Use of a tourniquet in lower limb amputations: Evaluating blood loss in peripheral arterial disease patients

A systematic review

by

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ELDOMA001

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Declaration

I, **Omar Eldurssi**, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature:

Signed by candidate

Date: 23-05-2021

Acknowledgements

To my supervisor: Dr Christo Kloppers for his mentorship.

To my parents: Ibrahim and Karima - my icons

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Part A - Study protocol

Study title: **Use of a tourniquet in lower limb amputations: Evaluating blood loss in peripheral arterial disease patients - A systematic review**

Principal investigator: **Dr Omar Eldurssi** Co-investigator: **Dr Christo Kloppers**

PROSPIRO Registration number**: CRD42021231657**

Introduction and background:

Above knee - and below knee amputations of the lower limb are major amputations and common procedures in acute care and vascular surgery [1]. These procedures are associated with blood loss and from this realization, surgeons should not underestimate the blood loss recorded during an amputation because of the adverse effects that may emerge, threatening the survival rates of individuals in the post-operative phase. The average blood loss is 400ml (IQR 200-500ml). However, limiting this loss can have an economic impact due to transfusion requirements and hospitalization costs [2,3].

The use of a pneumatic tourniquet is standard practice in many orthopedic procedures, where they provide a near bloodless field and minimize blood loss. Most of these patients are elderly and are likely to have some degree of undiagnosed peripheral vascular disease [4]. There are also reports of the use of tourniquets during the construction of infra inguinal, arterial anastomoses during bypass surgery to avoid clamping of the vessels [5].

Tourniquets do carry some risk, which has limited their use in general vascular and amputation surgery. These risks include the development of ischemia-reperfusion injury and damage to the underlying vessels [4,6]. The risk to the vessels may be overestimated, as a

previous randomized trial in transtibial amputations have shown no difference in wound healing or sepsis between groups with and without the use of a tourniquet [7,8]. A study, by Middleton and Varian reported that the incidence of tourniquet complications in Australia in the 1970s was approximately one in 5000 applications on the upper limb and one in 13 000 on the lower limb [9]. It appears that the historical hesitance to use a tourniquet in ischemic limbs is anecdotal and not based on good evidence.

A randomized controlled trial of the use of a tourniquet to reduced blood loss during transtibial amputation for peripheral arterial disease was performed in a larger tertiary vascular unit. They concluded that the use of a tourniquet reduces blood loss and need for transfusion without increased complications [10]. This strong evidence base has changed practice in our unit as tourniquets are now routinely used for below knee amputations.

Objectives:

The aim of this study is to investigate the effectiveness of using a pneumatic tourniquet as an adjunct in lower limb amputations in peripheral arterial disease to reduce the amount of blood loss and the requirement for blood transfusions. Stump revision rate, complication rate and mortality rate will be assessed as secondary objectives.

Study design:

This study will be conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis for Protocol (PRISMA-P).

PICO:

To conduct this systematic review, the participants, intervention, comparison and outcomes (PICO) framework are illustrated here:

Table 1: PICO

Participants	Intervention	Comparison	Outcomes
Patients with peripheral arterial disease who underwent lower limb amputation	Tourniquet	Amputation without tourniquet	Post-op blood transfusion requirement. Hb level Revision rate Operative time Mortality

Search strategy:

Keywords, rephrasing are identified to be used in the search, different databases have been used which are: PubMed/Cochrane Google Scholar Library /Scopus includes EMBASE, exclude Primo/ Web of Science exclude Medline theses & conference proceedings Medline / EBSCOHOST: Africa Wide, CINAHL Timeframe was not included.

Key words are: (Blood loss, Tourniquet, peripheral artery disease, amputation).

Studies selection criteria:

All extracted articles from previous mentioned search strategies will be collected and populated into a spread sheet and duplications will be removed. The remaining will be assessed by two separate reviewers (Dr C Kloppers and Prof W Sibanda); first evaluating the title and abstract following with the complete manuscript to assess eligibility for inclusion as per PRIMSA flow diagram. Non-English articles will be excluded.

Eligibility criteria:

1. Patient's aged 18 years and above with peripheral arterial diseases such as diabetes, hypertension dyslipidemia, HIV or ABI less than 0.9.
2. Lower limb amputations
3. Use of tourniquet

Exclusion criteria:

1. Traumatic amputation
2. Amputation for oncology

Data extraction:

All data collected will be put on a separate sheet under the last name of the first author and year published. Size of population, median age, country, type of operation, estimated blood loss (EBL), will be collected.

Data analysis

The data analysis will be evaluating the difference in EBL and in tourniquet group against non-tourniquet group. Narrative synthesis, strength of evidence, meta-analysis will be conducted.

Ethics

The study will be conducted on published data; therefore, ethical approval and consent are not required. For degree purposes the protocol was approved by the local ethics committee. (HREC/512/2020).

Budget

Apart from basic stationary no expense is anticipated.

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Part B: Literature review

Major lower limb amputations in peripheral arterial disease

Peripheral arterial disease is a high-risk condition that results in amputation of the lower limb. Statistics reveal that peripheral arterial disease results in a high mortality rate and numerous complications. The disease process causes ischemia, a condition treated through amputation or re vascularization procedures that improve blood flow. The latter might even be needed after amputation to improve stump healing. Lower-extremity amputation is a life-changing procedure, resulting in significant morbidity, social implications, low capacity to work and devastating life-image. Lower limb amputation is also done to patients with diabetic foot disease, acute and chronic limb ischemia. Major amputation levels include above and below the knee.

Lower limb amputation is a surgical procedure with some discrepancies regarding exact distal boundaries and dissection.

Peripheral arterial disease stems from atherosclerosis of the lower extremity arteries [1]. Due to occlusive disease the arteries narrow, creating severe cardiovascular conditions and high-risk ischemic events, which accelerate the disease's progression [2].

The evidence for the oldest confirmed amputation in Europe, was found in France, dating back to 4900–4700 BC and was re-introduced in 1529 by a French military surgeon called Ambrose Pare. However, the earliest account of amputation was recorded in 484 B.C. by Herodotus, who cut off his bad leg before replacing it with a wooden piece. James Hanger was the first recorded amputee who underwent the surgical procedure before being exposed to the world of prosthesis. He founded a prosthetic company that produced different parts that are critical in the rehabilitation after amputation. Major lower limb amputation, including above knee amputation (AKA), below knee amputation (BKA) and through knee amputation,

has a historical background that includes congenital diseases, sepsis, and trauma. Vascular disease, diabetes mellitus, and cancer are the most susceptible to infections which leads to microvascular dysfunction [3].

The causes of amputation vary from one country to another, but diabetic complications are central to most. Atherosclerosis is a significant risk factor for peripheral arterial disease and amputation. Atherosclerosis has led to the prevalence and progression of peripheral arterial diseases by reducing lower extremity arterial perfusion [1]. Peripheral arterial disease has also increased chronic limb-threatening ischemia and diabetes is a significant risk factor to infra-popliteal pattern of disease. Tibial artery disease is often a vessel calcification among diabetic patients, causing infections, peripheral neuropathy and impaired wound healing [4].

Decision to choose between above and below knee amputations

Deciding on the ideal level for amputation in patients with peripheral arterial disease is often complex and needs multidisciplinary team input. Generally, the knee joint should be preserved as it improves post-operative rehabilitation and mobility. Major lower limb amputation is associated with increased energy expenditure: 10 - 40% in unilateral below knee amputation and 50 - 70% in above knee amputation. The three most common used adjuncts to assess the level of amputation are clinical assessment, doppler ultrasound and transcutaneous oxygen tension (TcPO2).

Clinical judgment is accurate in predicting stump healing in about 80 % for BKA and 90% for AKA. The doppler ultrasound is used to measure the ankle/brachial pressure index (ABI) and if larger than 0.77 and/or TcPO2 > 40 mmhg the wound has a good chance to heal primarily [5].

Surgical technique for above knee amputation

Above knee amputation is recommended in peripheral disease patients who have non re constructible aorto-iliac or fem-pop disease and tibio-peroneal disease with fixed flexion deformity of the knee more than 15 degrees or hip joint more than 30 degrees There are three levels for AKA: proximal, mid or high AKA depending on the degree of blood supply for the future stump. Locally we prefer mid-thigh AKA with preservation of the adductor muscles as it improve walking if a prosthesis is planned. Although many patients do not have the resources to obtain a prosthesis, mid-thigh amputation does decrease the energy required to ambulate than high one.

Surgical steps in patients with Chronic limb-threatening ischemia (CLTI), start with adequate broad-spectrum antibiotic. However, patients with dry gangrene receive only a preop prophylactic dose of antibiotics. Mark the level of amputation approximately 12 cm from the knee joint, then apply pneumatic tourniquet at adequate level. A fish mouth incision is created using sharp and cautery dissection to expose the subcutaneous tissue. Sutures ligate the great saphenous vein and any other vessels in the field. Anterior and medial compartments of the thigh should then be transected at the level of femur while the posterior compartment (hamstrings) is transected two fingerbreadths distal to the femur [8]. On the medial side, identify the femoral artery and vein: double suture ligation of these are performed. The femur is divided using a -, Gigli - or electrical saw. The sciatic nerve is identified and transected under tension then left to retract. Release the tourniquet, if it was used, check for hemostasis and wash with saline. Use interrupted absorbable suture to approximate the fascia and subcuticular absorbable sutures to close the skin.

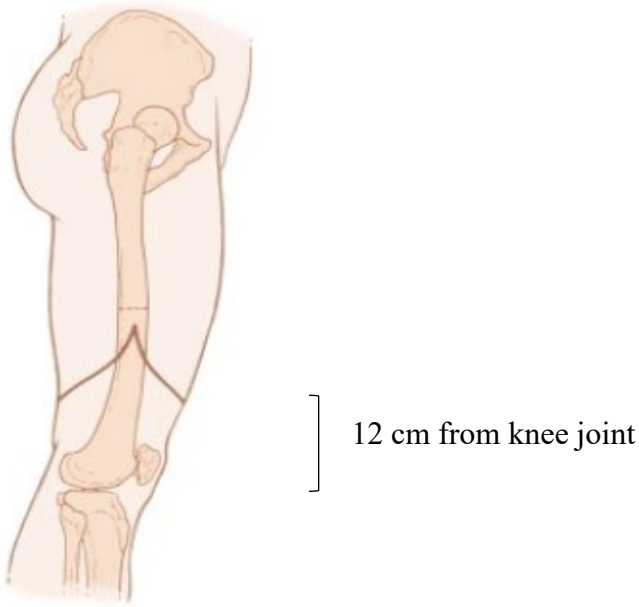

Figure 1: Incision in above-knee amputation [6]

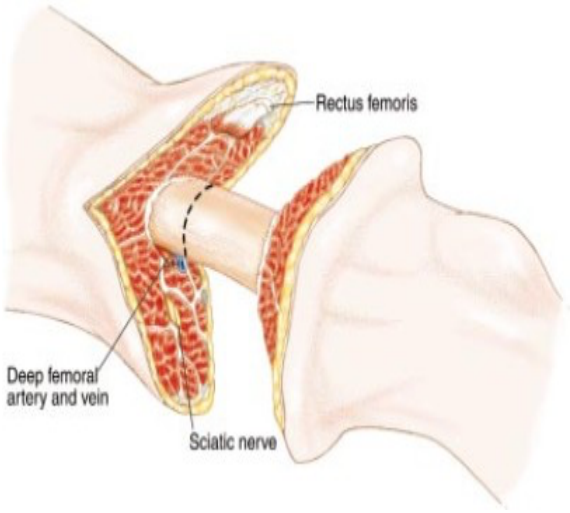

Figure 2: Transectional muscle and bone [6]

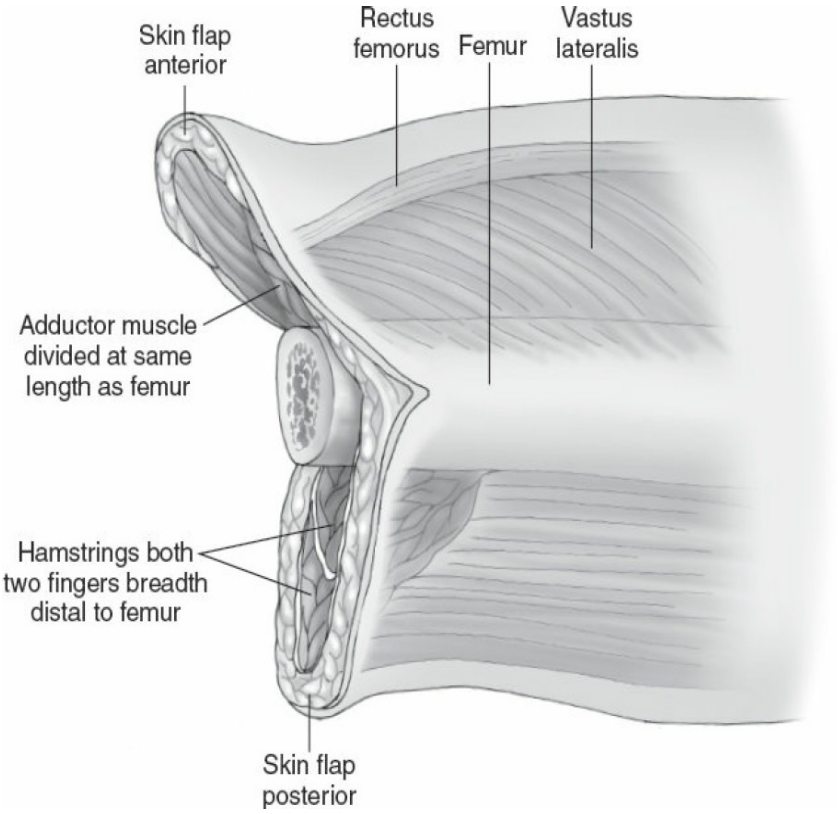

Figure 3 Muscle division in relation the femur division in Above knee amputation [8]

Surgical technique for below knee amputations

Below knee amputation is indicated in patients with diabetic foot sepsis or intractable foot pain secondary to advanced peripheral arterial disease with intact infra popliteal circulation suitable for stump healing.

The most commonly technique used is Burgess or the long posterior myocutaneous flap, which is made up of skin, gastrocnemius muscle and part of the soleus muscle. The procedure is started by administrating a broad-spectrum antibiotic, marking incisions, and applying a pneumatic tourniquet above the knee. A transverse skin incision is made 12 cm distal to the tibial tuberosity, the medial and lateral landmark of the incision is the anterior third of the leg circumference. Extending the incision longitudinally to a length of 1.5 times the length of the transverse incision to form the posterior flap ended by creating a transverse incision [8].

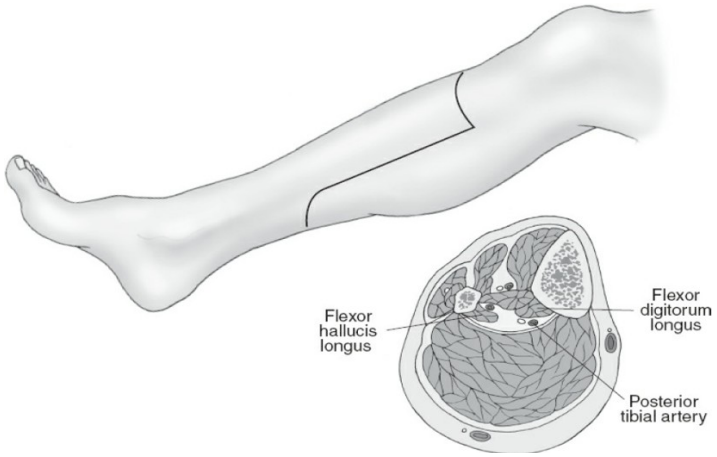

Figure 4: Skin incision for Burgess below-knee amputation [8]

A good anatomical knowledge of the leg assists in identifying the sites where the neurovascular bundle occurs and can be easily controlled by ligation and transection. Figure 4 illustrates the three compartments of the leg and their vascular bundles.

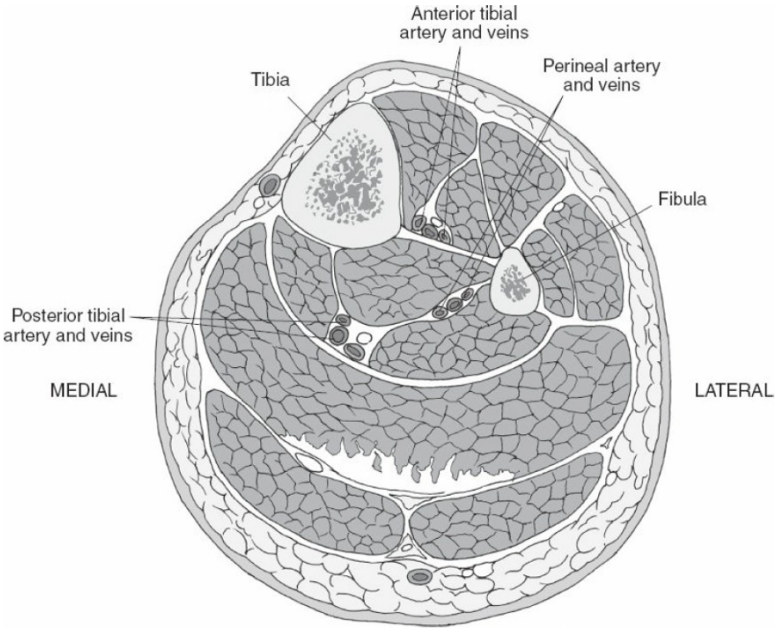

Figure 5: Locations of anterior tibial, posterior tibial and peroneal vasculatures [8]

Deepening the skin incision to expose the periosteum of the tibia, which is then dissected, and the tibia is divided 2 cm proximal to the skin incision and beveled. The fibula is cut 2 cm proximal to the tibial transection. Sutures ligate major vessels, transect nerves under tension and leave them to retract. Create the posterior flap by leaving gastrocnemius and part of the soleus muscle (see figure 6). Deflate tourniquet if used, check for any visible bleeder, and control it. Good wash, facial closure by absorbable suture and skin with subcuticular absorbable monofilament suture.

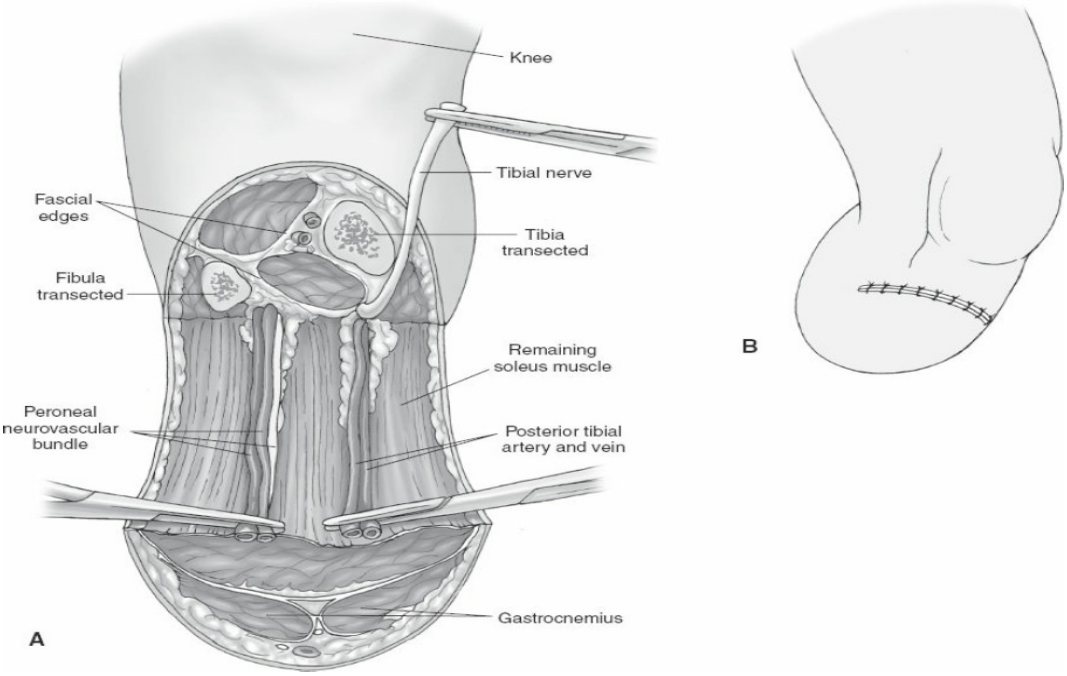

Figure 6: A. Posterior flap with remaining soleus and gastrocnemius.

B. Reconstruction after below knee amputation [8]

Blood loss in lower limb amputation

Several scholars have established that the total blood loss incurred by patients during amputation is twice the intra operative loss. The reasons for this difference are diffuse hematomas occurring postoperatively and a possible underestimation of the OBL by the

operating surgeons. Average blood loss varies between IQR 200-500, which translates to 400ml [9].

Tourniquet in major lower limbs amputation in peripheral arterial disease

The use of tourniquets goes back to 199BCE-500CE, where literature reports that it was used by the Romans to control bleeding during amputation [10]. Romans first used tourniquets comprising a narrow strap made of bronze with leather for comfort [11].

Figure 7 Pneumatic tourniquet application for below knee amputation

Other types of tourniquets include Esmarch tourniquets, a type of rubber band tied to the distal extremity to enable bloodless surgery [12]. The shortfall of Esmarch tourniquets is the high pressure generated that leads to skin and nerve trauma. As a result of the disadvantages of Esmarch tourniquets, pneumatic tourniquets were introduced by Harvey Cushing in 1904

[13]. Pneumatic Tourniquets create a bloodless environment, which is thought to facilitate surgery and reduce time, potential errors, and subsequent complications [14]. Despite some concerns over their potential to cause lasting pain, ischemia, and deep vein thrombosis, such complications are rare and usually resolve over time [14]. To reduce the chance of undesirable complications during lower limbs operations where pneumatic tourniquet is used, we should follow the modified rules of Burner (Table 1).

Table 1: Burner's ten rules for safe tourniquet [15]

Application	Apply only to a healthy limb or with caution to an unhealthy limb
Size of tourniquet	15 cm or wider in large legs
Site of application	Upper arm; mid/upper thigh
Padding	At least two layers of orthopedic wool
Skin preparation	Occlude to prevent soaking of wool.
Pressure	50–100 mm Hg above systolic for the arm; double systolic for the thigh; or arm 200–250 mm Hg; leg 250–350 mm Hg (large cuffs are recommended for larger limbs instead of increasing pressure
Time	Absolute maximum 3 hours (recovers in 5–7 days) generally, not to exceed 2 hours
Temperature	Avoid heating (e.g., hot lights), cool if feasible, and keep tissues moist
Documentation calibration and maintenance	At least weekly against mercury manometer or teat gauge; 3-monthly maintenance

Above knee amputations (AKA) are performed for patients with peripheral vascular disease as well as in patients with diabetes and diabetic foot ulceration [16]. AKA is a major operation with significant mortality and morbidity due to pre-existing diseases. Complications include, but not limited to, blood loss with need for transfusion, sepsis,

breakdown and revision [17,18]. Reducing these complications can allow patients to recover faster. Several studies have determined the efficacy and benefits of using tourniquets in lower extremities surgery like below knee amputation (BKA), knee surgery, and varicose veins. Tourniquets were also found to significantly reduced intra-operative blood loss, drop in hemoglobin levels, and requirements for transfusion (255mL, 1g/dL, and 33% respectively) when compared to controls (no tourniquet) (550mL, 1.8g/dL, and 50% respectively) among patients with peripheral arterial disease undergoing BKA [18]. However, the rate of breakdown and revision in the tourniquet group (0% and 14% respectively), although lower than the controls (9% and 9% respectively), were insignificant ($p > 0.05$) [19]. This could be the effect of the type of tourniquet used and more specifically on the accurate maintenance of pressure and bloodless field. The Boazul cuff, although effective, is known to show inaccurate pressure gauge measures [15]. Further, a study had found that the use of a pneumatic tourniquet with accurate control of air pressure was effective in significantly reducing revision rates by over 50% in patients with peripheral arterial disease (14.3% in the tourniquet group compared to 38.3% in the control group, $p < 0.05$) [20]. In a previous study that used Boazul cuff tourniquets shown reduced amount of blood loss during varicose vein surgery (5 - 158mL) when compared with controls without tourniquets (17-610mL) ($p < 0.0001$) [18].

The requirements for blood transfusion in lower limb amputation have been shown to be significantly less with the use of tourniquets [19,20]. Another study determined that in the absence of tourniquet use, the median total blood loss among patients with trans-femoral amputation was 964mL and two units of RBC transfusion was given on average [18].

In conclusion, there is evidence suggesting that the use of tourniquets do reduce the amount of intra-operative blood loss and transfusion requirements. It might also decrease the rates of

revision and sepsis in patients with lower extremity amputations. However, complications arising as a result of improper tourniquet use must be taken into consideration and safe ways of using them to maximize recovery must be implemented.

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Part C: Publication ready original manuscript

Use of a tourniquet in lower limb amputations: Evaluating blood loss in peripheral arterial disease patients - A systematic review

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Keywords: Tourniquet, blood loss, revision, amputation, lower limb, pain

Abstract

Background: Tourniquets have become an inseparable part of many different types of intricate and major surgeries, including amputation. Tourniquets create a bloodless environment, which is thought to facilitate surgery and reduce time, potential errors and subsequent complications.

Objectives: To investigate the effectiveness of using a pneumatic tourniquet as an adjunct in lower limbs amputation in peripheral arterial disease to reduce blood loss and requirement for blood transfusions. Stump revision rate, complication and mortality will be assessed as secondary objectives.

Method: For this systematic review, a search was performed using the keywords phrases, "peripheral arterial disease", "lower limb amputation" and "tourniquet" in PubMed, Medline, Embase and Google scholar.

Results: Based on univariate analysis, to determine the relationship between risk factors and blood loss, the study demonstrated the use of tourniquet significantly reduces the amount of blood loss during lower limb amputation (LLA), F (21.01), P=0.044. An independent t -test, demonstrated that there was a statistically significant difference in mean blood loss between tourniquet and non-tourniquet studies, (T=-2.588, P=0.049). In this review the mean blood loss was 251.67±2.89 and 462.5±137.69ml for tourniquet and non-tourniquet studies respectively.

Conclusion: Using a tourniquet is a technically feasible approach to LLA, and effectivelyreduces the amount of blood loss and requirements of blood transfusion. No change in revision rates were noted.

Background and aim

Major limb amputation is a common surgical operation for patients with diabetic foot sepsis and critical limb ischemia who failed or are not candidates for revascularization. These patients often have significant co morbidities and outcomes are generally guarded. Post-operative hemorrhage is a common complication that can occur after any surgical procedure. A tourniquet is a device that prevents blood flow in the limbs and has the advantage of improving the surgical field and decreasing the blood loss Its usage is universal, but many controversies remain about it and with passage of time some principles have changed. In general, there are two types of tourniquets, namely surgical and emergency. Surgical tourniquets are used in orthopedic and plastic surgeries for creation of a bloodless field, greater safety, better precision, and convenience for the surgeon. Another use of the tourniquet is as an adjunct for regional anesthetic. Emergency tourniquets are used out of hospital to control traumatic bleeding in limbs. A tourniquet can be either pneumatic or elastic (Esmarch). In recent times,most tourniquets are of the pneumatic design.

Currently the use of a tourniquet during amputation is not universally practiced, mostly due to surgical anecdote. With this review we aim to evaluate the current literature on the use of a tourniquet to prevent blood loss during amputation.

Methods

Protocol and registration

The study is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis for Protocol (PRISMA-P).

Statement of human rights and ethics

This is a systematic review and does not involve patients directly. The protocol has been approved by the local institutional ethic committee (HREC/ REF/512/2020).

Eligibility criteria

Randomized controlled trials (RCTs) and retrospective studies comparing tourniquet with non-tourniquet amputations of the lower limb, for patients aged 18 and above, with peripheral arterial disease (PAD), with the following risk factors, diabetes mellitus (DM), HPT, smoking, hyperlipidemia, and HIV.

Information sources

Two review authors searched the PubMed, Cochrane, Google Scholar Library and EmBase databases for all results.

Search

A simple, but exhaustive keyword search was performed using the keyword "tourniquet" in EmBase and as a MeSH term in PubMed. Other keywords used were amputations with tourniquet, peripheral arterial disease (PAD), blood loss, Amputation.

Study selection criteria

The search results were captured on an online data repository. Two review authors independently reviewed all results, based on the study inclusion and exclusion criteria. Any discrepancies for each step were resolved before proceeding to the next step. Extracted articles were first evaluated for the title, abstract and the complete manuscript to assess eligibility as per PRISMA flow diagram. Non-English articles were excluded.

Data Collection Process

All data collected will be put on a separate sheet under the last name of the first author, year, size of population, median age, country, and type of operation. One author developed the data capture repository,while the other author extracted the relevant data.

Data items

Primary data extraction concerned only patients with peripheral arterial disease (PAD), who underwent lower limb amputation (LLA), with tourniquet. Secondary data extraction concerned lower limb

amputation outcomes such as blood loss, revision rate, operative time, complication, and mortality. Othervariables collected were country of study, study design, number of participants and characteristics of study participants (age, sex, fracture type and length of stay in hospital) and operation characteristics (data on the use of a tourniquet and surgery duration).

Summary measures

Primary outcomes, blood loss, revision rate, operative time, number of complications and mortality were reported across the studies. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using the SPSS version 26 software.

Study selection

The study selection process is outlined in the Preferred Reporting Items for Systematic Reviews (PRISMA) diagram (*Figure* 1). A total of 75 articles were identified during the initial search. After removal of six duplicate records remaining with 69. A further review of the 69 abstracts, resulted in the removal of 11 citations that were not related to the research, giving 58 full manuscripts that were related to the research question. Screening the remaining 58 manuscripts based on the minimum eligibility criteria excluded 43 articles that did not meet the minimum eligibility criteria. A total of 15 full manuscripts met the minimum eligibility criteria.

Results synthesis

Fifteen studies met the minimum inclusion criteria and were included in this systematic review as shown in table 1. The number of participants ranged from 42 to 138 and except for one study [8] there was a surplus of males included. Amputations among men were higher compared to women, 11 studies showed (92%) amputations among men were above 50% and five studies (42%) amputations were above 60% compared to women. Prevalence of DM varied between 35% and 58% for the 15 studies.

Figure 1. PRISMA flow diagram of the screening process

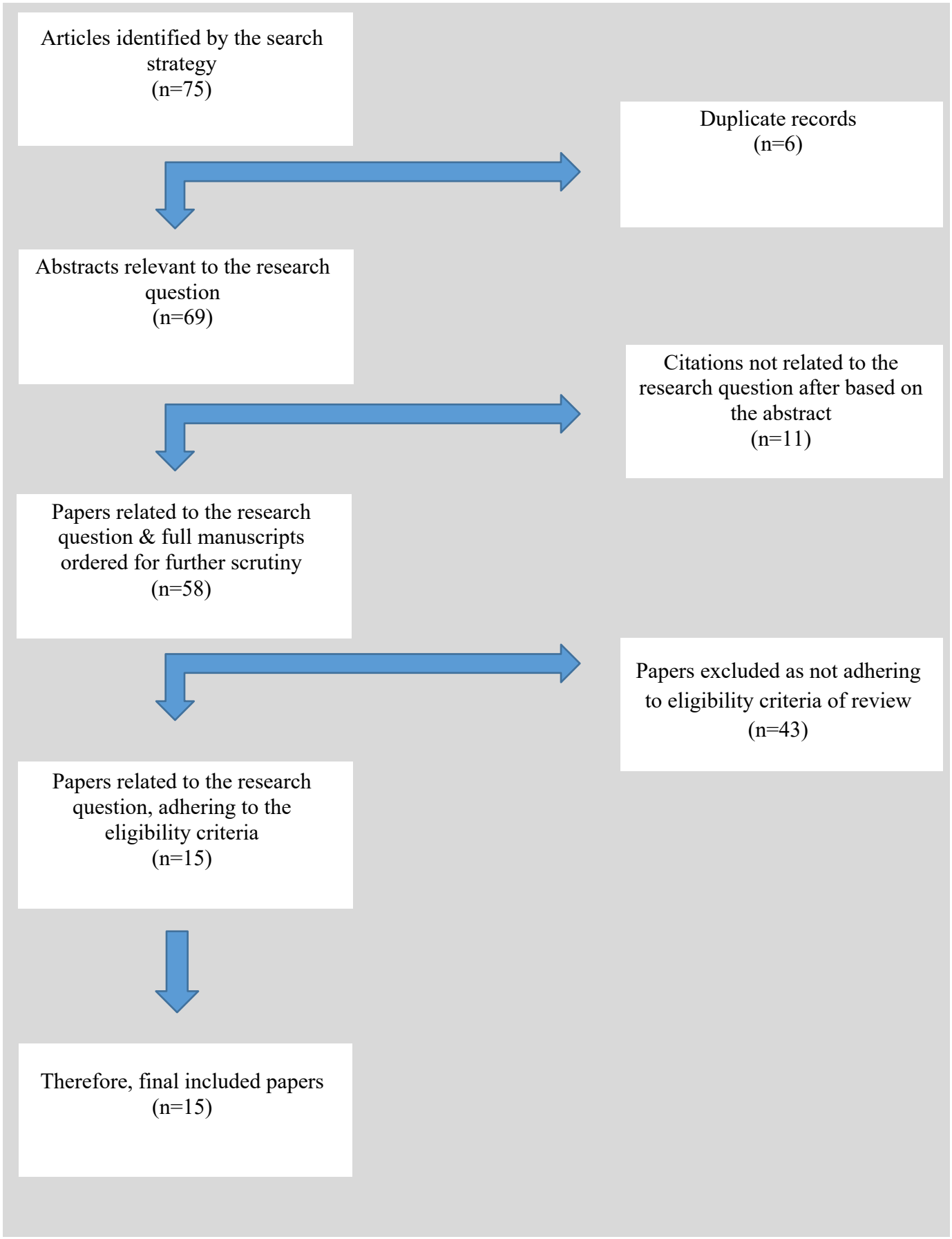

Table 1: Study characteristics of the included studies

Study	**Country**	**Amputation**	**Follow-up**	**Tourniquet**			**No tourniquet**		
				n	**Mean age (SD)**	***M/F* %**	***n***	**Mean age (SD)**	***M/F* %**
Berli et al. [9]	Switzerland	BKA, AKA	814 days	182	66.5 (31-93)	69/31	-	-	-
Carmona et al. [10]	Switzerland	BKA, AKA	9–32 months	40	52 (6.4)	83/17	198	78 (7.5)	56/45
Choksy et al. [11]	UK	BKA	1-6 weeks	25	69 (60-75)	84/16	29	69 (63-77)	86/14
Fortington et. al [12]	Netherlands	BKA, AKA	24 months	-	-	-	299	74.1 (11.2)	60/40
Hsu et. al [13]	Netherlands	BKA, AKA	5.7 years	-	-	-	69332	62.6 (13)	49/51
Jain et. al [14]	USA	BKA, AKA	-	-	-	-	14012860	69±12.3	49/51
Kolossvary et. al [15]	Hungary	BKA, AKA	-	-	-	-	32 084	63.9 (11.5)	65/35
Malyar et. al [16]	German	BKA, AKA	4 years	-	-	-	24687	72.1±10.3	52/48
Rowe et. al [17]	German	BKA, AKA	-	-	-	-	48293	72.1±27	52/48
Scott et. al [18]	UK	BKA, AKA	12 months	-	-	-	339	73(162-79)	69/31
Spoden et. al [19]	German	BKA, AKA	-	-	-	-	55595	74 (64-81)	69/31
Wolthuis et. al [20]	UK	BKA, AKA	-	42	76	60/40	47	72	53/47
Wied et.al (2017a) [21]	Denmark	TTA	30 days	38	71±9.8	71/29	36	73±12	61/39
Wied et.al (2017b) [22]	Denmark	AKA	-				81	77±11	48/52
Mohd et. al [23]	India	AKA	1, 3, 6 weeks	20	65	75/25	20	64	60/40

In this systematic review, one article reported on re-operation after lower limb amputation in PAD patients [1], three articles [2,5,6] on the role of diabetes in increasing the risk of LLA in PAD patients, two articles on application of tourniquets to reduce blood loss in LLA in PAD patients [3,23], two articles on mortality rate after LLA for PAD patients [11,21] and three articles on trends in LLA for PAD patients [8,16,20]. A detailed analysis of profile of patients in the studies and complications associated with LLA surgery is given in Table 2 and table 3 respectively.

Table 2: Showing profile of patients included in this study

Paper	Sample	Mean age (SD)	Gender		Diabetes	Revision/ Reamputation	Mortality/ year	Hypertension	Obesity	Dyslipidemia	Smoking	Myocardial Infarction	Ischemic stroke	Sepsis
			F	M										
Spoden et al [19]	55595	74 (64-81%)	17234 (31%)	38361	26686 (48%)	5646 (10%)	4276 (7.7%)							
Malyar et al [16]	24687 (61.8%)	72.1±10.3	11742 (47.6%)	12945 (52.4%)	8652 (35%)			15955 (64.6%)	1186 (4.8%)	7471 (30.3%)	3418 (13.8%)	149 (0.6%)	62 (0.3%)	1870 (7.6%)
Carmona et al [10]	209		93 (44.5%)	116 (55.5%)	101 (48.3%)	23 (11%)	80 (38.3%)	100 (47.8%)	87(41.2%)		47 (22.5%)		17 (8.1%)	
Jain et al [14]	14 012 860	69±12.3	6 067568 (43.3%)	7 945 292(56.7%)			434 39 (3.1%)	10 467 606 (74.7%)		6 249 736 (44.6%)	3 349 074 (23.9%)			
Berli et al [9]	180	66.5 (31-93)	55 (31%)	125 (69%)	104 (57.8%)	54(30%)	34 (18.9%)							
Hsu et al [13]	69332	62.6±13	35359 (51%)	33973 (49%)			13850 (20%)	51028 (73.6%)				1444 (4.5%)	3754 (11.7%)	
Kolossvary et al [15]	38084	63.9±11.5	11229 (35%)	20855 (65%)	16170 (50.4%)							1444 (4.5%)	3754 (11.7%)	
Rowe et al [17]	48293	72.1±27	23084 (48%)	25209 (52%)										
Choksy et al [11]	25	69 (60-75%)	4 (16%)	21 (84)	13 (52%)									7 (28%)
Wolthuis et al [20]	42	76	14 (33%)	28 (67%)	19 (45.2%)	6 (14.3%)	3 (7.1%)	25 (59.5%)						
Scott et al [18]	339	73 (26-92%)			131 (39%)	5 (15%)	121 (35.7%)							

Fortington et al [12]	299	74.1±11.2	121 (40%)	178 (60)	150 (50.2%)		231 (77%)				228 (76%)			
Wied et al [21]	40	72.3±11.0	25 (34%)	49 (66%)	39 (53%)		6 (8.1%)							
Wied et al [22]	81	76.8±11.2	42 (52%)	39 (48%)	22 (27%)		11 (13%)							
Mohd et. al [23]	40	65 (50-75%)	13 (33%)	27 (67%)	23 (58%)	7 (18%)								

Table 3: Detailed analysis of complications

Study	**Tourniquet Complications n (%)**		**Non-tourniquet complications n (%)**	
Berli et. Al [9]	Skin necrosis	1		
	Soft tissue infection	1		
	Delayed wound healing	2		
	Necrotizing fasciitis	1		
Choksy et al [11]	Wound breakdown	0 (0)	Wound breakdown	9 (3)
	Revision of amputation stump	1 (4)	Revision of amputation stump	9 (3)
	Wound healing	57 (14)	Wound healing	59 (17)
	Myocardial infarction	4 (1)	Myocardial infarction	7 (2)
	Cardiac arrhythmias	12 (3)	Cardiac arrhythmias	10 (3)
	Pulmonary edema	8 (2)	Pulmonary edema	3 (1)
	Intraoperative blood loss (OBL)	255 (155-572.5)	Intraoperative blood loss (OBL)	550 (255-1058)
	Hemoglobin concentration	1.0 g/dl (0.6–2.4)	Hemoglobin concentration	1.8 g/dl (0–1.2)
Malyar et. Al [16]			Acute renal failure	218 (0.9)
			Myocardial infarction	149 (0.6)
			Ischemic stroke	62 (0.3)
			Infections	1870 (7.6)
			Sepsis	398 (1.6)

			Deaths	579 (2.3)
Wolthuis et. Al [19]	Pulmonary edema	1	Pulmonary edema	
	Pulmonary embolism	1	Pulmonary embolism	
	Clostridium difficile diarrhea	2	Clostridium difficile diarrhea	1
	Acute myocardial infarction	1	Acute myocardial infarction	
	Urinary tract infection		Urinary tract infection	1
	Cerebrovascular accident		Cerebrovascular accident	1
	Post-operative death	1	Post-operative death	2
	Death after revision procedure	1	Death after revision procedure	1
	Disseminated ovarian cancer	1	Disseminated ovarian cancer	
	Drop in hemoglobin	5.6%	Drop in hemoglobin	14.3%
	Revision rate	14.3%	Revision rate	38.3%
	Mortality	7.1%	Mortality	6.4%
Brien et. Al [24]			Early amputation failure	1130 (13%)
			30-day mortality	626 (7.1%)
			Wound complications	805 (9.1%)
			Non-wound complications	1903 (21.4%)
			Post-operative hospitalization	6 (4.7%)
Bourke et. al. [25]			Bone pathology	13 (18.3%)
			Soft tissue pathology	22 (31%)
			Infection	22 (31%)
			Pain (neuroma)	10 (14.1%)
			Pain (other)	5.6%
Iannuzzi et. Al [26]			Respiratory complication	910 (8.2%)
			Venous thromboembolism	190 (1.7%)
			Renal	259 (2.3%)
			Neurologic	124 (1.1%)
			Cardiac	14 (3.5%)
			Graft/Prosthesis	59 (0.5%)
			Post-operative bleeding	620 (5.6%)
			Minor complications	1380 (12.5%)

		Wound disruption	182 (1.6%)
		Incisional infection	924 (8.4%)
Wied et. al (2017 a) [20]	Seepage of blood from wound due to damaged vessels by tourniquet	More Intraoperative blood loss (OBL)	
	Late onsets drop in Hemoglobin (Hgb)	More blood transfusions	
	Increased postoperative bleeding		
	Exsanguinated limbs swell by 10% after removal of tourniquet		
	Total Blood loss (TBL) 773 (336-1218) ml	Total Blood loss 859 (383-1315) ml	
	Intraoperative Blood loss (OBL) 250 (150-500) ml	Intraoperative blood loss (OBL) 300 (225-600) ml	
Wied et. al. (2017 b) [21]		22 amputations due to diabetes-related complications	9 (41%) post-operative complications
		52 amputations due to atherosclerotic complications	16 (31%) post-operative complications
		Blood loss (median) 964 mL (IQR 443-1558)	
		Intraoperative blood loss (OBL) 400ml	
Mohd et. Al [23]	1x1l Transfusion 2 (10%)	1x1l Transfusion 12 (60%)	
	Wound break down 3 (15%)	Wound break-down 6 (30%)	
	Revision amputation 2 (10%)	Revision amputation 5 (25%)	
		Hip disarticulation 1 (5%)	
	Blood loss (median) 250ml	Blood loss (median) 600ml	
	Drop in hemoglobin (mean) 0.82gm/dl	Drop in hemoglobin (mean) 1.72gm/dl	

By using univariate analysis to determine the relationship between risk factors and blood loss, the study demonstrated the use of a tourniquet significantly reduces the amount of blood loss during lower limb amputation, F = 21.01, P = 0.044 (Table 5). An independent t -test, demonstrated that there was a statistically significant difference in mean blood loss between tourniquet and non-tourniquet studies, (T = -2.588, P = 0.049). The mean blood loss was 251.67±2.89 and 462.5±137.69 milliliter for tourniquet and non-tourniquet studies respectively.

Table 4: Univariable analysis with linear regression of association between risk factors for the total blood loss

Dependent variable- Blood loss		
Variable	F-value	P-value
Intercept	351.7	0.0030
Age (Years)	16.6	0.055
Tourniquet (Y/N)	21.01	0.044
Sex (M/F)	0.50	0.553

Discussion

In this systematic review, there were studies suggesting that PAD stage was not predictive of the need for revision surgery [1]. In a study by Carmona in Geneva between the year 1990 and 1999, the rate of amputation for PAD patients increased from 1.8 to 11.4/10 000 patients/year and the increase was observed to be associated with age and male gender of patients [2]. In addition, this group demonstrated that diabetes was present in 48% of patients, conferring a 10 times risk of lower limb amputation (LLA). In the same cohort it was demonstrated that major lower limb amputation has a poor prognosis, characterized by 40% mortality in a two-year period. Another study by Scott, similarly, showed that major lower limb amputation is a high-risk procedure with a high 30-day mortality of 12.4% and that an increase in age was associated with an increase in the risk of mortality following LLA for PAD patients [18]. Rowe et al reported that there was an association between increased application of endovascular technology and reduced rates of amputation in patients with PAD [16].

Jain et al demonstrated that individuals with PAD and DM1 are more likely to be amputated compared to PAD and DM2 (17.7% vs 10.6%). However, PAD and DM2 patients were observed

to be older than PAD and DM1. Kolossvary reported that 50.4% of LLA for PAD had diabetes [8].

In a study by Wolthuis the drop in hemoglobin following surgery was higher among non-tourniquet patients (14.8%) compared to tourniquet patients (5.6%), with a higher need for transfusion in the non-tourniquet group. The revision rate was 14.3% in the tourniquet group and significantly higher in the non-tourniquet group (38.3%) [23]. Interestingly, according to thiswork, mortality was higher among tourniquet (7.1%) than non-tourniquet patients (6.4%),however the difference in mortality was not statistically significant, P = 0. 895.

According to Choksy intraoperative blood loss was higher among non-tourniquet patients; 550 (255-1058) ml compared to tourniquet patients 255 (155-572.5) ml [3]. In addition, there was a significantly greater drop in hemoglobin concentration (median and IQR) in non-tourniquet compared to the tourniquet group (1.8 g/dl (0–1.2) vs1.0 g/dl (0.6–2.4) and the difference was statistically significant, P = 0.035. Therefore, the requirement for blood transfusion was lower in the tourniquet group. The rate of wound healing, breakdown and revision were similar in the tourniquet and non-tourniquet groups, respectively (59 vs 57%, 0 vs 9%, 14 vs 9%).

Conclusion

The study provides valuable insight into the differences between tourniquet and non-tourniquet for lower limb amputations, with respect to outcomes such as blood loss (both intraoperative blood loss and total blood loss), revision rate, operation time, complications and mortality. However, not all the studies provide the entire list of outcomes. The weakness of the study is that there is a paucity of randomized control studies (RCTs) investigating tourniquet use in lower limbs amputation in PAD patients. We recommend doing more prospective investigation for lower limb amputations.

Conflicts of interest

The authors declare no conflict of interest.

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Part C - Supporting documents

Addendum A: Abbreviations

Addendum B: Index of tables

Addendum C: Author guidelines of South African Journal of Surgery

Addendum D: Departmental Research Committee Approval

Addendum E: HREC Approval

Addendum A- Abbreviation

ABI	Ankle Brachial pressure Index
CLI	Critical limb Ischemia
DM	Diabetes
EBL	Estimated Blood Loss
HIV	Human Immunodeficiency Virus
HPT	Hypertension
IHD	Ischemic Heart Disease
LEA	Lower Extremity Amputation
PAD	Peripheral Arterial Disease
TcPO2	Transcutaneous Oxygen Pressure

Addendum B-Index of tables

Part B

Part C

Addendum C-Author guidelines of South African Journal of Surgery

Authorship

Named authors must consent to publication. Authorship should be based on substantial contribution to:

(i) conception, design, analysis, and interpretation of data.

(ii) drafting or critical revision for important intellectual content; and

(iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org).

Conflict of interest

Authors must declare all sources of support for the research and any association with a product or subject that may constitute conflict of interest.

Research ethics committee approval

Provide evidence of Research Ethics Committee approval of the research where relevant.

Protection of patient's rights to privacy

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

Ethnic classification

References to ethnic classification must indicate the rationale for this.

Manuscripts

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

Original articles not exceeding 3 000 words, with up to 6 tables or illustrations, are usually observations or research of relevance to surgery. References should preferably be limited to no more than 15. Please provide a structured abstract not exceeding 250 words, with the following recommended headings: Background, Objectives, Methods, Results, and Conclusion.

Manuscript preparation

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

Qualification, affiliation, and contact details of ALL authors must be provided in themanuscript and in the online submission process.

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

Scientific measurements must be expressed in SI units except blood pressure (mmHg) and hemoglobin (g/dl). Liters is denoted with a lowercase 'l' e.g., 'ml' for milliliters). Units should be preceded by a space (except for %), e.g., '40 kg' and '20 cm' but '50%'.
Greater/smaller than signs (> and 40 years of age'. The same applies to ± and º, i.e., '35±6' and '19ºC'.

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

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

General formatting

The manuscript must be in Microsoft Word or RTF document format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, with the exception of Tables).

Illustrations and tables

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

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

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

References

Authors must verify references from the original sources. Only complete, correctly formatted reference lists will be accepted. Reference lists must be generated manually and not with the use of reference manager software. Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others. [3,4-6] All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order). Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus. Names and initials of all authors should be given if there are more than six

authors, the first three names should be given followed by et al. First and last page, volume and issue numbers should be given. Wherever possible, references must be accompanied by a digital object identifier (DOI) link and PubMed ID (PMID)/PubMed Central ID (PMCID). Authors are encouraged to use the DOI lookup service offered by CrossRef.

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

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

Proofs

A PDF proof of an article may be sent to the corresponding author before publication to resolve remaining queries. At that stage, only typographical changes are permitted; the corresponding author is required, having conferred with his/her co-authors, to reply within 2 working days for the article to be published in the issue for which it has been scheduled.

Addendum D: Departmental Research Committee approval

UNIVERSITY OF CAPETOWN

Department of Surgery
Departmental Research Committee
Dr Timothy Pennel
D24 Office, Groote Schuur Hospital
Observatory 7925
South Africa
Tel (021) 404 3430
Email: tim.pennel@uct.ac.za

27 Jul 2020

Dr O Eldurssi

Department of Surgery
University of Cape Town

Dear Dr Eldurssi

RE: Project 2020/108

PROJECT TITLE: Use of Tourniquet in Lower Limb Amputation: Blood Loss in Peripheral Arterial Disease Patients - A Systematic Review

The above protocol has been reviewed by the Department of Surgery Research Committee. I am pleased to inform you that the committee approved the scientific merit of the study and endorse the protocol for submission to the relevant ethics committee.

Although this letter serves as confirmation that the above protocol has successfully passed through the surgical DRC, respective ethics committees still require DRC chair signature before submission.

Please use the above project number in all future correspondence, Yours sincerely

DR TIMOTHY PENNEL
CHAIR: SURGICAL DRC

DR MARITZ LAUBSCHER
CHAIR: PROTOCOL REVIEW COMMITT

"OUR MISSION is to be an outstanding teaching and research university, educating for life and addressing the challenges facing our society."

Addendum E: HREC Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

03 September 2020

HREC/REF 512/2020

Dr C Kloppers
Department of General Surgery
J-Floor, OMB
Email: jckloppers@gmail.com
Student: Qaldresse@gmail.com

Dear Dr Kloppers

PROJECT TITLE: USE OF TOURNIQUET IN LOWER LIMB AMPUTATION: BLOOD LOSS IN PERIPHERAL ARTERIAL DISEASE PATIENTS - A SYSTEMATIC REVIEW-MMED CANDIDATE-DR OMAR ELDURSSI

Thank you for submitting your request to the Faculty of Health Sciences Human Research Ethics Committee.

The HREC note that the proposed study is a systematic review.

As the systematic review involves published literature available through publicly accessible electronic databases, research ethics review and approval is not required.

This is in accordance with Section 1.1.8 of the Department of Health's Ethics in Health Research: Principles, Processes and Structures (South African Department of Health, 2015), which states: *"Research that relies exclusively on publicly available information or accessible through legislation or regulation usually need not undergo formal ethics review. This does not mean that ethical considerations are irrelevant to the research."*

The HREC recommend that researchers refer to the PRISMA website, for the PRISMA statement and checklist, to facilitate the reporting of systematic reviews and meta-analyses. For more information, please refer to http://www.prisma-statement.org/.

Further, fundamental ethical principles for health-related research should be considered in the objectives and methods of the systematic review. See, for example, the Declaration of Helsinki (Fortaleza, Brazil, 2013) and the Department of Health's Ethics in Health Research: Principles, Processes and Structures (South African Department of Health, 2015).

The HREC acknowledge that the MMED Candidate, Dr Omar Eldurssi, was also involved in this project.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Hrec.ref512/2020sa