Al-Azhar Med. J. *Vol. 49(3), July, 2020, 1359-1368*
DOI : 10.12816/amj.2020.107131
https://amj.journals.ekb.eg/article_107131.html

ASSESSMENT OF MYOCARDIAL VIABILITY USING LOW DOSE DOBUTAMINE THREE DIMENSIONAL SPECKLE TRACKING STRESS TRANSTHORACIC ECHOCARDIOGRAPHY

By

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ABSTRACT

Background: Three-dimensional speckle tracking echocardiography (3D STE) is used recently to assess many cardiac diseases; it is considered as natural growth of two-dimensional speckle tracking echocardiography (2D STE). The LV mechanics is in nature a 3D phenomenon and its accurate assessment requires a 3D imaging method. 3DSTE has been implemented for measuring 3D strain, and has emerged as a more physiologically sound tool for analyzing the complexity of LV mechanics, overcoming the inherent limitations of 2D STE.

Objective: To determine the relative accuracy of area strain measured by 3D speckle-tracking echocardiography combined with low dose dobutamine for the detection of myocardial viability before coronary revascularization in comparison with MPI.

Patients and Methods: The study included 40 patients referred to Bab El-She'riya University Hospital nuclear lab for assessment of myocardial viability by MPI before coronary revascularization. Then all patients were referred to Islamic Cardiac Center Echo lab where complete conventional transthoracic echocardiography was done followed by Low dose dobutamine (LDD) stress transthoracic echocardiography with 3D STE then comparing results of 3D strain of viable segments with that of nonviable segments and with corresponding segments in MPI studies.

Results: The study showed that 241 segments in the 40 patients were assigned as abnormal segments, 114 were viable and 127 were nonviable, resting area strain (AS)was -18.7±2.5 for viable segments comparing to -12.6±5.3 for non-viable segment. A cut-off point of -16 was chosen to differentiate viable segments from non-viable ones with sensitivity 80.75% and specificity 83.1%. The average LDD AS value for viable segments was-24.5±2.7 and was -15.2±4.8 of non-viable segments with a cut-off point of -24 to differentiate viable segments from non-viable ones with sensitivity of 84.75% and a specificity of 89.1%. The average increase of AS of viable segments after LDD was -5.8±2.3 with a cut-off point to detect viability was a -0.24 increase in LDD from resting AS with a sensitivity of 95.75% and a specificity of 98.1%.

Conclusion: AS obtained from 3D STE may be used clinically as an indicator to detect myocardial viability with higher sensitivity and specificity when combined with LDD.

Keywords: Area Strain (AS), three dimensional (3D), speckle tracking echocardiography (STE), myocardial viability.

Abbreviations: AS: area strain- CS: circumferential strain – LS: longitudinal strain– RS: radial strain- 3D: three dimension – 3DSTE: there dimension speckle tracking echocardiography - MPI: myocardial perfusion image - LDD: low dose dobutamine - LDDSE: low dose dobutamine stress echocardiography.

INTRODUCTION

After myocardial infarction, both morbidity and mortality depend upon the extent of left ventricular (LV) systolic dysfunction. Not all dysfunctional myocardial segments are due to necrosis which is non-viable and cause irreversible damage; also hibernating and stunned segment which are viable and reversibly losing their contractile function *(Ryan and Perera, 2018)*. As for the hibernating or stunned myocardium, its contractile function may be recovered after revascularization; thus there is much-improved LV function and a higher proportion of survival in patients with ischemic cardiomyopathy (whose myocardium may be viable) than in those with large areas of nonviable or scarred myocardium *(Pegg et al., 2010)*.

Myocardial viability may be assessed by various methods that test the integrity of a number of cellular mechanisms of the viable cardiac myocytes. These mechanisms include the determination of maintained cell membrane integrity, preserved metabolic machinery, recruitable inotropic reserve (or contractile reserve), coronary micro vascular integrity and the absence of late enhancement. Viable myocardium is capable of augmenting its function in the presence of inotropic stimulus - a property called contractile reserve or recruitable inotropic reserve. The improvement in function of viable myocardium can be visualized either with echocardiography or other imaging techniques, like magnetic resonance imaging *(Adrián and Christopher, 2018)*.

Dobutamine stress echocardiography is an established method for the assessment of coronary artery disease with a sensitivity and specificity of 80% - 85% comparable to those of radio-isotopic myocardial perfusion studies *(Allman, 2013)*.

2D STE when combined with LDD stress echocardiography in assessing myocardial viability it increases the sensitivity, specificity and accuracy of echocardiography in comparison to late gadolinium enhanced cardiac MRI *(Wan, 2016)*.

Three-dimensional (3D) speckle-tracking echocardiography (3DSTE) is an advanced imaging technique designed for left ventricular (LV) myocardial deformation analysis based on 3D data sets. 3DSTE has the potential to overcome some of the intrinsic limitations of two-dimensional STE (2DSTE) in the assessment of complex LV myocardial mechanics, offering additional deformation parameters (such as area strain) and a comprehensive quantitation of LV geometry and function from a single 3D acquisition. Albeit being a relatively young technique still undergoing technological developments, several experimental studies and clinical investigations have already demonstrated the reliability and feasibility of 3DSTE, as well as several advantages of 3DSTE over 2DSTE. This technique has provided new insights into LV mechanics in several clinical fields, such as the objective assessment of global and regional LV function in ischemic and non-ischemic heart diseases *(Muraru et al., 2018)*.

The present work aimed to determine the relative accuracy of area strain measured by 3D speckle-tracking echocardiography combined with low dose dobutamine for the detection of myocardial viability before coronary revascularization in comparison with MPI.

PATIENTS AND METHODS

This study included 40 patients went to our Cardiology Department of Bab Alshe'ria University Hospital, in the period from April 2018 to- December 2019 for assessment of myocardial viability for possibility of myocardial revascularization. We exclude those with significant valvular heart disease as severe AS and severe MR and those with contraindication to dobutamine including unstable patients, such as those with decompensated heart failure or unstable angina, hypertrophic cardiomyopathy, arrhythmias that interfere with interpretation of dobutamine stress echocardiography or perfusion scintigraphy. Patients with bad echo window or when echo study protocol cannot be completed or who refuse to be included in the study all are excluded.

All Subjects underwent the following:

1. **Myocardial perfusion imaging (MPI):**

   The entire 40 patients underwent myocardial single photon emission computed tomography using Tc-99m Sestamibi (Tc-99m-sestaMIBI SPECT). The studies were done in two settings one at rest and the second at rest with nitrate potentiation in the next day, Beta-blockers, calcium antagonists and nitrates were discontinued in patients at least 24 hours before the study. Computed tomography images were acquired one hour after infusion of the radiotracer. Image acquisition was achieved with a dual head gamma camera (Siemens) without attenuation or scatter correction, using a low energy, all-purpose collimator. Trans axial tomograms were reconstructed for each patient, at short-axis, horizontal and vertical long axis slices and were analyzed. A total of 17 myocardial segments per patient were studied.

2. **Conventional transthoracic echocardiographic assessment:**

   Standard Echo-Doppler examinations were performed using a 2.5 multi frequency 1.7- 4 MHz transducer (GE Vivid 9 Ultrasound Machine). All the patients were examined in the left lateral decubitus position and echocardiographic images were acquired from the standard views (parasternal long-axis, parasternal short axis at papillary muscle level, apical four –chamber, apical five –chamber and apical two- chamber). Recordings and calculations of different cardiac chambers and ejection fractions were made according to the recommendations of the American Society of Echocardiography *(Lang et al., 2015).*

3. **Low Dose Dobutamine Stress Echocardiography (LDDSE):**

   Beta-blockers, calcium antagonists and nitrates were discontinued in patients at least 48 hours before low dose dobutamine echocardiography. Low dose dobutamine (LDD) infusion was administered using automated infusion pump. Dobutamine was delivered intravenously using 3 minutes staged protocol starting from 5 µg/kg/min for three minutes, then 10 µg/kg/min for another three minutes period, then 3 minutes recovery without dobutamine. 3D echocardiographic acquisition of full volume scan was acquired from apical window (will be verified later on). The recorded 3D image loops were digitally stored at rest and at 10 µg/kg/min LDD echocardiography for later offline analysis. Patients were continuously monitored by ECG and blood pressure measurement during the test.

4. 3 Dimension Speckle tracking echocardiography study (3D STE):

A full-volume scan was acquired by harmonic imaging from an apical approach, using a frame rate (in volume per second) higher than 40% of the individual heart rate in order to increase the possibility that the "speckles" could be recognizable in successive frames. Accordingly, four electrocardiogram-gated consecutive beats were acquired while holding the breath in expiration. The quality of acquisition was verified in each patient, before storing the volume data set, by selecting a 12-slice display mode available on the machine to ensure the entire LV cavity and wall were included in the full volume. Data sets were stored digitally in raw data format and equipped with commercially available software (4D Auto LVQ software), for analysis of LV volumes, EF, LV mass, and 4D STE deformation parameters. LV analysis was performed according to a previously described methodology *(Muraru et al., 2010)*.

RESULTS

Table (1): Demographic and risk factors data among studied group:

Factors \ Variables	Frequency (N= 40)		Percent
Age	**Mean ± SD: 56.1 ± 9.7**		
Male	**31**		**77.5%**
Female	**9**		**22.5%**
HTN	**Negative**	**19**	**47.5**
	Positive	**21**	**52.5**
DM	**Negative**	**22**	**55**
	Positive	**18**	**45**
Dyslipidemia	**Negative**	**16**	**40**
	Positive	**24**	**60**
Smoking	**Negative**	**13**	**32.5**
	Positive	**27**	**67.5**
Family history	**Irrelevant**	**21**	**52.5**
	Relevant	**19**	**47.5**

Table (2): Conventional TTE measurements:

Descriptive Statistics						
	Range			**Mean**	±	**SD**
LVIDD	**4.800**	**-**	**6.900**	**5.830**	±	**0.48**
LVISD	**3.000**	**-**	**4.700**	**3.962**	±	**0.44**
LVEDV	**100.000**	**-**	**190.000**	**145.160**	±	**13.440**
LVESV	**40.000**	**-**	**95.000**	**43.640**	±	**10.830**
EF	**29.000**	**-**	**58.000**	**39.600**	±	**7.420**

Percentage of viable and non-viable segments by MPI: A Total of 241 segments in the 40 patients were assigned as abnormal segments (viable or nonviable) by MPI with nitrate potentiation, 114 out of 241 segments revealed viability while 127 segments were assigned as non-viable, The number of viable and non-viable segments as identified by MPI after nitrate potentiation using MPI as a gold standard to distinguish between viable and non-viable segments (Table 3)

	Number	Percent
Viable	**114**	**47.3%**
Non-viable	**127**	**52.7%**
Total	**241**	**100%**

3D speckle tracking echocardiography reading Mean ± SD of different segments grouped by MPI readings both during rest and after LDD and mean difference between resting and LDD of viable and nonviable segments showing that comparing to MPI for viability detection, AS measured by 3 D STE is highly sensitive and specific tool in detecting myocardial viability especially when adding LDD. (Table 4)

	3 D speckle tracking Echo		Difference between resting and LDD	
		Mean value ±SD	**Mean difference ±SD**	**P value**
AS Viable	**Resting**	**-18.7±2.5**	5.806± 2.3-	**<0.0001**
	LDD	**-24.5±2.7**		
AS Non-viable	**Resting**	**-12.6±5.3**	2.838±**3.1-**	**<0.0001**
	LDD	**-15.2±4.8**		
LS Viable	**Resting**	**-13.3±5.3**	4.054±**2.9-**	**<0.002**
	LDD	**-17.5±1**		
LS Non-viable	**Resting**	**-9.8±3.7**	2.013±**2.1-**	**<0.001**
	LDD	**-11.1±3.8**		
CS Viable	**Resting**	**-15.8±1.5**	-2.000±**1.7**	**0.034**
	LDD	**-18.1±1.2**		
CS Non-viable	**Resting**	**-10.6±3.1**	.892±**2.04-**	**0.04**
	LDD	**-12.02±3.5**		
RS Viable	**Resting**	**15.82±1.3**	1.287±**1.3**	0.12
	LDD	**17.12±1.1**		
RS Non-viable	**Resting**	**9.54±2.3**	0.595±**0.9**	0.6
	LDD	**10.16±2.5**		

DISCUSSION

In our study we found that AS obtained from 3D STE may be used clinically as an indicator to detect myocardial viability with higher sensitivity and specificity when combined with LDD. The classic methodological gold standard for detecting myocardial viability has been positron emission tomography (PET). Since this technique is costly and not widely available, another most widely applied nuclear technique which is single-photon emission computed tomography (SPECT) utilizing the tracers 201Thallium, 99mTechnetium sestamibi, or 99mTechnetium tetrofosmin has long been used to evaluate viability. Besides these nuclear studies, the most widespread technique to assess regional myocardial viability and the potential for functional recovery has been dobutamine echocardiography *(Mansour and Zhong – hua 2014).*

Dobutamine stress echocardiography is an established method for the assessment of coronary artery disease with a sensitivity and specificity of 80% - 85% comparable to those of radio-isotopic myocardial perfusion studies *(Allman 2013).*

2D STE was approved in assessing regional wall motion abnormalities with longitudinal strain being the most sensitive parameter by detecting regional myocardial deformation. 2D STE when combined with LDD stress echocardiography in assessing myocardial viability it increases the sensitivity, specificity and accuracy of echocardiography in comparison to late gadolinium enhanced cardiac MRI *(Wang, 2016).*

3DSTE is being a relatively young technique still undergoing technological developments, several experimental studies and clinical investigations have already demonstrated the reliability and feasibility of 3DSTE, as well as several advantages of 3DSTE over 2DSTE. This technique has provided new insights into LV mechanics in several clinical fields, such as the objective assessment of global and regional LV function in ischemic and non-ischemic heart diseases *(Muraru et al., 2018).*

Several studies assessed normal individual 3D strain to detect reference values of 3D strain as *Muraru et al., 2014* and *Kleijn et al., 2013*.

Wang and his Colleagues (2015) evaluate myocardial infarction size with three-dimensional speckle tracking echocardiography in comparison with single photon emission computed tomography and they find correlation between global 3D strain detected by 3DSTE and infarction size detected by MPI

3DSTE might have potential for detection of myocardial viability in patients with cardiac dysfunction due to MI. *(Hong et al., 2016)* who compare viable myocardial segments detected by MPI as a gold standard with strain of the segments detected by 2DSTE and 3DSTE to compare between the results of viable and non-viable segments.

Our study results wers generally in agreement with the mentioned studies that used 3DSTE facility.

CONCLUSION

3D speckle tracking when added to LDD SE M increased the sensitivity and specificity of echocardiography in detection of myocardial viability and this when generally applied makes detection of viability more easy and decreases the cost and hazards of radiation exposure so.

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تقييم حيوية عضلة القلب بواسطة الموجات فوق الصوتية على القلب ثلاثية الأبعاد مع الدبيوتامين باستخدام التتبع النقطى

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خلفيـــة البحـــث: أصـــبح التتبـــع النقطـــى لعضـــلة القلـــب مـــن خـــلال الموجـــات فـــوق الصـــوتية ثلاثيـــة الابعـــاد يســـتخدم فـــى تقـــيم العديـــد مـــن الأمـــراض ، كمـــا أنـــه يعتبـــر التطـــور الطبيعـــى للتتبـــع النقطـــى لأنســـجة القلـــب مـــن خـــلال الموجـــات فـــوق الصـــوتية ثنائيـــة الأبعـــاد. وتـــأتى أفضـــلية التتبـــع النقطـــى ثلاثـــى الأبعـــاد عـــن ثنـــائى الأبعـــاد فـــى كونـــه أكثـــر محاكـــاة للحركـــة الميكانيكيـــة الطبيعيـــة لأنســـجة القلـــب. وفـــى الســـنوات الأخيـــرة أصـــبح يســـتخدم لقيـــاس إجهـــاد أنســـجة القلـــب بصـــورة ثلاثيـــة الأبعـــاد ممـــا جعلـــه أداه أفضـــل فـــى تحليـــل الحركـــة الميكانيكيـــة المعقـــدة للبطـــين الأيمـــن وأزال الكثيـــر مـــن القيـــود الموجودةعنـــد قيـــاس إجهـــاد عضـــلة القلـــب مـــن خلال التتبع النقطى ثنائى الأبعاد.

الهـــدف مـــن البحـــث: تحديـــد مـــدى دقـــة قيـــاس الإجهـــاد النطـــاقى لعضـــلة القلـــب مـــن خـــلال التتبـــع النقطـــى ثلاثـــى الأبعـــاد فـــى تشـــخيص حيويـــة عضـــلة القلـــب قبـــل عمليـــة إعـــادة إرواء شـــرايين القلـــب التاجيـــة مصـــحوبا باســـتخدام عقـــار الـــدوبيوتامين كمجهد دوائى للقلب مقارنة بالمسح الذرى لعضلة القلب.

المـــرض وطـــرق البحـــث: أجريـــت الدراســـة علـــى 40 مريضـــا قـــدموا إلـــى وحـــدة المســـح الـــذرى بمستشـــفى بـــاب الشـــعرية الجـــامعى لعمـــل مســـح ذرى علـــى عضـــلة القلـــب لتقيـــيم حيويـــة عضـــلة القلـــب قبـــل إجـــراء إعـــادة إرواء الشـــريان التـــاجى ثـــم تـــم تحويـــل المرضـــى للمركـــز الإســـلامى لأمـــراض القلـــب ، حيـــث تـــم عمـــل موجـــات صـــوتية علـــى القلـــب ثلاثيـــة الأبعـــاد باســـتخدام عقـــار الـــدوبيوتامين لإجهـــاد عضـــلة القلـــب حيـــث تـــم قيـــاس التتبـــع النقطـــى ثلاثـــى الأبعـــاد لتحديـــد قـــيم الإجهـــاد ثلاثـــى

الأبعـــاد لكـــل جـــزء مـــن اجـــزاء عضـــلة القلـــب ومقارنـــة هـــذه القـــيم بنتيجـــة المســـح الذرى لكل قطعة مقابلة لها.

نتـــائج البحـــث: اظهـــرت نتـــائج المســـح الـــذرى وجـــود 241 قطعـــة غيـــر طبيعيـــة فـــى إجمـــالى مرضـــى الدراســـة وهـــم 40 مريضـــا ، حيـــث تبـــين وجـــود حيويـــة فـــى 114 قطعـــة أمـــا البـــاقى وهـــم 127 قطعـــة فلـــم تظهـــر فيهـــا حيويـــة ، وكـــان متوســـط الإجهـــاد النطـــاقى فـــى أثنـــاء الراحـــة فـــى القطـــع التـــى ظهـــرت فيهـــا حيويـــة -18.7±2.5 مقارنـــــة للقطـــــع التـــــى لا يوجـــــد بهـــــا حيويـــــة (-12.6±5.3) وإذا أخـــــذنا -16 كنقطـــــة فاصـــــلة كانـــــت حساســـــيتها 80.75٪ وخصوصـــــيتها 83.1٪. فـــى تحديـــد القطـــع ذات الحيويـــة. بينمـــا كـــان متوســـط قـــيم الإجهـــاد النطـــاقى بعـــد إجهـــاد القلـــب باســـتخدام عقـــار الـــدوبيوتامين -24.5 ± 2.7 للقطـــع ذات الحيويـــة مقارنـــة بـــــ -15.2 ± 4.8 للقطـــع الغيـــر حيويـــة وإذا أخـــذنا -26 كنقطـــة قاطعـــة لتميـــــز القطـــــع ذات الحيويـــــة تبـــــين أن حساســـــيتها 84.75٪ وخصوصـــــيتها 89.1٪. وكـــان متوســـط زيـــادة قـــيم الإجهـــاد النطـــاقى للقطـــع القابلـــة للحيـــاة -5.8 ± 2.3 مـــع نقطـــة فاصـــلة لتميـــز القطـــع ذات القابليـــة للحيـــاة وهـــى -0.24 زيـــادة فـــى قيمـــة الإجهـــاد النطـــاقى بعـــد تنـــاول عقـــار الـــدوبيوتامين مـــن القيمـــة الأساســـية وقـــت الراحة.

الإســـتنتاج: قـــيم الإجهـــاد النطـــاقى مـــن خـــلال التتبـــع النقطـــى للقلـــب المقـــاس بالموجـــات الصـــوتيه ثلاثيـــة الأبعـــاد يمكـــن اســـتخدامها كمؤشـــر للكشـــف عـــن حيويـــة عضـــلة القلـــب، وتـــزداد دقـــة الاجهـــاد النطـــاقى فـــى تحديـــد حيويـــة عضـــلة القلـــب إذا ما كان فحص القلب مصحوبا باستخدام الدوبيوتامين كعقار مجهد للقلب.