AFS in those who survived at least 2 years, and angioplasty-first was appropriate for those with a shorter life expectancy. Because randomization for BASIL required suitability for both types of revascularization, patients with similar anatomy presenting with CLI in our study, and other studies like Dosluoglu et.al[43],Bisdas et al[51], most probably were treated with endovascular therapy, and therefore, the patients who actually had bypasses likely represent a very different group of patients. Therefore, the issue with the BASIL trial is not only its nongeneralizability but also that its results in the angioplasty or the bypass arms cannot be compared with our study and modern series. Despite this overall mortality is similar and comparable with BASIL trail.

There have been number of single-center reports of CLI patients[55,56,57] with open or endovascular interventions , however, some of these studies had only femoropopliteal interventions, whereas others included all levels, suggesting that the patient selection and referral patterns vary, thus attempting to make meaningful comparisons between studies and subgroups diffificult.

Soderstrom et al[45] compared only infrapopliteal interventions in CLI patients and found AFS, and survival rates were similar overall.In the present study Amputation Free survival in open surgical group is more compared to Endovascular group study with 6months of follow up.log rank test is performed between the two groups which is statistically significant (p-0.037) and Hazards ratio when compared is 2.378 which favoured open surgical group. In a study by Bisdas et al[51] for a follow up 1year the Amputation Free Survival rate was 75% in endovascular group and 72% in Bypass group and log rank test was performed between two groups which showed no significant difference . In other study by Dosluoglu et al[43] also showed the similar result AFS in Endovascular group was 30% and Open surgical group was 39% and there was no statistical significant difference between two groups . In other studies by Hicks et al[44] and F.Gentile et al[47] also showed similar result stating that AFS was similar in both groups

Wound healing is the other primary endpoint of our study .In both the groups wound healing status is not statistically significant between the two groups . Mean wound healing duration for open surgical group was around 2.61 months and in Endovascular group was 3.2months which shows wound healing duration was less in open surgical group but they are not statistically significant(p value-0.06).

In previuos studies like Spillerova et al[50] wound healing was better in bypass group compared to endovascular group which is not same when compared with our study.In other study done by F.Gentile et al[47] showed bypass surgery group achieved better wound healing compared to endovascular group.In BASIL-2 study showed time to healing of tissue loss was 70% higher in favour of bypass group than endovascular group, but this was not statistically significant ,but relief of rest pain was more than twice in the bypass group.

In our study **primary patency** in follow up was based on whether ABIor TBI or TcPO2 was maintained or improved when compared to the post operative measurements.All patients underwent all the three measurements,decrease in ABI >0.15,TBI>0.1,TcPO2>10 from the maximum post procedural level is considered as significant.

Based on ABI the primary patency in Endovascular group is 73% and 90% in the open surgical group at the end of 6months follow up As mentioned in the fig(1)at 1,3 and 6month of follow up ABI in both groups was similar and there was no statistical difference . However ABI was not available when the patient has non compressible vessels.In our study >40-50% patients in both groups had Non compressible(N/C) vessels hence non measureable ABI.with suchdearth of data,to consider ABI as the primary modality for determining primary patency is not a standard option.

To overcome the problem of N/C ABI is the measurement of TBI as the foot vessels are less prone for medial calcification.Based on TBI,the primary patency in the Endovascular group was 74% and 90% in the open surgical group .TBI was not available when 1st and 2nd toe was amputated.TBI was available for 45 in 1st ,43 in 3rd ,42 in 6th month in open surgical group,and 93 in 1st ,85 in 3rd and 82 in 6th month in Endovascular group for analysis.However on comparing the values at the end of 6months follow up there was no statistical difference in patency based on TBI levels between the Endovascular group and open surgical group.To our knowledge no study has included TBI in thier follow up protocol.

ABI and TBI are direct monitors of detrmining the patency of a vessel post intervention.The same cannot be told to **TcPO2** as it provides the perfusion at the tissue level and is not direct modality to determine whether a vessel is patent or not.This is because TcPO2 may be maintained by collateral supply even in the presence of a blocked major artery.this was how ever not noticed in our study as every patient who had drop in ABI,TBI had drop in

thier TcPO2 values.Also availability of TcPO2 is an advantage as there are not much factors which make it non measurable.however multitude of factors which may vary the actual level should be kept in mind before proceeding with the measuring the TcPO2.Maintenance of foot perfusion by measurement of TcPO2, is taken as a surrogate for primary patency TcPO2 was measured in the supine and in the dependent foot down provocative position. Only for a few patients in both groups, TcPO2 was not available in follow up ,**Foot perfusion** was maintained in 64% in endovascular group and 80% in the open surgical group and there was no statistical significance between both the groups. Considering overall Athere was no significant difference in primary patency between the two groups in the 6months of follow up. As of our knowledge no previous studies used the TcPO2 values in thier protocol for patency.

In most of the studies primary patency is not taken as the clinical end point rather an angiographic or duplex based end point where late lumen loss or binary restenosis was considered to determine the outcome. Dosluoglu et al study[43] loss of patency was defifined as occlusion, 70% restenosis, an elevated ratio of velocity to the proximal segment being 300% by duplex examination, loss of a previously palpable pulse, dampened PVR, or decrease in ABI of 0.2. in this study TBI and TcPo2 was not taken into consideration, According to this study there was no significant difference in patency between both groups . In Hicks et al[44] patency was primarily based on clinically palpable pulse and duplex study of the index limb according to this study during 1year follow up bypass group has low patency compared to endovascular group and was statistically significant and this study was done only in below knee vessels. In ROBUST trial[58] conducted by Mahmoud .b.Malas et al, compaared patency using duplex imaging and ABI,TBI for 1year folow up,according to this study primary patency was better in bypass group and stenting of femoral artery in endovascular group improved the patency . In Siracuse et al[42] study conducted on patients with intermittent claudication primary patency was measuerd using angiogram and duplex in the follow up bypass group patients had higher freedom from restenosis when compared to endovascular group.

MACE(major adverse cardiac event) is one of major complications which lead to mortality in majority of the vascular surgery procedures, 15.5% (23 of 148) and 7.1% (4 of 56) of the patients in the endovascular and open surgical groups respectively had cardiac events in the 6months of follow up. Patients in Endovascular group suffered with more cardiac events compared to open surgical group but statistically there is no significant difference in cardiac events between two groups (p value- 0.114). In previous study conducted by dosluoglu et al

during 1year of follow up cardiac events were more in open surgical group when compared with Endovascular group and was statistically significant(11%vs4.9% p-0.01).

In Infrapopliteal Bypass versus Angioplasty in the BASIL trial ,cardiac events happened in 11 patients in vein bypass group and 9 patients in endovascular group, and was not statistically significant.In other study conducted by F.Gentile et al[47] cardiac events occured in very less number of patients in both groups and there was no statistical significance between both groups(p-371).In other study done by Hicks et al[44] showed the no significant difference in cardiac events between the two groups and was comparable with the present study .

Major adverse Limb event (MALE) occurred in 11.5% (17 of 148) in Endovascular group and 17.9% (10 of 56) in open surgical group of the patients in the endovascular and open surgical groups respectively. There is no significant difference in MALE between two groups (p value- 0.231).

Previous studies found that diabetes, dialysis dependence, need for infrapopliteal interventions, poor functional capacity, and presence of gangrene independently predicted limb loss. These were previously reported to be associated with poor outcomes after even successful endovascular[59] or bypass interventions.[60]

In Dosluoglu et al[43] study primary amputation was 17% in Endovascular group and 19% in open surgical intervention group and there was no significant difference in limb events in both groups ,similar to that of the present study.

In study conducted by F.Gentile et al[47] The ipsilateral major amputation rate for all patients was 3% below knee and 1% transfemoral at 30 days, and 6% below knee and 2% transfemoral at 1 year. The open cohort had more complications reported at 30 days. There was a trend towards a higher rate of below knee amputations in the open surgical group, and more transfemoral amputations at 1 year. When all major amputations are compared more occurred in the open surgical group (7% vs. 2%; p- .013) at 30 days but not at 1 year (11% vs. 7%; p- .21)no difference between two groups.

In other study by Hicks et al[44] showed similar risks of MALE in both endovascular and bypass groups at the end of 1year follow up.In Infrapopliteal bypass versus angioplasty BASIL trial[7] M.A.Popplewel et al only two patients in bypass group had major amputation and one patient had major amputation in endovascular group.In Bisdas et al[51] study major ampuataion was 3% in Endovascular group and 4% in open surgical group(p-0.84) there was no statistical significance in both groups .

Mortality from all causes occured 5.4% (3/56) in open surgical group and 15.5% (23/148) in endovascular group .Mortality at the end of 6months follow up was similar between two

groups and there is no significant difference in both groups (p value -0.069).In endovascular group 7patients in <1 month ,10 in1- 3months and 6 in 3- 6months and in open surgical group 1patient in< 1 month,2patients in 1-3 months and 0 in 3-6months ,had mortality.Five patients who underwent amputation had mortality at the end of 6months in endovascular group.

In BASIL trial[7] by Bradbury the overall survival was similar in both endovascular and byapss group at the end of 2years but the morbidity was more in the bypass group.

In a study by Bisdas et al[51] over survival was 81% in endovascular group and 84% in open surgical group and there was no significant difference between mortality between two groups .

In other study by Dosluoglu et al[43] with the follow up of 5years the mortality/over all survival in the endovascular group was 36% and 46% in open surgical group and there was no statistical significant difference between two groups(p-146). other study by Hicks et al[44] with 1year of follow up showed the mortality of 4% in bypass group and 6% in endovascular with pvalue of 0.15 showing no significant differnce between two groups which was similar to the present study.similarly.Our study results also indicate the all cause mortality in the same rate with Endovascular and open surgical procedure.

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