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## Correspondence

## Quantitative detection of inducible ischemia during dobutamine stress by speckle tracking echocardiography: A dream comes true

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Patients with three-vessel or left main (LM) obstructive coronary artery disease (CAD) represent a life-threatening population [1]. In this clinical setting, early detection of inducible myocardial ischemia would be desirable for appropriate risk stratification and management. However, both myocardial perfusion SPECT [2] and dobutamine stress echocardiography (DSE) [3] may be challenging in these patients. In particular, DSE is limited by visual, semi-quantitative evaluation of regional wall motion abnormalities (WMAs) and has therefore a relatively poor reproducibility, even when handled by expert operators [4].

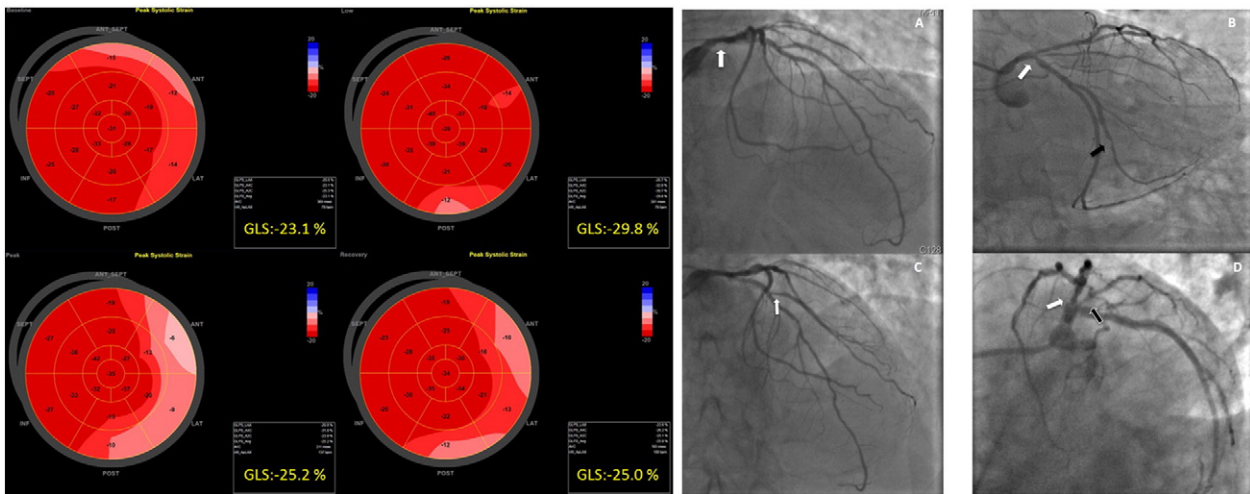
Speckle tracking echocardiography (STE) allows quantitative and relatively operator-independent evaluation of WMA. It is based on grey scale map, frame-to frame tracking of “speckles” within the myocardium that are followed during the cardiac cycle by softwares on dedicated workstations [5]. Among the different strain components quantifiable by STE, longitudinal strain (LS) is the most sensitive to myocardial ischemia, it reflects changes of subendocardial fibers which are maximally exposed to the ischemic damage [5]. A good concordance between strain and sonomicrometry has been reported experimentally, a finding which points out the possibility of using it at an elevated heart rate (HR), own of DSE [6]. Accordingly, LS has shown a diagnostic accuracy for CAD detection during DSE which is higher (85.2%) than circumferential and radial strain and comparable to wall motion core index (WMSI), and is substantially increased (94.9%) when combined with the same WMSI [7].

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Automated Function Imaging (AFI), thanks to on-line application of STE, allows a faster assessment of regional LS and global longitudinal strain (GLS) and clear result presentation as a polar map. AFI-derived LS is very sensitive in diagnosing CAD in emergency [8] and correlates well with STE-derived strain both at rest and during DSE [9]. However, at the highest HR occurring during DSE, both AFI and STE may provide suboptimal imaging and results. Accordingly, operators prefer to use STE or AFI during early recovery, as surrogate of maximal stress acquisition [10,11]. Very recent advancement of AFI system could overcome this limitation but this system has not been tested during DSE.

We present a case of a 69-year old man with chronic CAD. Four years before our evaluation, he had undergone a percutaneous coronary intervention with drug eluting stent implantation on obtuse marginal (OM) branch of circumflex coronary artery (CCA). At that time, concomitant intermediate stenosis of left anterior descending (LAD) artery, judged not “angiographically” significant, had not been treated. The patient was referred for short duration effort angina. After obtaining the patient’s informed consent, a DSE (Vivid E95, GE, Horten, Norway) was performed by an expert operator according to a standardized staged protocol [3], including visual analysis of WMA and quantification of regional LS and GLS by AFI system. At rest, despite no detection of ECG alteration and visual WMA, a mild reduction of LS in basal segments of anterior septum, anterior and lateral walls, was evidenced (Fig. 1). Ejection fraction (67%) and GLS (-23.1%) were normal. At low dose dobutamine, GLS improved substantially, with viability of anterior septum and lateral wall (Fig. 1). At maximal dobutamine dose, the patient referred angina, again without ECG abnormalities or visual WMA (Fig. 2). Nevertheless, despite a still normal GLS, a LS reduction in basal segments of lateral and posterior walls and in both basal and middle segments of anterior wall was observed (Fig. 1). During early recovery, regional LS and GLS remained substantially unchanged (Fig. 1). On the grounds of the pure AFI assessment, the patient was scheduled for coronary angiography that showed a patent right coronary artery and a moderate LM stenosis involving either CCA (75% ostium lesion) and LAD (critical ostium lesion). Critical stenosis of second diagonal branch, moderate stenosis of intermediate branch and significant OM stenosis, distal to the previous implanted stent, were also found (Fig. 1). The global syntax score calculated was 35. The patient underwent cardiac surgery with successful sequential grafting in left internal mammary artery to LAD and diagonal branch, and in saphenous vein to OM and intermediate branch.



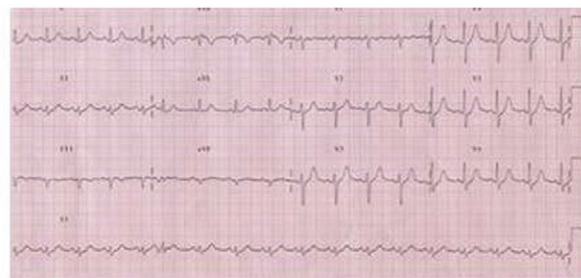
**Fig. 1** STE derived bull's eye before, during and after dobutamine (left panel) and coronary angiography (right panel). Left panel. Head to head comparison of STE derived bull's eye at rest (upper left), at low-dose dobutamine (upper right), at maximal stress (lower left) and during early recovery (lower right). At rest a mild reduction of LS in basal segments of anterior septum, anterior and lateral walls was detected. At low dose dobutamine a substantial improvement of GLS and regional strain of anterior septum and lateral wall was evident. At maximal stress and during early recovery, STE analysis revealed a substantial reduction of regional strain in basal segments of lateral and posterior walls and in both basal and middle segments of anterior wall. Right panel. Coronary angiography. (A). Cranial right anterior oblique angiogram of left coronary artery demonstrating a moderate stenosis of left main. (B). Caudal right anterior-oblique angiogram showing 75% stenosis of the origin of the circumflex branch (white arrow) and a 80% stenosis of obtuse marginal branch (black arrow). (C). Right anterior oblique cranial angiogram showing a severe stenosis of ostium of second diagonal branch. D. Critical lesions of the origin of LAD (white arrow) and of the intermediate branch (black arrow) observed in the "spider" view.

The present clinical case demonstrates the incremental value of the very novel AFI-derived regional LS upon visual WMA assessment during DSE. By using previous software, the main limitation corresponded to the possible suboptimal identification of speckles at highest HR [9,10]. This "on board" software advancement overcomes this limitation, due to confocal imaging which allows to obtain an enhanced spatial resolution, even at the HR achieved at maximal DSE. This characteristic is very useful for both imaging acquisition and subsequent reading procedures. Moreover, the new machine allows to store different bull eye's plots corresponding to sequential DSE stages into AFI cell inside the stress template and to visualise them side by side, thus making the comparison of regional LS and GLS during DSE test very easy. Globally, this new technology allowed us to achieve an appropriate diagnosis

of inducible ischemia in LAD and CCA territories, despite the absence of stress-induced ECG abnormalities and visual WMA. The diagnosis was subsequently confirmed by coronary angiography and the patient addressed towards a successful cardiac surgery.

STE derived regional LS corresponds to longitudinal function of subendocardial fibers, which is the most sensitive marker of myocardial ischemia. LS alterations precede visually detectable WMA during DSE [7, 8]. Our clinical case goes beyond this advantage and points out for the first time how the quantitative analysis of regional LS stand alone could lead to diagnose an inducible ischemia not detectable by the visual WMA at dobutamine peak dose.

In conclusion, we speculate that, by utilizing the novel AFI system, the application of regional LS to DSE might induce an important increase



**Fig. 2** ECG and stress echo at maximal dobutamine dose. In the upper panel 12-leads ECG. No repolarization alteration was observed. In the lower panel 2D-derived quad screen reconstruction: apical 4-chamber, 2-chamber and 3-chamber views from left to right. No WMA was detectable.

of diagnostic accuracy, driving a better decision making in patients with three vessel and LM disease. The use of this technology could make stress echo operators much more confident with clinical choices of patients referring for chest pain. Confirmation on large populations with suspected or ascertained CAD as well as feasibility and reproducibility analyses of the novel AFI system during DSE are needed to hypothesize a routinary use of this technique in the clinical setting.

#### Conflict of interest

No conflict of interest to declare.

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