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Original Article

Occult Left Ventricular Dysfunction Assessed by Three-Dimensional Echocardiography in Patients with Significant LAD Single Vessel Disease; A Prospective Study

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ABSTRACT

Article information

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Background: Ischemic heart disease persists as the leading global cause of death and lost life years in adults. The assessment of cardiac function by measuring LVEF using echocardiography is the most common method in daily clinical practice.

The Aim of the work: This study aims to assess the accuracy and feasibility of three-dimensional echocardiography in the detection of occult left ventricular dysfunction in comparison with the two-dimensional speckle tracking echocardiography.

Patients and Methods: This study enrolled 100 participants in 2 groups, Group I included 50 patients with single LAD lesion eligible for PCI withp normal 2D LV EF compared to Group II including 50 healthy participants with the same demographic matched as a control group. All patients were subjected to conventional echocardiography, Three-Dimensional Echocardiography, and 2D speckle tracking before and one month after the PCI.

Results: In terms of 2D Echocardiography parameters, we found no statistically significant differences between the 2 groups in all parameters [p-value > 0.05], except for GLS [p-value = 0.001]. As regards 3D Echocardiography parameters, we found no not statistically significant differences between the 2 groups in all parameters. We compared the mean EF of 2D and 3D before and after PCI in Group I patients, and we found no statistically significant difference between 2D, and 3D in the estimation of LV volumes and LVEF before PCI [p-value = 0.7], and after PCI [p-value = 0.26].

Conclusion: There are no significant differences between 2D and 3D echocardiography in the estimation of LV volumes and LVEF in patients with significant LAD single vessel disease before and after PCI. Also, we found that the 2D Global longitudinal strain, based on speckle tracking imaging, is a potentially useful method to detect the occult LV dysfunction.

Keywords: Ischemic heart disease; Three-Dimensional Echocardiography; 2D Echocardiography.

INTRODUCTION

Ischemic heart disease remains the primary cause of death and lost life years worldwide in adults. There is a lack of consistency in the reductions of morbidity and mortality among different subgroups, as younger individuals continue to experience persistently high mortality rates. Overall, IHD continues to be a global public health issue that requires attention [1].

Chronic Coronary Syndrome [CCS] is commonly known as stable ischemic heart disease, characterized by a typical history of angina pectoris in individuals with risk factors for or existing atherosclerotic cardiovascular disease. Angina pectoris, also known as angina, is a condition characterized by chest discomfort that arises when the heart's demand for oxygen surpasses its supply. Stable angina is characterized by chest discomfort that occurs consistently and can be relieved by rest or nitroglycerin. The occurrence of anginal symptoms can differ and is believed to be less common among patients living in the community compared to those participating in clinical trials [2].

Ischemic heart disease [IHD], also known as coronary artery disease [CAD], is a condition where the myocardium does not receive enough blood flow due to blockage of the coronary arteries, typically caused by atherosclerosis. Patients can present with either acute or chronic coronary artery disease [CAD] [3].

Consistent evidence has challenged the idea that revascularization improves CCS prognosis more than OMT. The lower prevalence of severe disease in current populations and the prognostic efficacy of OMT targeting established risk determinants of coronary atherosclerosis and/or ischemia may explain these findings. Clinical practice still follows the idea that revascularization can improve symptoms and prognosis in obstructive CAD patients. Referring stable patients to invasive coronary angiography [ICA] based only on clinical suspicion and without objective evidence of inducible myocardial ischemia is still common [4].

The risk of annual cardiac death in patients with established CCS is used to describe the event risk. As in the previous version of the Guidelines, a cardiac mortality rate of more than 3% per year is considered to have a high event risk, and one of less than 1% per year is considered to have a moderate event risk [5].

In routine clinical practice, the most common method for evaluating cardiac function is the measurement of LVEF using echocardiography. There are a number of issues with this method, including low sensitivity to small changes in myocardial function, low correlation with symptoms, and inter- and intra-observer variability that is affected by preload conditions [6].

Advancements in 3-dimensional echocardiography [3DE] have led to the creation of more compact probes, improved data acquisition speed, and expanded areas of use. However, there is still a continuing discussion regarding its potential to offer supplementary insights to 2DE in the context of general hospital clinical practice [7].

So, this study aims to assess the accuracy and feasibility of three-dimensional echocardiography in the detection of occult left ventricular dysfunction in comparison with two-dimensional speckle tracking echocardiography.

PATIENTS AND METHODS

This study enrolled 100 participants in 2 groups, Group I included 50 patients with single LAD lesion eligible for PCI with normal 2D LV EF at Al-Azhar University Hospital, compared to Group II including 50 healthy participants with the same demographic match as control groups. After approval of the ethics committee at Al-Azhar University, and informed written consent from all patients, we recruited the patients according to the following criteria;

The inclusion criteria were: Patients with CCS eligible for PCI to LAD according to recent guidelines, but with normal LVEF by conventional 2D echocardiography: Severe angina symptoms, noninvasive testing indicates high risk of coronary disease, Symptoms of angina and positive stress test, Inadequate information from noninvasive testing.

The exclusion criteria were; Patients who refused to share in the study, Acute MI, Heart muscle disease [cardiomyopathy], other causes of cardiomyopathy [as severe valvular heart disease, hypertrophic cardiomyopathy …etc.], significant arrhythmia, previous pacemaker implantation, poor image quality, another significant lesion other than LAD, patients when the follow-up cannot be done, and non-viable LAD territory.

Data collection: All patients were subjected to the following; 1] Complete medical history to detect gender, age, smoking, diabetes, hypertension, ischemic heart disease, chronic kidney diseases, and other risk factors also to detect the nature and type of chest pain and to exclude unstable patients. 2] Complete physical examination including special attention to cardio-vascular to obtain clinical information such as symptom onset, and cardiovascular risk factors including smoking, hypertension, and diabetes. Then the clinical data, including heart rate [HR], systolic blood pressure, diastolic blood pressure, and body mass index [BMI], were measured. 3] A basal standard 12 leads Electrocardiogram for each patient to detect heart rate, rhythm and chamber enlargement, and ischemic changes [ST deviation or T wave inversion]. 4] Routine laboratory tests: Including complete blood count, lipid profile [low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides], liver functions, renal functions [creatinine level.], and virology. 5] Echocardio-graphy; conventional echocardiography, Three-Dimensional Echocardiography, and 2D speckle tracking were performed before and one month after the PCI.

Echocardiography: All echocardiographic studies [Conventional echocardiography, Three-Dimensional Echocardiography, and 2D speckle tracking] were performed in the left lateral decubitus position with ECG monitoring, using Philips EPIQ Cvx-3D Ultrasound System with X5-1 probe.

Conventional echocardiography: Standard views will be used to get images for the LAD territory including, Parasternal long- and short-axis views and apical four- and two-chamber views. All the patients were examined in the left lateral decubitus position. Echocardiographic images were acquired from the standard views [parasternal long-axis, parasternal short axis at the level of the great vessels, apical four–chambers, apical five–chambers, and apical two-chambers]. Recordings and calculations of different cardiac chambers and ejection fractions were done according to the recommendations of the American Society of Echocardiography.

Three-Dimensional Echocardiograph: Measuring [LV] volume at end-diastole [LVEDV], at-end systole [LVESV], Ejection Fraction [EF], and stroke volume [SV]. Patients with poor visualization [more than 2 segments] were excluded from further investigation.

Two-Dimensional speckle tracking: The aim of 2D speckle tracking Echocardiography is to obtain the global longitudinal strain [GLS].

Statistical analysis: All statistical analysis was done using the SPSS version 26 [IBM Corp., Armonk., NY., USA]. Continuous data were first examined for normality using the Kolmogorov-Smirnov test. Parametric continuous data were represented as mean and SD, and were compared by the t-test [independent t-test if not paired, and paired t-test if paired]. However, nonparametric continuous data were described as medians and IQR and were compared by using the Mann-Whitney U-test. Categorical data were described as numbers and percentages [%] and were compared by using the chi-square test. p-values less than 0.05 were considered statistically significant.

RESULTS

Our results regarding the demographic, and clinical characteristics of the participants demonstrate that both groups matched to be compared in this study. The mean age of the patients was 57.12 ± 9.8 years, which was similar to the mean age of the control group [p-value = 0.8]. The mean BMI was 25.8 ± 2.4 Kg/m2 for the patients, and 26.5 ± 1.9 Kg/m2 for the control, with no significant difference between the 2 groups [P = 0.1]. As regards the gender distribution of the participants, 58% of them were male, and 42% were female. History of the patients revealed that; 30 [60%] were smokers, 14 [28%] were diabetics, 27 [54%] were hypertensive, 11 [22%] had ischemic heart disease, and 17 [34%] had dyslipidemia [Table 1, Figure 1].

In terms of 2D Echocardiography parameters between group I and group II, we found no statistically significant differences between the 2 groups in all parameters except GLS [p-value = 0.001]. [Table 2]. Also, in the comparison between group I and group II in the term of 3D Echocardiography parameters, we found no statistically significant differences between the 2 groups in all parameters [Table 3].

We compared the mean EF of 2D and 3D before and after PCI, in Group I, and we found no statistically significant difference between 2D, and 3D before PCI [p-value = 0.7], and after PCI [p-value = 0.26] [table 4].

In Group I [patients with LAD lesion], we compared the 2D results before and after PCI, and we found that LVs and LVD didn't change after PCI [p-value = 0.7], however, the mean Ef [M-mode] increased from 63.6% to 66.9% after PCI [p-value = 0.02], Ef [Simpson] increased from 62.4% to 65.3% [p-value = 0.03], LV volume s decreased from 42.6 to 37.2 [p-value = 0.01], LV volume d decreased from 88.4 to 80.8 [p-value = 0.03], and GLS increased from 16.6 to 19.5 [p-value = 0.001] [Table 5]. According to the 3D assessment, SV increased from 76.2 to 81.6 after PCI [p-value = 0.035] [table 6].

Table [1]: Demographic and clinical characteristics of the patients

Variables		Group I [n = 50]	Group II [n = 50]	P value
Age [Years] [Mean ± SD]		57.12 ± 9.8	57.4 ± 5.3	0.8 [a]
BMI [Kg/m²] [Mean ± SD]		25.8 ± 2.4	26.5 ± 1.9	0.1 [a]
Gender, n [%]	Male	31 [62%]	27 [54%]	0.4 [b]
	Female	19 [38%]	23 [46%]	
History of smoking, n [%]	Smoker	30 [60%]	16 [32%]	0.4 [b]
	Not smoker	20 [40%]	34 [68%]	
Comorbidities, n [%]	Diabetes	14 [28%]	0 [0%]	0.002 [b]
	Hypertension	27 [54%]	0 [0%]	0.001 [b]
	Ischemic heart disease	11 [22%]	0 [0%]	0.02 [b]
	Chronic kidney disease	0 [0%]	0 [0%]	0.1 [b]
	Dyslipidemia	17 [34%]	0 [0%]	0.03 [b]

a; independent t test. b; Chi square test

Table [2]: Comparison between the 2 groups as regards the results of 2D

Variables	Group I	Group II	P value [a]
LVs	3 ± 0.52	3.5 ± 0.2	0.09
LVD	5 ± 0.61	4.5 ± 0.8	0.2
Ef [M-mode]	63.6 ± 8.8	65.5 ± 3.2	0.1
Ef [Simpson]	62.4 ± 8.8	66.1 ± 3.4	0.06
LV volume s	42.6 ± 14.5	39.5 ± 10.9	0.8
LV volume d	88.4 ± 20.5	88.2 ±18.1	0.5
GLS	16.6 ± 1.3	20.5 ± 2.9	0.001*

a: independent t test. *: significant p value

Table [3]: Comparison between the 2 groups as regards the results of 3D

3D Variables	Group I	Group II	P value [a]
EDV [ml]	109.4 ± 33.2	147.9 ± 29.1	0.08
ESV [ml]	70.3 ± 19.8	60.7 ± 19.4	0.07
EF [%]	62.9 ± 8.7	66.6 ± 4.1	0.06
EDL [cm]	8.5 ± 0.8	8.6 ± 0.97	0.3
ESL [cm]	7.7± 0.8	7.6 ± 1.2	0.64
SV [ml]	76.2 ± 17.5	109.1 ± 25.5	0.06
ED mass [g]	139.9 ± 38.4	136 ± 15.2	0.08

a: independent t test. *: significant p value

Table [4]: Comparison between the EF results of 2D and 3D in LAD group

EF [%]	2D	3D	P value
Before PCI	62.8 ± 8.8	62.9 ± 8.4	0.77 [a]
After PCI	65.3 ± 7.3	63.6 ± 7.6	0.26[a]
Difference ¶	0.2 [-3.3 – 11.5]	1.3 [- 6.12 – 8.05]	0.2[b]

a: independent t test; **b:** Mann Whitney test.

Table [5]: Comparison between the results of 2D in LAD group

Variables	Before PCI	After PCI	P value [a]
LVs	3 ± 0.52	3.07 ± 0.4	0.7
LVD	5 ± 0.61	4.92 ± 0.5	0.5
Ef [M-mode]	63.6 ± 8.8	66.9 ± 6.1	0.02*
Ef [Simpson]	62.4 ± 8.8	65.3 ± 7.3	0.03*
LV volume s	42.6 ± 14.5	37.2 ± 8.6	0.01*
LV volume d	88.4 ± 20.5	80.4 ±19.05	0.03*
GLS	16.6 ± 1.3	19.5 ± 1.3	0.001*

Data represented as mean and SD. **a:** paired sample t test. *: significant p value

Table [6]: Comparison between the results of 3D in LAD group

Variables	Before PCI	After PCI	P value
EDV [ml]	109.4 ± 33.2	109.6 ± 34.1	0.94
ESV [ml]	70.3 ± 19.8	70.3 ± 18.8	0.93
EF [%]	62.9 ± 8.7	63.6 ± 7.6	0.05*
EDL [cm]	8.5 ± 0.8	8.6 ± 0.79	0.22
ESL [cm]	7.7± 0.8	7.6 ± 0.82	0.64
SV [ml]	76.2 ± 17.5	81.6 ± 17.5	0.035
ED mass [g]	163.9 ± 38.4	158.7 ± 36.1	0.4

Data represented as mean and SD. **a:** paired sample t test. *: significant p-value

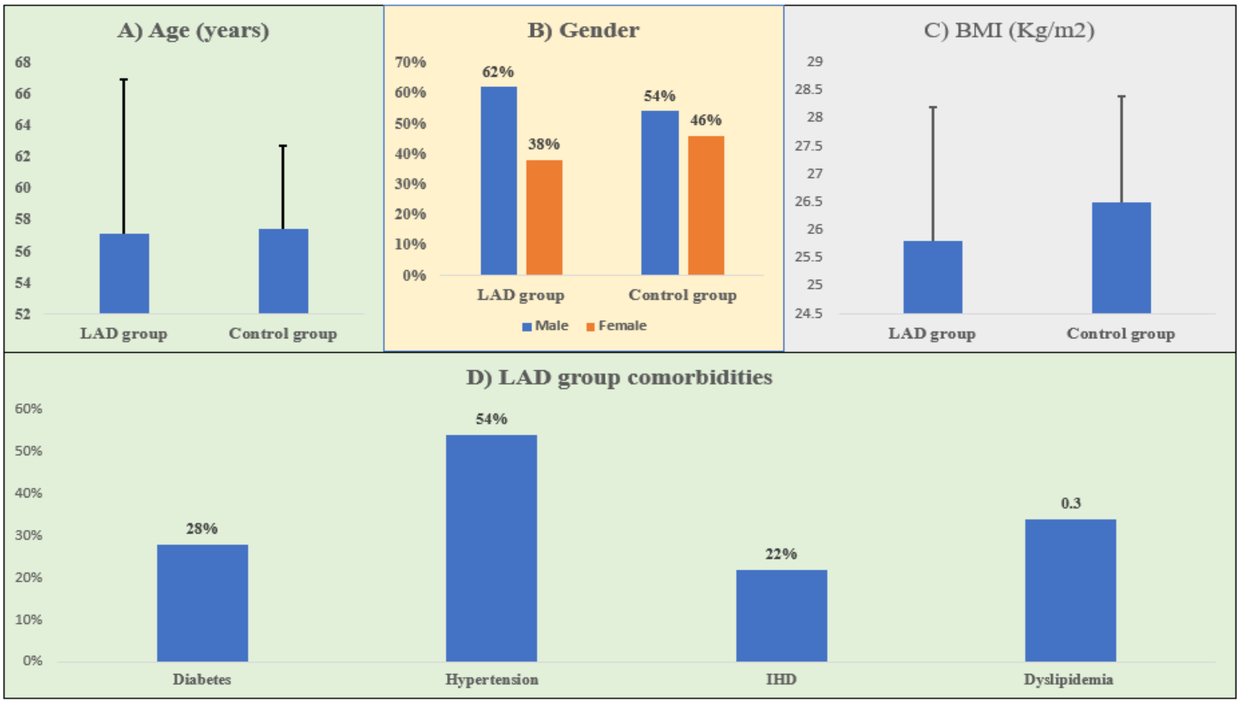

Figure [1]: Demographic data including A] Shows the mean ± SD age of the study participants, B] Shows the gender distribution of the study participants, C] Shows the mean ± SD BMI of the study participants, and E] Shows the comorbidities distribution of the included patients

DISCUSSION

In our study that conducted on 50 patients [56% males and 44% females], and 50 statically matched healthy control, regarding sex and age, also, we found that there is a significant improvement in the EF before and after PCI, using M-mode [Before = 63.6 ± 8.8, After = 66.9 ± 6.1, P = 0.02], Simpson method [Before = 62.4 ± 8.8, After = 65.3 ± 7.3, P = 0.03], and 3D model [Before = 62.9 ± 8.7, After = 63.6 ± 7.6, P = 0.05]. There was a statistically significant difference between pre and post PCI according to GLS by 2D speckle tracking Echocardiography [with p-value = 0.001] [Before = 16.6 ± 1.3, After = 19.5 ± 1.3]. In the term of LV volumes there was significant decrease in the LV volumes during systole [Before = 42.6 ± 14.5, After = 37.2 ± 8.6, P = 0.01], and during diastole [Before = 88.4 ± 20.5, After = 80.4 ± 19.05, P = 0.03]. By comparing the differences in EF before and after the PCI we found that there are no significant differences between 3D echocardiography and 2D echocardiography in detecting the change in LV function before PCI [2D = 62.8 ± 8.8, 3D = 62.9 ± 8.4, P =0.77], after PCI [2D = 65.3 ± 7.3, 3D = 63.6 ± 7.6, P =0.26], also in the changes occurs in the function [2D = 0.2 [-3.3 – 11.5], 3D = 1.3 [-6.12 – 8.05], P = 0.2]. By comparing the group with LAD to healthy control we found that there were no significant differences in the term of Ef [M-mode], Ef [Simpson], LV volume during systole, EDV, ESV, EF, EDL, ESL, SV, except GLS group I [p-value = 0.001].

In **Özbek *et al.*** [7] that conducted on 1171 patients who underwent coronary angiography for any reason and were found to have CTO in any coronary artery. They found that GLS is a valuable marker of cardiac subclinical dysfunction for all caused mortality in CTO patients.

Monitoring via STI has diagnostic and prognostic value in heart failure, ischemic heart disease, valvopathies, chemotherapy-induced cardiotoxicity, and cardiac resynchronization therapy because the change in longitudinal strain can serve as an early marker of the left ventricular systolic dysfunction. The method is effective in evaluating the function of the right ventricle and left atrium as well as arterial stiffness, despite the lack of standardization [8].

Measurement of global systolic function is crucial for risk assessment and management of all patients with cardiac disease, according to previous studies that showed similar results. GLS has shown new pathological features in cases where diastolic dysfunction was thought to be the only abnormality, and it improves the detection of systolic dysfunction beyond LVEF. The use of reduced GLS is currently well-justified for risk evaluation due to its consistent independent association of GLS with adverse outcomes [9].

In Egypt a prospective study conducted at Al-Azhar University, Assiut, Egypt, showed that the effect of PCI on LV systolic function using GLS is associated with a significant improvement in LV systolic function as shown by the significant improvement in GLS [mean GLS before PCI was −7±2.1%, which significantly improved after PCI to −13.9±1.7%; P<0.001]. they also found that PCI is associated with a significant improvement in LV systolic function as shown by the significant improvement in LVEF [mean EF before PCI by was 47.8±4.1%, which significantly improved after PCI to 57.4 ± 2.0%, and mean EF before PCI by modified Simpson’s method was 43.5±3.9%, which significantly improved after PCI to 52.8 ± 2.2%, P<0.001] [10].

In the term of occult LV disfunction previous studies showed similar results suggest that 3D echocardiography has a role in the clinical application but no additional value over 2D echocardiography can be demonstrated [11-14].

Also, both procedures showed no significant difference during stress echocardiography [15]. A previous meta-analysis included 23 paper that analyze data from 1174 patients conclude that 3D echocardiography underestimates the values of LV volumes and LVEF especially in patients with poor images or large ventricles. They also report that the 3D may has precision advantages in the term of LV volumes, but it has a little advantage in the term of LVEF. 3D echo-cardiography was found to result in slightly larger LV volumes than 2D echocardiography, whereas LVEF was similar between both methods [16].

A previous systematic review conducted by **Ruddox *et al.*** analyze data from 20 paper report that the 3D accuracy is superior to 2D in measuring LV volume and LVEF using MRI as a reference in the comparison. They also considered the 3D results is the gold standard in long term follow up. However, these mentioned advantages there are a limitation of 3D in daily practice especially in patients with poor image quality and Atrial fibrillation [AF]. Despite the clear benefits, 3DE has some technical limitations, represented by difficulty in imaging parts in LV due to the confusion occurs by ribs. Even after new small transducers the lower line density led to low spatial and temporal resolution 3D image [17].

Although 3D echocardiography makes no assumptions regarding the structure of the LV, it performs poorly in sicker individuals with bigger ventricles [18]. The large ventricles may not fit within the scanning sector allotted by the probe [19].

However, the 3D echocardiography has the ability to analyze LV segments wall motion rapidly by imaging 93-98% of LV segments wall during parasternal volume set, and 85-89% of LV segments wall during apical volume set [20, 21]. The clinical practice demonstrates no significant difference between 2D and 3D echocardio-graphy in the term of accuracy and time to perform the examination. The time necessary to 3D imaging optimization was have prolonged significantly the examination time [15].

Although it has its limitations, 3DE has the potential to outperform 2D methods. When it comes to volumes, 3DE fails to accurately portray the actual values by approximately 50% and only has half of the 95% confidence interval when compared to 2DE. Yet LVEF is the basis for a greater number of clinical decisions. There is no variation in the bias between 3DE and 2DE when using LVEF, and the variation in variance is small [±4.7%]. When looking at the intraobserver and interobserver variability, we can see that 3DE has significantly less variance, which is a benefit. For patients undergoing repeated exams to detect clinical deterioration, as well as for real-world echocardiographic labs with multiple readers and sonographers, low observer variability is of the utmost importance [16].

The accuracy of both 2D and 3D echocardiography was found to be significantly lower when using unenhanced echocardiography with state-of-the-art harmonic imaging, as compared to CMR. In a recent study, various imaging techniques were examined, including CMR, cardiac computed tomography, cine ventriculography, and 2D and 3D echocardiography. Interestingly, the study did not find any significant differences in volumes between 3D echocardiography and 2D echocardiography. This mean that 2D echocardiography has a limitation in visualization of endocardial border contours, and that need for geometric assumptions. The contrast enhancement during echocardiographic study resulted in high accuracy and better correlation to the reference values obtained by CMR, cardiac computed tomography, or cine ventriculography [22, 23].

The evidence of single and multicenter studies on LV volumes and LVEF using 2D or 3D echocardiography report the similarity of both procedures in assessing LV volumes and LVEF, and the underestimation of both procedures when compared to CMR, also some reports recommended the contrast administration which minimize the difference in volume measurements compared with CMR [24].

2D contrast imaging is superior to non-contrast 2D echocardiography regarding to LVEF and LV volume. As the measures obtained by 2D contrast was closer to CMR measures. The 2D contrast echocardiography recommended in the patient with poor acoustic windows [25, 26].

Some studies report the superiority of non-contrast 3D over non-contrast 2D ECHO [27]. Some evidence showed no significant difference between 2D and 3D echocardiography, However, 3D echocardiography showed underestimated results in patient with ventricular Desynchrony or enlarged LV [28].

Numerous studies have examined various recording and analysis techniques for non-contrast 3D ECHO. The voxel count is the most technique used with 3D echocardiography. The difference of measures between 3D software's depends on the number of 2D slices which used for tracing of the endocardium. Whereas, QLAB uses 2 orthogonal views, Tom-Tec uses at least 3 planes, however, after segmentation all further measurements are performed via voxel count [29]. The voxel counting method show superiority compared with biplane Simpson and multiplane measurements of LVEF [30].

There was no significant difference between the QLAB and Tom-Tec voxel methods, however the Tom-Tec volume measurements was closer to CMR measurements [31, 32].

The papers that study 3D echocardiography used a multi beat acquisition which mean the data needed by 3D can be acquired by small datasets during 4 or more consecutive beats assembled together electronically. **Macron *et al.*** study that compared between single beat versus multi beat 3D echocardiography reported that single beat acquisition associated with variable result of LVEF [bias 5%]. The multi beat 3D echocardiography was able to scan patients with AF [27, 33].

The comparison of 2D contrast and 3D non-contrast and contrast research cannot be concluded till now. A study by **Caiani *et al.*** that compared Simpson's biplane in 3D and 2D echocardiography with CMR in 46 patients [14 patient consented for contrast infusion during 3D]. The results showed no significant difference between two methods in the term of LVEF, while the results of EDV and ESV became worse when a contrast agent was used. This bias resulted from bubble destruction, resulting from the high density of scanlines required for full volumetric acquisition. **Thavendiranathan *et al.*** recommended non contrast 3D over contrast 3D echocardiography in patient with good image quality [27, 34].

Conclusion: There were no significant differences between 2D and 3D echocardiography in the estimation of LV volumes and LVEF in patients with significant LAD single vessel disease before and after PCI. Also, we found that the 2D Global longitudinal strain, based on speckle tracking imaging, is a potentially useful method to detect the occult LV dysfunction.

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