Evaluation of Heart Failure Prognostic Factors in Patients Referred for Heart Transplantation

Cleópatra Medina Noronha Areosa, Dirceu Rodrigues Almeida, Antônio Carlos C. de Carvalho, Angelo A. V. de Paola
Universidade Federal de São Paulo - Escola Paulista de Medicina - São Paulo, SP - Brazil

Summary

Objectives: To evaluate the survival of patients with heart failure submitted to cardiac transplantation screening as well as identify poor prognostic factors using a risk score to identify patients with higher death risk.

Methods: 330 male and female patients aged 12 to 74 years old, referred for heart transplantation from January 1986 to November 2001 were evaluated. Clinical, laboratory, electrocardiographic, Holter monitoring, echocardiographic and radionuclide ventriculography data were analyzed.

Results: The median follow up period was 5 years; patients' survival rate was 84.5% in the first year, 74.3% in the second year, 68.9% in the third year and 60.5% in the fifth year. The prognostic variables selected through the univariate analysis were: age, Chagas' disease etiology for cardiomyopathy, NYHA functional classes III and IV, orthopnea, systolic blood pressure, mean blood pressure, pulse pressure, plasma urea, sodium, glucose, albumin, bilirubin, hemoglobin, and mean heart rate. The prognostic variables at the multivariate analysis were: ejection fraction, blood urea, and hemoglobin. The risk score: RR=exp[(-0.0942401 x ejection fraction) + (0.0105207 x blood urea) + (-0.2974991 x hemoglobin) + (-0.0132898 x age) + (-0.0099115 x blood glucose)] discriminated the population with a higher death risk.

Conclusion: Patients' survival was satisfactory despite heart failure severity, suggesting they can be maintained on optimized clinical treatment until persistent clinical deterioration takes place. Ejection fraction, ventricular diameters, and clinical functional class alone should not be used as an indication for heart transplantation. The risk score could help discriminate the population with the poorest prognosis. (Arq Bras Cardiol 2007;88(6):590-595)

Key words: Heart failure, cardiac transplantation, survival, prognostic factors.

Introduction

Approximately 5,000,000 North-Americans present heart failure (HF), with an incidence of 10/1,000 among individuals older than 65 years. HF is the cause of around 20% of all hospital admissions among individuals older than 65 years[1]. In Brazil, the importance of HF is similarly significant and according to data from the Ministry of Health (DATASUS/2000), there are currently 2,000,000 patients with HF and 240,000 new cases are diagnosed yearly[2]. Despite the therapeutic advances that have taken place in the last decades, HF is a disease with a severe prognosis, showing an annual mortality of 30 to 50% for the most critical patients[3]. Heart transplantation is currently the only broadly accepted surgical alternative to treat these patients with severe HF; however, there are limitations created by the higher number of receptors compared to the permanent scarcity of donors. The transplantation priority for hospitalized patients in critical condition is accepted worldwide; as for the outpatients, the conditions that are associated with HF mortality (prognostic factors) have been used as determinant factors for the heart transplantation indication and waiting list position in Brazil and other countries, as a priority criterion in this group of patients.

The aim of the present study was to find the prognostic factors of HF in our country that would take clinical parameters into account and could contribute to the identification of patients with a higher death risk among those referred for heart transplantation and attempt to establish a risk score considering these factors.

Methods

The study group consisted of 330 patients referred for heart transplantation assessment, from January 1986 to November 2001, in a Reference Center for Heart Transplantation. Mean age was 43 ± 12 years (ranging from 12 to 74 yrs); 77.3% of the patients were males with chronic HF: 124 had idiopathic dilated cardiomyopathy (IDCM), 94 had Chagasic cardiomyopathy (CCM), 64 had ischemic cardiopathy (IC) and 48 had other etiologies. Patients were selected according to the inclusion criteria: 12 to 75 years of age, left ventricular ejection fraction ≤ 40% at the two-dimensional echocardiography, symptomatic HF, New York Heart Association (NYHA) functional class II, III or IV, undergoing conventional drug therapy and being referred for heart transplantation. Patients were excluded when they presented severe concomitant

Mailing address: Cleópatra Medina Noronha Areosa •
Rua Tókio, 160/101 - Bloco Açaí - 69045-200 - Manaus, AM - Brazil
E-mail: cmedina@cardiol.br
Manuscript received June 6, 2006; revised received November 8, 2006; accepted January 17, 2007.

diseases that could affect the prognosis (chronic obstructive pulmonary disease, hepatic failure, insulin-dependent diabetes mellitus, stroke with severe sequelae and dementia, positive serology for HIV and chronic renal failure under dialysis treatment). The study protocol was approved by the Committee of Ethics on Research of our Institution.

The beginning of the study enrolment coincided with the first outpatient visit with data collection on clinical history, usual medications, symptoms and physical examination; other variables were NYHA functional class, hospital admissions due to HF, use of vasoactive drugs, routine laboratory assessment, electrocardiogram (ECG), two-dimensional transthoracic echocardiogram with Doppler, radionuclide ventriculography and Holter monitoring. The functional analysis with a direct measurement of oxygen consumption (VO_2) was carried out in a small number of patients and therefore, it was not included among the studied variables. Hemodynamic variables obtained through right and left heart catheterization, although available for most of the patients, were not considered for the assessment in the present study, due to its low level of feasibility at obtaining it by the clinicians who treat patients with HF.

For the statistical analysis, the event of interest was death due to cardiovascular disease; heart transplantation and other causes of death were suppressed. The descriptive analysis is demonstrated by mean ± SD and median and the survival curve by the actuarial method[4] for the analysis of long-term survival.

The prognostic assessment was carried out using the survival curve by the Kaplan-Meier method and the curves were compared using the log-rank test[4] to identify a combination of significant prognostic factors. To determine independent survival predictors, Cox proportional hazards regression model[5] was used. The significant predictors of the univariate analysis of the Cox proportional hazards regression model ($p< 0.10$) and other variables that were considered significant in other studies were analyzed at the multivariate model[6]. To explore the association between the selected variables, Spearman's correlation coefficients and phi[7] were calculated. The prognostic score was calculated for each patient (excluding the patients who underwent heart transplantation) as an exponential value of the sum product of the prognostic variables and their coefficient ($RR=\exp(\beta_1 x_1 + \beta_2 x_2 + ... + \beta_n x_n)$, where $x_1, x_2, ... x_n$ are the values of the variables and $\beta_1, \beta_2, ... \beta n$ are the coefficients assigned to each variable. To establish a cutoff for this prognostic score, the ROC (Receiving Operating Characteristic) curve was used in order to show the clinical implications of accepting the different cutoff levels of the calculated prognostic score[8].

The statistical analysis was carried out using the STATA 7.0 software.

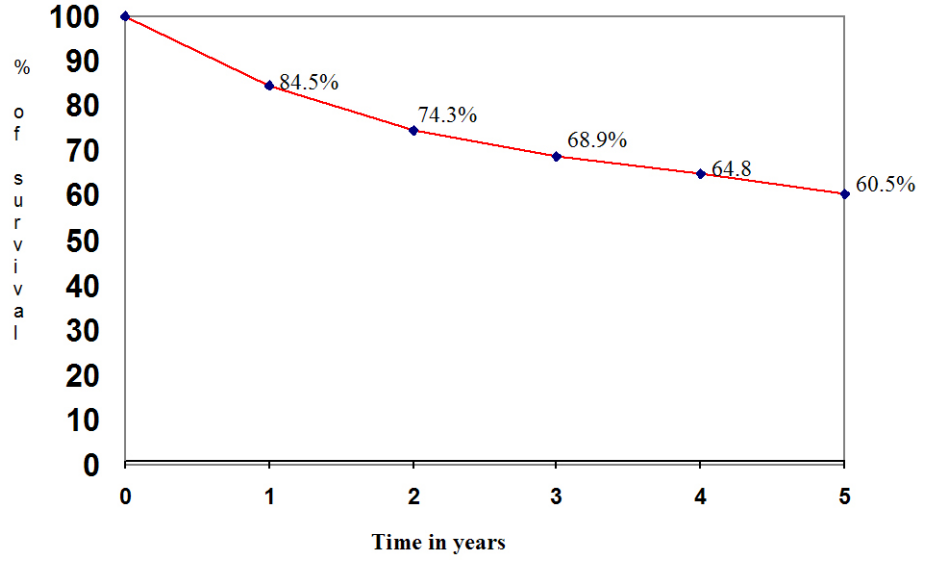
Results

The final study group consisted of 330 patients (77.3% males, mean age 43 ± 12 yrs). Eighty-five (20.4%) of the 415 patients that were initially selected were excluded as they did not meet the inclusion criteria.

The patients' follow-up period had a median of 1,780 days (ranging from 7 to 5,574); 99 patients (30%) died and 123 (37.3%) underwent heart transplantation due to terminal HF.

All of the patients were submitted to the conventional therapy, advised to maintain a low-sodium diet, hydric restriction and pharmacological treatment, which included angiotensin-converting enzyme inhibitors (ACEI), digitalis, diuretics, and in some patients, betablockers, amiodarone and oral anticoagulants.

Long-term survival (actuarial method) was 84.5%, in the 1st year, 74.3% in the 2nd year, 68.9% in the 3rd year and 60.5% in the 5th year (Graphic 1).



Graphic 1 - 5-year actuarial survival curve for the 330 patients in the sample.

At the assessment of the prognostic factors, the univariate analysis selected 15 variables (Table 1) as potential prognostic predictors (age, Chagasic etiology, functional class III or IV, orthopnea, systolic arterial pressure, mean arterial pressure, pulse pressure, plasma urea, plasma sodium, glycemia, albuminemia, serum total bilirubin, hemoglobin and mean HR at Holter monitoring). At the multivariate analysis (Table 2), the left ventricular ejection fraction (LVEF) by the radionuclide method (Hazard ratio [Hr] 0.091, p=0.004), plasma urea (Hr 1.01, p=0.007) and hemoglobin (Hr 0.742, p=0.003), were independent predictors of mortality. The left ventricular ejection fraction by the radionuclide method decreased the death risk by 9% for each 1% increase in its value. Plasma urea increased the death risk by 1% for each 1mg/dl increase in plasma levels. Hemoglobin decreased the death risk by 74% as the hemoglobin levels increased 1g%. To adjust the statistical model and improve the information obtained from the set of data, age and plasma glycemia, which were not significant at the multivariate analysis, were maintained.

The prognostic score was calculated for each patient individually, with individual risk factors being identified at the multivariate analysis (excluding the patients that were submitted to heart transplantation). The individual relative risk calculated for each patient varied from 0.0000424 to 0.0019156. The score cutoff was established at 0.0011851, (Graphic 2), with a sensitivity of 82.86% and a specificity of 67.61%. The one-year and two-year event-free survival for low and high-risk patients were 92% and 76.06% and 82.68% and 70.88% respectively (log rank p=0.00001) (Graphic 3).

Discussion

There are several studies in the literature regarding prognostic factors and risk scores for patients with HF followed at an outpatient clinic. However, there is a heterogeneity concerning these data. We analyzed the clinical and laboratory data of a sample of patients referred for heart transplantation, allowing us to select prognostic variables and, based on these variables, establish a prognostic score.

Many studies suggest that the etiology of HF is an important prognostic factor[9,10], despite being conflicting; there is a general trend that the ischemic etiology has a worse prognosis when compared to the non-ischemic etiology, which was not observed in the present study. Studies carried out in our country indicate that the Chagasic

Table 1 - Variables selected for the multivariate analysis by the Cox Regression Model

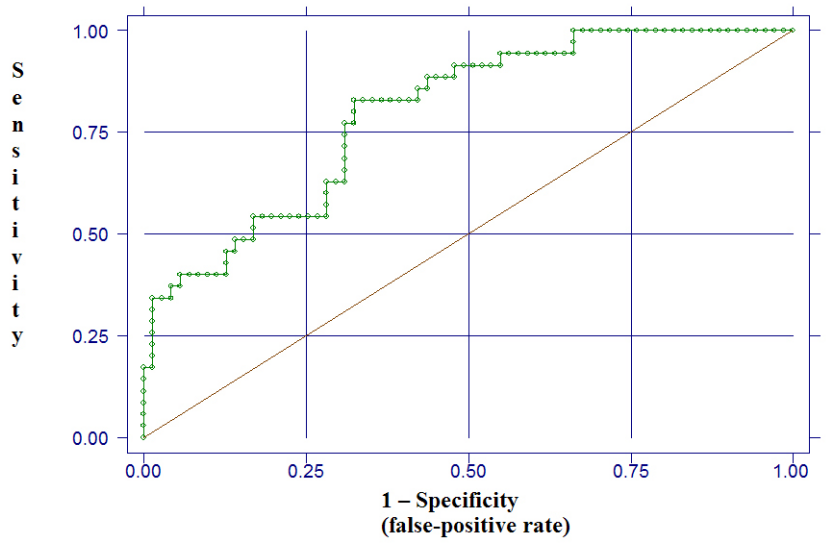
Variable	Hazard ratio	Standard error	Z	p>| z |	[95% CI]
Diastolic d.	0.9820524	0.0234101	-0.76	0.447	0.9372248-1.029024
EF (echo)	2.2516628	5.123265	0.36	0.721	0.0260439-194.6645
EF (RI)	0.9061327	0.0325586	-2.74	0.006	0.8445142-0.9722471
SAP	0.9873396	0.012824	-0.98	0.327	0.9625223-1.012797
Urea	1.008917	0.0048126	1.86	0.063	0.999528-1.018393
Sodium	0.9743023	0.0411025	-0.62	0.537	0.8969835-1.058286
Glycemia	0.9912635	0.007233	-1.2	0.229	0.9771879-1.005542
Hemoglobin	0.7860301	0.0833328	-2.27	0.023	0.6385533-0.9675675
Age	0.9913893	0.0164288	-0.52	0.602	0.9597067-1.024118
FC	1.466586	0.6007324	0.93	0.350	0.6571199-3.273185
Etiology	0.7617017	0.1532818	-1.35	0.176	0.5134433-1.129997
Sex	0.8414009	0.4206375	-0.35	0.730	0.3158391-2.241507

EF - ejection fraction; EF (RI) - left ventricular ejection fraction by radionuclide; SAP - systolic arterial pressure; FC - functional class; 95% CI – 95% confidence interval.

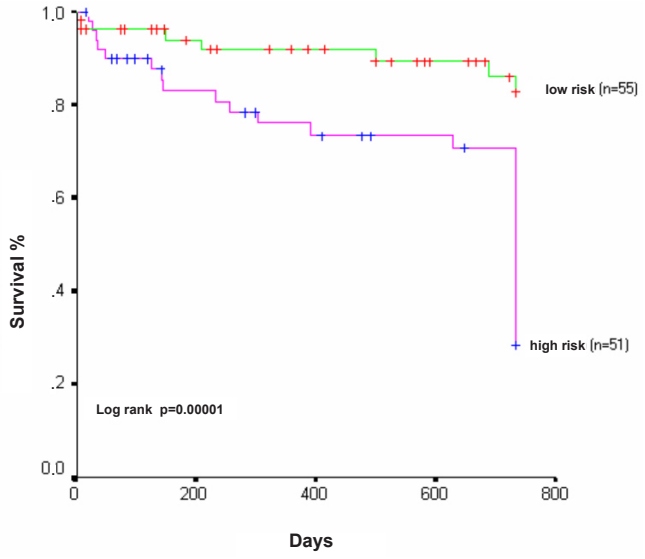
Table 2 - Cox proportional hazards regression model of the prognostic variables

Variable	Coefficient	Hazard ratio	Standard error	z	p>| z |	95% CI
EF (RI)	-0.0942401	0.09100642	0.0300951	-2,85	0.004	0.8529497 - 0.9710031
Urea	0.0105207	1.010576	0.0039576	2.69	0.007	1.002849 - 1.018363
Hemoglobin	-0.2974991	0.7426733	0.0740307	-2.98	0.003	0.61087 - 0.9029148
Age	-0.0132896	0.9867981	0.014454	-0.91	0.364	0.9588717 - 1.015538
Glycemia	-0.0099115	0.9901375	0.0056338	-1.74	0.082	0.9791568 - 1.001241

EF (RI) - left ventricular ejection fraction by radionuclide; 95% CI – 95% confidence interval.



Graphic 2 - ROC Curve for the level of the individual relative risk cutoff. Area under the curve = 0.7952.



Graphic 3 - Survival curve by the Kaplan-Meier method, for the individual relative risk, according to the ROC curve cutoff point, defined in Chart 2.

etiology is an independent factor of worse prognosis[11,12]. At the survival rate analysis, we observed that Chagasic patients presented a worse evolution when compared to patients with ischemic etiology. The Chagasic etiology showed to be an independent prognostic factor at the univariate analysis, which was not maintained at the multivariate analysis. Additionally, we did not observe a higher incidence of sudden death in this group.

Whenever the severity of HF symptoms is evaluated using the NYHA functional class classification, the functional classes III and IV seem to have the worse prognosis[13-15]. In our sample, the univariate analysis showed that functional classes III and IV were factors of worse prognosis, with no difference observed between them. However, at the multivariate analysis, the functional classes III and IV did not remain as indicators of worse prognosis.

In our sample, the laboratory variables plasma bilirubin, albumin, glycemia, hemoglobin, urea and sodium were factors of worse prognosis at the univariate analysis. However, at the multivariate analysis, only plasma urea and hemoglobin remained as important prognostic factors. The serum sodium level have a strong inverse correlation with plasma renin activity

and is considered an important factor of worse prognosis in HF[10,15-20]. Our sample presented a median sodium level of 137 ± 4.96, which probably reflected the optimized treatment with ACEI and was not significant as a prognostic factor, even when the subgroups with sodium levels > or < 130mEq/l were analyzed. The increase in plasma urea and creatinine seems to be the worst prognosis factor in HF[15,19-23].

The studies that assessed the influence of renal failure as a prognostic factor in HF indicated the importance of serum creatinine levels[15], plasma urea and the estimated creatinine clearance[22,23]. In the present study, serum creatinine was not significant as a prognostic factor; however, plasma urea showed to be a strong predictor of mortality in both multi- and univariate analyses, which has been corroborated by other autors[15].

Recent studies investigated a correlation between anemia and HF severity and showed that there was an improvement in the ejection fraction (EF), functional class and exercise capacity when anemia improved[24-26].

According to Horwich et al[27], there is a correlation between low hemoglobin and the symptoms, exercise capacity and prognosis in patients with advanced HF; therefore, moderate anemia is not associated with increased morbidity and mortality in patients of both sexes. However, Sales et al[28], evaluating hemoglobin and hematocrit levels in hospitalized elderly individuals, observed that male individuals with anemia presented higher mortality in comparison with female individuals and that anemia was an independent marker of in-hospital mortality.

In our sample, we did not consider the cases in which anemia was associated to the chronic disease and observed that male patients presented higher mortality when hemoglobin levels were < 14g/dl; such association was not observed in female patients when hemoglobin levels were < 12g/dl. In the general analysis, after adjusting the variables, hemoglobin levels remained as an important prognostic factor in our sample. This information is in agreement with literature data and increases the interest on the role of erythropoietin in HF treatment.

The left ventricular ejection fraction obtained through radionuclide ventriculography[10,13,17] has been increasingly appreciated as a strong prognostic indicator[29]. This variable showed to be discriminant as a high risk of death predictor at the multivariate analysis.

In our sample, the survival rate of patients referred for heart transplantation was 84.5% in the first year, 74.3% in the second year, 68.9% in the third year and 60.5% in the fifth year. When survival was assessed between the sexes, male sex survival in the first year was 85.7%, and the female was 81%; in the second year, it was 76.9% for males and 67.5% for females and in five years, it was 62.4% for males and 64.8% for females. These survival rates are identical to those reported after heart transplantation published by "The Registry of the International Society for Heart and Lung Transplantation"[30].

In comparison to literature data, the survival rate of patients in our sample was better, although they were critical patients referred for heart transplantation. When patients submitted to heart transplantation were excluded, the first-year survival was 75.8% and the 2-year was 61%; considering only patients that were referred for heart transplantation, the first-year survival was 62.5% and the 2-year survival was 49.6%. These numbers suggest that the decision and the criteria used for patients' transplantation referral were correct.

The assessment of the best moment for heart transplantation referral in outpatients remains difficult, as the criterion selection is not universally accepted and therefore, the establishment of a score has been used to try to help in this decision-making. The use of variables that are usually part of the clinical and laboratory assessments makes it more feasible to use the score routinely, although variables that are obtained invasively are equally important.

Among the previously developed scores, some authors used variables that are not obtained by invasive methods, such as the score developed by Maeda et al[21], who used HR, hemoglobin, serum potassium, serum total protein, albumin/globulin ratio, plasma urea, degree of hepatomegaly and the number of episodes of cardiac decompensation. The score by Aaronson et al[10] considered the following variables: ischemic etiology, HR at rest, radionuclide EF, maximum oxygen consumption, intraventricular conduction delay and serum sodium. The score by Alla et al[31] used: HR, serum creatinine, serum sodium, cardiac decompensation and age > 70 years. Among the studies that used data obtained from invasive methods in their scores are: Campana et al[14], who used pulmonary diastolic arterial pressure minus the pulmonary capillary pressure, mean blood pressure, cardiac output, valvular heart disease, presence of B3 and functional class IV, whereas Martí et al[32] used the mean pressure of the right atrium, the cardiac index and functional class IV. Of the aforementioned scores, only the one by Aaronson et al[10] has a reasonable clinical acceptance, being the only one that has been validated prospectively.

The non-conformity of the described scores is also an indication of the difficulties in considering the isolated weight of each prognostic factor in the evolution of heart failure.

In our sample, the worse prognosis factors were the low ejection fraction at the radionuclide ventriculography, increase of plasma urea and low hemoglobin levels; based on these variables, we sought to establish a prognostic score that could objectively help determine the best moment for heart transplantation referral. This score showed to have reasonable sensitivity and specificity in the identification of patients at high risk of death. We believe the present study has created perspectives for carrying out a broader, prospective study that can validate an easy-to-apply score with a potential clinical usefulness.

Study limitations - The fact that this is a retrospective study initiated in January 1986, a time when IECA, spironolactone and betablockers were still not established as first-choice therapy in the treatment of HF might somehow have interfered with the prognostic markers. Other study limitations were the non-systematic use of the direct measurement of O_2 consumption and the measurement of neurohormones (brain natriuretic peptide – BNP and plasma norepinephrine) and pro-inflammatory activity, which are seen as independent predictors of death.

A prospective study with a larger sample size is necessary to validate the prognostic factors and the risk score presented here.

Acknowledgements

To Professor Dr. Meide Silva Ançao, Clovis de Araujo Teles, Neil Ferreira Novo, Yara Juliano, to the Post-Graduate student Gizelton Pereira Alencar and the systems analyst Kelsy Catherina Nema Areco, for their advice and statistical analysis.

Potential Conflict of Interest

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

References

1. Jessup M, Bronzena S. Medical progress heart failure. N Engl J Med. 2003; 348: 2001-18.
2. Ministério da Saúde, Datasus. Óbitos de residentes – Brasil. [citado 2002 24]. Disponível em: URL: <http//www.datasus.gov.br>.
3. Muntwyler J, Abetel G, Gruner C, Follath F. One-year mortality among unselected outpatients with heart failure. Eur Heart J. 2002; 23: 1861-6.
4. Lee ET. Nonparametric methods of estimating survival functions. In: Lee ET. Statistical methods for survival data analysis. California: Wadsworth; 1980. p. 75-118.
5. Cox DR. Regression models and life-tables (with discussion). J Royal Stat Soc B. 1972; 34: 187-220.
6. Harrell FE Jr, Lee KL, Matchar DB, Reichert TA. Regression models for prognostic prediction: advantages, problems, and suggested solutions. Cancer Treat Rep. 1985; 69: 1071-7.
7. Siegel S. Estatística não-paramétrica. São Paulo: McGraw-Hill; 1975.
8. Sackett DL, Haynes RB, Tugwell P. Diagnosis. In: Sackett DL, Haynes RB, Tugwell P. Clinical epidemiology, a basic science for clinical medicine. Boston: Little Brown; 1985. p. 3-139.
9. Franciosa AJ, Wilen M, Ziesch S, Cohn JN. Survival in men with severe chronic left ventricular failure due to either coronary heart disease or idiopathic dilated cardiomyopathy. Am J Cardiol. 1983; 51: 831-6.
10. Aaronson K, Schwartz JS, Chen TM, Wong KL, Goin JE, Mancini DM. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. Circulation. 1997; 95: 2660-7.
11. Mady C, Cardoso RHA, Barretto ACP, Luz PL, Bellotti G, Pileggi F. Survival and predictors of survival in patients with congestive heart failure due to Chagas' cardiomyopathy. Circulation. 1994;90:3098-102.
12. Oliveira Jr MT. Características clínicas e prognósticas de pacientes chagásicos e não-chagásicos em pacientes com insuficiência cardíaca avançada. [Tese de Doutorado]. São Paulo: Faculdade de Medicina. Universidade de São Paulo; 1999.
13. Keogh AM, Baron DW, Hickie JB. Prognostic guides in patients with idiopathic or ischemic dilated cardiomyopathy assessed for cardiac transplantation. Am J Cardiol. 1990; 65: 903-8.
14. Campana C, Gavazzi A, Berzuini C, Larizza C, Marioni R, D'Armini A, et al. Predictors of prognosis in patients awaiting heart transplantation. J Heart Lung Transplant. 1993; 12: 756-65.
15. Madsen BK, Hansen JF, Stokholm KH, Brons J, Husum D, Mortensen LS. Description and survival of 190 consecutive patients with a diagnosis of chronic congestive heart failure based on clinical signs and symptoms. Eur Heart J. 1994; 15: 303-10.
16. Stevenson LW, Tillisch JH, Hamilton M, Luu M, Chelimsky-Fallick C, Moriguchi J, et al. Importance of hemodynamic response to therapy in predicting survival with ejection fraction < 20% secondary to ischemic or nonischemic dilated cardiomyopathy. Am J Cardiol. 1990; 66: 1348-54.
17. Parameshwar J, Keegan J, Sparrow J, Sutton GC, Poole-Wilson PA. Predictors of prognosis in severe chronic heart failure. Am Heart J. 1992; 123: 421-6.
18. Saxon LA, Stevenson WG, Middlekauff HR, Fonarow G, Woo M, Moser D, et al. Predicting death from progressive heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. Am J Cardiol. 1993; 72: 62-5.
19. Spinar J, Vitovec J, Spac J, Blaha M, Spinarova L, Toman J. Non-invasive prognostic factors in chronic heart failure: one-year survival of 300 patients with a diagnosis of chronic heart failure due to ischemic heart disease or dilated cardiomyopathy. Int J Cardiol. 1996; 56: 283-8.
20. Gronda EG, Barbieri P, Frigerio M, Mangiavacchi M, Oliva F, Quaini E, et al. Prognostic indices in heart transplant candidates after the first hospitalization triggered by the need for intravenous pharmacologic circulatory support. J Heart Lung Transplant. 1999; 18: 654-63.
21. Maeda K, Tanaka Y, Tsukano Y, Fujita K, Tanaka C, Takeuchi K, et al. Multivariate analyses using a linear discriminant function for predicting the prognosis of congestive heart failure. Jpn Circ J. 1982; 46: 137-42.
22. 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: 681-9.
23. Mahon NG, Blackstone EH, Francis GS, Starling RC, Young JB, Lauer MS. The prognostic value of estimated creatinine clearance alongside functional capacity in ambulatory patients with chronic congestive heart failure. J.Am Coll Cardiol. 2002; 40: 1106-13.
24. Silverberg DS, Wexler D, Blum M, Keren G, Sheps D, Leibovitch E, et al. The use of subcutaneous erythropoietin and intravenous iron for the treatment of the anemia of severe, resistant congestive heart failure improves cardiac and renal function, and functional cardiac class, and markedly reduces hospitalizations. J Am Coll Cardiol. 2000; 35: 1737-44.
25. Silverberg DS, Wexler D, Sheps D, Blum M, Keren G, Baruch R, et al. The effect of correction of mild anemia in severe, resistant congestive heart failure using subcutaneous erythropoietin and intravenous iron: a randomized controlled study. J Am Coll Cardiol. 2001; 37: 1775-80.
26. Mancini D, Katz S, Lamarca J. Erythropoietin improves exercise capacity in patients with heart failure [abstract]. Circulation. 2001; 104: II438.
27. 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.
28. Sales ALF, Villacorta H, Reis L, Mesquita ET. Anemia como fator prognóstico em uma população hospitalizada por insuficiência cardíaca descompensada. Arq Bras Cardiol. 2005; 84 (3): 237-40.
29. Rashid H, Exner DV, Mirsky I, Cooper HA, Waclawiw MA, Domanski MJ. Comparison of echocardiography and radionuclide angiography as predictors of mortality in patients with left ventricular dysfunction (studies of left ventricular dysfunction). Am J Cardiol. 1999; 84: 299-303.
30. Hertz MI, Taylor DO, Trulock EP, Boucek MM, Mohacsi PJ, Edwards LB, et al. The Registry of the International Society for Heart and Lung Transplantation: Nineteenth Official Report-2002. J Heart Lung Transplant. 2002; 21: 950-70.
31. Alla F, Briançon S, Juillière Y, Mertes PM, Villemot JP, Zannada F. Differential clinical prognostic classifications in dilated and ischemic advanced heart failure: The EPICAL study. Am Heart J. 2000; 139: 895-904.
32. Martí V, Ballester M, Marrugat J, Augé JM, Padró JM, Narula J, et al. Assessment of the appropriateness of the decision on heart transplantation in idiopathic-dilated cardiomyopathy. Am J Cardiol. 1997; 80: 746-50.