Correlation of Anemia and Clinical Outcomes in Heart Failure at Rajavithi Hospital

Surapun Pongsuthana MD*,
Vithitta Tanghongse MD*

* Division of Cardiology, Department of Medicine, College of Medicine, Rangsit University, Rajavithi Hospital, Bangkok, Thailand

Background: Anemia is one of the precipitating factors leading to congestive heart failure. Although much data indicate that anemia is associated with worsening clinical outcomes in heart failure patients, only few studies have been conducted on the subjects in Thailand. Hence, the researchers decided to study about this issue.

Objective: The present study aimed to evaluate whether anemia could have adverse effects on mortality and morbidity rates in patients with a diagnosis of heart failure.

Material and Method: A retrospective cross-sectional study was performed by collecting data from medical records of patients who were admitted in Rajavithi Hospital due to congestive heart failure from January 1, 2011 to December 31, 2012. Those data showed a total 486 patients with congestive heart failure treated during the period. Of the 486 patients, 18 were excluded on the basis of selection criteria, a total of 468. These selected patients were divided in two groups, one group of congestive heart failure patients with anemia (n = 221) and another group of congestive heart failure patients without anemia (n = 247).

Results: The study showed that the mortality rate in patients with the anemia group was 8.6%, whereas among nonanemic patients no deaths were reported (0%) [p-value <0.0001]. Patients with anemia had a higher incidence of no restoration of spontaneous circulation after Cardiopulmonary resuscitation (3.62%) than nonanemic patients (0%) [p-value = 0.002]. No difference was observed in the use of inotropic drugs between the two groups [p-value = 0.078]. The patients with anemia (14.75$\pm$20.31 days) had a longer duration of hospital admission than nonanemic patients (7.12$\pm$8.57 days) [p-value <0.0001].

Conclusion: Anemia was associated with increased morbidity and mortality rate among heart failure patients. The mortality rate tended to increases in correlation with the severity of the anemia. Moreover, blood transfusion after congestive heart failure occurrence may not reduce the mortality rate.

Keywords: Anemia, Congestive heart failure, Morbidity, Mortality

Congestive heart failure is a major problem in public health; over 20 million patients around the world are affected and the incidence increases with age[1]. Several factors precipitate heart failure including anemia. Anemia is associated with worsening symptoms, impairment in functional capacity and increasing mortality rate among heart failure patients. However, previous studies have difficulty correlating anemia with mortality rate[2-7]. Only a few studies have been conducted on subjects in Thailand. In this research the authors studied anemia correlated to clinical outcomes (both morbidity and mortality) among heart failure patients.

Material and Method

A retrospective review was performed on the inpatients medical record forms of patients admitted with the diagnosis of heart failure using ICD-10 code I50.0[8]. Initial blood test at the emergency room was collected for hemoglobin level (Hb) and other baseline characteristics for clinical correlation. The study was approved by the ethics committee of Rajavithi Hospital.

Study populations

The present study reviewed the inpatient medical record forms of patients admitted with the diagnosis of heart failure from January 2011 to December 2012. Heart failure patients of either sex were

Correspondence to:
Pongsuthana S, Division of Cardiology, Department of Medicine, Rajavithi Hospital, 2 Phayathai Road, Ratchathewi Bangkok 10400, Thailand.
Phone: 0-2354-8108 ext. 5504
E-mail: surpng@yahoo.com

eligible for inclusion in the present study if they were at least 40 years of age.

Patients were excluded if the diagnosis was unclear or diagnosis of heart failure was uncertain.

Study protocol

Baseline characteristics such as age, sex, body weight, height, underlying disease, medication, left ventricular ejection fractions (LVEF), myocardial infarction[9] and Hb level were recorded.

The use of inotropic drugs[10], endotracheal intubation[11], cardiopulmonary resuscitation (CPR) with/without restoration of spontaneous circulation (ROSC)[12] and mortality rate were determined.

Anemia was defined by the World Health Organization (WHO) criteria by hemoglobin level below 12 gm/dl in females and hemoglobin below 13 gm/dl in males[13].

Outcome

The primary end point was the relationship of anemia on the mortality rate in patients with heart failure. The secondary end points evaluated the relationship of anemia on morbidity such as need for inotropic drugs or duration of admission.

Statistical analysis

The estimated sample size was based on previous studies[6]. It was estimated that mortality rate in patients with anemia would be 27.8% compared to 15.7% in those without anemia. Using a 2-sided type 1 error of 5%, 85% power, a sample of 207 patients per group was required.

Baseline characteristics were described as number (percentage), median (range) and mean $\pm$ standard deviation (SD). Chi-square test/Fisher exact test was employed to test the difference in qualitative variable (i.e., mortality and morbidity) between patients with and without anemia, whereas 2-sample t-test was used for quantitative variabes and Mann Whitney U test was used for non-normal distributions with a p-value <0.05 using SPSS program, version 17.

Results

From January 1, 2011 to December 31, 2012 a total 486 patients were admitted with heart failure. Eighteen patients were excluded because of age below than 40 years old. In all, 468 patients were enrolled in the present study.

The baseline characteristics (Table 1) show two groups. A total of 221 patients comprised the anemic patient group and 247 comprised the nonanemic patient group. The mean age was 67.06$\pm$12.43 years and the patients were mainly female. Underlying diseases were mainly diabetes mellitus, hypertension and dyslipidemia. Patients mainly had preserved LVEF (67.09%). The anemia group had a significantly higher prevalence of diabetes mellitus, chronic kidney disease than the nonanemic patient group. As to the medication prescribed in the present study, use of angiotensin-converting enzymes inhibitors (ACEIs) was significantly higher in the nonanemic patient group than the anemic patient group and use of calcium channel blockers (CCBs) was lower in the nonanemic patient group than the anemic patient group as shown in Table 1. In the anemic patients group, significantly more patients were intubated than in the nonanemic patient group (18.10% and 4.45% respectively, p-value <0.0001).

The mortality rate in the anemic patient group was higher (19 deaths versus no deaths) than in the nonanemic patient group (8.60% and 0% respectively, p-value <0.0001) as shown in Table 3.

The average duration of admission was 10.72$\pm$15.73 days. The average length of hospitalization was significantly higher in the anemic patient group than the nonanemic patient group as shown in Table 3. Two patients in the anemic group had prolong hospitalization which caused standard deviation to vary excessively but after calculate with Mann Whitney U test was shown different significant between two groups. The patients who were intubated had similar lengths of hospitalization (23.22$\pm$38.67 and 23.10$\pm$36.36 days respectively, p-value = 0.875). No difference was observed in the rate of inotropic drug use between the two groups, but in the subgroup, dopamine, levophed and adrenaline were more frequently used in the anemic patient group and significantly higher than in the nonanemic patient group. CPR was performed in only one patient in the nonanemic patient group with successful ROSC but in the anemic patient group 19 deaths were recorded and only 10 patients received CPR and 2 patients had ROSC as shown in Table 3.

The association between the level of hemoglobin and mortality rate is shown in Table 4. Patients with lower hemoglobin levels had nonsignificant higher mortality rate. In patients with marked anemia (Hb <10 gm/dl) the mortality rate was 10% and patients with mild anemia had a mortality rate of 7.63% (p-value = 0.538). In the nonanemic patient group, 33.48% received blood transfusion, but no difference was found in the mortality rate between

Table 1. Baseline characteristics divided in anemic and nonanemic patient groups

	Number (%)			p-value
	Total (n = 468)	Anemia (n = 468)	No anemia (n = 247)	
Age (years): mean $\pm$ SD	67.06$\pm$12.43	68.98$\pm$12.37	65.34$\pm$12.27	0.100
Female	273 (58.33)	136 (61.54)	137 (55.47)	0.064
Weight (kg) mean$\pm$SD	63.33$\pm$7.12	62.18$\pm$7.19	64.36$\pm$6.91	0.206
Height (cm) mean$\pm$SD	162.51$\pm$6.41	162.01$\pm$6.22	162.95$\pm$6.56	0.207
Underlying disease				
Diabetes mellitus	225 (48.08)	130 (58.82)	95 (38.46)	<0.001
Hypertension	395 (84.40)	188 (85.07)	207 (83.81)	0.707
Dyslipidemia	355 (75.85)	171 (77.38)	184 (74.49)	0.467
Atrial fibrillation	83 (17.74)	36 (16.29)	47 (19.03)	0.439
Valvular heart disease	51 (10.90)	24 (10.86)	27 (10.93)	0.980
Coronary artery disease	116 (24.79)	53 (23.98)	63 (25.51)	0.703
Chronic kidney disease	81 (17.31)	61 (27.60)	20 (8.10)	<0.0001
GFR <15 ml/min/1.73 m^2	12 (2.56)	11 (4.98)	1 (0.40)	
GFR 15-59 ml/min/1.73 m^2	69 (14.74)	50 (22.62)	19 (7.69)	
COPD	12 (2.56)	6 (2.71)	6 (2.43)	0.845
Medication				
ACEIs	214 (45.73)	79 (35.75)	135 (54.66)	<0.001
Beta-blockers	124 (24.36)	57 (25.79)	67 (27.13)	0.744
Calcium channel blockers	161 (32.97)	90 (40.72)	71 (28.74)	0.006
Diuretics	324 (47.86)	153 (69.23)	171 (69.23)	1.000
Digitalis	51 (10.90)	20 (9.05)	31 (12.55)	0.225
Statin	355 (75.85)	165 (74.66)	190 (76.92)	0.586
Aspirin	345 (73.72)	162 (73.30)	183 (74.10)	0.847
Preserve LVEF	314 (67.09)	152 (68.78)	162 (65.59)	0.463
Myocardial infarction	57 (12.18)	33 (14.93)	24 (9.72)	0.085
On endotracheal tube	51 (10.97)	40 (18.10)	11 (4.45)	<0.0001

GFR = glomerular filtration rate; COPD = chronic obstructive pulmonary disease; ACEIs = angiotensin-converting enzyme inhibitors; LVEF = left ventricular ejection fraction

Table 2. Hemoglobin level in anemic and nonanemic patients

Hemoglobin (gm/dl)[#]	Number (%)	
	Anemia (n = 221)	No anemia (n = 247)
Normal	0	247 (100)
Mild	131 (59.3)	0
Low	90 (40.7)	0

[#] Normal ($\geq$13 and $\geq$12 for males and females respectively), Mild (10-12.9 and 10-11.9 for males and females respectively), Low (<10 for both males and females)

patients that received or did not receive blood transfusions (10.81% and 7.48% respectively, p-value = 0.405).

Discussion

    Previous studies have difficulty correlating anemia with mortality rate among heart failure patients.

Table 3. Morbidity and mortality divided in anemic and nonanemic patient groups

	Number (%)			*p*-value
	Total (n = 468)	Anemia (n = 221)	No anemia (n = 247)	
Length of hospitalization (days) mean ± SD	10.72±15.73	14.75±20.31	7.12±8.57	<0.0001#
Length of hospitalization (days) median (min, max)	7 (1, 213)	10 (1, 213)	6 (1, 126)	
Blood transfusion	74 (15.81)	74 (33.48)	0 (0)	<0.0001
On inotropic drug	114 (24.36)	62 (28.05)	52 (21.05)	0.078
Dobutamine	97 (20.73)	48 (21.72)	49 (19.84)	0.616
Dopamine	22 (4.70)	16 (7.24)	6 (2.43)	0.014
Levophed	11 (2.35)	10 (4.52)	1 (0.40)	0.003
Adrenaline	10 (2.14)	9 (4.07)	1 (0.40)	0.008
No inotrope	354 (75.64)	159 (71.95)	195 (78.95)	0.078
CPR				
ROSC	3 (0.64)	2 (0.90)	1 (0.40)	0.604
No ROSC	8 (1.71)	8 (3.62)	0 (0)	0.002
Dead	19 (4.06)	19 (8.60)	0 (0)	<0.0001

CPR = Cardiopulmonary resuscitation, ROSC = Restoration of spontaneous circulation
# calculated with Mann-Whitney U test

Horwich et al[2] showed that anemia deteriorated heart failure symptoms and increased mortality and duration of hospital admission. Anand et al[3] showed that anemia will increase mortality and duration of hospital admission. Diastolic heart failure mortality rate was correlated with anemia as well[4]. Not all studies have supported the association of anemia and adverse outcomes in heart failure. A study by Kalra et al[7] found a significant incidence of anemia in this cohort (18%) but no association between baseline Hb and survival after adjustment for other variables. Ezekowitz et al[5] did not find that anemia to be associated with mortality rate. Mazaffarian et al[6] also showed that anemia did not increase mortality but severe anemia was correlated with higher mortality rates. The present study showed a correlation of anemia with higher mortality rate among heart failure patients similar to previous studies. However, the baseline characteristics of the two groups were markedly different. In the anemic patient group, more patients had diabetes mellitus and chronic kidney disease, which increased the risk for cardiovascular death and received less ACEIs drug to treat heart failure than the nonanemic patient group. The mortality rate shows a nonsignificant increased with the severity of anemia which is similar to a previous study[6].

The anemic patient group had a significantly longer length of hospital admission than the nonanemic patient group similar to other studies[2,3]. In the anemic patient group two patients were admitted for 213 and 131 days which may explain the longer hospital admission as compared with the nonanemic patient group. In the anemic patient group, more patients were intubated. The reason for this may be from the greater severity of underlying diseases or myocardial dysfunction in the anemic patient group. However, anemia did not affect the duration of hospital admission among patients who underwent endotracheal intubation. The intubated patients were a sicker group of patients and anemia may have had less of an effect on this group of patients.

No significant difference in inotropic drug use was found between the two groups. The majority of patients received dobutamine but dopamine, levophed and adrenaline were used more commonly in the anemic patient group. It may reflect that the anemic patient group had more hypotension that needed vasoconstrictor drugs to raise blood pressure. Patients with normotension/hypertension used only dobutamine or had no need for inotropic support. However, vasoconstrictor drugs were used in very few patients, which may explain why no difference was observed between the two groups.

Garty et al[14] studied acute decompensated heart failure patients, of whom 7.1% received blood

Table 4. Cause of death by hemoglobin level and blood transfusion in 221 anemia subjects

	n	Death	Cause of death							
			CHF	HAP	VAP	Stroke	MI	Secretion obstruction	Septicshock	Unknown
Hb level (p = 0.538)										
Mild	131	10 (7.6%)	-	2	2	-	2	1	2	1
Low	90	9 (10.0%)	2	1	1	1	3	-	1	-
Blood transfusion (p = 0.405)										
Yes	74	8 (10.8%)	1	2	2	1	1	-	1	-
No	147	11 (7.5%)	1	1	1	-	4	1	2	1

Hb = hemoglobin; CHF = congestive heart failure; HAP = hospital-acquired pneumonia; VAP = ventilator-associated pneumonia; MI = myocardial infarction

transfusions. In the hospital, 30-day mortality rates were higher among blood transfusion patients, but short term mortality tended to lower with blood transfusion. In the present study, only some patients in the anemic patient group received blood transfusions. Blood transfusions had no significant effect on the mortality rate in contrast with a previous study. Blood transfusions are supportive treatment only and may have had no effect on the underlying diseases.

Limitation

The present study was a retrospective study reviewing medical records resulting in incomplete data in some cases. Some patients with heart failure at admission were not included in the present study because of misdiagnosis. Selection bias in the present study was likely. The mortality rate among heart failure patients is affected by many factors such as underlying disease and medication received in addition to anemia. The difference in baseline characteristics between the anemic and nonanemic patient groups (both underlying disease and medication received) probably affected the mortality rate. The correlation between anemia and mortality among heart failure patients needs further investigation for confirmation.

Conclusion

Anemia was associated with increased mortality rate among heart failure patients. The mortality rate tend to increases in line with the severity of the anemia. Moreover, blood transfusion after congestive heart failure occurrence may not reduce mortality rates. The length of hospital admission was increased in the anemic patient group, but no difference was found in inotropic drug use between the two groups.

Potential conflict of interest

None.

References

1. Mann DL. Heart failure and cor pulmonale. In : Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al, editors. Harrison's principles of internal medicine. 17th ed. New York: McGraw-Hill; 2008: 1443-55.
2. Horwich TB, Fonarow GC, Hamilton MA, MacLellan WR, Borenstein J. Anemia is associated with worse symptoms, greater impairment in functional capacity and a significant increase in mortality in patients with advanced heart failure. J Am Coll Cardiol 2002; 39: 1780-6.

3. Anand I, McMurray JJ, Whitmore J, Warren M, Pham A, McCamish MA, et al. Anemia and its relationship to clinical outcome in heart failure. Circulation 2004; 110: 149-54.
4. Tehrani F, Phan A, Morrissey R, Chien C, Rafique A, Schwarz ER. The prognostic value of anemia in patients with diastolic heart failure. Tex Heart Inst J 2009; 36: 220-5.
5. Ezekowitz JA, McAlister FA, Armstrong PW. Anemia is common in heart failure and is associated with poor outcomes: insights from a cohort of 12 065 patients with new-onset heart failure. Circulation 2003; 107: 223-5.
6. Mozaffarian D, Nye R, Levy WC. Anemia predicts mortality in severe heart failure: the prospective randomized amlodipine survival evaluation (PRAISE). J Am Coll Cardiol 2003; 41: 1933-9.
7. Kalra PR, Collier T, Cowie MR, Fox KF, Wood DA, Poole-Wilson PA, et al. Haemoglobin concentration and prognosis in new cases of heart failure. Lancet 2003; 362: 211-2.
8. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012; 33: 1787-847.
9. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. Eur Heart J 2012; 33: 2551-67.
10. Overgaard CB, Dzavik V. Inotropes and vasopressors: review of physiology and clinical use in cardiovascular disease. Circulation 2008; 118: 1047-56.
11. Endotracheal intubation. Medical dictionary [Internet]. 2014 [cited 2014 Jun 26]. Available from: http://www.medical-dictionary.thefreedictionary.com/endotracheal+intubation
12. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation. Circulation 2004; 110: 3385-97.
13. World Health Organization. Hemoglobin concentrations for the diagnosis of anemia and assessment of severity. VMNIS: Vitamin and mineral nutrition information system [Internet]. Geneva: WHO; 2011 [cited 2014 Jun 26]. Available from: http://www.who.int/vmnis/indicators/hemoglobin.pdf
14. Garty M, Cohen E, Zuchenko A, Behar S, Boyko V, Iakobishvili Z, et al. Blood transfusion for acute decompensated heart failure—friend or foe? Am Heart J 2009; 158: 653-8.

ความสัมพันธ์ของภาวะโลหิตจางต่อผลทางคลินิกของผู้ป่วยที่มาด้วยภาวะหัวใจวายในโรงพยาบาลราชวิถี

สุรพันธ์ พงศ์สุธนะ, วิทิตตา ตั้งหงส์

ภูมิหลัง: ภาวะโลหิตจางเป็นปัจจัยหนึ่งที่กระตุ้นทำให้ผู้ป่วยเกิดภาวะหัวใจวาย แม้ว่าในปัจจุบันจะมีข้อมูลส่วนใหญ่ ที่บ่งบอกว่าภาวะโลหิตจางจะก่อให้เกิด ผลลัพธ์ที่เลวลงในผู้ป่วยที่มีภาวะหัวใจวาย แต่ก็ยังไม่มีการศึกษามากนักในประเทศไทย ดังนั้นผู้นิพนธ์จึงเลือกศึกษาถึงความสัมพันธ์และผลลัพธ์ของภาวะ โลหิตจางว่าจะมีผลอย่างไรต่อผู้ป่วยที่มีภาวะหัวใจวาย

วัตถุประสงค์: เพื่อศึกษาว่าการมีภาวะโลหิตจางมีผลต่อการเพิ่มอัตราการเสียชีวิตและมีผลต่อการเพิ่มอัตรา การเกิดทุพพลภาพหรือไม่ในผู้ป่วยภาวะหัวใจวาย ในโรงพยาบาลราชวิถี

วัสดุและวิธีการ: เป็น Retrospective cross-sectional study เก็บข้อมูลจากเวชระเบียนของผู้ป่วยที่รับการรักษาในโรงพยาบาลราชวิถีตั้งแต่วันที่ 1 มกราคม พ.ศ. 2554 ถึง 31 ธันวาคม พ.ศ. 2555 พบว่ามีจำนวนภาวะหัวใจวาย ที่เข้ารับการรักษาทั้งหมด 486 ราย และมีผู้ป่วยที่ไม่เข้าเกณฑ์ การคัดเลือกอยู่ 18 ราย เหลือจำนวนผู้ป่วยที่ใช้ในการศึกษา 468 ราย แบ่งผู้ป่วยเป็น 2 กลุ่ม คือ กลุ่มที่มีภาวะหัวใจวายและมีภาวะโลหิตจาง (n = 221) และกลุ่มที่มีภาวะหัวใจวาย แต่ไม่มีภาวะโลหิตจาง (n = 247)

ผลการศึกษา: พบว่ามีการเสียชีวิตในกลุ่มผู้ป่วยที่มีภาวะโลหิตจาง (8.6%) ในขณะที่กลุ่มผู้ป่วยที่ไม่มีภาวะโลหิตจางไม่มีการเสียชีวิตเลย (0%) [p-value <0.0001], ส่วนของการมีภาวะหัวใจหยุดเต้นพบว่ากลุ่มผู้ป่วยที่มีภาวะโลหิตจาง มีโอกาสเกิดภาวะหัวใจหยุดเต้นและไม่สามารถช่วยฟื้นคืนสัญญาณ ชีพได้สำเร็จ (3.62%) มากกว่ากลุ่มผู้ป่วยที่ไม่มีภาวะโลหิตจาง (0%) [p-value = 0.002], ส่วนของการให้ยากระตุ้นหัวใจ พบว่าทั้ง 2 กลุ่ม ไม่ได้มี อัตราการใช้ยาที่แตกต่างกัน [p-value = 0.078], ส่วนของจำนวนวันที่ต้องนอนในโรงพยาบาลพบว่ากลุ่มผู้ป่วยที่มีภาวะโลหิตจาง (14.75±20.31 วัน) มีการนอนโรงพยาบาลนานกว่ากลุ่มผู้ป่วยที่ไม่มีภาวะโลหิตจาง (7.12±8.57 วัน) [p-value <0.0001]

สรุป: ภาวะโลหิตจางมีผลต่อการเพิ่มอัตราการเสียชีวิต และเพิ่มอัตราการเกิดทุพพลภาพในผู้ป่วยที่มีภาวะหัวใจวาย และอัตราการเสียชีวิตมีแนวโน้ม ที่จะมากขึ้นตามความรุนแรงของระดับโลหิตจาง นอกจากนี้การเติมเลือดให้เพิ่มขึ้นหลังการเกิดภาวะหัวใจวายไปแล้วอาจไม่ได้ช่วยลดอัตรา การเสียชีวิตลงได้