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Prophylactic and Therapeutic Fasciotomy for Acute Compartment Syndrome after Revascularization for Acute Lower Limb Ischemia – Renal and Wound Outcomes

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Author contribution

EK, FE, TB, SA. contributed to the design and implementation of the research, to the statistical analysis, interpretations of the results, and to the writing of the manuscript. EK, TB, SA performed the data collection.

Abstract

Objectives

Acute Compartment Syndrome (ACS) is a significant complication after revascularization for Acute Lower Limb Ischemia (ALI). High risk patients sometimes undergo prophylactic fasciotomy (PF) to prevent ACS. Patients that develop ACS undergo therapeutic fasciotomy (TF). The optimal timing of fasciotomy has been debated. The aim of this study was to describe and compare renal and wound outcomes in patients undergoing PF and TF.

Methods

A retrospective cohort study including 76 patients undergoing PF (n=40) or TF (n=36) after revascularization for ALI between 2006 and 2018. Estimated Glomerular Filtration Rate (e-GFR) was used to evaluate renal function and compare within (paired-samples t-test) and between (ANOVA) groups. Wound complications and healing time were compiled from the complete wound healing period and compared between groups with Pearson's chi^2- and log-rank test, respectively.

Results

E-GFR improved over the in-hospital period with 8.2ml/min/1.73m^2 (95% CI 2.4-14.1, p=0.007) in the PF group and 4.4ml/min/1.73m^2 (95% CI 1.2-7.7, p=0.010) in the TF group, with no significant difference between the two groups (0.3ml/min/1.73m^2, 95% CI -6.7-7.4, p=0.93). The rate of wound infections was higher after TF (PF=60.6 % and TF=82.4 %, p=0.048), whereas rate of other wound complications (PF=61.3 % and TF=35.3%, p=0.036) was higher after PF.

Conclusion

Overall wound complications were high, whereas renal function improved during in-hospital stay. A more conservative approach to fasciotomy could avoid unnecessary fasciotomies and reduce wound complications, while have the potential to sufficiently preserve renal function if fasciotomy is needed for ACS. This would be possible and safe if an early diagnosis and treatment of ACS can be ensured.

Key words: acute lower limb ischemia, acute compartment syndrome, prophylactic fasciotomy, therapeutic fasciotomy, renal function, wound infection

1.1 Introduction

Acute lower limb ischemia (ALI) is caused by sudden onset of reduced blood flow to the limb. It is usually a result of thrombosis, which may develop in atherosclerotic and aneurysmatic arteries, or embolism from a proximal source, obstructing arteries to or in the limb [1]. Depending on the severity of ALI, the limb can be salvaged through urgent revascularization, performed either through open vascular surgery, endovascular procedures or hybrid vascular surgery [1,2]. After revascularization, the limb muscles may swell due to inflammation and endothelial injury [1].

The muscles are contained in compartments enclosed by fascia and can only expand to a certain degree. Acute compartment syndrome (ACS) develops if the muscle cannot sufficiently expand within the compartment and thus increasing intracompartmental pressure (ICP) with constriction of blood flow [3,4]. The ischemia from ACS alone is limb threatening while it also causes rhabdomyolysis resulting in release of certain toxic metabolites, such as myoglobin, into the circulation [5]. Myoglobin is excreted through the urine, but an excessive amount can lead to acute kidney injury (AKI) [5,6]. In addition to the threat of renal injury from rhabdomyolysis, patients who develop ALI often have diabetes mellitus [1,2], often undergo contrast enhanced imaging with nephrotoxic iodine contrast before and during treatment [7], which all could contribute to renal injury.

The only curative treatment of severe ACS is a fasciotomy, a procedure which entails incisions along the fascia to relieve the ICP, thereby allowing the muscle to expand [3]. If ACS is expected, a prophylactic fasciotomy (PF) can be performed [1]. This will potentially protect against ACS and prevent additional limb ischemia. If ACS has already developed, a therapeutic fasciotomy (TF) must be performed [3].

While there may be intuitive reasons for performing a PF to prevent ACS, the vast majority of patients who undergo revascularization for ALI will not develop ACS [8]. Fasciotomies are associated with a wide range of complications [9,10,11] and should not be performed on dubious indications. It is however possible that a PF could protect against adverse events caused by ACS, such as renal injury, amputation and neuro-muscular sequelae. The environment in the muscle after development of ACS is characterized by a high degree of proinflammatory cytokines, cellular debris from necrotic cells, damaged endothelium with high permeability, and oxygen free radicals [12]. This edematous and inflammatory environment could be hostile to the healing process and a breeding ground for infections. A PF could prevent ACS and with that potentially have fewer wound complications and faster healing than a TF. Previous studies comparing amputation rates after PF and TF have shown conflicting results regarding 30-day amputation outcome [10,13], which makes it difficult to determine if a PF is beneficial in practice, and if so, in what patient groups.

It is unknown if a PF can be limb or lifesaving, protect against neuromuscular sequalae and renal injury, and if it is associated with fewer complications than a TF. Therefore, the aim of this study is to describe the change in renal function and frequency of wound complications, and to examine potential differences in renal and wound outcomes between patients who undergo PF and TF after revascularization for ALI.

1.2 Methods

1.3 Study design and setting

This study is a retrospective observational study of patients with ALI between 2006 and 2018 at a tertiary referral vascular center with an estimated catchment population of 1.9 million inhabitants in 2021.

1.4 Study population

ALI was defined as any acute onset of lower limb threatening ischemia with a maximum duration of 14 days. All patients who underwent revascularization procedures for ALI between 2001 and 2018 were entered in a register. Patients who were treated primarily conservatively, with primary amputation of the limb or with palliative care were excluded. In total, 843 revascularizations were included in the register, of whom 76 underwent fasciotomy between 2006 and 2018. The study center joined a new patient record system on a digital platform in January 2006, which simplified data collection, and 2006 was therefore chosen as starting point of this study

1.5 Procedures for Revascularization

The patients underwent either primary open vascular surgery or endovascular procedures as treatment for ALI. Primary open vascular surgery included open thrombo-embolectomy or bypass surgery. Endovascular procedures were predominantly catheter directed thrombolysis (CDT). Thrombolysis was sometimes followed by adjunctive transluminal angioplasty, and/or deposition of stents and/or stent grafts.

1.6 Fasciotomy definition and wound treatment

PF was any fasciotomy performed prior to signs of ACS, otherwise it was categorized as a TF.

When fasciotomy was performed, a four-compartment fasciotomy was usually chosen. The fasciotomy wounds were dressed using negative pressure wound therapy (NPWT) or compresses and gauze dressings. NPWT was started at the time of fasciotomy or the following day, after wound revision, or when it was deemed necessary. A black poly urethane or white polyvinyl alcohol sponge (KCI Medical, San Antonio, Texas, USA) was applied with a topical continuous negative pressure of 125 mm Hg. Changes of NPWT dressings were usually performed three times per week. The first re-dressings were sometimes performed at the operation room. In addition to NPWT, reduction of oedema in the fasciotomy wound was treated by positioning the leg above heart level (approximately 10 cm), physiotherapy program including concentric activity of calf muscles and use of intermittent pneumatic compression of the calf and feet. Staged interrupted skin suturing was performed when needed for closure of the skin edges. Sometimes split skin graft transplant was needed to cover the wound bed to promote wound healing. NPWT using white polyvinyl alcohol sponge on top of a fresh split skin graft transplant was sometimes used to improve graft take [14].

1.7 Baseline comorbidity prior to admission

Ischemic heart disease was defined as any prior history of myocardial infarction or invasive treatment for angina pectoris. Atrial fibrillation was defined by previous history, evidence from electrocardiogram or echocardiography. Previous claudication was defined by a history of claudication in the affected limb prior to onset of ALI. Diabetes mellitus was defined by having a diagnosis of diabetes mellitus, type 1 or type 2, prior to hospitalization for ALI. Current smoker was defined by being a regular smoker at admission, or cessation within a one-year period prior to admission. Previous smoker was any patient with a history of regular smoking with a cessation date more than one year prior to admission. Hypertension was defined by the usage of antihypertensive drugs, or a prior diagnosis of hypertension. Dialysis prior to admission was defined by undergoing dialysis regularly for chronic renal failure.

1.8 Patient symptoms and findings at admission

Anemia was present if blood-hemoglobin was lower than 134mg/L in male and 117mg/L in female patients. Renal insufficiency was defined as a relative estimated-Glomerular Filtration Rater (e-GFR) of less than 60ml/min/1.73m^2 at admission. The severity of the ischemia was ranked according to Rutherford's Criteria, where presence of motor deficit was labelled as Rutherford IIb [15].

1.9 Renal function

The e-GFR was calculated using an established formula based on patients' serum-creatinine levels, age, and sex [16]. Serum-creatinine values during in-hospital stay period were collected at admission, when highest and at discharge. Dialysis following revascularization was defined as any new onset of dialysis during the in-hospital period after revascularization.

2.0 Wound outcomes

Major amputation was defined as amputation at tibial level or proximal thereof. Wound infection was assessed according to the Centers for Disease Control and Prevention (CDC) classification [17]. Other wound complications were skin necrosis, significant bleeding and wound rupture. Healed fasciotomy was accomplished when there was full skin epithelialization of every eligible fasciotomy wound. Reduced motor function was defined as peroneus paresis, any sign of new onset of reduced motor function, need of physiotherapy or new need of walking aid at discharge.

2.1 Data sources

Data regarding patient characteristics, laboratory data, status at admission, and outcome was collected from medical records. The records are linked to each patient's unique social security number in Sweden. Patients with open fasciotomy wound were regularly followed up at the vascular out-patient clinic until complete wound healing. Uncomplicated procedures were followed up once at 30 days and one year post discharge. Additional follow up was only performed when needed. If needed, fasciotomy wound treatment was performed at the vascular center outpatient clinic and rarely at primary care facilities. Data from primary care facilities was not included. Data on patients who returned to hospitals outside of the local municipality after initial treatment of ALI were usually retrieved by receiving copies of patient records upon request. Information regarding survival and date of death was collected from the National Population registry.

2.2 Sample size

Consecutive patients identified during the study period that met the inclusion criteria were included. No estimations of sample size were performed due to the exploratory aim.

2.3 Statistical analysis

The statistical analysis was performed using SPSS version 27 and 28 (IBM, Armonk, New York, USA). Nominal data was expressed in proportions and compared between groups using Pearson's Chi^2-test. Continuous data that was not normally distributed was expressed in median and interquartile range. Normally distributed data was expressed with mean and standard deviation. The difference in e-GFR at the three time points during in-hospital stay between the PF and TF group were analyzed using analysis of variance (ANOVA), adjusting for sex and

Rutherford IIb. To analyze the change in e-GFR in between two different timepoints from admission to discharge in the PF and TF groups paired samples T-test was used. The mean change in e-GFR from admission to discharge was compared between the PF and TF groups using univariate ANOVA, adjusting for e-GFR at admission, Rutherford IIb and sex. Potential confounders were included in the model if inclusion resulted in change in results of more than 15%. Comparison of complete wound healing time of fasciotomies between PF and TF was performed using Kaplan-Meier survival analysis with Life Tables, and difference between groups with the log-rank test. A p-value of less than 0.05 was considered significant.

2.4 Ethical considerations

Ethical approval was granted by Swedish Ethical Review Authority (Dnr 2020/00764).

2.5 Results

2.6 Patient characteristics

In the PF group 37.5% were female, 35.3% were smokers, 17.5% had diabetes, 66.7% had renal insufficiency at admission and 2.6% routinely underwent dialysis. In the TF group 25% were female, 22.9% were smokers, 25.0% had diabetes, 44.4% had renal insufficiency at admission and 0% routinely underwent dialysis (Table I).

2.7 Patient symptoms and findings

In the PF group median symptom duration was 13.5 hour from onset to start of treatment, in comparison to a median of 48.0 hours in the TF group. Motor deficit (Rutherford IIb) was found in 92.5% of patients in the PF group and 58.3% in the TF group. Primary open vascular surgery was chosen for 100% of patients in the PF group and 36.1% of patients in the TF group (Table II).

2.8 Renal outcomes

The PF (8.2mL/min/1.73 m^2, 95% CI 2.4-14.1, p=0.007) and TF (4.4mL/min/1.73 m^2, 95% CI 1.2-7.7, p=0.010) -groups had both improvements of e-GFR from admission to discharge (Figure I), (Table III), with no observed difference between the two groups (0.3mL/min/1.73 m^2, 95% CI -6.7-7.4, p=0.93) regarding improvement. There were neither significant differences between the two groups regarding e-GFR at the three different time points, nor for the need of new-onset dialysis-treatment following revascularization (Table IV).

2.9 Wound outcomes

The fasciotomy wounds were completely healed in a higher proportion in the TF group (PF=57.5% versus TF=80.6%, p=0.031). NPWT was applied more frequently to the TF group (PF=38.9% versus TF=63.9%, p=0.034). The combined wound complication rates were high in both groups (PF=78.8% versus TF=91.2%, p=0.16) but with no significant difference. The infection rate was overall high (71.6%) and higher in the TF-group than the PF-group (PF=60.6% versus TF=82.4% p=0.048). The PF group had a higher rate of other wound complications (PF=61.3% versus TF=35.3% p=0.036). There were no significant differences regarding total wound complications, wound healing time (Figure II), wound revisions done in the operation room, readmission for wound complications or any other wound outcome (Table V).

3.0 Short-term major amputation and mortality

The combined major amputation/mortality rate at 90 days was borderline-significantly higher in the PF group (PF=37.5% versus TF=17.1%, p=0.050). The mortality rate at 90-days did not differ significantly (PF=10.0% versus TF=5.7%, p=0.50), nor did the amputation rate at 90-days (PF=17.5% versus TF=8.6%, p=0.26) (Table VI).

3.1 Discussion

Renal function improved in both groups over the in-hospital period with no significant difference in improvement between the two groups. High rates of wound complications, predominantly wound infections were found in both PF and TF groups. A fasciotomy was also associated with a long median wound healing time, over two months in both groups.

The improvement in renal function from admission to discharge can be counter intuitive. Initial kidney injury could be explained by hypovolemia [18] and ischemia-induced rhabdomyolysis [19,20]. During the in-hospital period, renal function was expected to deteriorate more in the TF group, compared to the PF group, due to ACS and rhabdomyolysis and exposure to higher doses of repeated iodine contrast in patients mainly undergoing CDT. A recent report showed an association between higher iodine-contrast dose/e-GFR ratio and contrast-associated AKI in patients undergoing CDT for ALI [21]. Other potential risks for renal injury during the in-hospital period would be multi-organ failure from systemic inflammatory response syndrome or septicemia. Even with the exposure to iodine contrast and risk of rhabdomyolysis from muscle ischemia, renal function was, after an initial ischemia-reperfusion insult, not worsened in either group in the present study. This suggests that a TF, in most cases, is not associated with permanent renal injury. It is important to note, though, that two patients in each group developed severe renal injury with need of temporary dialysis, showcasing the impact of ALI, potentially resulting in severe deterioration of renal function irrespective of ACS or not.

The TF group had more wound infections but a lower rate of other wound complications. Muscle necrosis might be widely prevalent in the TF group, potentially caused by a longer ischemia time in general and, importantly, subsequent development of ACS. This could make the TF group more susceptible to infections. On the other hand, a fasciotomy done at the time of revascularization would expose a muscle that had been under severe ischemic insult and potentially still were ischemic, if the revascularization procedure was not entirely successful. The wound infection rate in the present study was overall 71.6%, which is more than twice the rates seen in two previous studies [10,11]. This difference may be attributed to the documentation of wound complications until healed wound in the present study, compared to either 30-day [10] or unclear [11] follow-up time. The wide definition of wound infection, including all patients who received antibiotic treatment for suspected fasciotomy wound infection might overestimate the true number of wound infections. This might be caused by a low threshold for antibiotic treatment for suspected fasciotomy wound infections by the treating physician, especially in an out-patient setting where active surveillance of the wound is difficult. Nevertheless, the criteria of surgical site infection according to CDC classification guidelines [16], the most established and widely used definition, was used. In contrast, a previous study failed to find any significant difference between rates of wound infections after PF versus TF, with a somewhat higher observed rate of wound infection in the PF-group [10]. All things considered, patients undergoing treatment for ALI often have multiple comorbidities, high age, reduced limb circulation, two large wounds with a long healing time, and possibly necrotic tissue underneath. With all these risk factors it is not unreasonable to think that wound infection rates over the whole wound healing period would be high, and potentially as high as this study suggests.

Fasciotomies results in large wounds on both sides of the lower leg, resulting in wound healing periods of over two months, and an SSI could arise at any point during that period. NPWT of fasciotomy wounds has shown greater daily wound size reduction, fewer dressing changes, shorter wound closure time, shorter hospital stay and less resource use in retrospective studies comparing NPWT with gauze dressings [22, 23]. The present study results indicate, however, that irregular use of NPWT resulted in high wound complication rates in both the PF and TF group. To optimize fasciotomy wound care, a bundle of care approach appears to be necessary: Fasciotomy wound care should preferably be performed by the surgeon who performed the fasciotomy. Meticulous wound revisions to remove necrotic muscle and skin tissue, regular NPWT dressing changes, secondary wound suture closure as soon as it is possible and use of proper per oral antibiotics after sampling of targeted wound cultures and testing of bacterial resistance [24].

A shorter time to full skin epithelialization would reduce the time window for the development of SSI. One RCT on deep groin infections after vascular surgery suggested that NPWT improved wound healing with significantly shortened time to full skin epithelialization, without an increased cost or loss in quality-of-life measures [25, ,26]. A meta-analysis has suggested that fasciotomy wounds treated primarily with NPWT had low rates of wound complications but failed to promote healing without the need of split skin grafts compared to different primary closure techniques [27].

A few major differences between the PF and TF groups makes comparison regarding major amputation and mortality hard. Firstly, the difference in revascularization procedures between the two groups with only primary open surgery in the PF group and mainly CDT in the TF group. Though an updated meta-analysis has not concluded that either method is superior in terms of limb salvage and/or death, whereas the risk of major bleeding and distal embolization was found to be higher after thrombolysis [28]. Secondly, the PF-group had a higher proportion of motor deficit (Rutherford IIb) at admission, indicative to severe ischemia. Far from all patients with ALI and motor deficit undergo PF [8], therefore something persuaded the surgeon to opt for a fasciotomy, potentially anticipating a high risk of poor outcome. This could explain the borderline higher rate of combined major amputation and mortality at 90 days, and the lower proportions of healed fasciotomies, in the PF group. If ACS is a result of successful revascularization of a limb, a TF would be a proxy for this, giving a better chance of short-term limb patency. On the other hand, the TF group did develop ACS which resulted in subsequent ischemia to the limb, especially worsening limb status in a group who nonetheless had significant proportion of motor deficit at admission.

The main limitations of this study were the retrospective design, the major differences between the two groups and the low sample size. The major amputation rate at 30 days was twice as high in the PF group compared to the TF group, but insignificantly higher, which may be attributed to a type II statistical error. With the retrospective design the only data available was the one already recorded. This introduced the need for interpretation of available data, and acceptance of lack of data. The low numbers made it difficult to adjust for multiple confounders and it increased the risk of false associations, and lack of evidence for actual associations, though some adjustments of confounding factors were included when evaluating differences in renal function between PF and TF groups. There could to some extent be censoring of cases affecting both the development of e-GFR and wound complications. Firstly, this would be the case if severe renal injury contributes to a higher mortality risk prior to discharge and thus censoring patients with negative development of e-GFR. At 30-days post revascularization, four and two patients had died in the PF and TF group respectively. Secondly, if major amputation or mortality occurred prior to any wound complication, the patient was censored. This would have resulted in an underestimation of complications, mainly in the PF group, as the PF group had a higher loss of data due to these severe adverse events and it can be presumed that the patients with poor outcome would have had a high risk of wound complications.

The study population consisted of consecutive patients at this center, from a 13-year data collection period, and the results of this study may be applicable to centers with a full range of facilities to manage patients with emergent vascular diseases. Larger prospective multi-center studies would be warranted to be able to adjust for all confounders in the comparison between PF and TF, since a randomized controlled trial (RCT) comparing PF and TF in patients revascularized for ALI would be unethical. Prospective studies are also warranted to accurately determine the rates and extent of neuromuscular sequelae, as this factor is usually poorly described and imprecise in patient records.

To reduce the numbers of wound complications a conservative approach to fasciotomy would be beneficial, where fasciotomy is done only when ACS is emerging. An early diagnosis would offer the highest chance to mitigate the effects of the ACS induced ischemia. The ESVS guidelines suggests that a fasciotomy should be performed preferably within two hours of the development of ACS and no later than six [1]. Irreversible damage due to ACS can develop within hours [29]. As of now diagnosis of ACS is done through signs and symptoms combined with a clinical examination. The signs for ACS are either unspecific or present late, which could prolong the time to diagnosis and fasciotomy [30]. Invasive measurement of the ICP is possible, but it is not routinely used in the clinic [1]. A potential risk with invasive measurements is bleeding complications, with the risk of causing or worsening ACS, especially when done in juncture to CDT. Novel non-invasive techniques for detection of ACS have shown early promise but are still under development [30]. For a safe conservative approach to fasciotomy, introduction of non-invasive surveilling techniques for early diagnosis of ACS are needed.

3.2 Conclusion

A fasciotomy, whether prophylactic or therapeutic, was associated with alarmingly high rates of wound infection and other wound complications. It was also associated with a long wound healing time. TF appears to have the potential to sufficiently preserve renal function caused by ACS. A conservative approach in performing fasciotomy could be beneficial, with active surveillance of the limb and performing a fasciotomy only when ACS is developing, thus reducing the number of unnecessary fasciotomies. This would warrant noninvasive monitoring of the limb for early diagnosis of ACS, which is not yet in practice.

3.3 Funding

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3.4 Declaration of interest

None.

3.5 References

[1] Björck M, Earnshaw JJ, Acosta S et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2020 Clinical Practice Guidelines on the Management of Acute Limb Ischaemia. Eur J Vasc Endovasc Surg. 2020 Feb;59(2):173-218.

[2] Olinic D-M, Stanek A, Tătaru D-A et al. Acute Limb Ischemia: An Update on Diagnosis and Management. Journal of Clinical Medicine [Internet]. 2019 Aug 14;8(8):1215

[3] Schmidt AH. Acute Compartment Syndrome. Orthop Clin North Am. 2016 Jul;47(3):517-25. doi: 10.1016/j.ocl.2016.02.001.

[4] Guo J, Yin Y, Jin L et al. Acute compartment syndrome: Cause, diagnosis, and new viewpoint. Medicine (Baltimore). 2019 Jul;98(27):e16260.

[5] Cone J, Inaba K. Lower extremity compartment syndrome. Trauma Surg Acute Care Open. 2017 Sep 14;2(1):e000094.

[6] Khan FY. Rhabdomyolysis: a review of the literature. Neth J Med. 2009 Oct;67(9):272-83.

[7] Saphir E, Svensson-Björk R, Acosta S. Performance of Computed Tomography Angiography Before Revascularization Is Associated With Higher Amputation-Free Survival in Rutherford IIb Acute Lower Limb Ischaemia. Front Surg. 2021 Oct25;8:744721.

[8] Karonen E, Wrede A, Acosta S. Risk Factors for Fasciotomy After Revascularization for Acute Lower Limb Ischaemia. Front Surg. 2021 Mar29;8:662744.

[9] Rush DS, Frame SB, Bell RM et al. Does open fasciotomy contribute to morbidity and mortality after acute lower extremity ischemia and revascularization? J Vasc Surg. 1989 Sep;10(3):343-50

[10] Wesslén C, Wahlgren CM. Contemporary Management and Outcome After Lower Extremity Fasciotomy in Non-Trauma-Related Vascular Surgery. Vasc Endovascular Surg. 2018 Oct;52(7):493-97.

[11] Grip O, Lindahl P, Pärsson H. Acute Compartment Syndrome Following Thrombolysis For Acute Lower Limb Ischemia. Ann Vasc Surg. 2022 Feb;79:182-90

[12] Merle G, Harvey EJ. Pathophysiology of Compartment Syndrome. 2019 Sep 3. In: Mauffrey C, Hak DJ, Martin III MP, editors. Compartment Syndrome: A Guide to Diagnosis and Management [Internet]. Cham (CH): Springer; 2019. Chapter 3.

[13] Rothenberg KA, George EL, Trickey AW et al. Delayed Fasciotomy Is Associated with Higher Risk of Major Amputation in Patients with Acute Limb Ischemia. Ann Vasc Surg. 2019 Aug;59:195-201.

[14] Yin Y, Zhang R, Li S et al. Negative-pressure therapy versus conventional therapy on split-thickness skin graft: A systematic review and meta-analysis. Int J Surg. 2018 Feb;50:43-48.

[15] Rutherford RB, Baker JD, Ernst C et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. J Vasc Surg. 1997 Sep;26(3):517-38.

[16] Björk J, Grubb A, Sterner G et al. Revised equations for estimating glomerular filtration rate based on the Lund-Malmö Study cohort. Scand J Clin Lab Invest. 2011 May;71(3):232-9.

[17] National Healthcare Safety Network, Centers for Disease Control and Prevention. Surgical site infection (SSI) event. Updated Jan 2022. Accessed March 10th, 2022, at http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf.

[18] Basile DP, Anderson MD, Sutton TA. Pathophysiology of acute kidney injury. Compr Physiol. 2012 Apr;2(2):1303-53.

[19] Wilhelm MP, Schlensak C, Hoh A et al. Controlled reperfusion using a simplified perfusion system preserves function after acute and persistent limb ischemia: a preliminary study. J Vasc Surg. 2005 Oct;42(4):690-4.

[20] Currie IS, Wakelin SJ, Lee AJ et al. Plasma creatine kinase indicates major amputation or limb preservation in acute lower limb ischemia. J Vasc Surg. 2007 Apr;45(4):733-9.

[21] Butt T, Lehti L, Apelqvist J et al. Contrast-Associated Acute Kidney Injury in Patients with and without Diabetes Mellitus Undergoing Computed Tomography Angiography and Local Thrombolysis for Acute Lower Limb Ischemia. Vascular and Endovascular Surgery. 2022;56(2):151-157.

[22] Saziye K, Mustafa C, Ilker U, Afksendyios K. Comparison of vacuum-assisted closure device and conservative treatment for fasciotomy wound healing in ischemia reperfusion syndrome: preliminary results. Int J Wound J 2011; 8: 229 - 236.

[23] Zannis J, Angobaldo J, Marks M, et al. Comparison of fasciotomy wound closures using traditional dressing changes and the vacuum-assisted closure device. Ann Plast Surg 2009; 62: 407 - 409.

[24] Acosta S, Björck M, Wanhainen A. Negative-pressure wound therapy for prevention and treatment of surgical-site infections after vascular surgery. Br J Surg 2017; 104: e75-e84.

[25] Monsen C, Wann-Hansson C, Wictorsson C et al. Vacuum-assisted wound closure versus alginate for the treatment of deep perivascular wound infections in the groin after vascular surgery. J Vasc Surg. 2014 Jan;59(1):145-51.

[26] Monsen C, Acosta S, Mani K et al. A randomised study of NPWT closure versus alginate dressings in peri-vascular groin infections: quality of life, pain and cost. J Wound Care. 2015 Jun;24(6):252, 254-6, 258-0.

[27] Jauregui JJ, Yarmis SJ, Tsai J et al. Fasciotomy closure techniques. J Orthop Surg (Hong Kong). 2017 Jan;25(1):2309499016684724.

[28] Darwood R, Berridge DC, Kessel DO et al. Surgery versus thrombolysis for initial management of acute limb ischaemia. Cochrane Database Syst Rev. 2018 Aug 10;8(8):CD002784.

[29] Farrow C, Bodenham A, Troxler M, Acute limb compartment syndromes. Continuing Education in Anaesthesia, Critical Care & Pain Volume 11, Issue 1. 2011 Feb,24–28.

[30] McMillan TE, Gardner WT, Schmidt AH et al. Diagnosing acute compartment syndrome-where have we got to? Int Orthop. 2019 Nov;43(11):2429-2435.

Figure legends

Figure 1. Estimated glomerular filtration rate (e-GFR) (mL/min/1.73m^2) at different time points during in-hospital period in patients undergoing prophylactic and therapeutic fasciotomy after revascularization for acute lower limb ischemia.

Figure 2. Kaplan-Meier estimates of cumulative proportion of healed fasciotomies in patients undergoing prophylactic and therapeutic fasciotomy. Life table showing open, non-healed, fasciotomy wounds at each time point in respective groups. Patients whose fasciotomy did not heal were not included.

Table I. Patient characteristics prior to admission

	All (n=76)	Prophylactic fasciotomy (n=40)	Therapeutic fasciotomy (n=36)
Age, mean (SD) (n=76)	71.6 (11.7)	72.3 (10.7)	71.0 (11.3)
Female % (n=76)	31.6 (24)	37.5 (15)	25.0 (9)
Smoking % (n=69)	29.0 (20)	35.3 (12/34)	22.9 (8/35)
Previous smoking % (n=69)	37.7 (26)	38.2 (13/34)	37.1 (13/35)
Hypertension % (n=76)	77.6 (59)	75.0 (30)	80.6 (29)
Anemia % (n=73)	17.8 (13)	23.1 (9/39)	11.8 (4/34)
Diabetes mellitus % (n=76)	21.1 (16)	17.5 (7)	25.0 (9)
Atrial fibrillation % (n=76)	34.2 (26)	37.5 (15)	30.6 (11)
Ischemic heart disease % (n=76)	35.5 (27)	30.0 (12)	41.7 (15)
Previous claudication % (n=76)	40.8 (31)	37.5 (15)	44.4 (16)
Renal insufficiency % (n=75)	56.0 (42)	66.7 (26/39)	44.4 (16/36)
Dialysis prior to admission % (n=73)	1.4 (1)	2.6 (1/38)	0.0 (0/35)

SD=standard deviation

Table II. Patient symptoms and findings prior to intervention and management

	All (n=76)	Prophylactic fasciotomy (n=40)	Therapeutic fasciotomy (n=36)
Symptom duration (hours), median (IQR) (n=75)	18.5 (6.8–48.0)	13.5 (6.0-45.0)	48.0 (14.0-120.0) (n=35)
Ankle-brachial index, median (IQR) (n=49)	0.0 (0.0-0.0)	0.0 (0.0-0.0) (n=20)	0.0 (0.0-0.0) (n=29)
Rutherford class IIb % (n=76)	76.3 (58)	92.5 (37)	58.3 (21)
CT-angiography pre intervention % (n=76)	51.3 (39)	50.0 (20)	52.8 (19)
Bilateral arterial occlusions % (n=76)	17.1 (13)	25.0 (10)	8.3 (3)
Supra-inguinal occlusion % (n=76)	34.2 (26)	42.5 (17)	25.0 (9)
Native artery thrombus % (n=76)	23.7 (18)	32.5 (13)	13.9 (5)
Native artery embolus % (n=76)	27.6 (21)	35.0 (14)	19.4 (7)
PAA occlusion % (n=76)	17.1 (13)	15.0 (6)	19.4 (7)
Primary open vascular surgery % (n=76)	69.7 (53)	100.0 (40)	36.1 (13)
CDT % (n=76)	28.9 (22)	0.0 (0)	61.1 (22)
Other endovascular procedure % (n=76)	1.3 (1)	0.0 (0)	2.8 (1)

CDT= Catheter directed thrombolysis, CT= Computed tomography, IQR= Inter quartile range, PAA=Popliteal artery aneurysm

Table III. Development of e-GFR over in-hospital period

	Admission e-GFR, mean (SD)	Discharge e-GFR, mean (SD)	Change in e-GFR, mean (95% CI)	P-value
All n=69	56.6 (SD: 23.1)	63.0 (SD: 24.0)	6.4 (95% CI: 3.0-9.8)	<0.001
Prophylactic fasciotomy n=36	53.8 (SD: 26.5)	62.0 (SD: 28.1)	8.2 (95% CI: 2.4-14.1)	0.007
Therapeutic fasciotomy n=33	59.8 (SD: 18.7)	64.2 (SD: 18.8)	4.4 (95% CI: 1.1-7.7)	0.010
***Difference in change in e-GFR between PF and TF**			0.3 (95% CI:-6.7-7.4)	0.93

CI=confidence interval, eGFR= estimated glomerular filtration rate ml/min/1.73m^2, SD=standard deviation

*= Adjusted for sex, motor deficit and admission e-GFR.

Table IV. Comparison of eGFR at different time points, change in eGFR and new onset dialysis

	All (n=76)	Prophylactic fasciotomy (n=40)	Therapeutic fasciotomy (n=36)	Mean difference between groups	p-value
***eGFR admission, mean (SD) (n=75)**	56.6 (SD: 23.2)	53.3 (95% CI: 43.8-62.8)	59.4 (95% CI: 51.1-67.7) (n=39)	-6.1 (95% CI: -17.8-5.5)	0.30
***eGFR lowest point, mean (SD) (n=75)**	44.4 (SD: 23.6)	43.6 (95% CI: 33.8-53.3)	45.7 (95% CI: 37.2-54.3) (n=39)	-2.2 (95% CI: -14.1-9.8)	0.72
***eGFR discharge, mean (SD) (n=69)**	63.0 (SD: 24.0)	60.8 (95% CI: 50.3-71.2)	64.4 (95% CI: 55.4-73.5) (n=36)	-3.7 (95% CI: -16.5-9.2) (n=33)	0.57
New onset temporary dialysis following revascularization % (n=71)	5.6 (4)	5.7 (2/35)	5.6 (2/36)	-	0.98

CI=confidence interval, eGFR= estimated glomerular filtration rate ml/min/1.73m^2, SD=standard deviation

*=Adjusted for sex and motor deficit in comparison between PF and TF.

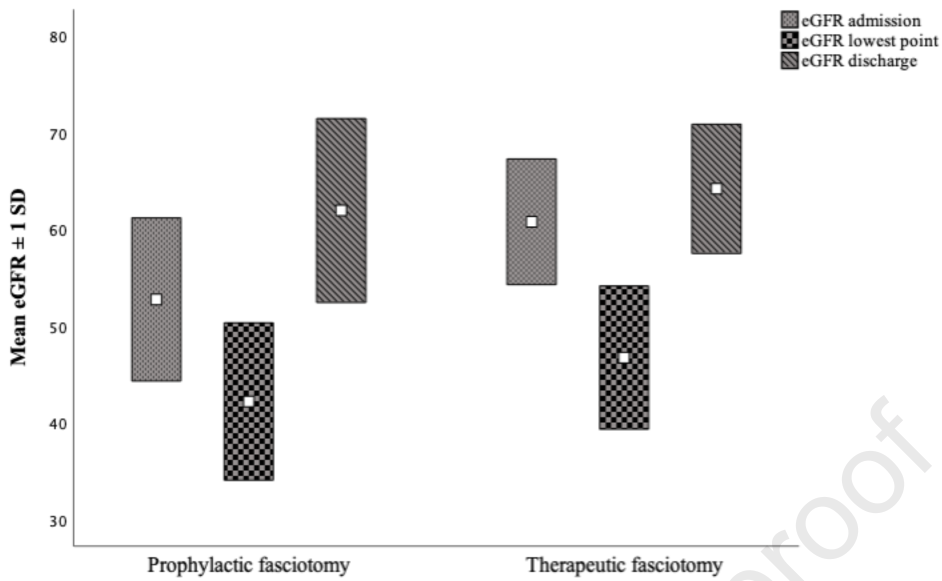
Table V. Wound outcomes regarding timing of fasciotomy

	All n=76	Prophylactic fasciotomy (n=40)	Therapeutic fasciotomy (n=36)	p-value
Bilateral fasciotomies % (n=76)	7.9 (6)	12.5 (5)	2.8 (1)	0.49
Four compartments fasciotomy % (n=76)	92.1 (70)	97.5 (39)	86.1 (31)	0.13
Fasciotomy wound healed % (n=76)	68.4 (52)	57.5 (23)	80.6 (29)	0.031
Fasciotomy healing time, median days (IQR) (n=51)	73.0 (55.0-96.0)	67.5 (53.3-94.5) (n=22)	73.0 (52.0-94.5) (n=29)	0.44
Any wound complication % (n=67)	85.1 (57)	78.8 (26/33)	91.2 (27/35)	0.16
Wound infection % (n=67)	71.6 (48)	60.6 (20/33)	82.4 (28/34)	0.048
Other wound complications % (n=65)	47.7 (31)	61.3 (19/31)	35.3 (12/34)	0.036
Wound revision performed in OR % (n=67)	55.2 (37)	51.5 (17/33)	58.8 (20/34)	0.55
Secondary suture % (n=71)	64.8 (46)	66.7 (24/36)	62.9 (22/35)	0.74
NPWT % (n=72)	51.4 (37)	38.9 (14/36)	63.9 (23/36)	0.034
Split skin graft % (n=71)	40.8 (29)	33.3 (12/36)	48.6 (17/35)	0.19
Readmission for wound complication % (n=62)	16.1 (10)	13.8 (4/29)	18.2 (6/33)	0.64
Reduced neuro-muscular function at discharge % (n=60)	30.0 (18)	34.4 (11/32)	32.1 (9/28)	0.86

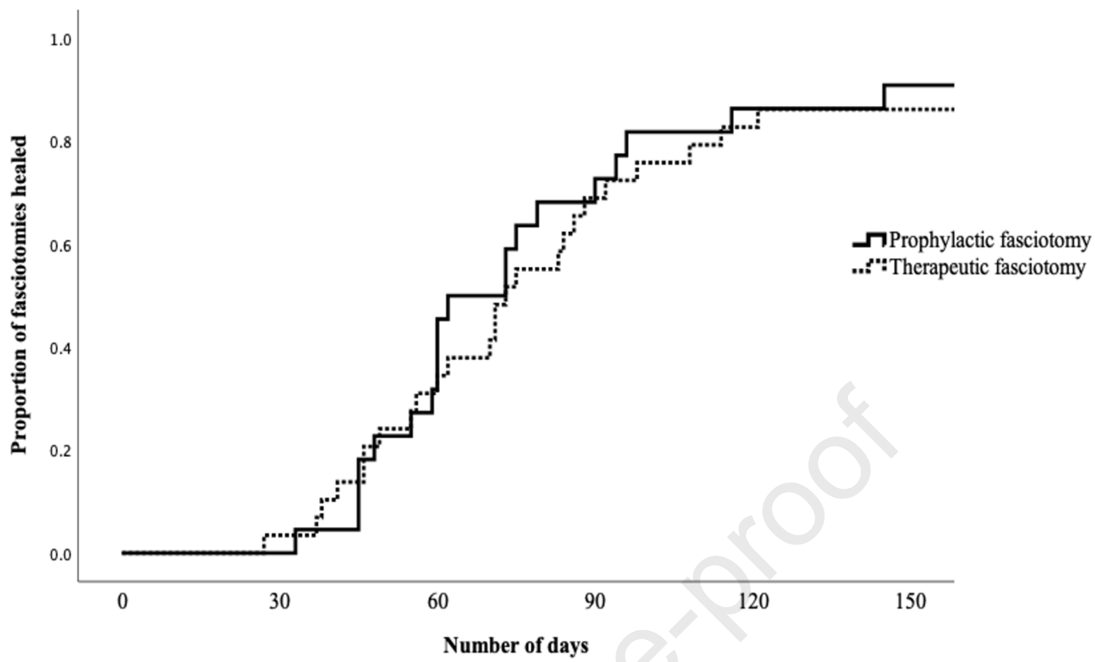
IQR= inter quartile range, NPWT=negative pressure wound therapy, OR=operating room

Table VI. Major amputation and mortality at 30-days and 90-days

	All n=76	Prophylactic fasciotomy (n=40)	Therapeutic fasciotomy (n=36)	p-value
Major amputation 30-days % (n=75)	13.3 (10)	17.5 (7/40)	8.6 (3/35)	0.26
Mortality 30-days % (n=75)	8.0 (6)	10.0 (4/40)	5.7 (2/35)	0.50
Major amputation and/or mortality 30-days % (n=75)	18.7 (14)	25.0 (10/40)	11.4 (4/35)	0.13
Major amputation 90-days % (n=75)	13.3 (10)	17.5 (7/40)	8.6 (3/35)	0.26
Mortality 90-days % (n=75)	17.3 (13)	22.5 (9/40)	11.4 (4/35)	0.21
Major amputation and/or mortality 90-days % (n=75)	28.0 (21)	37.5 (15/40)	17.1 (6/35)	0.050



eGFR admission
eGFR lowest point
eGFR discharge
80
70
60
50
40
30
Mean eGFR ± 1 SD
Prophylactic fasciotomy
Therapeutic fasciotomy



22	22	12	6	3	2	Prophylactic fasciotomy
29	28	19	9	5	4	Therapeutic fasciotomy

Highlights

- Wound infection rate was higher after therapeutic fasciotomy (TF)
- Rate of other wound complications where higher after prophylactic fasciotomy (PF)
- Fasciotomies are prone to wound healing times of over two months after TF and PF
- Renal function improved equally over the in-hospital period in the TF and PF group