Myocardial perfusion echocardiography: a novel use in the diagnosis of sepsis-induced left ventricular systolic impairment on the intensive care unit

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Impaired left ventricular systolic function secondary to sepsis can occur in up to 20% of patients with septic shock. The electrocardiogram (ECG) and echocardiographic changes it produces can be very similar to those occurring during acute coronary syndromes (ACS). Myocardial contrast echocardiography (MCE) allows assessment of myocardial perfusion. This technique can be performed at the bedside of the critically unwell patient. We describe a patient presenting with septic shock secondary to pneumonia. While sedated and ventilated in the intensive care unit, the patient developed marked ECG changes, a troponin rise and widespread left ventricular wall motion abnormality. The clinical picture suggested ACS or stress cardiomyopathy was unlikely and was more in keeping with a diagnosis of sepsis-induced left ventricular systolic dysfunction. To support this, resting and flash impulse MCE was performed which revealed normal perfusion in areas of both normal and abnormal wall motion. This suggested that the cardiac presentation was more likely to be due to left ventricular impairment secondary to sepsis and ACS therapy was discontinued. Pre-discharge ECG and transthoracic echocardiogram were normal. Percutaneous coronary angiography 6 weeks later was also normal. This is the first described case of MCE being used to aid in the decision-making process in distinguishing between ACS, stress cardiomyopathy, and left ventricular systolic impairment secondary to sepsis.

Keywords: Perfusion • Echocardiography • Contrast • Sepsis

Introduction

Sepsis is the systemic inflammatory reaction made in response to an infectious agent. It can result in septic shock and ultimately multi-organ failure.1 This syndrome is the leading cause of mortality in intensive care units in the developed world.

For many years it has been recognized that a proportion of patients with sepsis develop left ventricular systolic impairment. This is a well-described but poorly understood phenomenon with epidemiological data suggesting that it may occur in up to 20% of patients with septic shock.1 The pathophysiology of this condition remains the subject of much debate. Microvascular changes, autonomic dysregulation, metabolic changes, and inflammatory signalling have all previously been hypothesized as potential mechanisms for cardiac dysfunction.2

Myocardial contrast echocardiography (MCE) is a relatively new technique in which microbubbles are infused into the peripheral venous circulation. The bubbles are small enough to pass through the lung vasculature, into the left ventricular cavity and subsequently into the coronary microcirculation where they can be then be visualized using two-dimensional cardiac ultrasound at a low mechanical index (MI).

The ability of microbubbles to enter the coronary microcirculation has allowed this technique to be used in the assessment of left ventricular myocardial perfusion and tissue viability.3 The presence or absence of microbubbles in the myocardium provides information as to the perfusion state of the tissue. If the pattern of perfusion is homogenous this indicates normal myocardial perfusion. However, absent or patchy perfusion can indicate myocardial ischaemia, infarction, or scar tissue.4,5 Flash impulse destruction of microbubbles either at rest or during stress with subsequent delayed reperfusion can indicate the presence of flow-limiting coronary artery disease.6

MCE assessment of left ventricular perfusion after myocardial infarction has been shown to be superior to SPECT in the prediction of hard cardiac events, recovery of regional wall motion.

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abnormalities and left ventricular systolic function. Importantly, a recent review found the use of contrast agents in patients with coronary artery disease to be safe.

To our knowledge, there have been no reported cases of MCE assessment of myocardial perfusion in patients with sepsis-induced left ventricular systolic impairment. We present a case in which we have used this technique to aid in the decision-making process of distinguishing between sepsis-induced left ventricular systolic impairment and acute coronary syndrome (ACS).

**Case report**

A 66-year-old lady presented to the Emergency Department with severe breathlessness. There was no history of recent emotional stress. She had a past medical history of hypertension and chronic obstructive pulmonary disease of moderate severity due to smoking. Clinical examination revealed a severely distressed patient with a respiratory rate of 50 breaths/min and bilateral wheeze in her lungs. Her blood pressure was 110/68 with normal heart sounds. Arterial blood gas analysis was consistent with severe type two respiratory failure and lactic acidosis. Her chest X-ray revealed right lower zone consolidation consistent with a diagnosis of pneumonia. Endotracheal intubation was performed in the Emergency Department and intavenous antibiotics were administered. The patient was moved to the intensive care unit, where she became hypotensive. A noradrenaline infusion was therefore started with good effect.

The following day a routine ECG showed new, deep symmetrical T-wave inversion in the inferior and anterolateral leads. Echoangiography demonstrated severely impaired left ventricular systolic function with akinesis of all walls except the basal segments which contracted normally. There was mild pulmonary artery hypertension. The troponin T was raised at 1.01 (normal <0.03). A diagnosis of ACS was made and aspirin, clopidogrel, and low-molecular-weight heparin were therefore prescribed. A cardiology opinion was requested. We felt that ACS was unlikely as there was no history of chest pain and the widespread ECG and wall motion abnormalities did not correspond to any single coronary artery territory. We also felt that stress (Tako-Tsubo) cardiomyopathy was unlikely as in a recent large series this condition was only associated with infection in 2% of cases and was more likely to present following an emotionally stressful event and with chest pain and ST segment elevation on ECG.

Although multivessel coronary artery disease or stress cardiomyopathy remained a possibility, we suggested that a diagnosis of left ventricular systolic impairment secondary to sepsis would be more in keeping with the clinical findings.

MCE assessment of myocardial perfusion was performed to aid in our decision-making process. Our hypothesis was that if the akinetic areas of myocardium had both normal perfusion at rest and on replenishment imaging, this would suggest that there was no chronic infarction or hibernation present. It would also make a diagnosis of stress cardiomyopathy less likely as previous work has shown that this condition often results in perfusion defects on MCE imaging. Although a normal study would not rule out the possibility of stress cardiomyopathy or myocardial stunning after ACS, it would add further evidence to the clinical suspicion of left ventricular systolic impairment as a result of sepsis. This was particularly so considering that the wall motion abnormalities did not occur in a recognized coronary artery distribution and so were very unlikely to be a result of an ACS from a single vessel. Therefore if ischaemic heart disease was the underlying problem, it is likely to be due to multivessel coronary artery involvement with at least some of the akinesis occurring as a result of either chronic infarction or hibernation.

MCE was performed 2 days after the original ECG changes had occurred. Although at present the summary of product characteristics for SonoVue document that it is contraindicated in recent ACS, it (and a number of other different contrast agents which are now licensed for use in ACS) has safely been used in many patients with this condition. Furthermore, considering the clinical findings, we felt that ACS was an unlikely diagnosis. We therefore believed that it was safe to use SonoVue in this scenario.

The study was performed with the patient intubated and while an infusion of noradrenaline was running at a dose of 0.1 μg/kg/min to maintain the blood pressure of the patient. This drug has been previously shown to cause coronary vasoconstriction and decrease coronary blood flow at low doses. Previous work has shown that mechanical ventilation does not affect the transit of SonoVue. At the time of the study, the patient had a pulse rate of 82 beats/min and a blood pressure of 116/69. We performed both real-time imaging to assess wall motion, and low-power MCE with triggered imaging following microbubble destruction to assess myocardial perfusion. Excellent image quality was obtained with all 17 left ventricular segments adequately visualized. End-systolic images were recorded with a low MI of 0.1 and high-intensity pulses (MI: 1.0) to facilitate microbubble destruction followed by acquisition of 10 end-systolic frames. There was uniform, normal uptake of contrast throughout the left ventricular myocardium both in the normal and akinetic segments. After bubble destruction, replenishment was seen in <5 s in all 17 segments of the left ventricular myocardium (Figures 1 and 2).

Following the investigation, the patient was monitored closely with a three lead ECG and haemodynamic measurements with no adverse effects seen over the next few hours.

We did not perform a stress vasoconstrictor study as we felt that it would be potentially unsafe to do so in an unstable patient. Furthermore, it would have been difficult to interpret the results of the stress study because of the noradrenaline infusion potentiating a reverse, vasoconstrictive effect. Overall we believed that, if normal, the resting study would give us enough information to support a diagnosis of sepsis-induced myocardial dysfunction rather than ACS.

These results suggested to us that coronary artery disease was unlikely to be responsible for the ECG changes and regional wall motion abnormalities and that the most likely cause was sepsis induced left ventricular dysfunction. The treatment for ACS was therefore discontinued.

The ECG and echocardiogram were repeated 9 days after the original study was performed. By this time, the clinical state of the patient had improved and she was well enough to be discharged from hospital. The T-wave changes on the ECG had returned to normal and the echocardiogram showed normal
left ventricular systolic function with no regional wall motion abnormalities. Six weeks after discharge a coronary angiogram was performed to ensure that we had not missed a diagnosis of significant coronary artery disease. This was normal.

**Discussion**

In patients with septic shock, up to 20% will develop left ventricular systolic dysfunction. This can result in a variety of biochemical, ECG, and echocardiographic abnormalities. This diagnosis needs to be distinguished from an ACS, which may present in a similar manner. Treatment for the latter condition involves anti-platelet and anti-thrombotic therapy, which increase the risk of bleeding complications in intensive care patients and will likely lead to invasive investigation of the coronary arteries. Non invasive techniques that could help to rule out the coronary arteries. Non invasive techniques that could help to rule out the coronary arteries. There are numerous available non-invasive modalities, which allow investigation of patients with potential coronary artery disease such as CT coronary angiography, myocardial perfusion scintigraphy, and cardiac MRI, but these cannot be performed at the bedside. The use of MCE in the assessment of perfusion is a safe procedure that can be carried out at the bedside in the intensive care unit, making it a much safer and easier investigation to perform than the other techniques in the critically unwell patient.

In this case we used MCE to assess left ventricular perfusion to aid in differentiating between sepsis-induced systolic dysfunction and ACS. This novel application of MCE is only of value if myocardial perfusion is not affected by sepsis. Early hypotheses regarding the pathophysiology of this syndrome did propose a role for myocardial hypoperfusion, however, a number of subsequent human and animal studies have found no evidence of either macrovascular or microvascular perfusion abnormalities occurring. MCE cannot, however, differentiate between stunned myocardium as a result of ACS and sepsis-induced left ventricular systolic dysfunction. Both conditions behave in a similar manner, with no decrease in myocardial perfusion occurring in either. Therefore, when deciding upon a diagnosis, the whole clinical picture will need to be considered with MCE potentially providing helpful additional information to aid in the decision-making process.

In the case presented, the MCE study showed normal left ventricular perfusion which suggested that the wall motion abnormalities seen were not due to chronically infarcted or hibernating myocardium, but could still be a result of stunning after ACS or stress cardiomyopathy. However, the wall motion abnormalities did not correspond to a single coronary territory and the clinical picture was more in keeping with sepsis-induced left ventricular dysfunction, allowing us to make this diagnosis with reasonable certainty.

This is the first case report suggesting that MCE assessment of left ventricular myocardial perfusion could be used to aid in distinguishing between the regional wall motion abnormality potentially caused by either sepsis or ischaemic heart disease.

**Conflict of interest:** none declared.

**References**


