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Percutaneous transluminal angioplasty improves glucose control and quality of life in patients with critical limb ischemia

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Abstract. – AIM: To evaluate the benefit of endovascular peripheral revascularization on glucose control in patients with chronic limb ischemia.

METHODS AND RESULTS: Over a 12 month period, 61 patients (41 male, range 49-88 years of age) presenting with critical limb ischemia (CLI) were treated according to the Trans Atlantic Inter Society Consensus (TASC II) guidelines. After discharge, all patients were asked to measure their glucose level three times daily, and glycated hemoglobin was checked monthly up to 12 months, as well as to fill a questionnaire to assess their Quality of Life (QoL). The revascularization procedure was successful in 90% of cases. Glycemic control and glycated hemoglobin in 22 diabetic patients subgroup were significantly improved after the treatment and remained stable over the follow-up period. There was a significant improvement in QoL that increased steadily from the operation and to reach a plateau after six months.

CONCLUSIONS: Peripheral percutaneous angioplasty in subjects with CLI significantly improves glycemic control and ameliorates QoL. Revascularization positively effects also long-term diabetes control as well as QoL.

Key Words:
Percutaneous transluminal angioplasty (PTA), Quality of Life (QoL), Critical limb ischemia (CLI), Limbs amputation, Peripheral arterial disease, Arterial stenting, Diabetes mellitus, Subintimal angioplasty, Revascularization.

Introduction

Aim of this study is to evaluate the benefit of endovascular peripheral revascularization on glucose control in patients with chronic limb ischemia comparing also Quality of Life (QoL) data using Short Form 8 protocol. According to Trans Atlantic Society Consensus II (TASC II) consensus on peripheral arterial disease the definition of critical limb ischemia (CLI) should be used for all patients with chronic ischemic rest pain, ulcers or gangrene attributable to objectively proven arterial occlusive disease and referring to chronic and not to acute symptoms[1]. Lower limbs vascular lesions affect about 10% of over 50 and 20% of the population over age 70[2,3,12]. In 1991 a European Consensus[4] estimated the incidence of CLI to be in the range of 500-1.000 per million population per year.

Materials and Methods

From December 2009 to December 2010, 61 patients were admitted to our Unit for CLI, 22 patients were affected by type I and II diabetes. Predisposing factors and comorbidity in CLI were evaluated and represented in Table II. All patients presenting to the Unit with CLI as defined by TASC II Consensus were enrolled for filling a Short Form 8 (SF8)[15]. Post operative controls were scheduled during vascular examination follow up (F.U.) at 1, 4, 8, 12 months after endovascular procedure. Other data were: presence of rest pain/paresthesia, patient walking autonomy (PWA) in meters, the ankle brachial index (ABI) at rest, vascular ultrasound for assessing the arterial patency and $tcPO^2$ measured at the dorsum of the foot. Arterial lesions sites were divided in 4 groups: iliac artery, femoral artery, popliteal artery and tibial artery (Table I). CLI with loss of tissue was sized and photographed. Diabetics filled an extra form for evaluating glucose values, diabetes type and insulin therapy pre- and post-operatively.

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Table I. Anatomical PTA site.

Site	Total N°	Type of lesion	
		Occlusion	Stenosis
Common iliac artery	6	2	4
External iliac artery	2	0	2
Superficial femoral artery	26	8	18
Popliteal artery	9	1	8
Tibial artery	18	10	8
Total	61		

Patients with unstable angina, recent stroke, and lack of compliance in following the insulin therapy were excluded.

Statistical Analysis

All data were collected on a customized FileMaker Pro and analyzed using Microsoft Excel. QoL scores were normally distributed. The Kruskal Wallis analysis of variance (KWANOVA) was used to assess change over time of clinical indicators of CLI and SF8.

Results

We analyzed the results of 61 patients treated with percutaneous transluminal angioplasty (PTA) for CLI in period of 12 months. 41 male and 20 females, with a median age of 74 years (range 49-88 years), suffering for CLI since 6 months. 9 patients (14%) were admitted with lower limb tissue loss and 3 patients (4%) had digital gangrene. PWA ranged from 0 to 50 meters. Night rest pain/paresthesia and concomitant reactive foot were present in 55 patients (90.1%). ABI ranged from 0.22 up to 0.45. Ultrasound evaluation was executed in 100% of patients. SF-8 was filled in 100% preoperatively. All patients underwent unilateral procedures. In 17 cases we used a nitinol stent. Technical success was achieved in 55 patients (90.1%). In 6 cases endovascular procedure failed for long, severe and chronic calcifications and patients underwent surgical below the knee femoro-popliteal bypass and were excluded from the follow up. There were no arterial worsening or complications due to endovascular procedures. In Table IV are showed data at discharge about PWA, night rest pain and ABI.

Compliance to fill SF8 rates were 98%, 92%, 90% and 88% at 1, 4, 8 and 12 months, respectively. Diabetic controls were completed in 90%, 85%, 85% and 80% in the same intervals. SF8 showed a significant improvements of QoL after PTA in physical functioning, role physical, pain, vitality, social functioning and mental health. Comorbidities (Table II) were not bias for SF8 preop and post-op results. Increasing of QoL is clearer in the first 6 months in all domains (Figures 1 and 2). At 12 months follow up we noted a downward on some physical domains that could be related to arterial re-stenosis that we noticed increasing since the second follow up (Figures 1

Table II. Preoperative comorbidity and predisposing factors.

	N°	%
Diabetes	22	36
Glycated hemoglobin (HbAC1) > 7%	19	83.6*
Cronic obstructive pulmonary disease	29	47.5%
Asymptomatic cardiac ischemic disease (remote MI)	27	44.2
Ejection fraction < 60% - > 25% pre operative echocardiogram	24	39.3
Hypertension	57	83.6
Hyperlipidemia	38	62.2
Cerebrovascular disease (remote stroke, RIND, cognitive decay)	18	29.5
Smoking	34	55.7
Obesity	29	47.5
Total	61	100

*Referred to diabetes group (22 patients).

Table III. Pharmacological therapy.

	N°	%
Beta blockers	55	90.1
Ca^{++} antagonists	16	26.2
Angiotensin II receptor antagonists	44	72.3
Nitrates	12	20.8
Insulin therapy	9	40.9*
Oral hypoglycemics	13	59.1*
Antiplatelets	55	90.1
Anticoagulants	6	9.8
Diuretics	31	50.8
L-Thyroxine	19	31.9
Total	61	100

*Referred to diabetes group (22 patients). Exclusion criteria.

and 5). Drug therapy (Table III) still remain the same during the follow up period, except for insulin therapy. Diabetologists reduce insulin intake in patients with lowered glycated hemoglobin levels since first control remaining stable during all the follow up period. Patients treated for iliac lesions were the best subgroup for arterial patency, scoring an highest QoL respect totals (Figure 2) in almost all domain, improving ABI and TcO^2 (Figures 3 and 4) and reducing glycated hemoglobin percentage (Figure 6). Tibial lesions in diabetic patients were the worst subgroup for QoL improving. PTA sites at risk of restenosis/occlusion were the popliteal-tibial territories as already many studies has shown[3,4,6]. Improvements were observed of QoL (according with SF8) in 90% of patients at 1 month, 83% of patients at 4 months, 76% of patients at 8 months and 71% at 1 year. No clinical deterioration were observed in the treated population.

Discussion

The fate of patients with mild peripheral artery obstructive disease (PAOD) is relatively benign but 25-30% of these patients will worsen to critical limb ischemia (CLI) within 5 years from the first diagnosis[1,2,12]. The definition of CLI according to the TASC II refers to all patients with chronic ischemic rest pain, ulcers or gangrene attributable to objectively proven arterial occlusive

Table IV. Clinical and instrumental findings at discharge.

	Pre-op	Discharge
Night rest pain	61 patients	6 patients*
ABI	0.35 (median)	0.74 (median)
PWA	25 meters (median)	80 meters (median)

*Open surgery 2 weeks later.

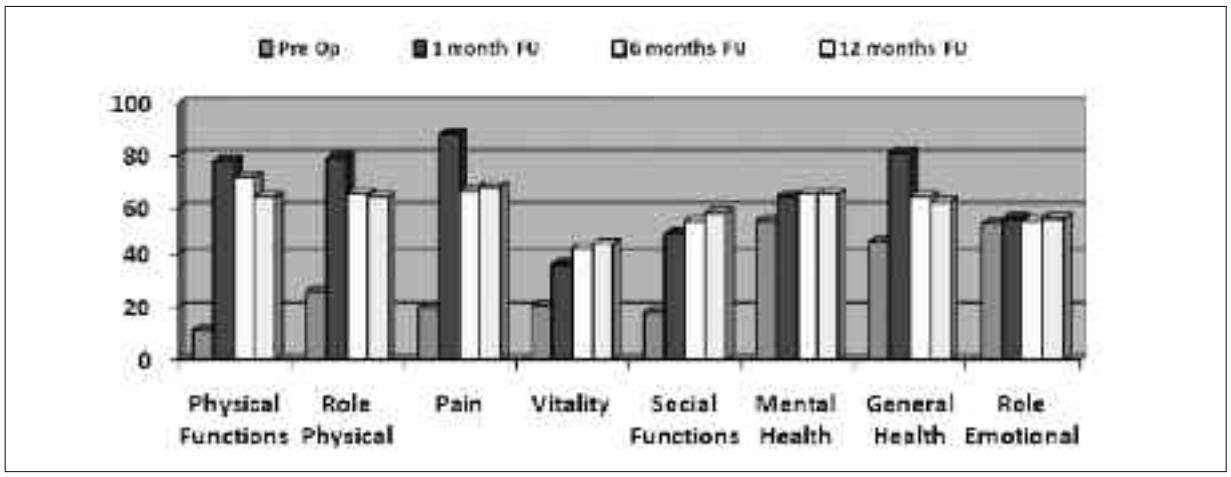

Figure 1. Total SF 8 median results on all domains ($p < 0.01$ by KWANOVA).

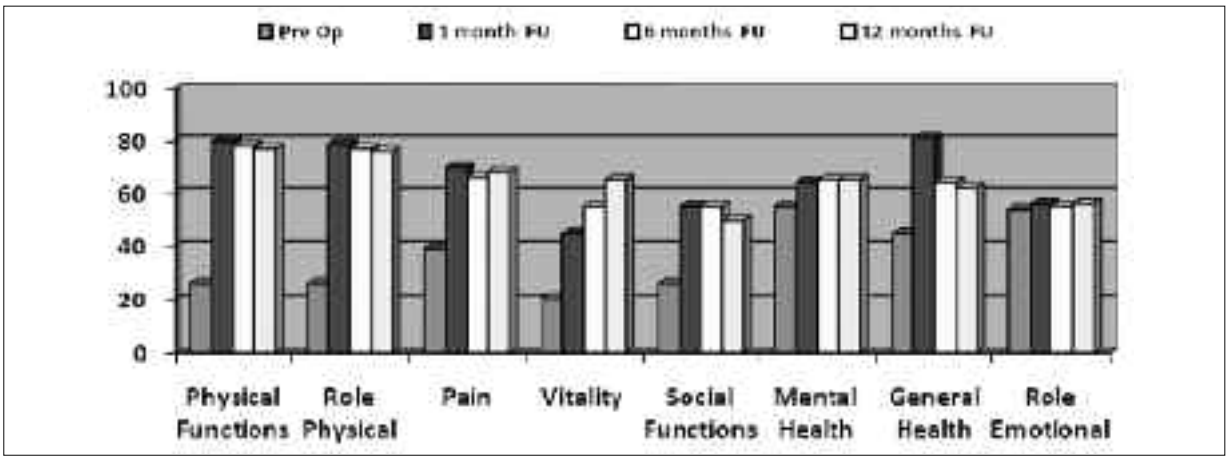

Figure 2. Iliac subgroup SF8 median results (stability of physical domains, $p < 0.1$).

disease and referring to chronic and not to acute symptoms[1,3]. This condition bears a primary amputation rate between 10% and 40% and a mortality rate of 20% at 1 year, between 40% and 70% at 5 years, and reaching 80%-95% at 10 years[5].

Chronic limb ischemia (CLI) means pain in the lower extremity at rest or ulceration with and without tissue necrosis. Aggressive treatment of CLI is needed, as progression to amputation is frequent. In patients with wound ulcers treated without revascularization, a high incidence of amputation has been reported particularly in patients with an ABI < 0.5[1,14,15]. Monitoring of QoL in CLI population permit to survey not only the mortality rate of these patient but also their comorbidity. Comorbidity and risk factors reduction can decreases mortality rates. The SF8 has demonstrated acceptable validity and reliability in population studies[13,14]. As reported by the ARISCAT group[15] the SF-8 is a feasible, reliable, valid, and responsive instrument for assessing health-related quality of life in a broad-spectrum surgical population. What primary emerged from our studies is the high rate of attendance at follow up. As we already said, SF8 is, on the whole, as valid reliable, and responsive as the SF36, but importantly takes less time to complete, appears to be less confusing, and is, therefore, likely to be more acceptable to the patient across the disease spectrum of CLI[13]. QoL index scores provide an appropriate tool for independent outcome reporting following intervention in claudicants. Mazari et al.[4] report data about the disease-specific "VascuQoLindex" that appears to correlate more closely than generic indices with changes in clinical indices of lower limb ischemia with treatment. The Authors[4] noted that the VascuQoL index demonstrated a greater degree of improvement compared with generic QoL instruments. Use of QoL evaluating tools in endovascular surgery really increase during the last decade. Clinical and instrumental results not always match with the patients everyday life. Mazari et al[4] and other Authors[12] report that easier is the test the higher will be its relia-

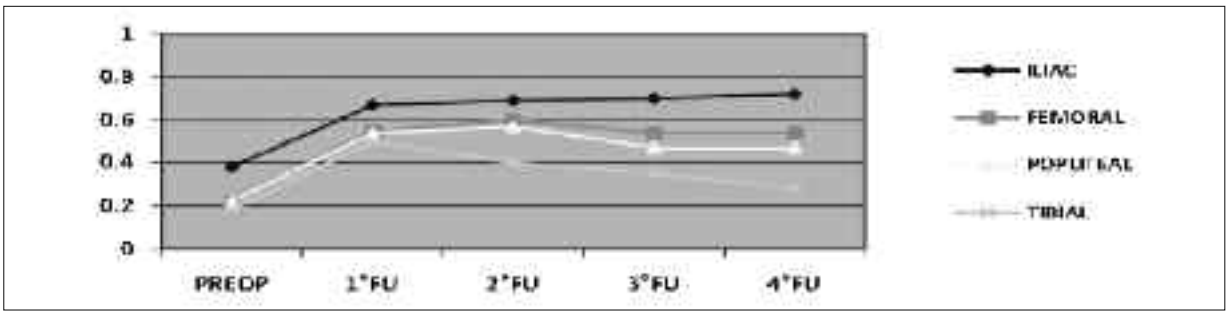

Figure 3. Pre-op and post-PTA ABI for different PTA sites (F.U.: follow up).

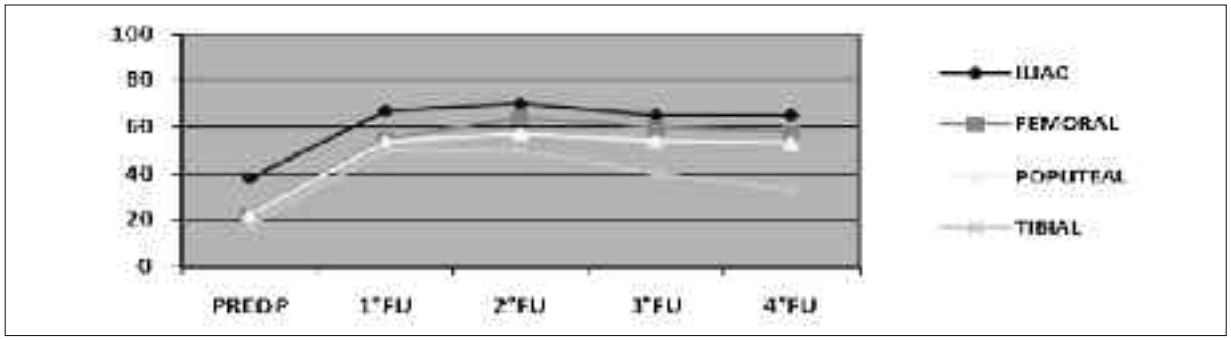

Figure 4. Pre-op and post-PTA TcO^2 for different PTA sites (F.U.: follow up).

bility, and what we noted is that, since SF8 has been used for this paper instead of SF36, we reduced bias due to mistakes. The age range, sex ratio, factors predisposing to peripheral vascular disease, and levels of comorbidity were as expected in a group of patient with CLI. We had 9% of technical failure rate for PTA according with other endovascular team. One year arterial patency is (50/55) 90.9% ranging from 100% for iliac artery to 45.5% (8/18) on the tibial vessels and QoL is related with the technical success. Glycemic test showed a correlation with arterial lesion site (Figure 6). Ileo-femoral arterial lesions had best long term results in terms of QoL and glycated hemoglobin. Indeed the benefits of regular physical activity for the prevention and management of diabetes are becoming well known[9]. It has been shown that physical activity improves glycemic control through increased insulin sensitivity and glucose tolerance[9,12]. Even physical activity of moderate intensity can improve insulin sensitivity[9,10], leading to potential reductions in the dosage of hypoglycemic agents as well as additional benefits for cardiovascular health, functional status, and longevity. Importantly, increased insulin sensitivity occurs within weeks of the adoption of a program of regular physical activity[9]. It is important to demonstrate that any intervention in claudicants has an immediate and relatively lasting impact on patient-reported QoL[13]. Peripheral angioplasty helps patients in "pain free" walking and this event permits to improve their physical activity leading to a metabolism increase[9,10,12]. We noted that patients with an amelioration of their "pain free" walking distance in diabetic group had a decrease of HbA1 that can be related to a better metabolic performance. In Figure 6 diabetic patients who underwent to iliac artery angioplasty (with a better results in terms of PWA, ABI and TcPO2) reported a significant reduction of HbA1. As described by others, intermittent claudication has a serious inhibitory effect on QoL. Chetter et al[13] reported that the only SF36 domains not affected by PTA are role limitations due to emotional problems and general health. What we noted in our study, even if related to SF8 domains, is that emotional problems are affected positively by successful PTA. As in other papers[5,12] has been noted general health perception can downward during the follow up period because of the co-morbidities progression.

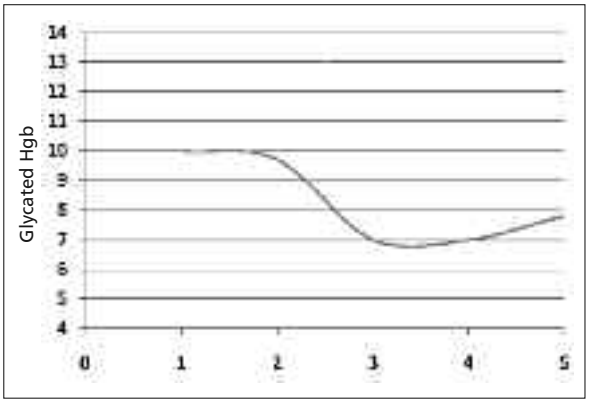

Figure 5. Time trend of glycated hemoglobin (in diabetic group) and PTA ($p < 0.1$) (1: pre op; 2-5: follow up).

There are some limitations to this study. First, the overall numbers are small, and when divided into subgroup (site of lesion, diabetic) they become even smaller. What we can extrapolate is that if a trend is significant for small numbers it will be significant for larger numbers. Another limitation is the follow up period. QoL to one year is not QoL for the rest of life, although the trend is positive we can't exclude worsening of QoL due to progression of the vascular lesions in other sites.

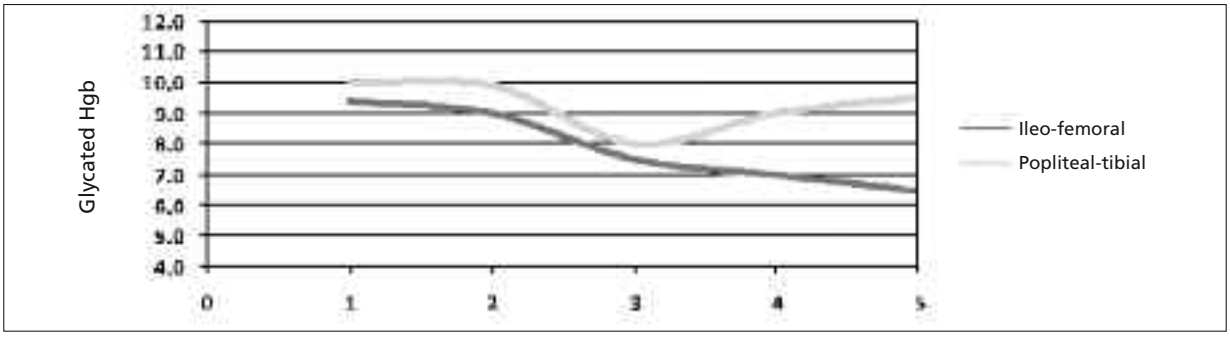

Figure 6. Time trend of glycated hemoglobin and PTA sites (in diabetic group) ($p < 0.1$) (1: pre op; 2-5: follow up).

In conclusion, despite some limitations, we report a significant improvement in QoL after peripheral PTA in subjects with CLI in the short and medium term. PTA is also effective positively for diabetes control in terms of glycemic levels during all the period of study. Finally patients with iliac-femoral lesions appear to have a better result for QoL, ABI and glycated hemoglobin respect tibial vascular lesions.

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