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Risk Factors that Influence Hospital Length of Stay in Diabetic Foot Ulcer with Negative Pressure Wound Therapy at RS. dr. Cipto Mangunkusumo

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Abstract

Introduction. It estimated that around 15% of diabetic patients would experience diabetic foot ulcer (DFU) in their lifetime. Negative pressure wound therapy (NPWT) is proven to be more effective than conventional treatments. NPWT creates a moist wound environment, increases local blood flow, and stimulates tissue granulation, thereby accelerating wound healing. This study conducted to determine the risk factors that affect the length of stay of DFU with NPWT.
Method. A retrospective study with a cross-sectional design carried out from January 2016 to December 2018 at RS. dr. Cipto Mangunkusumo Hospital, Jakarta. Subjects' characteristics and risk factors taken from medical records. The length of stay and application of NPWT was the focus of interests. The correlation to the risk factors was analyzed.
Results. Out of 105 subjects enrolled, the length of stay of DFU with NPWT was 19.9 ± 19.3 days. Risk factors affecting the length of stay were history of ulcers (r = 0.01; p = 0.034), wound depth (r = 0.292; p = 0.003), Hb (r = 0.05; p = 0.039), HbA1c (r = 0.06; p = 0.033), Albumin (r = 0.06; p = 0.017), PCT (r = 0.10; p = 0.035), and duration of DM (r = 0.193; p = 0.009).
Conclusion: The length of stay of DFU with NPWT influenced by systemic factors (duration of DM, Hb, HbA1c, albumin, and PCT) and local factors (history of previous ulcers and wound depth). The depth of the wound was the most positively related factor to the length of stay in DFU after NPWT (r = 0.292; p = 0.003). Interventions on factors that can be corrected before the application of NPWT may amplify the result of NPWT and reduce the length of treatment.

Keywords: Diabetic foot ulcer, negative pressure wound therapy

Introduction

Diabetes mellitus (DM) is one of the biggest problems in the global health system. The prevalence of diabetes mellitus has increased in the last two decades. Epidemiology studies showed the number of DM cases have continuously increased from 177 million in 2000, to 415 million in 2015, and likely to achieve 624 million by 2040.[1] Currently, Indonesia ranked seventh worldwide with 10 million people estimated to have diabetes.[1] Diabetic foot ulcer (DFU) is one of the most common complications of DM. It predicted that around 15% of subjects with diabetes would experience DFU in their lifetimes. Furthermore, almost 4-27% of people with DFU complications end up with many disabilities, such as amputation of the feet and mortality rate as high as 16%.[2,3,13] Three main factors for DFU formation are peripheral vascular disease, neuropathy, and infected trauma.[11, 12] Peripheral arterial diseases has been shown as the main factor that leads to a worse outcome and prognostic.[15,16] Principles of DFU treatment include: 1) wound treatment; 2) debridement and antibiotic therapy; 3) mechanical off-loading; 4) revascularization to improve blood flow; 5) control of systemic metabolic issues and comorbidities.[4]

With the advancements of modern wound treatment, negative pressure wound therapy (NPWT) became an integral part of DFU treatment. NPWT has shown remarkable benefits in the treatment of DFU, which was: reducing edema, increasing granulation tissues, improving blood flow, and in certain studies, may lower bacterial colonization in wounds.[4,5] However, the prolonged usage of NPWT may lead to exudate retention and infection.[6, 10] In the use of NPWT, the application of negative pressure in adult subjects recommended at 50–175 mmHg either continuously or intermittently.[5] There are four primary mechanisms of NPWT: 1) It causes wound shrinkage secondary to wound contraction. 2) Inflammatory modulation by reducing tissue macrophage infiltration and reducing expression (IL-1β) and (TNFα) results in decreased inflammation. 3) Reducing excessive exudate fluid and infectious material like bacteria by sucking it continuously. 4) Creating an optimal wound environment (moist condition and thermoregulation).[4] Moreover, we understand that the condition of the patient may also influence the outcome of the treatment. They are the systemic condition of the patient and the local status of the affected foot. These factors have to be taken consideration in the treatment of the diabetic foot ulcer with negative pressure wound treatment. This study aimed to obtain risk factors that affect the length of stay of the patients with DFU after utilizing NPWT.

Method

This study was a retrospective study with a cross-sectional design carried out from January 2016 to December 2018 at RS. dr. Cipto

Mangunkusumo Hospital, Jakarta. The study aimed to determine risk factors that affect the length of stay of DFU subjects with NPWT in RSCM.

The accessible population of this study was subjects who come to RSCM and managed by staff of vascular surgery division or consulted or treated together with the Internal Medicine department within 36 months (January 2016 – December 2018). Total population sampling method applied in this study, which means all DFU subjects with NPWT listed in the medical records of the Surgery Department of RSCM during the period were enrolled. Those includes were all subjects with diabetic foot ulcers who received wound care with NPWT at RSCM and had complete medical record. While those not treated with NPWT, or NPWT treated in hospital other than RSCM and incomplete medical record were excluded. Subjects' characteristics (age, gender), duration of DM, sepsis condition, smoking status, laboratory findings (Hba1c, albumin, hemoglobin, leukocyte, lymphocyte, creatinine, PCT, RBS), comorbid (hypertension, cardiac heart disease, chronic kidney disease) and subject feet characterized using PEDIS classification were the variables of interests. Subjects undergo debridement in the operating room, before the application of the NPWT, the negative pressure was kept continuously at -125mmHg for 3-5 days. And the removal or re-application of the NPWT carried out at the operating theater.

Univariate analysis carried out to find out the distribution frequencies of each variable. Because the dependent and independent variables were numerical and categorical, the Spearman test used. Linear regression also used to evaluate whether there were correlations between risk factors and the length of stay for DFU with NPWT or not. Significance (alpha) $\leq$ 0.05 and 95% confidence interval.

The Committee of Ethics, Faculty of Medicine, Universitas Indonesia approved the study No.456/UN2.F1/ETIK/PPM.00.02/2019 and Research bureau of RSCM No. LB.02.02/II.1/638/2019.

Results

Of 106 DFU subjects enrolled, the mean age was 55.3 $\pm$ 9.2 years old. Females were dominant (52.4%) than males (46.6%). The duration of DM was 6.7 $\pm$ 5.3 years, and subjects experiencing sepsis were 44.8%. Of 69 subjects who underwent NPWT once (65.7%), and thirty-six subjects (34.2%), underwent NPWT >1 time; the maximum usage of NPWT was four times.

Out of 69 subjects, thirty-two subjects underwent definitive therapy, thirty-one of those subjects underwent STSG (29.5%), while one subject underwent approximation suture (1%). More than half of the subjects were discharged as outpatients for further evaluation (63.8%). Fifteen subjects experienced adverse outcomes, namely major amputation (4.8%), died (4.8%), and discharged against medical advice (4.8%). These subject characteristics are shown in Table 1.

In general, subjects managed in the Emergency Room of RSCM presented in relatively severe and infected wound conditions. According to PEDIS classification, 68.6% of subjects showed grade 3 wound extension, and compromised distal vascularization with ABI score = 0.8 $\pm$ 0.3. Furthermore, about 37.1% subjects showed a history of ulcer and 32.4% experienced osteomyelitis. All subjects underwent debridement before using NPWT.

Table 1. Subjects characteristics

Characteristics	Total (n = 105)
Age (year)	55.3 ± 9.2
Gender	
Male	50 (47.6%)
Female	55 (52.4%)
Duration of DM	6.7 ± 5.3
Sepsis	
Yes	47 (44.8%)
No	58 (55.2%)
Smoker	
Yes	41 (39%)
No	64 (61%)
Laboratory findings:	
HbA1c (%)	7.7 ± 4.5
Albumin (g/L)	2.6 ± 0.8
Hemoglobin (mg/dL)	10.2 ± 1.4
Leukocyte	12425.0 ± 5446.7
Lymphocyte	15.1 ± 9.5
Creatinine	1.3 ± 0.99
PCT	2.5 ± 8.7
Random Blood Glucose	195.4 ± 69.4
Comorbid	
Hypertension	74 (70.5%)
Cardiac heart disease	22 (21%)
Chronic kidney disease	46 (43%)
NPWT	
1 time	69 (65.7%)
2 times	27 (25.7%)
3 times	5 (4.8%)
4 times	4 (3.8%)
After NPWT length of stay	19.9 ± 19.3
Total length of stay	26.0 ± 22.5
Outcome:	
Approximation suture	1 (1%)
STSG	31 (29.5%)
Outpatient	58 (63.8%)
Discharge against medical advice	5 (4.8%)
Amputation	5 (4.8%)
Died	5 (4.8%)

Note: DM: diabetes mellitus; PCT: procalcitonin; NPWT: negative pressure wound therapy; STSGL split thickness skin graft.

Table 2. PEDIS characteristic in subjects with DFU

Characteristics	Total (n = 105)
ABI Score (mean $\pm$ SD)	0.8 ±.0.3
PEDIS	
Perfusion (mean $\pm$ SD)	2 ± 0.6
Grade 1	56 (53.3%)
Grade 2	43 (41%)
Grade 3	6 (5.7%)
Extension (mean $\pm$ SD)	3 ± 0.0
<2cm	5 (4.8%)
2-5cm	28 (26.7%)
>5cm	72 (68.6%)
Depth (mean $\pm$ SD)	2 ± 0.6
Grade 1	35 (33.3%)
Grade 2	57 (54.3)
Grade 3	13 (12.4%)
Infection	3 ± 0.9
Grade 1	0
Grade 2	49 (46.7%)
Grade 3	28 (26.7%)
Grade 4	28 (26.7%)

Table 3. PEDIS characteristic in subjects with DFU (cont)

Characteristics	Total (n = 105)
Sensation (mean ± SD)	1,6 ± 0,5
Present	55 (52.4%)
None	50 (47.6%)
Osteomyelitis	
Yes	34 (32.4%)
No	71 (67.6%)
History of ulcer	
Yes	39 (37.1%)
No	66 (62.9%)
Debridement (mean ± SD)	1±0.67
1 time	74 (70.5%)
2 times	25 (23.8%)
3 times	4 (3.8%)
4 times	2 (1.9%)

Table 4. Bivariate analysis between risk factors and length of stay after NPWT

Variables	r	p
Age (years)	0.03	0.98
Gender		
Female Male	-0.01	04.6
Sepsis:		
Yes No	0.03	0.06
Smoker:		
Yes No	-0.08	0.148
ABI	-0.03	0.478
History of Ulcer:		
Yes No	0.01	0.034*
PEDIS		
Perfusion		
Grade 1 Grade 2 Grade 3	0.233	0.372
Extension		
<2 cm 2-5 cm >5 cm	0.019	0.419
Depth		
Grade 1 Grade 2 Grade 3	0.292	0.003*
Infection		
Grade 1 Grade 2 Grade 3 Grade 4	0.089	0.256
Sensation		
Present None	0.044	0.589
Laboratory		
Hb (mg/dL)	0.05	0.039*
HbA_1C (%)	0.06	0.033*
Albumin	0.06	0.017*
Leucocyte ($x10^3$)	0.08	0.225
Creatinine	0.06	0.075
PCT	0.10	0.035*
Osteomyelitis		
Yes No	-0.042	0.335
Duration of DM:		
≤ 10 years > 10 years	0.193	0.009*

Note: *Spearman test; DM: diabetes mellitus; ABI: *ankle brachial index*; Hb: hemoglobin content; HbA1c: Hemoglobin A1c; PCT: procalcitonin.

Subjects of DFU with risk factors were: the history of ulcers (r = 0.01; p = 0.034), wound depth (r = 0.292; p = 0.003), Hb (r = 0.05; p = 0.039), HbA1c (r = 0.06; p = 0.033), albumin (r = 0.06; p = 0.017), PCT (r = 0.10; p = 0.035), and duration of DM (r = 0.193; p = 0.009) show a positive correlation with the length of stay after NPWT. The risk factors and length of stay after NPWT presented in Table 3.

Discussion

The treatment of DFU is a multimodality approach. The treatment, including surgical debridement, administration of antibiotics, and treat the wound environment. The use of NPWT in the treatment of DFU has been proven to be more practical benefits than conventional treatment.5 The purpose of this study was to determine which risk factors affect the length of stay of DFU compared to NPWT. In this study, the mean length of stay of DFU subjects afters NPWT was 19.9 ± 19.3 days. All subject underwent surgical debridement before NPWT application. Therefore, the mean total length of stay was 26 ± 22.5 days

A total of 105 subjects with DFU and treated using NPWT enrolled in this study. Female (52.4%) predominant though not significant. This finding consistent with data of the Ministry of Health, Republic of Indonesia (2018). The mean age of subjects was 55.3 ± 9.2 years, consistent with the range age group of the highest prevalence in DM, i.e., 55–64 years;[17] all subjects were people with DM for 6.7 ± 5.3 years.

The subjects with DFU presented in the Emergency Room obtained a prompt treatment. They presented with severe infected ulcers, which was marked by leukocytosis and increased PCT. Such a condition was requiring debridement for source control. Almost half of the subjects (44.8%) were in septic conditions. The level of PCT has a positive relationship with the length of stay (r = 0.10, p = 0.035). However, leucocyte levels did not have any positive correlation in this study (r = 0.08, p = 0.225). Infection eradicated with wound debridement before the NPWT application. Some subjects underwent debridement more than once. Debridement is essential in the management of DFU that control local factors and to manage infection and inflammation.

The DFU itself assessed using PEDIS classification, which consists of perfusion, extent, depth, infection, and sensation. Almost all subjects (68.6%) found to have grade 3 extension of their wound, which sized >5 cm. The measures larger compared to published studies overseas. This finding might be found since RSCM as a referral hospital, yet most cases presented were the complex ones.

Although statistically, the ulcer size was not an affecting factor in the length of stay in the study (r = 0.292; p = 0.003), the author realized that the wound size and depth affect the healing process of DFU. A study of Chuan et al. (2015) reported that subjects with different extent grade to have different outcomes and ulcers with wide extension might be incurable.[19]

In this study, the depth of wounds has a positive correlation with the length of stay after NPWT (r = 0.292, p = 0.003). This risk factor has a strong correlation compared to other factors. More than fifty percent of subjects found with ulcer depth of grade 3 (54.3%). A history of previous ulcers found in 31.7% and showed a positive correlation with the length

of stay in bivariate analysis (r = 0.01, p = 0.034). The correlation the weakest compared to other related risk factors. A study by Martins-Mendes et al. (2014) showed that subjects with a history of DFU have more severe wounds and chronic conditions that hinder their healing process. Furthermore, the history of DFU was also related to the risk of lower extremity amputation.[20]

In a routine ABI measurement, it found subjects showed vascular compromise with ABI 0.8 + 0.3. ABI assessment may become an initial referral sign of peripheral vascular disease. Therefore, impaired vascularization was also found and may increase the mortality and morbidity of DFU subjects. However, in bivariate analysis, the ABI score did not affect the length of stay in this study (r = -0.03, p = 0,478). A previous study in RSCM showed found that ABI as an independent risk factor of the morbidity of major amputation in the Emergency Department.21 Therefore, it is essential to assess the ABI score in subjects with DFU, although the length of stay was not affected in this study.

The bivariate analysis of risk factors, namely the history of ulcer, duration of DM ≥10 years, Hb, HbA1c, albumin, and PCT showed a positive correlation with the length of stay (r = 0.01 p = 0.034; r = 0.193, p = 0.09; r = 0.05, p = 0.039; r = 0.06, p = 0.017; r = 0.10, p = 0.035). Hemoglobin content, albumin, HbA1c, and PCT levels were laboratory findings that should be considered concerning the length of stay. Those laboratory findings represent the systemic condition, blood glucose regulation, and inflammation in subjects with DFU underwent NPWT. The comorbidities of the subjects may explain the low values of these laboratory findings. Regarding these situations, around 70.5% of subjects have hypertension, 21% of subjects have cardiac diseases, and 43% have chronic kidney failure. In this study, 67 subjects (63.8%) found to have HbA1c ≥7%.

Mantoyani (2016) stated that HbA1c was one of the substantial predictive factors in wound healing. The higher the HbA1c concentration was, the less time required for the wound healing process. Meanwhile, in a prospective study performed by Al Golban et al. (2016), in 140 subjects with DFU, it was discovered that wound healing in subjects with HbA1c (< 7 mmol/L) was much faster compared to subjects with improperly controlled HbA1c during three months of observation.

The duration of DM >10 years showed a positive correlation with the length of stay in bivariate (r = 0.193, p = 0.009) and multivariate analysis (p = 0.002). A study by Ziang et al. (2014) in subjects with DM for more than ten years has a higher risk of DFU than newer ones.

Unfavorable outcomes experienced in 15 subjects, which were major amputations, discharged against medical advice, and died during the admission. We must keep in mind that subjects with DFU have comorbidities and other underlying diseases, which may worsen the subject's condition. Therefore, it is essential to consider the subjects' condition to obtain desirable outcomes instead of the opposite.

Retrospective studies have unavoidable risks. Available data from medical records have a possibility of not being complete, such as several laboratory variables that were not always tested, such as PCT and HbA1c. Moreover, it may lead to selection bias based on the available data.

There are two risk factors that affect the length of stay of patients with DFU treat using NPWT showed in the study, which is systemic factors and local factors. Local factors include the duration of DM >10 years and history of ulcer. Systemic factors evaluated from laboratory findings, namely hemoglobin content, serum albumin, HbA1c, and PCT. Meanwhile, the local state may be assessed using the PEDIS classification. Systemic factors could be managed aggressively with adequate debridement, administration of antibiotics based on culture results to suppress the infection in subjects,[5] and nutritional improvements to improve serum albumin. By paying attention to those risk factors, we could be more selective in choosing and determine the use of NPWT.

Conclusion

Risk factors that affect the length of stay of DFU patients with NPWT are wound depth, levels of hemoglobin content, albumin, HbA1c, PCT, and duration of DM. The depth of the wound was the most significant related factor to the length of stay in DFU after NPWT (r = 0.292; p = 0.003). Interventions on these factors should be corrected before the application of NPWT may improve the result and reduce the length of treatment.

Disclosure

The authors report no conflicts of interest in this work.

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