Anemia, Renal Dysfunction and Malnutrition Associated with Heart Failure in Patients with Valvulopathy

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Abstract

Background: Valvular disease can course with heart failure (HF), anemia and renal dysfunction (RD), increasing the nutritional risk and worsening patient prognosis.

Objective: To evaluate the prevalence of anemia and RD in patients with valvulopathy with or without HF, as well as establish a correlation with the nutritional status.

Methods: A total of 104 patients admitted at the Clinic of Valvulopathy of PROCAPE/UPE, during the period of Aug-Oct/2008. The data were obtained from the nutritional and medical follow-up files. The collected variables were: sex, age, nutritional status according to the body mass index (BMI), presence of HF, anemia and RD. Anemia was considered when hemoglobin values were < 13 g/dl in men and < 12 g/dl in women. RD was established according to the glomerular filtration rate (GFR) and it was calculated through the formula proposed by Cockcroft and Gault.

Results: The prevalence of anemia and RD was 71.1% and 68.8%, and 48.1% and 60.0%, in patients with and without HF, respectively, with a statistically significant difference for anemia (p = 0.022). Of the patients, 48.1% were eutrophic, 26.9% had excess weight and 25.0% presented some degree of malnutrition. The patients with HF presented a higher frequency of low weight (p = 0.020). The nutritional status was not associated with anemia (p = 0.117), but it was associated with RD, with renal function being decreased more often in patients with low weight (p = 0.000).

Conclusion: When the prevalence of malnutrition, anemia and RD was compared between patients with and without HF, it showed statistical significance. (Arq Bras Cardiol 2010;94(6) : 745-749)

Key words: Heart failure; anemia; malnutrition; heart valve diseases.

Introduction

Valvular disease has increased in the last years, as a result of several factors, including the undeniable increase in age-related degenerative valvulopathies due to the increase in life expectancy[1].

The prevalence of valvular heart disease, although lower than other cardiovascular diseases such as heart failure or ischemic cardiopathy, persists as one of the main sources of medical assistance and use of healthcare resources. Although the prevalence of valvulopathy is high in Brazil, data on its actual prevalence and clinical profile are still scarce[1,2].

Heart failure (HF), common in patients with valvular disease, is a clinical syndrome that results from the deterioration of the cardiac function, which generates a series of hemodynamic and neurohumoral alterations, manifesting as dyspnea, fatigue, reduced functional capacity, fluid retention, with consequent pulmonary congestion and peripheral edema[3]. Patients with HF, mainly after a hospital admission, present a poor prognosis[4]. Recently, it was demonstrated that these patients often present anemia, with increased prevalence with the disease severity and an association with mortality[5-7].

The renal dysfunction (RD) is also common in these individuals and can interfere in symptom intensity, change the clinical course and alter the response to treatment, influencing the prognosis[8].

Malnutrition results in significant loss of skeletal muscle mass, and it is common in patients with valvulopathies and HF, contributing to the increased prevalence of comorbidities, mortality and postoperative hospital stay duration[9].

Therefore, malnutrition, together with RD and anemia, can be risk factors associated with the HF prognosis, and can also be related among them. Anemia promotes the activation of the sympathetic nervous system, which, in the presence of an increase in preload, increases cardiac remodeling, with posterior ventricular dilatation. As the kidney is an organ

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that is directly related with the cardiovascular function, the neurohumoral and inflammatory activation, present in HF, contributes to the progressive loss of renal function. A cycle, known as the cardio-renal-anemia syndrome (CRAS) is thus created[10].

Considering the importance of CRAS and the fact that malnutrition is frequent in patients with HF, it becomes crucial to carry out a nutritional assessment to diagnose and correct the nutritional status and decrease the renal overload, thus decreasing hospital costs and mortality.

The objective of the present study was to evaluate the prevalence of anemia and RD in patients with valvulopathies, with and without HF, and investigate the association of these variables with the nutritional status.

Methods

The present cross-sectional case-series study was carried out in patients with valvulopathies admitted at the Cardiology Emergency Room of Pernambuco (PROCAPE/UPE), deform August to October 2008. The data were collected from medical and nutritional follow-up files of 104 patients of both sexes, with or without surgical intervention.

The exclusion criteria were the presence of pathologies that could have a negative influence on localized or general muscle trophism or hypercatabolic pathologies, such as acquired immunodeficiency syndrome (AIDS), neoplasias, disabsorptive diseases and chronic degenerative diseases.

The collected variables were: sex, age, weight, height, presence of HF, hemoglobin and hematocrit levels. The patients were weighed in the standing position, wearing light clothes and barefoot, on a *Filizola*™ digital scale, with a maximum capacity of 300 kilograms and 100-gram increments. Height was verified sing a 2-meter metallic anthropometric measuring tape, with 1-cm increments, coupled to the digital scale platform. The patients remained standing, barefoot, on the center of the platform, with the feet side by side in parallel position and upper limbs hanging along the trunk, in respiratory apnea.

Hemoglobin values < 13 g/dl in men and 12 g/dl in women were considered anemia, according to the World health Organization (WHO)[11].

The presence of RD was assessed through the glomerular filtration rate (GFR), calculated through the formula proposed by tfgpor meio Cockcroft and Gault[12], after which the renal function was reclassified in two categories: ≥ 60 ml/min/1.73 m^2, normal; and < 60 ml/min/1.73 m^2, decreased. The stage of life was classified in adults and elderly according to the criteria of the WHO (1997) and the biochemical measurements collected from the files were classified according to Waitzberg[13]. The diagnosis of HF was obtained from the patients' files.

The nutritional assessment was carried out through the body mass index (BMI), using the criteria of the WHO for adults[14] and of ímcLipschitz[15] for the elderly.

The creation of the database and the statistical analysis were carried out using the program Statistical Package for Social Sciences (SPSS), release 13.0 (SPSS Inc., Chicago, IL, USA)[16].

The categorical variables were presented in proportions, where the binomial distribution was close to the normal distribution through the 95% confidence interval.

The association between the analyzed variables was evaluated through Pearson's correlation. The level of significance for all tests was set at 5.0%.

The study followed the ethical rules for research involving human beings, as described in the Resolution #196 of the National Council of Health and was submitted to and approved by the Ethics Research Committee of Faculdade Mauricio de Nassau (resolution# 004/2008). The patients who agreed to participate in the study received all the information on the study and signed the Free and Informed Consent Form.

Results

The series consisted of 104 patients, with a similar distribution between the sexes and a mean age of 49.4 ± 16.2 years, with a higher prevalence of patients younger than 60 years.

The presence of HF, anemia and decreased renal function were diagnosed in 47.1%, 58.8% and 64.1% of the patients, respectively (Table 1). The assessment of the nutritional status showed that 48.1% of the patients were eutrophic, 26.9% had excess weight (overweight and/or obesity) and 25.0% presented some degree of malnutrition.

The diagnosis of HF was not associated with renal function impairment in the studied patients, considering that the distribution of patients with normal and decreased renal function was similar between patients with and without HF. However, it was observed that patients with HF presented a higher incidence of anemia, in comparison with patients without HF ($p = 0.022$). Similarly, patients with HF presented a higher frequency of low weight, in comparison with patients without HF, who presented a higher frequency of eutrophia and excess weight ($p = 0.020$) (Table 2).

The presence of anemia showed no statistical difference regarding the patients with low weight, eutrophia or excess weight. On the other hand, the renal function showed a highly significant difference regarding the nutritional status of the assessed patients, with the decreased renal function being more frequent among patients with low weight and normal renal function more frequent in patients with excess weight (Table 3).

Discussion

Anemia is common in patients with HF and its etiology is multifactorial, being associated with high mortality[7,17]. Its prevalence ranges from 5.0% to 55%, depending on the criteria used and the studied population[18].

In the present study, the prevalence of anemia in patients with HF was similar to that demonstrated by the study of Silverbeg et al[19], where 55.0% of the patients with HF presented hemoglobin levels < 12 g/dl. The study developed by Sales et al[20] showed a high incidence of anemia (63.0%) in patients with HF, whereas Ezekowitz et al[87], when analyzing non-selected patients with HF, found that only 17% of them

Table 1 - Characteristics of the patients with valvulopathy admitted at the PROCAPE/UPE, from August to October, 2008

Variables	N	%	95%CI*
Sex			
Female	49	47.1	37.3 - 57.1
Male	55	52.9	42.9 - 62.7
Stage of life			
< 60 years	72	69.2	59.3 - 77.7
> 60 years	32	30.8	22.3 - 40.7
Nutritional status			
Low weight	26	25.0	17.3 - 34.6
Eutrophia	50	48.1	38.3 - 58.0
Excess weight	28	26.9	18.9 - 36.7
Presence of HF			
Yes	49	47.1	37.3 - 57.1
No	55	52.9	42.9 - 62.7
Anemia			
Yes	57	58.8	48.3 - 68.5
No	40	41.2	31.5 - 51.7
Renal function			
Normal	37	35.9	26.9 - 46.0
Decreased	66	64.1	54.0 - 73.1

95%CI = 95% Confidence Interval.

presented anemia. It is noteworthy the fact that the heart failure in the two aforementioned studies was not due to valvulopathies.

The anemia in patients with HF can occur due to several factors, such as decreased intestinal absorption of iron, caused by either insufficient ingestion of iron or intestinal loop edema and the chronic gastric loss of blood among patients who use acetylsalicylic acid.

Table 2 - Distribution of renal function, presence of anemia and nutritional status according to the diagnosis of HF in patients with valvulopathy admitted at the PROCAPE/UPE, from August to October 2008

Variables	With HF		Without HF		χ^2	P*
	n	%	n	%		
Renal function						
Normal	15	31.2	22	40	0.853	0.356
Decreased	33	68.8	33	60		
Total	48	100	55	100		
Anemia						
Yes	32	71.1	25	48.1	5.282	0.022
No	13	28.9	27	51.9		
Total	45	100	52	100		
Nutritional status						
Low weight	18	36.7	8	14.5	7.817	0.020
Eutrophia	22	44.9	28	50.9		
Excess weight	9	18.4	19	34.6		
Total	49	100	55	100		

*χ^2 = Pearson's Chi-square. *value of significance.*

The increase in cytokines, such as the tumor necrosis factor alpha (TNF-α), which produce bone marrow depression, is another reported factor. The activation of the renin-angiotensin-aldosterone system (RAAS) causes sodium and water retention, resulting in anemia due to hemodilution.

Similarly, the renal dysfunction, which affects patients with HF, partly due to vasoconstriction and renal ischemia, causes a decrease in the production of erythropoietin and loss of erythropoietin and transferrin due to the coexistence of proteinuria.

In addition to the treatment with angiotensin-converting enzyme (ACE) inhibitors, which can alter the production of

Table 3 - Distribution of the presence of anemia and renal function according to the nutritional status, in patients with valvulopathy admitted at the PROCAPE/UPE, from August to October 2008

Variables	Low weight		Eutrophia		Excess weight		χ^2	P*
	N	%	n	%	n	%		
Anemia								
Yes	19	76.0	24	51.1	14	56.0	4.294	0.117
No	6	24.0	23	48.9	11	44.0		
Total	25	100	47	100	25	100		
Renal function								
Normal	3	11.5	16	32.7	18	64.3	16.729	0.000
Decreased	23	88.5	33	67.3	10	35.7		
Total	26	100	49	100	28	100		

*χ^2 = Pearson's Chi-square. *value of significance.*

erythropoietin in the kidney, especially at high doses, the anticoagulant treatment can contribute to the presence of anemia, producing blood loss[21].

On the other hand, the anemia contributes to the HF, as there is higher cardiac expense to provide the necessary oxygen supply to the tissues, which produces the stimulation of the sympathetic nervous system with vasoconstriction and tachycardia. The renal vasoconstriction activates the RAAS, with decrease in the renal flow and water retention, causing secondary renal failure that aggravates anemia and causes, in the long term, ventricular hypertrophy and remodeling, worsening the HF[22]. This anemia and HF cycle was observed in our study, where the prevalence of anemia was quite high in patients with HF, thus demonstrating the contribution of these two comorbidities to a worse prognosis.

Anemia and RD are common comorbidities currently recognized as risk factors that modify the course of HF[8]. RD is an increasingly more frequent finding in patients with HF and its early detection, correct staging and control represents a clinical challenge. Most of the clinical studies in HF exclude patients with RD; therefore, even the use of medications employed in the treatment of HF presents potential risks to renal function. The RD causes imbalance in the cardio-renal system and can cause HF instability in the short-term[23].

Currently, the RD is considered an independent risk factor for the prognosis in hospitalized patients with decompensated HF[25,10,24]. Several studies have assessed the presence of anemia in patients with a GFR < 60 ml/min/1.73 m^2 [5], demonstrating a great impact, in hospitalized patients, of the association of RD, HF and anemia on mortality[26]. In our series, only 1/3 of the patients presented a GFR > 60 ml/min/1.73 m^2.

No positive correlation was found between RD and the presence of HF in the studied population, which can be attributed to a possible higher prevalence of patients with non-severe HF; that could not be measured in our study, as the HF severity was not assessed, neither classified.

Malnutrition, as well as RD and anemia, is frequently observed among patients with valvulopathies, especially those with HF. In our series, the correlation between anemia and malnutrition was not observed. On the other hand, the study by Horwich et al[6] oushowed a possible association between anemia and malnutrition, considering the association between the serum levels of albumin and BMI.

The available clinical and experimental data indicate an association between HF and malnutrition[27]. There are some doubts on which mechanisms lead to malnutrition and what the importance of each mechanism is in the maintenance and aggravation of the condition[28]. Krummel[29] ratifies what was observed in the present study, when affirming that de 35.0% to 53.0% of the patients with HF presented malnutrition. The prevalence of malnutrition in our series was 69.2% in patients with HF. In a retrospective study carried out by Herreros et aland[30], a prevalence of 28% of malnutrition was observed in patients with valvulopathies, confirming our findings once again.

Veloso et al[27] suggest that the impact of the nutritional status on advanced heart failure, although it results from the left ventricular contractile dysfunction as a common etiological factor, have as its main determinant factors, in each individual, other factors that go beyond the involvement of the cardiac pump. The nutritional involvement could be better understood within the scope of the complex peripheral adaptation and the neurohumoral response to myocardial failure[27].

The malnutrition in these patients can also be explained by the increase in levels of cytokines such as TNF-α and interleukin-6. The cytokines are also quite increased at the advanced stages of the disease and studies have demonstrated an association between the increase in their levels and weight loss[31].

Conclusion

The prevalence of anemia, RD and malnutrition was high in the study population, especially in patients with HF, which can contribute to a worse prognosis; thus, it is necessary to establish the early diagnosis and treatment of such comorbidities.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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