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Determinants of prognosis among Black Africans with hypertensive heart failure

AS Isezuo [1], ABO Omotoso [1], MA Araoye[1], J Carr [2] and T Corrah[3]

Department of Medicine, University of Ilorin Teaching Hospital, Ilorin, Nigeria[1], Royal Victoria Hospital, Banjul, The Gambia[2] Medical Research Council, Fajara, The Gambia[3]

Summary

One hundred and seven consecutive Black Africans hypertensive heart failure patients made of 52 Gambians and 55 Nigerians (51 males + 56 females) aged 53.6 ± 12.1 years were followed-up for 12 months or till death. One-year survival curve was determined using Kaplan-Meiers method. The survivors and the deceased were compared using univariate and multivariate analysis. Mean blood pressures were 180.4 ± 28.2 mmHg (range: 130-250 mmHg) systolic and 117.0 ± 12.9 mmHg (range: 100-160 mmHg) diastolic. Duration of hypertension ranged from 0.5 to 23 years. The rate of undetected hypertension was 44%. Overall one-year survival rate was 71%. Twenty two percent of deaths occurred within the first 3 months of HHF. One-year survival rate among the survivors of this period was 89.4%. A strong negative correlation existed between cumulative survival and the duration of heart failure ($y=0.9812, x_2=0.1173, R=0.965$). Compared to the survivors, the deceased had significantly higher systolic blood pressure (191.9 ± 32.2 mmHg versus 175.1 ± 25.2 mm Hg; $P<0.05$), diastolic blood pressure (123.7 ± 15.8mmHg versus 114.3 ± 10.3 mm Hg; $P<0.05$), cardio-thoracic index (69.2 ± 3.9% versus 66.2 ± 4.2%; $P<0.05$) and serum creatinine (148.6 ± 42.2umol/L versus 113.8 ± 36.4umol/L; $P < 0.05$). Compared to the patients aged 40 or more years, patients aged below 40 years had significantly lower one-year survival rate (41.7% versus 74.1%; $P<0.05$). One-year survival rate was significantly higher among patients on captopril medication than those without (75% versus 52.6%; $P<0.05$). However, only serum creatinine had statistically differing values between the deceased and survivors ($df=1$ SS=10272, $F=7.60$, $p=0.007$). Basic clinical and biochemical parameters could therefore be useful prognostic markers in hypertensive heart failure.

Keywords: *Hypertension, heart failure, prognosis, black Africans.*

Correspondence: Dr ABO Omotoso, Department of Medicine, University of Ilorin, PMB 1515 Ilorin, Nigeria.
E-mail: abomotoso@hotmail.com

Résumé

Cent et sept malades de l'arrêt du coeur de l'hypertensive des Africains, faisant de 52 Gambiens et 55 Nigérians (51 mâles + 56 femmes) de l'age 53.6 ± que 12.1 ont été suivies pour 12 mois ou mort de la caisse. La courbe de la survie d'une année a été déterminée en utilisant la méthode Kaplan-Meiers. Les survivants et les défunts ont été comparés en utilisant l' analyse d' univariate et de multivariate. Les pressions du sang de la moyenne étaient 180.4 ± 28.2 mm Hg (gamme: 130-250 mm Hg) systolique et 117.0 ± 12.9 mm Hg (gamme: 100-160 mmHg) diastolique. La durée d'hypertension a aligné de 0.5 à 23 années. Le taux d'hypertension non détectée était 44%. Le taux total de la survie d'une année était 71%. Vingt deux pour cent de morts se sont produits dans les premiers 3 mois de HHF. Le taux de la survie d'une année parmi les survivants de cette période était 89.4%. UNE corrélation forte négative a existé entre la survie cumulative et la durée d'arrêt du coeur ($y=0.9812, x2=0.1173, R=0.965$). Comparé aux survivants, les défunts avaient considérablement plus haute tension du systolique (191.9 ± 32.2 mmHg contre 175.1 ± 25.2 mm Hg; $P<0.05$), tension du diastolique (123.7 ± 15.8mmHg contre 114.3 ± 10.3 mm Hg; $P<0.05$), index cardio-thoracique (69.2 ± 3.9% contre 66.2 ± 4.2%; $P<0.05$) et créatinine du sérum (148.6 ± 42.2umol/L contre 113.8 ± 36.4umol/L; $P<0.05$) Comparé aux malades a vieilli 40 ou plus d'années, les malades vieillis en dessous 40 années avaient le 1-year taux de la survie considérablement inférieur (41.7% contre 74.1%; $P<0.05$). Le taux de la survie d'une année était considérablement plus haut parmi malades sur médicament du captopril que ce sans (75% contre 52.6%; $P<0.05$). Cependant, seulement créatinine du sérum avaient être différent des valeurs entre les défunts et survivants statistiquement ($df = 1$ SS =10272, $F=7.60$, $p = 0.007$). Les paramètres clinique et biochimiques de base pourraient être des marqueurs du pronostic utiles dans arrêt du coeur de l'hypertensive par conséquent.

Introduction

Heart failure is a global public health problem. Its public health significance as an important cause of morbidity mortality among Nigerians would potentially rise because of increasing lifespan, adoption of affluent lifestyle and

rising prevalence of cardiac-related non-communicable diseases. Though community based studies are rare, hospital-based data showed that hypertension is the predominant precursor of HF among Black Africans [1,2]. Information on the prognostic indices of HF is important in identifying patients at high risk of mortality and requiring a more aggressive intervention or care. This information including clinical, laboratory, haemodynamic and therapy-related variables are abundantly available among Caucasians [3,4].

However, in spite of HF being an endpoint of varieties of process, its prognosis is largely dependent on aetiology. The 5-year survival rates among Japanese with HF secondary to coronary artery disease, idiopathic dilated cardiomyopathy, rheumatic valvular heart disease and hypertensive heart disease, for example were 35%, 40%, 53% and 80% respectively [5]. Furthermore, the dominant aetiologies of HF vary from population to population. In the study of left ventricular dysfunction (SOLVD), hypertensive aetiology of left ventricular dysfunction occurred in 32% of Blacks and 4% of Whites, whereas, an ischaemic aetiology occurred in 73% of Whites and 36% of Blacks [6]. In Africa, hypertension is the dominant precursor of heart failure [1,2]. The prognosis of heart failure may also be dependent on racial factor. The one-year survival rates among Blacks and Whites with dilated cardiomyopathy were, for example, 92% and 71.5% respectively [7]. Furthermore, hypertension has 1.5 cardiac-related deaths among Blacks than White Americans [8].

The prognostic indices of heart failure may therefore vary from population to population. We have previously reported that hypertensive heart failure (HHF) has poorer prognosis among Black Africans than the Caucasians [9]. The current study determines the prognostic factors of HHF among Black Africans.

Patients and methods

One hundred and twenty-six consecutive patients with newly diagnosed HHF and made of 69 Gambians (33 males + 36 females) and 57 Nigerians (29 males + 28 females) were recruited at the Royal Victoria Hospital, Banjul, The Gambia and University of Ilorin Teaching Hospital, Ilorin, Nigeria between January 1994 and December 1996. One hundred and seven (107) patients (52 Gambians and 55 Nigerians) made of 51 males and 56 females were followed up for 12 calendar months or till death while 19 patients were lost to follow-up.

Information on age, sex, occupation, educational status, alcohol intake and cigarette smoking was obtained. Socioeconomic status was determined using the British Registrar General Scale [10]. Intake of 20 or more units of alcohol and smoking of 20 or more sticks of cigarettes daily were considered significant alcohol consumption and cigarette smoking respectively [11,12]. The duration of diagnosis of hypertension was considered as the period between the diagnosis of hypertension and presentation with heart failure. Weight and height were measured with patients lightly clothed without shoes on. Obesity was defined as body mass index greater than or equal to 30K gm/m^2

A detailed clinical cardiovascular evaluation was carried out to detect the symptoms and signs of heart failure. These were grouped into the major and minor criteria of HF [13]. The major criteria included orthopnoea, paroxysmal nocturnal dyspnoea, raised jugular venous pressure, cardiomegaly, third heart sound with or without gallop rhythm and pulmonary rales while the minor criteria included dyspnoea on exertion, dry cough, pedal oedema, tachcyardia, tender hepatomegaly and ascites. A minimum of two major criteria or one and major plus two or more minor criteria are required to make a diagnosis of HF provided they are not attributable to causes other than HF [13].

Blood pressure was measured on the right upper arm after 10-15 minutes of rest using standard procedures and aneroid sphygmomanometer (Accoson), of size 15cm breadth and 100cm length. Three readings were taken. The average of the last two was taken as the blood pressure. Systolic blood pressure (Korotkoff sound phase I) > or = 140 mmHg and/or diastolic blood pressure (Korotkoff sound phase V) > or = 90 mmHg were required to make a diagnosis of hypertension [14].

All patients were evaluated for evidence of chronic hypertensive cardiovascular disease including thickened arterial wall or locomotor brachialis, accentuated aortic component of the second heart sound, retina artero-venous nipping and radiological evidence of unfolded aorta. Common causes of heart failure other than hypertension (anaemia, rheumatic heart disease, cardiomyopathy, pericardial diseases and congenital heart diseases) were excluded by clinical examination.

Laboratory evaluation included chest x-ray, 12-lead electrocardiography, packed cell volume, serum creatinine, urea, sodium, potassium and fasting blood sugar.

The followings were required to make a diagnosis of HHF:

1 Heart failure.
2 Hypertension.
3 Three or more evidence of chronic hypertensive cardiovascular disease.

4 Exclusion of causes of heart failure other than hypertension.

Patients with serum creatinine in excess of 200 umol/L were excluded from the study.

All patients had frusemide. This was substituted with bendrofluazide in some patients after recovery from HF. Oral potassium supplements were given except where contraindicated by concomitant use of captopril, an angiotensin converting enzyme inhibitor and potassium sparing agent. Single or combination antihypertensive therapy with captopril, alpha methyldopa, hydrallazine, prazosin and reserpine were used. Patients were responsible for procurement of drugs. The target blood pressure were systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mm Hg.

Follow-up was done at the outpatients' departments of the respective hospitals. All patients were counselled on compliance with medications and clinic appointments. The services of two indigenous Field Assistants (one in each country) and telephone enquiries where available, were utilized in tracing defaulters.

Endpoints: The endpoints of the study were:

1 Completed 12 months of follow-up.
2 Death.

Where death occurred, the duration of survival was considered as the period between the diagnosis of HHF and death.

Statistical analysis

Continuous variables are presented as Mean ± SD. Comparison of means between two groups were done using student's t-test while proportions were compared using chi-square test with Yate's correction as appropriate. Analysis of covariance (ANCOVA) was used to determine the difference between outcomes (survivor or deceased) adjusted for co-variables. Survival curve was determined using Kaplan-Meier's method [15].

Results

Of the 126 patients recruited, 107 (51 males + 56 females) made of 52 Gambians and 55 Nigerians aged between 17 and 79 years (mean 53.6 ± 12.1 years) completed the study. Nineteen patients were lost to follow-up. Of the 107 patients studied, 47 (44%) were previously unknown to be hypertensive. The duration of diagnosis of hypertension among the previously diagnosed hypertensive ranged from 0.5 to 23 years (mean 4.3 ± 4.7 years). Blood pressure ranged from 130 to 250 mmHg (mean 180.4 ± 2 mm Hg) systolic and 100 to 160 mmHg (mean 117.0 ± 12.9 mm Hg) diastolic. Only 10 (9.4%) and 21 (28.4%) patients were ethanol consumers and cigarette smokers respectively. Ten patients (9.4%) were obese. The mean packed cell volume; serum creatinine and urea were 38.1 ± 8.7%, 122.2 ± 39.9 umol/L and 6.1 ± 1.4 mmol/L respectively. Mean serum sodium and potassium levels were 140.8 ± 10.1 mmol/L and 4.3 ± 1.7mmol/L respectively. Mean fasting blood glucose was 4.8 ± 0.9mmol/L.

All patients had frusemide. Twenty-five patients (23.4%) had potassium supplementation. Potassium supplements were contraindicated in the remaining patients by concomitant use of captopril, an angiotensin converting enzyme inhibitor and potassium-sparing agent.

Table 1: Baseline characteristics of Nigerian and Gambian patients

Characteristics	Nigerians (N=55)	Gambians (N=52)
Sex: Female (%)	27 (49.1)	27 (51.9)
Male (%)	28 (50.9)	25 (48.1)
Undetected hypertension (%)	21 (38.2)	26 (50)
Cigarette smoking (%)*	2 (3.6)	19 (36.5)
Ethanol consumption (%)	7 (12.7)	3 (5.8)
Atrial fibrillation (%)	4 (7.3)	5 (9.6)
Anti HF treatment: Frusemide (%)	55 (100)	52 (100)
Captopril (%)	49 (89.1)	39 (75)
Digoxin (%)	7 (12.7)	5 (9.6)
Anticoagulant (%)	4 (7.3)	6 (11.5)
Anti-HF: Alpha methyl dopa (%)	45 (81.1)	37 (72.5)
Bedrofluazide (%)	15 (27.3)	15 (28.8)
Hydrallazine (%)	18 (32.7)	20 (68.5)
Prazosin (%)	6 (10.9)	4 (7.7)
Reserpine (%)	6 (10.9)	3 (5.8)
Age (years)	53.3 ± 11.5	52.3 ± 13.2
Systolic blood pressure mmHg	175.2 ± 22.2	183.0 ± 28.5
Diastolic blood pressure mmHg	115.7 ± 11.6	117.8 ± 12.7
Duration of hypertension (years)	3.9 ± 4.4	4.7 ± 4.7
Body mass index (Km/m²)	20.4 ± 6.3	20.2 ± 9.0
Cardio-thoracic index (%)	67.3 ± 4.0	66.3 ± 5.0
Serum creatinine umol/L	122.7 ± 41.9	121.5 ± 40.9
Serum urea mmol/L	6.0 ± 0.9	5.7 ± 1.2
Packed cell volume (%)	38.4 ± 6.4	40.1 ± 8.8

* $P<0.05$

Antihypertensive drugs and the proportions of patients who had them were alpha methyldopa (76.6%), captopril

(82.2%), bendrofluazide (28%), hydrallazine (26.2%), prazosin (9.4%) and reserpine (8.4%). Seventy-nine (73.8%) patients were on combination (two or more drugs) while 28 (26.2%) were on single anti-hypertensive therapy. The characteristics of The Gambian and Nigerian patients are shown in table 1. They were similar except that The Gambians had a higher proportion of tobacco users.

Of the 107 patients studied, 76 made of 38 Gambians and 38 Nigerians survived, whereas, 31 made of 14 Gambians and 17 Nigerians died, giving a one-year survival rate of 71%. One-year survival rate did not differ among the Gambians and Nigerian patients (73.1% versus 69.1%; x^2=0.06, P >0.05). Of the 31 deaths that occurred, 22 (71%) occurred during the first 3 months of HHF. This is reflected by a rapid fall in the survival curve during this period (Figure 1). One-year survival rate was significantly higher among the survivors of the first three months of HHF, compared to the patients as a whole (89.4% versus 71%; x^2=8.6, P <0.05). There was a strong negative correlation between cumulative survival and the duration of HHF (y=0.9812, x_2=0.1173, R=0.965) as shown in the trend line analysis in Figure l.

Compared to the survivors, the deceased (Table 2) had significantly higher systolic blood pressure (191.9 ± 32.2mmHg versus 175.1 ± 25.2mmHg; P <0.05), higher

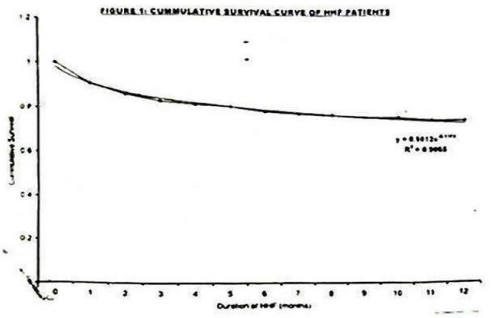

Fig. 1: Cummulative survival of HHF patients

Table 2: Univariate comparison of survivors and deceased HHF patients

Characteristics		Survivors (N=76)	Deceased (N=31)
Sex: N (%):	Females	36 (70.6)	15 (29.4)
	Males	40 (71.4)	16 (28.6)
Socioeconomic class N (%):	Upper/middle	27 (84.4)	5 (15.6)
	Lower	49 (65.3)	26 (34.7)
Knowledge of being hypertensive N (%)	Yes	47 (78.3)	13 (21.7)
	No	29 (61.7)	18 (34.7)
First 3 months of HHF N (%):*	All HHF patients	76 (71)	31 (39)
	Survivors of the first 3 months of HHF	76 (89.4)	9 (10.6)
Captopril medication N (%):*	Yes	66 (75)	22 (25)
	No	10 (52.6)	9 (47.4)
Age category N (%):*	< 40 years	5 (41.7)	7 (58.3)
	> or = 40 years	71 (74.1)	24 (25.3)
Mean age (years)*		55.6 ± 12.1	49.8 ± 13.3
Systolic blood pressure (mmHg)*		175.1 ± 25.2	191.9 ± 32.2
Diastolic blood pressure (mmHg)*		114.3 ± 10.3	123.7 ± 15.8
Body mass index (kg/m²)		22.1 ± 4.6	23.6 ± 6.4
Serum creatinine (umol/L)*		113.8 ± 36.4	148.6 ± 42.0
Cardio-thoracic index (%)*		66.2 ± 4.2	69.2 ± 39.0
Packed cell volume (%)		37.0 ± 4.3	35.0 ± 4.3

*P< 0.05

diastolic blood pressure (123.7 ± 15.8mmHg versus 114.3 ± 10.3mmHg; $P < 0.05$), higher cardio-thoracic index (69.2 ± 3.9% versus 66.2 ± 4.2%; $P < 0.05$) and higher serum creatinine (148.6 ± 42.2umol/L versus 113.8 ± 36.4umol/L; $P < 0.05$).

Mean age was significantly lower among the deceased than the survivors (49.8 ± 13.3 years versus 55.6 ± 12.1 years; $P < 0.05$). Compared to the patients aged 40 or more years, patients aged below 40 years had significantly lower one-year survival rate (41.7% versus 74.1%; $P < 0.05$), higher systolic blood pressure (200.2 ± 35.1mmHg versus 178.6 ± 26.3mmHg; $P < 0.05$), higher diastolic blood pressure (128.0 ± 16.4 mm Hg versus 116.4 ± 12.0mmHg; $P < 0.05$) and higher serum creatinine (152.0 ± 46.6umol/L versus 120.0 29.1umol/L; $P < 0.05$).

One-year survival rate was significantly higher among patients with captopril medication than those without (75% versus 52.6%; $P < 0.05$). Though one-year survival rate was higher among patients on multiple anti-hypertensive therapy than those on monotherapy (74.3% versus 68.8%), the difference was not statistically significant ($P > 0.05$).

One-year survival rate did not differ significantly between male and female patients (71.4% versus 70.6%; $P > 0.05$), between previously diagnosed and previously undiagnosed hypertensives (78.3% versus 61.7%; $P > 0.05$) and between tobacco users and non-tobacco users 71.4% versus 72.1%; $P > 0.05$). Though one-year survival was higher among patients in the upper/middle socioeconomic class than those in the lower class (84.3% versus 65.3%), the difference was not significant ($P > 0.05$).

After adjusting for co-variables, only serum creatinine had statistically differing values between the deceased and survivors ($df=1$ $SS=10272$, $F=7.60$, $p=0.007$).

The proportion of patients with alcohol intake (9.4%), atrial fibrillation (8.4%), obesity (9.4%), and those with digoxin (10.3%) and anticoagulant medications (10.3%) were each too small for meaningful statistical analysis.

Discussion

This study showed that the survivors and the deceased HHF patients differed in blood pressure levels, mean age, serum creatinine and cardio-thoracic index. The first three months of HHF appeared critical for survival since 71% of the total number of deaths occurred during this period. Furthermore, one-year survival rate was significantly higher among the survivors of this period compared to the study population as a whole. It was probable that the survivors of the first three months of HHF had sufficiently preserved systolic and diastolic functions, and responded early to anti-heart failure treatment. Early response to anti-heart failure treatment has been shown to be associated with good prognosis [16]. Trend line analysis also showed a strong negative correlation between cumulative survival and duration of HHF. This may enable projection of survival rate of HHF patients beyond a period of twelve months in the current report.

Increased blood pressure levels were associated with poor prognosis among HHF patients. This contrasts the findings in a report on Caucasians with HHF in whom no significant correlation between mortality and degree of hypertension was observed [17]. The differed findings may be explained by the presence of co-existing coronary artery disease among 64% of patients among the latter [17].

However, the prognostic value of blood pressure levels in HHF may not be uniform. Longstanding HHF may be associated with irreversible myocardial damage with consequential fall in cardiac output such that an elevated or even normal blood pressure cannot be sustained (Grade III HHF) [18]. In Grade III HHF, low or normal blood pressure in the absence of anti-hypertensive medication may therefore be an indicator of severely compromised myocardial function and poor prognosis. Low blood pressure has in fact been shown to be associated with poor prognosis among HF patients with impaired systolic function, whereas an opposite trend occurred in those with sufficiently preserved systolic function [19]. It is therefore probable that the majority of our patients had sufficiently preserved systolic function since they presented with the first attack of HF, and low blood pressure was associated with good prognosis.

Our patients also presented at a relatively younger mean age than the Caucasians (53 years versus 63 years) [17]. This may be because the African population has shorter life span and poorer blood pressure control. The prognostic value of age in HF is controversial. Advance age is generally thought to be associated with poor prognosis [6]. Analysis of the data from Veteran Affairs Co-operative Heart Failure Trials (V-HeFT) I and II however showed that though age correlated with the incidence of coronary artery disease and arrhythmias, it had no independent prognostic effect on survival [20].

In investigating the prognostic effect of age in HHF, the heterogeneous of hypertensive population has to be taken into consideration. It appears as shown in the current report that young age is associated with poor prognosis in a hypertensive population of relatively young mean age. The young hypertensive patients are more predisposed to higher frequency of undetected hypertension and renal impairment. Below the age of 70

years, mortality was highest among HHF Caucasians in the youngest age group, and this was also attributed to renal impairment among the younger patients [17].

Renal function is generally impaired in HF because of renal hypo-perfusion resulting from reduced cardiac output. The poor prognostic effect of serum creatinine in HF has been reported in a previous report [3]. Serum creatinine is however of particular interest in the current report because it is the only variable having independent prognostic value. Furthermore, the hypertensive kidney is at additional risk of arteriolonephrosclerosis. Therefore, the mean serum creatinine obtained among our patients is higher than the value reported in HF from other causes [3].

The prognostic value of cardio-thoracic index obtained in the current report does not differ from that reported in HF from other causes [4]. Autopsy studies have shown that Nigerians who died from HHF had large flabby hearts [21].

The positive influence of captopril (angiotensin converting enzyme inhibitor) on survival in HHF is probably due to its combined cardio-reparatory, anti-heart failure, anti-hypertensive and potassium conserving effects. The efficacy of angiotensin converting enzyme inhibitor in reduction of intra-hospital mortality among Nigerians with heart failure has been previously demonstrated [22]. However, the effect of captopril in the current report might be interpreted with caution because the study was not a double blind or controlled one primarily aimed at determining drug efficacy. Furthermore, confounding factors including compliance with medications was not measured; an important limitation given that medications were not free.

The influence of gender on the outcome of HF appears to differ according to its aetiology. In a population where HF is predominantly secondary to coronary artery disease, female gender is associated with a favorable prognosis [23]. This is because of the lipid lowering effect of estrogen and lower prevalence of coronary artery disease in premenopausal females [24]. Contrary to the findings among HHF Caucasians with a background of coronary artery disease [17], gender did not influence prognosis of HHF in the current report. This was because our study population is free of the burden of coronary artery disease. Furthermore, male and female indigenous Black African hypertensives have been shown not to differ strikingly in plasma lipid concentrations [25]. Consequently, feminine gender offered no prognostic advantage among indigenous Black Africans with HHF.

Cigarette smoking adversely influenced the outcome of HF secondary to dilated cardiomyopthy [7]. We were however unable to demonstrate a similar effect in the current report probably because of the relatively lower prevalence of tobacco users and lower quantity of tobacco intake among our patients. It has been shown that indigenous Black Africans smokers have less intake of tobacco than the Caucasians [26]. We were also unable to demonstrate the confirmed negative effect of ethanol consumption in HF because the proportion of patients with ethanol intake in the current report is too small for meaningful statistical analysis. This low prevalence of ethanol consumers is due to the dominance of Islamic faith that prohibits ethanol intake among our study population.

In conclusion, clinical and basic laboratory parameters could be useful prognostic indices of HHF. Contrary to the findings among Caucasians, gender has no prognostic value and young age conferred poor prognosis. The first three months of HHF was critical for survival.

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