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Original Article

Echocardiographic Assessment of Left Ventricle Torsion by Tissue Doppler and Velocity Vector Imaging

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Abstract

Introduction
Left ventricular (LV) twist is believed to store potential energy and plays an important role in generating diastolic suction. Recent advances in echocardiography techniques have allowed quantification of LV twist. The aim of the present study was to compare LV twist and torsion in healthy human subjects determined by velocity vector imaging (VVI) and tissue Doppler imaging (TDI) at rest.
Materials and Methods
All volunteers (72 healthy subjects) underwent complete echocardiographic study and LV torsional parameters were assessed using VVI or TDI methods. LV rotation at apical and basal short-axis levels was calculated throughout cardiac cycle and LV twist was defined as net difference between rotation angles of the two levels. The LV torsion was calculated as the LV twist divided by the LV end-diastolic length.
Results
Twist degree was significantly lower in the VVI group than the TDI group (11.4±2.4º vs.14.1±3.0º, $p<0.001$), but when LV twist was normalized by LV end-diastolic length, there was no statistically significant difference between the two groups (1.9±0.7 º/cm vs. 2.1±0.6 º/cm, $p=0.142$).
Conclusion
Normalized LV twist or LV torsion values were comparable for both imaging techniques (TDI and VVI methods). Results suggest that these methods may be interchanged for serial assessment, but needs additional studies and preferably larger populations to confirm it.
Keywords: Echocardiography, Left Ventricle, Torsion.

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1. Introduction

The torsional parameters of the left ventricle (LV) are sensitive indicators of the cardiac performance [1,2]. The twist of the LV is the wringing motion of the heart around its long axis created by oppositely directed apical and basal rotations and is determined by contracting myofibers in the LV wall [3,4] which are arranged in opposite directions between the subendocardial and subepicardial layers. This motion is essential for regulating the LV systolic and diastolic functions [2,5]. There is a consensus that the LV twist, expressed in degrees, and LV torsion, expressed in degrees per centimeter, both refer to the same phenomenon in the cardiac function and define the base-to-apex gradient in a rotational angle along the longitudinal axis of the LV. When viewed from the apex, the systolic rotation of the base is clockwise or negative polarity and that of the apex is counterclockwise or positive polarity [6].

The LV twist is measured by means of echocardiography. Initially, the measurement was done by studying the rotational motion of the papillary muscles [7]. Recently, however, the LV twist has been assessed by measuring rotational mechanics via tissue Doppler imaging (TDI) and speckle tracking echocardiography (STE) based on different concepts [8-11]. TDI can be derived from primary velocity data with higher temporal resolution but with intrinsic angle dependency constraints common to all Doppler methods and STE by frame-to-frame tracking of unique speckle patterns created by the interference of ultrasound beams within the tissue. The accuracy of these novel technologies has recently been validated by sonomicrometry and tagged magnetic resonance imaging [9-11]. In a study, the ability of STE to assess the LV torsional deformation was validated against the TDI method and tagged MRI [11]. In another study, the LV torsional deformation was studied in a closed-chest animal model, using both tissue Doppler and STE [12].

Velocity vector imaging (VVI) is a novel sophisticated STE that involves endocardial border tracking performed with Fourier techniques, which can track routine two-dimensional (2D) echocardiographic images. Using VVI, the tissue velocity is displayed as a vector projected on a 2D echocardiographic image where the vector shows the direction and velocity of the myocardial movement [8]. The evaluation of LV torsion can be challenging and warrants the use of sophisticated tools such as VVI. The aim of our study was to compare LV torsion as determined by VVI and TDI in healthy human subjects.

2. Materials and Methods

2.1. Study population

Seventy-two adult healthy men and women (48±14 years old) were included in the present study. They were randomly divided into two groups and two different vendor platforms were used to assess LV torsion. All of the volunteers underwent complete echocardiographic study (2D, m-mode, and Doppler).

None of the study participants had a history of cardiovascular disease and all had normal physical examinations, ECG, and resting echocardiography. Exclusion criteria were diabetes mellitus, smoking, obesity, hypertension, and other risk factors. The study was approved by the institutional Ethics Committee, and informed consent was obtained from all of the participants.

2.2. Echocardiography

Transthoracic echocardiography was performed with commercial GE Vivid System (Horten, Norway) and equipped with an M3S multi-frequency harmonic phased array transducer (Horten, Norway) for the assessment of LV torsion via the tissue Doppler-based method and MyLab50 (ESAOTE, Florence, Italy) for the VVI method. Images were acquired with the subjects at rest while lying in the left lateral supine position at the end of expiration. Two-dimensional ECG was superimposed on the images and end-diastole was considered at the peak R-wave of the ECG.

2.3. Doppler myocardial imaging and off-line analysis

Measurement of the LV torsion using tissue Doppler velocity data sets was introduced recently by Notomi et al. [9]. In the present study, this method was employed for the assessment of the LV function. Using standard LV parasternal short-axis views in two base and apical levels, color Doppler myocardial imaging (CDMI) was recorded throughout the three cardiac cycles according to the guidelines of the American Society Echocardiography (ASE) [13]. An appropriate velocity scale was chosen to avoid CDMI data aliasing and sector angle was adjusted to ensure the highest possible sampling frequency. Care was taken to keep the anterior and posterior LV segments perpendicular to the ultrasound beam and aligned at as near zero degrees as possible to the radial motion. Moreover, the images were stored digitally in cine-loop format in the memory of the scanner. The digitally stored CDMI data sets were processed off-line using the EchoPac quantitative analysis software (GE, Horten, Norway) and equipped to obtain the regional myocardial velocity. The tissue velocity imaging analysis with 8-mm volume samples was conducted from the anterior and posterior segments of the LV walls for extracting radial velocity-time curves and the lateral and septal segments for extracting the tangential component of velocity (Figure 1) in both base and apical short-axis levels. Because TDI method is angle dependent, the measurements were limited to LV anterior, posterior, lateral, and septal segments.

The velocity-time data set of each sample throughout the cardiac cycle was saved on compact disc using the CD writer of the system and transferred to Excel 2003 spreadsheet program for the basal and apical rotations, LV twist, and torsion calculations. All of the calculations were averaged for at least three consecutive heart beats.

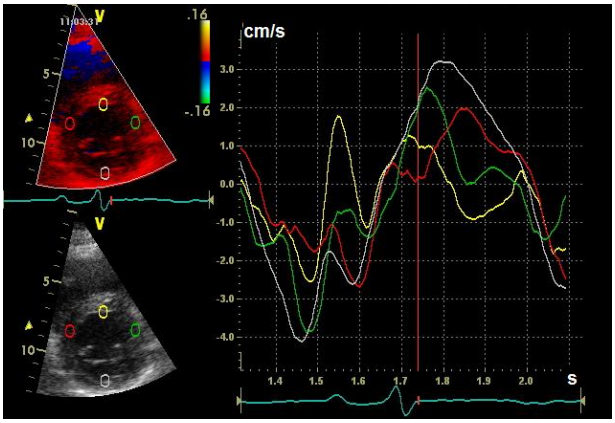

Figure 1. The profile curves of the myocardial anterior and posterior velocities (yellow and white volume samples, respectively) used to track the LV radius and the profile curves of the myocardial septal and lateral tangential velocities (red and green volume samples, respectively) used to calculate the LV rotational velocity in the basal level throughout one cardiac cycle.

To convert the tangential velocity (cm/s) into angular velocity (degree/s), the time-varying radius of the LV [r(t)], both at the basal and apical levels, was estimated using the anterior and posterior velocity data sets (Figure 1) [14]:

$$r(t) = r(0) + \frac{\int_0^t [Va(t) - Vp(t)].dt}{2}$$

Where Va and Vp are the myocardial velocity at the anterior and posterior regions and r(0) is the end-diastolic radius.

From the lateral and septal velocity data sets, the LV rotational velocity was estimated from the averaged tangential velocity corrected with r(t) as follows:

$$Vrot(t) = \frac{(Vl(t) - Vs(t))}{2 \times r(t)} \times \frac{180}{3.14}$$

Where Vl and Vs are the myocardial velocity at the lateral and septal regions and Vrot(t) is the LV rotational velocity (degree/s) both at the basal and apical levels. The LV rotation (degrees) at the basal and apical levels was calculated rotational velocity (degree/s) at the apical and basal levels as follows:

$$LV\,Apical\,Rotation(t) = \int_0^t Apical\,Vrot(t).dt$$

and

$$LV\,Basal\,Rotation(t) = \int_0^t Basal\,Vrot(t).dt$$

The LV twist (degrees) was calculated as LV apical rotation minus LV basal rotation and the time sequence was normalized to the percent of systole duration (t=100% at end-systole). The peak systolic twist was measured as is demonstrated in Figure 2. LV length was measured in the two-dimensional echocardiography images in end-diastole (distance between apex and mitral valve mid-point). LV torsion was calculated as the LV twist divided by the LV longitudinal length in diastole.

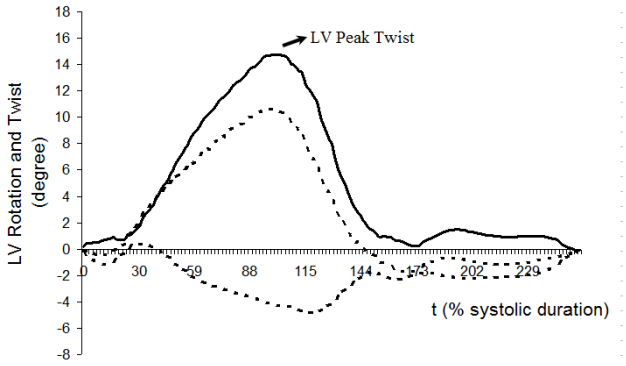

Figure 2. The profile curves of the LV rotation in the basal (negative dashed curve) and apical (positive dashed curve) levels and the LV twist and untwisting (thick continued curve) throughout one cardiac cycle via the TDI method.

2.4. Vector velocity imaging and off-line analysis

Two standard parasternal short-axis views in the basal and apical levels were subsequently processed off-line by the speckle tracking XStrain software (ESAOTE, Florence, Italy). For the initial position of the tracking points based on the ASE's 18 segments segmentation of the heart, the aided heart segmentation (AHS) mode was utilized to insert well equal-spaced tracking points over the 2D echocardiographic images and the points were tracked automatically. Accordingly, at the end of diastole, 12 and 8 tracking points were positioned at the basal and apical levels (Figure 3), respectively. The system then applied a sequence of processing steps to track the motion of the segments from frame to frame. The rotation of the LV segments about the LV central axis at each short-axis level was calculated separately based on the average motion of the three points.

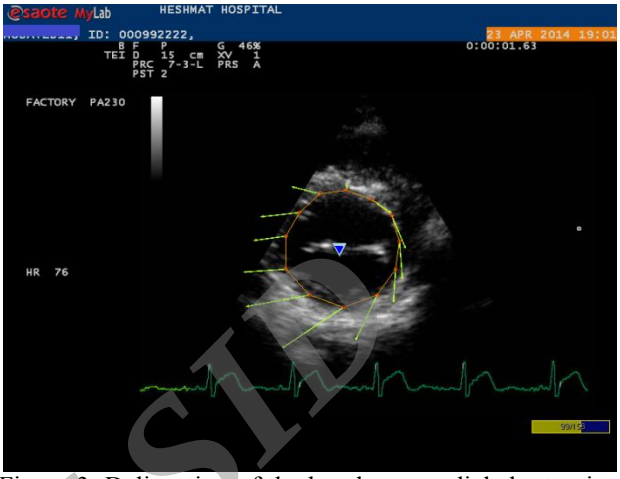

Figure 3. Delineation of the basal myocardial short-axis view during VVI analysis.

The data of all the sample regions tracking (6 segments for basal and 4 segments for apical levels) were transferred to Excel spreadsheet program for the LV average rotation and rotational velocity calculation. For example, Figure 4 shows the plots of the LV rotation versus time derived from each segment of the basal short-axis and also the average values throughout one cardiac cycle. The LV twist (degrees) was calculated as LV apical rotation minus LV basal rotation. The counterclockwise LV apical rotation and torsion as viewed from the apex were expressed as positive values, and their clockwise LV rotation were expressed as negative values for the basal level in both TDI and VVI analyses. Similar to the TDI method, peak systolic twist was measured as is demonstrated in Figures 4. LV torsion was calculated as the LV twist divided by the LV length in diastole.

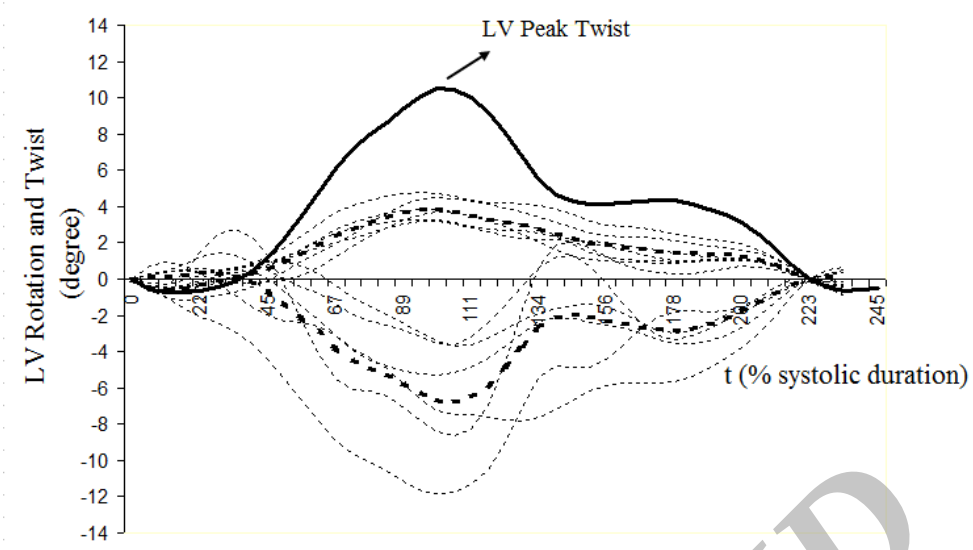

Figure 4. The profile curves of the apical (positive thin dashed curve), basal (negative thin dashed curve) segmental, average apical and basal rotations (positive and negative thick dashed curves, respectively) and the LV twist and untwisting (thick continued curve) via the VVI method throughout one cardiac cycle.

2.5. Statistical analysis

All of the statistical analyses were performed using the SPSS version 13.0 software package (SPSS Inc. Chicago, IL, USA). All of the continuous variables are presented as mean±standard deviation (SD). The data were tested for normal distribution using the Kolmogorov-Smirnov (K-S) test. To determine whether the difference in the values between the two methods was statistically significant, independent samples t-test analysis was performed. A p-value $\leq$ 0.05 was considered statistically significant.

3. Results

The clinical characteristics and echocardiographic data of the two groups are summarized in Table 1. The results of the comparisons between the two study groups showed no significant difference in terms of the demographic, hemodynamic, and echocardiographic characteristics.

Table 1. Demographic, hemodynamic, and resting echocardiographic characteristics of the study participants.

Variable	VVI group	TDI group	P-value
Gender (male/female)	18/18	18/18	NS
Body surface area (m2)	1.8±0.2	1.7±0.2	NS
Age (year)	48±14	49±15	NS
Heart rate (beats/min)	75±8	75±9	NS
SBP (mmHg)	125.7±9.0	123.8±6.2	NS
DBP (mmHg)	78.6±8.6	79.0±8.3	NS
LA volume (ml)	37.9±9.3	38.6±8.4	NS
LA volume/BSA (ml/m2)	21.8±4.9	22.9±4.5	NS
LVEDD (cm)	6.4±1.6	6.9±1.5	NS
LVEDD/BSA (cm/m2)	3.7±0.8	4.0±0.7	NS
LVESD (cm)	3.8±0.5	3.7±0.5	NS
LVESD/BSA (cm/m2)	2.2±0.5	2.3±0.4	NS

SBP=Systolic blood pressure, DBP=Diastolic blood pressure, LA=Left atrium, BSA=Body surface area, LVEDD=Left ventricular end diastolic diameter, LVESD=Left ventricular end systolic diameter, NS=Non significant (p-value $\leq$ 0.05).

The twist degree was significantly lower in the VVI group compared with the TDI group (11.4±2.4º vs.14.1±3.0º, p<0.001). However, when LV twist was normalized by LV end-diastolic length, there was no statistically significant difference between the two groups (1.9±0.7 º/cm vs. 2.1±0.6 º/cm, p=0.142).

4. Discussion

In this study, we demonstrated that LV torsional deformation assessed by VVI was comparable with those by TDI in healthy human subjects.

Ventricular torsion is a sensitive marker of dysfunction and is a useful clinical measure for the early recognition of subclinical LV dysfunction before other indices of the systolic and diastolic functions are impaired [14]. Over the years, different methods have been employed for the assessment of the LV torsion: cine-angiographic markers, rotational devices, echocardiography, and tagged MRI [15-20]. For a long time, cardiac magnetic resonance with tissue tagging was deemed gold standard for the quantification of the LV rotation, twist, and absolute myocardial torsion between the basal and apical LV slices. Nevertheless, it is not a practical technique for routine clinical use on account of the fact that it is a costly and cumbersome technique, is not widely available, and has a long analysis time with low temporal resolution [2, 3, 8, 21]. In recent years, echocardiography has evolved from a diagnostic tool into a complex technique able to provide quantitative information to alter the management of most cardiac diseases.

TDI is used to quantify myocardial regional function. Unfortunately, TDI suffers from the angle dependency, which may compromise the validity of results. As a case in point, when the angle between the ultrasonic beam and the tissue is >20º, real velocity is underestimated and thus loses its validity [22], which is a major limitation for the evaluation of the rotation and the measurement of the LV angular velocities because it is limited to two septal and lateral segments in the short-axis views. STE as another echocardiographic technique was first introduced in 2004. It has been validated as a feasible method for measuring the LV rotation and torsion [11, 23, 24]. This technique is based on the frame-by-frame tracking of the ultrasound speckles within the image. Using this method, myocardial strain and torsion can be assessed from the displacement of theses speckles relative to each other and angle dependency can thus be overcome. VVI is an advanced STE method based on myocardial feature tracking and assesses the myocardial motion in two dimensions [25-27].

Yoon et al. showed both TDI and speckle tracking imaging as sufficiently accurate and reliable alternatives to MRI in the non-invasive assessment of the LV torsion [28]. Because our center was not equipped with an MR tagging system, we could not compare our results with those that could have been obtained by that system. Baykan et al. evaluated the VVI method for the assessment of the different parameters of the LV wall motion and found VVI as a reliable non-invasive method for evaluating the LV torsional deformation and synchronization in both dilated cardiomyopathy patients and normal individuals [29]. In the current study, we used two different vendor platforms and compared the normalized LV twist obtained by the TDI and VVI methods in two healthy populations. The profile curves of the LV twisting and untwisting by the TDI and VVI methods in our healthy study population are represented in the result section.

Notomi et al. assessed the LV twist in 13 patients with a variety of cardiac pathologies. Regression analysis by repeated-measures regression models for the measurement of the LV twist and LV twisting velocity by STE indicated a strong correlation with those estimated by MRI and TDI (r=0.93, p<0.001). The limits of agreement analysis demonstrated a non-significant mean difference in the measurement of the LV twist [11]. Moreover, Kim et al. compared the twist-related values determined by VVI and STE and found that the peak twist as determined by STE and VVI was

well correlated regarding the twist [24]. We used VVI and TDI methods to extract LV normalized twist in healthy human subjects at rest.

4.1. Study limitation

Both TDI and VVI techniques are regarded as time-consuming and difficult to measure LV twist and thus have limited routine application for studying human heart. The fact that we included different healthy subjects in the study groups at rest (with the limitation of assessment during stress) and tried to match them with respect to demographic, hemodynamic, and echocardiographic characteristics precluded a comparison between the results of the two methods by regression and Bland-Altman analyses. Further studies are required to probe into this issue in a more meticulously matched study population.

The frame rate in TDI was significantly higher than that in VVI (130+20 fps vs. 60+10 fps, $p<0.05$). It is conceivable that at least some of our findings may have been affected by the difference in time resolution between the methods.

5. Conclusion

Our findings showed that there was a significant difference in the twist between the two methods, however, when the LV twist was normalized to the LV length (torsion), the values were comparable in both imaging techniques. Results suggest that these methods may be interchanged for serial assessment, but needs additional studies and preferably larger populations to confirm it.

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References

1. Moustafa SE, Kansal M, Alharthi M, Deng Y, Chandrasekaran K, Mookadam F. Prediction of incipient left ventricular dysfunction in patients with chronic primary mitral regurgitation: a velocity vector imaging study. Eur J Echocardiogr. 2011 Apr; 12(4):291-8.
2. Ennis DB, Nguyen TC, Itoh A, Bothe W, Liang DH, Ingels NB, et al. Reduced systolic torsion in chronic pure mitral regurgitation. Circ Cardiovasc Imaging. 2009 Mar; 2(2):85-92.
3. Partho P. Sengupta, Tajik AJ, Chandrasekaran K, Khandheria BK. Twist mechanics of the left ventricle: principles and application. J Am Coll Cardiol. 2008 May; 1(1):366-76.
4. Phan TT, Shivu GN, Abozguia K, Gnanadevan M, Ahmed I, Frenneaux M. Left ventricular torsion and strain patterns in heart failure with normal ejection fraction are similar to age-related changes. Eur J Echocardiogr. 2009 Aug; 10(6):793-800.
5. Shawa SM, Foxa DJ, Williams SG. The development of left ventricular torsion and its clinical relevance. Int J Cardiol. 2008 Nov; 130(3):319-25.
6. Takeuchi M, Otsuji Y, Lang RM. Evaluation of left ventricular function using left ventricular twist and torsion parameters. Curr Cardiol Rep. 2009 May; 11(3):225-30.
7. Garot J, Pascal O, Diebold B, Derumeaux, Gerber BL, Dubois-Rande JL, et al. Alterations of systolic left ventricular twist after acute myocardial infarction. Am J Physiol Heart Circ Physiol. 2002;282:357-62.
8. Deng Y, Alharthi MS, Thota VR, Yin L, Li C, Emani UR, et al. Evaluation of left ventricular rotation in obese subjects by velocity vector imaging. Eur J Echocardiogr. 2010; Jun 11(5):424-8.
9. Notomi Y, Setser RM, Shiota T, Martin-Miklovic MG, Weaver JA, Popovic ZB, et al. Assessment of left ventricular torsional deformation by Doppler tissue imaging: validation study with tagged magnetic resonance imaging. Circulation 2005;111:1141-7.
10. Helle-Valle T. Crosby J, Edvardsen T, Lyseggen E, Amundsen BH, Smith HJ, et al. New non-invasive method for assessment of left ventricular rotation: speckle tracking echocardiography. Circulation 2005;112:3149-56.

11. Notomi Y, Lysyansky P, Setser RM, Shiota T, Popovic ZB, Martin-Miklovic MG, et al. Measurement of ventricular torsion by two dimensional ultrasound speckle tracking imaging. J Am Call Cardiol. 2005 June; 45(12):2034-41.
12. Ferferieva V, Claus P, Vermeulen K, Missant C, Szulik M, Rademakers F, et al. Echocardiographic assessment of left ventricular untwist rate: comparison of tissue Doppler and speckle tracking methodology. Eur J Echocardiogr. 2009 Jul; 10(5):683-90.
13. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et all. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr. 1989; 2: 358-67.
14. Han W, Xie MX, Wang XF, Lu Q, Wang J, Zhang L, et al. Assessment of left ventricular torsion in patients with anterior wall myocardial infarction before and after revascularization using speckle tracking imaging. Chin Med J. 2008 Aug; 121(16):1543-8.
15. Nakai H, Takeuchi M, Nishikage T, Kokumai M,Otani S, Lang R.M. Effect of aging on twist-displacement loop by 2-dimensional speckle tracking imaging. J Am Soc Echocardiogr. 2006 Jul; 19(7):880-5.
16. Ingels NB Jr, Hansen DE, Daughters GT 2nd, Stinson EB, Alderman EL, Miller DC. Relation between longitudinal, circumferential, and oblique shortening and torsional deformation in the left ventricle of the transplanted human heart. Circ Res. 1989 May; 64(5): 915-27.
17. Gibbons-Kroeker CA, Ter-Keurs HE, Knudtson ML, Tyberg JV, Beyar R. An optical device to measure the dynamics of apex rotation of the left ventricle. Am J Physiol 1993 Oct;265(4):1444-9.
18. Kim HK, Sohn DW, Lee SE , Choi SY, Park JS, Kim YJ, et al. Assessment of left ventricular rotation and torsion with two-dimensional speckle tracking echocardiography. J Am Soc Echocardiogr. 2007 Jan; 20(1):45-53.
19. Kroeker CA, Tyberg JV, Beyar R. Effects of ischemia on left ventricular apex rotation. An experimental study in anesthetized dogs. Circulation 1995; 92:3539-48.
20. Knudtson ML, Galbraith PD, Hildebrand KL, Tyberg JV, Beyar R. Dynamics of left ventricular apex rotation during angioplasty: a sensitive index of ischemic dysfunction. Circulation 1997; 96:801-8.
21. Esch BT, Warburton DER. Left ventricular torsion and recoil: implication for exercise performance and cardiovascular disease. J Appl Physiol. 2009 Feb; 106(2):362-9.
22. Kowalski M, Kukulski T, Jamal F, D'hooge J, Weidemann F, Rademakers F, et al. Can natural strain and strain rate quantify regional myocardial deformation? A study in healthy subjects. Ultrasound in Med & Biol. 2001 Aug; 27(8):1087-97.
23. Leitman M, Lysyansky P, Sidenko S, Shir V, Peleg E, Binenbaum M, et al. Two dimensional strain: a novel software for real-time quantitative echocardiographic assessment of myocardial function. J Am Soc Echocardiogr. 2004 Oct; 17(10):1021-9.
24. Kim DH, Kim HK, Kim MK, Chang SA, Kim YJ, Kim MA, et al. Velocity vector imaging in the measurement of left ventricular twist mechanics: head-to-head one way comparison between speckle tracking echocardiography and velocity vector imaging. J Am Soc Echocardiogr. 2009 Dec; 22(12),1344-52.
25. Jarnert C, Melcher A, Caidahl K, Persson H, Ryden L, Eriksson MJ. Left atrial velocity vector imaging for the detection and quantification of left atrial diastolic function in type II diabetes. Eur J Heart Fail. 2008 Nov; 10(11):1080-7.
26. Liu X , Zhian Li Z. Assessment of cardiac twist in dilated cardiomyopathy using velocity vector imaging. Echocardiography 2010 Apr; 27(4):400-5.
27. Pirat B, Khoury DS, Hartley CJ, Tiller L, Rao L, Schulz DG, et al. A novel feature-tracking echocardiographic method for the quantification of the regional myocardial function: validation in an animal model of ischemia-reperfusion. J Am Coll cardio. 2008 Feb; 51(6):651-9.
28. Yoon AJ, Bella JN. New option in noninvasive assessment of left ventricular torsion. Future Cardiol. 2009 Jan; 5(1):51-61.
29. Hegazy AM, Akbar MA, Al-Sayegh A, Abdulkader BA. Predictive accuracy of tissue Doppler imaging for assessment of non-infarcted myocardial region in patients with acute myocardial infarction. Med Princ Pract. 2007;16(1):40-6.