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Galactin-3 and brain natriuretic peptide versus conventional echocardiography in the early detection of cirrhotic cardiomyopathy

LIVER

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Original Article

ABSTRACT

Background/Aims: Cirrhotic cardiomyopathy (CCM) is defined as an abnormal heart structure and function in cirrhotic patients. CCM includes systolic and diastolic dysfunction, electrophysiological abnormalities, and structural changes, both microscopic and macroscopic. Currently, there is no one diagnostic test that can identify patients with CCM. Evaluation of the validity of galactin-3 and brain natriuretic peptide (BNP) as biomarkers in the early detection of CCM in comparison to conventional echocardiography.

Materials and Methods: A case control study was carried out in the Departments of internal medicine and tropical Medicine, Assuit University, Egypt. Seventy-one subjects were divided into the following three groups: 26 cirrhotic patients without ascites, 25 cirrhotic patients with ascites, and 20 healthy controls. All groups underwent clinical examination, and laboratory investigation including BNP, galactin-3, and echocardiography.

Results: There was a significant difference between the three groups ($p<0.001$) with regard to corrected QT (cQT), BNP and galactin-3. Left ventricular diastolic dysfunction with different grades was the most recorded cardiac abnormality in the patient group I and II (88.5% and 96%; respectively) with significantly increased frequency and severity in ascetic patients and with the advancement of liver cirrhosis. BNP and galactin-3 were sensitive and specific biomarkers for the detection of diastolic dysfunction in cirrhotic patients (77.6%, 95.5%, 89.9% and 86.4%; respectively).

Conclusion: Diastolic dysfunction is a common cardiac abnormality in cirrhotic patients that worsens with the advancement of cirrhosis. BNP and galactin-3 had higher sensitivity and specificity in the early detection of CCM compared with those of conventional echocardiography.

Keywords: Liver cirrhosis, cardiomyopathy, ascites, cardiac function, BNP, galactin-3

INTRODUCTION

Both cardiac dysfunction and peripheral vascular changes were detected in patients with decompensated liver cirrhosis, and these changes are now termed CCM (1,2). CCM includes diastolic and systolic cardiac dysfunction. The pathogenesis of CCM is complex with various neuro-humoral and cellular pathways. The proposed diagnostic criteria of CCM are now well-established according to the EASL 2010 published review (3). Despite these efforts, the characterization of CCM among patients with and without ascites has not been completely evaluated. Cirrhotic patients undergo electrophysiological changes like increased repolarization time and impaired excitation contraction coupling (4).

Heart failure due to CCM is claimed to be the third cause of mortality after rejection and infection in the transplanted patients (5). Therefore, early diagnosis, accurate screening tests, and assessment criteria for CCM severity seem to be essential in the management of cirrhotic patients.

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Serum cardiac markers including atrial natriuretic peptide, BNP, and troponin-I, which are signs of stress and volume overload within the heart, were found to be elevated in cirrhotic patients due to the increased activity of renin–angiotensin–aldosterone system, caused indirectly by diastolic dysfunction of CCM (3). Recently, a new serum biomarker, galectin-3, was found to cause myocardial fibrosis and to be increased in cirrhosis. Furthermore, it was reported that galectin-3 binding protein concentrations increased in patients with cirrhosis (6).

Therefore, we tried to evaluate the validity of galactin-3, BNP, and echocardiography in diagnosis of diastolic dysfunction in cirrhotic patients with and without ascites.

MATERIALS AND METHODS

Patients' recruitment/categorization

A case control study was designed to enroll cirrhotic patients at both Gastroenterology Unit of Internal Medicine department and Tropical Medicine department, Assiut University School of Medicine, over a period of 4 months (between August and November, 2015). The study was approved by the Ethics Committee of Assiut Medical College. After obtaining written consent from the subjects, they were counseled and explained about the objectives of the study by a qualified medical doctor.

A total of fifty-one patients were enrolled [26 cirrhotic patients without ascites (group I) and 25 cirrhotic patients with ascites (group II)]. Another 20 apparently healthy subjects were recruited as controls (group III).

Diagnosis of cirrhosis was carried out based on clinical findings (chronic liver disease stigmata, jaundice, ascites, and esophageal varices), impaired liver function laboratory tests ultrasonographic features consistent with cirrhosis (diffuse alteration of liver parenchyma, irregular border, and dilated portal vein). Presence and absence of ascites was detected according to clinical and ultrasound examination.

Exclusion criteria

1) History or clinical signs of cardiovascular disease; 2) major lung disease (chronic obstructive lung disease, or interstitial lung fibrosis); 3) diabetes mellitus; 4) major arrhythmias (heart block, atrial fibrillation, frequent atrial, or ventricular ectopies); 5) severe anemia (Hb<7 gm/dL); 6) grade III and IV hepatic encephalopathy according to the West Haven Criteria; 7) renal failure (creatinine>1.5 mg/dL); 8) drugs that may affect the parameters of the study such as sympathomimetics, nitrates, or anti-hypertensive in the past 4 weeks before examination; 9) history of or presence of hypertension according to JNC 8 criteria for hypertension (7).

Study procedures

Evaluation of asymptomatic cardiac dysfunction in cirrhotic patients and controls was conducted using the following:

- Resting 12-lead surface ECG was obtained from all subjects at a speed of 25 mm/s for the prediction of dysrhythmias and calculation of corrected QT (cQT) interval. The cQT interval was calculated manually using Bazett's formula: cQT=QT interval (s)/(R-R interval 1/2) (s). Bazett's formula has been shown to be a predictor of cardiovascular mortality. Lead II was used as the first choice for calculating cQT. cQT decrease was defined as a reduction of ≥60 ms. A prolonged cQT interval was defined as a cQT of >440 ms for men and >460 ms for women (8).
- Resting trans-thoracic echocardiography (TTE): Using (Philips Envisor 2002; Andover, Massachusetts, USA). The procedure was done with a 2.5 MHz multiphase array probe in standard parasternal and apical views according to the recommendations of the American Society of Echocardiography (9).
- Ejection fraction (EF) was assessed using modified biplane Simpson's method from the apical two and four chamber view (10).
- The diastolic function was assessed using the following parameters: left ventricular filling derived from mitral valve diastolic flow velocity curve, such as the ratio of E and A wave velocities (E/A); the atrial deceleration time (ADT). The E wave corresponds to the peak initial mitral inflow velocity and the A wave corresponds to the velocity caused by atrial contraction. ADT is associated with the left ventricular relaxation and corresponds to the slope of a straight line from the peak to half of the E velocity. The normal value of the E:A ratio is ≥1.0 ms, ≤250 ms for ADT, and ≤80 ms for isovolumetric relaxation time (IVRT). Diastolic dysfunction (Dd) was present if one or two of the above were detected.
- Laboratory investigations: Venous blood samples were collected from patients and healthy controls under standardized conditions. After centrifugation, serum samples were divided and stored in aliquots at –80°C until analysis. Citrated plasma samples were used for the assay of prothrombin concentration and international normalized ratio (INR) by (Sysmex® CA-1500 System; Siemens, Germany). Serum bilirubin, albumin, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were measured using Cobas Integra 400 (Roche, Switzerland). Serum galectin-3 level was measured using an enzyme linked immunosorbent assay based on the biotin double antibody sandwich technology (Gen Asia kit, Catalog number GA-E1968HM). Measurement of BNP was performed using the competitive enzyme linked immunosorbent assay using a kit provided by Elabscience (catalog number E-EL-H0598).
- Diagnosis of CCM was done according to the EASL 2010 published review (3).

Table 1. Demographic data and laboratory values of the groups

Variables		Control (No=20)	Group I (No=26)	Group II (No=25)	p
Age in years (mean±SD)		54.5±7.2	54.1±9.1	53.9±11.0	0.980*
Sex	Male	22 (84.6%)	20 (80.0%)	12 (60.0%)	0.129**
	Female	4 (15.4%)	5 (20.0%)	8 (40.0%)	
BMI kg/m^2 (mean±SD)		22.3±1.5	22.6±1.5	29.7±2.9	<0.001*
AST IU/L (Median & Range)		8 (6–18)	38 (7–246)	55 (17–88)	<0.001***
ALT IU/L (Median & Range)		16.5 (10–24)	44 (10–391)	38 (10–87)	<0.001***
Albumin g/L (Median & Range)		40.3 (34–45)	32 (19–43)	24.5 (2.4–58)	<0.001***
Bilirubin Umol/L (Median & Range)		9.8 (6–17)	24 (8.7–89)	43 (7.1–103)	<0.001***
INR (Median & Range)		1 (0.9–1.1)	1.3 (1.1–80)	1.4 (1.1–4.7)	<0.001***
Child Class	A	-	18 (4.5%)	0 (14.1%)	<0.001**
	B	-	8 (4.5%)	8 (14.1%)	
	C	-	0 (4.5%)	17 (55.0%)	
cQT interval ms (mean±SD)		440±6.2	472±36.8	531±49.8	<0.001*
Galactin-3 pg/mL (Median & Range)		99 (37–129)	242 (35–790)	408 (212–1280)	<0.001***
BNP pg/mL (Median & Range)		99 (75–105)	146 (19–425)	329 (98–574)	<0.001***

*ANOVA test was used to compare the mean difference between the groups.
**Chi-square test analysis was used to compare the difference in proportions between the groups.
***Kruskal–Wallis H test was used to compare the mean difference between the groups.
BMI: Body Mass Index; AST: aspartate aminotransferase; ALT: alanine aminotransferase; INR: international normalized ratio; cQT: corrected QT; BNP: brain natriuretic peptide

Statistical analysis and ethics

Statistical Package for Social Sciences (SPSS) version 16.0 for Windows (SPSS Inc.; Chicago, IL; USA), was used for data analysis. Parametric data are expressed as mean or median values±standard deviation (SD) and categorical variables as percentages. The Chi-square test or Fischer's exact was used for the comparison of dichotomous variables and the Student's *t* test for continuous variables. ANOVA was used to calculate p values in comparisons of more than two continuous variables. A p value of ≤0.05 was considered statistically significant.

The study was approved by the local ethics committee and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients enrolled into this study.

RESULTS

Fifty-one cirrhotic patients were included in the study. Table 1 shows demographic and baseline characteristics. A highly significant statistical difference between three groups (p<0.001) was observed with respect to BMI, AST level, ALT level, albumin, bilirubin, INR, Child Class, cQT interval, galactin-3, and BNP, where all of these parameters, except albumin, were observed to be higher in group II compared to those in group I and III.

Corrected QT was more prolonged in cirrhotic patients with ascites than patients without ascites with statistical difference between groups (p<0.001) (Table 1), it was positively correlated with Child Pugh class C with a significant statistical difference (p<0.001) (Table 2).

With regard to the cardiac events recorded in the studied population (Table 3), Figure 1 depicts a highly statistically significant difference (p<0.001) between the studied groups, where LAD and Dd are more common in group II. Furthermore, a statistically significant difference was observed between the groups with regard to the left ventricular hypertrophy and segmental wall motion abnormalities (SWMA) (p=0.025 and p=0.016, respectively), where LVH is more common in group I (26.9%) and SWMA is more common in group II (24%). A statistically insignificant difference was observed between groups with regard to systolic dysfunction (Sd) (p=0.138) in spite of significant difference in both EF, Fractional shortening (FS) between the three groups.

Diastolic dysfunction in its different grades is the most common cardiac event that was recorded in our patients using the E/A ratio, IVRTT, and deceleration time, with statistically significant difference between all studied groups. Advanced Dd (grade II and III) with shorter IVRT time and shorter diastolic time (DT) were common in cirrhotic patients with ascites (group II) (Table 4).

Child C patients experienced a significantly more prolonged cQT interval; more prevalent LAD, Sd, SWMA; lower EF; higher BNP; galactin-3 levels (Table 2).

Table 2. Electro-physiological, echocardiographic, and laboratory markers of cirrhotic cardiomyopathy in different Child class

Variables	Child Classification			p	Spearman ratio
	A (n=18)	B (n=16)	C (n=17)		
cQT interval (mean±SD)	451±21.9	497±29.1	556±36.5	<0.001*	0.830
LAD	7 (38.9%)	12 (75%)	17 (100%)	<0.001**	0.557
LVH	2 (11.1%)	5 (31.2%)	6 (35.3%)	0.102**	0.232
Sd	0 (0%)	1 (6.2%)	3 (17.6%)	0.095**	0.271
Dd	15 (83.3%)	15 (93.8%)	17 (100%)	0.114**	0.275
SWMA	0 (0%)	5 (31.2%)	6 (35.3%)	0.011**	0.359
EF%	68±4.7	62±5.2	58±6.5	<0.001*	0.609
Galactin-3 (Median & Range) pg/mL	188 (35–477)	388 (212–790)	568 (287–1280)	<0.001***	0.744
BNP (Median & Range) pg/mL	38 (19–187)	226 (130–425)	391 (98–574)	<0.001***	0.831

*ANOVA-test was used to compare the mean difference between the groups.
**Chi-square test analysis was used to compare the difference in proportions between the groups.
***Kruskal–Wallis H test was used to compare the mean difference between the groups.
cQT: corrected QT; LAD: left atrial dilatation; LVH: left ventricular hypertrophy; Sd: systolic dysfunction; Dd: diastolic dysfunction; SWMA: segmental wall motion abnormalities; EF: ejection fraction; BNP: brain natriuretic peptide

Table 3. Cardiac events in the groups

	Control (No=20)	Group I (No=26)	Group II (No=25)	p
LAD	1 (5%)	13 (50%)	23 (92%)	<0.001*
LVH	0 (0%)	7 (26.9%)	6 (24%)	0.025**
Sd	0 (0%)	1 (3.8%)	3 (12%)	0.138**
EF% (mean±SD)	70±3.4	65±6.1	60±6.4	<0.001**
FS% (mean±SD)	47±3.2	36±4.9	34±6.9	<0.001**
Dd	2 (10%)	23 (89%)	24 (96%)	<0.001**
SWMA	0 (0%)	5 (19.2%)	6 (24%)	0.016**

*Chi-square test was used to compare the difference in proportions between the groups.
**Fisher's exact test was used to compare the difference in proportions between the groups.
LAD: left atrial dilatation; LVH: left ventricular hypertrophy; Sd: systolic dysfunction; EF: ejection fraction; FS: fractional shortening; Dd: diastolic dysfunction; SWMA: segmental wall motion abnormalities

Table 4. Diastolic dysfunction in the groups

(Mean±SD)		Control (No=20)	Group I (No=26)	Group II (No=25)	P
Grades of diastolic dysfunction		19 (95%)	1 (3.8%)	0 (0%)	<0.001*
	G I	1 (5%)	16 (61.6%)	9 (36%)	
	G II	0 (0%)	8 (30.8%)	14 (56%)	
	G III	0 (0%)	1 (3.8%)	2 (8%)	
IVRT		76±6.4	101±12.5	82±13.5	<0.001**
DT		208±16.8	227±48.5	198±25.2	0.039**

*Fisher's exact test analysis was used to compare the difference in proportions between the groups.
**ANOVA-test was used to compare the mean difference between the groups.
IVRT: isovolumetric relaxation time; DT: deceleration time

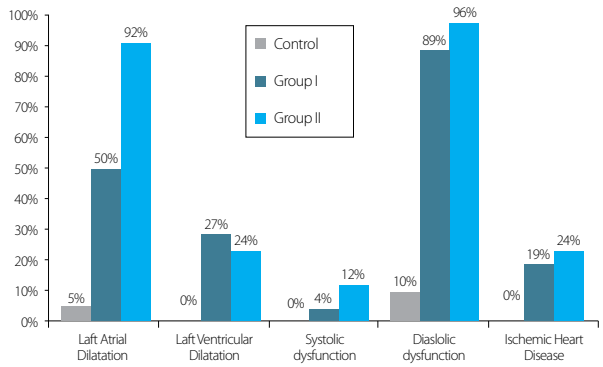

Figure 1. Prevalence of cardiac events in the groups

Galactin-3 was 89.9% sensitive for Dd detection with 86.4% specificity at a cut off value of 132 pg/mL as observed using ROC curve with AUC 0.94 (p<0.001) (Table 5, Figure 2).

Brain natriuretic peptide was 77.6% sensitive for Dd with 95.5% specificity at a cut off value of 104 pg/mL as observed using ROC curve with AUC 0.81 (p<0.001) (Table 6, Figure 3).

Positive correlation between BNP and galactin-3 (r=0.697, p>0.001) was observed in the studied groups (Figure 4).

IVRT showed a high sensitivity and specificity in the detection of Dd (91.8%, 81.1%, respectively) at a cut off value of 88 ms with AUC 0.91 (Table 7, Figure 5).

DISCUSSION

Cardiac dysfunction among cirrhotic patients has been recently recognized, it is usually asymptomatic at rest because of the reduced afterload as a result of decreased peripheral vascular resistance (11).

Table 5. Validity of Galactin-3 for diastolic dysfunction discrimination

	Galactin-3			
	AUC	**SE**	**p**	**95% CI⁺**
Dd	0.94	0.03	<0.001	0.88–0.99
	Sensitivity	**Specificity**		
At 132 pg/mL	89.9%	86.4%		

AUC: area under the curve; SE: standard error; CI: confidence interval; Dd: diastolic dysfunction

Table 6. Validity of BNP for diastolic dysfunction discrimination

	BNP			
	AUC*	**SE****	**p**	**95% CI⁺**
Dd	0.81	0.05	<0.001	0.71–0.91
	Sensitivity	**Specificity**		
At 104 pg/mL	77.6%	95.5%		

AUC: area under the curve; SE: standard error; CI: confidence interval; BNP: brain natriuretic peptide; Dd: diastolic dysfunction

Table 7. Validity of IVRT for diastolic dysfunction discrimination

	IVRT			
	AUC*	**SE****	**p**	**95% CI⁺**
Dd	0.91	0.04	<0.001	0.84–0.98
	Sensitivity	**Specificity**		
At 88 ms	91.8%	81.8%		

AUC: area under the curve; SE: standard error; CI: confidence interval; IVRT: isovolumetric relaxation time; Dd: diastolic dysfunction

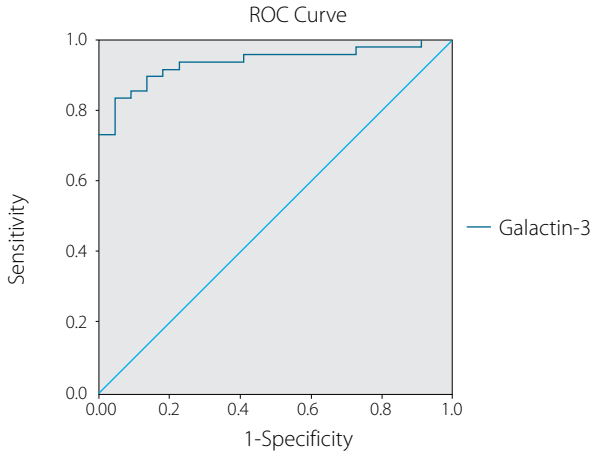

Figure 2. ROC curve for galactin-3 validity in diastolic dysfunction discrimination

Although CCM is clinically not so problematic in a resting state, stressful conditions like exercise, infections, drugs, and bleeding and any procedure, such as insertion of transjugular intrahepatic portosystemic shunts (TIPS) or liver transplantation, can make the latent form of CCM to overt heart failure (12). Therefore, the need of a more accurate screening test and assessment criteria for CCM severity estimation seems to be essential in the management of cirrhotic patients.

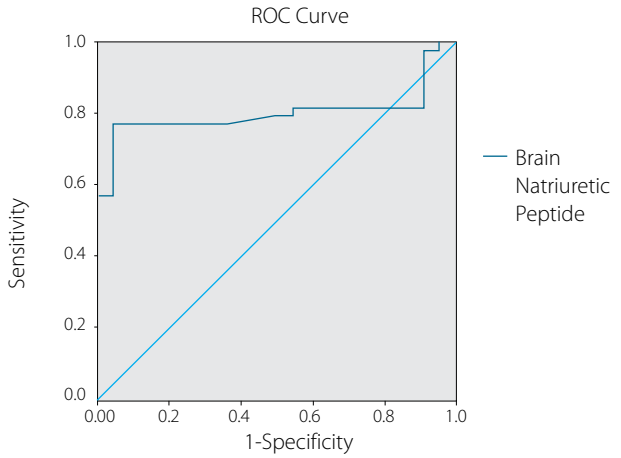

Figure 3. ROC curve for BNP validity in diastolic dysfunction discrimination

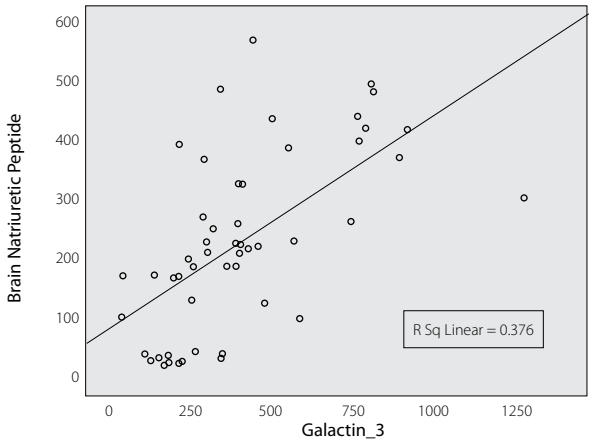

Figure 4. Correlation between galactin-3 level and BNP

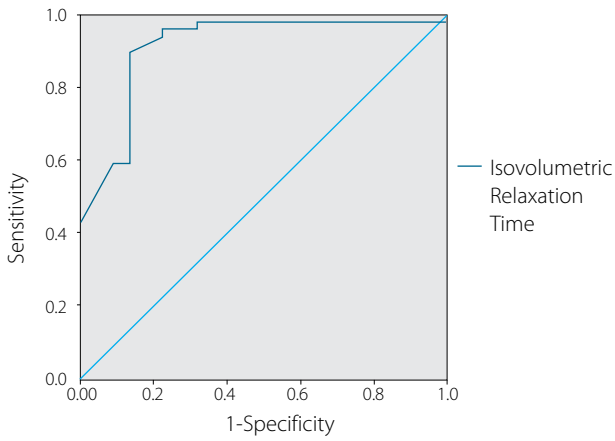

Figure 5. ROC curve for IVRT validity in diastolic dysfunction discrimination

To achieve this goal, investigations such as new laboratory markers, ECG, and echocardiography, particularly in combination, will be useful because of the latent course of CCM (13).

The electrophysiological abnormalities include prolonged repolarization, which manifests itself in the form of a prolonged

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cQT interval that was present in cirrhotic patients with and without ascites (472±36.8, 531±49.8) with a significant positive correlation with the severity of cirrhosis and the presence of ascites ($p<0.001$, $r=0.83$). Prolonged cQT has been associated with an increased risk of life-threatening cardiac arrhythmias, such as torsades de pointes and ventricular fibrillation, as well as with sudden cardiac death**.** These results are in agreement with previous studies that found cQT prolongation is common among cirrhotic patients and has direct correlation with the severity of liver dysfunction (Child-Pugh score) and ascites and portal hypertension (14-16).

These electrophysiological abnormalities occurred as a result of a combination of ion-channel dysfunction, plasma membrane abnormalities, β-adrenoceptor, post-receptor pathway defects, and volume overload (17).

Cardiac abnormalities such as heart stiffness due to fibrosis and circulatory problems may contribute to worsening of cardiac function in the late stage of cirrhosis (18).

In the current study, cirrhotic patients with and without ascites had both morphological and functional cardiac dysfunctions. Cardiac dimensions are mainly enlarged toward the left side.

Left ventricular Dd with different grades particularly grade II (86.8%) was present in majority of cirrhotic patients (88.5% in cirrhosis without ascites and 96% in patients with ascites), whereas systolic dysfunction was present in few cases with an insignificant difference between groups ($p>0.09$), and both were correlated with the severity of cirrhosis and presence of ascites.

Grade I Dd was commonly seen in cirrhotic patients without ascites (61.6%) compared to that in cirrhotic patients without ascites (36%).

Although grade II and III Dd were recorded in cirrhotic patients without ascites (30.8% and 3.8%, respectively), they were more common in ascetic patients with ascites (56% and 8%, respectively). Similar to previous studies that showed Dd to increase with the degree of liver fibrosis (19,20). Mild Dd was most prevalent in cirrhotic patients in previous studies, and severe Dd was less common; these findings are similar to our result (21).

Incidence of Dd was higher in our study as compared with that in previous studies; this may be due to multiple factors: firstly, many patients in both groups were above 60 years, and this participates to diastolic dysfunction; secondly, the presence of ascites in the second group leads to diaphragm shift-up and intrathoracic pressure increase that could prevent the required relaxation of the ventricle, causing an overestimation of Dd particularly when using E/A ratio.

In most of the studies performed recently, diagnosis of LVDD was based on an E/A ratio of <1 using 2-D Doppler echocardiography. Valeriano et al. (22) also founded a similar lower mean E/A ratio in both the left and right ventricles in an ascetic subgroup than in a non-ascetic subgroup.

Pozzi et al. (23) showed that the removal of ascites by rapid complete paracentesis reduced the A wave velocity and increased the E/A ratio to values near to those of cirrhotic patients without ascites; however, it remained abnormal when compared with those in healthy controls**.** Isovolumic relaxation time (IVRT) is measured using simultaneous Doppler and M-mode echo or simultaneous phonocardiogram and transmitral Doppler. When it is prolonged, it indicates poor myocardial relaxation. A normal IVRT value is about 70±12 ms, it may be 10 ms longer in those above 40 years of age. With an abnormal relaxation, the value is usually over 110 ms, with restrictive filling, under 60 ms (24).

In our study IVRT showed high sensitivity and specificity in the detection of Dd (91.8% and 81.1%, respectively) at a cut off value 88 ms with AUC 0.91. Although it has reasonable sensitivity and specificity in the detection of Dd and may be superior to transmitral flow velocity in the estimation of Dd in our patients as the latter was greatly affected by the volume status of the patients, the former is age dependent, sensitive to change in heart rate, and does not give information on LV filling, which lowers its specificity.

Cardiac natriuretic peptides have been generally considered as markers of volume overload rather than markers of cardiac dysfunction; however, numerous recent studies have shown that patients with cirrhosis have increased plasmatic concentrations of BNP and NT-pro-BNP, representing as markers of early ventricular dysfunction. Recently, Wong and colleagues proposed that BNP could be an indicator of CCM (25).

With respect to BNP levels between our three study groups, a statistically significant difference was observed and was higher in the patient groups ($p<0.001$); the levels increased with the severity of cirrhosis, and our results are in agreement with previous studies that showed BNP level to be significantly increased with degree of liver cirrhosis, liver failure, and portal hypertension (26,27).

Our study revealed that BNP is a valid marker for Dd in cirrhotic patients ($p<0.001$, 95% CI 0.71–0.91) with a sensitivity and specificity of 77.6% and 95.5%, respectively, at a cutoff value of 104 pg/mL.

Galectin-3 is a novel biomarker and has been shown to mediate myocardial fibrosis and to be expressed in cirrhosis. Furthermore, galectin-3 binding protein concentrations have also been found to be increased in patients with cirrhosis (6).

Our study revealed that galectin-3 is a valid marker for Dd in cirrhotic patients ($p<0.001$, 95% CI 0.88–0.99) with a sensitiv-

ity and specificity of 89.9% and 86.4%, respectively, at a cutoff value (132 pg/mL).

We found a significant positive correlation between serum galectin-3 levels and the severity of cirrhosis (Child class). Furthermore, there was a positive correlation between the levels of BNP and galectin-3 in the detection of Dd.

Galactin-3 was more sensitive than BNP despite the latter being more specific in the detection of Dd. This correlates with the results of Yin et al. (28) who suggested that galectin-3 is more sensitive, whereas BNP is more specific in HF diagnosis, and both are important biomarkers for HF diagnosis. If used together, they could provide early non-invasive accurate diagnosis of Dd**.**

Pereira et al. (29) also proved that galectin-3 appears to have a higher prognostic value than BNP when assessed separately; however, when combined together their prognostic value is even higher**.** In our study, galactin-3 level positively correlated with IVRT time in the detection of Dd and had nearly the same sensitivity of IVRT time but had a higher specificity in the detection of Dd in cirrhotic patients; therefore, it may be elevated in early Dd before it could be detected in TTE as cirrhotic patients have many factors affecting Dd.

The main limitation of our study was the lack of follow up of the patients and further assessment of the cardiac function, portal hypertension, and liver fibrosis. Furthermore, it was a single center study and patient number was limited.

Cardiac dysfunction was found to be directly proportional to the severity of cirrhosis, which in turn associated with electrophysiological, echocardiographic, and laboratory changes. Dd is the most common cardiac abnormality that worsens with the advancement of cirrhosis. BNP and galactin-3 have high sensitivity and specificity than those of conventional echocardiography in the early detection of Dd, particularly when combined. The use of new modality tissue Doppler and speckle tracking echocardiography may increase the sensitivity and specificity of early detection and treatment before TIPS and liver transplantation. Furthermore, a large-scale prospective study is recommended, using MELD score, for patient assessment.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Assiut Medical College.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - W.A.A., S.M.K.A., A.M.A.A.; Design - S.M.K.A., M.A.A, A.K.I., A.M.A.A.; Supervision - W.A.A., M.O.A.; Funding - W.A.A., S.M.K.A., A.M.A.A., M.O.A., A.K.I., M.A.A.A., A.A.M., M.A.M.; Materials - W.A.A., S.M.K.A., M.A.A.A., A.M.A.A., A.A.M.; Data Collection and/or Processing - S.M.K.A., A.M.A.A., A.K.I., M.A.M.; Analysis and/or Interpretation - A.K.I., W.A.A., A.A.M., M.O.A.; Literature Review - M.A.M., S.M.K.A., M.O.A.; Writer - S.M.K.A., W.A.A.; Critical Review - W.A.A., M.A.M.

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