Platelet count: A predictor of sepsis and mortality in severe burns

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ABSTRACT

Background: Platelet cells, or thrombocytes, have additional roles to haemostasis. After burn injury, platelet counts drop to a nadir at days 2–5 then rise to a peak between days 10–18. The nadir has previously been associated with mortality but there is currently no thorough investigation of its potential to predict sepsis in adults. The primary objective of this study is to assess whether platelet count can predict survival and sepsis in adults with severe burn injuries.

Methods and findings: A retrospective cohort analysis of platelet count and other blood parameters in 145 burn patients with a TBSA greater than 20%. AUROC analysis revealed that the platelet count and rBaux score together produce moderate discrimination for survival at less than 24 h after injury (AUROC = 0.848, 95%CI 0.765–0.930). Platelet count at day 3 combined with TBSA has a modest association with sepsis (AUROC = 0.779, 95%CI 0.697–0.862). Multivariable Cox regression analysis revealed platelet peak was the strongest predictor of mortality.

Conclusions: A reduced peak platelet count is a strong predictor of 50-day mortality. Platelet count nadir may have some association with sepsis.

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1. Introduction

Platelets are known traditionally for their essential roles in haemostasis and thrombosis. However, their non-haemostatic roles as sentinels of the innate immune system during infection and inflammation are becoming increasingly recognised [1–3]. Several large clinical studies conducted in intensive care units suggest that thrombocytopenia is predictive of mortality and multiple organ failure during sepsis [4–6]. However, in burn injury, the diagnosis of sepsis is often more difficult due to a profound systemic inflammatory response obscuring the classical signs and diagnostic criteria. Intriguingly, platelet counts after burn injury tend to follow a distinct pattern; falling to a nadir at days 2–5, then rising to a peak value

at days 10–18. This has been investigated within animal models, case reports [7–9], and a number of larger scale studies [10–12]. A number of these studies have compared platelet counts and mortality [10,11,13]. More recently, Marck et al. investigated platelet counts within a large heterogeneous group (N=244) of adult and paediatric burns patients, where 80% of the cohort had burns covering less than 29% total body surface area (TBSA). They compared both the nadir and peak values with mortality [14]. Both the mean nadir and peak platelet counts were significantly lower in both septic and non-surviving patients with lower peak counts predicting 50day mortality (p<0.05). However, Marck et al. had very few septic patients in their cohort; hence, there has not been a proportional hazards model applied to an adult dataset of burns patients to investigate platelet count and sepsis.

In this retrospective study of 145 patients with severe burn injuries (≥20% TBSA) we investigate whether the classical pattern of post-burn platelet counts are able to predict outcomes. In addition, we also examine if other routinely measured haematological parameters are helpful to the clinician in their assessment of the patient.

2. Materials and methods

2.1. Patient cohort

This retrospective cohort study was conducted from January 2007 to May 2015. All burn patients were screened for eligibility. Table 1 shows the inclusion and exclusion criteria for the study. Clinical data were collected from the electronic patient record (EPR) and UK International Burn Injury Database (IBID) including: age at injury; gender; body mass index (BMI); length of stay in total (LOS) and in intensive care episodes (LOS ICU); mechanism of injury; inhalation injury status and severity; TBSA%; sepsis and mortality. Each patient was assessed for the presence of sepsis through appraisal of the EPR, paper records and observation charts. As a retrospective study of clinical data, ethical approval by the University Hospitals Birmingham (UHB) trust Clinical Governance Department was granted.

2.2. Routine haematological and pathology measurements

Routine haematological parameters were extracted from the EPR for 50days after burn injury. These included: platelet count; white blood cell counts including the differential of lymphocytes and neutrophils and C-Reactive protein (CRP). All

cellular parameters were measured in the routine cellular pathology laboratories at Queen Elizabeth Hospital Birmingham (QEHB) using a Beckman Coulter UniCel DxH 800 Cellular Analysis System from 2010 to 2015, and with a Beckman Coulter LH750 from 2007 to 2010. Both analysers use impedance based analysis for platelets with similar accuracy and precision [15,16]. Quality control was ensured by regular measurement of internal and external quality control samples.

2.3. Clinical definitions

The primary outcomes were in-hospital 50-day mortality and incidence of sepsis. Sepsis was defined as a patient meeting a score of 3 or more using the 2007 American Burn Association criteria plus a temporally relevant positive microbiological culture result, (±5days from the ABA indicated sepsis) [17]. Severity of injury was reported using the revised-Baux (rBaux) score, defined by Osler et al. [18]. This was preferred over other mortality scoring systems such as the abbreviated burn severity index (ABSI) as previous diagnostic test accuracy studies show it has greater accuracy in predicting mortality in severe burns [19,20]. Thrombocytopenia was defined as a platelet count of less than 150×10^9/L, and thrombocytosis as a platelet count of greater than 400×10^9/L [21]. The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were also calculated from routine parameters. Inhalational injury was defined as the presence of carbonaceous deposits, erythema, oedema, bronchorrhea or obstruction observed with or without the aid of bronchoscopy. Severity of inhalational injury was divided into mild, moderate or severe: mild was defined as minor/patchy areas of erythema and carbonaceous deposits in the proximal or distal bronchi; moderate as erythema with carbonaceous deposits, bronchorrhea with or without compromise of the bronchi; and severe was defined as any of the following: strong inflammatory response with friability, copious carbonaceous deposits, bronchorrhea, or bronchial obstruction.

The nadir platelet count was defined as the lowest value between days 2–5. The peak platelet count was the highest value observed between days 11–17. These values are based on previous figures from the literature and experimental models [7–12,14].

2.4. Statistical methods

Variables were assessed for normality both graphically, using Q-Q plots, and quantitatively using the Shapiro-Wilk test. The

Table 1 – Inclusion and exclusion criteria.	
Included	Excluded
• Aged 16-99 • Total body surface area percentage (TBSA%) is greater than or equal to 20% • At least one platelet count within 48h of injury • A minimum of 4 platelet counts within the first 7 days of admission	• Non-acute burn injury • Diagnosed with platelet disorders • Patients diagnosed with skin blistering conditions (such as TENS) • Chemical burn injury • Patients admitted for comfort care (where a decision is made within the first 24h) • Incomplete data or unable to obtain medical notes