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Comparative Outcomes of Conservative Surgery versus Early Surgical Intervention in Diabetic Foot Ulcers

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ABSTRACT

Background: Diabetic foot ulcers (DFUs) are a severe complication of diabetes, often requiring intervention. Comparing conservative treatment and early surgical intervention is essential to optimize patient outcomes.

Objectives: To evaluate the effectiveness of conservative surgery and early surgical intervention in the management of DFUs and to assess the association of clinical outcomes with biomarkers such as C-reactive protein (CRP) and glycated hemoglobin (HbA1c).

Methods: A comparative study was conducted at different tertiary care center in Lahore between January 2024 and October 2024. A total of 300 patients with DFUs (Wagner grade 2-4) were included, with 150 receiving conservative surgery and 150 undergoing early surgical intervention. Outcomes measured included wound healing time, revision surgeries, and amputation rates. The association of these outcomes with CRP and HbA1c levels was analyzed.

Results: Patients in the conservative surgery group had a higher rate of revision surgeries (53% vs. 41%, $p = 0.04$) and longer hospital stays (median 20 vs. 16 days, $p < 0.01$). Elevated CRP levels (median 58 mg/L, IQR 15–170) were significantly associated with clinical failure (HR = 1.8, $p = 0.03$), as were elevated HbA1c levels (median 8.2%, IQR 7.5–9.0; HR = 1.5, $p = 0.02$). Early surgical intervention was linked to lower revision rates and quicker recovery but at the cost of increased limb loss.

Conclusion: Conservative surgery preserves limbs but often requires revisions and longer treatment durations, while early surgery shortens recovery time but raises amputation risks. Biomarkers like CRP and HbA1c are critical for guiding personalized treatment decisions.

Keywords: Diabetic foot ulcers, conservative surgery, early surgical intervention, revision surgery, biomarkers, C-reactive protein, glycated hemoglobin, wound healing.

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INTRODUCTION

Diabetic foot ulcers (DFUs) are one of the most severe and most common complications of diabetes, contributing to substantial patient morbidity, hospitalization, and risk of lower limb amputation [1]. With that said, the global increase in diabetes prevalence has seen DFUs become a greater concern to global healthcare providers[2]. The pathophysiology of DFUs is a complex process involving a combination of peripheral neuropathy, peripheral arterial disease (PAD) associated with ischemia, and a propensity to infection. However, the combination of these factors together results in chronic wounds that are difficult to treat. Historically, the management of DFUs has revolved around two primary strategies: surgical interventions and conservative treatments. Conservative management aims at the preservation of limb function using wound care, infection control, and offloading [3]. Regular debridement of necrotic tissue, use of topical antibiotics or dressings, and offloading to reduce the pressure on the affected area are common conservative measures. Less severe ulcers or those in patients with high risks of surgery from comorbidities usually get conservative treatments. Nevertheless, several studies have shown that conservative treatment, although less invasive, usually results in higher recurrence and longer healing times, resulting in longer patient discomfort and higher healthcare costs[4, 5]. Early surgical management, including debridement, revascularization, or minor amputation, has been used as a more aggressive approach to DFU. However, surgery is usually indicated when extensive tissue necrosis, deep infection, or osteomyelitis has failed to respond to conservative measures. The main goal of surgical debridement is to remove all necrotic tissue, thereby lowering the bacterial load and creating a better environment for the wound to heal.[6]. The studies have shown that, in the short term, surgical intervention can shorten healing time and reduce rates of infection. The downside is the higher risk of functional impairment by amputations and the psychosocial burden of limb loss, especially with higher levels of amputation.[7]. The optimal approach to DFU management has been debated in the literature. A few studies have shown that conservative treatments are a better option in patients where limb preservation is still an option because they are not invasive and may produce better long-term results by preventing needless amputations. Yet other studies suggest that early surgical intervention, especially when the infection is deep or critical ischemia, may represent better definitive treatment, decrease the risk of severe complications, and promote rapid recovery.[8, 9].The presence of infection and progression to osteomyelitis are important factors in determining treatment outcomes. Conservative management versus surgery of diabetic foot osteomyelitis has been compared in studies, and surgery may be more efficacious in eradicating deep infection and its recurrence. While conservative management with prolonged antibiotic therapy has also been successful in selected cases, this has been shown in particular for conservative management, in combination with initial treatment response, the severity of the condition, and the presence of comorbidities in the patient.[10]. In addition, patients with PAD have PAD which can further complicate wound healing by decreasing blood flow to the affected area. However, management of DFUs with PAD has included revascularization procedures, whether surgical or endovascular, which have decreased healing rates and reduced the risk of amputation in patients with PAD. If revascularization is successful, it improves the effectiveness of both conservative and surgical treatments, and therefore should be assessed in all DFU patients, reported the literature.[11].

While many studies have sought to delineate the comparative effectiveness of conservative and surgical treatment, results have been mixed, and some have failed to show significant differences in long-term outcomes between conservative and surgical treatment. Surgical interventions, although providing faster initial healing, have higher risks of complications including amputation and functional impairments. Conservative treatments, although they do not promote wound closure as quickly, may help to preserve more of the foot's function, and reduce the psychological impact of amputation[12]. This study seeks to extend existing research by providing a comparative analysis between conservative and surgical interventions for the management of DFU. The scope of the analysis will be on the long-term patient outcomes such as wound healing rate, amputation rate and need for revision surgery and the aim is to provide insights that can help to develop more targeted and individualized diabetic foot treatment strategies. This study uniquely highlights the role of CRP and HbA1c in guiding personalized treatment strategies for diabetic foot ulcers.

MATERIALS AND METHODS

The present study was designed as a comparative study at different tertiary care centers in Lahore, Pakistan between January 2022 to October 2024. The objective of this study was to compare long-term outcomes of conservative versus surgical intervention in diabetic foot ulcers (DFUs). The study was approved by the institutional review board approval ref no. (ERC/22D/2022) and informed consent was obtained from all participants before inclusion in the study. The study population included adult patients (aged 18 years or more), who were diagnosed with DFUs, Wagner grades 2-4. Patients were recruited consecutively and stratified into two groups based on their treatment modality or early surgical intervention. Patients were excluded who had undergone a major amputation (above the ankle), severe peripheral arterial disease (PAD) not amenable to revascularization, or received pharmacological treatment only without surgical intervention. The study included a total of 300 patients of whom 150 were in the conservative group and 170 in the surgical group. Nonsurgical management included debridement of the wound and control of the infection with antibiotics based on culture, pressure offloading, and advanced wound care techniques constituted conservative treatment. Microbiological cultures were obtained and antibiotic regimens were selected based on the sensitivities of the organisms identified. Healing progression, infection status, and the need for other interventions were assessed weekly, and data were collected. The minor amputation group in the early surgical intervention group included the removal of one or more of the toes or part of the foot. Clinical indicators of osteomyelitis, ischemia, and the severity of the infection were used to determine whether surgery should be performed. Debridement and appropriate antibiotic therapy were usually required to accompany surgery. Patients were then monitored postoperatively for signs of wound healing, wound infection recurrence, and complications until complete epithelialization occurred with standard wound care. Time to complete wound healing, amputation rates, both minor and major, and incidence of revision surgeries were the primary outcomes measured in this study. Complete epithelialization without further need for surgical intervention was defined as wound healing. The note was made of minor amputation (toe or partial foot amputation) or major amputation (above the ankle). Non-healing ulcers or recurrent infections at the same site defined revision surgeries as any subsequent operation. The secondary outcomes were the quality of life (assessed with the SF-36 questionnaire), length of hospitalization, and

overall functional recovery. Minimum of 12 months follow up, and assessment performed at 1, 3, 6, and 12 months after treatment. Follow-up visits were clinical evaluation, wound assessments, and documentation of any complications or further intervention. During these follow-up periods, new infections or new ulcers were recorded. The data were analyzed using SPSS (version 28.0) and R (version 4.3.2). Data were expressed as means with SD or medians with interquartile range as appropriate for the distribution of the data. Categorical variables were summarized as frequencies and percentages. The Chi-square test for categorical variables and the student's t-test or Mann-Whitney U test for continuous variables were used to perform bivariate comparisons of the conservative and surgical groups. Time-to-event outcomes were time to wound healing or revision surgery and Kaplan-Meier survival curves were constructed, and differences between the two groups were compared using the log-rank test. The association between treatment modality and time to wound healing was evaluated by multivariable Cox proportional hazards models adjusting for key confounders such as age, sex, duration of diabetes, severity of PAD, infection severity, and preoperative antibiotic use. Schoenfeld residuals were used to test the proportional hazards assumption. For amputation and revision surgery odds ratios (ORs) were assessed via logistic regression analysis, with confounders adjusted where appropriate. To explore variation in outcomes by wound severity (Wagner grade), presence of ischemia, and antibiotic regimen type, subgroup analyses were performed. Test robustness was performed on the findings of the sensitivity analysis in cases where there was missing or incomplete follow-up data. The sample size for this study was calculated to have an expected 10 percent difference in wound healing rates between the conservative and surgical groups. A power analysis of 95% confidence and 80% power gave a required sample size of 150 patients per group to achieve statistically significant differences in outcomes. Analyses were considered statistically significant ($p \leq 0.05$) for all.

RESULTS

The study included 300 patients, 150 in the Conservative Surgery Group and 150 in the Early Surgical Intervention Group. Median age was 61 years (IQR 50-70) for patients in the conservative group versus 68 years (IQR 60-75) in the surgical group, and this was a statistically significant ($P<0.01$) difference. There was no difference between the groups in the distribution of male patients, 80% in the conservative group and 82% in the surgical group ($p = 0.75$). In the conservative group, the median BMI was 27 kg/m², and in the surgical group, 29 kg/m² ($p = 0.22$), no significant difference in body mass between the groups. Glycated hemoglobin (HbA1c) levels, a key marker for glycemic control, were also evaluated in the study. The median HbA1c of patients in the conservative group was 8.2% (IQR 7.5-9.0), and 8.4% (IQR 7.7-9.2) in the surgical group, with no statistically significant difference ($p = 0.12$). This was because the conservative group had significantly longer durations of follow up a median of 2.0 years (IQR 2.1 – 6.8), compared to 1.0 years (IQR 1.0 – 4.6) in the surgical group ($p< 0.01$), reflecting the more prolonged management needed for conservative treatment. Ulcer localization was significantly different between the two groups. Table-1 shows that 61% of the ulcers were in the midfoot in the conservative group compared to 64% in the forefoot in the surgical group ($p<0.01$). Localization of this mass is also different and may influence the treatment strategy and long-term outcome.

Table-1: Comparative Characteristics, Biomarkers, and Treatment Outcomes for Conservative Surgery vs. Early Surgical Intervention

Characteristics and Biomarkers	Conservative Surgery (n = 150)	Early Surgical Intervention (n = 150)	*p-Value*
Age, years (median, IQR)	61 (50-70)	68 (60-75)	<0.01
Male sex, n (%)	120 (80)	140 (82)	0.75
BMI (kg/m², median, IQR)	27 (24-32)	29 (26-34)	0.22
Years of diabetes (median, IQR)	16 (8-25)	18 (10-27)	0.46
Glycated hemoglobin (HbA1c, %) (median, IQR)	8.2 (7.5-9.0)	8.4 (7.7-9.2)	0.12
Duration of follow-up, years (median, IQR)	2 (2.1-6.8)	1 (1.0-4.6)	<0.01
Forefoot, n (%)	32 (21)	110 (64)	<0.01
Midfoot, n (%)	92 (61)	50 (29)	
Hindfoot, n (%)	26 (18)	10 (7)	
Coronary artery disease, n (%)	55 (36)	75 (44)	0.14
Peripheral arterial disease, n (%)	90 (60)	115 (68)	0.20
Preoperative CRP, mg/L (median, IQR)	58 (15-170)	30 (10-80)	0.02
Creatinine value, µmol/L (median, IQR)	105 (80-140)	110 (85-150)	0.24
GFR (mL/min/1.73m², median, IQR)	55 (40-78)	52 (35-80)	0.18
Preoperative antibiotic treatment, n (%)	110 (73)	125 (74)	0.89
Days of hospitalization (median, IQR)	20 (12-35)	16 (10-28)	<0.01
Duration of total antibiotic therapy, days (median, IQR)	35 (22-52)	22 (16-34)	<0.01
Negative microbiologic sample, n (%)	12 (8)	15 (9)	0.70
Polymicrobial infection, n (%)	65 (43)	75 (44)	0.86
Clinical failure, n (%)	45 (30)	35 (21)	0.06
Microbiological recurrence, n (%)	15 (10)	14 (8)	0.42
Revision surgery, n (%)	80 (53)	70 (41)	0.04

Patients in the conservative group had significantly higher preoperative C-reactive protein (CRP) (median 58 mg/L, IQR 15–170) than in the surgical group (30 mg/L, IQR 10–80; p=0.02). The higher rate of revision surgeries seen in the conservative group may be explained by elevated baseline inflammation, as reflected by elevated CRP levels. Table 1 shows that creatinine levels and GFR were similar between the two groups and that there were no statistically significant differences in renal function.Patients in the conservative group had much longer days of hospitalization compared to patients in the surgical group, median of 20 days (IQR 12–35) versus 16 days (IQR 10–28), p<0.01. The total duration of antibiotic therapy

was longer in the conservative group (median 35 days versus 22 days in the surgical group, p<0.01). These results emphasize the more intensive medical management in the conservative treatment group. Revision surgeries were more common in the conservative group (53% vs 41% in the surgical group, p = 0.04) although no clinical outcomes were found to be superior in either group. Despite no statistical difference between the groups for clinical failure (p = 0.06), clinical failure was more common in the conservative group (30% vs 21% in the surgical group). Table- 2 showed that the multivariable analysis showed that higher preoperative CRP and HbA1c were significantly associated with an increased risk of clinical failure. Both treatment approaches also led to a higher likelihood of clinical failure due to the involvement of polymicrobial infections.

Table-2: Biomarkers and Risk Factors for Clinical Failure (Multivariable Analysis)

Risk Factors and Biomarkers	HR (95% CI)	p-Value
Age	1.1 (0.9-1.2)	0.45
Male sex	1.6 (1.1-3.2)	0.10
Peripheral arterial disease	1.1 (0.6-1.9)	0.74
Preoperative CRP	1.8 (1.1-2.6)	0.03
Glycated hemoglobin (HbA1c)	1.5 (1.2-2.1)	0.02
Polymicrobial infection	1.4 (1.0-2.3)	0.04
Preoperative antibiotic therapy	1.2 (0.9-2.2)	0.18
Conservative surgery (main exposure)	1.3 (0.8-2.0)	0.32

The Fig-1 Kaplan-Meier survival plot compares the probability of survival (wound healing) over time between two treatment groups: surgical intervention and conservative surgery. Prolonged healing times are reflected by a slower decline in survival probability in the conservative surgery group. Initially patients in the surgical intervention group recover faster, but all converge to the same probabilities over time. This is represented by the risk table below showing the number of patients at risk for different time points.

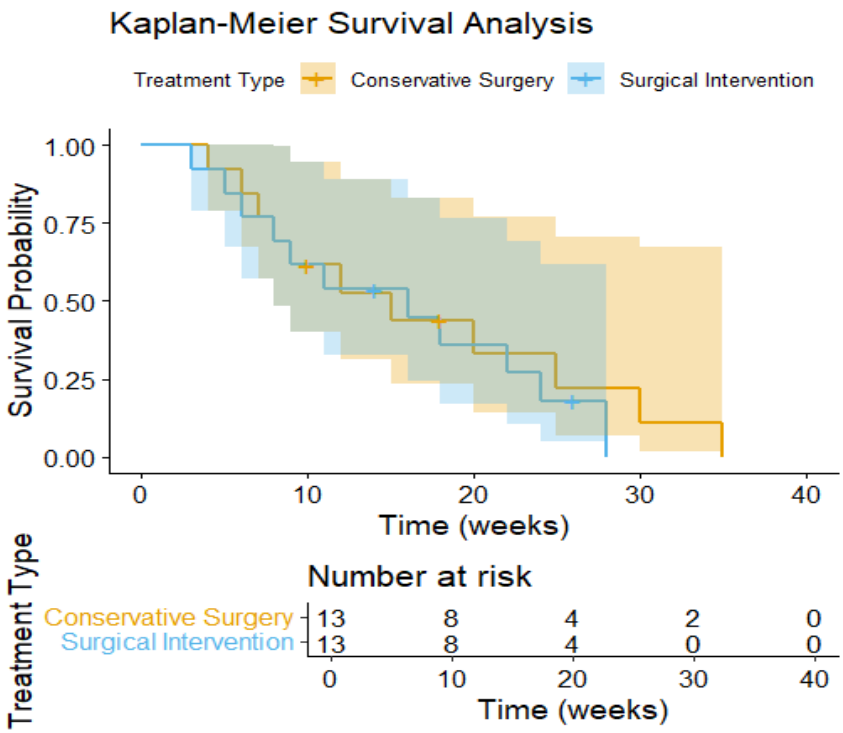

Fig-1: Kaplan-Meier Survival Curves for Wound Healing in Conservative Surgery vs. Surgical Intervention

These results demonstrate that conservative surgery while offering the potential for limb preservation, requires more frequent medical interventions and longer hospital stays. Patients in the conservative group had higher.

DISCUSSION

This study revealed some important information about the comparative effectiveness of conservative surgery versus early surgical intervention (minor amputation) in DFU management. The findings underscore the difficulty of picking the best treatment strategy and highlight trade-offs between limb preservation, the need for additional interventions, and patient outcomes[13]. Results show a significantly higher rate of revision surgery in patients undergoing conservative surgery versus those undergoing early surgical intervention (53% versus 41%, p=0.04). That's consistent with previous studies showing that conservative treatment keeps more of the limb but more often requires more frequent follow-up surgery because of infection recurrence or nonhealing wounds. Conservative surgery can initially preserve the limb but with prolonged healing times and increased incidence of secondary complications, the treatment burden is heavier[14]. Early surgical intervention for limb loss results in a profound impact on patients' psychosocial well-being, with depression, anxiety, and diminished quality of life frequently present. Therefore, these efforts include incorporating psychological counseling, such as peer support programs as well as preoperative education into treatment protocols to help mitigate this burden. In this study, elevated CRP levels reflecting systemic inflammation were associated with poor outcomes. Preoperative targeting of infection control with antibiotics and anti-inflammatory therapies might optimize CRP levels and improve healing. As with the HbA1c, effective glycemic management with intensive insulin therapy and dietary modification along

with glucose monitoring can decrease HbA1c levels improve preoperative preparation, and decrease complications. These measures emphasize the value of a patient-centered approach to DFU management. We found biomarkers such as C-reactive protein (CRP) and glycated hemoglobin (HbA1c) to be significant predictors of clinical outcomes. Significantly associated with clinical failure were elevated CRP levels indicative of systemic inflammation (HR = 1.8, p = 0.03) and elevated HbA1c levels indicating poor glycemic control (HR=1.5,p=0.02) [15]. The findings are consistent with a well-established role for inflammation and poor glycemic management in delaying wound healing and increasing susceptibility to infections. As conservative or surgical intervention did not influence the outcome of the patients, higher CRP and HbA1c levels predicted worse outcomes, emphasizing the need to control these biomarkers to improve the patient outcome[16]. Polymicrobial infection was also important in predicting clinical failure (HR = 1.4, p = 0.04) and supports the importance of aggressive infection control. The prevalence of polymicrobial infections was similar in the conservative and surgical groups, but patients with polymicrobial infections had a greater incidence of complications. Both treatment approaches, with targeted antibiotics and with continued vigilant monitoring of wound progression, should be focused on infection control, particularly in the context of complex infections comprising multiple pathogens.[17]. We also note that patients in the conservative surgery group need longer hospitalization and antibiotic therapy. Median hospital stay in these patients was 20 days versus 16 days in the early surgical group ($p<0.01$), and longer antibiotic courses (median 35 days in the conservative group versus 22 days in the surgical group, $p<0.01$) [18]. The extended period of treatment was due to the more intensive management needed for patients with conservative surgery persistent infections and delayed healing. Many cases are treated conservatively while limb preservation is achieved, but the conservative approach consumes a greater number of medical resources and places a greater commitment on the patient's recovery times.[19]. Despite early surgical intervention with minor amputations, early recovery, and fewer revisions, concern for long-term functionality and quality of life exist if the permanent loss of part of the limb. With this decision to be personalized then, based on the overall health of the patient, the severity of the ulcer, and concerning the presence of infection, and the patient’s preferences, the patient must decide to opt for conservative surgery or early surgical intervention. In some patients, early surgical intervention is probably the best choice, particularly if they are at risk for significant complications with conservative management. However, conservative surgery, while having a longer course, and a higher revision rate, may be preferred for some, especially for limb preservation[20]. Despite this, this study has limitations which have to be acknowledged. The generalizability of these findings to other populations was limited by the fact that the cohort was drawn from a single center. Furthermore, although we adjusted for important confounders including age, sex, glycemic control, and infection status, other unmeasured factors (e.g., patient adherence to wound care and differences in post-operative care) could affect outcomes. Further research is needed to determine the most effective approach to the treatment of DFU through multi-center studies and randomized controlled trials.[21].

CONCLUSION

Conservative surgery for diabetic foot ulcers preserves limbs but requires more revisions and longer treatment, while early surgery offers faster recovery but risks limb loss. Biomarkers

like CRP and HbA1c are crucial for predicting outcomes and guiding personalized care. Treatment strategies should be tailored to individual conditions, focusing on infection control, glycemic management, and multidisciplinary care to optimize outcomes.

Conflict of interest:

The authors declared no conflict of interest during the research

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Authors Contribution:

MI: Conceptualized the study, supervised the overall research process, and ensured data accuracy.

II: Conducted the literature review and contributed to data collection and analysis.

ZS: Designed the methodology and performed statistical analyses.

AF: Coordinated participant recruitment and assisted in data acquisition.

FJ: Drafted the manuscript and reviewed the discussion section.

MIq: Managed references and ensured proper formatting of the manuscript.

MNS: Provided critical revision of the manuscript and final approval for publication.

All authors have read and approved the final manuscript.

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