Clinical Characteristic and In –Patients Mortality among 100 Patients with Heart Failure Admitted to Ibn Seena Central Hospital, Mukalla, Hadhramout- Yemen.

Ahmed Ali Bahaj *MBPP, MB (Medicine).*

Abstract

Background: The rate of heart failure in Hadhramout is steadily increasing.

Objective: To determine the clinical characteristic and the predictors of in –hospital mortality of heart failure patients.

Method: The first 100 consecutive patients with heart failure admitted to Ibn Seena central hospital in Mukalla for whom clinical history, physical examination and the basic investigations(including hemogram, blood sugar, chest X-Ray. Renal function test, serum cholesterol, electrocardiogram and echocardiogram) were performed during the period from October 2007 to June 2008.

Results: In this study**,** we found male were more affected than female (65% versus 35%). The mean age of the patients was 57 ±12.1 years for males and 59 ±12.2 years for females. The most common underlying causes in all the patients were IHD in 52% followed by AHT 25%. IHD was more in males and AHT was more in females, while valvular heart diseases was the cause of HF in only 7%. The most common associated co-morbidities were renal dysfunction, anemia, dyslipidemia, diabetes mellitus and stroke in 43%, 41%, 35%, 25% and12% respectively. Patients of heart failure with impaired left ventricular function were 67.8%. And it was more in males than in females (52.7% &15.1%). The most common presenting symptoms was dyspnea of different classes in all of the patients and the most common sign was cardiomegaly in 89% of the patients followed by pulmonary crackles in 82%. And the most common arrhythmia were ventricular ectopic in 28% and atrial fibrillation in 21%. During the admission period 9 out of 100 patients died. The most common underlying causes were IHD, AHT and DCM and the most common co-morbidities of death were elder age of the patients, male sex, anemia, renal failure, DM, Stroke, impaired systolic ventricular function, and class IV NYHA dyspnea.

Conclusion: This study revealed that HF is common in our community and it is recommended that early detection and management of the underlying etiology and associated co-morbidities could reduce the morbidity and mortality of HF

Key words: Heart failure, clinical presentation, predictors, outcome. Mukalla, Yemen

IRAQI J MED SCI, 2010; VOL.8 (3): 60-68

Introduction

Heart failure (HF) is the end stage of many cardiovascular disorders [(1)]. It is a global serious health problem especially in people aged above 65 years [(2).] It is estimated that nearly 6.5 million people in Europe, five million people in the USA, and 2.4 million people in Japan suffer from HF. Overall; it appears that HF affects 1–3% of the general population and 10% of the elderly.

In developing countries its incidence is steadily increasing [(3)].

HF is a broad clinical syndrome with many different underlying etiologies. In some studies ischemic heart disease (IHD) was the commonest cause and in other studies arterial hypertension (AHT) was the most common [(4, 5)]. However, the etiology of HF varies with different population, in developed countries it is usually due to IHD and AHT. In developing countries viral and bacterial infection as streptococcal infection and its role in the etiology of rheumatic heart disease play an important role [(6)].

Dept. Medicine, College of Medicine, Hadhramout University,
Address Correspondence to: Dr. Ahmed Ali Bahaj, E- mail: aaobaaj@yahoo.com
Received: 13th March 2010, Accepted: 29th June 2010.

Recently, evidence-based pharma-cological and device therapies indicated the decrease in heart failure symptoms, hospitalization, mortality and improve quality of life of patients with HF, still many patients treated with these regimens often remain burdened by dyspnea and fatigue, diminished exercise tolerance, reduced quality of life, recurrent hospitalizations and early mortality, and if underlying cause is not corrected , more than half of the patients with HF will die within 1-4 years depending on the severity of the disease [7].

Several indicators were developed for prediction of risk and prognosis and to determine the guideline for management of patients with HF. The three most predictors were elder age of the patient, Low left ventricular ejection fraction, and presence of diabetes mellitus. Other risk predictors include high class dyspnea of New York Heart Association (NYHA), male sex, low diastolic blood pressure [8].

In Yemen, few studies were conducted regarding cases of HF and in Hadhramout this is the first study aimed to identify the clinical characteristics and mortality among patients admitted to Ibn Seena central hospital in Al-Mukalla city in Hadhramout governorate, Yemen, during the period from October 2007 to June 2008.

Patients & methods

Study design: This is a hospital-based, prospective study.

Study population: 100 patients who met the modified Framingham criteria of diagnosis of HF [9] were admitted to the Intensive care unit (ICU) and medical wards from the period from October 2007 and their investigations were completed including (CBC, blood sugar, blood urea, serum creatinine, serum cholesterol , Chest X-ray, echocardiography , electrocardiogram). Readmitted patients were included in their first admission

Settings: This study was conducted in Ibn Seena central hospital in Mukalla. It is the central hospital in Hadhramout governorate. However in this hospital there is no specialized cardiac unit (CCU) and all the patients of heart diseases are admitted in ICU or general medical wards.

Exclusion criteria: All the patient who due to any reason dropped from follow up before complete his investigations (died, transferred, discharged)

Data collection: Data were collected by direct interviewing of the patients or their relatives and from the medical records of the patients using closed - end questionnaire.

Ethical consideration: The purpose and the method of the study were explained to the patients and their relatives and oral consent was given.

Study variables:

Ischemic heart disease: was considered if the patient is diagnosed before as IHD, presence of ischemic ECG changes or having wall motion abnormality in echocardiography.

Arterial hypertension: was considered if patient has history of hypertension and on anti- hypertension treatment or if there is more than three readings of systolic BP > 140 mmHg and/or diastolic BP >90mmHg during admission period [10].

Valvular heart disease: was considered if there is clinical and echocardiography evidence of valvular disease.

Dilated cardiomyopathy (DCM): was diagnosed when echocardiography shows heart chambers enlargement and diastolic dysfunction and no evidence of other underlying cause.

Anemia: was considered when hemoglobin concentration was <11g/dl.

Diabetes Mellitus: was considered when the patient was diagnosed as

diabetic case and on regular treatment or repeated fasting blood sugar was more than 126mg/dl during admission period.

***Renal insufficiency*:** was considered if serum creatinine >2mg/dl.

Hypercholesterolemia: was considered if a patient with fasting total cholesterol more than 240mg/dl according to guidelines of the third report of the American national cholesterol education program [(11)].

Stroke: referred to clinical syndrome of vascular origin manifested by rapid development of signs of focal or global disturbance of cerebral function, lasting for more than 24hours.

Cardiomegaly: in chest X-ray is defined when C/t ratio is more than > 0.5.

Data analysis:

Was performed using SPSS-15 statistical program. P value < 0.05 was considered statically significant. Qualitative data were tested by Chi-square test, while quantitative data were tested by student t-test

Results

Table 1: Distribution of the patients according to age &sex

Age group in Years	male		Female		Total	
	No	%	No	%	No	%
<35	3	4.6	1	2.9	4	4
35-44	5	7.7	2	5.7	7	7
45-54	9	13.9	4	11.4	13	13
55-64	22	33.8	8	22.9	30	30
>65	26	40.0	20	57.1	46	46
Total	65	100	35	35	100	100

- Percentage is calculated in relation to total in the columns.
- Mean age of the patients 58 ±12.3 years.
  (male 57.6 ±12.1 years & Female 59±12.2 years) (P = 0.08)

Table 1 shows that 65 of the admitted patients with HF during this period were male and 35 were female, with male to female ratio of 1.86 : 1. The frequency of HF cases increasing with age, the most common age group were > 65 years representing 46% of the patients followed by age group of 55-64 years in 30% of cases. This table also shows that in the age group of more than 65 years, 26 were males and 20 were female indicating that male were affected more than female (56.5% &43.5%) respectively.

Our study showed that, the most common symptom among our patients of HF was dyspnea in 100% of the patients, 63% had dyspnea class IV according to NYHA classification and 37% had class III. Fatigability, cough and palpitation were present in 81%, 65%, and 20% respectively, while 18% had chest pain and/or tightness.

Regarding physical findings, cardiomegaly was the most common in 89%, followed by crackles of different types, basal, mid-chest and diffuse was found in (82%) of the patients (82%), while other findings like peripheral or generalized edema was present in 62%, Gallop rhythm in 39%, high jugular venous pressure in 31% hepatomegaly in 20% and ascitis in10%. There is a significant number of patients of HF had arrhythmias, and the most common arrhythmias were ventricular ectopic beats in 28% and Atrial fibrillation in 21%.

Table 2: Distribution of the underlying causes according to age & sex

Underlying cause	Male		Female		Total	
	No	%	No	%	No	%*
Ischemic heart disease (IHD)	37	71.2	15	28.8	52	52
Arterial hypertension (AHT)	13	52	12	48	25	25
Idiopathic dilated cardiomyopathy (IDCM)	7	63.6	4	36.4	11	11
Valvular heart disease (VHD)	4	57.2	3	42.8	7	7
Corpulmonale	4	80	1	20	5	5
Total	65	100	35	100	100	100
*Percentage were calculated in relation to total of the column while the rest to total of rows. The difference between causes of HF in both sexes was statically not significant (P = 0.22)						

Table 2 shows that the most common underlying cause of HF in all the patients was IHD in 52% followed by AHT in 25% , IDCM (11%), VHD (7%) and pulmonary heart disease in 5%. Distribution of the underlying causes of HF among male and female showed that male have higher prevalence in all the causes. The difference between causes of HF regarding sexes was not statically significant (P value > 0.05)

Regarding left ventricle function, 63 out of 93 patients had HF with impaired ventricular function (ILVSF) and 30 patients had preserved left ventricular systolic function (PLVSF) representing 67.8% & 32.2% respectively, that was statically significant (P = < 0.05 and X^2 = 18.69). In 7 of our patients, HF was due to valvular heart disease (VHD), so LVSF was not calculated because most of the valvular lesion out of aortic valve lesions; it interferes with measurement of LVSF.

Regarding sex distribution, male patients with ILVSF was higher than in female (80.9% & 19.1% respectively). Whereas PLVSF was higher in female patients than male (56.7% & 43.3% respectively).

Table 3: Distribution of associated co-morbidities among patients with HF (n = 100)

Associated co-morbidity	No.	%
Renal dysfunction	43	43%
Anemia	41	41%
Dyslipidemia	35	35%
Diabetes Mellitus	25	25%
Ischemic stroke	12	12%

Table 3 shows that the most common co-morbidities among our patients with HF were renal impairment (43%) followed by anemia (41%), Dyslipidemia (35%), DM (25%) and ischemic stroke (12%)

Table 4: Distribution of dead patients (n = 9) according to age &sex:

Sex	45-54		55-64		>65		Total	
	No.	%	No.	%	No.	%	No.	%
Male	1	11.1	1	11.1	5	55.6	7	77.8
Female	0	0	1	11.1	1	11.1	2	22.2
Total	1	11.1	2	22.2	6	66.7	9	100

Table 4 shows that 9 of 100 patients died during their stay in the hospital and 91 patients discharged alive, giving overall mortality rate of 9%. The dead patients were 7 out 65 male (10.8%) and 2 out 35 female (5.7%). Among dead patients, males were more than female representing 77.8% and 22.2% respectively. Most of the dead patients (66.7%) were in the elder age group (> 65 years)

Table 5: distribution of the dead patients (n =9) according to clinical features underlying cause, co-morbidities and left ventricular systolic function

	No.	%
Clinical features:		
NYHA class:		
III	1	11.1
IV	8	88.9
Edema:		
Generalized	4	44.4
Peripheral	8	88.9
Gallop rhythm	5	55.6
Underlying cause:		
IHD	6	66.7
AHT	2	22.2
DCM	1	11.1
Co-morbidity:		
Anemia	6	66.7
Renal impairment	5	55.6
DM	4	44.4
Stroke	3	33.3
LVSF:		
Impaired	7	77.8
Preserved	2	22.2

Table 5 shows that the main symptoms in the dead patients was dyspnea class IV in 88.9% and the main signs were peripheral/ general edema in all the patients followed by gallop rhythm in 55.6%.. The most common underlying cause of HF among of dead patients was IHD representing 66.7% followed by AHT in 22.2% and DCM in 11.1%.

Regarding co- morbidities, anemia was the commonest findings in 66.7% followed by renal impairment, DM and stroke in 55.6%, 44.4% and 33.3% respectively. In regard to left ventricular systolic function, it was impaired in 77.8% and preserved in 22.2%.

Discussion

This is a hospital – based study and does not reflect the epidemiology of HF in the community because there are many patients with heart diseases don't come to our hospital and are treated in other private and governmental hospitals.

In our studied HF patients, males were more than female (65% versus

35%) and this was consistent with several local, regional and international studies. In a study conducted by Ba-Ishen in Aden/ Yemen, he found that 70% of HF were male and 30% were female [12]. and in other study from a neighboring country, Oman, A.K. Agarwal found that 62.3% of HF were males and 38.7% were females [13] . In Framingham study and other studies from Singapore and Malaysia indicated that HF is lower in females than in males [14-16]. The preponderance of HF in male may be attribute to high incidence of IHD in male and the effect of estrogen protection against cardiovascular diseases in female.

In regards to age of the patients, the mean age of the patients in our study was 58 ± 12.3 years and this was similar to that is studies from Yemen [12], Pakistan [17] and Nigeria [18] which it was 57.1 ± 13.3 years, 61 years and 57.6 ± 15.9 years respectively, but less than those from Japan where it was 70.0 ± 12 years [19].

Our study showed that most of the patients with HF were the age groups of 55-64 years and > 65 years and this support the high prevalence of this condition in the older population. With advance of age, the sex ratio is narrowed and in the age of more than 65 years in our study 56.5% were male indicating that male were affected more than female and this close to study by Stromberg et al on 2003 [20] and this may be due to the increasing number of postmenopausal females with AHT and IHD.

The underlying cause of HF in our study was IHD (52%) AHT (25%), DCM (11%), VHD (7%) and Corpulmonale (5%). This was close to the study of Agarwal et al from Oman who reported IHD (51.7%), AHT(24.9%), DCM (8.3%), VHD (4.0%) and Corpulmonale (4.3%) [13], Framingham study and other studies by Chong A, et al in Malaysia and Leong KTG, et al in Singapore which showed that IHD was the most common underlying cause of HF followed by AHT [14-16].

In our study, the patients had HF with impaired systolic function (HF-ISF) was more than HF with preserved systolic function (HF-PSF) with 67.8% and 30 % respectively. This was consistent with study from Aden/Yemen by Al-khameri et al on 2005 who reported HF-ISF in 66.4% versus 33.6% of HF-PSF [17] and a study by Ibrahim et al on 2003 from Egypt who found HF- ISF in 66% versus 34% had HF- PSF) [22].

Our study showed that HF-ISF was more in male than in female (52.7% versus 15.1%) and this may be attributed to high prevalence of IHD in males than in females. On the other hand HF-PSF was more in females (19.3% & 12.9% respectively) and this was consistent with other studies and this presumed to be due to difference in ventricular remodeling in response to pressure overload and post-infarction remodeling between males and females[23,24] .

The most common associated co-morbidity in our patients of HF was renal impairment which was found among 43% and this was the same as in the study by Smith, et al. (2006) who found that renal impairment was present in 43% of his patients [25] .Renal impairment in the patients with HF is due to hemodynamic changes and renovascular abnormalities occurred secondary to heart failure.

Anemia was found in 41% of our patients, and this is consistent with other study who found that anemia is a common associated co-morbidity in patients with HF [26]. Presence of anemia in HF patients is because of hemodilution due to fluid retention, depressed erythropoisis due renal dysfunction, anorexia and malnutrition and the old age of most of the patients.

In this study Diabetes mellitus (DM) was present in 25% of our patients and this was similarly observed by Berry et al who reported DM in 24% of his HF cases [27] . DM is known to accelerate coronary atherosclerosis and increase of myocardial infarction, besides it is now recognized as independent risk factor for development of HF by inducing specific cardiomyopathy characterized by myocardial hypertrophy, fibrosis and microangiopathy. Also this study revealed that stroke is associated in 12% of our cases, all of them were of ischemic type and this was more than 5.3% reported by barsheshet A et al [28].

Regarding the clinical manifestations, Dyspnea was the most distressing symptoms. NYHA class III dyspnea was present in 37% and 63% was having dyspnea class IV and the same was reported was in some other studies [29].

Fatigue was the second most common symptoms; it was present in 81% of the case and this close to 83% and 84% reported by other studies. Signs of congestion (rales, peripheral edema, high jugular pressure, hepatomegaly and Ascitis) was present in 82%,62%,31%, 20% and 10% respectively and this almost the same as reported by others [30, 31] .

During the study period 9 out of 100 patients died in the hospital and this represents overall mortality 9% which is higher than 6.4% reported by Baishen from Aden/Yemen [12] and close to that by Lee, et al who reported mortality rate of 8.6% [32] . Most of the dead were males (77%) and 22.2% were females and the mortality rate was higher among older age patients, 66.7% of them were aged 65 years or more, while 22.2% were in the age group of 55-64 years and this could be related to complex interaction between advancing age and high frequency of non cardiac co-morbidity in elderly than in younger patients. The most common underlying cause of death in all patients was IHD which was present in 66.7%

It is well known that the presence of non cardiac co-morbid conditions in HF increase hospitalization and death. The most common co-morbidity was anemia which was present in 66.7% of dead patients. It is documented that when it is present in patients with HF lead to poor prognosis and increase mortality [33 -34]. In the current study, 5 of 9 dead HF patients had evidence of renal dysfunction which is reported that it is associated with adverse outcome in HF and this may be due to increased retention of fluid and salts, effect of HF on peripheral vessels and because of limited use of life-saving intervention in HF like use of ACE inhibitors which were stated to induce renal impairment [35].

4 of 9 dead patients (44.4%) detected to have DM which is reported to influence survival and a predictor of adverse outcome in HF with ischemic etiology [28, 36].

Also in this study 7 of 9 dead patients had impairment systolic function representing 77.8% and only 2 patients (22.2%) were with preserved systolic function. McCarthy, et al. identified impaired LSVF as a predictor of increase mortality in HF [37]. In DIAMOND study survival decreased with decreasing LVSF [38] This can be attributed to many reasons, patients with impaired LVSF are predominantly male, the majority with ischemic etiology and significantly associated with renal impairment. All of these factors carry poor prognosis with HF.

In our patients, dyspnea class IV NYHA, advanced edema and presence of gallop rhythm were present in 88.9%, 66.7% and 55.6% respectively, this was mentioned in several studies

to be associated with increasing mortality among patients of HF [12, 39].

Conclusion & Recommendations:

This hospital-based study of heart failure patients in central Mukalla hospital revealed that male patients were affected more than females and the frequency increased with advancing age.IHD was the most common cause of heart disease in HF-ISF while AHT was the other significant etiology in HF-PSF. The most common presenting symptom was dyspnea and the most common sign was cardiomegaly followed by pulmonary crackles and edema. The most common co-morbidities were renal dysfunction; anemia and DM. Mortality rate during admission period was 9% and was associated with old age, male sex, impaired systolic function, high HYHA class, anemia, DM and renal impairment. It is recommended that increase the awareness of the patient's early detection and management of the underlying causes and morbidities associated with HF could decrease the burden of morbidity and mortality of HF.

Acknowledgement

Deep thanks and gratitude to my students, Maysoon, Wisam, Yaser, Saeed, Ali and others who helped me in collection of the data and to Mr. Ahmed Muhdar from medical statistical unit in Ibn Seena Hospital for his keen cooperation

References

1. Davis RC, Hobbs FDR, Lip GYH. ABC of heart failure: History and epidemiology. BNJ 2000; 320:39-42.

2. Sanderson JE, Tse TF. Heart failure a global disease requiring a global response. Heart 2003; 89:585-586.

3. Barker WH, Mullooly JP, Getchell W. Changing incidence and survival for heart failure in a well-defined older population, 1970-1974 and 1990-1994. Circulation. 2006; 113(6):799-805.

4. Lip GYH, Gibbs CR, Beevers DG.ABC of heart failure etiology. BMJ.2000; 320: 104-107.

5. Fox KF, Cowie MR, Wood DA, et al. Coronary artery disease as a cause of incident heart failure in population. Euro Heart J.2001; 22(3): 228-236.

6. Rich MW. Epidemiology, pathophysiology, and etiology of congestive heart failure in older adults. J Am Geriatr Soc 1997; 45:968 - 74.

7. Fonarow GC, Adams KF, Abraham WT, et al. Risk stratification for in-hospital mortality in acutely decompensated heart failure. JAMA. 2005; 293: 572-580.

8. Pocock SJ, wang D, Pfeffer MA, et al, Predictors of mortality and morbidity in patients with chronic heart failure. European heart J. 2005; 27(1):65-75.

9. Schellenbaum GD, Rea TD, Heckbert SR, Smith NL, Lumley T, Roger VL, et al Survival associated with two sets of diagnostic criteria for congestive heart failure. Am J Epidemiologyv2004; 160(7): 628- 635.

10. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the joint national committee on prevention, evaluation and treatment of high blood pressure. Hypertension 2003; 42: 1206-1252.

11. National Cholesterol Education program Expert Panel. Executive summary of the third report of the national cholesterol education (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adult. JAMA 2001; 285:2486 -2496.

12. Baishen I. Study of clinical Epidemiology of heart failure cases admitted to Algomhoria Teaching hospital, Aden 2004, Master thesis, Aden University, Yemen.

13. Agarwal A, Venungopalan P, et al. Prevalence and etiology of heart failure in an Arab population. Eur J Hear fail 2001; 3(3): 301-305.

14. Ho KKL. Pinsky JL, Kannel.WB, Levy D. the epidemiology of heart failure. The Framingham study. J Am Coll Cardiol 1993; 22(suppl A): 6-13.

15. Leong KTG, Goh PP, and Chang BC, et al. Heart failure cohort in Singapore with defined criteria: Clinical characteristics and prognosis in multi-ethnic hospital based cohort in Singapore. Singapore Med J 2007; 48(5):408-414.

16. Chong A, Rajaratnam R, Hussain N, et al. Heart failure in population in Kuala Lampur, Malaysia. Eur J Heart failure 2003; 5(4(:569-574.

17. Vim S, Ahmadi H. Factors influencing the length of hospital staying the patients with

heart failure. Pakistan J Cardiol. 2005;16(1):29-34

18. Familoni OB, Olufemi BW. A clinical study of pattern and factors affecting outcome in Nigerian patients with heart failure. Cardiovasc J Afr 2007;18:308 311.

19. Sakatani T, Shirayama T, Suzaki Y, yamamoto T, Mani H, Kawasaki T. The association between Cholesterol and Mortailty in heart failure Comparison between patient with and without coronary heart disease. Int Heart J 2005; 46(4): 619-629.

20. Stromberg A, Mastersson J. Gender difference in patients with heart failure. Eur J cardiovasc nursing 2003; 2: 2105-2111.

21. Al- Khamri MG. Role of arterial hypertension in heart failure. Algomhoria teaching hospital. 2005: Master Thesis, Aden University, Yemen.

22. Ibrahim BS. The frequency of systolic versus diastolic heart failure in an Egyptian cohort.Eur J haeart fails 2003; 5(1):41-45.

23. Hellerman JP, Jacobsen SJ, Reeder GS, et al. Heart failure after myocardial infarction: prevalence of preserved left ventricular systolic function in the community. Am Heart J 2003; 145:742-748.

24. Krumholz HM, Larson M, Lvy D. Sex difference in cardiac adaptation to isolated systolic hypertension. Am J Cardiol 1993; 72:310-315.

25. Smith GL, Lichtman JH, Bracken MB, et al. Renal impairment and outcome in heart failure. J Am Coll Cardiol 2006; 47:1987-1996.

26. Tanner H, Moschovititis G, Kuster GM, et al. The prevalence of anemia in chronic heart failure. Int J cardiol 2002; 86:115-121.

27. Berry C, Brett M, Stevenson K, et al. Nature and prognostic importance of abnprmal glucose tolerance and diabetes in acute heart failure. Heart 2008; 94:296 -304.

28. Barsheshet A, Gary M, Grossman E, et al. Admission blood glucose level and mortality among nondiabetic patients with heart failure. Arch Intern medicine 2006:166:1613-1619.

29. Wang Cs, Fitzerald JM, Schulzer M, et al. Does this dyspnic patient in the emergency department have congestive heart failure. JAMA 2005; 294:1944-1956.

30. Thomas JK, Kelly RF, Thomas SJ, et al. Utility of history, physical examination, echocardiogram and chest radiography for differentiating normal from decreased systolic function in patients with heart failure. Am J MED 2002; 112:437-445.

31. Malki Q, Sharna ND, Afzal A, et al. Clinical presentation, hospital length of stay, and readmission rate in patients with heart failure with preserved and decreased left ventricular systolic function. Cli Cardiol 2002;25: 149-152

32. Lee DS, Austin PC, Rouleau JL, et al. Predicting mortality among patients hospitalized with heart failure.JAM 2003; 290: 2581-2587.

33. Ezekowitz J, McAlister Fa. Anemia is common in heart failure and is associated with poor outcomes. Circulation 2003; 107: 223-225.

34. Felker GM, Gattis WA, Leimberger JD, et al. Usefulness of anemia as a predictor of death and rehospitalization in patients with decompensated heart failure. Am J cardiol 2003; 92:625-628.

35. Dries DL, Exner DV, Donaski MJ, et al. The prognostic implications of renal insufficiency in asymptomatic and symptomatic patients with left ventricular systolic dysfunction. J Am Coll Cardiol 2000; 35:681-689.

36. De Groote P, Lamblin N, Mouquet F, et al. Impact of diabetes mellitus on long term survival in patients with congestive heart failure. Eur Heart J 2004; 25:656-662.

37. McCarthy PA, Kearney MT, Nolan J, et al. Prognosis in heart failure with preserved left ventricular systolic function.BMJ 2003; 327:78-79.

38. Gustafsson F, Torp-Pedercen C, Brendrop B, et al. The DIAMOND study group, long term survival in patients hospitalized with congestive heart failure: relation to preserved and reduced left ventricular systolic function.Eur Heart J 2003; 24:863-870.

39. Bouvy Ml, Heerdink ER, Leufkens HG, et al. predicting mortality in patients with heart failure: a pragmatic approach 2003;89:605-609