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Original Article

Clinical characteristics and prognostic significance of changes in platelet count in an internal medicine ward

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ABSTRACT

Background: The clinical characteristics and prognostic significance of changes in platelet count (PC) during hospitalization in internal medicine wards have not been well investigated.
Methods: Demographic, clinical and laboratory data were collected from 345 patients admitted to an internal medicine ward. Following discharge, all-cause mortality was recorded. These data were compared, according to deltaPC (PC on discharge minus PC on admission): group 1 (drop in PC, deltaPC -50×10^9/l), group 2 (no significant PC changes, deltaPC up to 50×10^9/l) and group 3 (rise in PC, deltaPC $+50 \times 10^9$/l).
Results: Groups 1, 2 and 3 comprised 64 (18.5%), 200 (58%) and 81 (23.5%) patients, respectively. Patients from group 3 were younger, more likely admitted for infection and less likely for cardiovascular disorder, and less often presenting with coronary artery disease, complex nursing care and thrombocytosis on admission or thrombocytopenia on discharge than patients from groups 1 and 2. Mean platelet volume was higher in group 2 on admission and lower in group 3 on discharge. During a median follow-up of 25 months, 146 (42.3%) of 345 patients died. The survival rate was higher for group 3 (65.4%) than for groups 1 (45.3%) and 2 (58.5%), $p = 0.003$. In the entire cohort, each 100×10^9/l increment of deltaPC was a powerful predictor of lower mortality ($p = 0.03$, relative risk = 0.83, 95% confidence interval = 0.71–0.98).
Conclusions: Increased PC throughout hospitalization was associated with better prognosis than a drop or blunted rise in PC. The assessment of PC changes in an internal medicine ward may provide useful prognostic information.

1. Introduction

The average platelet life span in blood is 7–10 days [1–3]. Therefore, platelet count (PC) may change significantly within several days as a result of altered production and increased destruction and sequestration of thrombocytes [4–6]. These pathogenic mechanisms may be encountered in acute conditions such as severe infection, inflammation, trauma, major surgery, mechanical ventilation, bleeding and transfusions [4–9]. Changes in PC may also be caused by a variety of chronic disorders, including malignant diseases, nutritional deficiencies or liver failure and certain drugs [4,8,9]. Decreased PC over time may indicate a failure of the bone marrow to achieve an adequate compensatory response and may be due to severe infection, secretion of toxic substances or inflammatory mediators and administration of medications [4–9]. On the other hand, a rise in PC can reflect appropriate activation of bone marrow, as the acute phase response to infection and inflammation is mediated by various growth factors and cytokines, especially thrombopoietin and interleukin-6 [2,3,5,6].

Thrombocytopenia is recognized as a marker of disease severity and an independent risk factor for mortality in critically ill patients [4,6,8,9]. Yet the prognostic significance of time-dependent PC changes has been investigated in only few studies involving intensive care unit (ICU) patients. The development of thrombocytopenia was found to be associated with a worse prognosis among such patients [6]. Moreover, a relative drop in PC ≥ 30% [7,10] and a blunted rise in PC [5] were associated with increased mortality in the ICU.

Many internal medicine inpatients suffer from conditions that may result in thrombocytopenia or thrombocytosis on admission. In addition, PC may change significantly during hospitalization, even within the normal range. For such patient population, the clinical characteristics associated with PC changes throughout hospitalization and the prognostic significance of these changes have not been investigated. Therefore, the aim of this study was to compare the characteristics and long-term survival among groups of internal medicine patients with a drop in PC, no significant changes in PC and a rise in PC from admission to discharge.

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2. Methods

2.1. Study population and design

The study population consisted of adult patients admitted to the emergency department during November 2009–December 2011 due to a variety of acute medical disorders and then hospitalized arbitrarily to our ward (38 beds), which is one of the six departments of internal medicine in our medical center. Included in the study were 345 patients with available complete blood count (CBC) on admission and discharge (the minimal interval between the two determinations was 3 days). CBC was determined routinely within 24 h from admission and, according to the decision of the attending physician, at least 48 h before discharge or death. PC was measured by Coulter® A84148-AB counter (Beckman Coulter, Inc., CA, USA) with LH 750 control system (coefficient of variability 10%–20%). Patients with severe thrombocytopenia on admission (PC $\leq 20 \times 10^9$/l), primary hematological disorders (leukemia, immune thrombocytopenia, myelodysplastic syndrome, myeloproliferative disease, etc.) and platelet transfusion were excluded from the study.

Patients were divided into 3 main groups for analysis, according to deltaPC (PC on discharge minus PC on admission): group 1 (drop in PC, deltaPC -50×10^9/l), group 2 (no significant PC changes, deltaPC up to 50×10^9/l) and group 3 (rise in PC, deltaPC + 50×10^9/l). The deltaPC of more than 50×10^9/l was determined to minimize the chance of misclassification of patients due to known normal individual PC variability [5,11] or variability of PC measurement by the counter.

We also analyzed the impact of time-dependent PC changes on survival according to the ratio of PC on admission to discharge: relative drop >20% (group A), no significant changes (up to 20%, group B) and rise >20% (group C) in PC. In addition, an association between changes in mean platelet volume (MPV) and mortality was assessed by comparing patients according to a relative increase (>10%), no significant change (up to 10%) and a decline (>10%) in MPV.

The study was carried out in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee.

2.2. Data collection

Demographic, clinical and laboratory data were collected from patients' charts and hospital records. Recurrent hospital admissions and all-cause mortality, following discharge, were registered. Death was confirmed by hospital or outpatient death certificates.

2.3. Definitions

Thrombocytopenia and thrombocytosis were defined as PC below ($<140 \times 10^9$/l) and above (450×10^9/l) normal range values, respectively. The cutoff points were chosen as the lowest/highest values within the normal range provided by the laboratory device manufacturer. Renal function was assessed by estimating the glomerular filtration rate (GFR) using the modification of diet in renal disease (MDRD) equation [12]. Renal dysfunction was defined as GFR <60 ml/min/1.73 m^2. Anemia, according to the World Health Organization criteria, was defined as a hemoglobin concentration of <13 g/dl in men and <12 g/dl in women.

2.4. Statistical analysis

The data were analyzed using BMDP Statistical Software [13]. The results were expressed as mean ± SD for the data with normal distribution, or as median (range), as raw data or as percentages in case of non-parametric data. Pearson's chi-square was used for comparison of qualitative variables. Analysis of variance (ANOVA), with Bonferroni correction for multiple comparisons, was applied for quantitative variables. Log transformation or the Kruskal–Wallis non-parametric test was used for comparison of variables that did not have Gaussian distributions. Survival curves were plotted using the Kaplan–Meier estimate. Mantel–Cox and Breslow tests were used to evaluate the differences between the curves. Variables found to be associated with survival using the Kaplan–Meier method ($p \leq 0.1$) were re-evaluated by the Cox proportional hazards model to identify those variables most significantly associated with mortality. A p-value ≤ 0.05 was considered statistically significant.

3. Results

3.1. Characteristics of the patients

3.1.1. Entire group

The demographic, clinical and laboratory characteristics of the 345 patients are presented in Table 1. The overall mean age was 66.2 ± 19 years. Groups 1, 2 and 3 comprised 64 (18.5%), 200 (58%) and 81 (23.5%) patients, respectively. The respective median duration of hospital stay and interval between measurements of PC were 8 and 6 days.

3.1.2. Comparisons among groups 1 (DeltaPC -50×10^9/l), 2 (DeltaPC 50×10^9/l) and 3 (DeltaPC $+50 \times 10^9$/l) (Table 1)

Patients with rising PC during hospitalization (group 3) were younger, more likely admitted for infectious/inflammatory disease and less likely for cardiovascular disorder than patients from groups 1 and 2.

Patients from group 3 less often presented with coronary artery disease, complex nursing care and thrombocytosis on admission or thrombocytopenia on discharge. Patients from group 3 were more likely than those in groups 1 and 2 to present with thrombocytopenia on admission and thrombocytosis on discharge. The mean values of PC were higher in group 1 on admission and in group 3 on discharge. Values of C-reactive protein (CRP) were higher in group 3. MPV was higher in group 2 on admission and lower in group 3 on discharge. Higher counts of leukocytes and neutrophils on discharge and of lymphocytes on admission were observed in group 1.

The median length of hospital stay and the time lapse between PC measurements were shorter for group 2. No statistically significant difference was observed among the groups in recurrent hospital admissions.

3.2. Survival

3.2.1. Entire group

The follow-up period was up to 42 months (median 25 months). All-cause mortality in the entire group was 42.3% (146 patients); 43 patients (12.5%) succumbed during the current hospitalization and 103 (29.8%) died in the follow-up period.

3.2.2. Comparison of survival rates among groups 1–3

During current hospitalization, mortality was 21.9% in group 1, 10.5% in group 2 and 9.9% in group 3 ($p = 0.04$). Fig. 1A illustrates survival curves in groups 1–3. Declining PC (group 1) was associated with shortened survival and rising PC (group 3) with longer survival, $p = 0.003$. The respective mean survival durations and survival rates were 20.5 months and 45.3% in group 1 compared with 26.9 months and 58.5% in group 2 and 30.2 months and 65.4% in group 3. The differences in the slopes of the survival curves were the most prominent for the first 90 days of the study.

3.2.3. Comparison of survival rates among groups A, B and C

In analysis of the impact of time-dependent PC changes on survival, according to the ratio of PC values at admission and discharge, a drop in PC of >20% (group A) during hospitalization remained to be associated with decreased survival, while a rise in PC >20% (group C) was still associated with better outcome ($p < 0.001$, Fig. 1B).