The Outcome of Diabetic Patients with Cardiomyopathy in Critical Care Unit: Hospital and Short-Term Outcome in a Period of Six Months to One Year

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Abstract

BACKGROUND: Diabetes mellitus (DM) is a major risk factor for heart failure (HF) and coronary artery disease (CAD). DM may cause structural changes involving the left ventricle (LV) systolic and diastolic function.

AIM: To compare patients who have diabetes and ischemic cardiomyopathy (ICM) to those with diabetic cardiomyopathy (DMCMP) regarding LV systolic function, diastolic function, in hospital long term and short-term mortality.

METHODS: Ninety diabetic patients with heart failure and left ventricular ejection fraction (LVEF) ≤ 35%, admitted to Critical Care Medicine department Cairo University were divided into two groups based on coronary angiography results; group I (ICM) n = 48 patients and group II (DMCMP) n = 42 patients.

RESULTS: Group I patients had higher mean age (63 ± 7 years), (p = 0.004), Hypertension (p < 0.001) and dyslipidemia (p = 0.008) were significantly more present in group I compared to group II. No significant differences were found regarding LVEF, global longitudinal strain (GLS), E/A and E/É ratio in both groups. A significant difference in the wall motion score index (WMSI) in group I; (1.4 ± 0.4) versus group II; (1.1 ± 0.2), (p = 0.005) was found. In the study, 6 patients had a cardiogenic shock with no documented in-hospital mortality. At 6 months, statistically, significantly higher mortality rates were found in group I, (p = 0.006), while at one year there was no significant difference in the mortality between the two groups, (p = 0.077). In comparison of the survived and non-survived patients at 6 months and one year in group I (ICM) there was a significant difference in LVEF (40 ± 6% vs 23 ± 6%, p < 0.001), GLS (- 8.1 ± 2.4 vs - 4.6 ± 2.6, p = 0.007), E/A (1.25 ± 0.91 vs 1.8 ± 0.5, p = 0.038), E/É (11.68 ± 7.5 vs 21.3 ± 3.6, p = 0.001) respectively. In group II (DMCMP) there was no documented mortality at 6 months follow up, however, at one year there was statistically significant difference in the mortality between survived and non-survived patients; the LVEF (35 ± 8% vs 25 ± 2%, p = 0.014), GLS (-7.9 ± 2.9% vs -5 ± 0.1%, p = 0.032), E/A (1.45 ± 0.8 vs 3.3 ± 0, p = 0.006) respectively. The E/É ratio in group II was not significantly different between the groups (15.73 ± 5.3 vs 15 ± 1, p = 0.873).

CONCLUSION: The combination of cardiomyopathy and diabetes affects LV systolic and diastolic function; however; ischemic cardiomyopathy and diabetic cardiomyopathy had a similar systolic and diastolic function. Ischemic cardiomyopathy is associated with worse prognosis compared to diabetic cardiomyopathy.

Introduction

Diabetes mellitus (DM) is a major risk factor for cardiovascular diseases, including coronary artery disease (CAD), congestive heart failure (CHF) and atrial fibrillation [1]. DM is associated with increased risk of cardiovascular-related deaths. Diabetes can lead to heart failure not only by augmenting coronary artery disease through macroangiopathy but also through structural changes involving the left ventricle (LV) causing systolic and diastolic dysfunction [2].

We aimed to compare diabetic patients, who have ischemic cardiomyopathy (ICM) to those with diabetic cardiomyopathy (DMCMP) in terms of clinical course, left ventricular (LV) systolic function, diastolic function, in-hospital long and short-term mortality.

Methods

Our study included 90 diabetic patients with decompensated heart failure due to cardiomyopathy with LVEF ≤ 35% admitted to Critical Care Medicine department over 16 months (March 2016- July 2017). Excluded from the study were patients with valvular heart disease, patients with diastolic heart failure and those with poor echocardiography window. The study was approved by the ethical committee at the faculty of medicine at Cairo University. Written consent was taken from all patients on admission.

Complete disease history was performed for all patients, analysis of risk factors of coronary artery disease (CAD) and heart failure such as arterial hypertension, dyslipidemia, smoking and family history of CAD; detailed physical examination with special emphasis on Killip classification; coronary angiography to differentiate ischemic from diabetic cardiomyopathy and echocardiographic assessment of LV systolic and diastolic function using ultrasound machine (Philips ultrasound,100-127/220240V~50/60Hz,1010 VA).

Echocardiography included the conventional 2D examination and speckle tracking to assess LV strain. The study was stored in a digital format with patient identity and file number.

The study was analysed by two experienced echocardiographers blinded to the study; the following parameters were measured for evaluation of LV geometry and function: left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left ventricular ejection fraction (LVEF) measured using the modified Simpson's method.

Figure 1: Example of assessment of global longitudinal myocardial strain (GLS) as provided by the EchoPAC software: apical long-axis view, 4-chamber view, and 2-chamber view. In the lower panel, the "bull's eye" plot, using a 17-segment model, provides the value of longitudinal strain for each segment of the left ventricle and the values of longitudinal strain of apical long-axis (GLPSS-LAX), 4-chamber (GLPSS A4C), 2-chamber (GLPSS A2C), and the value of GLS(GLPSS Avg)

Quantification of LV mechanics was done according to the recommendation using 2D speckle tracking echocardiography. A standard 2D ultrasound images were obtained. Three waves were analysed for longitudinal LV strain in the apical 4 chamber, apical 3-chamber and apical 2-chamber views. Cut off values of less than -20% were used as indicators of systolic dysfunction.

The regional wall motion abnormality (RWMA) was expressed by wall motion score (WMSI) which was calculated according to American Society of Echocardiography 17-segments model in which (normal = 1, hypokinetic = 2, akinetic = 3, dyskinetic = 4, aneurysmal = 5) Score was calculated by averaging the sum of the 17 segments. RWMA was considered present if WMSI > 1 [3].

Assessment of diastolic function was done according to the update of the American society of echocardiography imaging and the European association of cardiovascular imaging (2015) [4]. Mitral inflow was assessed by pulsed-wave Doppler from apical four-chamber view during diastole.

A one or two mm sample volume was placed between the tips of mitral flow leaflets during diastole and the following parameters were measured: peak E velocity (m/s), peak A velocity (m/s), E/A ratio, annular É (m/s) by tissue Doppler at the level of mitral annulus and the E/É ratio. The E/É ratio > 15 indicates elevated left ventricular filling pressure (LVFP), whereas E/É < 8 indicates normal left ventricular filling pressure [5].

The study population was divided into two groups based on coronary angiography data: Group I included patients with ischemic cardiomyopathy (n = 48). Group II included patients with diabetic cardiomyopathy (DMCMP) (n = 42).

Ischemia was defined as inadequate blood supply (circulation) to a local area due to blockage of the blood vessels supplying that area. Stenosis of 70% in a main coronary artery (> 2.5 mm) in one angiographic projection, or 50% in two projections, and 50% of the left main coronary artery [6].

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 24. Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis and Mann-Whitney tests _(Chan, 2003a)_ [7]. For comparing categorical data, Chi-square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5 _(Chan, 2003b)_. P-values less than 0.05 were considered statistically significant [8].
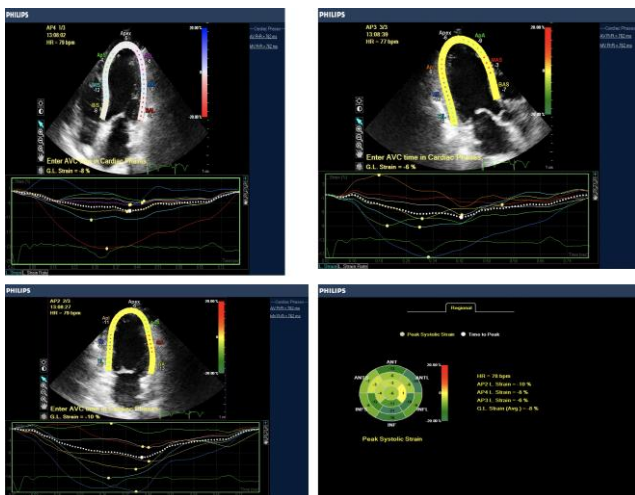
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Results

The mean age of the whole study group was 60 ± 10 years, with 18/90 females (20%) and 72/90 males (80%). The mean age in group I was 63 ± 7 years and 55 ± 11 years in group II with a statistically significant difference, (p = 0.004). Both groups had the same gender distribution (9 females in each group), (Table 1).

Table 1: Mean age of study groups

ICM n = 48		DMCMP n = 42	
Age	Mean ± SD	Mean ± SD	p-value
	63+7	55 +11	0.004

There was a statistically significant difference between both groups regarding HTN and dyslipidemia, both with a higher incidence in group I, p < 0.001; p = 0.008 respectively, (Figure 2).
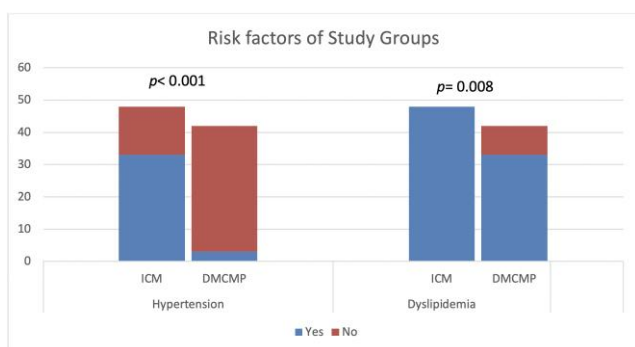

Figure 2: Hypertension and dyslipidemia as risk factors in both groups and p-value

There was no statistically significant difference between both groups regarding the type and duration of DM, wherein group I; 27/48 patients (57%) had non-insulin dependent type two diabetes mellitus (T2DM) and the mean duration of DM was 7.7 ± 2.6 years. In group II; 21/42 patients (50%) were non-insulin dependent T2DM, and the mean duration of DM was 8.3 ± 3.8 years.

All studied patients were classified according to Killip classification; with no statistically significant difference between the two groups, (p = 0.131), (Table 2).

Table 2: Killip classification in both groups

Killip Classification	ICM n = 48 (%)	DMCMP n = 42(%)	P-value
Class II	15/48 (32)	18/42 (43)	
Class III	30 /48 (62)	21/42 (50)	
Class IV	3/48 (6)	3/42 (7)	0.131

Out of the studied population, 33 patients (36%) were on inotropic and vasopressor support, namely dobutamine and norepinephrine, out of whom 21 patients were in group 12 patients and I in group II.

Comparison of both systolic and diastolic function of both groups

The left ventricular internal dimensions were not statistically significantly different between both groups; the mean LVEDD was 6.1 ± 0.9 cm in group I and 6.1 ± 1.2 cm in group II with p = 0.926, the mean LVESD in group I was 4.8 ± 1 cm and 5 ± 1 cm in group II with p = 0.682.

There was no statistically significant difference between the two groups regarding global LV systolic function. The mean LVEF was (36 ± 9% in group I versus 35 ± 8% in group II, P = 0.497). The mean GLS was (-7.7 ± 3% in group I vs -7.9 ± 2.9% in group II p = 0.674). The mean WMSI was statistically significantly different in both groups, (1.4 ± 0.4 vs 1.1 ± 0.2, respectively, p = 0.005).

There was no statistically significant difference between both groups as regards to LV diastolic function except for annular É. The mean E/A ratio was (1.5 ± 0.9 in group I vs 1.45 ± 0.8 in group II, p = 0.417) while the mean É was statistically significant (4.6 ± 1.3 m/s in group I vs 6.1 ± 2.7 m/s in group II, p = 0.009), the mean E/É ratio was (15.6 ± 5 in group I vs 15.73 ± 5 in group II, p = 0.278).

In-hospital survival at 6 months and one year of both groups

All patients had survived in-hospital course with no documented mortality, even those admitted with cardiogenic shock. After 6 months, 9 patients died in group I and non in group II with a statistically significant difference, p = 0.006. After one year 3 patients died in group II with no other documented mortality in group I and non-statistically significant difference, p = 0.077. So, the total mortality was 12 patients in the whole study population (Figure 3).
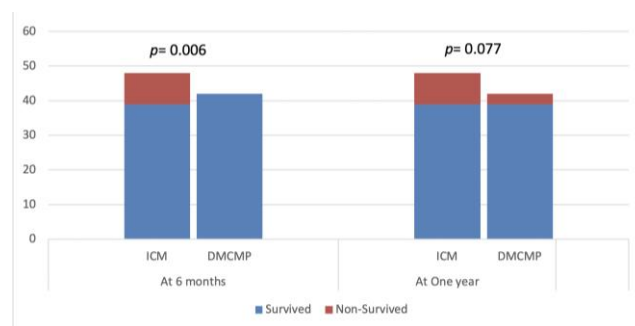

Figure 3: Survival rates at 6 months and one year in both study groups and p-value

The relation of the mean duration of diabetes mellitus to the mortality of patients in both groups was not statistically significant at both 6 months, and one year (p = 0.955 and 0.837 respectively).

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Relation of systolic and diastolic function to survival at 6 months and one year in group I

We studied the relation of different echocardiographic values to the mortality after 6 months and one year in group I; there was a statistically significant difference between survived and non-survived patients in terms of LV systolic and diastolic function, with mean LVEF 40 ± 6% vs 23 ± 6%; p < 0.001 respectively, and mean GLS of -8 ± 2.4% vs -4.67 ± 2.6%, p = 0.007 respectively. The mean E/A ratio was 1.25 ± 0.91 vs 1.8 ± 0.5, p=0.038 and the mean E/É was 11.68 ± 7.5 vs 21 ± 3.6, p = 0.001 respectively in the group of survivors versus non-survivors. These findings remained constant after one year as there were no new mortalities recorded in this group (Figure 4).
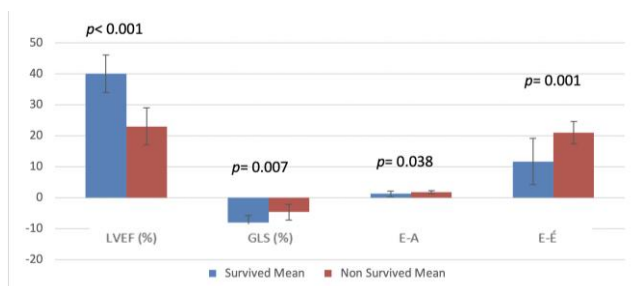

Figure 4: Systolic and diastolic echocardiography values at 6 months and one year in ICM

Relation of systolic and diastolic function to survival at 6 months and one year in group II

We studied the relation of echocardiographic values to the mortality after 6 months and one year in group II; at 6 months there was no mortality in this group, and the mean systolic function for survived patients was; LVEF (35 ± 8%), GLS (-7.9 ± 2.9%) respectively. The mean diastolic LV function for the survived group was: E/A (1.45 ± 0.8), E/É (15.7 ± 5.3) respectively.
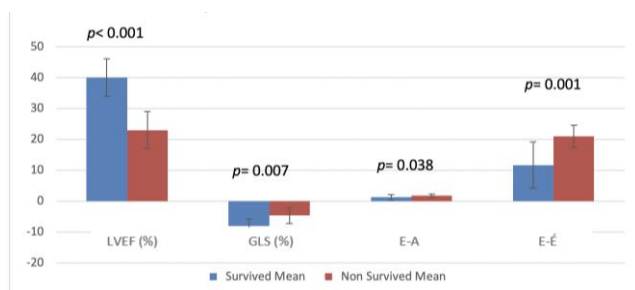

Figure 5: Systolic and diastolic echocardiography values at 6 months and one year in DMCMP

However, there was a statistically significant difference between survived and non-survived patients after one year in LV systolic and diastolic function, where the mean LVEF was 35 ± 8% vs 25 ± 2%, p = 0.014 and the mean GLS was -7.9 ± 2.9% vs

-5 ± 0.1%, p = 0.032 respectively for the group of survivors and non-survivors. The mean E/A ratio in survived patients was 1.45 ± 0.8, and in the group of non-survivors 3.3 ± 0, p = 0.006. However, the mean E/É was non-significantly different in both groups of patients (15.73 ± 5.3 vs 15 ± 1, p = 0.873), (Figure 5).

Discussion

Diabetes mellitus (DM) is a chronic metabolic disorder with steadily increasing prevalence all over the world [9]. Diabetic cardiomyopathy (DMCMP) [10] is a cardiac dysfunction which affects approximately 12% of diabetic patients, leading to overt heart failure and death. However, there is no efficient and specific methodology for the diagnosis of diabetic cardiomyopathy, possibly because molecular mechanisms are not fully explained, and it remains asymptomatic for many years [11].

Left ventricular systolic function is routinely quantified by measuring LVEF [12]. Two-dimensional speckle tracking echocardiography in recent years has emerged as a method for assessing LV systolic function. Global longitudinal strain (GLS), obtained by 2-dimensional speckle tracking echocardiography is a measurement that has previously been demonstrated to be of prognostic value, GLS provided incremental prognostic information when added to a model including conventional echocardiographic parameter and clinical predictors [13].

In our study, the mean age in group I was 63 ± 7 versus 55 ± 11 years in group II with a statistically significant p = 0.004. Diastolic echocardiography indices in group I was higher with advanced age compared to group II, indicating the effect of age on diastolic function. These findings in our study were similar to that of Kane et al., (2011) who studied the effect of age on diastolic dysfunction. The study concluded that age-related progression of diastolic dysfunction in the population contributes to the pathophysiologic changes which cause severe heart failure in these patients [14].

In a group, I (57%) had non-insulin dependent T2DM, and the mean duration of DM was 7.7 ± 2.6 years while in group II (50%) were non - insulin-dependent with a mean duration of diabetes of 8.3 ± 3.8 years. We compared our study findings with that of _Zoungas S et_ al., (2014), who studied the effect of mean age at diagnosis of diabetes and the duration of the disease which was 7.9 ± 6.4 years. He stated that the long duration of diabetes was associated with the risk of microvascular events and this effect was greater in the younger patients. No interaction was observed between diabetes duration, age and the risk of macrovascular events or death [15].

In our study we measured both LVEF and GLS in both our study groups as a marker of systolic function and we compared our results to Sengeløv et al., (2015) who stated that speckle tracking echocardiography, specifically GLS, is superior to conventional echocardiographic parameters, including left ventricular ejection fraction, in predicting all-cause mortality in patients with heart failure with reduced ejection fraction (HFrEF) [13].

Senglov et al. also investigated the prognostic value of global longitudinal strain (GLS) about the patient with HFrEF and concluded that GLS is an independent predictor of cause mortality and is a superior prognosticator compared to all other echocardiographic parameters in predicting mortality in these patients [13], [16].

The finding goes hand in hand with our results since the mortality rate was higher in patients with low GLS and low LVEF in both our study groups.

Also, Argulian et al., (2016) stated that the GLS is the most reliable method of detecting systolic dysfunction and that cut off value of (-20%) is considered normal while values less than (-20%) are abnormal and indicate systolic dysfunction [16]. We found that most of our patients had a GLS of less than (-15%), which indicated systolic dysfunction.

Radwan et al., in (2016) assessed the GLS in 80 patients who had cardiomyopathy and were divided into two groups, one with CAD and the other without CAD according to angiography. The study showed that the GLS measure is a sensitive and accurate tool in predicting severe CAD. The study used a low cutoff value of GLS -15.6% in which patients with GLS less than -15.6% had significant obstructive CAD stenosis > 70% [17].

In our study, the RWMA was assessed by measuring the (WMSI). There was a statistically significant difference between both study groups.

The wall motion score index (WMSI) in group I with ICM was higher than that in group II and this was explained by the presence of CAD and risk factors such as hypertension, dyslipidemia, and positive family history of CAD which played a role in the occurrence of wall motion abnormalities. In group II with DMCMP, the presence of wall motion abnormality might be explained by atherosclerotic changes which are pronounced in diabetic patients and also the development of micro thrombosis.

The findings in our study go hand in hand with Esmaeilzadeh et al. (2013) who studied the correlation between WMSI with coronary artery lesions. The study stated that a normal LV has a wall motion score index of 1 and the index increases as wall motion abnormalities increase in severity. The study concluded that a WMSI of 1.1-1.9 could predict small infarct size, and an index greater than 2.0 predicts the occurrence of complications and increase mortality [18]. However, a combined study of LVEF, WMSI and GLS proved superiority and accuracy of GLS in predicting long term outcome in ischemic cardiomyopathy [19].

LV diastolic function is assessed by many indices, such as the ratio of peak early to late diastolic filling velocity E/A ratio and tissue doppler mitral early diastolic velocity (E) combined with peak transmittal annular early diastolic velocity (É) in order to obtain a dimensionless index E/É, which provides a fair estimate of LV filling pressure [20], [21].

In group I; the mean É was (4.6 ± 1.3 m/s) while in group II the mean É was (6.1 ± 2.7 m/s) higher than that in group I with a statistically significant difference between the two groups, (p 0.009). However, the E/É ratio in group I was 15.6 ± 5 compared to a ratio of 15.73 ± 5 in group II with no statistically significant difference between the two groups. These findings showed that hypertension and CAD in patients with diabetes added to the risk of developing LV diastolic dysfunction. The E/E' of > 15 in patients with DM is associated with subsequent HF and increased mortality independent of HTN, CAD, or other echocardiographic parameters [22].

In our study, the mean E/A ratio for those who survived at 6 months was (1.25 ± 0.91 vs 1.8 ± 0.5) for non- survived patients in group I, while for group II there was no mortality at 6 months, and the mean E/A was 1.45 ± 0.8. The Strong Heart Study follow-up (2002) showed that, a transmitral E/A ratio < 0.6 (pattern of abnormal relaxation) is associated to a doubled increase of mortality risk and an E/A ratio > 1.5 (pattern pseudonormal/restrictive) is associated to a threefold increase of cardiac mortality [23].

In our study in terms of outcome and complication, both groups had survived the in-hospital course despite the presence of patients with cardiogenic shock. We had nine patients who died in group I after 6 months, and three patients died in group II after one year. Short term outcome goes in hand with Johansson et al., (2016) who found that type two diabetes mellitus (T2DM) was shown to be a predictor of mortality in both ischemic and non-ischemic heart failure, although the presence of ischemic heart disease (IHD) with T2DM appeared to have the worst outcome [24].

Our results also were similar to that of Sarma et al., (2013) who demonstrated in his study that diabetic patients with HF and low LVEF tend to have more co-morbidities and worse long- term outcomes after hospitalization, specifically increased rates of cardiovascular mortality and re-hospitalization after discharge, than those without DM, even after adjusting for baseline risk factors and medications, DM was associated with a (17%) increased risk for cardiovascular mortality and hospitalization for HF over a median follow-up of 9.9 months [25].

Limitation: We excluded a rather big sample from our final study results as the views were not

analysed by speckle tracking software and this was due to poor quality of images. The values for the strain parameters measured in this study were calculated using feature tracking post-processing software. This remains a research application and lacks the clinical validation to enable its adoption into routine clinical practice for the screening of diabetic cardiomyopathy.

In conclusion, the combination of cardiomyopathy and diabetes affects LV systolic and diastolic function; however; ischemic cardiomyopathy and diabetic cardiomyopathy had a similar systolic and diastolic function. Ischemic cardiomyopathy is associated with worse prognosis compared to Diabetic cardiomyopathy. We recommend conducting a larger study to evaluate the impact of DM on heart failure patients over a long period. Further studies are warranted to detect early signs of heart failure in diabetic patients to prevent deterioration of LV function.

References

1. Chiha M, Njeim M, Chedrawy EG. Diabetes and coronary heart disease: a risk factor for the global epidemic. International journal of hypertension. 2012; 2012. https://doi.org/10.1155/2012/697240 PMid:23119148 PMCid:PMC3483823

2. Rosano GM, Vitale C, Seferovic P. Heart failure in patients with diabetes mellitus. Cardiac failure review. 2017; 3(1):52-55. https://doi.org/10.15420/cfr.2016:20:2

3. Lebeau R, Serri K, Morice MC, Hovasse T, Unterseeh T, Piéchaud JF, Garot J. Assessment of left ventricular ejection fraction using the wall motion score index in cardiac magnetic resonance imaging. Archives of cardiovascular diseases. 2012; 105(2):91-8. https://doi.org/10.1016/j.acvd.2012.01.002 PMid:22424327

4. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. European Heart Journal-Cardiovascular Imaging. 2015; 16(3):233-71. https://doi.org/10.1093/ehjci/jev014 PMid:25712077

5. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging's. European Heart Journal-Cardiovascular Imaging. 2016; 29(4):277-314. https://doi.org/10.1016/j.echo.2016.01.011 PMid:27037982

6. Thomas J Ford, David Corcoran. Stable coronary syndromes: Pathophysiology, diagnostic advances and therapeutic need. Heart. 2018; 104:284-292.

7. Chan YH. Biostatistics 102: Quantitative Data - Parametric & Non-parametric Tests. Singapore Med J. 2003; 44(8):391-396.

8. Chan YH. Biostatistics 103: Qualitative Data -Tests of Independence. Singapore Med J. 2003; 44(10):498-503.

9. Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman medical journal. 2012; 27(4):269-273. https://doi.org/10.5001/omj.2012.68 PMid:23071876 PMCid:PMC3464757

10. Seferović PM, Paulus WJ. Clinical diabetic cardiomyopathy: a two-faced disease with restrictive and dilated phenotypes. European heart

journal. 2015; 36(27):1718-27. https://doi.org/10.1093/eurheartj/ehv134 PMid:25888006

11. Lorenzo-Almoros A, Tunon J, Orejas M, Cortés M, Egido J, Lorenzo Ó. Diagnostic approaches for diabetic cardiomyopathy. Cardiovascular diabetology. 2017; 16(1):28. https://doi.org/10.1186/s12933-017-0506-x PMid:28231848 PMCid:PMC5324262

12. Kumar N, Oommen R, Thomson VS, Jose JV. Assessment of left ventricular systolic function by velocity vector imaging. Indian heart journal. 2012; 64(2):146-9. https://doi.org/10.1016/S0019-4832(12)60050-9

13. Sengeløv M, Jørgensen PG, Jensen JS, Bruun NE, Olsen FJ, Fritz-Hansen T, Nochioka K, Biering-Sørensen T. Global longitudinal strain is a superior predictor of all-cause mortality in heart failure with reduced ejection fraction. JACC: Cardiovascular Imaging. 2015; 8(12):1351-9. https://doi.org/10.1016/j.jcmg.2015.07.013 PMid:26577264

14. Kane GC, Karon BL, Mahoney DW, Redfield MM, Roger VL, Burnett JC, Jacobsen SJ, Rodeheffer RJ. Progression of left ventricular diastolic dysfunction and risk of heart failure. Jama. 2011; 306(8):856-63. https://doi.org/10.1001/jama.2011.1201 PMid:21862747 PMCid:PMC3269764

15. Zoungas S, Woodward M, Li Q, Cooper ME, Hamet P. Impact of age, age at diagnosis and duration of diabetes on the risk of macrovascular and microvascular complications and death in type 2 diabetes. Diabetologia. 2014; 57(12):2465-74. https://doi.org/10.1007/s00125-014-3369-7 PMid:25226881

16. Argulian E, Sengupta PP. Speckle Tracking Echocardiographic Imaging in Metabolic Cardiomyopathies. Current Cardiovascular Imaging Reports. 2016; 9(10):26. https://doi.org/10.1007/s12410-016-9390-0

17. Radwan H, Hussein E. Value of global longitudinal strain by two dimensional speckle tracking echocardiography in predicting coronary artery disease severity. The Egyptian Heart Journal. 2017; 69(2):95-101. https://doi.org/10.1016/j.ehj.2016.08.001 PMid:29622962 PMCid:PMC5839366

18. Esmaeilzadeh M, Parsaee M, Maleki M. The Role of Echocardiography in Coronary Artery Disease and Acute Myocardial Infarction J Tehran Heart Cent. 2013; 8(1):1-13.

19. Stanton T, Leano R, Marwick TH. Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring. Circ Cardiovasc Imaging. 2009; 2:356-364. https://doi.org/10.1161/CIRCIMAGING.109.862334 PMid:19808623

20. Arindam Choudhury, Rohan Magoon, Vishwas Malik. Global Longitudinal Strain Is a Superior Predictor of All-Cause Mortality in Heart Failure With Reduced Ejection Fraction, 2015.

21. Flachskampf FA, Biering-Sørensen T, Solomon SD, Duvernoy O, Bjerner T, Smiseth OA. Cardiac imaging to evaluate left ventricular diastolic function. JACC: Cardiovascular Imaging. 2015; 8(9):1071-93. https://doi.org/10.1016/j.jcmg.2015.07.004 PMid:26381769

22. Bella JN, Palmieri V, Roman MJ, Liu JE, Welty TK, Lee ET, Fabsitz RR, Howard BV, Devereux RB. Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle-aged and elderly adults: the Strong Heart Study. Circulation. 2002; 105(16):1928-33. https://doi.org/10.1161/01.CIR.0000015076.37047.D9 PMid:11997279

23. From AM, Scott CG, Chen HH. The development of heart failure in patients with diabetes mellitus and pre-clinical diastolic dysfunction a population-based study. J Am Coll Cardiol 2010; 55:300-5. https://doi.org/10.1016/j.jacc.2009.12.003 PMid:20117433 PMCid:PMC3878075

24. Bella JN, Palmieri V, Roman MJ, Liu JE, Welty TK et al: Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle aged and elderly adults. The Strong Heart Study. Circulation, 2002. https://doi.org/10.1161/01.CIR.0000015076.37047.D9 PMid:11997279

25. Sarma S, Mentz RJ, Kwasny MJ, Fought AJ, Huffman M, Subacius H, Nodari S, Konstam M, Swedberg K, Maggioni AP, Zannad F. Association between diabetes mellitus and post-discharge outcomes in patients hospitalized with heart failure: findings from the EVEREST trial. European journal of heart failure. 2013; 15(2):194-202. https://doi.org/10.1093/eurjhf/hfs153 PMid:23059198 PMCid:PMC4176083