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Below Knee Angioplasty in Diabetic Patients: Predictors of Major Adverse Clinical Outcomes

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Abstract

Background: Tibial vessel disease (stenoses or occlusions) has a huge variety of outcomes either technical or clinical, which has an impact on the health authorities.

Aim of Study: To locate clinical outcome predictors following Plain Old Balloon Angioplasty (POBA) in diabetic patients with below knee atherosclerotic lesions causing Chronic Limb Threatening Ischemia (CLTI).

Patients and Methods: Over one year, 67 patients (CLTI 100%) underwent infragenicular angioplasty. Our main interest was Major Adverse Clinical Outcome (MACO) of thelimb operated upon at follow-up which was adressed as clinical failure, need for subsequent endovascular or surgical revascularization or amputation.

Results: Amputation free survival was seen in 88% with CLTI. Sound healing of wounds was achieved in 76% of cases with a mean value of healing timeof 10.7 months. Significant predictors of MACO were technical failure (*p*-value 0.002) and occlusive lesions (*p*-value 0.019). Freedom of MACO was achieved in 76.1%.

Conclusions: Infragenicular angioplasty is a feasible therapeutic option in diabetic population. Type ofthe lesions in addition to smoking may be predictors of adverse outcome.

Key Words: *Infra genicular angioplasty – Diabetic population – Adverse outcomes.*

Introduction

PERIPHERAL Arterial Disease (PAD), also known as chronic limb threateningischemia, is the most common cause of loss of normal walking ability seen by the vascular specialist. The presence of PAD is a strong marker for the presence of coronary artery and cerebrovascular disease **[1]**.

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Chronic Limbthreatening Ischemia (CLTI) is a severe form of PAD and it is defined as persistent, recurring ischemic rest pain that requires opiate analgesia for at least two weeks, ulceration or gangrene of the foot or toes with ankle systolic pressure less than 50mm Hg or toe systolic pressure less than 30mm Hg **[2]**.

The two major classifications based on the clinical presentations of CLTI and in general PAD into grades and categories are Fontaine classification, in which CLTI is classified as Fontaine III and Fontaine IV: In which ischemic rest pain is classified as Fontaine III and patients suffer tissue loss, such as ulceration or gangrene, is classified as Fontaine IV or Rutherford classification, in which CLTI is classified as: Patients with rest pain are classified as category 4 and grade II. While patients with tissue loss are classified as grade III, and category 5 and 6 **[3-5]**.

Surgery remains a good option for some patients with CLTI, but endovascular therapy offers the advantages of local anesthesia and shorter hospital stay when compared with infragenicular bypass surgery **[6-8]**.

Restenosis remains a major drawback of endovascular intervention and several trials to augment the patency after POBA have included anti ischemic drugs and endovascular brachytherapy, but these modalities have a very minimal role in preventing restenosis. Paclitaxel coated balloons are a new generation with a more primary patency rate **[9-11]**.

The purpose of this study was to locate predictors of clinical outcome after infra genicular angioplasty for occlusive lesions in diabetic patients.

Patients and Methods

We generated a prospective study of 67 patients following informed consent with symptomatic peripheral arterial disease, either rest pain or tissue loss, who underwent infra genicular angioplasty using plain balloons. Medical files, including inpatient and outpatient clinic visits and procedure details were reviewed.

Diabetic patients of different age & sex who were admitted to the Department of Vascular and Endovascular Surgery in Kasr Al-Ainy, Faculty of Medicine and National Institute of Diabetes and Endocrinology and scheduled for below knee angioplasty from the beginning of January 2013 till the end of December 2013 were included into the study. We excluded nondiabeticpatients, patients who had lesions (managed in previous session) proximal to the knee or compromised renal function patients were excluded. Follow-up period was about one year.

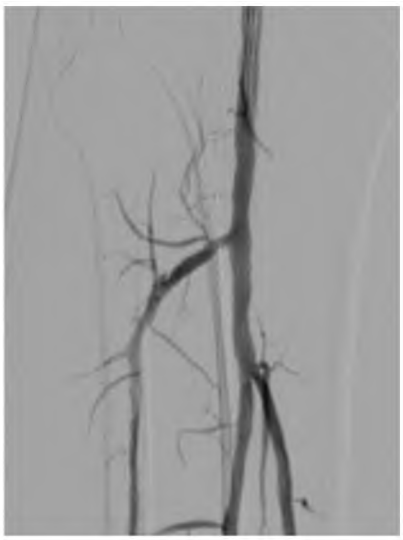
All patients had a thorough vascular examination, including detailed history, physical examination, ankle brachial index, assessment of risk factors and serum creatinine. All patients had a digital subtraction angiogram performed for diagnosis of lesions morphology.

Procedure details:

Angiographic data revealing the whole arterial treewas available on all patients prior to angioplasty. Treated arterial lesions were located at distal popliteal, tibioperoneal trunk or any of thecruralarteries. The atherosclerotic lesion was compared to that of the proximal non-diseased arterial segment to determine degree of stenosis, measured as a percentage.

Sheath insertion

CTA pre-intervention



DSA post-intervention

Before

During

One month later

Rt. Diabetic foot debridement
Computed Tomography Angiography (CTA), Digital Subtraction Angiography (DSA)

Fig. (1): A case of tibial angioplasty followed by debridement.

Then ipsilateral antegrade femoral was used in about 90% of patients (n=60). We performed a crossover technique using the contralateral femoral artery in seven patients (n=7). We injected 5000IU intra-arterial heparin via the sheath. The size of balloon was determined from the diameter of the proximal healthy arterial segment (range 3-6mm). The balloon was inflated to 8-10 atmospheres for 30-60s up to two minutes in resilient lesions with a mechanical inflator.

After deflation, completion angiogram was performed with the guidewire in place and procedure outcome was recorded. Subintimal angioplasty was used in small number of patients (n=9, 13%) due to lesion lengthand/or occlusion. The subintimal angioplasty followed Bolia's previously described techniques.

If arterial spasm occurred, 0.1mg nitroglycerine was given as an intra-arterial bolus. After the intervention, all patients were received an antiplatelet drug (clopidogrel 75mg daily for 3 months followed by acetylsalicylic acid 150mg daily thereafter). Together with lipid lowering agents (atorvastatin 40mg once daily) in dyslipidemic patients Fig. (1).

Post-operative follow-up:

Appropriate medical management was commenced, along with risk factor modification. Clinical outcomes, including improvement in the wound bed, were documented prior to discharge and at subsequent outpatient visits, with repeat Ankle Brachial Index (ABI) and/or Ankle Peak Systolic Velocity (APSV) performed within six weeks.

Statistical analysis:

The association of particular factors that might be incriminated in the development of Major Adverse Clinical Outcome (MACO) was analyzed by either Descriptive: e.g. number, percentage, range, mean and Standard Deviation (SD) or analytical: Fisher's exact test or Chi-Squared (χ^2) for qualitative variable or *p*-value which was significant difference if $p<0.05$, non-significant difference if $p>0.05$ or highly significant difference if $p<0.001$.

Results

No mortality related to surgery was reported and all patients have completed their follow-up; we conducted a prospective study of 67 consecutive patients; 47 males (70.1%) and 20 females (29.9) complained tissue loss; forty five patients (67.2%) had minor tissue loss (Rutherford V) and a number of 20 patients (29.8%) with major tissue loss (Rutherford VI).

Among the study population 64.2% (43/67) was current smokers and 35.8% were non smokers at the time of angioplasty. Smoking seem to be a predictor of MACO. Ten smoker patients (10/16) 62.5% developed MACO while six non smoker patients (6/16) 37.5% developed MACO (Table 1), Fig. (2).

Table (1): Prevalence of MACO and smoking.

Smoking	Healing		BKA & Redo		Total		*p*-value
	No	%	No	%	No	%	
Yes	33	64.7	10	62.5	43	64.2	NS
No	18	35.3	6	37.5	24	35.8	(0.0072)

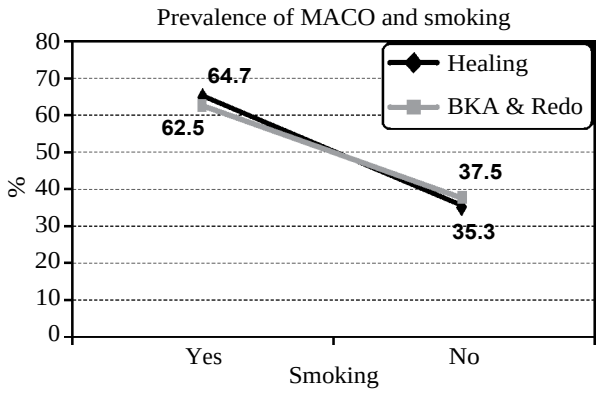


Fig. (2): Prevalence of MACO and smoking.

About the morphology of arterial lesions, we conducted in the current study 10 patients with stenotic lesions, 31 patients with variable lengths of occlusions and a number of 26 patients of mixed stenoses and occlusions. Of those who had stenotic tibial lesions, no one underwent major amputation or had another session of endovascular interventions (no MACO).

Of the group of occlusions or mixed lesions, eight patients underwent major amputations and another eight patients had second session of endovascular interventions in a follow-up period of one year and these results were statistically significant, thus we consider presence of occlusions is a significant factor contributing to MACO (Table 2), Fig. (3).

Table (2): Prevalence of MACO and type of lesions.

Type of lesions	Healing		BKA & Redo		Total		*p*-value
	No	%	No	%	No	%	
Stenosis	10	19.6	0	0.0	10	14.9	0.019
Occlusion	19	37.3	12	75.0	31	46.3	
Both	22	43.1	4	25.0	26	38.8	

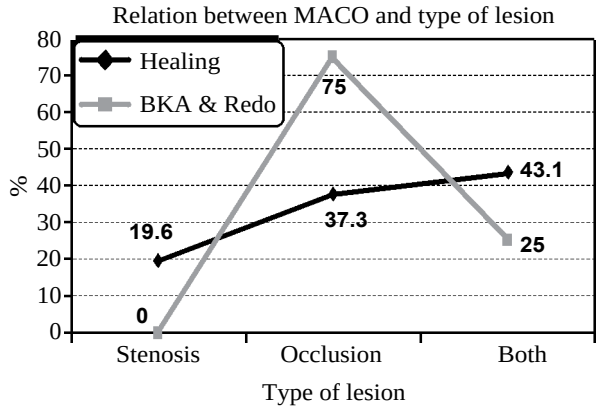


Fig. (3): Prevalence of MACO and type of lesions.

The rest of patients with minor tissue loss those suffered from gangrene of two or three toes [in 28 cases (28/67) 41.8%]. Seven patients of those 28 patients developed MACO either re-intervention (five patients) or major amputation (two patients). These results were of no significant statistical value (Table 3), Fig. (3).

Table (3): Prevalence of MACO and minor tissue loss.

Minor tissue loss	Healing		BKA & Redo		Total		*p*-value
	No	%	No	%	No	%	
No	30	58.8	9	56.2	39	58.2	NS
Toes	21	41.2	7	43.8	28	41.8	(0.856)

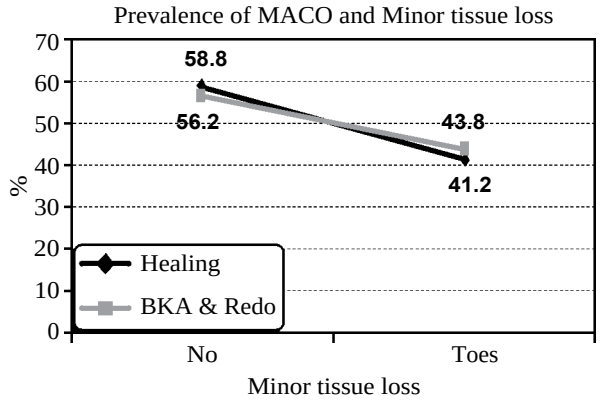


Fig. (4): Prevalence of MACO and Minor tissue loss.

We treated thirteen patients with major tissue loss (13/67) 19.4%, eleven patients with wounds located at forefoot (11/67) 16.4% while two patients with wounds at the heel of the foot (2/67) 3%. Six patients of those 13 patients developed MACO either re-intervention (two patients) or major amputation (four patients). These results were of no significant statistical value (Table 4), Fig. (5).

Sound healing ofwounds was achieved in 76% of cases with a mean value of healing time 10.7 months. But 8 patients (12%) required major amputation. In the current study, we reported a limb salvage rate of 88% and technical success rate of 95.5%. Freedom of MACO is achieved in 76.1%.

Table (4): Prevalence of MACO and Major tissue loss.

Major loss	Healing		BKA & Redo		Total		*p*-value
	No	%	No	%	No	%	
Forefoot	6	11.8	5	31.3	11	16.4	NS
Heel	1	2.0	1	6.3	2	3.0	(0.110)
No	44	86.2	10	62.4	54	80.6	

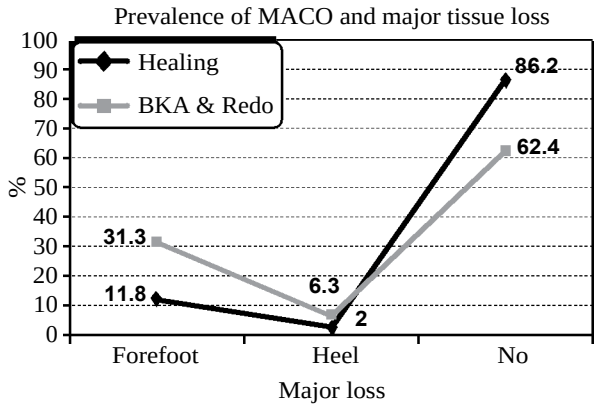


Fig. (5): Prevalence of MACO and Major tissue loss.

Discussion

Percutaneous Transluminal Angioplasty (PTA) is less invasive and is repeatable in case of recurrent ulcers; moreover, it can be used in multilevel lower limb arterial involvement and preserve the saphenous vein. Despite the technical and procedural advances in endovascular BTK revascularization, the stability and long-term patency of PTA is far from optimal, especially in diabetic patients. In addition to the higher incidence of BTK arteries lesions, in diabetic patients with CLI, collateral formation and arteriogenesis in response to ischemia is typically poor **[12]**.

In our study, 67 limbs of 67 patients with a mean age of 64.34±14.75 years were treated. Most of our patients were men 47 (70.1%). Gallagher et al., reported that patients with chronic limb threatening ischemia receiving infra genicular angioplasty, women had superior primary and secondary patency rates at all time points when compared to men **[13]**.

All patients were diabetics. The duration of diabetes was 20.68±9.79 years, and 55.8% of the patients were insulin dependent. Patients with diabetes and concomitant PAD are more likely to

have infrapopliteal atherosclerotic disease and are more likely to present with ischemic ulcers or gangrene **[14]**.

Diabetics are up to 15 times more likely than non-diabetics to suffer a major amputation. Diabetes is also associated with decreased primary patency following endovascular interventions. Cardiovascular outcomes are strongly related to tight glycemic control in patients with diabetes. Glycemic control may be associated with improved limb outcomes and vessel patency in patients undergoing endovascular intervention **[15,16]**.

Regarding other studies, another study by Kassaian, et al., treated 45 diabetic patients. Most of their patients were men (76%). Almost 70% of their patients had a positive history of hypertension and were under antihypertensive treatment, and 4% of their study population were current smokers [17].

In a multicenter study by Iida et al., hypertension was found in 73%. History of hyperlipidemia, coronary artery disease, and stroke was positive in 31, 51, and 24% of the patients, respectively, and 36% of their patients were current smokers. Freedom from MALE (major adverse limb events) rate was 57% and 47% at 1 and 2 years, respectively [18].

Sound healing of wounds was achieved in 76% of cases with a mean value of healing time 10.7 months. But 8 patients (12%) required major amputation. Four of them were categorized as Rutherford VI, three patients as Rutherford V and one patient of the amputee had rest pain (Rutherford IV). In our study, patients underwent major amputation because of tissue loss were seven. Six patients had below knee amputation and one patient underwent above knee amputation because of severe infection spreading to the thigh. The cause of amputation was either severe infection that the limb did not withstand (4 cases), or having peroneal artery as the only runoff vessel (3 cases).

Giles et al., reported on their experience with infrapopliteal angioplasty for CLTI in 176 limbs. At a mean follow-up of 12 months, they reported complete healing or improvement in 57% of limbs, with stable wounds in 22% and worsening of the wound in 21% **[6]**.

The larger the wound size or the volume of tissue loss may predict MACO. However, specific wound size information was not available on enough patients to analyze this factor in the current study. We categorized our patients as having minor or major tissue loss. The major goals to achieve in patients with CLTI are healing of chronic wounds, stopping of ischemic rest pain and limb salvage. Long patency rates are preferable but not strictly necessary. A lot of studies have been conducted but have some limitations.

Infra genicular endovascular interventions in the setting of CLTI have been extensively elaborated with mixed results. Romiti et al., showed in a meta analysis that one year primary and secondary patency rates of 58% and 68%, respectively, with a limb salvage rate of 86% and patient survival of 98% **[19]**.

We reported a limb salvage rate of 88%. Our limb salvage percentage was in accordance with that reported in the literature. In a review of ten largest studies on the endovascular treatment of CLI by Graziani, et al., the limb salvage rate was in the range of 80%-98% at six to 18 months of follow-up. Another study reported a limb salvage rate of 82% at six months after PTA **[8,20,21]**.

Schmidt, et al., treated 109 limbs (82.6%) for CLTI. The restenosis rate (>50%) at 1 year was 27.4%, with a limb salvage rate of 95.6% for patients with CLI. They used drug coated balloons in their study, thus they achieved higher limb salvage rate than ours **[22]**.

Our limb salvage rate is also lower than that previously quoted by Kalbaugh et al., of 90.0% at six months; however, we report a longer follow-up period **[23]**.

Mixed ischemic and infected diabetic foot is very common situation. This demonstrates the dilemma of determining the which first policy either debridement or angioplasty. Of courseprimary major amputation has a higher mortality rate than primary revascularization. Barshes et al., reported a 9.9% 30-day mortality rate after major amputation versus 6.5% in primary revascularization in high-risk patients **[24]**.

Conclusions:

Infra genicular angioplasty is a feasible therapeutic option in diabetic population. Type ofthe lesions in addition to smoking may be predictors of adverse outcome.

References

1- HIRSCH A.T., CRIQUI M.H., TREAT-JACOBSON D., REGENSTEINER J.G., CREAGER M.A., OLIN J.W., KROOK S.H., HUNNINGHAKE D.B., COMEROTA A.J., WALSH M.E., McDERMOTT M.M. and HIATT W.R.: Peripheral arterial disease detection, awareness,

and treatment in primary care. JAMA, 286: 1317-24, 2001.

2- NORGREN L., HIATT W.R., DORMANDY J.A., NEHLER M.R., HARRIS K.A. and FOWKES F.G.: TASC II Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J. Vasc. Surg., 45: S5-S67, 2007.

3- ROLLINS K.E. and COUGHLIN P.A.: Functional outcomes following revascularization of critical limb ischemia. European Journal of Vascular and Endovascular Surgery, 43: 420-5, 2012.

4- RUTHERFORD R.B., BAKER J.D., ERNST C., JOHNSTON K.W., PORTER J.M., AHN S. and JONES D.N.: Recommended standards for reports dealing with lower extremity ischemia: Revised version. J. Vasc. Surg., 26: 517-38, 1997.

5- SAYED A., TAHA A., ELKHOLY M., ELSHARNOBI H. and KHAIRY H.: Tibial angioplasty in diabetic patients: Should all vessels be treated? Int. Angiol., 31 (3): 239-44, 2012.

6- GILES K.A., POMPOSELLI F.B., SPENCE T.L., HAMDAN A.D., BLATTMAN S.B., PANOSSIAN H., et al.: Infrapopliteal angioplasty for critical limb ischemia: Relation of Trans Atlantic Inter Society Concensus class to outcome in 176 limbs. J. Vasc. Surg., Jul., 48 (1): 128-36, 2008.

7- GOSHIMA K.R., MILLS J.L. Sr. and HUGHES J.D.: A new look at outcomes after infrainguinal bypass surgery: Traditional reporting standards systematically underestimate the expenditure of effort required to attain limb salvage. J. Vasc. Surg., 39: 330-5, 2004.

8- GRAZIANI L. and PIAGGESI A.: Indications and clinical outcomes for below knee endovascular therapy: Review article. Catheterization and Cardiovascular Interventions, 75: 433-43, 2010.

9- DeRUBERTIS B.G., FARIES P.L., McKINSEY J.F., CHAER R.A., PIERCE M., KARWOWSKI J., et al.: Shifting paradigms in the treatment of lower extremity-vascular disease: A report of 1000 percutaneous interventions. Annals of Surgery, 246: 415-24, 2007.

10- DIEHM N.A., HOPPE H. and DO D.D.: Drug Eluting Balloons. Tech Vasc. Interv. Rad., 13: 59-63, 2010.

11- FAGLIA E., CLERICI G., CAMINITI M., QUARANTIELLO A., CURCI V. and MORABITO A.: Predictive values of transcutaneous oxygen tension for above-the-ankle amputation in diabetic patients with critical limb ischemia. Eur. J. Vasc. Endovasc. Surg., 33: 731-6, 2007.

12- GRAZIANI L., SILVESTRO A., BERTONE V., MANARA E., ANDREINI R., SIGALA A., MINGARDI R. and De GIGLIO R.: Vascular involvement in diabetic subjects with ischemic foot ulcer: A new morphologic categorization of disease severity. Eur. J. Vasc. Endovasc. Surg., 33 (4): 453-60, 2007.

13- GALLAGHER K.A., MELTZER A.J., RAVIN R.A., GRAHAM A., CONNOLLY P., ESCOBAR G., et al.: Gender differences in outcomes of endovascular treatment of infrainguinal peripheral artery disease. Vasc. Endovascular. Surg., 45: 703-11, 2011.

14- JUDE E.B., OYIBO S.O., CHALMERS N.R. and BOULTON A.J.: Peripheral arterial disease in diabetic and nondiabetic patients: A comparison of severity and outcome. Diabetes Care, 24: 1433-7, 2001.

15- ABULARRAGE C.J., SIDAWY A.N., AIDINIAN G., SINGH N., WEISWASSER J.M. and ARORA S.: Evaluation of the microcirculation in vascular disease. J. Vasc. Surg., 42: 574-81, 2005.

16- STRATTON I.M., ADLER A.I., NEIL H.W., MATTHEWS D.R., MANLEY S.E., CULL C.A., et al.: Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): Prospective observational study. Br. Med. J., 321: 405, 2000.

17- KASSAIAN S.E., MOHAJERI TEHRANI M.R., DEHGHAN NAYYERI A., et al.: Major Adverse Events, Six Months after Endovascular Revascularization for Critical Limb Ischemia in Diabetic Patients. Arch. Iran Med., 16 (5): 258-63, 2013.

18- IIDA O., SOGA Y., HIRANO K., KAWASAKI D., SUZUKI K., MIYASHITA Y., et al.: Midterm outcomes and risk stratification after endovascular therapy for patients with critical limb ischemia due to isolated below-the-knee lesions. Eur. J. Vasc. Endovasc. Surg., 43 (3): 313-21, 2012.

19- ROMANO M., MAINENTI P.P., IMBRIACO M., AMATO B., MARKABAOUI K., TAMBURRINI O., et al.: Multidetector row CT angiography of the abdominal aorta and lower extremities in patients with peripheral arterial occlusive disease: Diagnostic accuracy and interobserver agreement. Eur. J. Radiol., 50 (3): 303-8, 2004.

20- MENDIZ O.A., FAVA C.M., VALDIVIESO L.R., LEV G.A. and VILLAGRA L.G.: Angioplasty for treatment of isolated below-the-knee arterial stenosis in patients with critical limb ischemiat Angiology, 62: 359-64, 2011.

21- TAYLOR A.J., SULLENBERGER L.E., LEE H.J., LEE J.K. and GRACE K.A.: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol (ARBITER) 2: A double-blind, placebo-controlled study of extended-release niacin on atherosclerosis progression in secondary prevention patients treated with statins. Circulation, 110: 3512-7, 2004.

22- SCHMIDT A., PIORKOWSKI M., WERNER M., ULRICH M., BAUSBACK Y., BRÄUNLICH S., ICK H., SCHUSTER J., BOTSIOS S., KRUSE H.J., VARCOE R.L. and SCHEINERT D.: First experience with drug-eluting balloons in infrapopliteal arteries: Restenosis rate and clinical outcome. J. Am. Coll. Cardiol., 58: 1105-9, 2011.

23- KALBAUGH C.A., TAYLOR S.M., CULL D.L., et al.: Invasive treatment of chronic limb ischaemia according to the lower extremity grading system (legs) score: A 6 month report. J. Vasc. Surg., 39 (6): 1268-76, 2004.

24- BARSHES N., MENARD M., NGUYEN L., et al.: Infrainguinal bypass is associated with lower perioperative mortality than major amputation in high-risk surgical candidates. J. Vasc. Surg., 53 (5): 1251-9, 2011.

القسطرة التداخلية فى شرايين ما تحت الركبه فى مرضى السكر: تنبؤ النتائج الإكلينيكية الرئيسية السلبية

قصور الشرايين الطرفية يعد من أكثر أسباب الأمراض المزمنة ويكثر تشخيصه فى كبار السن المصابين بالداء السكرى. والقصور الحرج للشرايين الطرفية يعتبر مرحلة متأخرة قد تؤدى بحياة المريض أو تؤدى لبتر الساق والعجز الجزئى.

ذلك بالإضافة إلى المخاطر المصاحبة لعمليات توصيل الشرايين أدى إلى الإستثمار فى علاج قصور الشرايين بالقسطرة التداخلية.

تتضمن هذه الدراسة سبعة وستون مريضاً فى الفترة من يناير ٢٠١٣ إلى ديسمبر ٢٠١٣ وكانوا يعانون من القصور الحرج فى الدورة الدموية للأطراف السفلية وتم علاجهم بالتوسيع البالونى للشرايين القصبية. وهدف الدراسة هو تقييم فاعلية التوسيع البالونى للشرايين القصبية فى علاج القصور الحرج للدورة الدموية للأطراف السفلية وتحديد العوامل التى تنبئ بنتائج إكلينيكية سلبية كبرى مثل:

١- إعادة التدخل سواء بالقسطرة التداخلية أو بالجراحة.

٢- الفشل فى إلتئام جروح القدم السكرية.

٣- فشل التوسيع البالونى مما يؤدى إلى بتر الساق أسفل أو أعلى الركبة.

خطة العلاج كانت توسيع أكبر عدد من الشرايين القصبية فى المرضى المصابين بالغرغرينا وإلتهابات القدم السكرى بإستخدام البالونات العادية دون اللجوء إلى البالونات الدوائية أو الدعامات.

تم متابعة المرضى لمدة عام بعد إجراء التدخل وكانت النتائج كالتالى:

١- إلتئام الجروح تماماً فى عدد ٥١ مريض.

٢- بتر الساق لعدد ٨ مرضى.

٣- إعادة التدخل عن طريق القسطرة فى عدد ٨ مرضى.