Do diabetic patients who undergo transtibial amputation receive adequate treatment?

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Do diabetic patients who undergo transtibial amputation receive adequate treatment?

AIMS: *To determine if patients who undergo below-knee amputation (BKA) for intractable wounds caused by diabetes complications receive adequate treatment before surgery.*
MATERIALS AND METHODS: *The study included a total of 528 patients who underwent transtibial amputation for diabetic foot. All patients were assessed on the basis of duration of preoperative treatment, HbO therapy, negative wound pressure therapy (NPWT), peripheral vascular angioplasty (PVA) treatment, wound cultures, antibiotic medications, consultations with plastic and vascular surgeons, need for hemodialysis treatment, use of anticoagulant treatment as an inpatient, and assessment of blood sugar regulation by an endocrinologist. HbA1c, BUN, Creatinine, ESR, and CRP values attained for preoperative assessment were noted.*
RESULTS: *Eighteen patients (3.5%) received HbO therapy, 35 (6.7%) NPWT therapy and 347 (65.7%) anticoagulant treatment. Wound cultures were taken in 317 patients (60.5%) and 390 (73.9%) received preoperative antibiotic treatment. 45 (8.6%) patients were assessed by plastic surgeon with 22 (4.2%) subsequently undergoing surgery by the plastic surgeon. Vascular surgeons assessed 163 patients (30.9%) and performed procedures on 45 patients (8.6%). Endocrinologists assessed 316 patients (59.8%) and implemented blood sugar regulation. PVA treatment was performed in 246 patients (46.6%).*
Patients who were managed medically for more than 7 days after the initial assessment received more HbO therapy (p=0.037), anticoagulant treatment (p=0.015), IV antibiotics (0.001), blood sugar regulation attempts (p=0.001), and PVA therapy (0.001) and had more cultures taken (p=0.001). These patients also received overall more diagnostic and treatment modalities than those that received definitive surgical intervention within 7 days.
CONCLUSIONS: *The duration of time patients with diabetes-related foot problems who see orthopedic surgeons for longer periods of time receive more treatment modalities and are referred more often to specialists before transtibial amputation surgery. We believe that delayed presentation is one of the main obstacles prohibiting adequate treatment for these patients.*

KEY WORDS: Diabetic foot, Transtibial amputation, Treatment

Introduction

The etiology of diabetic foot ulcers can be grouped into three major classifications: neuropathic (due to damage of the nerves); ischemic (due to a poor blood supply); or neuroischemic (due to damage to the nerves and a poor blood supply). Although etiologies differ, treatment modalities are the same and include hyperbaric oxygen treatment (HbO), peripheral vascular angioplasty (PVA), negative pressure wound therapy (NPWT), blood sugar regulation, wound management, intravenous (IV) antibiotics etc [1-3]. Globally, a patient loses an extremity due to failed treatment for this condition every 30 seconds [4,5]. Criteria for below knee amputation criteria have been established by Weledji and Fokam as wet gangrene (infection + ischemia), life-threatening sepsis, extensive muscle necrosis, impossibility of revascularization, being bed-ridden, having a functionally useless limb, and unsuccessful revascularization[6].

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Diabetic foot problems have not historically drawn much attention from orthopedic surgeons due to their discouraging longevity and mortality rates and long-term follow-up needs. A multi-disciplinary approach is needed in the management of diabetic foot before the decision to amputate is made[7]. A variety of diagnostic and treatment modalities should be utilized in its treatment to either avoid the need for amputation or to contribute to positive postoperative outcomes. For these reasons, early presentation is vital for adequate treatment of diabetic foot problems. However, studies have reported that amputation scares diabetic patients even more than death and mean survival after transtibial amputation is less than 3 years[8, 9], which, along with other factors, might result in delayed presentation, limiting the feasibility of attempting various treatment modalities.

The aim of this study is to determine whether patients admitted for diabetic foot problems receive adequate therapy attempting to salvage the extremity before the decision for below-knee amputation procedure is made.

Methods

Patient Selection

A retrospective review of prospectively collected data from the Başkent University Research and Training Hospital orthopedic department database was performed. The files of 1401 patients who underwent lower extremity major amputation between 2000 and 2016 were analyzed. Of these, 802 underwent transtibial amputation. When including the International Classification of Diseases (ICD) codes E10 for type 1 Diabetes Mellitus (DM) and E11 for type 2 DM, the number of relevant patient files was reduced to 687. An additional 22 patients who underwent operation for intractable traumatic wounds (gunshot injuries and non-healing fracture wounds) and 137 patients with missing data were excluded from the study. The remaining 528 patient files were analyzed for the study.

Below-knee amputation was performed for patients with necrotic and gangrenous wounds that resulted in deterioration of the patient's general condition and/or in patients for whom below-ankle amputations were not possible. Transtibial amputations were all performed according the procedure described by Brückner in 1986 [10].

All patient files were assessed for age, gender, duration of preoperative management, HbO therapy, negative wound pressure therapy (NPWT), peripheral vascular angioplasty (PVA) treatment, wound cultures and intravenous antibiotic medications, plastic and vascular surgeons consultations, need for hemodialysis treatment, use of anticoagulant treatment as an in-patient, and assessment by an endocrinologist for regulation of blood sugar. Moreover, the duration of diabetes, body mass index (BMI), postoperative survival durations, and glycated hemoglobin (HbA1c), blood urea nitrogen (BUN), Creatinine, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) values attained for preoperative assessment were noted.

Statistical Analysis

The normality of distribution of continuous variables was tested using the Shaphiro Wilk test. The Student's t-test (for normal data) and the Mann-Whitney U Test (for non-normal data) were used to compare 2 independent groups for numerical variables. The Chi-square test was applied to investigate relationship between 2 categorical variables. The log-rank test was performed to compare 2 survival curves and hazard regression analysis to evaluate the effect of a numerical variable on survival times. Statistical analysis was performed with SPSS for Windows version 24.0 and a P value of < 0.05 was accepted as statistically significant.

Results

A total of 528 patients (337 men and 191 women) were enrolled in the study. Mean age was 64.5 years (range: 20-101 years). The mean age of the female patients was 66.63 years (range: 20-101 years) and was statistically higher (p=0.001) than the mean age of the male patients (63.33 years; range: 29-90 years). Mean HbA1c was 9.05% (range: 4.3-15.93%), mean ESR 89.96 mm/h (range: 7-204 mm/h), mean CRP 140mg/L (range: 0.26-90 mg/L), mean BUN 37.75 mg/dL (range: 4-144 mg/dL), mean creatinine 2.66mg/L (0.26-90 mg/L), and mean BMI 29.37 kg/m^2 (range: 18-49 kg/m^2), while mean diabetes period was 17.1 years (range: 1-40 years) (Table I).

Mean duration of preoperative management was 62.93 ± 133.91 days and mean postoperative survival was 852 ± 101 days. Of the total of 528 patients, 457 (86.5%) were under medical management for a mean of 69.9 ± 141.7 days and received at least one diagnostic and treatment modality whereas 71patients (13.5%) were

Table I - *Demographic characteristics of 528 patients.*

Variable	Mean	min-max	
Age (year)	64.52	20-101	11,47
Life period (day)	878	1-	926
HbA1c (%)	9.05	4,3-15,93	2,2
ESR (mm/h)	89,96	7-204	30.42
CRP (mg/L)	140	3-469	79.7
BUN (mg/dL)	37.75	4-144	24.43
Creatinin (mg/L)	2,66	0.26-90	4,58
BMI (kg/m^2)	29.37	18-49	4.35
Diabet period (year)	17.1	1-40	7.64

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TABLE II - *Treatment methods and percentages.*

Treatment methods	n	%
Hiperbaric Oxygen therapy		
Yes	18	3.5
No	510	96.5
Negative pressure wound therapy		
Yes	35	6.7
No	493	93.3
Anticoagulant therapy		
Yes	347	65.7
No	181	34.3
Wound culture		
Yes	319	60.4
No	209	39.6
Periferic vascular angioplasty		
Yes	246	46,6
No	282	53.3
Plastic surgery consultation		
Surgery (flep, greft, debridmant)	22	4,2
Yes	23	4,4
No	483	91.4
Vascular surgery consultation		
Surgery (Embelectomy,bypass)	45	8.6
Yes	118	22,3
No	365	69.1
Endocrinology Consultation		
Yes	316	59.8
No	212	40.2
IV antibiotics		
Yes	390	73.9
No	138	36.1

treated for a mean of 16.8 ± 36.9 days and received no diagnostic or treatment modality (p=0.001).
Eighteen patients (3.5%) received HbO therapy, 35 (6.7%) received NPWT therapy, and 347 (65.7%) anticoagulant treatment. Wound cultures were taken in 319 patients (60.4%) and preoperative IV antibiotic treatment was given in 390 patients (73.9%). Plastic surgeons assessed 45 patients (8.6%) and subsequently 22 patients (4.2%) underwent surgery (flap, graft, etc.). Vascular surgeons assessed 163 patients (30.9%) and performed procedures such as embolectomy or peripheral vascular by-pass on 45 (8.6%). Preoperatively, endocrinologists assessed 316 patients (59.8%) and initiated blood sugar regulation (continuous insulin infusion, blood glucose monitoring, etc.). PVA treatment was given to 246 patients (46.6%). Data is provided in detail in Table II. There were no statistically significant differences in variables between gender groups. However, a significantly greater number of wound cultures were taken from patients receiving dialysis treatment (p=0.042). These patients were less likely to be referred to HbO therapy (p=0.034), a peripheral vascular surgeon (p=0.002), or an endocrinologist (p=0.003).

Twenty percent of patients were administered only one treatment or diagnostic modality before surgery: 57 (10.8%) peripheral vascular angioplasty only, 43 (8.1%) IV antibiotics treatment only and 7 (1.3%) had wound cultures taken but no other intervention.
Wound cultures were performed in only 160 patients (30.3%) before administration of antibiotic treatment. Antibiotic treatment was given to 227 patients (43%) without any prior wound culture.
The majority (67.6%) of patients (362) underwent direct below-knee amputations while 119 patients (23.2%) had undergone prior toe amputations and 47 (9.2%) foot amputations (transmetatarsal, Chopart, Lisfranc). Mean follow-up period for patients with a prior history of amputation was 113.05 ± 179.84 days and that for those who did not was 40.09 ± 98.94 days. There was a statistically significant difference in survival between these two groups (p=0.001).
Anticoagulant therapy was administered in 197 of the 246 patients (80%) who received PVA as well as in 148 of the 280 (52.9%) who did not receive PVA intervention (p=0.001).
Patients who were managed medically for more than 7 days after admission were more likely to receive HbO therapy (p=0.037), anticoagulant treatment (p=0.015), IV antibiotics (p=0.001), blood sugar regulations (p=0.001), and PVA therapy (0.001) and had more cultures taken (p=0.001), Overall, these patients underwent more diagnostic and treatment modalities than those who received definitive surgical intervention within 7 days (p=0.001) (Table III).

Discussion

It is well known that extremity loss in patients with diabetes-related foot problems can be mitigated by education and early diagnostic and therapeutic intervention [11]. Many factors such as etiology, duration of diabetes disease, age, co-morbid conditions, and stage of the disease affect treatment success[12,13]. The aim of treatment in this patient group should focus on increasing oxygenation of the peripheral tissue, treatment of the infection in infected wounds, and protection of the tissue under pressure [14]. However, our study revealed that diabetic patients do not receive adequate therapeutic intervention before the decision to perform below-knee amputation is taken. We also found that patients who were managed medically for longer than 7 days prior to surgery received more diagnostic and therapeutic modalities than the patients who underwent surgery within 7 days. Any delays in seeking treatment may negatively affect the diagnostic and therapeutic interventions available to the patient.
Erratic blood glucose values and high HbA1c levels carry risk for amputation [15]. Glycemic control is difficult in patients with peripheral vascular disease and infection [15]. In our study we noted even though mean HbA1c% levels

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TABLE III - *Comparison of patients with less than 7 days of follow-up before the transtibial amputation surgery*

	<=7 day n (%)	>7 day n (%)	P value
Overall diagnosis and treatment			
Yes	176 (%79)	281 (%92)	0,001*
No	48(%21)	23 (%8)	
Hiperbaric oxygen therapy			
Yes	3 (%1)	15 (%5)	0,037*
No	221 (%99)	289 (%95)	
Negative pressure wound therapy			
Yes	7 (%3)	26 (%8)	0,015*
No	217 (%97)	279 (%92)	
Anticoagulant Therapy			
Yes	132 (%59)	215 (%71)	0,005*
No	92 (%41)	89 (%29)	
IV Antibiotic Therapy			
Yes	140 (%63)	250 (%82)	0,001*
No	84 (%37)	54 (%18)	
Endocrinology consultation			
Yes	87(%39)	229 (%74)	0,001*
No	137 (%61)	75 (%26)	
Periferic Vascular Intervention			
Yes	81 (36%)	165 (54%)	0.001*
No	143 (64%)	139 (46%)	
Culture			
Var	97 (43%)	222 (73%)	0.001*
Yok	127 (57%)	82 (27%)	
Plastic surgery Consultation			
Yes	3 (1%)	42 (14%)	0.001*
No	221 (99%)	262 (86%)	
Vascular Surgery Consultation			
Yes	53 (24%)	65 (23%)	0,642
Surgery (periferic vascular by-pass)	21 (9%)	24 (8%)	
No	150 (67%)	215 (71%)	

**Significant at 0,05 level; Chi-square test*

were 9.05% (normal value range 3.9%-6.1%), only 316 patients (59.8%) were assessed by an endocrinologist to regulate blood sugar after admission.

Ischemia in diabetic patients is caused by narrowing of large and small vessels [16]. Because vessels above the knee and below the ankle tend to be relatively spared, lower extremity atherosclerosis may be amenable to angioplasty or vascular bypass [17]. The use of anticoagulant drugs is recommended to prevent re-stenosis after peripheral vascular by-pass and PVA procedures and to protect the other extremity [18,19]. Anticoagulant drugs are also utilized to prevent thromboembolism following lower extremity amputation[20,21]. In our study, 246 patients (46.6%) received PVA therapy and 163 (30.9%) were assessed by peripheral vascular surgeon with 45 (8.6%) subsequently undergoing vascular surgery (embolectomy, by-pass). We also noted that while anticoagulant medication was given to all patients who underwent peripheric vascular surgery, only 197 of patients who underwent 246 PVA procedure (80%) received anticoagulant medications. Also noteworthy is the fact that patients who underwent PVA interventions received statistically more anticoagulant therapy than those that received no interventions. Beyaz et al. showed there is a correlation between longer survival and use of anticoagulants after PVA procedures [8]. However, our data did not reveal the specific indication for which the anticoagulants were administered. The fact that patients underwent amputation surgery despite undergoing PVA treatment raises questions over its indication and success.

Management of infected diabetic wounds caused by poor tissue oxygenation and pressure is difficult. In our study only 74% of patients received preoperative antibiotics despite an elevated mean ESR value of 90 and mean CRP of 140. Antibiotic therapy was based on tissue culture and specific to the bacteria identified in 160 patients (30.3%) while 228 (43.2%) received empiric antibiotic therapy. Because of the risk of bacterial resistance to antibiotics, chronic infections, and super infections encountered in empiric antibiotic use, it is advisable to use antibiotic treatment specific to bacteria identified on wound cultures [22]. Although vascular problems in these patients may limit

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systemic antibiotic distribution to the infected tissue the preferable method for administering antibiotics is intravenously[22]. In the current study only 143 patients (27.1%) received peripheral vascular intervention and wound culture-specific antibiotic treatment. We have no data to show whether the elevated ESR and CRP levels were directly due to the diabetic foot problems.

Studies have shown that HbO therapy greatly decreases the risk of major lower limb amputations in patients with chronic foot ulcers [2,23]. However, HbO therapy is a time consuming treatment that is only available in limited centers with requisite technique and technology. Only 18 of the 525 patients (3.5%) in the current study received HbO therapy prior to below-knee amputation. It is not clear whether this low number was due to the unavailability of the technique, lack of knowledge on the part of the surgeon, or co-morbid conditions.

A greater number of the 151 hemodialysis patients were referred to endocrinologists for blood sugar regulation and had a greater number of affected tissue cultures performed. We attribute this to the fact that these patients were hospitalized at least twice a week for dialysis. However, these patients were less likely to be referred to HbO therapy, or cardiovascular surgeons, an observation we attribute to the fact that these patients have co-morbid cardiac conditions and have therapy-resistant foot ulcers [24].

Diabetic foot requires multidisciplinary approach. Plastic and vascular surgeons play vital roles in this multidisciplinary treatment [25,26]. Chronic foot ulcers caused by diabetes have been successfully treated with flaps or grafts [27]. However, in the current study only 45 patients (8.6%) saw a plastic surgeon with 22 (4.1%) undergoing surgical procedures. Only 45 patients (8.6%) patients underwent peripheral vascular surgery. We believe that these low numbers are due to the popularization of minimally invasive peripheral vascular procedures.

NPWT reduces bacterial colonization and interstitial edema and increases capillary circulation and mitotic activity, enhancing re-epithelialization and collagen synthesis in the wound [28]. Clinical trials have shown that these cellular level activities reduce progression to amputation in both acute and chronic diabetic foot ulcers [29,30]. In our study only 35 patients (6.7%) received NPWT therapy.

In diabetic patients, problems other than acute ischemic arterial obstructions begin as a standing ulcer and swelling. Early diagnosis and comprehensive treatment can result in rapid healing and minimized morbidity and mortality rates and may prevent foot and leg amputations in the absence of ischemia and osteomyelitis[31]. There is a direct correlation between the wound severity of and amputation risk. Patients who are caught at an early stage have a higher chance of treatment [32].

The main limitation of our study is its retrospective design and the resultant gaps in information we were able to gather, including whether patients were managed at other centers or whether the patients declined any treatment. Similarly, records did not allow us to determine if patients delayed presentation and for what reasons. Finally, we do not have data on whether the problem in these patients was neuropathic or vascular in nature.

Conclusion

In diabetic patients with foot problems multidisciplinary approaches and treatment methods are vital. For these patients, amputation surgery should be the last treatment option. However, when other treatments fail or when treatment is not begun in time, amputation may be the only option to prevent mortality. Our results show that patients who were operated within 7 days did not have enough time to wait for the result of the treatment options. We believe that one reason for the low number of attempted treatment modalities was the patients' delayed presentation. Further studies into the relationship between the level of disease progression at time of presentation and the prescribed treatment modalities would be of significant value for the treatment of diabetic foot problems.

Riassunto

Si tratta di uno studio retrospettivo che copre un periodo di 16 anni di 528 pazienti sottoposti ad amputazione al di sotto del ginocchio a causa di complicanze da patologia fiabetica. Sono stati studiati la portata e l'uso di metodi convenzionali di diagnosi e trattamento universalmente accettati. In questo studio è stato esaminato il periodo di trattamento prima dell'amputazione sotto il ginocchio, la terapia antibiotica IV, la terapia anticoagulante, la terapia della ferita a pressione negativa, l'angioplastica vascolare periferica, la terapia iperbarica, la valutazione dei pazienti da chirurghi plastici, chirurghi cardiovascolari ed endocrinologi. La scoperta più interessante è stata che i pazienti sottoposti a intervento chirurgico nei primi 7 giorni di presentazione hanno ricevuto meno modalità diagnostiche e di trattamento rispetto a quelli con periodi di trattamento più lunghi. I problemi del piede diabetico non attirano molta attenzione dai chirurghi ortopedici a causa dei loro risultati scoraggianti e della necessità di un follow-up a lungo termine per la loro gestione. Questo studio è un primo in letteratura nel senso che evidenzia la necessità di una diagnosi precoce del piede diabetico e reindirizza la necessaria attenzione in questo campo.

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