

Original Paper

The Additive Value of 2D Longitudinal Strain During Stress Echocardiography in Coronary Artery Disease Detection in Low Risk Acute Coronary Syndrome - A Pilot Study

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REZUMAT

Valoarea cuantificării strainului longitudinal bidimensional în timpul ecocardiografiei de stres în detectarea bolii coronariene la pacienții cu sindrom coronarian acut cu risc scăzut – studiu pilot

Obiective: Evaluarea deformării miocardice (strain longitudinal) în timpul ecocardiografiei de stres farmacologic. Pornind de la acest studiu pilot aducem în discuție fiziopatologia și rolul alterării strainului longitudinal în detectarea bolii coronariene ischemice.

Metode: Studiul a inclus 10 pacienți care s-au prezentat la camera de gardă pentru durere toracică acută stratificată ca sindrom coronarian acut la risc scăzut pe baza scorului de risc GRACE. La 24 ore de la internare toți pacienții au fost evaluați prin ecocardiografie de stres utilizându-se protocoale standardizate: 5 pacienți au fost examinați cu dipiridamol, 5 cu dobutamină-atropină. Deformarea miocardică longitudinală a fost evaluată prin metoda speckle tracking în repaus, la fiecare treaptă de stres și în perioada de recuperare. În două cazuri s-a înregistrat scăderea strainului longitudinal la stres în absența tulburărilor de cinetică segmentară. Toți pacienții au fost explorați ulterior coronarografic, indiferent de răspunsul la proba de stres, dat fiind faptul ca au prezentat angina sau modificari electrocardiografice în timpul testului, în absența tulburărilor de cinetică segmentară. Doar cei doi pacienți care au avut valori alterate ale strainului longitudinal la stres au avut boală coronariană semnificativă.

Concluzii: Studiul ilustrează faptul că analiza cantitativă a deformării miocardice este superioară analizei vizuale a tulburărilor de cinetică în timpul ecocardiografiei de stres. Utilizarea strainului longitudinal alături de criteriile ecocardiografice convenționale ar putea conduce la creșterea sensibilității ecocardiografiei de stres în detectarea bolii coronariene ischemice. Această ipoteză trebuie verificată pe grupuri mai mari de pacienți.

Cuvinte cheie: ecocardiografie de stres, ecocardiografie speckle-tracking, deformare miocardică longitudinală, strain longitudinal, sindrom coronarian acut la risc scăzut

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ABSTRACT

Objectives: To assess the additive diagnostic value of longitudinal strain (LS) analysis during stress echocardiography and discuss the pathophysiological base and the role of LS alterations in coronary artery disease (CAD) detection.

Methods: We performed stress echocardiography 24 hours after admission in 10 patients presented with acute chest pain (ACP), stratified as low risk acute coronary syndrome (ACS) by GRACE score. Dipyridamole was used in 5 of the patients, while dobutamine-atropine protocol was employed in the other 5 patients, using state of the art protocols. Two dimensional (2D) speckle tracking derived LS was assessed using a semiautomated function imaging software at baseline, peak dose and recovery. All studies were negative by conventional 2D echocardiographical criteria but LS analysis showed altered values at peak stress in two cases suggestive of ischemic myocardium. All patients were referred to coronary angiography, due to the fact that they developed angina or ECG changes during the test, in the absence of wall motion abnormalities. Only those with altered LS values during stress showed significant CAD.

Conclusions: Our pilot study highlights that quantitative analysis of myocardial deformation appeared to be superior over conventional visual analysis of contractility for myocardial ischemia detection. Addition of LS analysis at conventional 2D echocardiographical criteria could lead to an increased sensitivity of pharmacological stress echocardiography. This hypothesis should be checked on a larger group of patients.

Key words: stress echocardiography, speckle-tracking echocardiography, two-dimensional longitudinal strain, low risk acute coronary syndrome

INTRODUCTION

Approximately 20% of patients arriving in the crowded emergency departments (ED) present with acute chest pain (ACP) and 60% are admitted in order to rule out an acute coronary syndrome (ACS). In the latter category, the ACS is confirmed only in 15% of patients thus resulting in a huge number of unnecessary admissions and wasted resources. (1) Stratifying ACP as low, moderate or high risk ACS allows physicians to take immediate action, initiate treatment and transfer the patient to the appropriate location.

The most problematic diagnosis and the most prevalent situation is encountered in patients classified as low risk ACS in whom the history, physical examination, ECG and cardiac biomarkers are not diagnostic. More than 5% of the initially presumed low risk patients develop a myocardial infarction after early discharge. (1) In order to reduce the crowding and length of stay in the ED and, to avoid the catastrophic consequences of the premature discharge of patients at risk for coronary events, new strategies should be considered in the evaluation of patients with moderate and low risk ACS.

Conventional tools for risk assessment

Common risk assessment tools including TIMI,

(2) PURSUIT (3), or GRACE risk scores (4) have been applied to predict outcomes in patients presenting to the ED with ACP. Unfortunately, no high sensitive tools exist to detect coronary artery disease (CAD) in low risk ACS patients and no definitive study has demonstrated the superiority of risk assessment scores or clinical prediction rules over clinician judgment, including the additional diagnosis testing. (5)

Accelerated diagnostic protocols in the ED

In the majority of patients with medium and low risk ACS noninvasive testing for diagnosis and further risk stratification is the appropriate initial strategy, as part of the accelerated diagnostic protocol recommended by the current guidelines. (5) The utility of these accelerated diagnostic protocols comprises in detecting patients with benign conditions versus those who require admissions for significant CAD. A negative accelerated diagnostic protocol evaluation allows the discharge, whereas patients with positive findings are admitted. Briefly, these protocols involve serial ECG and troponine measurements, both of which can be performed easily in the ED.

Some protocols also call for a functional or anatomical test (e.g., treadmill test, rest scintigraphy, coronary CT angiography, stress imaging).

Depending on the pretest probability of CAD in

each patient, a different type of stress test should be used. In young patients with very low pretest probability (<15%), no risk factors and TIMI score = 0, the best choice is CT coronary angiogram in order to assess coronary anatomy (IIa A) or rest myocardial perfusion imaging with a Technetium-99m radiopharmaceutical to exclude myocardial ischemia (IIa B). (5) However, it seems that the use of CT coronary angiogram lead to an increased number of coronary angiograms and percutaneous interventions without a certified long term benefit to this low-risk category of patients (6).

Non-invasive, imaging-based diagnostic methods for CAD have typical sensitivities and specificities of approximately 85%.

Stress echocardiography for detection of CAD

Compared with exercise treadmill test, stress echocardiography has an advantage in terms of sensitivity and an impressive advantage in terms of specificity. In patients who are able to exercise maximally, exercise rather than pharmacological stress echocardiography is recommended, as the exercise is the most physiological stressor. In patients who cannot exercise, dobutamine and vasodilator stress are alternatives. A meta-analysis considering original papers addressing head to head comparison between dobutamine stress echocardiography (DSE)(40 mcg/kg/min±atropine) and dipyridamole stress echocardiography (0.84 mg/kg plus atropine or 0.84 mg/kg in 6 minutes without atropine) showed similar accuracy (84% vs. 87%), sensitivity (86% vs. 85%) and specificity (86% vs. 89%) for detection of CAD, when state-of-the art protocols are followed (7). The sensitivity of stress echocardiography is greater when contrast is used (93% vs 82% without contrast) but the specificities for both with and without contrast are less consistent. (8)

Regional wall-motion abnormalities have for some time been the most commonly used markers of impaired myocardial perfusion. As the longitudinal myocardial deformation is an earlier sign of ischemia than the wall motion abnormalities, its assessment would result in a higher sensitivity of the stress test. Unfortunately, the physiological capabilities of the human eye limit the accurate assessment of the longitudinal myocardial motion in full detail.

Because longitudinal mechanical dysfunction predominates in the ischemia-vulnerable subendocardium, 2D- longitudinal strain (LS) imaging could

be used for a sensitive detection of myocardial ischemia. As a consequence, 2D- LS quantification by 2D speckle tracking echocardiography (STE) could increase the sensitivity of the stress test when added to conventional protocols. Using software which permits fast semiautomated functional imaging, this technique may be an easy to use tool even in the less experienced examiners.

METHODS

The study group consisted of ten patients (6 males), median age 56 year old, with cardiovascular risk factors presented in ED for ACP. Clinical examination was unremarkable. Serial ECG traces were within normal limits or showed non-evolutive, nonspecific ST-T abnormalities. Troponines were negative at two serial determinations and there were no wall motion abnormalities on 2D conventional transthoracic echocardiography. After 24-hours, a dipyridamole or a DSE was performed in each patient. Dipyridamole stress echocardiography was performed in 5 patients using high dose accelerated protocol with 0.84 mg/kg dipyridamole 6 min injection followed by 240 mg aminophylline administration. Three cine-loops were acquired from the apical 4-, 3- and 2-chamber views for assessment of myocardial deformation by STE in the end-expiratory holding state at baseline, at peak and after 6 minutes of dipyridamole infusion was stopped (recovery). The 2 dimensional frame rates ranged between 50/s and 70/s. Wall motion analysis was assessed using a 16 myocardial segment model at each stage. The segmental and global peak systolic LS was quantified at rest, peak and recovery using automatic functional imaging, a semiautomated 2D speckle tracking strain analysis (EchoPAC, version BT12; GE Healthcare, Horten, Norway).

In the other 5 patients, a DSE was performed using state-of-art protocol starting with 5 gamma/kg/min and increasing dobutamine dose at 10, 20, 30, 40 gamma/kg/min every 3 minutes with addition of atropine until the target heart rate was achieved. Three consecutive cine-loops with 64 FPS from apical 4-, 3-, 2- chamber view were acquired. Using semi-automated 2D STE analysis, segmental and global LS were also assessed in each stage.

All patients were referred for coronary angiogram, after the written informed consent was signed, regardless of the outcome of echocardiography stress test.

RESULTS

At peak dose dipyridamole one patient had typical angina with ECG changes 1 mm ST persistent horizontal depression in V4-V6 but no regional wall motion abnormalities were noticed. Semi-automated 2D STE analysis showed lower magnitudes of LS in the circumflex artery (CX) territory. (Fig. 1 a,b,c). The coronary angiogram revealed 90% stenosis of proximal CX (Fig. 2). The other 4 patients had angina with some ECG abnormalities, no wall motion abnormalities, no decreased LS values at peak stress or during recovery and normal coronary arteries at angiogram.

At peak dose dobutamine plus 0,25 mg atropine one patient presented typical angina in the absence of dynamic ECG changes and without any wall motion abnormalities on conventional 2D echocardiography. Two dimensional STE analysis showed lower magnitudes of LS in the left anterior descending artery (LAD) territory (Fig. 3 a,b,c,d). Coronary angiogram showed chronic occlusion of the medium LAD with CX retrograde loading, and chronic occlusion of medium right coronary artery (RCA) with LAD retrograde loading. (Fig. 4 a,b). The other 4 patients had negative dobutamine echo study on conventional criteria, but they presented angina with nonspecific ECG abnormalities. No LS alteration values at peak stress or during recovery were noticed and no coronary lesions on angiogram.

DISCUSSION

The presented case series shows the additive value of myocardial deformation parameters using semiautomated 2D LS analysis during pharmacological stress echocardiography with dipyridamole or dobutamine, in patients presented with ACP, classified as low risk ACS.

In the case of the patient with dipyridamole echo study, clinical and electrical changes along with LS alterations at peak dose dipyridamole, led to detection of significant CAD detection even in the absence of segmental wall motion abnormalities. This demonstrates that myocardial deformation parameters could detect subtle changes in ischemic myocardium which cannot be assessed by human eye. Interesting, the ECG changes and angina occurred prior the wall motion abnormalities in contrast with the previously described chronology of ischemic

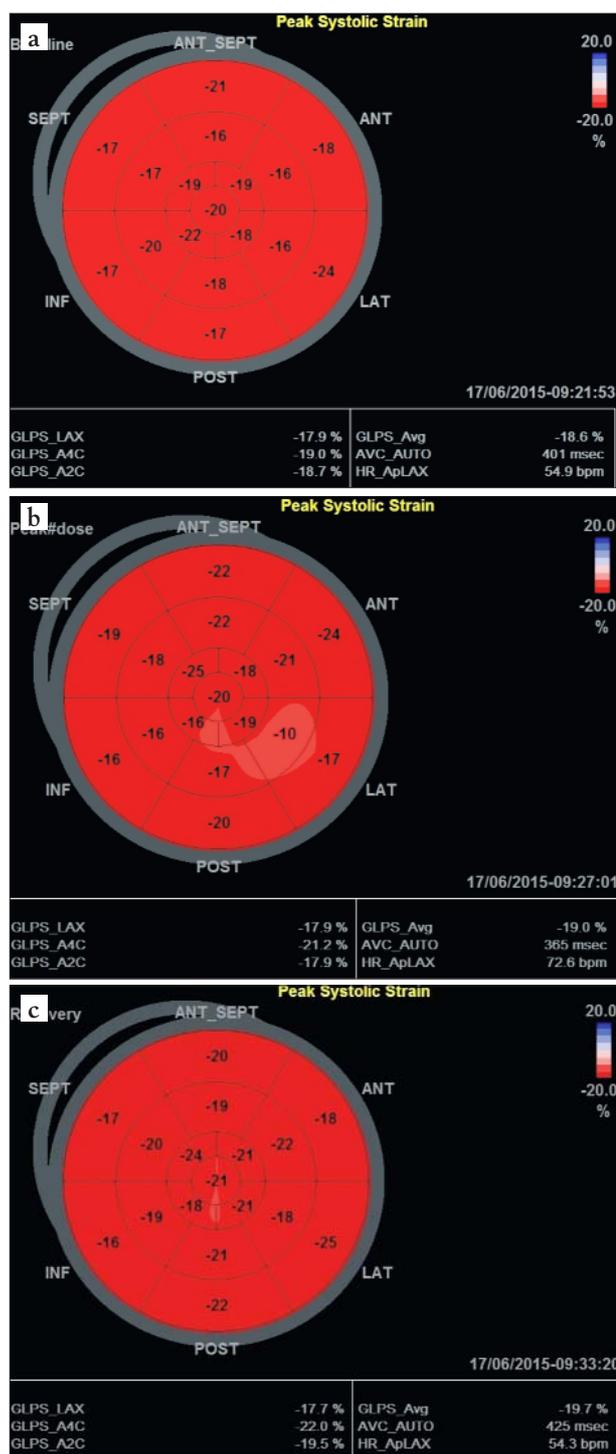


Figure 1. The systolic longitudinal strain was normal before the dipyridamole infusion (a), but lower magnitudes of strain can be observed in the circumflex artery territory at peak dose dipyridamole (b). During the recovery the longitudinal systolic strain return to normal values (c)

cascade. However, the alteration of longitudinal myocardial function appeared as early as electrical changes. It was described that stress-induced ST-segment depression is not per se a criterion of test positivity, since it can be frequently found in the

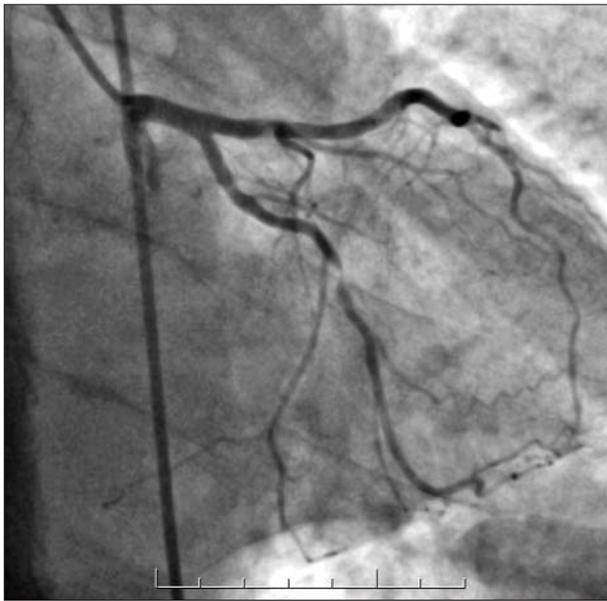


Figure 2. Coronary angiogram of the first patient showing 90% stenosis of proximal circumflex artery which was subsequently treated by a bare metal stent implantation

absence of wall motion abnormalities with angiographically normal coronary arteries, in the so-called microvascular coronary artery disease frequently found in women, hypertensives, and diabetics. (9)

The case of the patient with DSE highlights the potential additive value of 2D LS analysis during DSE even in the absence of ECG changes and wall motion abnormalities. It is important to mention that in the case of this patient, low magnitude of LS was noticed even at baseline, in contrast with the

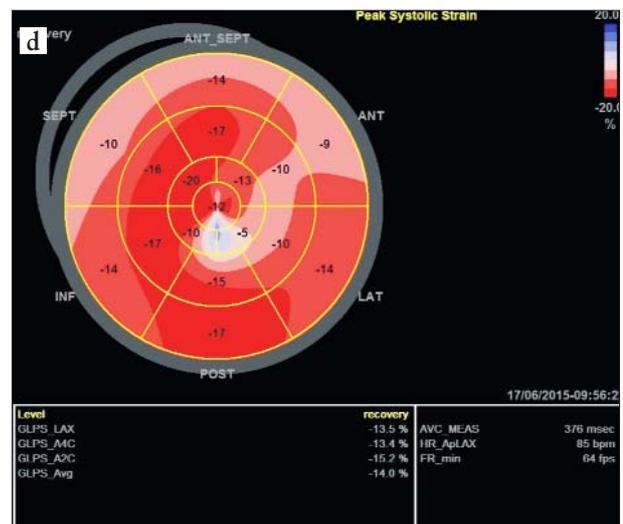
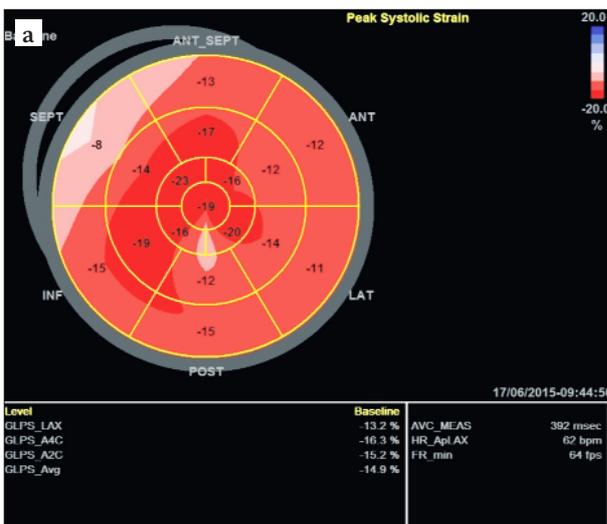
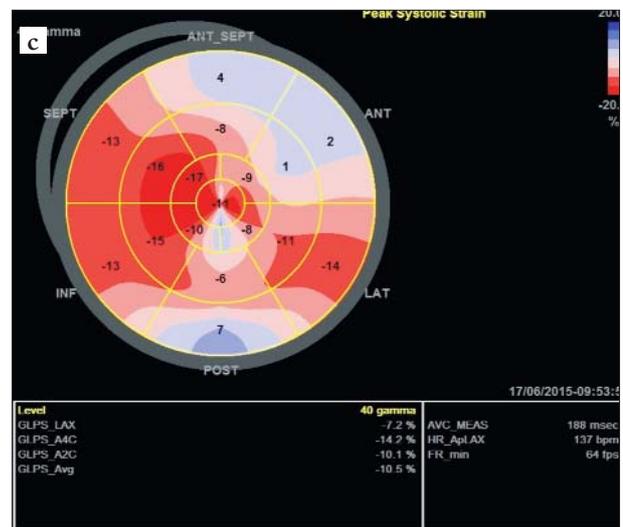
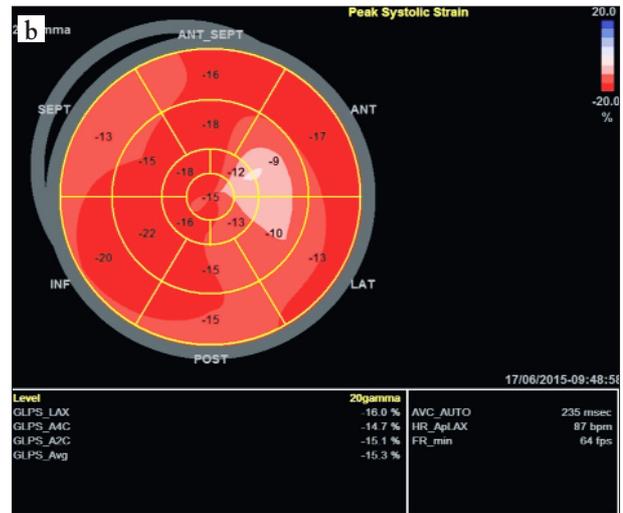


Figure 3. The systolic longitudinal strain was abnormal at baseline, with a patchy, non coronary distribution of the affected segments (a). During dobutamine infusion, the longitudinal strain further decreased reaching its lowest magnitude at peak dose dobutamine (b). During the recovery the longitudinal systolic strain returned to baseline values values (c)

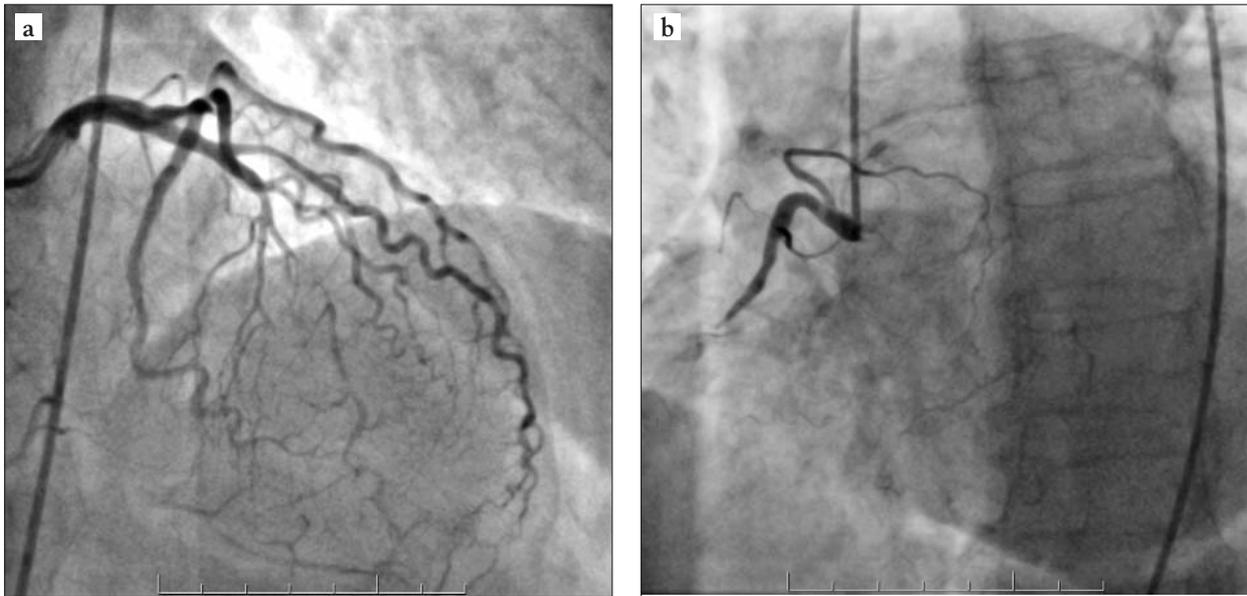


Figure 4. Coronary angiogram showing chronic occlusion of the medium left anterior descending coronary artery (LAD) with retrograde supply from circumflex artery (**a**), and chronic occlusion of medium right coronary artery with retrograde supply from the LAD (**b**)

other 4 patients.

Previous research indicate that LS may be modified even in rest conditions in patients with diabetes (10) or hypertension (11). In the case of this patient, the presence of hypertension could explain the altered LS at baseline. However, during dobutamine infusion, LS further decreased reaching its lowest magnitude at peak dose dobutamine. This response suggests the fact that even in the context of altered baseline LS, myocardial deformation imaging may still have an additive predictive value for the presence of significant CAD.

Myocardial deformation imaging during DSE has been previously studied using Doppler-derived LS techniques. According to these studies, Doppler-derived LS demonstrated similar value with wall motion assessment (12) in predicting significant CAD when combined with clinical data. Tissue Doppler-based techniques has the inherent disadvantages related to reverberations, angle deviation and noise.

The speckle tracking technique is angle independent but it may be limited by the inadequate low frame rate versus the high heart rate acquired at peak stress. Furthermore, myocardial tracking difficulties may result from failure of maintaining end-expiratory breath-hold in symptomatic patients, and the development of signal to noise due to hyperdynamic LV contractility and excessive annular

motion. (10 13) Perhaps this is why this novel method has not been largely used.

Another aspect that deserves attention is the accuracy of wall motion abnormalities at peak stress in CAD detection. It is known to be greater in patients with ischemia in the LAD territory than in patients with ischemia in the CX or RCA territory, and also in the multi-vessel disease cases than in the single vessel disease cases. (14) In the case of the patient with dipyridamol echo study, LS alterations were in the CX territory, suggesting that 2D strain imaging could have greater sensitivity than WMA for this territory. This hypothesis should be checked on a larger groups of patients.

CONCLUSIONS

A possible strategy to triage patients presented with ACP stratified as low risk ACS includes 2D LS analysis during stress echocardiography for rapid diagnosis and appropriate management. Our pilot study highlights that quantitative analysis of myocardial deformation appeared to be superior over conventional visual analysis of contractility for myocardial ischemia detection and could lead to an increased sensitivity of pharmacological stress echocardiography. More patients are needed for more consistent results.

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