Improved diagnosis of post-operative myocardial infarction by contrast echocardiography after coronary artery bypass graft surgery

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Objective
Contrast echocardiography is a more accurate means of assessment of left ventricular (LV) regional motion compared with non-enhanced echocardiography. Despite new tests, the diagnosis of post-operative myocardial infarction (MI) remains difficult. The aim of this study was to determine whether contrast echocardiography can facilitate this diagnosis.

Methods
We performed standard and contrast echocardiography in 79 consecutive patients before and up to 10 days after they underwent isolated coronary artery bypass graft (CABG) surgery.

Results
The post-operative intra- and interobserver reproducibility of echocardiographic measurements of the LV ejection fraction and wall motion score was significantly higher with than without contrast enhancement. The proportion of non-visualized LV myocardial segments was significantly greater with non-enhanced (6.6%) than with contrast (0.3%) echocardiography ($P < 0.0001$). The mean peak serum cardiac troponin (cTnI) concentration was significantly higher in the group of patients with new wall motion abnormalities detected with contrast-enhanced echocardiography. A correlation was found ($r = -0.43, P < 0.01$) between peak cTnI and changes in wall motion score only when a contrast agent was used.

Conclusion
Contrast echocardiography facilitated the detection of new LV wall motion abnormalities after CABG. This observation, added to other markers, might facilitate the diagnosis of post-operative MI.

Keywords
Contrast echocardiography • Cardiac wall motion • Post-operative myocardial infarction

Introduction
Post-operative myocardial infarction (MI) or ischaemia is prognostically important.¹ However, the diagnosis of MI early after coronary artery bypass graft (CABG) may be challenging, as chest pain is attenuated by sedation and analgesia, and ST-T changes may be attributed to common pericardial reactions and metabolic disturbances.²,³ Elevated cardiac troponin I (cTnI) and myocardial bounded fraction of creatine kinase (CK) are also very common and not invariable due to MI.⁴–⁷

Post-operative MI has been redefined by a joint consensus statement issued in 2007 by the European Society of Cardiology/American College of Cardiology/American Heart Association/World Heart Federation (ESC/ACC/AHA/WHF).⁸ This task force stated than an imaging study should be associated with measurements of cTnI to confirm the diagnosis of MI after CABG. While a correlation has been reported between (i) size of MI ascertained by cardiac magnetic resonance and (ii) blood MB-CK and cTnI concentrations after CABG,⁹,¹⁰ magnetic resonance cannot be used in most patients because of haemodynamic or rhythm instability.
and because of the complex nature. While bedside echocardiography might be the best imaging technique to estimate the amount of myocardial injury after CABG, the image quality is usually limited by pleural and pericardial effusions, fresh sternotomy, and abnormal ventilation. The echogenicity, hence the ability to analyze the contractility of 17 left ventricular (LV) myocardial segments, is a key factor, which needs to be improved upon to optimize the evaluation of regional myocardial dysfunction after CABG. The contributions of enhanced contrast echocardiography in the analysis of LV kinetics have been validated, however, not earlier after thoracic surgery.

The aim of our study was to determine whether the use of an intravenous contrast agent is of help in the analysis of LV kinetics in the post-operative period of CABG and contributes to the clinical diagnosis of MI after CABG surgery.

**Study population and methods**

Between July 2008 and September 2009, we prospectively enrolled 79 patients undergoing isolated CABG surgery. Patients (i) who had undergone prior coronary artery surgery, (ii) whose LV ejection fraction was <30%, (iii) urgent surgery, or (iv) who had a contraindication to the administration of intravenous contrast material, were excluded from enrolment.

**Study protocol**

Clinical data were recorded during the hospitalization for CABG surgery. Our cut-off value of cTnI was 0.50 ng/mL, as recommended in the ESC/ACCF/AHA/WHF consensus statement for post-operative MI. A baseline echocardiogram was recorded 24 h before surgery to analyze pre-operative wall motion. Laboratory measurements, including blood cTnI, total CK, N-terminal pro-brain natriuretic peptide concentrations, and electrocardiogram (ECG), were obtained (i) on the day before surgery, (ii) between 6 and 12 h after the operation, (iii) 1, 2, and 4 days after surgery, and (iv) on the day of discharge from the hospital, along with a follow-up echocardiogram, between 6 and 10 days after CABG surgery. Standard echocardiographic and Doppler examinations, using VIVID 7 instrumentation (GE Healthcare, Horten, Norway), were performed by the same operators (A.B., C.T.), and were repeated after the intravenous injection of contrast material to fill the LV cavity. The contrast material used in this study was Luminy (BMS Imaging). Before administration of Luminy, it was activated using a Vialmix. The recommended posology was a repeated injection of 0.1–0.4 mL followed by a bolus of 3–5 mL of sodium chloride 9 mg/mL or serum glucose 50 mg/mL in order to obtain optimal contrast. The total dose did not exceed 1.6 mL. A clinical supervision (rhythmic and haemodynamic) was performed during examination.

The echocardiograms were analyzed off-line by a single, blinded, observer (F.S.). The intra- (F.S.) and interobserver (F.S., E.D.) reproducibility of measurements was examined in 20 randomly selected patients. Considering pre- and post-operative echocardiograms, regional wall motion was assessed, using a 17-segment model and the scoring system recommended by the American Society of Echocardiography and European Association for Echocardiography as follows: unable to interpret = 0, normal or hyperkinesis = 1, hypokinesis = 2, akinesis = 3, dyskinesis = 4.

**Statistical analysis**

The intra- and interobserver variability was expressed as intraclass correlation and variation coefficient. Quantitative data are expressed as means ± standard deviations, and were compared, using Student’s t-test. Qualitative data are expressed as counts and percentage, and were compared, using χ² test. Pearson’s correlation coefficient was calculated for quantitative data. A P-value < 0.05 was considered statistically significant. The data were analyzed, using the 2006 STATISTICA, version 7.1. software (StatSoft, Maisons-Alfort, France).

**Results**

**Pre-operative observations**

The data collected pre-operatively are summarized in Table 1. The mean age of this mostly male population was 67 ± 8 years. The main indication for CABG was stable angina, surgery was elective in nearly 90% of patients, the mean EuroSCORE was 3.5%, two-thirds of patients had triple vessel or left main coronary artery disease, and one-fourth of patients had undergone prior percutaneous coronary procedures. The main pre-operative laboratory results are shown in Table 2.

**Operative characteristics**

The majority of patients was operated off pump (76%). Because of intolerance of dislodgement of the heart in one, and haemodynamically intolerable ventricular tachycardia in the other, two patients initially operated off pump had to be rapidly placed on cardiopulmonary bypass. Revascularization was complete in 72% of patients.

**Post-operative observations**

Haemodynamic instability requiring the administration of inotropes drugs was the main post-operative complication (40.5%). One patient needed intraaortic balloon contra-pulsation, and another needed a LV assist device. Three patients died of, respectively, gastrointestinal haemorrhage, stroke, and multiple organs failure, within the 30 first days after the index CABG operation.

**Diagnosis of myocardial infarction**

**Biological markers**

The mean peak serum cTnI concentration was 4.02 ± 9.64 ng/mL (Table 3). cTnI was above the threshold of 0.50 ng/mL in 62 patients (78.5%).
The initial ECG was non-contributory in seven patients because of complete left bundle branch in six and paced rhythm in one patient. A new Q-wave developed in 11 patients (16%), along with a peak cTnI > 0.5 ng/mL in all. Peak cTnI was significantly higher in patients with (16.4 ± 22.2 ng/mL) than in patients without (1.6 ± 1.8 ng/mL) new Q-waves (P < 0.0001).

**Echocardiographic studies**

**Safety of the contrast agent**
The injection of contrast material was uncomplicated in all patients. According to the recommendations we did not administer the contrast agent to artificially ventilated patients, precluding the collection of contrast-enhanced images in three patients.

**Effects of contrast-enhanced imaging on the test reproducibility in 20 patients**
The number of myocardial wall segments scored differently by the same observer was 1.5% with, vs. 7.5% without contrast (P = 0.002) pre-operatively, and 3.0% with, vs. 18.0% without contrast (P < 0.0001) post-operatively. A similar number of contrast-enhanced (12.0%) vs. non-enhanced (14.5%) myocardial wall segments were scored differently by two separate observers pre-operatively. However, post-operatively, significantly fewer contrast-enhanced (17.5%) than non-enhanced (24.0%) segments (P = 0.04) were scored differently by two different observers. The pre- and post-operative intra- and interobserver echocardiographic WMSI variation coefficients were both lower with than without the use of contrast material. Similar results were obtained in the analysis of WMSI intraclass correlation coefficient (Figures 1–4).

**Contributions of contrast-enhancement in the echocardiographic analysis of regional left ventricular wall motion and systolic thickening**
On pre-operative echocardiography in 79 patients, motion, and thickening could not be analysed in 0.6% of contrast-enhanced, vs. 3.0% of non-enhanced segments (P = 0.0002), while on post-operative echocardiography in 76 patients, motion and thickening of ≤ 0.5% of contrast-enhanced segments vs. 7.0% of non-enhanced segments could not be analysed (P < 0.0001) (Table 4).

**Contributions of contrast-enhancement in the echocardiographic diagnosis of myocardial infarction**
New wall motion abnormalities were detected on echocardiograms without intravenous contrast material in 28 patients (37%), in 8 of whom the peak serum cTnl concentration was ≤ 0.5 ng/mL. Peak cTnl was not significantly higher in the group with (5.45 ± 13.46 ng/mL) than in the group without (2.38 ± 3.14 ng/mL) new wall motion abnormalities (P = 0.13). We found no correlation between variations in WMSI and serum cTnl concentration (r = −0.15; P = 0.2).

New wall motion abnormalities were detected on echocardiograms with intravenous contrast material in 19 patients (25%), among whom the peak serum cTnl concentration was ≤ 0.5 ng/mL in only 1 patient. The peak serum cTnl concentration was significantly higher in the group with (9.06 ± 15.83 ng/mL) than without (1.66 ± 2.03 ng/mL) new wall motion abnormalities (P < 0.001). We found a correlation between variations in WMSI and serum cTnl concentration (r = −0.45; P < 0.001) (Figure 2).
Among 11 patients who developed a new Q-wave on the ECG, 1 died before an echocardiogram was recorded. Among the 10 remaining patients, 3 had new echocardiographic abnormalities of wall motion without, vs. 4 patients with the injection of intravenous contrast material (ns). Haemodynamic instability was observed in 53% of patients with new wall motion abnormalities detected by contrast echocardiography, vs. 43% of patients with wall motion abnormalities detected by non-enhanced imaging (ns) (Figure 5).

**Discussion**

Our study showed a facilitated diagnosis of MI by detecting new wall motion abnormalities after CABG with the use of
contrast-enhanced echocardiography, a technique recommended when ≥2 myocardial segments are not visualized by standard imaging. The use of contrast agent sharpens the definition of the endocardium, particularly in the near and far fields. Even in presence of limited acoustic windows, contrast echocardiography more accurately defines the LV shape, size, and function, and facilitates the measurements of LV regional wall motion and thickening. To the best of our knowledge, however, this has not been confirmed before and after CABG surgery. In our study, the use of intravenous contrast material increased the post-operative intra- and interobserver reproducibility of observations, with respect to the number of discordant segments and to the WMSI. The use of a contrast agent increases the reliability and the reproducibility of stress echocardiography.

We observed that the additive value of the contrast was most prominent post-operatively, when the acoustic window was the weakest, and was less distinct when analysing the pre-operative echocardiograms.

In a previous study, Whalley et al. evaluated the usefulness of contrast left ventricular opacification in healthy controls and in patients with heart failure. Even in controls, their results were worse than ours in term of percentage of non-visualized segments. Ikonomitos et al. demonstrated also that contrast use improve the assessment of wall motion, particularly of the basal lateral and anterior walls; it thus reduces the inter- and intraobserver variability of the wall motion score, especially for difficult patient like the ones we studied.

The percentage of non-visualized segments was 13.6% using fundamental imaging, 5.6% with tissue harmonic imaging, and 2.8% with left ventricular opacification ($P = 0.01$).
Our results are quite better with or without contrast. On pre-operative echocardiography, the percentage of non-visualized segments was 3.0% without contrast vs. 0.6% with contrast ($P = 0.0002$). On post-operative echocardiography, there were more segments not visualized without contrast 7.0% but only <0.5% with contrast ($P < 0.0001$). This can mostly be explained by the better quality of new ultrasound machines, our study was performed >4 years latter. The improved imaging of myocardial motion and thickening facilitates the diagnosis of post-operative MI. A higher correlation was observed between new wall motion abnormalities and other markers of MI, peak cTnI in particular, when using contrast-enhanced vs. non-enhanced imaging. Contrast-enhanced imaging was associated with significantly less discordance between measurements of serum cTnI concentration and echocardiographic observations, and a correlation between variations in WMSI and peak cTnI was observed only when the images were enhanced by the injection of intravenous contrast material. A moderate correlation between cTnI and amounts of myocardial necrosis after CABG surgery has been described with magnetic resonance imaging.1 However, in some patients, myocardial hibernation associated with abnormalities of regional wall motion probably occurs without increase in serum concentrations of cTnI.

Our study showed that the identification of wall motion abnormalities was facilitated by the opacification of the LV myocardium, a greater accuracy which might be applied to a new risk stratification scheme after CABG surgery. Dwivedi et al.20 found that contrast echocardiography accurately estimated the amount of LV remodelling better than conventional imaging. LV remodelling taking place during the first 72 h after the onset of MI is influenced by the size and location of infarction, and by the extent of transmural necrosis.1–21 It is also influenced by the transmurality of necrosis and presence of viable myocardium, both of which can also be ascertained with transthoracic ‘myocardial perfusion’ contrast echocardiography.23

Study limitations
We had no ‘gold standard’ definition of post-CABG surgery MI. Echocardiography at rest detects new wall motion abnormalities, though is not able of detecting a new loss of viable myocardium, which requires stress echocardiography or viability magnetic resonance imaging. For ethical reasons, we did not systematically obtain post-operative coronary angiograms as reference for the interpretation of new wall motion abnormalities and rises in serum cTnI concentration.

The contribution of this study was in the use of ECG, cTnI, and echocardiography at the bedside. The administration of contrast material (i) only needed an intravenous infusion, (ii) did not lengthen the examination, and (iii) was not associated with adverse events. The safety of intravenous contrast material, including when used for suspected acute coronary syndrome, has been reported in large studies.24

Conclusion
Contrast echocardiography facilitated the detection of LV wall motion abnormalities, and should thus facilitate the diagnosis of post-operative MI. Our results might impact the use of echocardiography in the peri-operative period in cardiac surgery.

Conflict of interest: none declared.

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