

Differences in Outcomes Between Major Amputation and Wound Debridement on Inflammatory Response and Length of Stay in Type 2 Diabetic Foot Ulcer Patients Treated at Airlangga University Hospital: A Retrospective Study

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Kontext: Podle Mezinárodní diabetologické federace (International Diabetes Federation, IDF) dosahovala v roce 2021 prevalence diabetes mellitus (DM) v Indonésii 10,8 % (toto onemocnění tam bylo diagnostikováno přibližně u 19,4 milionu osob). Pokud se týče nejčastější komplikace, tedy syndromu diabetické nohy (diabetic foot ulcer, DFU), existuje u diabetiků 15–34% riziko vzniku tohoto postižení s recidivou ve výši 40–60 %. V časném stadiu DFU je třeba odstranit detritus z rány, ale se stupňující se bolestí a imobilitou nakonec vyvstává nutnost amputace. Význam této studie spočívá ve srovnání předoperačních a pooperačních počtů leukocytů, poměru neutrofilů/lymfocytů (neutrophil-lymphocyte ratio, NLR) a délky hospitalizace (length of stay, LOS) při odstraňování detritu z rány versus vysoká amputace, stejně jako účinek odstranění detritu na DFU zamezující nutnosti amputace.

Metody: V tomto článku popisujeme observační kohortní retrospektivní studii, v níž byla pro vyhledání potřebné zdravotnické dokumentace uložené ve fakultní nemocnici Airlangga University ve městě Surabaya a zahrnující období od ledna do června 2024 použita metoda totálního výběru. Zkoumanou populací byli dospělí pacienti ve věku nad 18 let s diagnózou DM 2. typu a s DFU stupně 0–5 ve Wagnerově klasifikaci, u nichž bylo provedeno odstranění detritu nebo vysoká amputace. Mezi hodnocené proměnné patřily předoperační a pooperační hodnoty leukocytů, diferenciální rozpočet leukocytů, předoperační a pooperační hodnoty NLR, předoperační a pooperační LOS a celková LOS. Uvedené proměnné jsme srovnali u dvou skupin pacientů, jedné s odstraněním detritu z rány a druhé s vysokou amputací. Údaje byly analyzovány s použitím softwaru SPSS 27 a Microsoft Excel, verze 16.102.2.

Výsledky: Mezi oběma skupinami jsme našli statisticky významný rozdíl v předoperačním počtu leukocytů a diferenciálním rozpočtu leukocytů ($p < 0,05$); rozdíly mezi ostatními proměnnými nebyly statisticky významné ($p > 0,05$). Skupina s odstraněním detritu z rány vykazovala nižší předoperační počty leukocytů a menší pokles počtu leukocytů než skupina s vysokou amputací, což ukazuje na méně intenzivní zánětlivou odpověď u pacientů s odstraněním detritu z rány ve srovnání s pacienty s vysokou amputací. I když pooperační hodnoty nejsou statisticky významné, rozdíl předoperačních a pooperačních hodnot statisticky významný byl, což ukazuje na větší pokles počtu leukocytů po vysoké amputaci a odráží potlačení zánětu.

Závěr: Odstranění detritu z rány je spojeno s nižšími předoperačními počty leukocytů a s menším rozdílem mezi jejich předoperačními a pooperačními počty. K bližšímu poznání zánětlivých procesů u pacientů s DFU se doporučuje zkoumat i ostatní proměnné.

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Keywords:

Diabetic foot ulcer

Major amputation

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Wound debridement

ABSTRACT

Background: According to the International Diabetes Federation (IDF) in 2021, Indonesia had a diabetes mellitus (DM) prevalence of 10.8% out of the total population, approximately 19.4 million individuals. The most common complication, diabetic foot ulcer (DFU), has a 15–34% risk of developing in diabetic patients and

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a 40–60% recurrence rate. The early stage of DFU requires wound debridement, but as pain and immobility worsen, the need for amputation ultimately rises. The importance of this study is to compare preoperative and postoperative level of leukocyte, neutrophil-lymphocyte ratio (NLR), and length of stay (LOS) between wound debridement and major amputation, as well to evaluate wound debridement's healing factor on DFU to avoid amputation.

Methods: This is an observational cohort retrospective study. A total sampling method was used to retrieve medical records from Airlangga University Hospital, Surabaya, with the study period of January–June 2024. The population was adult patients above 18 years old and diagnosed with type 2 DM with DFU in Wagner scale of 0–5 that had received wound debridement or major amputation. The research variables were preoperative leukocyte, postoperative leukocytes, leukocyte difference, preoperative NLR, postoperative NLR, preoperative LOS, postoperative LOS, and total LOS. We compared those variables between two groups, which are wound debridement and major amputation. Data were analyzed using SPSS 27 and Microsoft Excel version 16.102.2.

Results: We found that there is a significant difference between the two groups in terms of preoperative leukocyte and leukocyte difference ($p < 0.05$), while other variables were found not significant ($p > 0.05$). Wound debridement groups had lower preoperative leukocytes and a smaller leukocyte decrease compared to those undergoing major amputation. This represents lower inflammation response in patients receiving wound debridement compared to major amputation. Although postoperative leukocytes aren't significant, the leukocyte difference between preoperative and postoperative was significant. This marks a greater reduction in leukocytes following major amputation, reflecting inflammation suppression.

Conclusion: Wound debridement has lower preoperative leukocyte and leukocyte difference. Further studies on other variables are recommended to describe inflammatory processes in patients with DFU.

Introduction

Diabetes mellitus (DM) is characterized by either a deficiency of insulin (type 1 DM) or insulin dysfunction (type 2 DM). According to the International Diabetes Federation in 2021, Indonesia has a DM prevalence of 10.8% of the total population, approximately 19.4 million individuals.⁸ This finding is supported by the Indonesian Ministry of Health, reporting 19.5 million people with DM in 2024, with an increased prediction of 28.5 million by 2045.⁷ In terms of cost, it was reported that the direct medical cost for DM care amounted to USD 576 million, with 56% represented by hospital inpatient care.⁶

Type 2 diabetes mellitus (T2DM) is responsible for 90–95% of all DM cases globally and is characterized by insulin resistance in pancreatic cells. One of the most adverse chronic complications of T2DM is diabetic foot ulcer (DFU), which is classified as a type of peripheral artery disease (PAD). DFU can lead necrotic tissue in the affected limb. According to recent studies, patients with T2DM have a 15–34% lifetime risk of developing DFU and a 40–60% recurrence rate.^{4,12} DFU is also a risk factor to nontraumatic lower extremity amputations (LEA) in diabetic patients, which is responsible for 85% of total cases. DFU consists of pain and immobility, which can ultimately reduce quality of life. Mortality rates associated with DFU are approximately 11% annually and increased to 22% among patients who underwent LEA.

Because of the urgency in terms of high cost inpatient care and increasing postoperative amputation mortality, this study is crafted to evaluate the alternative intervention to DFU treatment. This retrospective study aims to assess the effect of wound debridement therapy on DFU healing, specifically analyzing reductions in leukocyte counts and length of hospital stays (LOS) among patients treated at Airlangga University Hospital, Surabaya, Indonesia. The goal of this study is to provide insights in DFU healing from wound debridement as a form of prevention to amputation.

Methods

This study is an observational cohort retrospective study. Samples were taken from medical records of the Airlangga University Hospital, Surabaya, Indonesia from January–June 2024 period. This research conducted total sampling methods. The inclusion criteria were adult patients above 18 years old and diagnosed with T2DM with DFU in Wagner scale of 0–5 that had wound debridement or major amputation interventions. This research excludes data of patients besides T2DM, mortality during treatment, and incomplete medical records. Dependent variables such as, preoperative leukocyte, postoperative leukocytes, leukocyte difference, preoperative NLR, postoperative NLR, preoperative LOS, postoperative LOS, and total LOS are being analyzed and grouped based on the independent variables, which are wound debridement and major amputation. Data were analyzed with SPSS 27 and Microsoft Excel version 16.102.2.

Results

Data analysis of patient's characteristics have proven that there are 34 samples with frequencies almost equal between 16 male (47%) and 18 female (53%) (**Table 1**). This indicates that in this research, DFU isn't necessarily bound to genders, because of the relatively equal frequencies between male and females. Most of the sample, which is 30 patients (88%) are from the age range of 18–65 years old, meanwhile there are only four patients (12%) that are >65 years old (**Table 1**). There are 30 patients (88%) that don't have hypertension (**Table 1**). Most of the DFU samples occurred in the left side of the limb in 19 patients (56%), right side in 13 patients (38%), and bilateral in two patients (6%) (**Table 1**). These findings proved that DFU most likely occurred unilaterally. Meanwhile, findings in terms of Wagner scale mostly occurred in scale of 2–4. Whereas level 2 in two patients (6%), Wagner 3

in 15 patients (44%), and Wagner 4 in 17 patients (15%). Lastly, patients receiving wound debridement occurred in 25 patients (74%) and major amputation in nine patients (26%) (**Table 1**).

Based on total descriptive analysis of DFU patients, data showed the mean and standard deviation of preoperative leukocyte were 18.25 ± 8.8 (**Table 2**), which decreased in postoperative to 15.51 ± 6.94 (**Table 2**), with a mean leukocyte difference of 2.66 ± 6 (**Table 2**). The preoperative neutrophil-lymphocyte ratio (NLR) has 15.55 ± 16.05 (**Table 2**), while postoperative NLR was 13 ± 13.28 (**Table 2**). The results of preoperative and postoperative LOS, respectively, were 2.94 ± 1.75 days and 3.76 ± 3.08 days (**Table 2**). Meanwhile, the total LOS is 6.71 ± 4.17

Table 1 – Sample characteristics

Characteristics	Frequency	Percentage
Gender		
Male	16	47%
Female	18	53%
Age		
18–65 years	30	88%
>65 years	4	12%
Hypertension history		
Yes	4	12%
No	30	88%
Ulcer location		
Left	19	56%
Right	13	38%
Bilateral	2	6%
Wagner classification		
1	0	0%
2	2	6%
3	15	44%
4	17	50%
5	0	0%
Intervention		
Debridement	25	74%
Amputation	9	26%

Table 2 – Total descriptive inflammation markers

Characteristics	Mean $\pm$ SD (n = 34)
Preoperative leukocyte	18.25 ± 8.8
Postoperative leukocyte	15.51 ± 6.94
Leukocyte difference	2.66 ± 6
Preoperative NLR	15.55 ± 16.05
Postoperative NLR	13 ± 13.28
Preoperative LOS	2.94 ± 1.75
Postoperative LOS	3.76 ± 3.08
Total LOS	6.71 ± 4.17

Table 3 – Patient's characteristics with debridement

Characteristics	Mean $\pm$ SD (n = 25)
Preoperative leukocyte	15.17 ± 6.15
Postoperative leukocyte	14.52 ± 6.57
Leukocyte difference	1.15 ± 4.63
Preoperative NLR	14.04 ± 15.82
Postoperative NLR	11.07 ± 7.96
Preoperative LOS	2.72 ± 1.56
Postoperative LOS	3.88 ± 3.33
Total LOS	6.6 ± 4.54

Table 4 – Patient's characteristics with major amputation

Characteristics	Mean $\pm$ SD (n = 9)
Preoperative leukocyte	25.3 ± 11.39
Postoperative leukocyte	18.28 ± 7.6
Leukocyte difference	6.84 ± 7.57
Preoperative NLR	19.75 ± 16.86
Postoperative NLR	18.34 ± 22.23
Preoperative LOS	3.56 ± 2.18
Postoperative LOS	
Total LOS	7 ± 3.12

Table 5 – Comparison of mean values between wound debridement and major amputation

Characteristics	p-value
Preoperative leukocyte	0.018
Postoperative leukocyte	0.166
Leukocyte difference	0.012
Preoperative NLR	0.301
Postoperative NLR	0.922
Preoperative LOS	0.224
Postoperative LOS	0.827
Total LOS	0.324

days (**Table 2**). The data from **Table 2** provide a general overview of inflammatory response before and after intervention, as well as the overall LOS.

Based on analysis of 25 samples from the wound debridement group, it was found that preoperative leukocyte was 15.17 ± 6.15 , postoperative leukocyte was 14.52 ± 6.57 , and leukocyte difference was 1.15 ± 4.63 (**Table 3**). This indicates decrease in leukocytes preoperative to postoperative measurements within the wound debridement group, although high standard deviation is present in this variable, which suggests high heterogeneity among patients. Meanwhile, preoperative and postoperative NLR was 14.04 ± 15.82 and 11.07 ± 7.96 , respectively (**Table 3**). This finding suggests a potential reduction in NLR following wound debridement. Preoperative, postoperative, and total LOS were 2.72 ± 1.56 days, 3.88 ± 3.33

days, and 6.6 ± 4.54 days, respectively. This indicates longer LOS postoperatively compared to preoperative LOS in the wound debridement group.

Based on analysis of nine samples from the major amputation group, it was found that preoperative leukocyte was 25.3 ± 11.39 , postoperative leukocyte was 18.28 ± 7.6 , and leukocyte difference was 6.84 ± 7.57 (Table 4). This indicates prominent decrease in leukocytes preoperative to postoperative measurements within the major amputation group, which suggests positive inflammatory response reduction. Meanwhile, preoperative and postoperative NLR was 19.75 ± 16.86 and 18.34 ± 22.23 , respectively (Table 3). This finding suggests a potential reduction in NLR following wound debridement, although high standard deviations are present, which indicate variability in inflammatory response. Preoperative, postoperative, and total LOS were 3.56 ± 2.18 days, 3.44 ± 2.4 days, and 7 ± 3.12 days, respectively. This indicates relatively balanced LOS in both preoperative and postoperative in the major amputation group.

After analyzing 34 samples, it was found that few variables are significant ($p < 0.05$), which are leukocyte preoperative with p -value of 0.018 and leukocyte difference with 0.012 in (Table 5). These proved that there are significant differences in both variables between wound debridement and major amputation. Meanwhile, other variables weren't found to have any significant difference in p -value between the two groups.

Discussion

Preoperative leukocytes function as an indicator of the severity of inflammatory response in patients with DFU. Based on (Table 5) a significant difference was found in preoperative leukocytes between patients who receive wound debridement and major amputation, with a p -value of 0.018. The analysis showed that reduction from preoperative to postoperative leukocyte in the wound debridement group only has minimal reduction. Another study also supports this finding, where the preoperative and postoperative leukocytes are 13.902 g/dL and 13.804 g/dL, respectively, among DFU patients undergoing debridement.⁹ The previous study was aligned with this research, which also indicates a relative small difference in preoperative and postoperative leukocytes.

The significant difference between preoperative leukocytes between the two groups suggests a distinct inflammatory response in patients undergoing wound debridement and major amputation prior to the procedure. Additional findings support this research, which identified elevated leukocyte as a predictor of prolonged wound healing duration.² Another findings also mentioned, that the presence of wound infection can delay the healing process.² Significant differences of leukocyte prior to procedure are important for surgeons to pick the most optimal option to treat wounds in DFU patients. Another study supports this research, by reporting that preoperative leukocyte tends to be higher in patients who receive amputation.⁵ Therefore, it can be summarized that lower preoperative leukocytes are associated with wound debridement as intervention to treat DFU, where-

as higher preoperative leukocytes may lead surgeons to consider major amputation as more suitable.

Postoperative leukocytes reflect the inflammatory response reduction following intervention either wound debridement or major amputation. Conversely, the difference between preoperative and postoperative leukocytes represents the effectiveness of intervention in reducing inflammation. Based on data that were analyzed in Table 5, the difference between the two groups in terms of postoperative leukocyte was not significant ($p = 0.166$). However, the reduction of leukocyte from preoperative to postoperative between wound debridement and major amputation was significant ($p = 0.012$). The mean postoperative leukocytes for wound debridement and major amputation were 14.52 (Table 3) and 18.28 (Table 4), respectively, while the mean of leukocyte differences were 1.15 (Table 3) and 6.82 (Table 4). This analysis indicates although postoperative leukocytes did not differ between the two groups, the significance in reduction did.

NLR represents neutrophils as mediators of acute inflammation and lymphocytes which serve in adaptive immune response. Another study stated that NLR is an indicator of chronic inflammatory response.¹¹ Neutrophil reflects ongoing inflammatory response, while reduction in lymphocytes is a characteristic of T2DM. Additionally, increase in neutrophil and lymphocyte reduction is a key characteristic of T2DM.³ Recent study also suggests that NLR in T2DM patients that had amputation is equivalent as NLR on chronic wound infection.¹⁰ Based on data from (Table 5), there were no significant differences in preoperative and postoperative NLR between the two groups, with p -values of 0.301 and 0.922, respectively. However, each group reported a consistent reduction trend from preoperative to postoperative NLR. In the wound debridement group, the mean NLR decreased from 14.04 to 11.07 (Table 3), meanwhile in the major amputation group, it decreased from 19.75 to 18.34 (Table 4). These findings suggest a general reduction trend in inflammatory postintervention. On the other hand, the absence of significant difference indicates that NLR may not be an effective parameter for predicting the severity of infection in DFU patients.

LOS reflects the duration of recovery and potential cost of hospitalization. From Table 5, it was found that the comparison between preoperative, postoperative, and total LOS between the two groups was not statistically significant, with p -values of 0.224, 0.827, and 0.324, respectively. This indicates no significant difference in duration of stay in hospital between patients who underwent wound debridement and major amputation. Mean of preoperative and postoperative LOS in wound debridement group were 2.72 and 3.88 days, respectively (Table 3), whereas for the major amputation group were 3.55 and 3.44 days (Table 4). This aligns with another study, which suggests mean LOS of 8.13, 8.86, and 9.8 days for patients undergoing mild, moderate, and severe debridement treatment, respectively across 75 DFU cases.¹ Shorter LOS in this research may be attributed to different clinical pathways and postoperative management protocols. Since there are no significant differences in preoperative, postoperative, and total LOS, this suggests

that both wound debridement and major amputation have the same effectiveness in managing inflammatory responses, as reflected from hospitalization duration.

Conclusion

After analyzing medical records of samples with DFU, there are several conclusions that can be drawn. Firstly, there are differences in preoperative leukocytes that may serve as potential considerations for surgeons in determining the approach for DFU treatment. Although postoperative leukocytes were relatively similar in both groups, differences in leukocyte reduction are significant between patients who receive wound debridement and major amputation. Preoperative and postoperative NLR showed no significant difference between both groups, which suggests that NLR may not be effective to assess severity of infection. Preoperative, postoperative, and total LOS did not show any difference between both groups, indicating wound debridement and major amputation are equally effective in managing DFU in terms of hospitalization duration. Additional research is required to assess other inflammatory markers such as, HbA_{1c}, C-reactive protein, procalcitonin, and other mediators to determine effectiveness of wound debridement and major amputation.

Conflict of interest

The authors declare no conflict of interest for this article.

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