Evaluation of Clinically Significant Cardiac Abnormalities in Patients With Normal Electrocardiogram Using Transthoracic Echocardiography

Hameed A. Alhibaly[1], Hameed Hussein Al-Jameel[1], Ban Waheed Hussein Bdair[2], Satar Jabbar Rahi Algraittee[2]

[1] Department of Internal Medicine, College of Medicine, Kerbala University, Imam Al-Hussein Medical City, Kerbala, Iraq
[2] Department of Medical Microbiology and Immunology, College of Medicine, University of Kerbala, Kerbala, Iraq

Received: 11 Jun. 2020; Accepted: 21 Dec. 2020

Abstract- Cardiac abnormalities have been suspected and identified using transthoracic echocardiography in patients with normal electrocardiographic results have been reported. It is, however, not clear whether these abnormalities are clinically significant or can lead to a change in clinical management. The aim of this study was to evaluate the prevalence and clinical significance of cardiac abnormalities found in patients with normal electrocardiographic results. Transthoracic echocardiography was conducted on outpatients on referral despite having normal electrocardiographic results. Clinical symptoms were identified, and parameters such as BMI, smoking status, blood pressure, blood glucose levels, and hypercholesterolemia status were evaluated. The data obtained from these parameters were compared with findings of cardiac abnormalities in the patients. Out of 552 patients analyzed with a mean age of 50.53±15.04 years, 412, representing 74%, had abnormalities in their transthoracic echocardiographic reports. The significant majority of active smoking patients (82.2%) had cardiac abnormalities. The major findings were valvular heart disease observed in 123 patients, grade I and II diastolic dysfunction in 85 patients, hypertensive heart disease in 76 patients, and non-significant valve disease reported in 50 patients. The common symptoms included atypical chest pain, shortness of breath, and epigastric pain. Hypertension, hypercholesterolemia, and diabetes mellitus were observed among patients with abnormal transthoracic echocardiographic reports. There is a high prevalence of clinically significant cardiac abnormalities evaluated using transthoracic echocardiography in patients with normal electrocardiographic results. These cardiac abnormalities are associated with symptoms, and cardiometabolic disease hence might warrant a change in clinical management.

Acta Med Iran 2021;59(2):97-107.

Keywords: Transthoracic; Echocardiography; Cardiac abnormalities; Cardio-metabolic diseases; Structural heart disease

Introduction

The effective evaluation of possible structural heart diseases surmised to be present in a patient can be achieved through the non-invasive imaging tool of transthoracic echocardiography (TTE). The TTE provides visual and numerical information on the overall status of the heart, including its thickness and size, evaluation of systolic and diastolic function, as well as evidence of structural defects (1). In clinical practice, the request, ordering, or referral for TTE to be performed by cardiologists are mostly diagnostic tests on patients with primary indications for conditions such as congestive heart failure, arrhythmia, endocarditis (known or suspected), pericardial disease, and presyncope or syncope. Others include pulmonary hypertension, dyspnea, valvular disease (native valves), murmur, chest pain, pulmonary embolism, ischemia, hypotension, cerebrovascular event, congenital heart disease, hypertensive heart disease, and so on (2,3)

Electrocardiography (ECG), on the other hand, is an economical, fitting, and widely used initial diagnostic tool for the evaluation of the cardiovascular well-being of patients. The ECG is useful in the exclusion of cardiac

Corresponding Author: S.J.R. Algraittee
Department of Medical Microbiology and Immunology, College of Medicine, University of Kerbala, Kerbala, Iraq
Tel: +9647722282830, Fax: +9647722282830, E-mail address: sattar.rahi72@gmail.com

arrhythmias from the causes of cardiac symptoms, and as such, cases of abnormal results frequently serve as suitable indications for echocardiography since they may indicate a basal structural heart disease (4). However, whether a normal ECG and the presence of structural heart disease are mutually exclusive remains unclear. Although studies have suggested that normal ECG results rule out indications for TTE, clinical experience has shown that the incidence of abnormal TTE in patients with otherwise normal ECG is common (5,6).

Over the years, researchers have conducted many studies on the diagnostic prowess of ECG in comparison with echocardiography. In these studies, the superiority of echocardiography over ECG has been widely reported (7,8). Despite being specific, the ECG has been shown to be insensitive in recognition of left ventricular hypertrophy (LVH) as echocardiographic LV mass evaluation showed superiority over ECG clinical criteria for clinical diagnosis of LVH (9). In 2016, Baturova *et al*., assessed predictors of paroxysmal atrial fibrillation using non-invasive ECG as well as TTE in patients with ischemic stroke but without documentation of atrial fibrillation. They reported that although TTE independently predicted atrial fibrillation in stroke patients, ECG markers were not predictive of atrial fibrillation in early after ischemic stroke (10). Another study conducted in 2019 on a wide peri-pubertal male athlete's population showed that ECG could only identify cardiac disease that requires sport disqualification, while TTE was able to identify abnormalities that predict the occurrence of cardiomyopathies or major cardiovascular events (11).

While clinicians have an obligation to recommend or utilize advanced and superior technology for diagnostic tests, considerations should be made on the cost implication of clinically insignificant tests to enable patients to receive affordable health care. Therefore, it is important to indicate that not all patients with normal ECG require echocardiographic referral. Studies have shown that unnecessary echocardiography can be performed on patients with normal ECG. Out of 870 patients with normal ECG in a study conducted by Gibbons *et al*., in 2018, 619 showed indications for echocardiography. Interestingly, however, only 12 actually had abnormal echocardiography, of which only 4 required change in clinical management (12).

Although the American College of Cardiology Foundation (ACCF) has developed the appropriate use criteria (AUC) to guide practitioners in the use of echocardiographic imaging procedures (13), there is a need for additional investigations on clinical conditions where the use of echocardiography is justified in patients with normal ECG. In line with this, our study aimed at identifying the prevalence of clinically significant TTE abnormalities among patients with normal ECG results. We evaluated the TTE of 552 out-patients suspected to have cardiac abnormalities undetected by ECG and were referred to Al-Hussein Medical City in Kerbala, Iraq. Our findings were juxtaposed with the presence of associated symptoms as well as cardiovascular/metabolic diseases to discern whether the identified abnormalities warrant a change in clinical management.

Materials and Methods

Study population

Our study collated TTE orders of adult outpatients referred to Al-Hussein Medical City in Kerbala, Iraq, following normal ECG but showing symptoms of cardiac abnormalities or preparation for major surgery, from June 2018 to April 2019. During this period, only the first TTE was considered in cases of repeated examination, and the patients were recruited based on informed consent, leading to a total of 552 TTEs data set. The protocol study was reviewed, and ethical approval was granted by the institutional ethical committee board.

Data collection

The TTE was performed on the patients using a 5.0 MHz Prob (S5) Philips Ultrasound Machine equipped with live 3-dimensional, B-mode color tissue Doppler software (Philips Sonos 7500, Andover, MA, USA). The data obtained were stored digitally and examined by an echocardiographer, and results were reported following recommendations of the European Association Cardiovascular Imaging (EACVI) Expert Consensus document (14).

The patients were briefly interviewed to determine their smoking status and identify clinical signs and symptoms that are relevant to their cardiovascular health.

Blood pressure (BP) was measured using a Mercury Sphygmomanometer (Riester Nova, Germany) at three intervals, each separated by a rest period of 5 minutes. The mean BP was calculated, and adult hypertension was defined as having a mean BP ≥130/80 mmHg (15). The patients' height weight and were measured (in triplicates) in light clothing with no shoes, and the body mass index (BMI) was computed as weight in kilograms divided by square of height in meters, from the mean values obtained (16).

Veinous blood samples were collected from the patients with minimal occlusion after a period of rest, and

serum lipid profile consisting of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) was determined using Hitachi 7020 automatic chemistry analyzer (Hitachi, Japan). Low-density lipoprotein cholesterol (LDL-C) was computed from the lipid profile report using the Friedewald equation; LDL-C=TC-(TG/5)-HDL-C (17). Hypercholesterolemia was defined as LDL-C >190 mg/dL or LDL-C >160 mg/dL with 1 major risk factor or LDL-C >130 mg/dL with 2 major risk factors. The risk factors include; Age (male ≥45 years; female ≥55 years), family history of atherosclerosis, presence of hypertension, diabetes, smoking, and low HDL-C (male <40 mg/dL; female <55 mg/dL) (18). Fasting blood sugar (FBS) was measured using a Hitachi 7020 automatic chemistry analyzer (Hitachi, Japan), and diabetes mellitus was defined as having FBS ≥126 mg/dL (19).

Data were presented as mean±standard deviation, or as percentages where appropriate. Chi-square test was used to determine statistical significance between abnormal TTE findings and normal TTE results with $P<0.05$.

Results

Over a study period of 11 months, we conducted TTE examinations on 552 patients with normal ECGs comprising 227 males and 325 females with a mean age of 50.53±15.04 years. Four hundred and twelve representing 74% of total patients, comprising of 171 males and 241 females, had abnormalities in their TTE reports while 140 patients comprising of 56 males and 84 females showed normal TTE results. The distribution of the patients with respect to TTE results across gender, age, BMI, and smoking status are presented in Table 1.

Table 1. Distribution of the patients with Abnormal TTE and Normal TTE across Gender, Age, BMI, and Smoking status

		Total	Abnormal TTE	Normal TTE	*P*
Number of patients *(n (%))*		552 (100)	412 (74.6)	140 (25.4)	0.001*
Gender	**Male *(n (%))***	227 (41.1)	171 (41.5)	56 (40.0)	0.001*
	Female (*n (%)*)	325 (58.9)	241 (58.5)	84 (60.0)	0.001*
Mean Age *(years)*		50.53±15.04	53.91±14.25	38.98±12.37	0.03*
Mean BMI *(Kg/m^2)*		27.02±3.82	27.18±3.71	24.79±4.24	0.16
Smoking Status	**Smokers (*n (%)*)**	258 (46.7)	212 (51.5)	46 (32.9)	0.001*
	Passive smokers *(n (%))*	73 (13.2)	64 (15.5)	9 (6.4)	0.001*
	Non-smokers (*n (%)*)	221 (40.1)	136 (33.0)	85 (60.7)	0.001*

*signifies the statistically significant difference between Abnormal TTE and Normal TTE at $P<0.05$

The mean age of patients with abnormal TTE was 53.91±14.25 years, which was significantly higher compared to that of patients with normal TTE reports, which was 38.98±12.37 years ($P<0.05$). The mean BMI of the total patients in the study was 27.02±3.82 Kg/m^{2,} which remained nearly unchanged in the patients with abnormal TTE, i.e., 27.18±3.71 Kg/m^2 but slightly lower in those with normal TTE results, i.e., 24.79±4.24 Kg/m^2. Analysis of data on the smoking status of the patients showed that 258 patients representing 46.7%, were active smokers, while 73 persons were passive smokers and 221 were non-smokers. Out of the 258 smokers, 212, representing 82.2%, had abnormalities in the TTE reports. From another angle, 51.5% of the patients with abnormal TTE reports were active smokers, which was significantly higher ($P<0.05$) compared to smokers with normal TTE, i.e., 32.9%. Also, 65 out of the 73 passive smokers, as well as 136 out of the 221 non-smokers, had abnormal TTE.

The echocardiographic reports of the 412 patients with abnormal TTE revealed findings of major cardiac abnormalities. The relative frequencies of these findings are presented in Table 2. The major TTE abnormalities findings were valvular heart disease (VHD), which had the highest frequency as it was observed in 123 patients representing 29.85% of the total abnormal TTE patients, followed by grade I and II diastolic dysfunctions (DD Grade I & II) in 85 patients with a prevalence of 20.63%, hypertensive heart disease (HHD) in 76 patients with a prevalence of 18.45% and non-significant valve disease (NSVD) reported in 50 patients representing 12.14%. Other findings include ischemic heart disease (IHD) in 31

patients (7.52%), dilated chamber with preserved ejection fraction (DC pEF) in 13 patients (3.16%), congenital defect (CD) in 9 patients (2.20%), duel contraction of the septal wall (DC septal wall) in 8 patients (1.94%), cardiomyopathy (CMP) in 7 patients (1.70%) while pericardial effusion (PE) and right ventricle overload in pulmonary hypertension (RVO in PHT) was reported in 5 patients (1.21%) each.

Table 2. Frequency of TTE findings of cardiac abnormalities in patients with normal ECG

S/N	Findings	Frequency *(n= 412)*	Percentage *(100%)*
1	**Congenital defect**	9	2.20%
2	**Hypertensive heart disease**	76	18.45%
3	**Ischemic heart disease**	31	7.52%
4	**Valvular heart disease**	123	29.85%
5	**Non-significant valve disease**	50	12.14%
6	**Right ventricle overload in pulmonary arterial hypertension**	5	1.21%
7	**Dilated chamber with a preserved ejection fraction**	13	3.16%
8	**Grade I and II Diastolic dysfunction**	85	20.63%
9	**Cardiomyopathy**	7	1.70%
10	**Pericardial effusion**	5	1.21%
11	**Deul contraction of septal wall**	8	1.94%

Figure 1 shows the summary and graphical presentation of TTE findings of cardiac abnormalities in patients with normal ECG.

Symptoms recorded from the clinical examination of the patients with abnormalities in TTE were cross-referenced with each TTE findings.

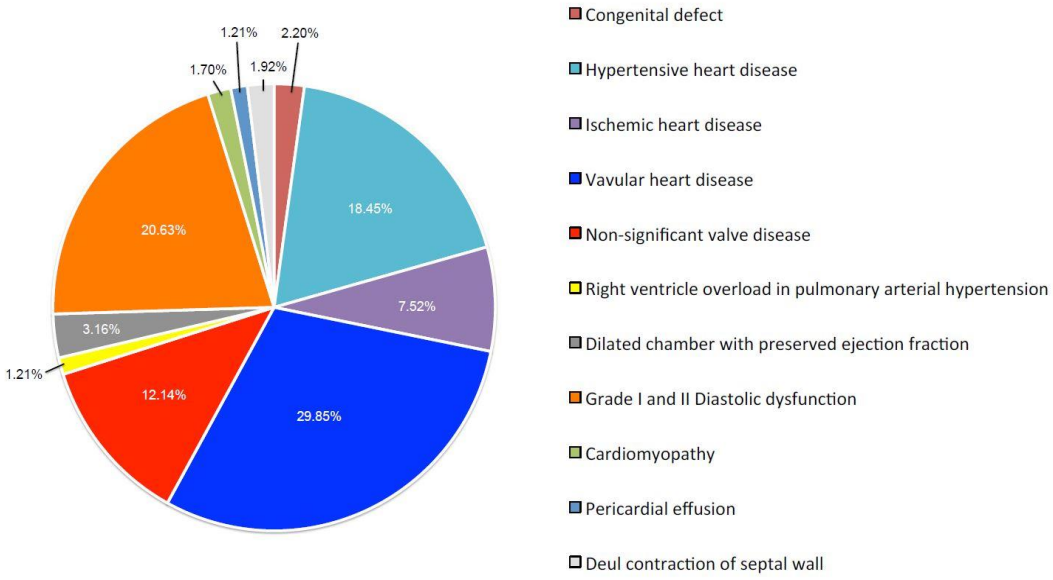

Figure 1. Summary and graphical presentation of TTE findings of cardiac abnormalities in patients with normal ECG.

The major TTE abnormalities findings were valvular heart disease, which had the highest prevalence of 29.85%, followed by grade I and II diastolic dysfunctions with 20.63%, then hypertensive heart disease with a prevalence of 18.45%, and non-significant valve disease with 12.14%. Other findings include ischemic heart disease (7.52%), the dilated chamber with preserved ejection fraction (3.16%), congenital defect (2.20%), duel contraction of the septal wall (1.94%), cardiomyopathy (1.70%) while pericardial effusion (1.21%) and right ventricle overload in pulmonary hypertension (1.21%).

Figure 2 presents the distribution of these symptoms among the different TTE findings. The common symptoms include atypical chest pain, shortness of breath (SOB), and epigastric pain. Others are typical chest pain, syncopal attack, palpitation, fatigue, and pregnancy. Out of 123 patients with VHD, 40 had atypical chest pain, 24 experienced SOB while palpitation was recorded in 14 patients. For DD Grade I & II, 21 patients experienced SOB, 14 had atypical chest pain. Twelve out of 76 patients with HHD had SOB, while atypical chest pain was recorded in 9 patients. Epigastric pain was most prevalent in 17 patients with NSVD, followed by atypical chest pain in 14 patients.

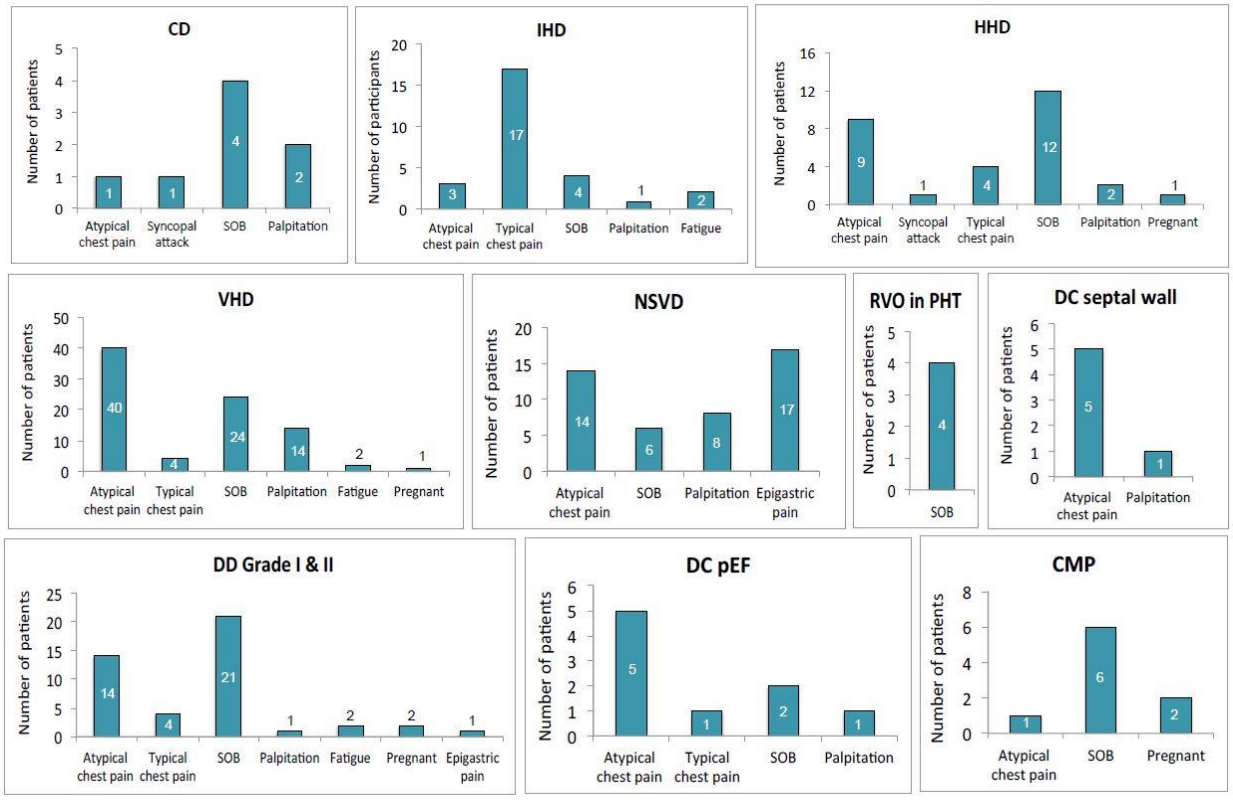

Figure 2. Distribution of clinical signs and symptoms among the different TTE findings

The relative frequencies of clinical signs and symptoms among the different TTE abnormalities findings in patients with normal ECG test results.

VHD (valvular heart disease); DD Grade I & II (grade I and II diastolic dysfunction); HHD (hypertensive heart disease); (HHD); NSVD (non-significant valve disease); IHD (ischemic heart disease); DC pEF (dilated chamber with preserved ejection fraction); (CD) congenital defect; DC septal wall (duel contraction of septal wall); CMP (cardiomyopathy); PE (pericardial effusion) and RVO in PHT (right ventricle overload in pulmonary hypertension).

The associated cardiovascular/ metabolic disease evaluated among patients with abnormal TTE includes hypertension (HTN), hypercholesterolemia (H. CHOL), diabetes mellitus (DM), and previously corrected atrial septal defect (PC. ASD). Out of 123 patients with VHD, 65 had DM, 61 had HTN, while H. CHOL was recorded

in 21 patients. For DD Grade I & II, 34 patients were diabetic, 32 had HTN, and 11 had H. CHOL. Fifty-four out of 76 patients with HHD were hypertensive, 8 were diabetic while H. CHOL was recorded in 9 patients. The prevalence of HTN and DM among the patients with NSVD was 19 patients for each, while 2 had H. CHOL. The PC. ASD was only recorded in 1 patient whose TTE report indicated RVO in PTH. The distribution of these associated diseases among the different TTE findings is shown in Figure 3.

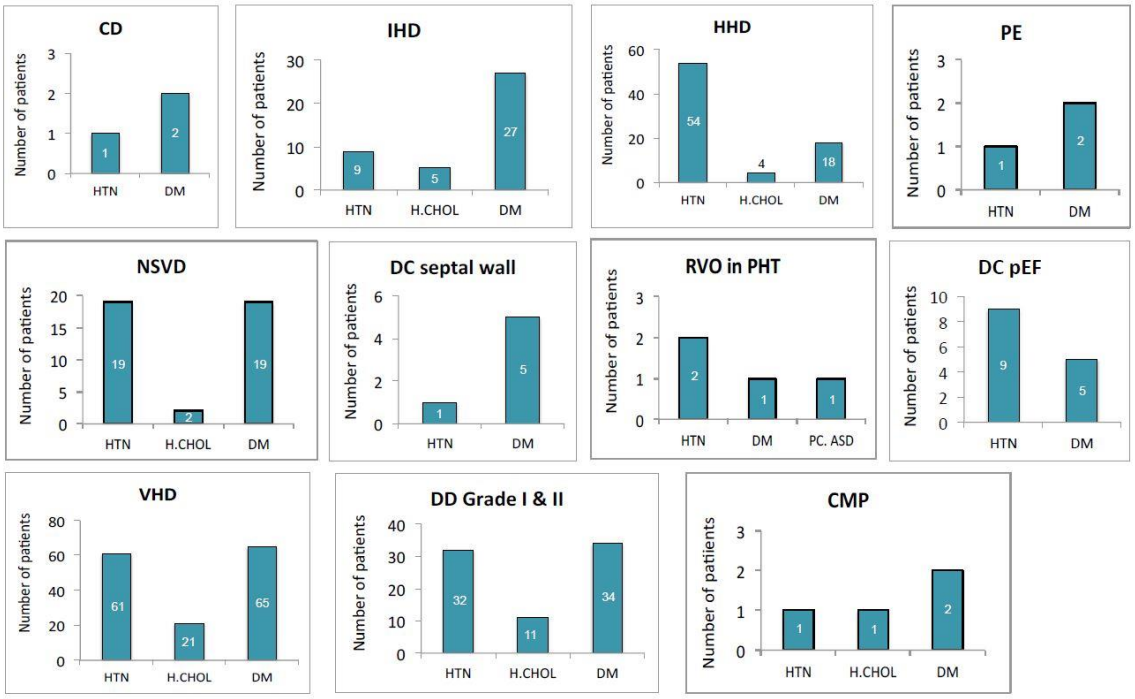

Figure 3. Distribution of associated cardiovascular/ metabolic diseases among the different TTE findings

The relative frequencies of associated cardiovascular/ metabolic disease evaluated among patients with abnormal TTE.
HTN (hypertension); H. CHOL (hypercholesterolemia); DM (diabetes mellitus) and PC. ASD (previously corrected atrial septal defect).

Discussion

The present study evaluated the supportive association between ECG and TTE, which are the two most commonly used assessment of cardiovascular health. In an ideal clinical setting, ECG is expected to be an office-based and cost-effective test that can be performed by clinicians for initial cardiovascular evaluations and based on its sensitivity, abnormalities detected by ECG strongly suggest the presence of structural heart defect that usually warrant confirmation by the usually expensive and not office based TTE. Conversely, normal ECG results clear the suspicion of structural heart defects and doesn't require further evaluation by TTE (19,20). Realistically, however, experiences in clinical practice, as well as studies conducted, indicates that there are scenarios where patients with normal ECGs exhibit signs and symptoms of cardiac abnormalities and hence providing the rationale of ordering TTE examinations (21,22). Other studies, on the other hand, have clarified that ECG and TTE are not competing for diagnostic tests, and as such, the cardiac abnormalities observed in TTE of patients with normal ECG might be ineffectual and not direct change in the clinical management of the patient (20,23). Therefore, there is a need to evaluate the frequency of cardiac abnormalities in patients with normal ECG using TTE and analyzing the clinical significance of these abnormalities.

Our study observed a high prevalence (74%) of TTE abnormalities in patients with normal ECG results,

indicating the presence of an underlying structural heart defect. Our findings are in accordance with those of previous studies where the notable frequency of TTE abnormalities in patients despite having normal ECG test results have been reported. These studies have correlated normal ECG results with the existence of underlying structural heart disease diagnosed using echocardiography, suggesting that normal ECG does not rule-out heart defects (12,24,25).

We also identified that factors such as age, BMI, and smoking status might increase susceptibility to cardiac abnormalities detected by TTE. The effect of age on cardiac structure and function (25), cardiac dysautonomia (26) as well as cardiac excitation-contraction coupling (27) have been previously reported. Rodicio *et al.*, in 2018, associated deterioration of cardiac health with the onset of overweight and obesity (28). Similarly, increased BMI and waist circumference have been shown to cause organ damage in patients on cardiac rehabilitation after acute coronary syndrome (29). Smoking, however, exhibits a major threat to cardiovascular health. Studies have implicated active or passive smoking with the peripheral arterial disease (30), circulating cardiac troponin I concentrations (31), cardiac hypertrophy and vascular inflammation (in an animal model) (32), and sudden cardiac death (33). Put-together, age, BMI, and smoking are factors that can promote the development of asymptomatic cardiac abnormalities that can be covert to ECG but detectable by TTE.

The findings of major TTE abnormalities recorded in this study were basically valve diseases. This includes VHD, which was the most common, with a prevalence of approximately 30%. The high prevalence of VHD in our study makes results from the consideration of any valvular stenosis as well as mild to moderate valvular regurgitation as abnormal. In other studies, however, a lower VHD prevalence was reported as VHD was graded as severe in order to be regarded as an abnormal finding (34-36). Traditional evaluation of VHDs using ECG P-waves has shown high sensitivity (37); however, the superiority of echocardiography over ECG in the diagnosis of VHDs has been reported in previous studies with emphasis laid on the ability of echocardiography to provide details of ejection fraction and heart volume (38). Magnetic resonance imaging is also a reproducible non-invasive method for the diagnosis of VHDs (39,40). These reports strongly suggest that normal ECG results do not preclude the presence VHDs, especially for asymptomatic diagnosis. In asymptomatic cases of suspected VHDs, caution should be taken during diagnosis as it has been reported that physical examinations are extremely important even when echocardiography is conducted (41). Another major abnormal TTE finding is the DD Grade I & II, which was diagnosed in 85 patients having normal ECG results. It was suggested in a previous study that the ECG criteria for diastolic dysfunctions are highly specific, which a very high left ventricular or atrial pressure threshold for diagnosis. The study indicated that intermediary values could be detected by echocardiography, thereby recommending the complementary use of ECG and TTE for the diagnosis of diastolic disorders (42). Although Khan *et al*., in 2016 have shown that prolonged ECG is a useful tool in predicting left ventricular diastolic dysfunction in patients with suspected heart failure, Buksinka-Lisink *et al*., in 2019 found TTE to show more details of subclinical changes in diastolic function compared to ECG (8,43). In line with our findings, it can be suggested that ECG might be useful in the diagnosis of severe cases of diastolic dysfunction but may not be significant in mild or subclinical cases. The HHD also exhibited a high prevalence (18%) among the abnormal TTE findings we recorded. The HHD encompasses abnormalities associated with protracted or sustained pressure overload, which could be from left ventricular hypertrophy (LVH), systolic or diastolic stiffness, left ventricular mass (LVM), or arrhythmias (44). Studies have shown that ECG can satisfactorily detect LVH and LVM (45,46), but with the advent of echocardiography, the relative insensitivity of ECG in detecting a prognostic increase in LVM has been identified; consequently, milder LVM can only be detected using echocardiography (46). Analysis of our findings in relation to available literature supports the suggestion that TTE could be a useful tool for early detection and predictive diagnosis of valve diseases (which could be asymptomatic or otherwise) that could go unnoticed in ECG reports.

It is important to ascertain whether these cardiac abnormalities were associated with clinically noteworthy signs and symptoms. Clinical examination of the patients with abnormal TTE results revealed symptoms that include typical and atypical chest pain, which has been implicated in numerous cardiovascular disorders. Studies have recorded experiencing atypical heart pain in patients with valve diseases. Specifically, symptoms of typical or atypical heart pain have been observed in patients with aortic regurgitation resulting from aberrant mitral chord transcending the aortic valve, as well as those with the anomalous left coronary artery (47,48). We also observed symptoms of SOB, epigastric pain, and palpitations in nearly all patients, irrespective of the type of TTE

abnormality. These symptoms have been previously reported in patients with the double-chambered left ventricle, mitral valve prolapse, and aortic valve stenosis (48-50). Symptoms of SOB have been reported in patients that have been echocardiographically diagnosed with chronic dyspnea and primary mitral valve disease (50).

We also evaluated the hypertensive, diabetic, hypercholesterolemia status as well as evidence of previous corrected atrial septal disease in the patients across the various abnormal TTE findings. Nearly all patients with cardiac abnormalities had hypertension or diabetes mellitus or both, while the majority of patients with hypercholesteremic were among those with VHD and DD Grade I & II. This was an expected outcome as the association between cardiometabolic diseases and cardiac abnormalities are well established both in literature and practice. As a pulmonary and cardiac disease that affects the pulmonary vasculature, hypertension is a cardiovascular condition that can be diagnosed using both ECG and TTE (51). The presence of cardiac abnormalities, like RVH in the form of an enlarged right ventricle and right atrium, as well as central pulmonary artery dilation, have been strongly associated with hypertension (52). Similarly, there is a body of evidence associating DM with cardiac abnormalities. Cardiac remodeling and adverse target organ damage have been reported in children/ adolescents with obesity and DM (53). In another study, echocardiographic screening has identified structural and functional cardiac abnormalities in type 2 DM patients without prior cardiovascular disease history (54,55). In 2018, Jia *et al*., identified the role of insulin resistance and hyperinsulinemia in diabetic cardiomyopathy, which is characterized by stress, fibrosis, hypertrophy, cardiac systolic and diastolic dysfunction, as well as systolic heart failure (56). Apart from familial forms of hypercholesterolemia, which are commonly associated with cardiac abnormalities (57,58), hypercholesterolemia in circadian abnormalities has to should to affect the progression of cardiovascular diseases (59). Also, a high risk of cardiac arrhythmias has been reported in hypercholesterolemia patients with liver cirrhosis (60). The correspondence between our abnormal TTE findings with clinical signs and symptoms as well as associated cardiovascular/ metabolic diseases buttresses the credibility of the clinical significance of the findings and their applicability in deciding whether a change in clinical management should be considered.

Therefore, we suggest that although there are concerns over the futile ordering of TTE for patients with normal ECG results, clinically significant cardiac abnormalities can be unraveled after TTE examinations, especially when clinical symptoms are manifested.

It is important to highlight some limitations of our study. The study does not suggest that TTE should replace ECG as a clinical diagnostic tool.

The categorization of our TTE findings as clinically significant might be rather subjective as it was based on prevalence, associated signs, and symptoms as well as the presence of cardio-metabolic diseases, rather than the severity of the cardiac abnormalities.

Also, we only analyzed the TTE findings of patients with normal ECG that were outpatients, i.e., referred to Al-Hussein Medical City in Kerbala, Iraq. Therefore, the prevalence of our findings does not represent that of all patients with the local population.

Our study reports a high prevalence of clinically significant TTE cardiac abnormalities in patients with normal ECG, thereby suggesting that patients with normal ECG should not be routinely exempted from undergoing further echocardiographic examination, especially when symptoms of the cardiac abnormality or structural heart defects are evident. We also propose that these cardiac abnormalities found in patients with normal ECG results might warrant a change in clinical management.

Acknowledgments

The authors wish to thank the Internal Medicine Department of the College of Medicine, University of Kerbala, and Imam Al-Hussein Medical City for their support.

References

1. Hung J, Lang R, Flachskampf F, Shernan SK, McCulloch ML, Adams DB, et al. 3D echocardiography: a review of the current status and future directions. J Am Soc Echocardiogr 2007;20:213-33.
2. Otto CM, Schwaegler RG, Freeman RV, Linefsky J. Echocardiography Review Guide E-Book: Companion to the Textbook of Clinical Echocardiography. Amsterdam: Elsevier Health Sciences, 2019.
3. Klein AL, Asher CR. Clinical echocardiography review: a self-assessment tool. Lippincott Williams & Wilkins: United States, 2011.
4. AlGhatrif M, Lindsay J. A brief review: history to understand fundamentals of electrocardiography. J Community Hosp Intern Med Perspect 2012;2:14383.
5. Stone JR, Lee L, Ward JP, Ward RP. High prevalence of clinically important echocardiographic abnormalities in

patients with a normal electrocardiogram referred for transthoracic echocardiography. J Am Soc Echocardiogr 2018;31:926-32.
6. Dasgupta S, Anderson S, Kelleman M, Sachdeva R. Application of pediatric Appropriate Use Criteria for initial outpatient evaluation of asymptomatic patients with abnormal electrocardiograms. Congenit Heart Dis 2019;14:230-5.
7. Tague L, Wiggs J, Li Q, McCarter R, Sherwin E, Weinberg J, et al. Comparison of left ventricular hypertrophy by electrocardiography and echocardiography in children using analytics tool. Pediatr Cardiol 2018;39:1378-88.
8. Buksińska-Lisik M, Litwin T, Pasierski T, Członkowska A. Cardiac assessment in Wilson's disease patients based on electrocardiography and echocardiography examination. Archives of medical science: Arch Med Sci 2019;15:857-64.
9. Moustafa MM, Shredah AAR, Marghany KA, Zakaria AYS. Electrocardiography versus Echocardiography for assessment of left ventricular hypertrophy in ischemic heart disease patients with and without cardiovascular risk factors. Egypt J Hosp Med 2019;74:1165-73.
10. Baturova MA, Sheldon SH, Carlson J, Brady PA, Lin G, Rabinstein AA, et al. Electrocardiographic and Echocardiographic predictors of paroxysmal atrial fibrillation detected after ischemic stroke. BMC Cardiovasc Disord 2016;16:209.
11. Calò L, Martino A, Tranchita E, Sperandii F, Guerra E, Quaranta F, et al. Electrocardiographic and echocardiographic evaluation of a large cohort of peri-pubertal soccer players during pre-participation screening. Eur J Prev Cardiol 2019;26:1444-55.
12. Gibbons RJ, Carryer D, Liu H, Brady PA, Askew JW, Hodge D, et al. Use of echocardiography in outpatients with chest pain and normal resting electrocardiograms referred to Mayo Clinic Rochester. Am Heart J 2018;196:49-55.
13. Fernando RJ, Goeddel LA, Shah R, Ramakrishna H. Analysis of the 2019 ACC/AATS/AHA/ASE/ASNC/HRS/SCAI/SCCT/SCMR /STS Appropriate Use Criteria for Multimodal Imaging in the Assessment of Structural Heart Disease. J Cardiothorac Vasc Anesth 2020;34:805-18.
14. Galderisi M, Cosyns B, Edvardsen T, Cardim N, Delgado V, Di Salvo G, et al. Standardization of adult transthoracic echocardiography reporting in agreement with recent chamber quantification, diastolic function, and heart valve disease recommendations: an expert consensus document of the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2017;18:1301-10.
15. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;73:3168-209.
16. Garvey WT. The diagnosis and evaluation of patients with obesity. Curr Opin Endocr Metab Res 2019;4:50-7.
17. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
18. Alfarisi HA, Mohamed ZB, Ibrahim MB. Basic pathogenic mechanisms of atherosclerosis. Egypt J Basic Appl Sci 2020;7:116-25
19. Aloia AA. Call to Standardize Diagnostic Practice for Type 2 Diabetes Mellitus World-Wide; A Review of Various Guidelines Used Internationally. Diabet Complications 2019;3:1-4.
20. Roth AR, Lazris A, Ganatra S. Overuse of cardiac testing. Am Fam Physician 2018;98:561-3.
21. Sachdeva R, Douglas PS, Kelleman MS, McCracken CE, Lopez L, Stern KW, et al. Effect of release of the first pediatric appropriate use criteria on transthoracic echocardiogram ordering practice. Am J Cardiol 2016;118:1545-51.
22. Kerkhof DL, Gleason CN, Basilico FC, Corrado GD. Is there a role for limited echocardiography during the Preparticipation physical examination? PM R 2016;8:S36-44.
23. Kroenke K. Diagnostic testing and the illusory reassurance of normal results: comment on "Reassurance after diagnostic testing with a low pretest probability of serious disease". JAMA Intern Med 2013;173:416-7.
24. Tewelde SZ, Mattu A, Brady Jr WJ. Pitfalls in electrocardiographic diagnosis of acute coronary syndrome in low-risk chest pain. West J Emerg Med 2017;18:601-6.
25. Hardy R, Maddock J, Ghosh AK, Hughes AD, Kuh D. the relationship between pubertal timing and markers of vascular and cardiac structure and function in men and women aged 60-64 years. Sci Rep 2019;9:1-10.
26. Prajna GS, Rao SKM, Devi GS. A Study on ECG Changes in Diabetic Patients and Its Relation to Cardiac Dysautonomia. Int J Sci Res 2019;8:73-5.
27. Dokuchaev A, Khamzin S, Solovyova O. A Population Modelling Approach to Studying Age-Related Effects on Excitation-Contraction Coupling in Human Cardiomyocytes. bioRxiv, 2019.
28. Rodicio MM, de Miguel VD, Jiménez MG, Guldrís SC,

Franco MML, Gestal AE, et al. Early cardiac abnormalities in obese children and their relationship with adiposity. Nutrition 2018;46:83-9.

29. Zhao H, Ma J, Zhou Q, Chen W, Zhu W, Cai Z, et al. Investigating the differences of body mass index and waist circumference in the follow-up assessment of patients to cardiac rehabilitation with acute coronary syndrome. Australas Phys Eng Sci Med 2016;39:1007-27.
30. Clark IIID, Cain LR, Blaha MJ, DeFilippis AP, Mentz RJ, Kamimura D, et al. Cigarette smoking and subclinical peripheral arterial disease in blacks of the Jackson heart study. J Am Heart Assoc 2019;8:e010674.
31. Skranes JB, Claggett BL, Myhre PL, Lyngbakken MN, Solomon SD, Sabatine MS, et al. Current Smoking Is Associated With Lower Concentrations of High-Sensitivity Cardiac Troponin T in Patients With Stable Coronary Artery Disease: The PEACE Trial. Circulation 2019;140:2044-6.
32. Al Hariri M, Zibara K, Farhat W, Hashem Y, Soudani N, Al Ibrahim F, et al. Cigarette smoking-induced cardiac hypertrophy, vascular inflammation and injury are attenuated by antioxidant supplementation in an animal model. Front Pharmacol 2016;7:397.
33. Aune D, Schlesinger S, Norat T, Riboli E. Tobacco smoking and the risk of sudden cardiac death: a systematic review and meta-analysis of prospective studies. Eur J Epidemiol 2018;33:509-21.
34. Anderson KL, Limkakeng A, Damuth E, Chandra A. Cardiac evaluation for structural abnormalities may not be required in patients presenting with syncope and a normal ECG result in an observation unit setting. Ann Emerg Med 2012;60:478-84.e1.
35. Chang NL, Shah P, Bajaj S, Virk H, Bikkina M, Shamoon F. Diagnostic yield of echocardiography in syncope patients with normal ECG. Cardiol Res Pract 2016;2016:1-7.
36. Han SK, Yeom SR, Lee SH, Park SC, Kim HB, Cho YM, et al. Transthoracic echocardiogram in syncope patients with normal initial evaluation. Am J Emerg Med 2017;35:281-4.
37. Beltrame M, Compagnucci P, Maolo A. P-Waves Are the Main Clues for Correct ECG Interpretation. In: Capucci A, ed. New Concepts in ECG Interpretation. Switzerland: Springer, Cham, 2019:1-7.
38. Nestaas E, Shih J-Y, Smedsrud MK, Gjesdal O, Hopp E, Haugaa KH, et al. Comparison of Electrocardiography Markers and Speckle Tracking Echocardiography for Assessment of Left Ventricular Myocardial Scar Burden in Patients With Previous Myocardial Infarction. Am J Cardiol 2017;119:1307-12.
39. Yousef HA, Hamdan AE, Elminshawy A, Mohammed NA, Ibrahim AS. Corrected calculation of the overestimated ejection fraction in valvular heart disease by phase-contrast cardiac magnetic resonance imaging for better prediction of patient morbidity. Egypt J Radiol Nucl Med 2020;51:1-11.
40. Nabeshima Y, Namisaki H, Teshima T, Kurashige Y, Kakio A, Fukumitsu A, et al. Impact of a training program incorporating cardiac magnetic resonance imaging on the accuracy and reproducibility of two-dimensional echocardiographic measurements of left ventricular volumes and ejection fraction. Cardiovasc Ultrasound 2019;17:23.
41. Nishimura RA, O'Gara PT, Bavaria JE, Brindis RG, Carroll JD, Kavinsky CJ, et al. 2019 AATS/ACC/ASE/SCAI/STS expert consensus systems of care document: a proposal to optimize care for patients with valvular heart disease: a joint report of the American Association for Thoracic Surgery, American College of Cardiology, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2019;73:2609-35.
42. Roslan A, Kamsani SH, Koh HB, Tey YS, Leong K, Tham CH, et al. Diastolic dysfunction grading, echocardiographic and electrocardiogram findings in 50 patients with apical hypertrophic cardiomyopathy. Med J Malaysia 2019;74:521-6.
43. Khan HS, Iftikhar I, Khan Q. Validity of Electrocardiographic QT Interval in Predicting Left Ventricular Diastolic Dysfunction in Patients with Suspected Heart Failure. J Coll Physicians Surg Pak 2016;26:353-6.
44. Khalique OK, Bello NA. Are We Getting Closer to the HEART of Hypertensive Heart Disease? Hypertension 2019;HYPERTENSIONAHA11913169 (Online ahead of print).
45. Dubey T, Paithankar U, Yadav B. Correlation of echocardiographic left ventricular mass index and electrocardiographic left ventricular hypertrophy variables. Int J Contemp Med Res 2016;3:1287-9.
46. Wilkinson IB, Raine T, Hall C, Wiles K, Goodhart A, O'Neill H. Oxford handbook of clinical medicine. Oxford: Oxford University Press, 2017.
47. Esfehani RJ, Hosseini S, Ebrahimi M, Jalalyazdi M, Gharaee AM. Anomalous Left Coronary Artery from the Pulmonary Artery Presenting with Atypical Chest Pain in an Adult: A Case Report. J Tehran Heart Cent 2017;12:128-30.
48. Henning RJ. Diagnosis and treatment of heart failure with preserved left ventricular ejection fraction. World j Cardiol 2020;12:7.

49. Li T, Han J, Li Y, Gao S, Hao X, He Y. Diagnosis of double-chambered left ventricle by echocardiogram and cardiac magnetic resonance imaging: A rare case in an adult. Echocardiography 2020;37:368-369.
50. Vijayalakshmi IB. Pregnancy with Mitral Stenosis and Mitral Regurgitation and Cardiac Failure. Ward Rounds Obstet Gynecol 2018;71:1-4.
51. Zhang W, Zhou Y, Bai B, Yu S, Xiong J, Chi C, et al. Consistency of left ventricular hypertrophy diagnosed by electrocardiography and echocardiography: the northern shanghai study. Clin Interv Aging 2019;14:549-56.
52. Waligóra M, Tyrka A, Miszalski-Jamka T, Urbańczyk-Zawadzka M, Podolec P, Kopeć G. Right atrium enlargement predicts clinically significant supraventricular arrhythmia in patients with pulmonary arterial hypertension. Heart Lung 2018;47:237-42.
53. Bacha F, Gidding SS. Cardiac abnormalities in youth with obesity and type 2 diabetes. Curr Diab Rep 2016;16:62.
54. Haley JE, Urbina EM. Insulin Resistance and Cardiovascular Disease. In: Insulin Resistance. New York: Humana: Cham, 2020:195-205.
55. Fumery M, Antakly Y, Garcon P, Abassade P, Boileve V, Rovani M, et al. Systematic echo-doppler screening identifies subtle structural and functional cardiac abnormalities in type 2 diabetes mellitus without documented cardio vascular disease: DIACAR a prospective study. Arch Cardiovasc Dis Suppl 2020;12:159-60.
56. Jia G, Hill MA, Sowers JR. Diabetic cardiomyopathy: an update of mechanisms contributing to this clinical entity. Circ Res 2018;122:624-38.
57. Luo Y, Zheng M, Zhang Y, He S, Zhang L, Sun H, et al. Familial hypercholesterolemia with early coronary atherosclerotic heart disease: A case report. Exp Ther Med 2019;18:981-6.
58. Ganjali S, Momtazi AA, Banach M, Kovanen PT, Stein EA, Sahebkar A. HDL abnormalities in familial hypercholesterolemia: Focus on biological functions. Prog Lipid Res 2017;67:16-26.
59. Akashi M, Matsumura R, Matsuo T, Kubo Y, Komoda H, Node K. Hypercholesterolemia causes circadian dysfunction: A potential risk factor for cardiovascular disease. EBioMedicine. 2017 Jun 1;20:127-36.
60. Calborean V, Miscoci SA, Istratoaie O, Galceava O, Alexandru DO, Guta MM, et al. Correlation Between Liver Cirrhosis and Risk of Cardiac Arrhythmias. Rev Chim (Bucharest) 2018;69:1527-32.