Utility of Complete Blood Picture for Predicting In-hospital Mortality in Patients with Acute Decompensated Heart Failure with Dilated Cardiomyopathy

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Indian J Cardiovasc Dis Women-WINCARS 2017;2:44–48.

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Abstract

Background Congestive heart failure (CHF) is one of the leading causes of acute hospital admissions. Despite recent advances in heart failure therapy, prognosis is still poor, rehospitalization rate is very high, and quality of life is worse. It is important to identify patients at increased risk of adverse events. We tried to investigate role of components of complete blood picture on in-hospital mortality in patients hospitalized with heart failure.

Methods It was an observational study of consecutive patients who admitted with a diagnosis of acute decompensated heart failure (ADHF) with dilated cardiomyopathy (DCM) in the our department between January 1, 2016 and December 31, 2016, age above 18 years. Ischemic cardiomyopathy was ruled by doing coronary angiograms either in this admission or previously known. Baseline investigations including complete blood picture were done and the patients were followed up till discharge or in hospital mortality.

Results A total of 74 patients (female:male::24:50) enrolled into the study (mean age 51.86 $\pm$ 13.5 years) in 12 months. A total of 8 (10.8%) patients died during hospitalization. Among the 74 heart failure patients, 24 (32.5%) had anemia. Group 1 included patients who died during index hospitalization ($n = 8$) and group 2 comprised patients who were discharged in a stable condition after index hospitalization ($n = 66$). Group 1 patients had low hemoglobin (12.34 $\pm$ 2.93 vs. 14.4 $\pm$ 0.21 g/dL, $p = 0.000$) and high leukocyte count (11,600 $\pm$ 2,780 vs. 9,047 $\pm$ 3,355 cells/mcL, $p = 0.040$) with more eosinophils (1 $\pm$ 1.06 vs. 4.16 $\pm$ 3.48%, $p = 0.000$) and lymphocytes (20.5 $\pm$ 0.53 vs. 17.56 $\pm$ 7.45%, $p = 0.002$). Regression analysis showed a significant association between low hemoglobin and low packed cell volume (PCV) with in-hospital mortality. Mean corpuscular hemoglobin (MCH) and mean corpuscular volume (MCV) rather than mean corpuscular hemoglobin concentration (MCHC) predicted worse outcome. There was a significantly higher risk of in-hospital mortality with increasing eosinophil count. On the other hand, there was no association between platelet count, total white blood cell (WBC) count, neutrophil, monocyte, or lymphocyte count with clinical outcome.

Conclusion Low hemoglobin, low PCV, and high eosinophil count have been shown to predict in-hospital mortality. Complete blood picture can, therefore, be utilized in risk-stratifying patients with ADHF due to DCM.

Keywords

- acute decompensated heart failure
- congestive heart failure
- dilated cardiomyopathy
- mean corpuscular hemoglobin

DOI https://doi.org/10.1055/s-0037-1607035.

Introduction

Congestive heart failure (CHF) is the leading cause of acute hospital admissions and one of the main causes of death.[1] Mortality rates approach 20% per year in spite of current medical therapy.[2] However, the clinical course of patients with CHF is variable.

Understanding what factors relate to subsequent mortality and morbidity may help in identifying which patients need more intense monitoring and therapy.

Several models predict outcome in patients with heart failure (HF), but most of them are very complex and may need wide range of investigations.[3] The purpose of this study is to assess the impact of components of complete blood picture (CBP) on in-hospital mortality in patients hospitalized with HF due to dilated cardiomyopathy (DCM).

Material and Methods

The study was conducted in our department of cardiology between January 1, 2016 and December 31, 2016. Seventy-four consecutive patients who were admitted with a diagnosis of acute decompensated heart failure (ADHF) due to DCM and met inclusion criteria were recruited. Patients with ischemic cardiomyopathy were excluded after doing coronary angiogram (CAG), or previous CAG within 6 months showed normal coronaries. The study was approved by the institutional review board. An informed written consent was obtained from the participants before recruiting them in the study.

Patients with medical conditions known to affect hematologic parameters, such as disorders of the hematopoietic system, history of cancer and/or previous treatment with chemotherapy, infection, and chronic inflammatory conditions; and/or histories of glucocorticoid use 3 months before the admission; and acute myocardial infarction or known coronary artery disease (CAD), were excluded. Eligible criteria for the study include any patient with age of at least 18 years; New York Heart Association (NYHA) class II, III, or IV symptoms; and an ejection fraction of $\leq$ 35% with normal coronaries.

We also excluded major comorbidities that may have independent influence on in-hospital mortality such as patients with acute and severe renal failure, active hepatic disease, severe pulmonary disease (e.g., chronic obstructive pulmonary disease), and acute infectious disease.

We divided the patients into two groups. Group 1 included patients who died during index hospitalization and group 2 comprised patients who were discharged in a stable condition after index hospitalization. Herein, we assessed the use of the white blood cell (WBC) count and other components of the CBP to predict in-hospital mortality. All patients were subjected to undergo routine investigations including complete blood counts. All data including patient's demographics, medical history, medications, clinical presentation, and electrocardiographic (ECG) and echocardiographic details were obtained. Hematologic parameters on date of admission were taken as parameters to predict in-hospital mortality. All blood samples were examined by the same experienced pathologist. Association between hematologic variables and in-hospital mortality was evaluated.

Statistical Analysis

Descriptive statistics for data with normal distribution were presented as means and standard deviations from the mean. Comparison between two groups was tested for continuous and dichotomous variables using Student's paired *t*-test and χ^2, respectively. Regression analysis of survival data based on a Cox proportional-hazards model was used to explain the effect of laboratory values on morbidity and mortality hazard rates. A p value < 0.05 was considered statistically significant.

Results

Participants were enrolled in this trial between January 1, 2016 and December 31, 2016. A total of 74 patients enrolled into the study (mean age 51.86 $\pm$ 13.5). Of these 74 patients, 50 (67.5%) were males and 24 (32.5%) were females. History of hypertension was present in 33 (44.6%) patients and diabetes mellitus (DM) in 25(33.8%) patients; 22 (29.7%) patients were smokers (►**Table 1**).

Mean hemoglobin and packed cell volume (PCV) were 12.56 $\pm$ 2.8 g/dL and 37.98 $\pm$ 8.6%, respectively. Among the 74 HF patients, 24 (32.5%) had anemia. Mean total leucocyte count was 9,323 $\pm$ 3,376 cells/mcL whereas mean red blood cell (RBC) count and mean platelet count were 4.39 $\pm$ 0.9 million cells/mcL and 123230 $\pm$ 33760 cells/mcL, respectively. The erythrocyte sedimentation rate (ESR) in our patients ranged from 5 to 170 mm/h (mean 28.34 $\pm$ 38.7). Low ESR ($<$ 5 mm) was found in only seven (9.5%) patients. Baseline CBP parameters are shown in ►**Table 2**.

Total 8 (10.8%) patients died during hospitalization. Group 1 included patients who died during index hospitalization ($n = 8$) and group 2 comprised patients who were discharged in a stable condition after index hospitalization ($n = 66$). We compared the white blood cell (WBC) count and other components of the CBP to predict in-hospital mortality (►**Table 3**).

Regression analysis showed a significant association between low hemoglobin and low PCV with in-hospital mortality. Mean corpuscular hemoglobin (MCH) and mean corpuscular volume (MCV) rather than mean corpuscular hemoglobin concentration (MCHC) predicted worse outcomes in patients admitted to the hospital with ADHF. There was a significantly higher risk of in-hospital mortality with

Table 1 Demographic features of study population

Variable	No.
Age (y)	51.86 $\pm$ 13.5
Total	74
Females	24 (32.5%)
Hypertension	33 (44.6%)
DM	25(33.8%)
SM	22 (29.7%)

Abbreviations: DM, diabetes mellitus; SM, smoking.

Table 2 Baseline complete blood picture

Variable	Mean ± SD	Minimum	Maximum
Age (y)	51.86 ± 13.5	20	80
ESR (mm/h)	28.34 ± 38.7	5	170
Packed cell volume (%)	37.98 ± 8.6	20.7	56
Hemoglobin (g/dL)	12.56 ± 2.8	7.1	18.5
Red cell count (million cells/mcL)	4.39 ± 0.9	2.81	6.43
MCH (pg/cell)	28.91 ± 2.3	22.7	32
MCHC (g/dL)	33.08 ± 1.4	29	34.8
MCV (fL/cell)	86.39 ± 6.1	73.1	94.2
Total leucocytes (cells/mcL)	9,323 ± 3,376	4,600	16,300
Reticulocyte (%)	0.53 ± 0.1	0.5	1
Eosinophil (%)	3.82 ± 3.4	0	12
Monocyte (%)	5.35 ± 2.9	0	10
Lymphocyte (%)	17.88 ± 7.09	4	30
Neutrophil (%)	72.74 ± 8.6	59	90
Platelet count (cells/mcL)	123,230 ± 33,760	1.3	3.5

Abbreviations: ESR, erythrocyte sedimentation rate; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; SD, standard deviation.

leucocytosis ($p = 0.047$) with increasing eosinophil count ($p = 0.000$). On the other hand, in this trial there was no association between platelet count and neutrophil, monocyte, or lymphocyte count with clinical outcome (►**Table 4**).

Table 4 Regression analysis

Parameter	Chi-square value	*p* Value
Age (y)	0.72	0.395
Hemoglobin (g/dL)	3.97	0.046
Red cell count (million cells/mcL)	0.74	0.389
MCH (pg/cell)	12.26	0
MCHC (g/dL)	0.02	0.875
MCV (fL/cell)	27.84	0
Total leucocytes (cells/mcL)	3.95	0.047
Eosinophil (%)	10.91	0.001
Monocyte (%)	0.77	0.382
Lymphocyte (%)	1.3	0.254
Packed cell volume (cells/mcL)	3.81	0.051
Neutrophil (%)	0.19	0.66
Platelet count	0	0.98

Abbreviations: MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume.

Discussion

In our study, anemia was frequently observed, found in over almost one-third of HF patients. A wide range of anemia prevalence in ADHF has been reported, ranging from 7% to over 50%.[4–11] This wide range in prevalence can be attributed to multiple factors, including the use of multiple definitions of anemia. The World Health Organization (WHO) criteria

Table 3 Comparison of completer blood picture parameters in both groups

Variable	Mean ± SD		*p* Value
	Death	Survive	
Number	8	66	
Age (y)	48 ± 17.1	52.33 ± 13.12	0.509
Packed cell volume (%)	37.33 ± 8.9	43.4 ± 1.17	0.000
Hemoglobin (g/dL)	12.34 ± 2.93	14.4 ± 0.21	0.000
Red cell count (million cells/mcL)	4.35 ± 0.96	4.65 ± 0.08	0.016
MCH (pg/cell)	28.65 ± 2.28	30.95 ± 0.05	0.000
MCHC (g/dL)	33.07 ± 1.41	33.15 ± 0.37	0.715
MCV (fL/cell)	85.54 ± 5.95	93.35 ± 0.90	0.000
Total leucocytes (cells/mcL)	11,600 ± 2,780	9,047 ± 3,355	0.040
Eosinophil (%)	4.16 ± 3.48	1 ± 1.06	0.000
Monocyte (%)	4.5 ± 3.74	5.45 ± 2.84	0.507
Lymphocyte (%)	17.56 ± 7.45	20.5 ± 0.53	0.002
Neutrophil (%)	74 ± 2.13	72.59 ± 9.09	0.301
Platelet count (cells/mcL)	2.35 ± 0.16	2.34 ± 0.69	0.922

Abbreviations: MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; SD, standard deviation.

were used in the majority of studies. Anemia in HF is considered to develop due to a complex interaction of iron deficiency, kidney disease, and cytokine production, although micronutrient insufficiency and blood loss may contribute. Plasma levels of tumor necrosis factor-α (TNF-α), interleukin-1, and interleukin-6 are elevated in HF, promoting iron storage by the reticuloendothelial system, likely contributing to the anemia of chronic disease. We did not differentiate anemia on etiologic basis for predicting mortality. Peripheral smear is a useful, inexpensive, widely available tool for the management and prognosis of HF.

Based on our study results, a significant relationship was observed between baseline hemoglobin and PCV and cardiac mortality in patient with ADHF. Anemia is associated with an increased mortality in patients with CHF in numerous previous trials.[4–15] Several authors speculated about the mechanisms behind the increased mortality risk observed in anemic CHF patients.[10,16,17] Anemia may lead to an increased workload, resulting from an increased heart rate and stroke volume. In response to the increased workload, the heart undergoes "remodeling" marked by left ventricular hypertrophy and dilation. This eventually may lead to CHF with an increased mortality risk. One interesting finding in this study was MCHC that was not the outcome predictor though MCV and MCH were one of the outcome predictors. Both MCH and MCHC reflect the average hemoglobin content of RBCs in slightly different ways. However, the MCHC, as measured by a multichannel analyzer nowadays, typically results in slightly increased hematocrit. This may explain the fact that MCHC did not predict in-hospital mortality though MCH and MCV did. This has not been documented in previous studies.[10,12–17]

Higher baseline WBC count was associated with worse short-term outcome in few trials, but it is not outcome predictor in the present study.[18] It is not WBCs as a whole that initiates and perpetuates various maladaptive cascades in HF. It is specific subset of WBCs that have main role in pathophysiology of HF.

Neutrophilia has been shown to be an independent predictor of mortality in patients with ADHF in some of the trials.[19–21] Most of the above trials did not exclude infection and other comorbidities that may increase neutrophil count.

Elevated monocytes count is an independent predictor of in-hospital mortality in the present study. Ziegler-Heitbrock et al reported that monocyte count is as a mortality predictor in HF patients.[22] Monocytes have been implicated in mechanisms of progression of atherosclerotic damage in experimental models and in human pathologies.[23] It is reasonable to hypothesize that selective modulation of monocyte expansion is likely to be relevant for the progression of CHF. Monocyte may provoke damage by infiltrating the failing myocardium and by contributing to the systemic inflammatory processes.

Our result did not suggest that the mortality risk increases with lower lymphocyte count. Thompson et al suggested that total lymphocyte count showed the best correlation and was the best predictor of survival in HF patients.[24] Charach et al demonstrated that low total lymphocyte counts has an association with increased mortality.[25] The prognostic value of low total lymphocyte counts was examined in several studies with greater emphasis on increased risk for mortality in HF patients HF.[26–28] lymphocytopenia is associated with the renin-angiotensin-aldosterone system and the adrenergic nervous system. Elevated adrenaline, angiotensin and cortisol levels have a proapoptotic effect on lymphocytes. Furthermore, all these hormones elevate the neutrophil count and will cause relative lymphocytopenia. Reason for this contradictory finding may be differences in selection criteria from previous trials.

This study findings do not support the classic teaching that the ESR is characteristically low in patients with CHF as only 10% of subsets have low ESR.[29] Low ESR is not an independent predictor of mortality in our study. ESR < 5 mm/h is defined as low ESR in the present study. Patients who had low ESR have worse clinical outcomes according to Eisenberg et al.[31] Haber et al and Eisenberg speculated that during periods of acute decompensation or when the clinical syndrome of right-sided HF ensues in patients with long-standing left ventricular failure, right atrial pressure rises, and hepatic congestion develops.[30,31] This increase in intrahepatic sinusoidal pressure might impair the formation or accelerate the degradation of fibrinogen. As we excluded patients with elevated liver enzymes more than three times in the present study irrespective of etiology, we might have missed patients with severe hepatic congestion that was postulated to cause low ESR.

Higher eosinophil count was found to have association with in-hospital mortality. This is not documented in previous studies. We hypothesized that this finding can be attributed to higher incidence of eosinophilic endomyocarditis due to dobutamine allergy as patients with severe disease are more likely to receive higher doses of dobutamine.[32]

Limitations

The major limitation of the present study was the relatively small numbers of patients who participated. Our study population of patients with advanced CHF may not reflect the characteristics of CHF patients in the general population. N-terminal of pro-brain natriuretic peptide (NT–proBNP) that has a proven value in prognostication of HF patients must have been used to compare predictive value of hematologic parameters.

Conclusion

In patients with acute HF, certain components of complete blood count can predict in-hospital mortality. Accordingly, CBP might be a very useful marker that can be utilized in risk-stratifying patients with ADHF. Moreover, it is inexpensive and easy to perform. Nonetheless, further larger-scale and multicenter studies were needed to confirm these findings.

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