Mean Corpuscular Hemoglobin Predicts Length of Hospital Stay Independent of Severity Classification in Acute Pancreatitis Patients: a Retrospective Study

Hao Lin (lh4621@126.com)  
Zhongda Hospital, Southeast University

Ting Yu  
Zhongda Hospital, Southeast University

Rong Xu  
Zhongda Hospital, Southeast University

Xing Li  
Zhongda Hospital, Southeast University

Research Article

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Abstract

**Background/Objectives:** The aim of this study is to explore the relationship between length of hospital stay and mean corpuscular hemoglobin (MCH) in acute pancreatitis (AP) patients.

**Methods:** The study included 273 AP patients without coronary heart disease, diabetes, hypertension, tumor, psychosis and anemia. The clinical data was collected from electronic medical records.

**Results:** We separated all data into three groups according to length of hospital stay. We observed that gender (P=0.017) and severity classification (P=0.000) were significantly correlated with length of hospital stay among three groups. Notably, MCH level was significant increased among three groups (30.02±1.91, 30.21±1.81, 30.92±2.47 pg, P=0.009). Thus, we separated all data into two groups according to MCH level, and observed significant increases of length of hospital stay between two groups (11.95±7.03, 13.96±8.18 days, P=0.030). A positive correlation between length of hospital stay and MCH was observed in these individuals (r=0.172, P=0.004). Multiple linear regression analysis showed that MCH was independent correlated with length of hospital stay, no matter whether severity classification of AP was included (beta=0.248, P=0.000; beta=0.212, P=0.000).

**Conclusions:** We concluded that length of hospital stay is correlated with MCH level in AP patients, and the MCH level may predict length of hospital stay independent of severity classification in this disease. Our results may provide a potential evaluation basis for the management of patients with AP.

Introduction

Acute pancreatitis (AP) is an acute inflammatory disease of the pancreas which can result in a systemic inflammatory response syndrome with significant morbidity and mortality, and the incidence rate of AP has increased in recent years. AP is one of the most common gastrointestinal causes of hospitalization and results in family financial burden. There is a lack of simple indicators to predict the length of hospital stay of AP. Therefore, the prediction of hospitalization time of patients with acute pancreatitis is conducive to the management of patients and the optimization of clinical diagnosis and treatment efficiency.

Severity classification is correlated with length of hospital stay in AP patients. Previous data showed that both Revised Atlanta Criteria (RAC) and Determinant Based Criteria (DBC), which stratify AP by severity, strongly predict length of hospital stay. But these indexes cannot predict length of hospital stay at the beginning of hospitalization. A recent work carried out among children demonstrated that certain demographic and clinical factor, such as gender and ethnicity, were independently associated with length of hospital stay for pediatric AP. However, few laboratory parameters are available to evaluate hospitalization in patients with AP.

Blood routine test is the most common clinical test at the beginning of hospitalization. White blood cell count (WBC) could predict severity of AP, but it hasn’t been tested in predicting of length of hospital stay.
Mean corpuscular hemoglobin (MCH) is the average amount of hemoglobin per red blood cell and is calculated by dividing hemoglobin (HGB) by red blood cell count (RBC). Mean corpuscular volume (MCV) is the average size of a red blood cell, and the Mean corpuscular hemoglobin concentration (MCHC) is the average concentration of hemoglobin per unit volume of red blood cells. The disease status of AP has a significant impact on blood routine test, and often abnormal hematological parameters predict adverse clinical events in patients with AP. For example, red cell distribution width (RDW) predicts the severity of AP patients in pregnancy. C-reactive protein (CRP) predicts systemic inflammatory response syndrome and death in AP. Total cholesterol concentration predicts the effect of plasmapheresis on hypertriglyceridemic AP. Increased circulating total bile acid levels were associated with organ failure in patients with AP. There are no studies investigating efficacy of MCH, MCV, MCHC, HGB or RBC in predicting length of hospital stay of AP.

Here, the purpose of our study was to evaluate the relationship between hematological parameters and length of hospital stay in patients with AP.

**Results**

1. The clinical and laboratory features

Table 1 included the characteristics of all participants. Because the average length of hospital stay for AP patients was 14 days in Zhongda Hospital, and the average length of hospital stay in three-A class hospitals of Nanjing city was 8 days., we separated all data into three groups according to 8 and 14 days of length of hospital stay. Significant difference in the value distribution of gender (P = 0.017) and severity classification (P = 0.000) was found. We observed significant increases of MCH among three groups (30.02 ± 1.91, 30.21 ± 1.81, 30.92 ± 2.47 pg, P = 0.009). We also noticed significant difference of RBC among three groups (4.75 ± 0.45, 4.77 ± 0.56, 4.54 ± 0.62 ×10^12/L, P = 0.007). There were no significant differences for other variables, including age, smoke, alcohol, cholecystectomy, WBC, HGB, MCV and MCHC.

**Table 1.** The clinical and laboratory data in whole population according to length of hospital stay
Due to the above interesting results between length of hospital stay and MCH, we separated all data into two groups according to the median number of MCH (Table 2). We observed significant increases of length of hospital stay between two groups (11.95 ± 7.03, 13.96 ± 8.18 days, P = 0.030). We also noticed significant difference of gender (P = 0.029), RBC (P = 0.000), MCV (P = 0.000), MCHC (P = 0.000) between two groups. There were no significant differences for other variables, including age, smoke, alcohol, cholecystectomy, WBC, HGB and severity classification.

Table 2. The clinical and laboratory data in whole population grouped according to MCH
| MCH (pg) | ≤ 30.3 | > 30.3 | P-value |
|----------|--------|--------|---------|
|          | N = 142 | N = 131 |         |
| Gender (male, %) | 77, 54.2% | 88, 67.2% | 0.029* |
| Age (year) | 44.3 ± 17.2 | 46.1 ± 15.7 | 0.363 |
| Smoke (n,% ) | 21, 14.8% | 27, 20.6% | 0.207 |
| Alcohol (n,% ) | 18, 12.7% | 22, 16.8% | 0.336 |
| Cholecystectomy (n,% ) | 10, 7.0% | 5, 3.8% | 0.243 |
| Severity classification | | | 0.067 |
| Mild (n, %) | 132, 48.4% | 113, 41.4% | |
| Moderately (n, %) | 1, 0.4% | 1, 0.4% | |
| Severely (n, %) | 9, 3.3% | 17, 6.2% | |
| WBC (10^9/L) | 10.65 ± 4.90 | 11.26 ± 4.78 | 0.294 |
| RBC (10^{12}/L) | 4.83 ± 0.57 | 4.53 ± 0.50 | 0.000*** |
| HGB (g/L) | 140.20 ± 16.57 | 143.68 ± 15.43 | 0.074 |
| MCV (fL) | 86.60 ± 4.10 | 92.51 ± 4.19 | 0.000*** |
| MCH (pg) | 29.04 ± 1.38 | 31.88 ± 1.76 | 0.000*** |
| MCHC (g/L) | 335.36 ± 10.84 | 344.76 ± 19.14 | 0.000*** |
| length of hospital stay (day) | 11.95 ± 7.03 | 13.96 ± 8.18 | 0.030* |

The demographic characteristics and laboratory parameters of study participants (n = 273) according to the median number of MCH. WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin content.

2. The correlation between length of hospital stay and laboratory data in whole population

As shown in Fig. 1, the positive correlation between length of hospital stay and MCH was observed in these individuals (r = 0.172, P = 0.004). In order to further explore the correlation between length of hospital stay and other laboratory data, we did the correlation between length of hospital stay and other laboratory data in whole population (Table 3). Length of hospital stay correlated with gender (r = -0.123, P = 0.042), severity classification (r = 0.182, P = 0.003), WBC (r = 0.128, P = 0.034), RBC (r = -0.190, P = 0.002). Length of hospital stay had no correlation with age, smoke, alcohol, cholecystectomy, HGB, MCV, MCHC.

Table 3. The correlation between length of hospital stay and other laboratory data in whole population
3. The correlation analyses in multiple linear regression analysis

The correlation analyses were carried out in all subjects. The basic demographic characteristics, such as gender, age and severity of AP, might influence length of hospital stay. The laboratory parameters of study participants, such as WBC and HGB, might influence length of hospital stay as well. Therefore, gender, age, severity classification, WBC, HGB and MCH were included as independent variables in multiple linear regression analysis. We did two regression models to investigate the correlation between length of hospital stay and laboratory data (Table 4). We did linear regression based on gender, age, WBC, HGB and MCH in model 1, and model 2 added severity classification on the basis of model 1. The results found that length of hospital stay was correlated with MCH in both model 1 and model 2 (beta = 0.248, P = 0.000 in model 1; beta = 0.212, P = 0.000 in model 2). Length of hospital stay was correlated with severity classification and gender independently (beta = 0.212, P = 0.000; beta = 0.211, P = 0.001; beta = -0.171, P = 0.015 respectively), as shown in Table 4.

**Table 4. The factors related to length of hospital stay in AP patients in multivariable linear regression analysis**

Model 1 (linear regression based on gender, age, WBC, HGB and MCH)
We found that length of hospital stay had a relationship with MCH level in AP patients, and the multiple linear regression analysis showed that MCH level positively correlated with length of hospital stay independent of severity classification of AP.

The severity classification of AP was a strong risk factor of length of hospital stay in AP patients, and the more serious the patient was, the longer they stayed in hospital (Table 1). We also found that gender was another a risk factor of length of hospital stay. The female patients stayed longer than male ones (Table 1), and this phenomenon consisted with previous report in pediatric AP patients. After adjustment for severity classification and gender, length of hospital stay still positively correlated with MCH (P = 0.000, Table 4).

At the beginning of data analysis, we also found a correlation between length of hospital stay and MCH without excluding anemic patients (data not show). We suspected that this correlation might due to the
reduction of HGB, so we excluded anemic patients in this study. Surprisingly, after excluding anemia, length of hospital stay and MCH are still correlated statistically (Fig. 1, Table 3), and HGB was not the risk factor of length of hospital stay according to the multiple linear regression analysis (Table 4). At the other hand, we also found that RBC was not a risk factor of length of hospital stay according to multiple linear regression analysis (P = 0.900, data not show). Because MCH is calculated by dividing HGB by RBC, these interesting results implied that MCH might affect length of hospital stay through mechanisms other than anemia.

Long hospital stay is associated with high hospital occupancy, increased costs, and adverse patient outcomes, such as persistent organ failure\textsuperscript{10–12}. The previous studies showed that low MCH level is one of the earliest and sensitive indicators of iron deficiency in different populations\textsuperscript{13–15}, suggesting that MCH positively correlated with iron level. Iron is one of the most important metal ions in human body, but it is also a potentially toxic element. So its systemic homeostasis is strictly regulated\textsuperscript{16}. Iron overload is a risk of pancreatic endocrine diseases, such as diabetes\textsuperscript{17}, and results in pancreatic β cell failure, impaired glucose tolerance and insulin sensitivity\textsuperscript{18,19}. Iron overload also cause the pancreatic exocrine diseases, such as pancreatitis and pancreatic adenocarcinoma\textsuperscript{20}. In the present study, length of hospital stay positively correlated with MCH probably because of higher iron level in these patients.

The present results had some limitations. First, this was a retrospective study from electronic medical records, serum samples of patients could not be obtained. Thus we could not measure concentration of iron or iron transporter in serum. Second, our sample size was small, and we needed to expand the sample to verify our conclusion in the future. Third, in different hospitals, there might be slight differences among treatment of AP, which might lead to different length of hospital stay data for same patients in different hospitals. Finally, the patients' financial situation and willingness of treatment might be a potential confounding factor that affects our final outcome.

In conclusion, the evaluation of length of hospital stay is conducive to the management of patients by hospital. We demonstrate that length of hospital stay is correlated with MCH level independent of severity classification in AP patients, and the MCH level may have an effect on predicting length of hospital stay in this disease.

**Materials And Methods**

**Data collection**

A total of 273 patients with AP from Zhongda Hospital, School of Medicine, Southeast University were included in the retrospective study, and the diagnosis of all patients with AP were defined in accordance with the criteria of IAP/APA evidence-based guidelines\textsuperscript{21}. Patients with known coronary heart disease, diabetes, hypertension, tumor and psychosis were excluded. Patients with anemia (HGB < 120 g/L for male and HGB < 110 g/L for female) were also excluded. Demographic and clinical characteristics of subjects were obtained from electronic medical records. Severity classification (mild, moderately,
severely) was performed according to Marshall scoring system22. The study was approved by Ethics Committee for Clinical Research of Zhongda Hospital, Affiliated to Southeast University and was performed according to the Declaration of Helsinki. The informed consent was waived by Ethics Committee for Clinical Research of Zhongda Hospital, Affiliated to Southeast University.

Statistical analysis

SPSS software version 23.0 was used to analyze all data. Continuous variables were shown as the means ± standard deviation, and categorical variables were presented as percentages. The comparisons among three groups of continuous variables were performed by One-Way ANOVA. The comparisons of ordinal categorical variables were performed by Rank Sum Test, and Chi-Square Test was used to compare unordered categorical variables among three groups. Spearman's correlation analyses were employed to examine the correlations between length of hospital stay and MCH appropriately. The multiple linear regression analysis was performed to analyze the independent effects of length of hospital stay in all subjects. A P-value of < 0.05 was considered to be statistically significant.

Declarations

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Author contributions

H.L. and T.Y. contributed equally. H.L. designed this project. H.L., T.Y. and R.X. collected data. H.L. and T.Y. did the statistical analysis. X.L. support the data of the average length of hospital stay. H.L. and T.Y. wrote the manuscript. All authors reviewed the manuscript.

Conflict of interest

We declare no conflict of interest.

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**Figures**
The correlation between length of hospital stay (length of hospital stay) and mean corpuscular hemoglobin (MCH) of study participants (n = 273). Spearman's correlation analyses were employed to examine the correlations between length of hospital stay and MCH appropriately. Correlation coefficient was 0.172, and P-value was 0.004.