Platelet distribution width associated with short-term prognosis and cost in paediatrics with partial-thickness thermal burns: A retrospective comparative study

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Abstract
Platelets exert important roles in burn wound healing and involving in inflammatory regulation and tissue repair. Platelet distribution width (PDW) is an indicator representing platelet morphology and activation. In this study, we try to evaluate the value of PDW in predicting short-term prognosis and cost of paediatrics with partial-thickness thermal burns. This retrospective study enrolled 73 children with partial-thickness thermal burns. The Ability of PDW to predict wound healing was evaluated by receiver operating characteristic (ROC) curve. All 73 patients were assigned into high and low PDW group according to optimal cut-off value from ROC curve. Associations between PDW and 2-weeks healing rate, time to wound healing, in-hospital cost and length of stay were evaluated. Furthermore, Univariate and multivariate logistic regression analysis were used to furtherly evaluate the significance of PDW in wound healing. We found that all baseline characteristics between groups were comparable (all \( P > .05 \)). High PDW group had a significant higher 2-weeks wound healing rate than those with a low PDW (66.7% versus 32.6%, \( P < .01 \)). Moreover, the mean time to wound healing of high PDW was obviously shorter than that of low PDW group (15.4 ± 10.1 vs 20.7 ± 10.9, \( P = .04 \)). Univariate (OR: 0.24, 95%CI: 0.09–0.65, \( P < .01 \)) and multivariate (OR: 0.15, 95CI%:0.05–0.52, \( P < .01 \)) analysis confirmed PDW as an independent marker for wound healing. Patients in high PDW group had a significant lower medical burden than low PDW group, including in-hospital cost (13.7 ± 10.6 vs 21.9 ± 16.7, \( \times 103 \) RMB, \( P = .02 \)) and length of stay (12.2 ± 8.8 vs 19.0 ± 10.8 days, \( P < .01 \)). In conclusion, PDW can sever as a potential indictor to predict the short-term prognosis of paediatrics with partial thickness thermal burns.

KEYWORDS
burns, children, platelet distribution width, prognosis, wound healing
Key Messages
- high PDW group had a significant higher 2-weeks wound healing rate than those with a low PDW
- the mean time to wound healing of high PDW was obviously shorter than that of low PDW group
- patients in high PDW group had a significant lower medical burden than low PDW group, including in-hospital cost and length of stay

1 | INTRODUCTION

Burns are a major traumatic pathology characterised by tissue destruction and cellular degradation resulted from energy transfer and mainly affected skin, which serve as a significant cause of paediatric morbidity and mortality.\(^1\) Partial thickness burns, a major constitution of thermal burns, mainly involve all epidermal and partial dermal layers and leave behind dermal appendages including sweat glands, hair follicles, and sebaceous glands.\(^3\)\(^,\)\(^4\) Currently, conservative therapy remains the primary treatment approach of partial thickness burns, such as wound dressings, systemic and topical medications.\(^5\) However, the wound healing of partial thickness burns may be delayed in setting of infection, destroyed epithelial island and granuloma, thereby requiring surgical skin grafting.\(^6\)\(^,\)\(^7\) Therefore, the optimal treatment of partial thickness burns remains an unsolved challenge in clinical practice due to the absence of a gold standard treatment. Optimal patient stratification and individual treatment planning based on wound healing related factors may serve as a promising option for paediatric patients with partial thickness burns.

Platelets play an important role in primary haemostasis, thrombosis, inflammation, tissue regeneration in the processes of wound healing.\(^8\) In details, platelets can contact exposed collagen and extracellular matrix, and releasing clotting factors to achieve haemostasis as well as essential growth factors (GFs) and cytokines to repair the wound.\(^9\)\(^,\)\(^10\) In clinical, platelet-rich plasma (PRP), as a concentrate of autologous platelets, has been used to effectively accelerate burn wound healing.\(^11\) Platelet distribution width (PDW) can reflect platelet area heterogeneity and is used as a routine serological indicator of platelet function and activation in clinical.\(^12\) Moreover, PDW has also been considered as a promising marker to predict prognosis in various types of critical illness including sepsis following severe burns.\(^13\)\(^,\)\(^14\) However, to date, there are no data on the significance of PDW in prognosis evaluation in burn patient. In this study, we evaluated PDW in paediatric patients with partial-thickness thermal burns and analyse the clinical significance in predicting short-term prognosis.

2 | MATERIAL AND METHODS

2.1 | Patients

This retrospective observational study was approved by the Institutional Review Board of the Forth Medical Center of Chinese PLA General Hospital. The study was conducted according to the principles of declaration of Helsinki and all patients were required for their signed and written informed consent. A total of 73 paediatric patients with partial-thickness thermal burns admitted at Department of Burn and Plastic Surgery, The Forth Medical Center of Chinese PLA General Hospital between Feb 1, 2019 and Feb 1, 2020 were enrolled in this study. All patients met the following inclusion criteria: age less than 18 years, partial thickness burns affected total body surface area (TBSA) less than 30%, primary admission following burn injury. Patients with comorbidities of psychiatric illness, critical illness under intensive care, and multiple traumas were excluded. Patients received previous burn therapy and complicated severe wound infection were also excluded. Following admission, all paediatrics received appropriate clinical evaluation and medical care according a standard protocol including laboratory tests, wound care, dressing changes, antibiotic therapy. Wounds dressings changes were performed every 2 days using topical bactericidal ointment and recombinant growth factors. According to reverent guidelines, if epithelialization of burn wounds cannot be achieved with conservative treatment in 3 weeks, surgical excision and grafting would be performed according to the discretion of senior surgeon.

2.2 | Data collection and outcome measurements

The demographic and clinical information of all enrolled patients including age, sex, body mass index (BMI), burn wound area and depth, burn location, length of stay, wound healing and in-hospital costs were collected from hospital information system. Wound healing was defined as burn wound achieved spontaneous full re-epithelialisation...
determined by burns surgeon. Burn wound area was expressed as percent total body surface area (%TBSA). Routine blood tests were conducted by central laboratory in our hospital immediately after admission, and within post-burn 6 hours, including platelet count, mean platelet volume (MPV) and PDW value.

The wound healing and cost-effectiveness characteristics were obtained and evaluated as short-term prognostic indicators. The primary outcome was defined as wound healing related indicators including 2-weeks wound healing rate and time to wound healing. The 2-weeks wound healing rate referred to incidence of wounds with a complete closure at the 2 weeks after burn injury. The cost-effectiveness evaluation was considered as the secondary outcome, including in-hospital costs and length of stay.

2.3 Statistical analyses

All statistical analyses were conducted by using the SPSS 20.0 software (IBM SPSS, USA). A two-sided P < .05 was considered as statistically significant. Normal distribution and homogeneity of variance of the data were evaluated. Continuous variables expressed as mean ± SD or median (range) according normal distribution and were compared by using analysis of independent t-test or Mann–Whitney U tests. Comparisons of categorical variables were conducted by using chi-square test, which were expressed as frequencies and percentages. Univariate and multivariate logistic regression were used to identify risk factors for wound healing.

3 RESULTS

3.1 Baseline characteristics

The baseline characteristics of all enrolled paediatrics are presented in Table 1. Total of 73 paediatric with partial-thickness burns were enrolled, with a median age of 2 years (range 0.8–17 years), consisted of 38 males and 35 females. The mean burn area was 8.5% ± 5.0% TBSA. Nineteen patients had burn wound on single site while 54 patients with wounds involving multiple sites. The overall 2-weeks healing rate was 44.6%. The mean platelet count was (353.8 ± 108.1) × 10⁹/L. The mean PDW and MPV was 10.8 ± 1.9 fl and 10.8 ± 7.9 fl, respectively. Among whole patients group, the mean time to wound healing was 18.7 ± 10.8 days. The mean length of stay and in-hospital cost were 16.3 ± 10.5 days and (18.5 ± 15.0) × 10³RMB.

3.2 Wound healing outcome

According to the results of ROC curve analysis, a PDW level of 10.9 (area under the curve, 0.66; 95% CI: 0.54–0.79; P = .02) was considered as the optimal cutoff level to predict 2-weeks wound healing in paediatrics with partial thickness burns, with a sensitivity of 59% and a specificity of 74.4%, respectively, see Figure 1. All 73 enrolled paediatrics were divided into a high PDW group (n = 30) or a low PDW group (n = 43) by using the optimal cutoff value of PDW. As showed in Table 1, patients with a high PDW had a significant higher 2-weeks wound healing rate than those with a low PDW (66.7% vs 32.6%, P < .01, Table 1). Moreover, the

| TABLE 1 Distribution of 73 paediatrics with partial-thickness thermal burns according to PDW level |
|---------------------------------|-----------------|-----------------|-------|
| All cases (n = 73)              | PDW, fl         |                  |       |
|                                 | <10.9 (n = 43)  | ≥10.9 (n = 30)  | P     |
| Male                            | 38              | 20 (46.5%)      | 18 (60.0%) | .26   |
| Age, years                      | 2 (0.8–17)      | 2 (0.8–14)      | 1 (0.8–17) | .63   |
| BMI, kg/m²                      | 17.4 ± 4.4      | 17.4 ± 5.2      | 17.4 ± 3.1 | 1.00  |
| Burn wound area, %TBSA          | 8.5 ± 5.0       | 8.4 ± 5.1       | 8.5 ± 5.1 | .93   |
| Burn wound location             |                 |                  | .23   |
| Single                          | 19 (26.0%)      | 9(20.9%)        | 10(33.3%) |       |
| Multiple                        | 54 (74.0%)      | 34(79.1%)       | 20(66.7%) |       |
| Laboratory tests                |                 |                  |       |
| Platelet count, 10⁹/L           | 353.8 ± 108.1   | 354.7 ± 107.8   | 352.5 ± 110.3 | .93   |
| MPV, fl                         | 10.8 ± 7.9      | 11.3 ± 10.2     | 10.1 ± 1.1 | .52   |
| Wound healing                   |                 |                  |       |
| 2-weeks wound healing           | 34(46.6%)       | 14(32.6%)       | 20(66.7%) | <.01  |
| Time to healing                 | 18.7 ± 10.8     | 20.7 ± 10.9     | 15.4 ± 10.1 | .04   |

Abbreviations: BMI, body mass index; MPV, mean platelet volume; PDW, platelet distribution width; TBSA, total body surface area.
Mean time to wound healing of high PDW was obviously shorter than that of low PDW group (15.4 ± 10.1 vs 20.7 ± 10.9, \( P = .04 \), Table 1). However, other characteristics including age, sex, BMI, burn wound area and location, platelet count and mean platelet volume were comparable between high and low PDW groups (all \( P > .05 \)). (Table 1).

Potential significance indicator (\( P < .05 \)) associated with 2-weeks wound healing in univariate and multivariate logistic analysis were shown in Table 2. In details, univariate analysis showed burn wound area (OR: 1.13, 95%CI:1.01–1.27, \( P = .03 \)) and PDW (OR: 0.24, 95%CI: 0.09–0.65, \( P < .01 \)) were significantly correlated to 2-weeks wound healing. In multivariate analysis, low PDW remain as an independent risk factor for 2-weeks wound healing in paediatrics with partial thickness thermal burns (OR: 0.15, 95CI%:0.05–0.52, \( P < .01 \), Table 2).

### 3.3 Cost-effectiveness evaluation

The results showed mean in-hospital cost of all 73 paediatrics with partial thickness burns was (18.5 ± 15.0) ×

| TABLE 2 | Univariate and multivariate analyses of indicators associated with 2-week healing |
|---------|--------------------------------------------------------------------------------|
|         | Univariate                        | Multivariate                        |
|         | OR      | 95% CI     | \( P \) | OR      | 95% CI     | \( P \) |
| Age, years | 0.95    | 0.85–1.06  | 0.34 | 1.15    | 1.01–1.30  | 0.04 |
| BMI, kg/m² | 2.59    | 1.00–6.66  | 0.05 |         |           |      |
| Burn wound area, %TBSA | 1.13    | 1.01–1.27  | 0.03 | 1.15    | 1.01–1.30  | 0.04 |
| Burn wound location | 0.78    | 0.27–2.25  | 0.65 |         |           |      |
| Platelet count, 10⁹/L | 1.39    | 0.53–3.67  | 0.50 |         |           |      |
| MPV, fL | 0.56    | 0.22–1.41  | 0.22 | 0.24    | 0.09–0.65  | <0.01 |
| PDW, fL |         |           |      | 0.15    | 0.05–0.52  | <0.01 |

Abbreviations: BMI, body mass index; MPV, mean platelet volume; OR, odd ratio; PDW, platelet distribution width; TBSA, total body surface area.
In this study, we found that PDW value was significantly lower in high PDW group (13.7 ± 10.6 vs 21.9 ± 16.7, ×10^3/RMB; P = .02, Figure 2A). Moreover, there was a similar difference in term of length of stay between groups (12.2 ± 8.8 vs 19.0 ± 10.8, days, P < .01, Figure 2A).

4 | DISCUSSION

In this study, we retrospectively evaluated the value of PDW in predicting short-term prognosis in paediatrics with partial thickness burns and found that patients with a high PDW level had a better wound healing and a lower cost than those with a low PDW. Furthermore, low PDW was significantly associated with poor wound healing in univariate and multivariate analysis. Both length of stay and in-hospital cost of high PDW group were lower than those of low PDW group. Therefore, we suggested that PDW level can sever as a predictor for short-term prognosis of paediatrics with partial thickness burns.

Partial thickness burns mainly affect all epidermal and partial dermal layers, and the healing of which mainly depend on extension of residual appendages. However, burn wound healing is a dynamic pathophysiological process involving dysregulated inflammatory host response, proliferation of residual appendages, and re-epithelialization and tissue remodelling. Platelets play crucial roles in whole process of burn wound healing, and mainly participating in inflammatory regulation and tissue repair. Platelet recruitment is immediately induced following burn injure, then forming clots, which provide a temporary shield for protection of burn wound, a matrix for cell migration involving tissue repair. Moreover, activated platelets can released various cytokines and growth factors involving inflammation regulation and tissue repair formation. Furthermore, interactions between platelets and inflammatory cells at wound sites also can regulate inflammatory host response, thus facilitating wound healing. PDW has been considered as an indicator of heterogeneity in platelet morphology and activation. In setting of burn injure, platelets are excessively activated, destructed and consumed, and immature platelets with a larger volume would be produced, which be presented as higher PDW values. In this study, we found that PDW value was significantly associated with wound healing, which was consistence with conclusions mentioned above. The PDW is considered as an indicator representing the heterogeneity of platelet size and also a potent marker of platelet activity, independent of platelet counts and mean platelet volume. A High PDW level indicates a higher production of larger reticulated platelets, which have larger and more metabolic activity, may promote the healing process of burn wound. It has been showed PDW was an independent risk factor for 120-day mortality in severe burn patients. Moreover, we found that burn wound area was also an independent factor associated with wound healing, which was consistence with previous study.

Besides wound healing, medical cost is another consideration for burn wound care. In this study, we found that patients with a high PDW value had a lower length of stay and in-hospital cost than those of patient with a low PDW. The wound healing process burn area and hospitalisation with autografting were important drivers for medical cost for burns patient. In this study, all patients received conservative treatments for burn wound, such as topical medication, dressing change. Therefore, we evaluated the association between PDW and medical cost in a more accurate aspect. High PDW presents an improved early wound healing, thereby decreasing length of stay and saving medical cost.

For children with burns injure, permanent scarring and poor cosmesis resulting from delayed wound healing is common and associated with long term quality of life. This study demonstrated that PDW value obtained from routine blood test was an independent marker of 2-weeks wound healing in paediatrics with partial thickness burns comparing with burn wound area. However, PDW level is not a direct contributor to wound healing, but a marker of activated platelets. In clinical of burn care, PDW can be applied to achieve optimal patient stratification and to plan individual treatment for burns patients, thereby prompting the prognosis.

This study had several limitations. The retrospective and single centre design may limit the effective and generalisation of conclusion of this study. A multicentre, prospective study with a large sample should be conducted to furtherly evaluated the effective of PDW. Furthermore, since PDW value was measured only one time on admission, which may be influenced by laboratory error, thus resulting in bias. We will furtherly evaluate dynamic changes of PDW during clinical course of burns, and confirmed the significance of PDW in burns, especially for paediatrics. Lastly, only Chinese paediatrics were enrolled in the study. The results of present study need to be further evaluated in adults.
5 | CONCLUSION

In conclusion, High PDW value is not only significantly and independently associated with improved wound healing outcome, but also predicts decreased medical burdens. The PDW value easily available from routine blood tests might be a potential indicator to predict the short-term prognosis of paediatrics with partial thickness thermal burns.

CONFLICT OF INTEREST
The authors declare no conflicts of interests.

ETHICS STATEMENT
This study was approved by the Ethics Committee of Forth Medical Center of Chinese PLA General Hospital.

INFORMED CONSENT
All patients were required for their signed and written informed consent.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author.

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How to cite this article: Liu H, Li D, Sun T, et al. Platelet distribution width associated with short-term prognosis and cost in paediatrics with partial-thickness thermal burns: A retrospective comparative study. *Int Wound J.* 2022;19(7):1853-1859. doi:10.1111/iwj.13791