Case Series

Angioplasty in Critical Limb Ischaemia: One-year Limb Salvage Results

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Abstract

Introduction: Lower extremity amputation prevention (LEAP) is an ongoing programme in our institution aimed at limb salvage in patients with critical limb ischaemia (CLI). Patients in the LEAP programme with reconstructible anatomy on initial Doppler imaging received either bypass surgery or percutaneous transluminal balloon angioplasty (PTA). We describe the 1-year limb salvage rates in 46 consecutive patients with CLI who received PTA in 2005. Clinical Picture: A total of 46 patients, 28 women and 18 men, between the ages of 40 and 91 years old (mean age, 70.8) received PTA in 2005. The most common presenting symptom was rest pain (n = 23), followed by pre-existing gangrene (n = 20), non-healing ulcer (n = 17) and cellulitis (n = 8). The majority of the patients (57%) had 3 to 4 risk factors. Diabetes mellitus (91%) and hypertension (80%) were the 2 most common risk factors. The patients were kept under surveillance for periods ranging from 12 to 21 months with a mean of 13.3 months, both clinically and with haemodynamic measurements [ankle-brachial index (ABI), toe pressure (TP) and digital-brachial index (DBI)]. Treatment: The aim of PTA is to achieve straight-line flow from the abdominal aorta down to either a patent dorsalis pedis or plantar arch with limb salvage as the ultimate goal. The patterns of the treated segments were as follows: aorto-iliac occlusions (n = 3), pure infrapopliteal disease (n = 5), femoropopliteal disease with at least 1 good infrapopliteal run-off vessel (n = 16) and combined femoropopliteal and infrapopliteal disease (n = 25). Technical success was achieved in 89% of patients (41 out of 46 patients). The most common cause of technical failure is the inability to cross long chronic total occlusions. Outcome: Paired T test was performed and showed statistically significant improvement in haemodynamic markers within the technically successful group. This included increase in the mean ABI from 0.62 (pre-angioplasty) to 0.91 (Day 1 post-angioplasty), an increase of 0.29 [95% confidence interval (95% CI), 0.1953 to 0.3875; *P* <0.001]. One year post-angioplasty, the mean ABI was 0.84, an increase of 0.22 (95% CI 0.1512 to 0.3121; *P* <0.001). There was also significant increase in the mean DBI of 0.17 from 0.23 to 0.41 (pre-angioplasty versus Day 1 post angioplasty – 95% CI of 0.1006 to 0.2433; *P* <0.001). In addition, significant increase in the mean TP of 28.2 mmHg from 36.8 to 63.2 mmHg (pre-angioplasty versus Day 1 post angioplasty – 95% CI, 18.493 to 37.939; *P* <0.001) was also noted. Of the 23 patients who presented with rest pain, total abolishment of symptoms was achieved in 21 patients (91%). Healing of pre-existing gangrene was attained in 15 patients (66%). Five patients subsequently received minor amputation for pre-existing gangrene. Clinical improvement in all the patients who presented with non-healing ulcers (n = 17) and cellulitis (n = 8) was attained. More importantly, all healed ulcers remained healed throughout the study period. The limb salvage rates were 93% at 1 month, 87% at 3 months, 82% at 6 months and 78% at 1 year. Conclusion: Angioplasty is a safe and effective limb salvage method in patients with CLI and has a high 1-year limb salvage rate.

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Key words: Angioplasty, Arterial occlusive diseases, Balloon, Lower extremity, Treatment outcome

Introduction

Critical limb ischaemia (CLI) is the most severe form of peripheral vascular disease where there is inadequate blood flow to a limb to maintain reasonable metabolic requirement of the tissues at rest. Eventual loss of limb is the feared sequelae of CLI. The TransAtlantic Inter-Society Consensus (TASC) defines CLI as persistently recurring ischaemic rest pain requiring opiates for at least 14 days, foot or toe ulceration or gangrene and ankle-brachial index (ABI)<0.40, toe pressure (TP) <30 mmHg, systolic ankle pressure <50 mmHg, flat pulse volume waveform and absent pedal pulses.[1]

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The lower extremity amputation prevention (LEAP) is a comprehensive programme aimed at reducing lower extremity amputations in individuals with peripheral vascular disease. The main aims of LEAP are to: 1) detect and treat early chronic ischaemic lesions, 2) offer alternatives to amputations in surgically untreatable patients, 3) preserve the remaining limb after major amputation, and 4) reduce global risk for cardiovascular disease. It is hence a multidisciplinary programme with involvement at various levels from risk factors modification and patient education at the primary healthcare level, to active treatment of critical limb ischaemia (CLI) at tertiary institutions. In our institution, all patients presenting with CLI are enrolled into the LEAP programme. Since its inception in 2001 up to 2005, a total of 301 patients with CLI had been enrolled.

Patients presenting with CLI to our institution first received Doppler vascular assessment of both lower limbs to assess anatomical "reconstructibility" of the lower limb arteries. Those with reconstructible anatomy received either bypass surgery or percutaneous transluminal angioplasty (PTA). The patients with non-reconstructible anatomy received hyperbaric oxygen, lumbar sympathectomies or pneumatic compression. Patients who were unfit for any of the above received primaryamputation and were put under close surveillance of the remaining limb.

Clinical Picture

In 2005, a total of 46 consecutive patients with CLI were enrolled into the PTA treatment arm. We studied the 1-year limb salvage results of these patients. The patients were enrolled in the PTA treatment arm based on the following inclusion criteria. 1) Patients who were medically unfit for bypass surgery; 2) Patients who were fit for bypass surgery but chose to have PTA; 3) All patients must have either a patent dorsalis pedis or a patent plantar arch on baseline Doppler vascular maps. Patients with long arterial occlusion >15 cm or those with occlusion of both the dorsalis pedis and plantar arch were excluded. The participants, 28 women and 18 men, were between the ages of 40 and 91 years (mean age, 70.8). The most common presenting symptom was rest pain (n = 23), followed by pre-existing gangrene (n = 20), non-healing ulcer (n = 17) (Fig. 1) and cellulitis (n = 8). The majority of the patients (57%) had 3 to 4 risk factors with 17% of the patients having more than 4. Diabetes mellitus (DM) (91%) and hypertension (80%) were the 2 most common risk factors (Fig. 2).

Treatment

The objective of the angioplasty (which is also the definition of technical success) was to achieve straight-line flow (SLF) from the aorta down to either a patent dorsalis

Fig 1a.

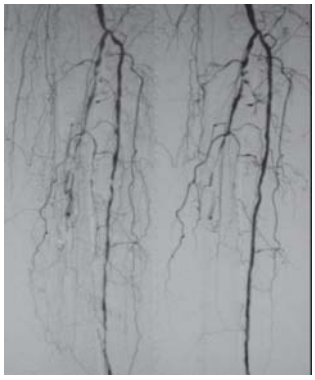

Fig 1b.

Fig 1c.

Fig 1c.

Fig.1. A 72-year-old diabetic with chronic non-healing heel ulcer (Fig 1a). Pre and post-percutaneous transluminal angioplasty (PTA) angiograms (Fig. 1b and 1c respectively) show extensive atherosclerotic disease with irregular lumen in opacified vessels. In the pre-PTA angiogram, there is poor infrapopliteal single vessel (anterior tibial artery) run-off into the foot. Long occlusions of the peroneal and posterior tibial arteries are also present but not angioplastied. The post-PTA angiogram demonstrates technical success in achieving "straight-line flow" into the dorsalis pedis. The patient needed repeat angioplasty at 4 months (not shown). Serial photographs (Fig 1d, left to right, 3 months, 6 months and 1 year post-PTA) over a 1-year period showing healing of the ulcer; this was accompanied by ankle-brachial index (ABI) improvement from 0.38 (pre-angioplasty) to 0.86 (1-year post-angioplasty).

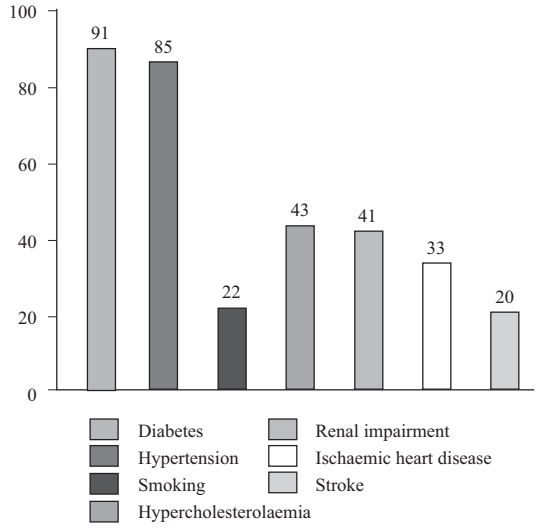

Fig. 2. Bar chart showing the incidence of risk factors for CLI in the study cohort. Diabetes mellitus and hypertension are the top 2 risk factors.

pedis or plantar arch. In addition, technical success was also considered if SLF was attained from the aorta into a peroneal artery that supplies either a patent dorsalis pedis or plantar arch via collateral reconstitution. All patients who were enrolled in the PTA treatment arm received PTA as the only form of treatment (apart from medical therapy for risk factors modification). The aim of treatment is limb salvage, i.e. to leave the patients who have CLI with a functional limb.

All angioplasties were performed by 1 of 3 interventional radiologists in our department. Antegrade arteriotomy was preferred and performed in all patients who had no evidence of aorto-iliac disease on Doppler arterial map. Vascular access was secured with a 5.5F vascular sheath (Terumo Corporation, Tokyo, Japan) in all cases. Intra-arterial heparin 3000 IU was routinely administered via the vascular sheath at the start of the procedure and intra-arterial glycerin trinitrate 200 mcg was administered before all tibial angioplasties. 0.035" wires (Terumo Corporation, Tokyo, Japan) were used to cross most femoropopliteal lesions while smaller diameter 0.018" wires (V-18 control wire; Boston Scientific) were used to cross infrapopliteal lesions. Balloons used for angioplasties included: 5 x 40 mm and 5 x 100 mm 5F (Ultrathin, Boston Scientific) for most superficial femoral artery lesions, 3 x 40 mm and 3 x 100 mm 3F microballoons (Savvy, Cordis/Johnson & Johnson) for most infrapopliteal lesions. Dissections (if any) were treated first line with prolonged balloon inflations. All vascular sheaths were removed 2 hours after angioplasty and haemostasis was controlled by manual compression for at least 10 minutes. Antiplatelet therapy was started immediately post-PTA using aspirin 100 mg or clopidogrel bisulfate 75 mg if there was aspirin contraindication.

A total of 42 femoral, 3 popliteal and 1 brachial arteriotomies were performed and the angiograms obtained. The patterns of treated stenoses were as follows: aorto-iliac occlusions (n = 3), pure infrapopliteal disease (n = 5), femoropopliteal disease with at least 1 good infrapopliteal run-off vessel (n = 16) and combined femoropopliteal and infrapopliteal disease (n = 25). Technical success was achieved in 89% (41 out of 46) of patients. The most common cause of technical failure was the inability to cross long chronic total occlusions (CTO). The locations of the CTOs in the failed cases were popliteal artery (n = 1; 2 cm in length), anterior tibial artery (n = 3; 15, 20 and 23 cm in lengths) and complete distal posterior tibial (n = 1). In all 5 failures, subintimal PTA was attempted with failed re-entry.

Transluminal angioplasty was performed in 37 patients and subintimal angioplasty was successfully performed in 4 patients. Only in 1 case was an endovascular stent deployed (over an iliac stenosis). In the technically successful group, repeat interval angioplasties were performed on 4 patients at 6 weeks (n = 2), 4 months (n = 1) and 7 months (n = 1).

Surveillance

Besides ABI, TP and digital-brachial index (DBI) measurements were also obtained before angioplasty and on Day 1 post-angioplasty. Post-procedure surveillance was in the form of 3 monthly clinic review by the referring vascular surgeon during which ABI as well as assessment for relevant clinical improvement (e.g. wound healing, rest pain) was performed. The patients were kept under surveillance for periods ranging from 12 to 21 months, with a mean of 13.3 months.

Outcome

Paired T test was performed and showed statistical improvement in the haemodynamic markers within the technically successful group. This included mean ABI improvement from 0.62 (pre-angioplasty) to 0.91 (Day 1 post-angioplasty), significant increase of 0.29 [95% confidence interval (95% CI), 0.1953 to 0.3875; P <0.001]. One year post-angioplasty, the mean ABI was 0.84, an increase of 0.22 (95% CI, 0.1512 to 0.3121; P <0.001). Significant increase in mean DBI of 0.17 from 0.23 to 0.41 (pre-angioplasty versus Day 1 post angioplasty) was also noted with a 95% CI of 0.10063 to 0.24326 (P <0.001). Significant increase in mean TP of 28.2 mmHg from 36.8 to 63.2 mmHg (pre-angioplasty versus Day 1 post angioplasty), with a 95% CI of 18.493 to 37.939 (P <0.001) was also noted.

Within the technically successful group, repeat angioplasty was performed on 4 patients. The reasons for repeat angioplasty included decreased in ABI by more than 0.15 (n = 2) and persistent non-healing of wound (n = 2) during follow-up. These 4 patients had intact limbs by the end of the study period.

Among the technical failures (n = 5), 3 went on to receive amputations (1 below-knee, 1 ray and 1 forefoot amputation). One patient underwent successful bypass surgery while another died of an unrelated cause 3 months later, with lower limbs intact. Within the study period, none of the patients within the technically successful group required bypass surgery.

There were no instances of significant distal embolisation, arterial perforations or procedure-related death or 30-day mortality. All intimal dissections encountered were successfully treated with prolonged balloon inflation with no case needing bail-out stenting. PTA-related complications encountered included 1 case of early arterial thrombosis (requiring an above-knee amputation after a failed thrombolysis), 2 cases of groin haematomas (resolved with conservative treatment) and 1 case of pseudoaneurysm (treated with ultrasound-guided compression).

The limb salvage rates were 93% at 1 month, 87% at 3 months, 82% at 6 months and 78% at 1 year. Minor amputations up to the level of Syme amputation as well as amputations of existing gangrenous lesions were not considered limb loss. Within the study period, there were 3 deaths from unrelated causes (sepsis, necrotising fasciitis of the elbow and pneumonia); more importantly, all 3 deceased patients had intact limbs at the time of death. Kaplan-Meier analysis of both the limb salvage rate and combined limb salvage and survival rate are illustrated in Figures 3 to 5.

Clinically, of the 23 patients who presented with rest pain, total abolishment of symptoms was achieved in 21 patients (91%). Healing of pre-existing gangrene was obtained in 15 patients (66%). Five patients within the technically successful group subsequently received minor amputation for pre-existing gangrene. Clinical improvement in the all the patients who presented with non-healing ulcers (partial or complete healing) and cellulitis was obtained. More importantly, all healed ulcers remained healed throughout the study period.

Discussion

CLI represents the most severe stage of peripheral vascular disease, with limb loss being a feared complication. The clinical presentations range from rest pain, ischaemic ulcers to gangrene. Apart from the potential loss of limb which is usually evident at presentation, the co-existent cardiovascular morbidity and mortality presents an even greater threats.[2] The above form the basis of the LEAP programme which targets both limb salvage as well as mortality reduction.

Studies have shown that the most important aspect of life quality for CLI patient is actually that of limb salvage[3] compared to other markers such as rest pain and ulcer healing, and it is believed that limb salvage should be the goal in most patients with CLI.[4,5] Hence, we believe that leaving the patient with an ambulatory foot should be the paramount goal. It has been shown that limb salvage by means of revascularisation in CLI is more cost-effective, leads to better quality of life for most patients, and is associated with lower perioperative morbidity and mortality compared to amputation.[4,5]

With conservative therapy (e.g. medical therapy, chemical lumbar sympathectomy), a 25% to 49% success rate with non-healing wounds and 1-year limb salvage rate up to 46% has been reported.[6,7] Both surgical bypass and endovascular revascularisation are currently accepted

	Superfical femoral artery	Infrapopliteal
Chronic total occlusion	n = 14, range: 1-25 cm, mean = 8.23 cm	n = 24, range: 1-23 cm mean = 9.92 cm
Severe lesions (>70% stenosis)	n = 42, range: 1-30 cm mean = 9.26 cm	n=22, range: 1-25 cm, mean = 9.50 cm

Fig. 3. Summary of the locations of the chronic total occlusions and severe stenosis.

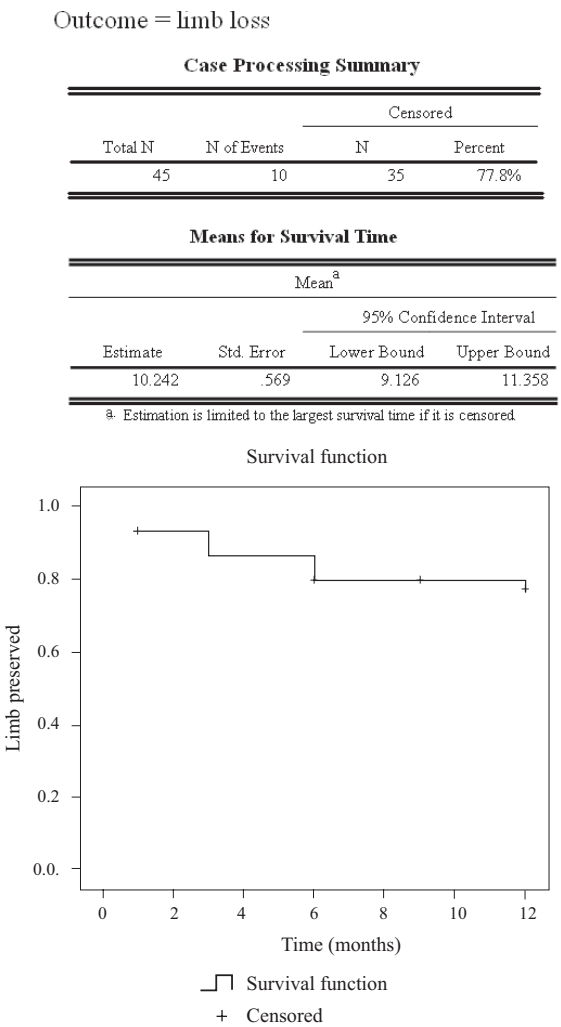

Fig. 4. Kaplan-Meier curve showing the relationship of limb loss over time.

Outcome = limb loss + death

Case Processing Summary

Total N	N of Events	Censored N	Censored Percent
45	13	32	71.1%

Means for Survival Time

Mean[a]			
		95% Confidence Interval	
Estimate	Std. Error	Lower Bound	Upper Bound
9.822	.597	8.652	10.993

a. Estimation is limited to the largest survival time if it is censored.

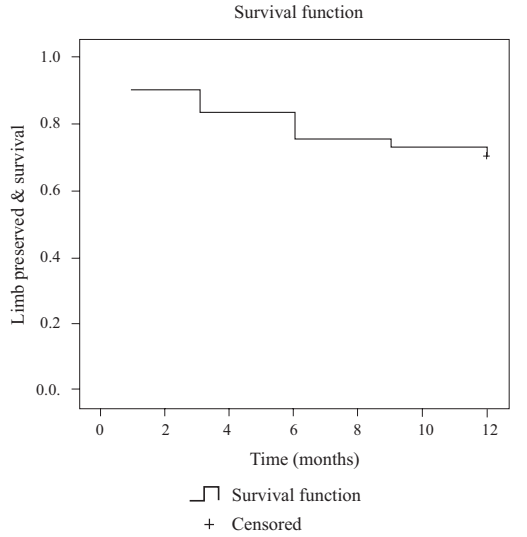

Fig. 5. Kaplan-Meier curve showing the relationship of limb loss and death over time.

modalities for CLI.[8,9] Surgical revascularisation (in the form of arterial bypass) has traditionally been the main treatment for CLI with a well-documented long-term patency and limb salvage rate.[10] In most surgical series, the 3-year bypass patency rates of calf arteries ranged from 40% for prosthetic bypasses to 85% for saphenous vein bypasses.[11-15] However, technical and anatomical limitations such as the availability of long vein-graft and the presence of infection near the site of planned distal anastomosis often make surgery technically challenging. To further compound the problem, patients with CLI often have multiple comorbidities (e.g. DM, cardiovascular disease) with increased general anaesthetic risk and poor tolerance for prolonged surgery. PTA is thus an attractive alternative in this subset of patients.

Although the long-term patency of angioplasty is not as good compared to arterial bypass surgery, it is still an attractive option if limb salvage is the ultimate goal, taken in the context of limited life expectancy in many of the patients with CLI. Notably, the clinical results and limb salvage after PTA are known to be higher than the haemodynamic patency rate and it has been repeatedly shown that healed ischaemic lesions do not recur even with restenosis of the dilated vessels. That is, less blood flow is required to keep tissues healed than to achieve healing. Surgical bypass patency, in contrast, always exceeds the limb salvage rate.[16] However, despite the lower long-term patency rate (versus surgery), it has been showed in a retrospective study by Kudo et al[9] that when compared to open surgery, angioplasty can replace open surgical procedure without compromise in outcomes. Furthermore, the authors also showed that open surgical procedures have been largely replaced by angioplasty procedure and that angioplasty is not only feasible and safe, but also an effective procedure and is the procedure of choice for the primary and secondary treatment of CLI. Lastly, from the results, the authors also advocated that open surgical procedures be reserved for lesions technically unsuitable for endovascular procedures and patients who do not demonstrate clinical improvement after angioplasty. The Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) multicentre trial[11] also further showed that a bypass-surgery-first and a balloon-angioplasty-first strategy, in suitable candidates with infra-inguinal disease, are associated with broadly similar outcomes in terms of amputation-free survival, and in the short term. In addition, the trial showed that open surgery is more expensive than angioplasty. Furthermore, the perimortality rate of PTA compares favourably at around 1%-3%[11,12] to 1.8%-6% for distal bypass surgery.[12,13]

The reported success rate of endovascular treatment of CLI is around 92% to 96% with a 1-year limb salvage rate of 68.6% to 90%[13-17] and our current study result (78%) is comparable to these published figures. The published 1-year limb salvage rate of surgical bypass is 81% to 87%.[18,19] The published 3-year limb salvage rate of PTA is around 77% to 94%[3,20,21] and this will serve as a comparison for our ongoing long-term study. Currently, many promising novel endovascular techniques such as cryoplasty, drug-eluting stenting, plaque debulking lasers and excision atherectomy are being investigated and are potentially useful adjuncts to PTA. Hopefully, these adjuncts will increase both the technical success and limb salvage rates in the future. However, a detailed discussion of these techniques is beyond the scope of this paper.

Besides lifelong anti-platelet therapy, our patients also undergo aggressive management of existing risk factor in a multidisciplinary setting to optimise PTA results. It is known that in patients with CLI, the co-existing cardiovascular morbidity and mortality pose an even greater risk.[22] Known risk factors for CLI include DM, advanced age (age >80 years), smoking, hypertension, hypercholesterolaemia and renal failure, with accelerated atherosclerosis as the main aetiology. Neuropathy, infection and vasculitides (e.g. thromboangiitis obliterans) are also less common, albeit known risk factors.

Singapore has one of the highest incidence of DM. It is estimated that 8.9% of the Singapore population between the ages of 18 and 69 years are diabetic.[23] This is reflected in our study where DM is the commonest risk factor for CLI in our cohort and we adopt an aggressive approach in treating DM. DM affects CLI in many ways. Premature and advance atherosclerosis, together with peripheral neuropathy, impaired cellular immunity and impaired wound healing make CLI a complex problem among diabetics. It has been shown that DM significantly increases the risk of CLI (up to 4 times compared to the general population).[24] Furthermore, it is estimated that 40% to 45% of all amputees are diabetic[25] and a diabetic patient with CLI is 10 times more likely than a non-diabetic to require an amputation.[26] The preferential involvement of distal calf vessels is commonly described in diabetics[27] and this probably can account for the distribution of the treated segments in our study where majority of the patients had infrapopliteal disease. In our institution, all the patients in our LEAP programme received endocrinologist evaluation for optimisation of glycaemic control.

There are several limitations to our study. Firstly, the anatomical success rate (i.e. vessel patency/restenosis) is not known because patients who improve haemodynamically and clinically do not routinely receive post-PTA imaging. For our future cohorts, perhaps non-invasive techniques such as Doppler ultrasound or magnetic resonance[28] should be considered for anatomical follow-up. Secondly, the functional improvement (e.g. walking distance) of our patients cannot be evaluated as functional status assessment is not performed routinely before PTA in our institution. Lastly, the compliance of the patients to risk factors and lifestyle modification that can impact the result of PTA is not known either.

In conclusion, our 1-year study shows that PTA in CLI patients is a safe and viable treatment option and can achieve a high short-term limb salvage rate. However, further long-term study will be needed to fully elucidate the actual potential of PTA at limb salvage.

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