

LIMB-SALVAGE ANGIOPLASTY IN POOR SURGICAL CHRONIC LIVER DISEASE AND DIABETIC PATIENTS

By

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Abstract

Critical limb ischemia (CLI) in high surgical risk patients with chronic liver diseases has a grave prognosis with a one-year mortality rate of 20% and a one-year amputation rate of 25% after the initial diagnosis. According to Trans-Atlantic Inter-Society Consensus (TASC)-II Guidelines, revascularization (surgical & endovascular) is the treatment of choice for patients with critical limb ischemia (CLI). The primary goal of revascularization is to relieve ischemic rest pain, heal ulcers, prevent amputation, improve patient's quality of life (limb salvage) and secondary goal was the periprocedural complications. Endovascular techniques include balloon angioplasty, stents, stent-grafts, and plaque debulking procedures. Surgical options, identification of patients at risk of postoperative complications could have an impact on the indications for a procedure as well as permitting modifications of treatment to reduce the surgical risk.

This study evaluated the treatment outcomes after limb salvage angioplasty for patients who otherwise would be candidates for primary amputation due to poor co-morbid conditions as chronic liver disease and diabetes.

The clinical evaluation, laboratory investigations and abdominal ultrasonography were performed to all patients to evaluate their liver status. Patients were classified according to Child-pugh classification into child A, B & C. All patients were subjected to either detailed arterial duplex or C.T. angiography to assess their arterial lesions from January 2008- January 2010. 95 patients with critical limb ischemia (Rutherford categories 4, 5, 6) were treated by primary percutaneous transluminal angioplasty (PTA). No patient was excluded on the basis of the extent of arterial occlusive disease. The primary end points were immediate technical success, clinical improvement and limb salvage rates. Secondary end points were periprocedural complications and mortality.

Most of the patients were male (54.7%) with mean age 62 (48-70 years). Underlying cirrhosis due to HCV was (82.2%), HBV (5.4%), while mixed viral infections was (12.4%). 54% were categorized as Child B, 32% as child A and 14% as child C. Associated diabetes mellitus was present in 96% of the cases, hypertension in 64.2%, ischemic heart disease in 74% and hyperlipidemia in 32%. Rest pain, tissue loss, or both, were the presenting symptoms in 83% while infec-

tion and ulcer were present in the other 17% of patients. The total numbers of interventions were 154; the treated lesions were 89 in the tibial arteries, 12 in the popliteal artery, 44 in the superficial femoral artery, 3 in the common femoral artery and 6 in the iliac arteries with initial technical success rate of 93.6% and periprocedural complications of 12.6%. All patients were in Rutherford clinical category 4, 5, 6 none of these patients had a previous bypass operation. Mean follow-up was 15 months. The limb-salvage rate was 87.4%. Eighty patients (84.2%) of toe amputation sites healed primarily. three patients with rest pain had resolution of their symptoms after angioplasty. All technical failures were due to inability to cross the lesions. Of the 6 technical failures, 4 required amputation, and 2 refused any further therapy.

Key words: Percutaneous Trans-luminal Angioplasty (PTA), Critical lower limb ischemia, Postoperative complications, Diabetes, Chronic Liver Disease.

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Introduction

The chronic critical lower limb ischemia occurs in the setting of severe peri-pheral arterial disease that is often characterized by advanced atherosclerosis at multiple level lesions in the lower extremity (Arora *et al*, 2013). Despite the challenges posed by complexity of arterial disease in such patients, endovascular intervention is a less invasive alternative to bypass graft surgery in most patients, with low procedural morbidity and mortality. Continual advances in percutaneous techniques have made it possible to revascularize lesions considered nonamenable for endovascular intervention. The development of dedicated peripheral wires, balloons, stents, and catheters allows recanalization and revascularization of almost any anatomy (Hiatt *et al*, 2007). Patients commonly presenting with critical limb ischaemia (CLI) are often elderly with multiple comorbid conditions (Park *et al*, 2007). Patients were considered poor bypass operation candidates on the basis of the

absence of an adequate greater saphenous vein for distal bypass, the presence of a poor distal bypass target vessel, or the presence of sever comorbid conditions.(Chronic liver disease, uncontrolled diabetes, recent myocardial infarction <6weeks, symptomatic coronary artery disease, or sever chronic obstructive pulmonary disease). Hepatitis C virus (HCV) infection is a major worldwide health problem that has an increasing prevalence and mortality. HCV is the most frequent cause of chronic liver disease and 20-30% of patients develop cirrhosis with a risk of hepatocellular carcinoma (El-Zayadi *et al*, 2005). It is estimated that 360 million suffer from chronic HBV infection worldwide. Both HBV & HCV are transmitted parentally and coinfection is not uncommon in intravenous drug users and in countries with a high prevalence of HBV, also may result in more severe liver disease than either infection alone (Ezzat *et al*, 2005). Also, the chronic liver disease association with diabetes mellitus may be attributed to common causes e.g.

alcoholism, hemochromatosis, and the possibly autoimmune conditions. Viral hepatitis (HBV & HCV) is established causes of chronic liver disease and seems to occur more frequently in diabetics than in the general population (Schreuder *et al*, 2008). This association may reflect epidemiological circumstances because of the frequent parenteral exposure of diabetics (Liao *et al*, 2009).

The purpose of this study was to evaluate the treatment outcomes after limb salvage angioplasty in high surgical risk patients with chronic liver diseases, otherwise for primary amputation.

Patients, Materials and Methods

A retrospective review of management of 95 patients with critical limb ischemia was classified according to Rutherford into the categories 4, 5, 6 (Rutherford, 2010), in association with chronic liver disease and diabetes were admitted to Theodor Bilharz Research Institute, National Institute of Diabetes and Endocrinology (NIDE), El-Gomhorya Hospital and El-Haram Hospital from January 2008- January 2010 treated by the primary percutaneous transluminal angioplasty (PTA). No patient was excluded on the basis of the extent of arterial occlusive disease. The primary end points were immediate technical success, clinical improvement and limb salvage rates. Secondary end points were periprocedural complications and mortality. All patients' demographic data including full history taking and clinical evaluation to assess the liver status, diabetes, cardiometabolic condition and other risk factors. History of previous attack of

bleeding (hematemesis or melena), cigarette smoking or myocardial ischemia was recorded.

Routine laboratory investigations including: complete blood picture, liver function tests, renal functions tests, total proteins, serum albumin, coagulation profile, hepatitis markers and fasting & postprandial blood sugar were done. Abdominal ultrasonography examination was performed to all patients. Diagnosis of liver cirrhosis was based upon sonographic findings of dilated portal vein, increased liver echogenicity, splenomegaly and/or ascites, upper endoscopy (gastroscopy) to verify of esophageal varices and its degree. Patients were classified according to Child-pugh classification into child A, B & C were collected and tabulated, clinical criteria including Rutherford category at baseline and during follow up were collected and analyzed. A Peri-procedural medication was acetylcysteine with good hydration at a rate of 0.5 ml/Kg/hr normal saline for 6 hrs before and after the procedure, intra-procedural 5000 units of unfractionated heparin.

The non-ionic contrast medium (ultravist) was used Post procedure, therapeutic low molecular weight heparin (LMWH) anticoagulation for 48 hrs. together with clopidogril loading dose (300mg), then statins (Atorvastatin; 20mg/day) and clopidogril (75mg/day) were continued on maintenance dose for 90 days and subsequently acetylsalicylic acid 100mg/day or ticlopidine 250mg/day indefinitely. The procedure was performed under local anesthesia through an antegrade approach of the

ipsilateral common femoral artery, or through a contralateral approach if obstruction of both iliac and common femoral artery. The trans-brachial and trans-popliteal approach was also used in patients with bilateral iliac artery occlusions. Procedural tools were invariably, a six French gauge sheath positioned to perform a preliminary angiographic study using diluted (50%) non-ionic contrast medium. 0.014-0.035 inch hydrophilic guide wire together with a diagnostic catheter (4-5 French) to locate the lesion and to support the wire and 3.0-5.0 French balloon catheter were used for the dilatation of 2-8 mm diameter arteries. The authors tried to avoid the use of stents especially in the infrapopliteal arteries since the risk of thrombosis is very high in such low-flow vessels. Stents were employed if there is subintimal dissection. Post-procedure, any minor amputations needed were to be done within 48 hrs. of the procedure, together with recording of periprocedural

adverse events. Follow up was scheduled at 1 month, 3 months, 6 months, and 1 year following the procedure for: (1) sustained clinical improvement based on absence of rest pain and/or progressive tissue healing; (2) Freedom from major amputation. All the data regarding patients who were not followed directly by the present authors were obtained from colleagues treating these patients.

Results

Ninety-five patients underwent percutaneous trans-luminal angioplasty (PTA) for critical limb ischemia (CLI) during our study period; we studied 52 males and 43 females, with a mean age of 62 years, associated with chronic liver disease. Diabetes (96%), hypertension (64.2%), ischemic heart disease (74%), smoking (32%), hyperlipidemia (32%) and cardiovascular stroke (16%) are associated risk factors.

Table 1: Patients' risk factors:

	No. patient	No. patient	No. patient
Underlying Cirrhosis	HCV 78 (82.1%)	HBV 5 (5.3%)	Mixed 12 (12.6%)
Child Pugh Classif.	Child A 31 (32.6%)	Child B 51 (53.6%)	Child C 12 (12.6%)
Associated risk factors:	1-Diabetis 91 (96%)	2-IHD 70 (74%)	3- Smoking 30 (32%)
	4- HTN 61 (64.2%)	5- Hlipid. 30 (32%)	6- CVS 15 (16%)

The clinical stratification of our patients at time of enrolment in our study showed unequal distribution between Rutherford categories 4, 5, 6. None of these patients had had a previous bypass operation.

Table 2: Clinical presentations

Clinical Presentations	No. Patients	Percentage
Gangrene	7	7.4%
Ulcer	11	12%
Infection	5	5%
Rest Pain	4	4%

Lesions were classified in the treated limbs according to the target vessel to

be treated which is the most likely to provide an in line flow down to the

foot. This was done during the intraprocedural preliminary selective contrast injection together with digital subtraction angiography (DSA) for proper visualization of the vessels and careful differentiation between a tight stenosis and total occlusion. In case of the presence of a simultaneous stenotic and occlusive lesions, or 2 lesions of the same type but with varying lengths in the same target vessel, we classified

the lesion according to the level of the lesion into one level lesion angioplasty (40 limbs), two level lesions (51 limbs) and three level lesions (4 limbs). Tibial vessels were the most commonly treated with a 57% preponderance, the superficial femoral artery was our target vessel in 29% of treated limbs, the popliteal artery (8%) while common femoral and iliac arteries where 2%, 4% respectively..

Table 3: Anatomical arterial lesions according to child-Pugh classification

Intervention	N= 154	percentage	Child A	Child B	Child C
Tibial a.	89	57%	18	34	7
Popliteal a.	12	8%	4	6	—
SFA	44	29%	5	10	1
CFA	3	2%	1	3	—
Iliac a.	6	4%	-	5	1

The technical characteristics of the procedure regarding guide-wire passage plane through the lesion were determined by the operator according to the guide-wire lesion interaction under fluoroscopic guidance, and were documented in the procedure details sheet.

Of 95 approaches 73 had (76.8 %) limbs through ipsilateral approach, 20 (21.1%) limbs through a contralateral approach, 1 (1.1%) limb through transbrachial, transpopliteal approaches respectively.

Table 4: Procedure technical approach

Ipsilateral	73	77%
Contralat.	20	21.1%
Brachial	1	1.1%
Popliteal	1	1.1%

Immediate technical achieved success, which was defined as residual angiographic stenosis of <30% of the target lesion, in 89 (93.6%) of our procedures with only 6 failures in 6 patients of those, 4 underwent major amputation and 2 patients refused further intervention and the reasons for failures were inability to cross a highly calcified chronic total occlusion. these patients were not suitable for surgical revascularization and had primary be-

low knee amputations. Limb-salvage rate was 87.4%. The eighty patients (84.2%) of toe amputation sites healed primarily, three patients with rest pain had resolution of their symptoms after angioplasty. There were 8 major amputations, limb loss occurred in four patients after technical failure and in four others, despite a technically successful angioplasty, limb loss was due to infection in four patients despite initial clinical improvement. Three patients died

due to myocardial infarction and one discontinued.

Table 5: Outcome, peri-procedural adverse events and mortality

Outcome	No. Patients	Percentage
Healing or minor amp.	80	84.2%
Rest Pain Improvement	3	3.2%
Major Amputation	8	8.4%
Discontinued	1	1.1%
Death	3	3.2%

During follow up, the recurrence of clinical symptoms correlated with recurrent arterial stenosis in 12 patients. Of the 12 patients in whom clinical restenosis occurred, PTA procedures were successfully repeated in 10 patients. In the other 2 patients (child C group), a further PTA was not feasible. All recurrence and clinical failures led to major amputation within 6 months of primary angioplasty.

Discussion

Chronic liver disease patients' requiring surgery were at greater risk for surgical and anesthetic related complications than those with a healthy liver. The risk magnitude depends upon the type of liver disease and its severity, the surgical procedure, and the type of anesthesia (Pandey *et al*, 2012). To quantify the surgical risk in vascular patients, there are three principle types of risk that must be assessed-the risk to the patient from the primary vascular disease, the risk to the patient from concomitant medical problems and the risks that each available treatment option holds (Patel *et al*, 2011). Multiple factors contribute to the increased risks that patients with liver disease have when undergoing surgery. Accurate preoperative identification of patients with liver disease allows their treatment plans to be adjusted accord-

ing to severity and nature of the underlying disease, as well as the type of surgery being undertaken. In patients with acute liver disease, elective surgery should be postponed until symptoms resolve. In patients with chronic liver disease, peri-operative risk increases with worsening severity of hepatic dysfunction as assessed by either the Child classification or MELD score (Davies and Ranaboldo, 1994). The preoperative management of complications related to patients' under-lying liver disease was essential to optimize their outcomes. Following surgery, patients with liver disease should be observed closely for the hepatic decompensating that often presented with worsening jaundice, encephalopathy, and ascites (Mohan *et al*, 2007). The best biochemical measures of liver function are probably the prothrombin time, serum albumin and serum bilirubin concentration. However, the serum bilirubin concentration usually rises, particularly after complicated surgery, multiple blood transfusions, excessive bleeding, hemodynamic instability, or systemic infection. Renal function, serum electrolytes, and glucose should also be monitored carefully (Hadziyannis, 1997). In spite of the commonly stated fact that cirrhosis protects from atherosclerosis, yet it was inter-

esting to notice that it was present in the present cases in both cardiac and vascular field. The least invasive options, such as angioplasty, or minimally invasive revascularization techniques, are likely recommended in patients with advanced cirrhosis. Although there is a role for primary amputation in patients who are poor candidates for surgical revascularization, the morbidity and mortality associated with major amputation remains high (Lowe *et al*, 1982). At the Wisconsin University, they have used arterial angioplasty as part of their endo-vascular program for treatment of limb threatening ischemia since 2001 (Jude *et al*, 2001). This treatment option is offered to patients considered high risk or poor candidates for surgical bypass. The main objective in CLI is limb salvage and therefore ambulatory function. Long-term patency comes second after this primary goal. The primary reason for the widespread adoption of endo-vascular intervention is based on the concept of repeatable recanalization with low complication rates (Kumpe and Rutherford, 1992). In the present protocol, the angiographic study and PTA were performed in the same session, this approach reduces both patient stress and the amount of contrast administered, which are particularly relevant in subjects with cardiac or renal insufficiency (London *et al*, 1995) The combination of a high technical success rate, a low complications rate and a high limb salvage rate are possible if the PTA physician is particularly skilled and patient care is performed by means of a skilled combined medical

and surgical team (Okazaki *et al*, 2011).

The present protocol employed PTA re-vascularization attempt irrespective of the length, number and localization of obstructions, which led to obtain a high number of technical success and a high limb salvage rate 87.4% and this was similar to other study that limb salvage was achieved in 96.6% of patients immediately after the procedure and in 88.3% a year after the procedure (Ostovan *et al*. 2011). Also, Zara (2011) achieved nearly the same results. In comparison to Cheng *et al*. (2003) in spite of insignificant differences of technical success rate, a year primary patency (56%) as well as secondary patency (69%) was significantly lower than in the group 96.6% of patients immediately after the procedure and in 88.3% one year after the procedure (Tsetis and Belli, 2004)

Conclusion

The endovascular management proved to be a good alternative to surgical interference in patients with high surgical as well as anesthetic risk because of their unfitness for general, epidural or spinal anesthesia, intolerance to surgical trauma (decompensation), bleeding tendency (hypoprothrombinaemia and thrombocytopenia), high incidence of wound infections (anergetic & defective power of wound healing). With recent advances in technology, long and multiple stenotic and occlusive lesions can be treated successfully carrying a lower morbidity and mortality and shorter hospital stay compared with surgery.

These figures showing the target vessels before and after angioplasty.

Fig. 1: PTA of Iliac artery occlusion



Fig. 2: PTA of superficial femoral artery occlusion

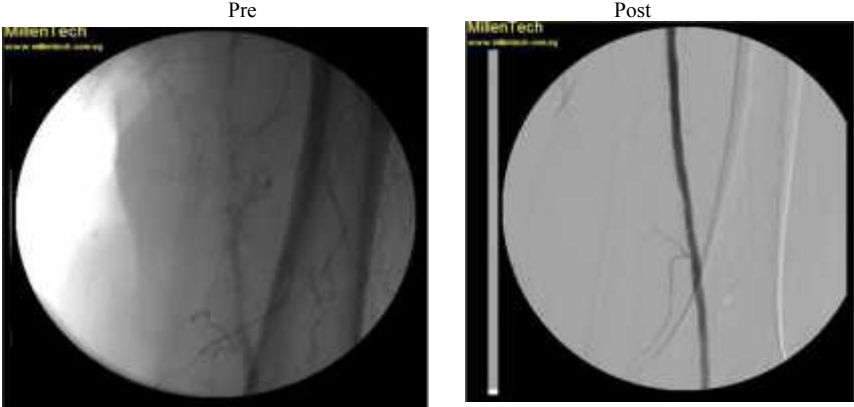


Fig 3: PTA of Popliteal artery occlusion



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