

ORIGINAL PAPER

THE LINK BETWEEN CHRONIC HEART FAILURE AND ANEMIA: INSIGHTS FROM CLINICAL PRACTICE

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SUMMARY

Background: Anemia is a frequent comorbidity in patients with chronic heart failure. The objective of the study was to evaluate the frequency of anemia and the clinical and paraclinical characteristics of patients with decompensated chronic heart failure admitted to the Internal Medicine Clinic of the Clinical Emergency Hospital of Bucharest, Romania, over a period of 6 months.

Methods: Between December 1st, 2014 and May 1st, 2015, the total number of admissions with the diagnosis of decompensated chronic heart failure was 309. From these, 78 patients had anemia (25.24%) and represented our group of study. We retrospectively analyzed the data from the hospital medical records database.

Results: The majority of patients had mild anemia (64%). Only one patient had severe anemia (2%), all the others having moderate anemia (34%). 64% of patients had normocytic hypochromic anemia, 21% had microcytic hypochromic anemia, 8% normocytic normochromic anemia and 7% had other forms of anemia. The distribution of chronic heart failure by NYHA class at admission was: 47% of patients had NYHA class IV, 37% had NYHA class III and only 16% were in NYHA class II.

Conclusions: In our study, 25% of the chronic heart failure patients had anemia, most often associated with chronic kidney disease. In the majority of the cases, patients with chronic heart failure presented anemia typical for chronic diseases (normocytic anemia), much rarely microcytic anemia. Our data did not prove a statistical correlation between the anemia severity and age of the patients or severity of chronic heart failure, evaluated by NYHA class.

Key words: anemia, chronic heart failure, chronic kidney disease

RÉSUMÉ

Le lien entre l'insuffisance cardiaque chronique et l'anémie: introspection dans la pratique clinique

Introduction: L'anémie est une comorbidité fréquente chez les patients atteints d'insuffisance cardiaque chronique. L'objectif de l'étude était d'évaluer la fréquence de l'anémie et les caractéristiques cliniques et paracliniques des patients avec insuffisance cardiaque chronique décompensée admis à la Clinique de médecine interne de l'Hôpital Clinique d'Urgence de Bucarest, Roumanie, sur une période de 6 mois.

Méthodes: Entre le 1er Décembre 2014 et le 1er Mai 2015, le nombre total d'admissions avec le diagnostic de d'insuffisance cardiaque chronique décompensée était 309. De ceux-ci, 78 patients avaient une anémie (25,24%) et ont représenté notre groupe d'étude. Nous avons analysé rétrospectivement les données de la base de données des dossiers médicaux de l'hôpital.

Résultats: La majorité des patients ont eu une anémie légère (64%). Un seul patient avait une anémie sévère (2%), tous les autres ayant une anémie modérée (34%). 64% des patients avaient une anémie hypochrome normocytaire, 21% souffraient d'anémie hypochrome microcytaire, 8% une anémie normochrome normocytaire et 7% avaient d'autres formes d'anémie. La distribution de l'insuffisance cardiaque chronique par classe NYHA à l'admission était: 47% des patients avaient classe NYHA IV, 37% avait de la classe NYHA III et seulement 16% étaient en classe NYHA II.

Conclusions: Dans notre étude, 25% des patients souffrant d'insuffisance cardiaque chronique souffraient d'anémie, le plus souvent associée à une maladie rénale chronique. Dans la majorité des cas, les patients souffrant d'insuffisance cardiaque chronique ont présenté une anémie typique pour les maladies chroniques (anémie normocytaire), anémie microcytaire bien rare. Nos données ne prouvent pas une corrélation statistique entre la gravité de l'anémie et l'âge des patients ou la sévérité de l'insuffisance cardiaque chronique, évaluée par classe NYHA.
Mots-clé: anémie, insuffisance cardiaque, maladie rénale chronique

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BACKGROUND

Anemia is a frequent comorbidity in patients with chronic heart failure (CHF). Symptoms of anemia, such as dyspnea and fatigue, may be difficult to distinguish from symptoms of heart failure. In patients with heart failure, symptoms of anemia may appear at lower levels of hemoglobin as compared with patients without heart failure; in patients with heart failure, oxygen delivery is impaired due to low cardiac output. The prevalence of anemia in patients with chronic heart failure with low ejection fraction varies between 4-61% (1-4). The prevalence of anemia is increased in patients with chronic heart failure with low ejection fraction and comorbid chronic kidney disease, more older and more symptomatic (30-61%) when compared with less symptomatic patients (4-23%) (1-4). Regarding patients with chronic heart failure and preserved ejection fraction, there are less epidemiologic studies, but the published reports indicate that anemia has also a high prevalence in this population (5-7). The recognition of anemia as a biomarker of chronic heart failure severity generated a high level of expectations regarding the possible beneficial effect of the treatment of anemia in patients with chronic heart failure.

AIM OF THE STUDY

The objective of the study was to evaluate the frequency of anemia and the clinical and paraclinical characteristics of patients with decompensated chronic heart failure admitted to the Internal Medicine Clinic of the Clinical Emergency Hospital of Bucharest, Romania, over a period of 6 months.

METHODS

Between December 1st, 2014 and May 1st, 2015, the total number of admissions with the diagnosis of decompensated chronic heart failure was 309. From these, 78 patients had anemia (25.24%) and represented our group of study. We retrospectively analyzed the data from the hospital medical records database (Hippocrate).

The distribution by sex in the group of study

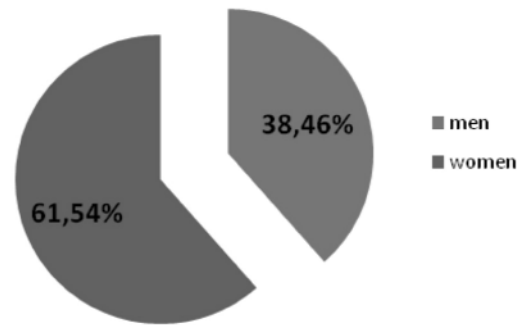


Figure 1 - The distribution by sex in the group of study

Degree of anemia in the group of study

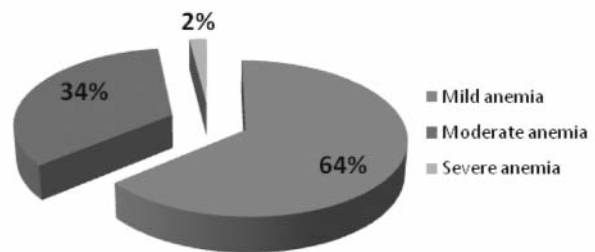


Figure 2 - Distribution of degree of anemia in the group of study

RESULTS

The distribution by sex in the group of study was: 48 women (61.54%) and 30 men (38.46%) (fig. 1). Mean age of the patients from the group of study was 76.42 +/- 10 years. We did not observe a statistical correlation between anemia severity and age.

The majority of patients had mild anemia (64%). Only one patient had severe anemia (2%), all the others having moderate anemia (34%) (fig. 2). 64% of patients had normocytic hypochromic anemia, 21% had microcytic hypochromic anemia, 8% normocytic normochromic anemia and 7% had other forms of anemia (fig. 3).

The distribution of chronic heart failure by NYHA

Types of anemia in the group of study

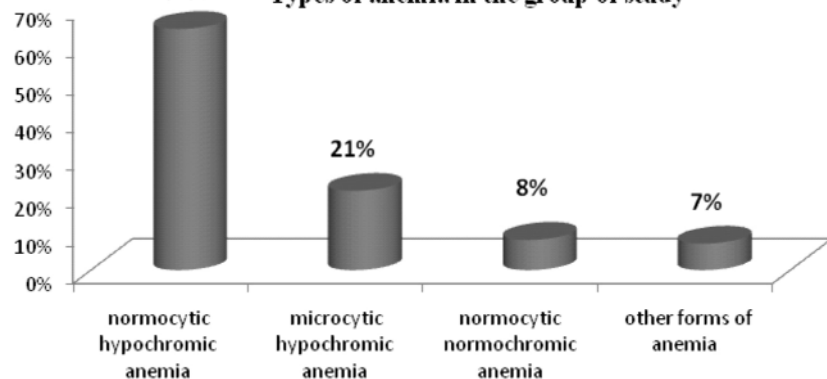


Figure 3 - Distribution of different types of anemia in the group of study

Figure 4 - The distribution of heart failure by NYHA class in the group study

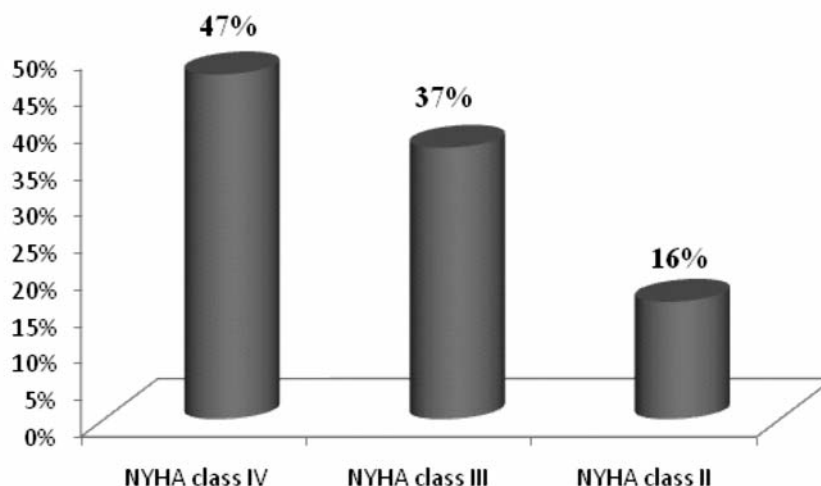
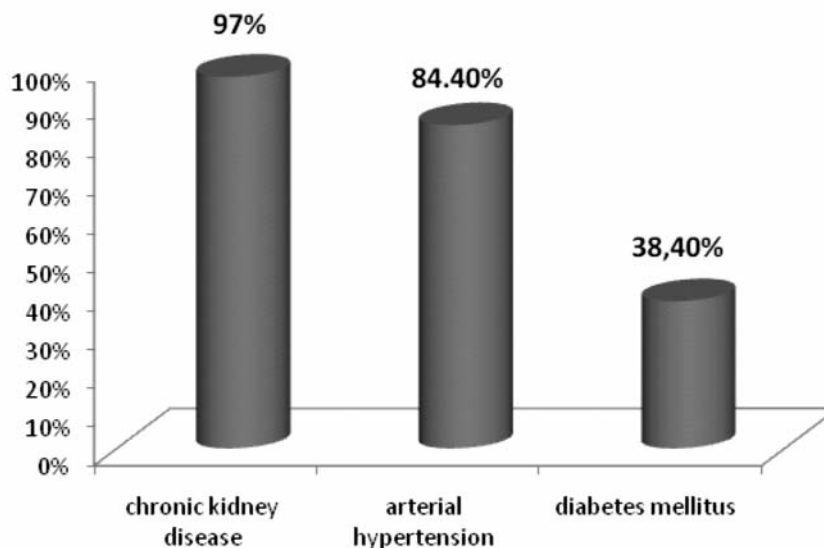


Figure 5 - The main comorbidities of patients with chronic heart failure and anemia



class at admission was: 47% of patients had NYHA class IV, 37% had NYHA class III and only 16% were in NYHA class II (fig. 4). We did not notice a significant statistical correlation between the severity of anemia and NYHA class. The most frequent comorbidities in the group of study were chronic kidney disease (97%) – the majority of the patients having chronic kidney disease class 3, arterial hypertension (84.6%) and diabetes mellitus (38.4%) (fig. 5).

DISCUSSION

Anemia appears when there is an imbalance between new erythrocyte production and the rate of removal of aged erythrocytes. The key component of the homeostatic system who regulates the red blood cell mass and tissue oxygen delivery is erythropoietin. Any abnormality that reduces renal secretion of erythropoietin or the bone marrow response to erythropoietin may result in anemia. The majority of patients with chronic heart failure have normocytic anemia, classified as anemia of chronic disease.

Chronic kidney disease is a frequent comorbidity in patients with CHF and also a strong independent predictor of the risk of anemia in several studies. In patients with moderate to severe chronic kidney disease (glomerular filtration rate, GFR < 60 ml/min/1.73 m²) without heart failure, erythropoietin production is diminished and hemoglobin decreases in parallel with GFR reduction (8). In patients with CHF, the estimated prevalence of mild to moderate chronic kidney disease is between 20-40% (1,9-11).

The etiology of anemia in patients with chronic heart failure is not well known. One study of patients with new heart failure and anemia found that the most common causes of anemia (iron, B12 or folate deficiency) were rare, in most cases no exact etiology could be found (12). One possible explanation may be the dysfunction of the bone marrow induced by low cardiac output. Other possible factors are: down regulation of erythropoietin by angiotensin converting enzyme inhibitors, cytokine activation, chronic bleeding secondary to anticoagulant or antiplatelet treatment, dilutional anemia. Some studies have found that iron deficiency is a major cause of anemia in nearly 80% of the

cases (13). Anemia in chronic heart failure patients must be considered multifactorial. In patients with anemia and chronic heart failure, a careful evaluation of the possible causes of anemia should be done. These initial evaluation should include complete blood count with peripheral blood smear, iron studies (serum iron, ferritin, transferrin, iron saturation), serum creatinine, creatinine clearance, erythrocyte sedimentation rate and C-reactive protein, seric vitamin B12.

In patients with heart failure, anemia is a risk factor for mortality, severity and hospital admissions (1,15,16). Lower levels of hemoglobin are associated with a poorer hemodynamic function, increases in creatinine and blood urea nitrogen, decrease of body mass index and a worse functional class in studies (1,16,17). One review suggested that anemia could be a marker of advanced disease, since it is associated with a worse functional NYHA class; correction of anemia improves the symptoms but not the mortality rate (18). Very interesting, on the other hand, hemoglobin level by itself is an independent predictive factor for mortality in patients with chronic heart failure, in both anemic or polycytemic patients (19). The presence of anemia can accelerate the progression of chronic kidney disease in patients with chronic heart failure and may be a risk factor and predictor for the development of heart failure in patients with end-stage chronic kidney disease (20). On the other hand, the renal function may be an indirect marker of cardiac function, together with ejection fraction and NYHA class (21,22). The results of our study did not prove a statistical correlation between the anemia severity and age of the patients or severity of chronic heart failure, evaluated by NYHA class. However, the small number of patients included in our study may be an important limitation.

Patients with chronic heart failure and anemia tend to be older, in NYHA functional class III-IV, with many drug treatments and more comorbidities, such as diabetes mellitus, chronic kidney disease, arterial hypertension, but these patients are not usually included in drug trials (1,16). The independent prognostic value of anemia in patients with chronic heart failure was described in a review of 1061 patients with heart failure functional class NYHA III or IV, with systolic dysfunction and left ventricular ejection fraction < 40% (23). This review noted that lower values of hemoglobin are associated with higher blood urea nitrogen and serum creatinine, together with lower seric albumin. Also, patients with lower hemoglobin values (< 13.6 g/dL) had a significantly greater frequency of NYHA class IV and a greater mortality (relative risk 1.13 for each 1 g/dL fall in hemoglobin concentration) (23). A much larger study, on over 50,000 patients ≥65 years of age hospitalized for heart failure, found that anemia was not an independent predictor of outcomes²⁴; the authors did not find any difference in mortality rates at one year between patients with a normal hematocrit (40-44%) and those with severe anemia (hematocrit ≤ 24 percent).

Treatment should be initiated according to the etiology of anemia. In heart failure patients with iron deficiency ane-

mia, intravenous iron may offer symptomatic amelioration. However, the long term effects of intravenous iron are not known. Treatment with erythropoietic agents in patients with heart failure is not beneficial; furthermore, they are associated with increased risk of thromboembolic events. There are no sufficient data about the use of blood transfusions in anemic patients with chronic heart failure. In clinical practice, we can use red blood cell transfusion strategy in asymptomatic patients with heart failure and a hemoglobin level between 7-8 g/dl, although a small proportion of patients may need transfusions at higher levels of hemoglobin, if the symptoms are severe and related to anemia.

CONCLUSIONS

Anemia is a frequent comorbidity in patients with chronic heart failure. In our study, 25% of the chronic heart failure patients had anemia, most often associated with chronic kidney disease. In the majority of the cases (72%), patients with chronic heart failure presented anemia typical for chronic diseases (normocytic anemia), much rare microcytic anemia. Our data did not prove a statistical correlation between the anemia severity and age of the patients or severity of chronic heart failure, evaluated by NYHA class. In patients with heart failure, it is not certain if anemia is an independent predictor of bad prognosis or a marker of more advanced disease.

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REFERENCES

1. 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;107:223-225.
2. Cromie N, Lee C, Struthers AD. Anaemia in chronic heart failure: what is its frequency in the UK and its underlying causes? *Heart*. 2002;87:377-378.
3. Tanner H, Moschovitis G, Kuster GM, Hullin R, Pfiiffner D, Hess OM, Mohacsi P. The prevalence of anemia in chronic heart failure. *Int J Cardiol*. 2002;86:115-121.
4. Wexler D, Silverberg D, Sheps D, Blum M, Keren G, Iaina A, Schwartz D. Prevalence of anemia in patients admitted to hospital with a primary diagnosis of congestive heart failure. *Int J Cardiol*. 2004;96:79-87.
5. Berry C, Hogg K, Norrie J, Stevenson K, Brett M, McMurray J. Heart failure with preserved left ventricular systolic function: a hospital cohort study. *Heart*. 2005;91:907-913.
6. Brucks S, Little WC, Chao T, Rideman RL, Upadhyaya B, Wesley-Farrington D, Sane DC. Relation of anemia to diastolic heart failure and the effect on outcome. *Am J Cardiol*. 2004;93:1055-1057.
7. Klapholz M, Maurer M, Lowe AM, Messineo F, Meisner JS, Mitchell J, Kalman J, Phillips RA, Steingart R, Brown EJ Jr, Berkowitz R, Moskowitz R, Soni A, Mancini D, Bijou R, Sehhat K, Varshneya N, Kukin M, Katz SD, Sleeper LA, Le Jemtel TH. Hospitalization for heart failure in the presence of a normal left ventricular ejection fraction: results of the New York Heart Failure Registry. *J Am Coll Cardiol*. 2004;43:1432-1438.

8. McCullough PA, Lepor NE. Piecing together the evidence on anemia: the link between chronic kidney disease and cardiovascular disease. *Rev Cardiovasc Med.* 2005;6(suppl 3):S4–S12.
9. McClellan WM, Flanders WD, Langston RD, Jurkovitz C, Presley R. Anemia and renal insufficiency are independent risk factors for death among patients with congestive heart failure admitted to community hospitals: a population-based study. *J Am Soc Nephrol.* 2002;13:1928–1936.
10. Dries DL, Exner DV, Domanski MJ, Greenberg B, Stevenson LW. The prognostic implications of renal insufficiency in asymptomatic and symptomatic patients with left ventricular systolic dysfunction. *J Am Coll Cardiol.* 2000;35:681–689.
11. Foley RN. Myocardial disease, anemia, and erythrocyte-stimulating proteins in chronic kidney disease. *Rev Cardiovasc Med.* 2005;6(Suppl3):S27–S34.
12. Cromie N, Lee C, Struthers AD. Anaemia in chronic heart failure: what is its frequency in the UK and its underlying causes? *Heart* 2002;87:377–8.
13. Nanas JN, Matsouka C, Karageorgopoulos D, Leonti A, Tsolakis E, Drakos SG, et al. Etiology of anemia in patients with advanced heart failure. *J Am Coll Cardiol.* 2006 19;48:2485-9.
14. Pascual Hernández D, Serrano Sánchez JA, García Robles JA, Muñoz Aguilera R, Prieto Arévalo R. Anemia e insuficiencia cardiaca. Manual de insuficiencia cardiaca (diagnóstico y tratamiento de una patología en expansión). Madrid: Just in Time; 2004. p. 70-3.
15. Silverberg DS, Wexler D, Blum M, Iaina A. The cardio-renal-anemia syndrome. Correcting anemia in patients with resistant congestive heart failure can improve both cardiac and renal function and reduce hospitalizations. *Clin Nephrol.* 2003;60 Suppl 1S:93-102.
16. Komajda M. Prevalence of anemia in patients with chronic heart failure and their clinical characteristics. *J Card Fail.* 2004;10:S1-4.
17. 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.
18. Roig E. La anemia en la insuficiencia cardiaca. Es un marcador de gravedad o un objetivo terapéutico? *Rev Esp Cardiol.* 2005;58:10-2.
19. Androne AS, Katz SD, Lund L, LaManca J, Hudaihed A, Hryniewicz K, et al. Hemodilution is common in patients with advanced heart failure. *Circulation.* 2003;107:226-9.
20. 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.
21. Gil P, Justo S, Castilla MA, Criado C, Caramelo C. Cardio-renal insufficiency: the search for management strategies. *Curr Opin Nephrol Hypertens.* 2005;14:442-7.
22. Caramelo C, Gil P. Insuficiencia combinada cardiorenal: una clave evolutiva y terapéutica en el fallo cardíaco. *Rev Esp Cardiol.* 2006;59:87-90.
23. Horwich TB, Fonarow GC, Hamilton MA, et al. 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.
24. Kosiborod M, Curtis JP, Wang Y, et al. Anemia and outcomes in patients with heart failure: a study from the National Heart Care Project. *Arch Intern Med* 2005; 165:2237.