Outcomes of Osteomyelitis in Patients with Diabetes: Conservative vs. Combined Surgical Management in a Community Hospital in Puerto Rico

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Objective: Diabetes predisposes patients to multiple complications, such as osteomyelitis, which, if not managed adequately, may result in amputation, sepsis, or death. This study aimed to compare the rates of amputation associated with two different treatment plans for osteomyelitis being utilized with a group of Puerto Ricans with diabetes.

Methods: We reviewed the medical records of adult patients with diabetes and osteomyelitis who had been admitted to a community hospital within a two-year timeframe; a total of 169 records were reviewed. Data were analyzed using descriptive statistics, chi-square, odds ratios, and multivariate logistic regression to compare the amputation rate of patients receiving conservative management (antibiotics and/or local care alone) with that of patients receiving combined surgical treatment (any modality consisting of an initial surgical treatment plus antibiotics and/or local care).

Results: We found a general amputation rate of 34.5%. Amputation was less likely in patients undergoing combined surgical treatment (OR: 0.22; 95% IC: 0.08-0.59) than it was in those patients whose disease management was conservative. In addition, men (OR: 2.09; 95% CI: 1.04-4.23) and non-geriatric patients (OR: 3.38; 95% CI: 1.65-6.94) had higher probabilities of amputation than did women and geriatric patients, respectively.

Conclusion: This study revealed an amputation rate among patients with diabetes that is higher than that reported in the United States (34.5% vs. 11.0% to 20.0%). We also found that the probability of amputation secondary to osteomyelitis among patients with diabetes is two times higher for men and three times higher for non-geriatric patients; combined surgical treatment was associated with a significant reduction (78%) of the probability of amputation. [*P R Health Sci J 2011;30:51-57*]

Key words: Osteomyelitis, Conservative treatment, Surgical treatment, Diabetes mellitus

Osteomyelitis is defined as an infection of the bone, bone marrow, or its structures that is secondary to inoculation (direct or contiguous) or to the hematogenous seeding of pathogenic bacteria at the site of infection (1, 2). Although it may occur in any individual, diabetic patients are especially prone to developing osteomyelitis. Peripheral neuropathy, impaired immune system, and peripheral vascular disease, all of which are common in diabetic patients, contribute to the development of lesions and infections that further progress to involve bone structures (3-7). The literature indicates that 30% to 40% of patients with diabetes develop osteomyelitis after a foot puncture, compared to only 16% of the general population sustaining a similar injury (8). These patients are at risk of amputation of the affected limb as well as other negative outcomes including generalized infection, sepsis, and death (8).

Conservative management (local care and antibiotic treatment, whether intravenous or oral) and surgical management (debridement and/or incision and the drainage of pus from the infected areas of the bone or the removal of the infected/necrotic pieces of bone themselves) are common approaches for the management of osteomyelitis (9). Each approach may be used alone or in combination with the other. Previous studies have compared the outcomes of conservative management and surgical approaches, and many of these studies confirm that the surgical approach tends to result in better outcomes, whether utilized alone or in combination with conservative measures (10-16). The majority of the studies took place in specialized

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treatment units rather than in community hospitals; Hispanics, a group at high risk for diabetes and its attendant complications, tended to be underrepresented (10-16).

Puerto Ricans living on the Island of Puerto Rico are 2.9 times more likely to have diabetes than are non-Hispanic white adults living in the United States (17). Prevalence rates for diabetes among adults in Puerto Rico range from 10.7% (data from the Center for Disease Control) (17) to 12.4% (self-reported prevalence from the Behavioral Risk Factor Surveillance System, 2008) (18). Because of the high prevalence of diabetes mellitus and the scarceness of specialized treatment units in the average community health care facility in Puerto Rico, patients arriving with a diagnosis of osteomyelitis present a special challenge in terms of disease management. The aim of this study was to describe and evaluate two different treatments for osteomyelitis, that is, combined surgical treatment (surgical plus conservative) and conservative treatment alone. This study also sought to compare the different outcomes (specifically, the rates of amputation) resulting from said treatments. The sample population consisted of Hispanic diabetics who had been admitted to a community hospital located in Puerto Rico.

Methods

This was a retrospective, chart-based, descriptive study that was performed in a community-based hospital (250 beds) in Puerto Rico located within the metropolitan area of San Juan. Our study population included all patients with diabetes (ICD-9 codes 250.01-250.09) who were admitted with a diagnosis of osteomyelitis (ICD-9 codes 730.0-730.2) from January 1, 2005, to December 31, 2006 (N = 218). We excluded several types of file: those representing relapsing patients or previously evaluated patients who were being readmitted; those of patients being transferred to or from another institution; those from which data were missing (incomplete medical records); those for which charts were unavailable; and those that detailed cases in which amputation had occurred for causes unrelated to osteomyelitis (49 excluded cases). A total of 169 records were analyzed. Information was retrieved from paper charts by two trained family medicine residents. Data that were gathered included demographics, diagnosis and treatment information, laboratory results (admission erythrocyte sedimentation rate [ESR]), and information regarding any existing complications. In this retrospective chart-review study, ethnicity was determined using self-reported data gathered during the admission interview (performed by the nursing staff) that is requested of all patients admitted to this institution.

The primary outcome was amputation (ICD-9-CM procedure codes 84.11, 84.12, 84.14, 84.15, and 84.17) of the affected extremity. The amputation rate was determined for our population and evaluated for its association with the modality of treatment (combined surgical [any modality consisting of an initial surgical treatment plus antibiotics and/or local care] or conservative [antibiotics and/or local care alone]) and other clinically important factors, such as age, sex, and ESR. The Internal Review Board of the University of Puerto Rico Medical Sciences Campus approved this protocol.

Data were analyzed using the statistical software Epi Info Version 3.5.1. Variables were evaluated using descriptive statistics (frequency, percentage, mean, and standard deviation). Comparative analysis was done using Odds Ratio and Chi-square for parametric data and Yates' Chi-square test for non-parametric data in order to evaluate the association between primary outcome (amputation) and clinically important variables, such as age, sex, modality of treatment, ESR, source of infection, etc. Finally, multivariate logistic regression was done to evaluate the probability of amputation as a function of modality of treatment when correcting for clinically and statistically significant covariates (trauma, sex, age, and ESR). Statistical significance was set at an α coefficient of 0.05.

Results

Demographic and clinical features

Table 1 shows an almost even sex distribution in our sample and a mean age of 55.9 ± 13.5 years. Interestingly, a predominance of patients under 65 years of age was observed. The great majority of our subjects were Hispanic (98.8%). In terms of modalities of treatment, we found 123 patients (72.8%) receiving conservative treatment alone and 46 patients (27.2%) receiving combined surgical treatment. Table 1 also shows a statistically significant difference in the initial modality of treatment according to age, with a mean age of 58.5 ±13.5 years in the conservative treatment group vs. one of 48.8 ± 10.7 years in the combined surgical treatment group (p value<0.001). Indeed, when treatment modality is compared in non-geriatric and geriatric patients, it can be seen that non-geriatric patients were more likely to have received surgical management (OR: 7.17; 95% CI: 2.09-24.49, p value<0.001). No statistically significant sex-based differences relating to the type of osteomyelitis management were found.

Our data revealed that ulcerated lesions were the most common source of infection (59.2%), followed by trauma (27.8%) (Table 2). The mean admission ESR was 100.3 ± 34.7 mm/hr, with a range of 19 to 150 mm/hr. Table 2 shows that 74.4% of our sample had ESR levels higher than 70 mm/hr upon arrival, which is compatible with a diagnosis of osteomyelitis (19). The most commonly reported complications/outcomes were bacteremia/sepsis (4.8%), skin and soft tissue infection (2.4%), death (1.2%), fracture (0.6%), and acute renal failure (0.6%). No significant differences in clinical characteristics were found when comparing combined surgical management and conservative management groups.

Table 1. Demographic characteristics of diabetic patients with osteomyelitis in a community hospital in Puerto Rico

	All patients n = 169	Modality of initial treatment		P
		Conservative n = 123	Surgical n = 46	
Age group (years), n (%)				
18-44	34 (20.1)	18 (14.6)	16 (34.8)	0.001
45-64	91 (53.8)	64 (52.0)	27 (58.7)	
65-74	29 (17.2)	26 (21.1)	3 (6.5)	
75-120	15 (8.9)	15 (12.2)	0 (0.0)	
Sex, n (%)				
Men	86 (50.9)	64 (52.0)	22 (47.8)	0.316
Women	83 (49.1)	59 (48.0)	24 (52.2)	

Table 2. Clinical characteristics and modality of treatment for patients with diabetes and osteomyelitis in a community hospital in Puerto Rico

	All patients n = 169	Modality of initial treatment		P
		Conservative n = 123	Surgical n = 46	
Source of infection, n (%)				
Pre-existing ulcer	100 (59.2)	73 (59.3)	27 (58.7)	0.538
Trauma	47 (27.8)	36 (29.3)	11 (23.9)	0.612
Hematogenous	8 (4.7)	5 (4.1)	3 (6.5)	0.377
SSTIs	8 (4.7)	6 (4.9)	2 (4.3)	0.793
Other source	6 (3.6)	3 (2.4)	3 (6.5)	0.418
Admission ESR (mm/hr) (based on 168 subjects), n (%)				
0-35	17 (10.1)	13 (10.7)	4 (8.7)	0.214
36-70	26 (15.5)	23 (18.9)	3 (6.5)	0.214
71-105	48 (28.6)	34 (27.9)	14 (30.4)	0.214
106-140	66 (39.3)	43 (35.2)	23 (50.0)	0.214
141-200	11 (6.5)	9 (7.4)	2 (4.3)	0.214
Complications/ Outcomes, n (%)				
Bacteremia/Sepsis	8 (4.8)	7 (5.7)	1 (2.2)	0.383
SSTI‡	4 (2.4)	3 (3.2)	1 (6.1)	0.640
Death	2 (1.2)	2 (1.6)	0 (0.0)	0.263
Fracture	1 (0.6)	1 (0.8)	0 (0.0)	0.726
Acute renal failure	1 (0.6)	1 (0.8)	0 (0.0)	0.726

ESR: Erythrocyte sedimentation rate; SSTIs: Skin and soft tissue infections

Diagnosis and management

A total of 159 cultures were performed, of which 112 were from blood and 47 from a given infection site (Table 3). Fifty-two positive cultures were obtained, most of them from samples taken from infected areas (39 vs. 13). Gram-positive organisms were present in 20.1% of the isolates (most of them from blood), and gram-negatives were present in 17.6% (most of them from infected site samples). The most common organism was Staphylococcus aureus (gram-positive) either in blood (38.5%) or in the infection-site cultures (28.2%). A total of 18 cultures presented more than one organism, 16 at the site of infection and two from blood cultures, which is common in SSTI among patients with diabetes.

Table 3. Prevalence of organisms cultured in patients with diabetes and osteomyelitis in a community hospital in Puerto Rico

	Blood cultures n = 47	Infected-area cultures n = 112	All cultures n = 159
Positive cultures, n (%)	13 (11.6)	39 (83.0)	52 (32.7)
Reported organisms*			
S. aureus	5	11	16
S. agalactiae	2	6	8
P. mirabilis	1	5	6
K. pneumonia	1	5	6
P. aeruginosa	0	6	6
E. coli	0	5	5
S. haemoliticus	3	0	3
E. faecalis	1	3	4
S. marcescens	0	4	4
Others	2	15	17

*Cultures may have more than one organism.

Table 4 details the different diagnostic approaches used by the medical staff. Admission ESR was the most widely used diagnostic tool, employed in 93.5% of cases and usually performed in combination with different imaging modalities (131 cases, 82.9%). No differences in diagnostic methodology were found between the two treatment modalities. Finally, among those receiving surgical treatment, the predominant procedures were debridement and incision and drainage (45.7% each), followed by removal of bone segments (6.1%).

Amputation rate

In this study, we found an amputation rate of 34.5% (58 cases) among patients with diabetes admitted because of osteomyelitis. Crude odds ratio for amputation for patients receiving combined surgical treatment vs. those receiving only conservative treatment was 0.20 (95% CI: 0.08-0.51; p value<0.001). Other variables found to have a significant association with amputation rate were age (p value = 0.009) (Figure 1) and sex (p value = 0.043). When patients were stratified as non-geriatric vs. geriatric, non-geriatric patients had a probability of amputation three times higher than did geriatric patients (OR: 3.38; 95%; CI: 1.65-6.94; p value<0.001). In the case of sex, women had a lower risk of amputation with an OR of 0.57 (95% CI: 0.30-1.08; p value = 0.043). Clinically important variables that presented a non-statistically significant tendency for higher amputation rates were admission ESR (Figure 1), history of trauma, and positive x-ray findings. Multivariate logistic regression analysis was done to evaluate the association

between modality of treatment and amputation rate after correcting for statistically and clinically significant variables such as sex, age, and ESR (Table 5). This regression model confirmed an increased probability for amputation among men and a 78.0% decrease in the probability of amputation among those patients receiving combined surgical management (Table 5).

Table 4. Diagnosis and management of patients with diabetes and osteomyelitis in a community hospital in Puerto Rico

		Modality of initial treatment		
	All patients n = 169	Conservative n = 123	Surgical n = 46	*P*
Diagnostic tools, n (%)				
Clinical diagnosis without imaging	26 (15.4)	22 (17.9)	4 (8.7)	0.141
Admission ESR	158 (93.5)	114 (92.7)	44 (95.7)	0.382
Positive conventional radiography	82 (48.5)	56 (45.5)	26 (56.5)	0.105
Bone scan	85 (50.3)	61 (49.6)	24 (52.2)	0.450
MRI	6 (3.6)	4 (3.3)	2 (4.3)	0.520
Probe-to-wound test	3 (1.8)	1 (0.8)	2 (4.3)	0.180
Types of initial surgical treatment, n (%)				
Debridement	21 (12.4)	---	21 (45.7)	
Incision & drainage	21 (12.4)	---	21 (45.7)	
Removal of bone segments	3 (1.8)	---	3 (6.5)	
Missed	1 (0.5)	---	1 (2.2)	
None	123 (72.8)	123 (100.0)	---	

ERS: Erythrocyte sedimentation rate; MRI: Magnetic resonance imaging

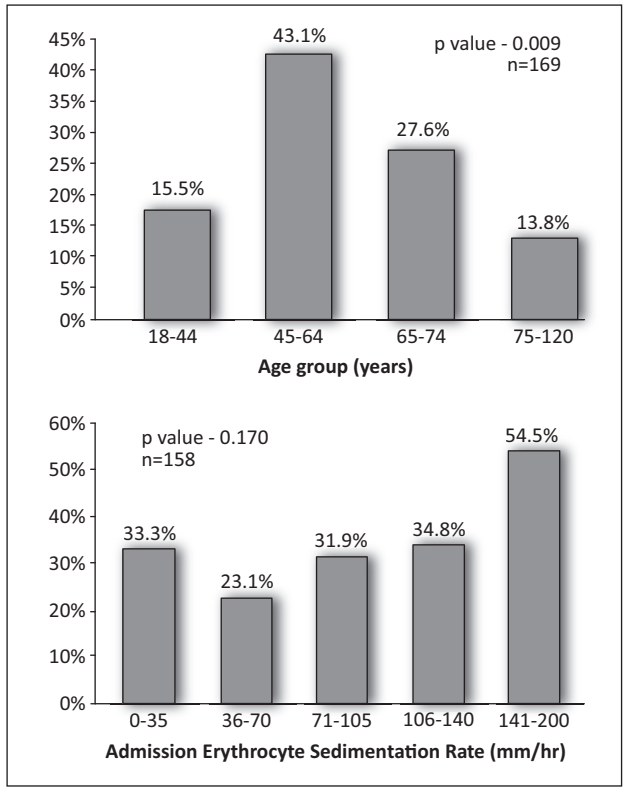

Figure 1. Amputation rate (%) as a function of age group and erythrocyte sedimentation rate (ESR) on admission

Table 5. Multivariate logistic model for amputation

	Odds ratio	95% confidence interval
Combined treatment	0.22	0.08-0.59
Sex (male/female)	2.09	1.04-4.23
Age	1.03	1.00-1.05
Admission ESR	1.00	0.00-1.01
Trauma	1.82	0.85-3.88

ESR: Erythrocyte sedimentation rate

Discussion

The most striking findings of our study are (1) that individuals receiving early combined surgical management had a probability of amputation 78.0% lower than that of those receiving conservative treatment alone; (2) that the men in our study had a probability for amputation that was twice as high as that of the women; and (3) an amputation rate higher than that reported for the general population living in the United States. Other important findings of this study include (1) the fact that there was a higher proportion of relatively younger patients with diabetes hospitalized with osteomyelitis than expected, and (2) the fact that younger patients were treated more aggressively.

In terms of demographics, our sample was evenly distributed by sex, but we found a predominance of patients with ages lower than 65 years (73.9%) (Table 1). It has been observed that as age increases, the prevalence of diabetes and its complications also increases (20), so we expected to have a higher proportion of geriatric patients than what we, in fact, observed. This issue needs further evaluation in prospective studies to determine the causes of this phenomenon or, alternately, to determine whether it is an isolated finding limited to our sample. We also found that although conservative management was the preferred modality of treatment overall, combined surgical treatment was more commonly used among younger patients. We believe this tendency for more aggressive management in the younger patient might be the result of bias among medical staff concerning the long-term implications of amputation for younger patients.

When the results of the clinical description are evaluated, it can be speculated that the real prevalence of trauma as the cause of infection may be higher than that found in our study because many patients remembered the development of an ulcer but failed to recall the initial trauma that may have been the cause of this ulcer (recall bias). Whichever might be the case, previous

ulcers and trauma continue to be the main triggers that lead to osteomyelitis; therefore, adequate and prompt management of these lesions at the primary care level is mandatory if this complication is to be prevented (21).

In terms of diagnostic methods, ESR was performed on 94.5% of the patients in our sample. ESR is commonly used as an element of the diagnostic work up, usually in combination with imaging studies and clinical findings as well as for the follow-up of osteomyelitis. Although ESR is a non-specific marker for disease, levels higher than 70 mm/hr have been described as being a sensitive and specific diagnostic modality for osteomyelitis (19). In our sample, the mean admission ESR was 100.7 ± 34.7, and 74.4% of our patients arrived with an ESR level higher than 70mm/hr (Table 2), which strongly supports the diagnosis of osteomyelitis in our sample.

Being that the contiguous spread of infection is the leading cause of osteomyelitis, it is not surprising to find a higher rate of positive cultures in samples taken from sites of infection than in blood samples. Infection-site cultures were done in only one fourth of the patients, with one third of these cultures presenting more than one organism. It is well known that polymicrobial infections are common among diabetic patients who present skin and soft tissue infections, which commonality explains this result. Concern about contaminants with normal skin flora is another issue to be considered. However, in this analysis, all culture results were evaluated, and organisms commonly considered as contaminants were found in 5.0% of the positive cultures coming from infection sites and in 38.4% of the positive blood cultures. Finally, Staphylococcus aureus was the most common individual organism reported as having been found in both culture sources, which is consistent with the description of the bacterial etiology of osteomyelitis in the literature (8, 11, 15, 22-24). Our findings support current guidelines that recommend the use of wide-spectrum antibiotics with adequate S. aureus coverage for the management of osteomyelitis in patients with diabetes.

Our study shows important findings with respect to amputation rates. First of all, in our study, the overall rate of amputation in patients with diabetes who were admitted with osteomyelitis was 34.5%. This rate was higher than that found in the data from the Nationwide Inpatient Sample, which reports that 8.5% of patients hospitalized for foot osteomyelitis had a leg or foot amputated and 23.0% had a toe amputated (80.0% of them with a diagnosis of diabetes) (1). Although at least one study reports an amputation rate of 36.0% for patients with diabetes who develop osteomyelitis (13), most studies report an amputation rate in the range of 11.0% to 20.0% (25-26). The underuse of early surgical intervention in our hospital and other hospitals in the US might be an important determinant for the high rate of amputation reported in some papers in the US and in our study. The second important finding of this study was that the men in our study were two times more likely than the women to have an amputation secondary to osteomyelitis. This finding agrees with the literature, including several population-based studies showing that being male is a risk factor for amputation in diabetic patients (27).

In terms of age, most of the literature suggests a tendency for a higher incidence or prevalence of diabetes complications, including osteomyelitis, as age advances. However, our sample was mainly composed of non-geriatric patients (73.9%) who presented a higher probability of amputation (crude OR: 3.38) despite having received combined surgical treatment more frequently than did geriatric patients. Although this association between age and higher probability of amputation was lost when the multivariate regression model was created, the issue of relatively younger people composing almost ¾ of our patients with osteomyelitis and being more prone to amputation is a worrisome finding. This number does not agree with published literature that suggests that older patients with diabetes and osteomyelitis are at an increased risk of amputation. Besides, this finding points to the possibility of age-related disparity issues in our non-geriatric patients with diabetes. In fact, further prospective studies are mandatory to evaluate whether this increased prevalence of osteomyelitis and the increased probability of amputation among relatively younger patients with diabetes is related to poor access to health care or medical insurance, poor compliance with treatment due to psycho-social factors, failure to recognize symptoms at the primary care level, or simply the failure of younger patients to adhere to proper medical treatment.

With respect to treatment, multivariate logistic regression analysis was done to evaluate the association between early combined surgical management and amputation rate after correcting for variables shown to be clinically or statistically associated with amputation rate in univariate analysis (age, sex, history of trauma, and admission sedimentation rate). This regression confirmed a 78.0% decrease in the probability of amputation among patients receiving combined surgical treatment. These results coincide with previous studies that report that patients that were treated only with antibiotics had a higher rate of amputation than did those receiving early surgical intervention (12, 16, 28). For example, a large secondary analysis of the National Inpatient Sample data revealed that medical therapy alone is inferior to combined medical and surgical therapy for wound healing and limb salvaging in patients with osteomyelitis (16). A similar tendency for lower amputation rates when antibiotic treatment is combined with local surgical management was reported in 2008 by Aragón-Sánchez et al in a chart review study in Spain (12).

Being a retrospective design, our study has various limitations. First, the reliability of our data depends on the written documentation of nurses and other medical staff. In order to overcome this limitation, we excluded all incomplete charts. Instructions regarding data collection were also used to standardize the process of data gathering from paper records.

Second, we were not able to evaluate pre-hospital data to better assess the severity of the disease upon admission. This last point is particularly important because we have no information documenting whether the decision to amputate was based solely on the severity of the infection or on other factors being taken into consideration (age, frailty of the patient, etc.). Moreover, our sample size was small, resulting in an underpowered analysis that precludes the integration of other clinically important variables in our regression model. A fourth limitation is that our study was conducted in only one hospital in Puerto Rico. As a result, generalization and application of our results to other populations in Puerto Rico or to other Hispanic groups is not possible. Finally, our study was focused on an acute treatment setting where admission time was less than that required for a complete cycle of antibiotic therapy. Therefore, documentation of follow up was not available in order to evaluate the completion of treatment; neither long-term sequelae nor amputations after discharge from the hospital could be assessed.

Despite these limitations, the current work is one of the first to describe osteomyelitis in Puerto Ricans, and it raises concerns about important issues regarding the well-being and the management of our patients with diabetes who present osteomyelitis. Therefore, the significance of our findings should not be minimized, given both the high prevalence of diabetes among Hispanics and the high rates of amputation observed in our study. We recommend that medical staff in our hospital and community take action in order to prevent osteomyelitis and to improve functionality and quality of life in our patients. To achieve this goal, standardized ambulatory and hospital protocols for the management of foot trauma, ulcers, and osteomyelitis in patients with diabetes should be developed or revised. These protocols must encourage a more aggressive osteomyelitis management. We also recommend paying special attention to relatively younger patients and men presenting this condition, since our results suggest that members of these groups are more vulnerable to amputation. Finally, primary care physicians should be aware that they are in the best position to start early treatment and, therefore, make a difference in the outcomes of these patients.

Resumen

Objetivo: Los pacientes con diabetes están en riesgo de múltiples complicaciones. Estas incluyen la osteomielitis, que, si no es manejada adecuadamente, puede resultar en amputaciones, sepsis o muerte. El propósito de este estudio fue comparar la tasa de amputación asociada con dos modalidades de tratamiento para osteomielitis que fueron utilizadas en un grupo de puertorriqueños con diabetes. Métodos: Se revisaron 169 expedientes médicos de pacientes con diabetes y osteomielitis admitidos a un hospital de comunidad durante un periodo de dos años. Los datos fueron analizados utilizando estadística descriptiva, chi-cuadrado, producto cruzado y regresión logística multivariada para evaluar la probabilidad de amputación en pacientes que recibieron tratamiento conservador (antibióticos y/o cuidado local) en comparación con los que recibieron tratamiento quirúrgico combinado (tratamiento quirúrgico y conservador). Resultados: Se encontró una tasa de amputación general de 34.5%. Los pacientes que recibieron tratamiento quirúrgico combinado tuvieron una menor probabilidad de amputación que los que solamente recibieron tratamiento conservador (OR: 0.22; 95% IC: 0.08-0.59). Además, se encontró que los varones (OR: 2.09; 95% IC: 1.04-4.23) y los pacientes no geriátricos (OR: 3.38; 95% IC: 1.65-6.94) tienen una mayor probabilidad de amputación en comparación con las mujeres y los pacientes geriátricos, respectivamente. Conclusión: Este estudio reflejó una tasa de amputación en pacientes con diabetes mayor a la reportada en los Estados Unidos (34.5% y 11.0%-20.0%, respectivamente). Además, se encontró que la probabilidad de amputación secundaria a osteomielitis en pacientes con diabetes es dos veces mayor para los varones y tres veces mayor en los pacientes no geriátricos. Por otro lado, se encontró que el tratamiento quirúrgico combinado se asocia con una disminución marcada (78%) en la probabilidad de amputación.

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