

Management and Outcomes in Patients with a Diagnosis of Myocardial Infarction but with Normal Coronary Arteries Angiographically

Abstract

The management of patients with chest pain, elevated troponin and unobstructed coronaries on coronary angiography poses a management dilemma. In such patients other differential causes of chest pain need to be excluded. The use of alternative imaging techniques such as intravascular ultrasound or optical coherence tomography enable direct visualisation of the coronary arteries to identify plaque rupture and coronary dissection. Cardiac magnetic resonance imaging is also useful in these patients as areas of myocardial necrosis can be identified. Making an accurate diagnosis is imperative as this has implications for treatment. If an incorrect diagnosis of acute coronary syndrome is made then dual antiplatelet therapy may be prescribed which is not without risk. Furthermore a diagnosis of an acute coronary syndrome has implications on psychological wellbeing, medical insurance and employment for the patient.

Review Article

Volume 7 Issue 4 - 2016

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Received: October 25, 2016 | **Published:** December 19, 2016

Introduction

Evidence surrounding the management of patients with chest pain, elevated troponin and unobstructed coronaries is scarce. Furthermore, the number of patients recruited in these trials have generally been limited. The current European Society of Cardiology and American College of Cardiology non ST-elevation myocardial infarction guidelines recommend early revascularisation in patients who have been diagnosed with an acute coronary syndrome if permitted [1,2]. In some circumstances the coronary angiogram may demonstrate unobstructed coronaries and this poses a management challenge as it is unclear whether these patients should continue on secondary prevention cardiac medications such as dual antiplatelet therapy. In this situation other causes of chest pain need to be ruled out. Troponin elevation may occur in a number of conditions including sepsis, atrial fibrillation, pulmonary embolus, hypovolaemia, congestive heart failure, myocarditis and renal failure. Some of these patients may have co-existing chest pain and in these cases troponin elevation is not necessarily due to thrombotic coronary artery occlusion. If there is a suspicion that the presentation is cardiac in origin despite unobstructed coronary arteries on coronary angiogram then alternative imaging techniques may provide better insight into the diagnosis.

Discussion

Approximately 10% of patients with cardiac sounding chest pain and elevated troponin have a normal coronary angiogram [3,4]. In such patients plaque rupture may have occurred but the coronary angiogram reveals a stenosis of less than 50% therefore making the diagnosis of an acute coronary syndrome (ACS) difficult. The mechanism includes arterial occlusion and recanalisation, coronary spasm or embolism [5]. There is a lack of data regarding the management of these patients and in addition

often a small number of patients have been recruited. According to the American College of Cardiology non ST elevation myocardial infarction guidelines, a class IIb recommendation has been given for the use of invasive physiological assessment in patients with raised troponin and normal coronaries if endothelial dysfunction is suspected [2]. Physiological assessment involves a pressure wire measurement where the pressure difference across a stenosis in an epicardial vessel is measured.

Patients without obstructive coronary artery disease are less likely to be prescribed conventional medications for the treatment of an ACS such as dual antiplatelet therapy (DAPT), angiotensin converting enzyme inhibitors, beta-blockers and statins. There is approximately a 2% risk of death or re-infarction over 6 to 12 months [6]. Furthermore in patients with cardiac chest pain, elevated troponin and unobstructed coronaries more than 15% of patients are readmitted within 6 months [7]. In patients without significant coronary artery stenosis the use of late gadolinium enhancement (LGE) cardiac magnetic resonance imaging (CMRI) may be useful in establishing an accurate diagnosis. CMRI is non invasive and can identify small areas of myocardial damage that may be due to myocardial infarction or myocarditis [8-10]. In a study of 91 patients with cardiac chest pain, positive troponin and unobstructed coronaries on angiography, the role of LGE-CMRI was assessed. The average time from coronary angiography to CMRI was 2 months. In 73% of patients the CMRI was reported as normal. 16% of patients had patchy LGE on CMRI consistent with myocarditis and 11% had findings consistent with a diagnosis of myocardial infarction. There were no deaths during a mean follow up of 21 months. The use of LGE-CMRI is therefore useful in patients with cardiac chest pain, elevated troponin and unobstructed coronaries on coronary angiography as this can help to establish a diagnosis and ensure patients are being managed appropriately.

Invasive imaging techniques involve the use of intracoronary imaging with intravascular ultrasound (IVUS) or optical coherence tomography (OCT). These techniques allow the identification of plaque rupture and the extent of atherosclerosis in patients with a possible ACS and angiographically normal coronary arteries [11].

In a study of 50 women with a diagnosis of non ST segment elevation myocardial infarction (NSTEMI) but without significant coronary artery stenosis on coronary angiography, IVUS and CMRI were used in combination to identify any cardiac abnormalities. CMRI was performed within 1 week of presentation. The median diameter of coronary stenosis on angiography was 20%. 30% of patients had normal angiograms. Plaque disruption was observed in 38% of patients when IVUS was used. CMRI revealed abnormalities in 26 of 44 patients (59%). LGE was present in 17 patients and oedema was seen in 9 patients when T2 imaging was used. The most common LGE pattern was that of subendocardial or transmural infarction. Nonischemic LGE patterns in the mid myocardium and subepicardium were observed. Plaque rupture and ulceration was commonly encountered in women with myocardial infarction without angiographically significant coronary artery stenosis. In this cohort abnormalities were seen in 70% of patients when IVUS and CMRI were used [11]. Both these imaging modalities are useful in patients without significant coronary artery stenosis on coronary angiography.

A further study of 504 patients admitted with a NSTEMI, assessed factors that predict normal coronaries on coronary angiogram. The long term outcomes in these patients were compared to a control group of 160 patients who were admitted with cardiac sounding chest, normal troponin levels and normal coronary arteries. The primary end point was the occurrence of coronary arteries without significant stenosis in the NSTEMI group. The secondary end point was the rate of death or myocardial infarction within a median of 3 years. 64 patients (13%) had coronary arteries without significant stenosis. The predictors of normal coronaries in the NSTEMI group were female sex ($P=0.0001$), age <55 years ($P=0.001$), absence of diabetes ($P=0.02$), no prior antiplatelet treatment ($P=0.007$) and lack of ST-segment depression ($P=0.008$) on the electrocardiogram. Female sex was strongly associated with unobstructed coronaries angiographically ($P=0.0001$). The combination of female gender as well as two additional predictive factors had a specificity of 85% and a sensitivity of 53% for coronary angiography showing no significant coronary obstruction. The rates of death or myocardial infarction were low during follow up in patients without significant coronary artery stenosis ($P=0.03$). There was no significant difference in the rates of death or myocardial infarction between patients who had an elevated troponin without significant coronary artery stenosis and the control group. In the NSTEMI population, patients without significant coronary artery stenosis had lower rates of death and myocardial infarction when compared to patients who had angiographically significant stenosis (6% and 27% respectively $P=0.0001$). Therefore, the long-term prognosis in patients with chest pain, elevated troponin and unobstructed coronaries appears to be good [12].

Conclusion

The diagnosis of an ACS can be difficult in patients with chest pain, elevated troponin but no obstructive coronary

disease angiographically. In these patients alternative imaging techniques such as IVUS, OCT and CMRI are useful in providing a definitive diagnosis so appropriate treatment can be initiated. To enable better understanding in the management and long term prognosis of these patients further trials recruiting larger number of patients are required.

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