

Echocardiographic and Clinical Correlates of Ejection Fraction Among 2000 Patients with Heart Failure in Western Saudi Arabia

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Introduction: Heart failure (HF) affects about 320,000 Saudi individuals and is associated with a considerable negative impact on the patients' quality of life. In literature, there is a lack of data about the echocardiographic abnormalities of HF patients in Saudi Arabia.

Aim of Work: To describe the echocardiographic findings of HF patients in Western Saudi Arabia.

Methodology: This was a retrospective record review study conducted on 2000 patients with chronic HF in Saudi Arabia. Demographic, clinical and echocardiographic data were collected and compared among patients with HF with reduced ejection fraction (HFrEF), ie, EF<40%; HF with mid-range EF (HFmrEF), ie, EF=41–49%; and HF with preserved EF (HFpEF), ie, EF≥50%.

Results: Among the 2000 patients studied, females constituted 46.3% of the sample. About 52% of females had HFpEF, whilst 70% of males had HFrEF ($p<0.0001$). Diastolic dysfunction occurred in 98% of HFpEF versus 78% of HFrEF ($p<0.0001$). Patients with HFrEF had higher left-ventricular diastolic (LVd) volume (1536 versus 826), higher left-ventricular systolic (LVs) volume (1660 vs 772), higher left atrial volume (1344 vs 875), higher aortic root dimension (1144 vs 929) and lower fractional shortening (FS) (267 vs 1213) than patients with HFpEF ($p<0.0001$).

Conclusion: HFpEF was more common among females and was associated with higher rates of diastolic dysfunction and higher FS. HFrEF was prevalent among males and associated with higher LVd, LVs, left atrium volume and aortic root dimensions.

Keywords: echocardiography, heart failure, Saudi Arabia, ejection fraction, HFpEF, HFmrEF, HFrEF

Introduction

Heart failure (HF) is the leading cause of cardiovascular morbidity and mortality worldwide.¹ It is estimated that HF affects about 1–2% of the adult population, and the prevalence increases to 10% among individuals above the age of 70 years.^{2,3} In developed countries, more than one million hospitalizations are attributed to HF, and the five-year mortality rate is estimated to be as high as 50%. Moreover, the burden of HF is anticipated to increase during the coming decades, due to the expanding pool of surviving patients and the growing elderly population.⁴ About 5 million individuals are diagnosed with HF worldwide, and the numbers are expected to increase by approximately 550,000 annually.³

Left-ventricular dysfunction is the initial pathophysiologic step in HF.⁵ It results from an insult to the myocardium (eg, ischemia) that leads to reduced systemic

perfusion and systemic venous congestion.⁶ The myocardium responds by remodeling and hypertrophy which, in turn, exacerbates the myocardial stress and results in mitral regurgitation.⁵ The diagnosis of HF is complex.⁷ Clinically, it is based on the patient's symptoms and clinical signs, which are sometimes non-specific, very subtle, or even absent. Less than 25% of the cases can be diagnosed clinically.⁸ Recent HF guidelines assert specific insights to detect subclinical left ventricular and diastolic dysfunction before the onset of symptoms. Though the standard physical examination can detect some signs of HF, the signs are seldom overt until advanced stages of HF, also, an accurate estimation of the cardiac output state and volume cannot be made solely based on clinical assessment.^{9,10} Echocardiography is the most appropriate diagnostic test for the initial assessment of HF patients, as recommended by the American College of Cardiology/American Heart Association guidelines for the diagnosis and management of HF.^{11,12} Echocardiography can evaluate the diastolic function, left-ventricular end-diastolic pressure and left atrial pressure, and demonstrate the morphologic, structural, functional and hemodynamic changes in HF, which give a clue for determining the etiology of the condition.¹³

Data about the prevalence, etiology, risk factors, diagnosis, and management of HF in the Middle East are scarce.^{14–19} About 320,000 individuals are being treated for HF in Saudi Arabia,¹⁷ and the etiological and risk factors for HF in Saudi Arabia are closely similar to those reported in western countries.^{20,21} There is a lack of data, however, on the echocardiographic findings of HF patients in Saudi Arabia. Hence, the main aim of this study was to examine and describe the echocardiographic findings of a sample of HF patients in Western Saudi Arabia.

Methodology

Study Design and Population

This was a retrospective record review study conducted on 2000 patients diagnosed with HF who were admitted at the King Abdulaziz University Hospital in Jeddah, Saudi Arabia during the years 2016 to 2018. All adult patients diagnosed with HF, based on both clinical and echocardiographic criteria, were eligible for recruitment to this study.^{22,23} Inclusion criteria included adult patients (≥ 18 years), both genders, any nationality, and chronic HF diagnosed based on the Framingham criteria for the

diagnosis of HF.²² Patients with acute HF and pediatric patients were excluded from this study.

Data Collection Procedure

The data were collected from the patients' records at the hospital. Both demographic data (ie, age, sex, and race), clinical data (ie, in-hospital mortality) and echocardiographic data (ie, ejection fraction (EF), left-ventricular diastolic volume (LVD), left-ventricular systolic volume (LVs), FS, left atrium volume, aortic root dimension and the existence of diastolic dysfunction) were collected. King Abdulaziz University Hospital granted access to the data for this study. All echocardiographic reports in our facility are written and/or approved by a cardiology consultant with echocardiographic experience. Diastolic dysfunction assessments were primarily made based on measurements in relation to mitral inflow, tissue doppler on the septum and lateral wall, pulmonary venous flow, and tricuspid velocity.

Statistical Analysis

Analysis of data was based mainly on the EF categories of the patients. All patients were divided according to their EF into three categories: patients with EF $\leq 40\%$, patients with EF between 41% and 49%, and patients with EF $\geq 50\%$. The distribution of EF was studied among the patients' demographic, clinical, and echocardiographic data. The impact of different variables on EF was also studied to determine which of them predicts the EF value.

All gathered data were fed into a computer, and analyzed using the IBM SPSS software version 20.0.^{24,25} Approximately 2.5% of data were missing. Categorical variables were expressed as frequency and percentages, while quantitative variables were presented as mean, standard deviation (SD) and mean ranks. The chi-square test of independence was conducted to explore the association of EF categories with various demographic and clinical factors. The Kruskal Wallis rank-sum test was conducted to examine the difference in mean ranks of various echocardiography variables with EF; differences in mean ranks were also presented with box-plots. Ordinal logistic regression was conducted to examine which demographic and echocardiographic variables had a significant effect on EF. The multivariate analysis Chi-Squared Automatic Interaction Detection (CHAID) classification algorithm was used to create a decision tree to select the most relevant covariate to predict the EF and to determine important cutoffs of significant predictors.

Ethical Considerations

All data collected from the patients' records were anonymous. On hospital admission, all patients sign a written informed consent that they agree to the use of their recorded data (anonymously and confidentially) for research purposes. A copy of these consents was taken, and the ethical committee of King Abdulaziz University, Jeddah, Saudi Arabia approved this study.

Results

Among the 2000 patients studied, Saudi individuals constituted 43.5% of the cases. The remaining patients were of different nationalities, including Pakistani, Yemeni, Sudanese, Palestinian, Philippine, and Mauritian. Females constituted 46.3% (n=925) of the recruited sample.

On studying the distribution of EF categories among the studied patients according to their demographics, there were significant differences according to patients' gender and diastolic dysfunction. Males constituted the vast majority of patients with EF of 40% or less and EF between 41% and 49% (70.1% and 63.5%, respectively), whereas females constituted more than half of the patients (52%) with EF \geq 50% ($p < 0.0001$). Similarly, the number of patients with diastolic dysfunction was significantly higher than those without diastolic dysfunction in all categories of EF (78% of patients with EF \leq 40%, 82.5% of patients with 41–49% and 97.9% of patients with EF \geq 50%, $p < 0.0001$). The detailed

description of EF category distribution among patients according to their demographics, clinical and diastolic dysfunction is depicted in [Table 1](#).

Concerning the echocardiographic findings, there was a significant association between the EF categories and all studied echocardiographic parameters ([Table 2](#)). It was noted that higher LVd (1536), higher LVs (1660), higher left atrium volume (1344), and higher aortic root dimensions (1144) were encountered among patients with EF \leq 40% ($p < 0.0001$). In contrast, lower FS (267.35) was associated with EF \leq 40% ($p < 0.0001$). [Figure 1](#) demonstrates the differences in LVd, LVs, FS, left atrium volume, and aortic root dimensions among different EF categories.

To study the odds of different demographic, clinical, and echocardiographic variables for determining the EF category, an ordinal logistic analysis was conducted. The model was evaluated based on an alpha of 0.05. The results of the model were significant ($\chi^2 = 1314.27$, $p < 0.001$). McFadden's R-squared was calculated to examine the model fit, where values greater than 2 were indicative of models with excellent fit.²⁶ The McFadden R-squared value calculated for this model was 0.48. The regression coefficient for LVd was significant ($B = -0.99$, $\chi^2 = 62.66$, $p < 0.001$), suggesting that a one-unit increase in LVd would decrease the odds of observing a higher category of EF by 62.91%. Similarly, the regression coefficient for FS was significant ($B = 0.16$, $\chi^2 = 292.69$, $p < 0.001$), suggesting that a one-unit increase in FS would increase the odds of observing a higher category of EF by

Table 1 Distribution of Ejection Fraction Categories Among HF Patients in Saudi Arabia According to Their Nationality, Sex, Associated in-Hospital Mortality and Diastolic Dysfunction (n=2000)

		Ejection Fraction						P-value
		≤40%		41–49%		≥50%		
		n	(%)	n	(%)	n	(%)	
Nationality	Saudi Non-Saudi	168 232	(42.0) (58.0)	49 76	(39.2) (60.8)	653 793	(45.2) (54.8)	0.274
Sex	F M	120 281	(29.9) (70.1)	46 80	(36.5) (63.5)	759 701	(52.0) (48.0)	0.000*
In-Hospital mortality	No Yes	379 22	(94.5) (5.5)	122 4	(96.8) (3.2)	1409 51	(96.5) (3.5)	0.171
Diastolic Dysfunction	No Yes	88 312	(22.0) (78.0)	22 104	(17.5) (82.5)	31 1427	(2.1) (97.9)	0.000*

Note: *Statistically significant.

Abbreviations: N, number; HF, heart failure.

Table 2 Distribution of Ejection Fraction Categories According to Different Echocardiographic Findings Among the Studied Patients (n=2000)

	EF (%)	n	Mean Rank	P-value
LVd	≤40%	398	1536.54	0.000*
	41–49%	126	1146.08	
	≥50%	1455	826.98	
LVs	≤40%	398	1660.32	0.000*
	41–49%	126	1388.51	
	≥50%	1455	772.13	
FS	≤40%	392	267.35	0.000*
	41–49%	122	511.52	
	≥50%	1447	1213.91	
Left Atrium	≤40%	391	1344.03	0.000*
	41–49%	125	1082.66	
	≥50%	1447	875.48	
Aortic Root	≤40%	388	1144.25	0.000*
	41–49%	125	1002.65	
	≥50%	1440	929.71	

Note: *Statistically significant.

Abbreviations: EF, ejection fraction; FS, fractional shortening; LVd, left-ventricular diastolic dimension; LVs, left-ventricular systolic dimension, n, number.

16.96%. The remaining studied variables were insignificant (Table 3).

The Chi-Squared Automatic Interaction Detection classification algorithm was used to create a decision tree to select the most relevant covariate to predict EF. Nationality, sex, in-hospital mortality, along with echocardiography variables (LVd, LVs, FS, left atrium volume, aortic root dimension, and diastolic dysfunction) were selected as input variables. LVs were found to be the most important and significant factor (Chi-Squared=1345.39, df=10, P-value=0.000): 97.5% of the cases with EF≥50 were observed to have an LVs of ≤2.77 (Node 1), whilst only 2% of cases with EF≥50 were found to have an LVs more than 4.62 (Node 6). Along with LVs, left atrium volume was also found to be significantly associated with EF in the LVs “≤2.77” subgroup (Chi-Square=26.32, df=4, P-value=0.003): 99.2% of the cases with EF≥50 were found to have a left atrium volume of 3.72 or less (Node 7). In the subgroup of patients with LVs between 3.19 and 3.6, LVd was noted to be significantly associated with EF (Chi-Square=64.3, df=2, P-value=0.000), ie, 92.7% of cases with EF≥50 were found to have an LVd of 4.79 or more (Node 11). In the subgroup of patients with LVs between 3.6 and 3.92, FS was significantly associated with EF (Chi-Square=78.6, df=2, P-value=0.000): 93.5% of cases with EF≥50 were found to have an FS>26.5

(Node 13). In the subgroup of patients with LVs between 3.19 and 3.60 and LVd more than 4.79, a significant association was noted between FS and EF (Chi-Square=29.59, df=2, P-value=0.000). About 99% of patients with EF≥50 were noted to have an FS of more than 32.3. The remaining studied variables (ie, sex, nationality, in-hospital mortality, aortic root dimension, diastolic dysfunction) were insignificant (Figure 2).

Discussion

Patients with HF are categorized according to their ejection fraction into patients with HF with reduced EF (HFrEF), ie, EF≤40%, patients with HF and mid-range EF (HFmrEF), ie, EF between 41% and 49% and patients with HF and preserved EF, ie, EF≥50% (HFpEF).^{27,28} This classification was proposed by the European society of cardiology (ESC) for the determination of the etiology of HF and for deciding the best treatment modality for different patients.^{11,28} In this study, echocardiographic findings were studied in 2000 patients with HF in Saudi Arabia. The findings were studied in correlation with different clinical and demographic variables.

In terms of gender, females recruited to this study were more likely to have HFpEF, whereas males were more likely to have HFmrEF or HFrEF. This is in accordance with data from reported literature, where HFpEF was more commonly encountered among females than males.²⁹ The results of previous studies demonstrated that HF among females is more likely to be caused by atrial fibrillation and hypertension, whilst the main cause of HF among males is ischemic heart disease.^{29–34}

Diastolic dysfunction was more prevalent among patients with HFpEF. In accordance with what was reported in the literature, patients with HFpEF are more likely to have diastolic dysfunction than patients with HFrEF owing to the pathophysiology of the HF.^{35,36} From the pathophysiology point of view, HFpEF is a disease of diastolic dysfunction.^{36,37} It manifests with raised end-diastolic pressure, raised left atrial filling pressure, increased myocardial wall stiffness and increased left atrial filling pressure, alteration in the preload, alteration in the end-diastolic volume and decreased elasticity and recoil of the myocardial vasculature.³⁸ Patients with HFpEF have more extensive perivascular fibrosis, more collagen crosslinking, more fibrotic signaling (eg tissue growth factor-beta 1), and more left-ventricular stiffness than patients with HFrEF.³⁹ This explains our findings.

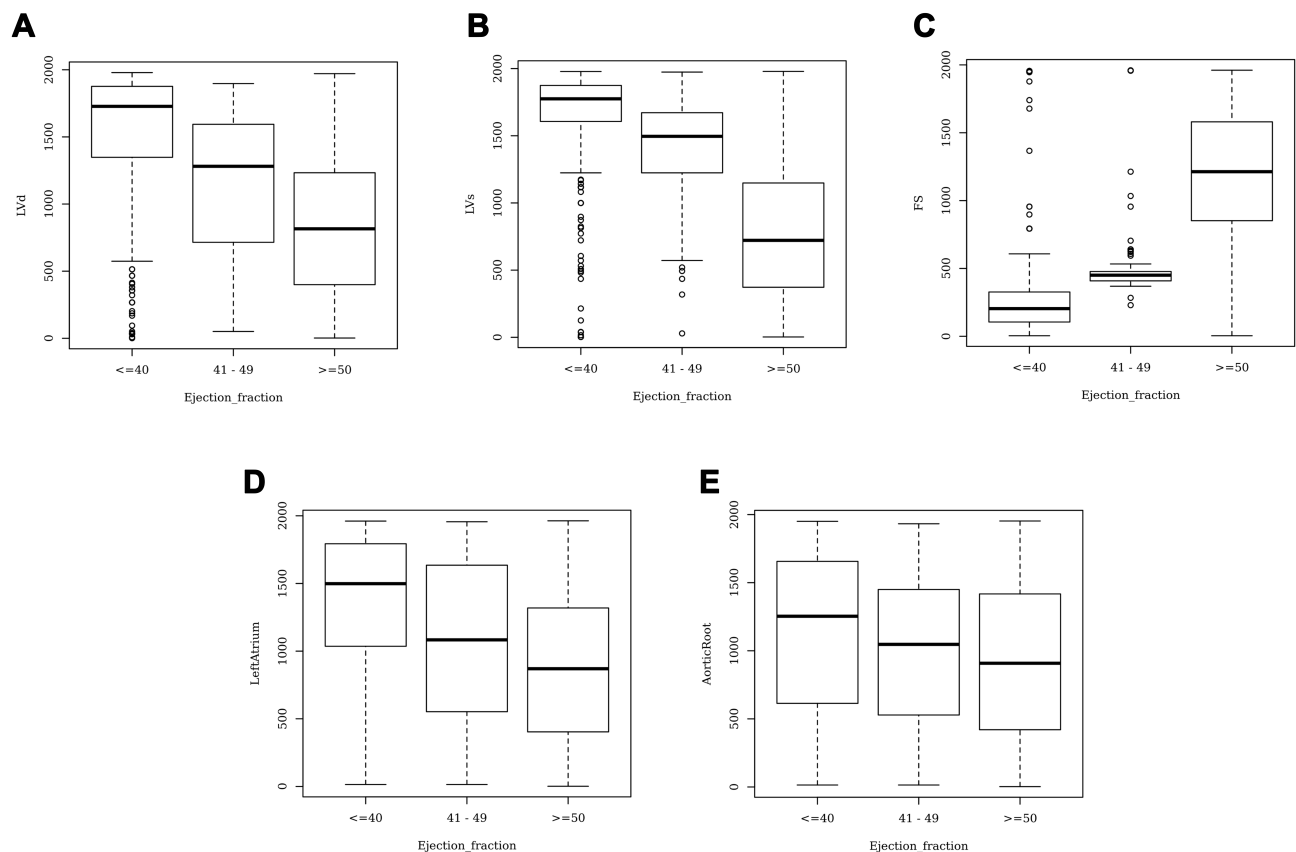


Figure 1 The differences in LVd (A), LVs (B), FS (C), left atrium volume (D) and aortic root dimensions (E) among the different ejection fraction categories in the studied patients (n=2000).

Abbreviations: LVd, left-ventricular diastolic volume; LVs, left ventricular systolic volume; FS, fractional shortening.

Mortality rates among patients with HFrEF, patients with HFmrEF, and patients with HFpEF were not significantly different. In disagreement with our results, patients with HFpEF had worse mortality rates than patients with HFrEF.⁴⁰ Patients with HFrEF were reported to improve on treatment and, therefore, achieve a better outcome, whereas patients with HFpEF worsened over time due to progressive myocardial remodeling, progressive systolic dysfunction, and deterioration of the EF.^{41,42} With regards to patients with HFmrEF, conflicting data exist in the literature.⁴³ HFmrEF patients may have one of the two courses; either remodeling of the myocardium and progressive reduction of EF, or improvement with therapy as patients with HFrEF.⁴¹ Such conflicting data may increase the importance of monitoring disease trends in HF, especially in the mid-range group, as improving or decreasing function may play a pivotal role in determining the prognosis in this group of patients.⁴³ The differences noted in our study may be either due to the different

demographic sample characteristics or due to the low number of in-patient mortalities encountered in our sample.

Upon studying the different echocardiographic findings among different types of HF, higher FS was commonly encountered among patients with HFpEF, whereas higher LVd, LVs, left atrial volume and aortic root dimension were encountered among patients with HFrEF. In the current study, diastolic dysfunction, LVd, and FS were the only significant correlates of the EF on logistic regression analysis. The higher the LVd, the lower the Fs, and the less the diastolic dysfunction, the more likely the EF would be decreased and the patient would have HFrEF. Interestingly, HFmrEF patients did not show echocardiographic signs of left-ventricular dysfunction as in the HFpEF group: their echocardiographic features were similar to HFrEF patients, which may indicate that those patients might be of the phenotype who would improve on a long-term basis with treatment. There was no significant difference between HFmrEF

Table 3 Ordinal Logistic Regression of Clinical and Echocardiographic Correlates of Ejection Fraction

Predictor	B	SE	95% CI	χ^2	OR	p
Sex (Male)	0.01	0.15	[-0.30, 0.29]	0.00	1.01	0.973
Nationality (None-Saudi)	-0.12	0.14	[-0.15, 0.38]	0.75	0.89	0.387
In-Hospital mortality (Yes)	-0.36	0.32	[-0.27, 0.98]	1.23	0.70	0.267
LVd	-0.99	0.13	[0.75, 1.24]	62.66	0.37	<.001
LVs	0.00	0.00	[-0.00, 0.00]	0.04	1.00	0.839
FS	0.16	0.01	[-0.17, -0.14]	292.69	1.17	<.001
Left Atrium	0.01	0.06	[-0.13, 0.11]	0.04	1.01	0.845
Aortic Root	-0.02	0.17	[-0.32, 0.36]	0.01	0.98	0.903
Diastolic Dysfunction (Yes)	1.05	0.24	[-1.52, -0.58]	19.00	2.86	<.001

Abbreviations: B, standardized coefficient; FS, fractional shortening; LVd, left-ventricular diastolic volume; LVs, left ventricular systolic volume; SE, standard error of the estimate; OR, odd's ratio; χ^2 , chi-square.

and HFrfEF in terms of left-ventricular dysfunction and wall changes, and ventricular dysfunction was significantly more common in HFpEF patients.

The strengths of this study are that it is, to the best of our knowledge, the first study to describe echocardiographic findings in patients with HF in Saudi Arabia; and that it was conducted on a large sample. One of the limitations of our study is that we could not track the patients longitudinally to track any changes in the EF in the future. Another limitation was that the mortality rates calculated were only the in-patient mortality, not the

overall mortality because a significant proportion of the patients could not be reached after discharge. Additionally, risk factors for HF (eg hypertension, smoking, diabetes, coronary artery disease, cardiomyopathy, etc.) were not included in our study. These limitations should be considered in future research.

Conclusion

Females with HF in Saudi Arabia were more likely to have HFpEF, whereas males were more likely to have HFmrEF or HFrfEF. In-hospital mortality rates were comparable

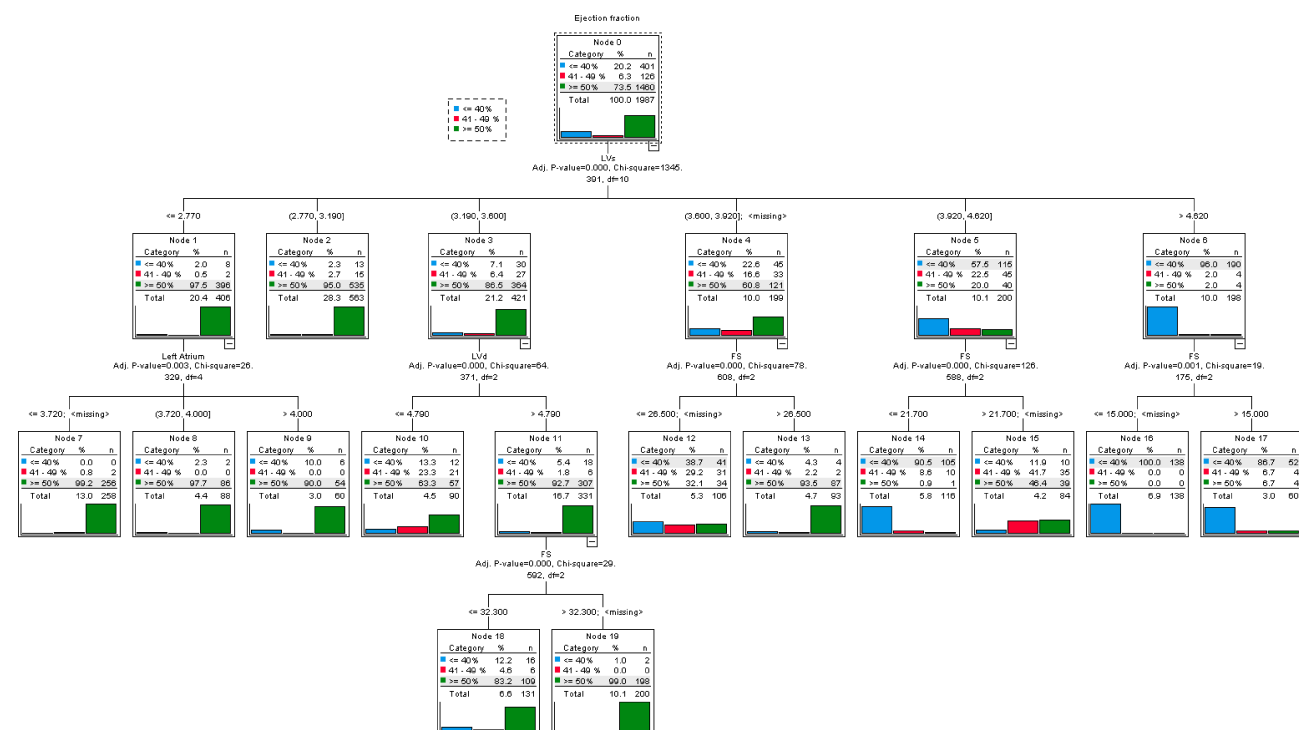


Figure 2 Tree diagram for ejection fraction with nationality, sex, in-hospital mortality, LVd, LVs, FS, left atrium volume, aortic root dimension, and diastolic dysfunction. **Abbreviations:** LVd, left-ventricular diastolic volume; LVs, left ventricular systolic volume; FS, fractional shortening.

between the three types of HF. FS was common among patients with HFpEF, whilst LVd, LVs, left atrium volume and aortic root dimensions were higher among patients with HFrEF. Knowledge about the echocardiographic findings among patients with HF in Saudi Arabia can provide a clue about the etiologies, risk factors, prognosis, and management plans required for those patients in the country, and therefore, assist in establishing appropriate preventive and therapeutic strategies for disease management.

Disclosure

The authors report no conflicts of interest in this work.

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