

## Percutaneous transluminal lower limb angioplasty [PTA] for chronic limb threatening ischaemia [CLTI] in a low resource setting - 4 year experience

Cassim MRN, Godahewa S, Paviththiran S, Wijeyaratne SM  
Department of Surgery, Faculty of Medicine, University of Colombo, Sri Lanka.

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### Introduction

With the emergence of diabetes mellitus, there is a significant burden of peripheral occlusive arterial disease [POAD] in Sri Lanka [1]. The age-sex standardized prevalence of diabetes mellitus for Sri Lankans aged 20 years and above was 10.3% [2]. The worldwide prevalence of POAD was evaluated from several studies and range from 3% to 10%, increasing to 15% to 20% in persons over 70 years [3]. A study done in elderly urban Chinese population reveals a 20% prevalence of POAD [4]. In another study done in South Indian population, the overall prevalence of POAD was 3.2% with higher prevalence [7.8%] in known diabetic patients compared to newly diagnosed diabetic patients [3.5%] [4]. Age and sex adjusted prevalence of POAD in Sri Lankan population was found to be 3.6% in a study done in 2013 [6].

A meta-analysis of 13 studies and 1527 patients with a median follow up of one year revealed that untreated chronic limb threatening ischaemia [CLTI] has a major amputation free survival rate of 56%. [7]. The definitive treatment for chronic limb threatening ischaemia is either lower limb bypass procedures or angioplasty with or without stenting [3, 8]. Revascularization is indicated for patients with either severe debilitating intermittent claudication, rest pain or tissue loss due to ischaemic ulcer or gangrene [8]. According to Inter-society consensus for the management of POAD, lower limb bypass surgery is preferred over angioplasty for TASC type C and type D lesions [3]. However, lower limb bypass surgery is unsuitable for patients with significant co-morbidities and poor cardiac function. It is also associated with significant postoperative complications when compared to angioplasty. Bypass surgery is also not suitable in some patients with poor runoff arteries i.e poor target arteries to bypass onto. If the stenotic segments are focal it may be easily treated with angioplasty as well. 30-day mortality following lower limb

bypass surgery is reported to be 2% to 8% and five-year graft failure rates vary from 50% to 90% [9].

In recent years, with continuing advances in imaging techniques, angioplasty equipment, endovascular expertise and unsuitability of patients for bypass procedures, the use of PTA as a primary treatment for ischaemic foot ulcers has been increasing [10, 11, 12].

In order to improve the primary patency rate and durability of the intervention, placement of a metallic stent following PTA became another fascinating step forward in the evolution of endovascular interventions. During 1978-1985, Julio Palmaz developed the first ever balloon expandable stent and it was approved by the FDA for peripheral arterial use in 1991 [13]. Self-expanding stents, with the ability of regaining their original configuration after compression were invented to be placed in arteries which are repeatedly subject to external forces, such as superficial femoral arteries.[14]. Drug Eluting Stent was introduced to prevent the stent failure from restenosis. DESs slowly release the drugs which inhibit cell proliferation, fibrosis and thereby prevent thrombi formation and restenosis.

Drug coated balloons were also introduced recently with hope of improving the primary patency rates by suppressing the neo-intimal hyperplasia and restenosis of diseased arteries. This method is a combination of balloon angioplasty and drug delivery to the local site. The balloon consists of drugs [commonly paclitaxel] which suppresses cell proliferation. The drug should also have the pharmacokinetic properties to be rapidly absorbed by the intima of arteries and to exert a sustained action to prevent restenosis [11,14,15].

Another alternative to balloon angioplasty is atherectomy, a procedure done to remove the atherosclerotic plaques from peripheral arteries. The atherectomy device consist of cutting blades which shave off the atherosclerotic plaques, which is aspirated through tip of catheter connecting to negative pressure system. There are four different types of atherectomy available to treat the peripheral arteries. They are directional atherectomy, rotational atherectomy, laser atheroablation and orbital atherectomy [14,16].

The amputations free survival for this patient population in a

Correspondence: Rezni Cassim

E-mail: rezni@srg.cmb.ac.lk

 <https://orcid.org/0000-0002-4826-6196>

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low resource setting is not known. In this setting drug eluting balloons, plain stents, drug eluting stents and atherectomy devices are limited due to cost. All the cases were done using only non-drug coated balloons and it's the first series of angioplasties done in Sri Lanka by vascular surgeons. The purpose of this study is to evaluate the effectiveness of PTA alone in limb salvage in patients with chronic limb threatening ischaemia.

## Methods

Patients who had ischaemic tissue loss or gangrene [Rutherford category 5 and 6] that were deemed non-healing with high risk of major amputation [below knee or above knee amputation] and had undergone PTA between January 2013 to April 2018 who consented were recruited into this prospective study. Patients who are in heart failure or left ventricular ejection fraction of less than 20% or known hypersensitivity to contrast were excluded. Ischaemia was diagnosed clinically and all of them had an arterial duplex scan to confirm it. All patients had an arterial duplex scan of the lower limb done before undergoing PTA. Some patients also had CT Angiography. The patients were on their routine medications for diabetes, hypertension, dyslipidemia and ischemic heart diseases. The patients who were on metformin had it withheld for 48 hours prior to the procedure and an alternative medication was used until it is restarted 48 hours after the procedure. The patients were admitted on the day of procedure. All of them had undergone PTA alone. No one was offered stenting. Almost all of them got discharged the following day with a period of hospitalization for less than 24 hours. A loading dose of Clopidogrel 300mg is given to patients who had a successful angioplasty if they were not on it already. It is then continued with 75mg of Clopidogrel daily for at least six months. Patients were hydrated with normal saline prior to the procedure and after the procedure. If renal impairment was present N-acetylcysteine was given with the pre-hydration for renal protection. Hydration was continued post procedure for at least six hours. In patients with a low cardiac ejection fraction the volume of hydration was reduced as necessary.

The procedure starts with cannulating the access site [common femoral artery] with a large bore needle and using an introducer wire to place an access sheath. Unfractionated Heparin is given through the sheath. Then an angiogram is done to identify the occlusive or stenotic lesions. Then a 0.014 or 0.035 wire is used to cross the occlusive or stenotic lesions and angioplasty is done with a percutaneous angioplasty balloon. Post procedure angiogram is performed to check the radiological success.

Following the angioplasty, the patients got their ulcers treated in ulcer clinics of their choice. The ulcer care was not

standardized. This was due to cost constraints of travelling for regular dressings.

Data was collected prospectively using a standard questionnaire and entered a computerized database. Patients were followed up using telephone interviews regarding limb salvage and survival. Follow up using telephone was necessary as patients go to local clinical settings for ulcer care once the angioplasty is done. Whether the ulcer has healed or not were asked on the same interview. The statistical analysis of determining long term results were done using Kaplan-Meier method and it was used to estimate the Survival rate, Amputation Free Survival and Death censored Limb Salvage.

## Results

The total number of 226 patients who were included in the study were followed up. 27[12%] of the patients were lost to follow up. All of them underwent plain balloon angioplasty alone. None of the patients were treated with stents, drug coated balloons and atherectomy devices. No procedure was abandoned.

199 patients who were followed up [median age 67 years, range 29-95: 119 men]. The percentage of patients with Diabetes, Hypertension, IHD and CKD are 91.5%, 56.7%, 39.7% and 12.5% respectively [Table 1].

Distribution of lesions treated were Iliac arteries 4%, superficial femoral arteries 39.7%, popliteal arteries 15.6% and tibial arteries 40% and the respective radiological success rates were 62.5%, 93.6%, 96.7% and 90.1% [Table 2].

The initial radiological success rate is 88.4%. Acute complications [<30 days] developed in 5% [10/199] of patients and that includes two deaths [Table 3].

A total of 66 patients died. Patient Survival rates, Amputation Free Survival and Death Censored Limb Salvage rates were calculated in the group of radiological success up to 5 years. The survival rate at 1, 2 and 4 years were 78.6%, 70.9%, 60% respectively.

Of the 176 patients who had radiologically successful PTAs 49 [28%] were found to have healed wounds and the median duration of wound healing is 6 months. Of the radiologically unsuccessful group [23] only one [5%] patient healed the ulcer. In the radiologically unsuccessful group 5 [22%] required bypass to salvage and another 5 [22%] underwent major amputations.

In amputees 45% stated that they had impaired activities of daily living [ADL]. In the limb salvaged group ADL was impaired only in 17%.

Of the limb salvaged group 28% were not wearing footwear despite advice. Even though the limb was salvaged only 63% were mobile without assistance while 5% were bed bound and 14% requiring wheelchairs for ambulation [Table 4].

Of the 22 amputees followed up 50% did not wear footwear. The percentage bed bound, limited to wheelchair and using crutches are 4.5%, 59% and 13% respectively. Only 22.7% were ambulant using a prosthesis [Table 5].

### Discussion

In our study the amputation free survival at 4 years was 52%. In a meta-analysis of angioplasty follow up it was reported that the 4 year amputation free survival was 48% [17]. Our results of AFS is comparable to the world reported rates even though non drug coated balloons were used. In our study the overall 3-year survival is 67%. The overall 3-year survival of the angioplasty done in the BASIL trial was 52% [18]. The increased survival in this group may be due to the lower median age [67 years] compared to BASIL group [greater than 70]. This is because the higher median age and higher incidence of age-related co-morbidities among the participants of BASIL trial have a negative impact on their overall survival. A significant limitation in this study is not tabulating the outcomes according to the Rutherford or Wiff classification. In Rutherford 6 category where multi-level occlusive disease is present the outcomes may be worse. A significant proportion of the population were in Rutherford 5 category. Hence treating single segments with plain old balloon angioplasty may bring better results.

Angioplasty with Drug coated Balloon [DCB] is becoming more preferred over conventional Plain Old Balloon Angioplasty [POBA] in developed countries. A recent meta-analysis of randomized controlled trials done to compare the use of DCB and POBA revealed that the use of DCBs is associated with improved vessel patency and a lower risk of target vessel restenosis when compared to POBA in patients with femoropopliteal disease [19].

Endovascular stent insertion for CLTI is becoming a more favorable option when compared to PTA alone [20,21]. A meta-analysis of randomized control trials comparing PTA alone and angioplasty with balloon expandable stents revealed higher primary patency rates at 6 months with stenting compared to PTA alone in the treatment of femoropopliteal artery occlusive disease.

However, there were no difference in long-term primary results and secondary patency rates [22].

In intrahospital arterial occlusive disease, although stenting is expected to have a higher primary patency rates, there is not enough evidence to support its superiority over PTA alone [23]. Insertion of Drug Eluting Stents [DES] for infrapopliteal arterial occlusive disease is superior to PTA alone or Angioplasty with Bare Metal Stents [BMS] because DESs significantly inhibit vascular restenosis and thereby improve primary patency rates, reduce risk of reintervention and amputation, improve wound healing and event free survival rate [24,25].

Since the resources available to us in Sri Lanka are limited due to cost factors, only plain angioplasty balloons were used in all the cases and drug coated balloons or stents were not used. Setting up the peripheral intervention program in Sri Lanka was a bit difficult at the beginning. Sri Lanka has an ongoing cardiac intervention program. The modification required the use of longer balloons that can be used in the lower limbs and longer wires that it requires to place them. Initially as the team was not experienced the procedure used to take about 2 to 3 hours and at the latter stages it took about 45 minutes to 90 minutes.

In our study the death censored limb salvage rate was 79.4%. This is in keeping with the world reported rates which is around 80% [26]. The drawback in our study is that radiological patency follow up was not done.

### Conclusion

The low incidence of serious complications makes PTA an attractive alternative in the treatment of patients with ischemic foot ulcers. Even in a low-resource setting, PTA is an attractive option for revascularization and wound healing for patients presenting with ischemic ulcers consistent with Rutherford category five [5] tissue loss. The amputation free survival in this group at 4 years [47,8%]. Poor ulcer healing rates may be due to noncompliance with offloading footwear. In the limb salvaged group only 63% were mobilizing without any walking aid while in the amputee group the only 22.7% mobilizing independently with a prosthesis. This reflects the need for higher intensity post procedure rehabilitation.

**Table 1. Comorbidity**

DM	91.5% [182/199]
Hypertension	56.7% [113/199]
IHD	39.7% [79/199]
CKD	12.5% [25/199]

**Table 2. Lesion distribution**

Lesion Treated	%		% Success	
Iliac	8/199	4%	5/8	62.5%
SFA	79/199	39.7%	74/79	93.6%
Popliteal	31/199	15.6%	30/31	96.7%
Tibials	81/199	40.7%	73/81	90.1%

**Table 3. Complications**

Death – Acute Heart Failure	2/199	1%
Dissection	6/199	3%
False Aneurysm	3/199	1%
AV Fistula	2/199	1%
Pulmonary oedema	1/199	0.5%
Haematoma	7/199	3.5%

**Table 4. Overall Survival**

Duration	% prediction of Survival
1 year	78.6%
2 year	70.9%
3 year	67.%
4year	60%

The amputation free survival at 1,2 and 4 years were 65%,57.5%,47.8%respectively.

**Table 5. Amputation Free Survival**

Duration	AFS %
1 year	65%
2 years	57.5%
3 years	52%
4 years	47.8%

**Table 6. Death censored limb salvage**

Duration	% Death Censored Limb Salvage
6 months	87.5
1 year	84%
2 year	81%
3 year	79.4%
4 year	79.4%

**Table7. Patients with salvaged limbs – 92/114**

Activities of daily living		
Impaired	16/92	17.3%
Not impaired	76/92	82.6%
Footwear		
Uses footwear	66/92	71.7%
Doesn't use footwear	26/92	28.2% [includes 5 healed wounds]
Drug compliance	100%	
Bed bound	5/92	5.4%
No mobilizing aids	58/92	63%
Wheelchair	13/92	14.1%
Crutches	1/92	1%
Walkers	10/92	10.8%
Walking stick	7/92	7.6%

**Table 8. Patients with Amputated Limbs.**

Activities of daily living		
Impaired	10/22	45.4%
Not impaired	12/22	54.5%
Footwear and care to other foot		
Uses footwear	11/22	50%
Doesn't use footwear	11/22	50%
Drug compliance	100%	
Bed bound	1/22	4.5%
Limb prosthesis	5/22	22.7%
Wheelchair	13/22	59%
Crutches	3/22	13.6%

Data available in 22 patients

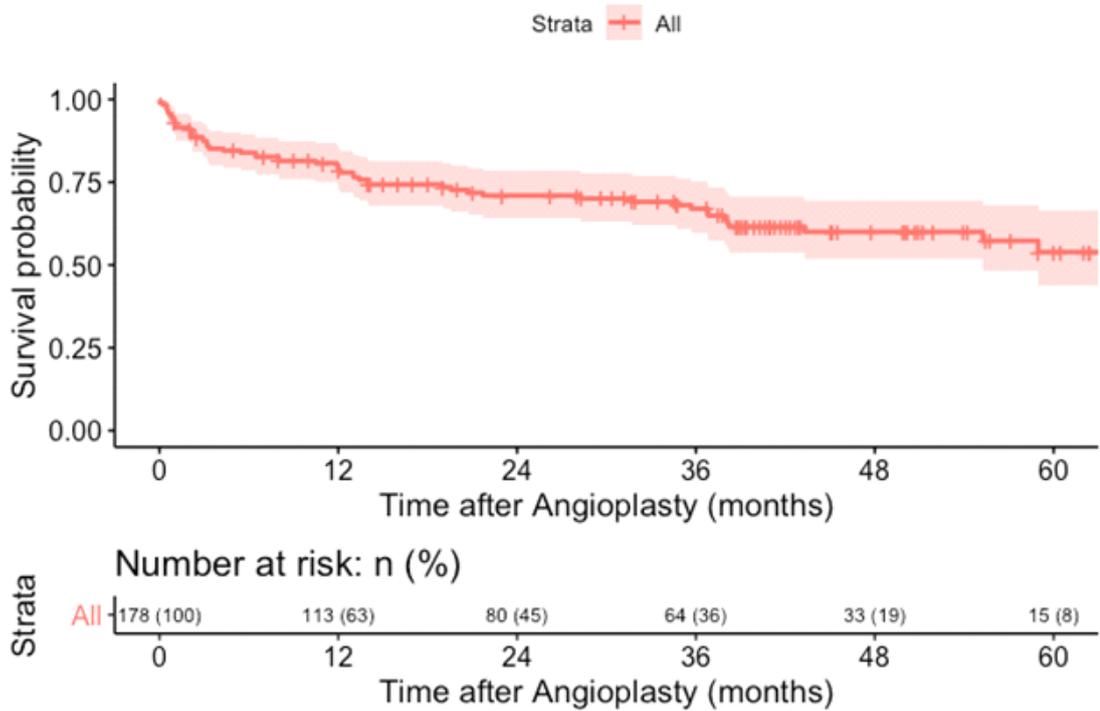


Figure 1. Overall Survival

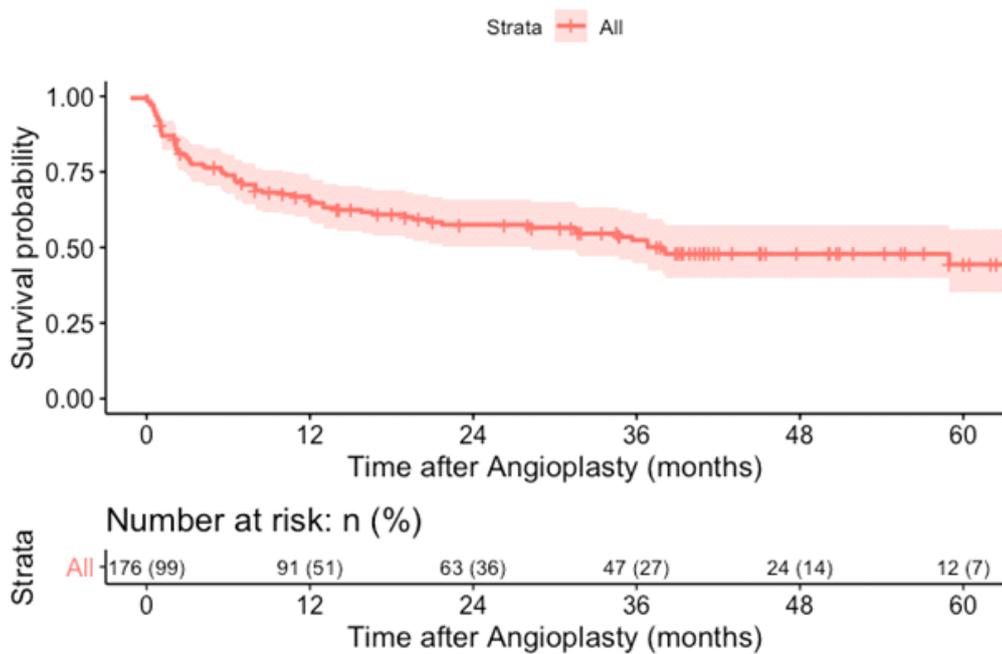
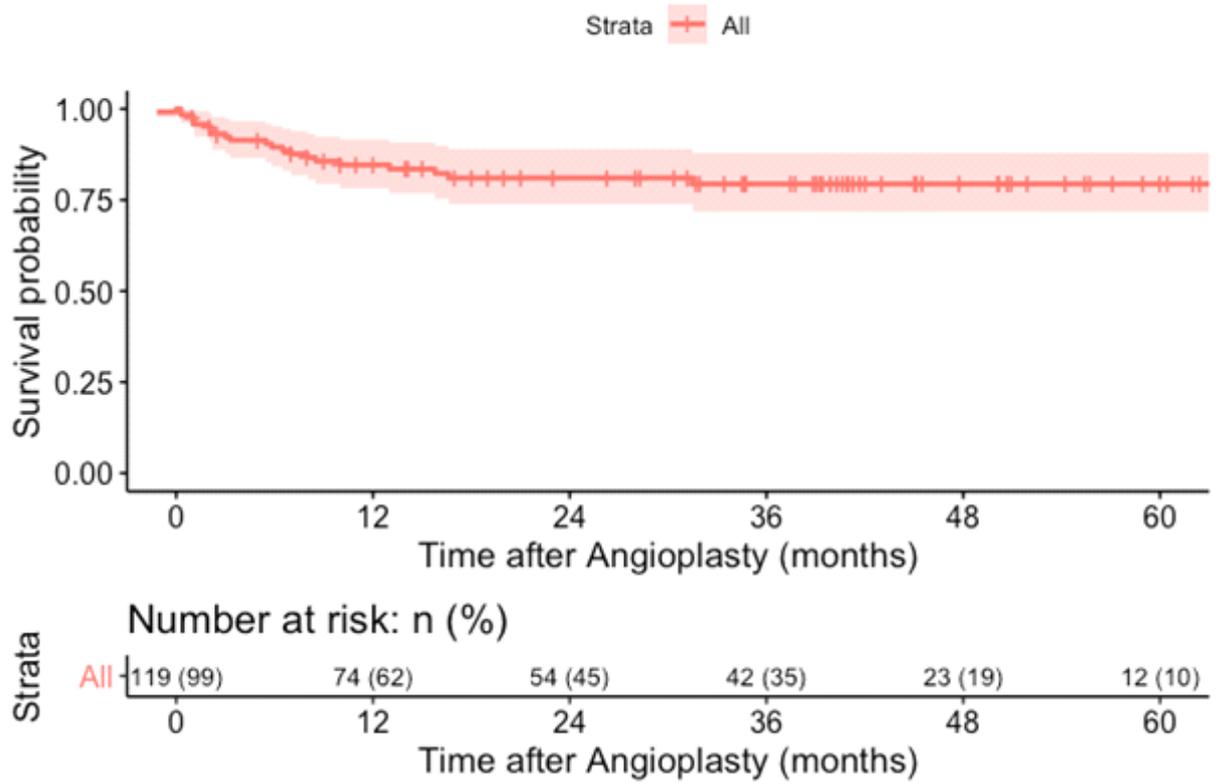


Figure 2. Amputation free survival



**Figure 3.** Death censored limb salvage

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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