

The Outcome of Percutaneous Transluminal Angioplasty in Patients with Critical Limb Ischemia and how Diabetes May Influence this Outcome

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Abstract

Purpose: This study sought to establish the outcome following percutaneous transluminal angioplasty (PTA) in patients with critical limb ischemia (CLI) and how diabetes may influence that outcome.

Method: A retrospective study included 49 consecutive patients with CLI who were managed by PTA between 2008 and 2011, with a follow-up period of 12 month. Analysis of data was done using the SPSS version 19 software. The χ^2 test, t-test, Z test, simple and multiple logistic regression analyses were performed.

Results: The study included 22 diabetic and 27 non-diabetic patients. The technical success was almost similar in both diabetic and non-diabetic groups (91% and 88% respectively). In the diabetic and non-diabetic groups, the limbs salvage rates were (72.7% and 88.9% respectively), rates of major amputation were (22.7% and 7.4% respectively), rates of minor amputation were (4.6% and 3.7% respectively) and ulcer healing rates were (90.0% and 93.3% respectively). There was higher percentage of ulcer or advance tissue necrosis among diabetics ($P=0.014$).

Conclusions: The technical success of angioplasty was almost similar in both groups. In both groups, having gangrene on initial clinical assessment is associated with seven folds increase in the risk of amputation when other factors are adjusted for.

Introduction

Critical limb ischaemia (CLI) is a manifestation of peripheral arterial disease (PAD) that is defined as patients with chronic ischaemic rest pain, or patients with ischaemic skin lesions, either ulcers or gangrene [1]. CLI is found in 12% of the adult population in the US [2], and it is presumed that there will be approximately 500 to 1000 new cases of CLI per million European or North American population per year [3]. Prevalence of CLI is projected to increase with the increasing prevalence of diabetes mellitus.[4] Evidence showed that diabetes mellitus increases the risk of PAD by 2-to-4 fold and is present in 12-20% of individuals with lower extremity PAD [5]. The risk of developing CLI is also greater in diabetics than nondiabetics [6].

Critical limb ischemia predisposes to a high risk of limb loss, fatal and non-fatal vascular events, myocardial infarction and stroke [3]. It has been reported that at 1 year, 25% of patients will be dead, 30% will have undergone amputation, and only 45% will remain alive with both lower limbs [2]. Improvement in the prognosis of CLI is expected with the increased availability of distal arterial revascularization by distal bypass surgery and by percutaneous transluminal angioplasty (PTA) [7,8]. The later technique is increasingly important as it is less invasive than open procedures and can be utilized in treating very distal arterial stenosis and/or obstructions. In addition, the risk profile with this procedure is much less than that with more extensive open procedures [9]. Comparable outcomes have been obtained when PTA and bypass surgery are compared [10] The use of PTA has increased in the management of patients with CLI [11,12]; however, there is little data

regarding outcomes of this intervention in the management of diabetic patients with CLI.

Purpose

The aim of this study is to assess the outcome of percutaneous transluminal angioplasty in patients with critical limb ischemia and how diabetes may influence this outcome.

Material and Methods

A retrospective record base study included consecutive patients who were admitted in our institution in the period between 2008 and 2011. Inclusion criteria were patients with a diagnosis of CLI as defined by TASC II Consensus (Rutherford category 4-6 [13]) and for whom the management protocol included early revascularization of the affected limb with percutaneous transluminal angioplasty (PTA). Patient who had other management modalities were excluded. Post procedure twelve months clinical follow up for the included patients were reviewed.

Patient's information regarding demography, history of smoking, clinical comorbidities (diabetes, cardiovascular diseases, hypertension, and hyperlipidemia) was assessed. History of type 2-diabetes mellitus was verified on the basis of the American Diabetes Association criteria [14]. The clinical outcome parameters used for assessment in this study were: limb salvage, amputation, and mortality. Primary success of angioplasty was defined as angiographic results with a residual stenosis of less than 30%.

Data was analyzed using the SPSS software version 19. Data was expressed as median, mean \pm SD. Comparisons between group characteristics were made with a χ^2 test (frequency data) t, or Z test (continuous data). Uni-variable logistic regression analyses were performed for potential predictor of amputation, with values presented as uni-variable odds ratio (OR) with the respective 95% CI. All potential predictors were entered in a multivariable regression and variable that best predicts outcome was identified. $P < 0.05$ was considered statistically significant.

The clinical audit was registered with the Trust Audit Office and Clinical Audit and effectiveness Committee of the Hull Royal Infirmary NHS Trust and approved. Informed consent was obtained from each patient as part of his or her routine care. All data analyzed were collected as part of routine diagnosis and treatment.

Results

A total of 49 patients with CLI were included of which 26 were male (53%) and 23 were female (47%), 22 patients (44.9%) were diagnosed to have type 2 diabetes and 27 (55.1%) were non-diabetic patients. The mean (SD) and median age values for diabetic patients were 73.6(\pm 10.47) and 74 years respectively, while for the non-diabetic patients they were 79.5(\pm 11.05) and 82 years respectively. Diabetic patients compared to non-diabetics, had higher frequency for hypertension (76.2% Vs 74.1, $P > 0.05$), hyperlipidemia (90.5% Vs 70.4%, $P > 0.05$) and history of CVD (90.5% Vs 55.6%, $P < 0.01$). History of smoking was reported by 11 diabetic (50%) and 17 non-diabetic (63%) patients, the difference was not significant ($Z = 0.36$).

Using Rutherford classification (Table 1), the percentage of patients with advance tissue loss (category 6 in Rutherford classification) was significantly higher among diabetic compared to non-diabetics (54.5% Vs 22.2%, $Z = 0.0196$). Significant association was noticed between diabetes and stage of presentation according to Rutherford classification ($\chi^2 = 8.6$, $P = 0.014$).

	Rutherford classification			P value
	4n (%)	5n (%)	6n (%)	
Non-Diabetics	6 (22.2)	15 (55.6)	6 (22.2)	0.014
Diabetics	0 (0.0)	10 (45.5)	12 (54.5)	

Table 1: The association between diabetes and stages of clinical presentation according to Rutherford classification in patients with critical limb ischemia.

The results of percutaneous transluminal angioplasty for diabetic and non-diabetic patients with critical limb ischemia (CLI) results are shown in Table 2. The percentage of technically successful angiographic investigation among diabetics Vs non diabetics was 90.9% Vs 85.2%. No significant association was found between having diabetes and the success of angioplasty. Table 3 shows that the percentage of patients having a 3 vessel distal run off is lower among diabetics Vs non-diabetics (18.2 % Vs 33.3%). However, no significant association was found between diabetes and number of distal runoff, $P = 0.266$.

The percutaneous transluminal angioplasty results	Non-Diabetics n (%)	Diabetics n (%)	P value
Successful (<30% stenosis)	24 (85.2)	20 (90.9)	0.643
Unsuccessful	3 (11.1)	2 (9.1)	

Number of distal run off	Non-Diabetics n (%)	Diabetics n (%)	P value
0	0(0.0 %)	2(9.1)	0.266
1	12(44.4)	9(40.9)	
2	6(22.2)	7(31.8)	
3	9(33.3)	4(18.2)	

Table 2: The results of percutaneous transluminal angioplasty for diabetic and non- diabetic patients with critical limb ischemia.

Variable	No Amputation no (%)	Amputation no (%)	P value
Non-Diabetics	24 (88.9)	3 (11.1)	0.159
Diabetics	16 (72.7)	6(27.3)	

Table 3: The number of distal runoff as shown by the percutaneous transluminal angioplasty.

During the 12-month follow-up period, nine patients had undergone limb amputation with a one year amputation rate of 18.4%. Table 4 shows the clinical outcome of the studied patients. The rate of amputation was higher among diabetic patients (27.3% Vs 11.1%), but the difference was not significant $Z = 1.4$, $P = 0.159$.

Variable	N	Predictors of limb amputation
		COR* (95% CI), P, AOR** (95% CI), P
Gender	Male	26, 1, 0.6, -
	Female	23, 1.53(0.36-6.55), 0.6, -

Table 4: Clinical outcome after 12 months follow-up.

Limb salvage rate (clinical improvement, not requiring amputation) at 12 month follow up was lower in the diabetic group than the non-diabetics (72.7% Vs 88.9%). Among diabetic patients, the amputations (total=6) were of the major and minor types in 22.7% (n=5) and 4.6% (n=1) respectively, while among the non-diabetic patients, the amputations (total=3) were of the major and minor types in 7.4% (n=2) and 3.7% respectively.

When smoking history was considered, the amputation rate among patients with CLI (both diabetics and non-diabetics) was higher among smokers (7 out of the 28, 25%) compared to non-smoker (2 out of 21, 9.5%, $Z = 1.4$, $p = 0.165$).

Table 5 shows the logistic regression analysis for the amputation predictors. It can be seen that the only significant predictor after controlling the confounding effect of other factors was the Rutherford category at time of presentation.

Variable	N	Predictors of limb amputation
		COR* (95% CI), P, AOR** (95% CI), P
Gender	Male	26, 1, 0.6, -
	Female	23, 1.53(0.36-6.55), 0.6, -

Hypertension	No	12	1		-	-
	Yes	36	1.33(0.24-7.4)	0.7		
Hyperlipidaemia	No	10	1		-	-
	Yes	38	1.02(0.18-5.78)	1		
CVD	No	14	1		1	0
	Yes	34	4.31(0.49-38.03)	0.2	3.137(0.28-35.08)	
Smoking	No	21	1		1	1
	Yes	28	1.64(0.358-7.478)	0.5	1.596(0.28-8.958)	
Diabetes	No	27	1			1
	Yes	22	3.0(0.65-13.76)	0.2	1.145(0.18-7.35)	
Rutherford Category	4 and 5	31	1		1	0
	6	18	9.23(1.66-51.42)	0	7.10(1.06-47.54)	
Number of distal runoff	3	13	1	0.3	1	1
	<3	36	3.43(0.39-30.52)		1.82(.016-21.34)	
Age (year)		49	0.99(0.93-1.06)	0.8	-	

*COR: Crude Odds Ratio; ** AOR: Adjusted Odds Ratio

Table 5: Logistic regression analysis: predictors of limb amputation

Discussion

Endovascular revascularization for the treatment of critical limb ischemia is the first-line approach in many centers [8]. In this study, 44.9% of patients with CLI studied had diabetes, and this is in agreement with the estimated rate of 40% reported earlier [15]. It has been suggested that premature and advanced atherosclerosis, together with peripheral neuropathy, impaired cellular immunity and impaired wound healing make CLI a complex problem among diabetic patients and if not adequately treated, may lead to amputation and death [16]. This could explain the higher rate of diabetic patients who had tissue loss or gangrene at time of presentation (Rutherford Classification grade 6) compared to non-diabetic patient observed in this study.

Although the technical success rate was higher among the diabetic group (91%); limb salvage rate, at 12 months follow up, was lower (72.7%). This is a multifactorial and could be explained by the significant increased frequency of gangrene, advance tissue necrosis, and delayed presentation in diabetic group.

In a prospective cohort study, with 1-year follow up of 383 patients, Dick et al. [15], found that the sustained clinical success of revascularization was significantly better in non-diabetic patients.

The higher percentage of clinical comorbidities, noticed among the diabetic patients compared to non-diabetics, is in agreement with another study which showed that history of hypertension, hypercholesterolemia, coronary artery diseases in addition to diabetes

are independent predictors of CLI recurrence [8]. Our findings showed a higher amputation rate among diabetics with CLI compared to non-diabetic group. Takahara et al. [17] study revealed that the main factors which affect the risk of amputation for CLI patients were the presence of diabetes and Hb A1C level ($P=0.012$ and $P=0.007$, respectively), whereas other clinical comorbidities (hypertension, dyslipidemia) were not significant factors.

The multiple logistic regression of current data revealed that having gangrene on initial clinical assessment of the patient is associated with seven fold increase in the risk of amputation when other factors are adjusted for. In addition, the risk of amputation was 14.5% higher among diabetics compared to non-diabetics, although such an increase was not statistically significant.

Several risk factors predisposing to amputations among CLI's patients have been reported. The relative risk of diabetic patients to undergo amputation over the course of their lives is 15 - 40 times greater than non-diabetic individuals [16]. In this study, the major amputation rate was higher among diabetic patients. An et al. [18] demonstrated similar trend of major amputations among diabetics versus non-diabetics after PTA (10 vs. 0%, $P<0.05$); the total amputation (12.0% vs. 8.7%, $P=0.62$) and restenosis rates (4.0% vs. 8.7%, $P=0.38$).

Lida et al. [19] identified diabetes to be a significant factor associated with major amputation after endovascular therapy on 465 limbs with CLI and isolated below-the-knee lesions.

It has been suggested that diabetic patients with CLI represent an extra challenge since, very often these patients have occlusion of crural vessels and it is thought that this can affect the outcome of those patient. In this study, the lower number (<3) of distal runoff vessels has 82% increase in the risk of amputation, and although that increase in risk was not statistically significant; it could suggest that it has a prognostic significance and this is in agreement with others finding [20].

Previous studies suggested older age as a risk factor for developing amputation [16,21]. On the contrary, the effect of gender or race was considered to be inconsistent [22,23]. Hence, age might play as a confounding factor on the studied participants. Adjusting for age and diabetes showed similar amputation and survival rates in women and men [24]. In this study both age and gender did not have significant impact on the risk of amputation.

Although, the use of anticoagulant therapy was not looked at in this study, the effect of anticoagulant therapy have been investigated in relation to their effect on the risk of re-occlusion following PTA [25]. Its usage, however, is not recommended routinely in the management of those patients [26]. Antiplatelet agent (either aspirin or clopidogrel) reduces both the incidence of cardiovascular events and risk of arterial occlusion; hence, its usage is recommended before endovascular and surgical procedures and should be continued, if not contraindicated, indefinitely post procedure [27].

Our data showed the significance of initial clinical assessment in determining the prognosis of patient presented with CLI. In patients with CLI, Rutherford category 6 at initial presentation is the only significant independent predictor of limb amputation when all other factors are adjusted for.

This study is limited by the retrospective, single center design, which may create a referral bias. The sample size is also small and would require greater validation from larger studies.

Conclusion

In our patient cohort, the technical success of angioplasty was almost similar in both diabetic and non-diabetic groups.

In both groups, having gangrene on initial clinical assessment is associated with seven folds increase in the risk of amputation when other factors are adjusted for.

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