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Clinical features of myocardial infarction and myocarditis in young adults: a retrospective study

Cyril Pellaton,[1] Pierre Monney,[1,2] Andrew James Ludman,[1] Juerg Schwitter,[1,2] Eric Eeckhout,[1] Olivier Hugli,[3] Olivier Muller[1]

[1]Department of Cardiology, University Hospital of Lausanne, Lausanne, Switzerland
[2]Cardiac MR Center, University Hospital of Lausanne, Switzerland
[3]Emergency Department, University Hospital of Lausanne, Lausanne, Switzerland

Correspondence to
Dr Olivier Muller;
olivier.muller@chuv.ch

ABSTRACT

Objectives: To evaluate the prevalence and clinical presentation of myocardial infarction (MI) and myocarditis in young adults presenting with chest pain (CP) and an elevated serum troponin I (TnI) to the emergency department (ED).

Design: Retrospective, observational, single-centre study.

Participants: All consecutive patients 18–40 years old admitted to the ED for CP with an elevated TnI concentration.

Primary outcome measures: Prevalence of MI, myocarditis and the characterisation of clinical presentation.

Results: 1588 patients between 18 and 40 years old were admitted to the ED with CP during 30 consecutive months. 49 (3.1%) patients with an elevated TnI (>0.09 μg/l) were included. 32.7% (16/49) were diagnosed with MI (11 ST-elevation myocardial infarction (STEMI) and 5 non-ST-elevation myocardial infarction (NSTEMI)) and 59.2% (29/49) with myocarditis. Compared with patients with myocarditis, MI patients were older (34.1±3.8 vs 26.9±6.4, p=0.0002) with more cardiovascular risk factors (mean 2.06 vs 0.69). Diabetes (18.8% vs 0%, p=0.0039), dyslipidaemia (56.2% vs 3.4%, p<0.0001) and family history of coronary artery disease (CAD) (37.5% vs 10.3% p=0.050) were associated with MI. Fever or recent viral illness were present in 75.9% (22/29) of patients with myocarditis, and in 0% of MI patients (p<0.0001). During follow-up, two patients with myocarditis were re-admitted for CP.

Conclusions: In this study, 32.7% of patients <40-year-old admitted to an ED with CP and elevated TnI had a diagnosis of MI. Key distinctive clinical factors include diabetes, dyslipidaemia, family history of CAD and fever or recent viral illness.

INTRODUCTION

Chest pain (CP) represents about 5% of admissions to emergency departments (ED), even in young adults.[1] Myocardial infarction (MI) and myocarditis are among the most important cardiac diagnoses to consider in

ARTICLE SUMMARY

Article focus
- Myocardial infarction (MI) in young adults has rarely been studied and limited epidemiological data are available.
- Differentiating between MI and myocarditis is a difficult diagnostic challenge.

Key messages
- MI is found in approximately one-third of patients <40 years old admitted to the emergency department with chest pain (CP) and elevated serum cardiac TnI concentration. The possibility of MI should not be overlooked in young adults.
- Key clinical features may help differentiate MI from myocarditis.

Strengths and limitations of this study
- This study provides an estimate of the prevalence of MI in young adults admitted with CP to a single centre.
- This study demonstrates the usefulness of clinical features in differentiating MI from myocarditis and the role of early cardiac MRI.
- Limitations of this study include the relatively small number of patients and the retrospective design.

patients with CP and elevated cardiac biomarkers. Clinical and ECG findings are not specific for either condition and separating both diagnoses is often a challenge.

The requirement for and timing of coronary angiography is a recurrent question in young patients who usually present with fewer coronary risk factors, and therefore a lower pretest probability of MI than older patients. Only a few small epidemiological studies have been published in this specific age group.[2–5] A recent prospective cohort study of 28 778 patients with acute coronary syndrome (ACS) found that 195 patients (0.7%) were 35 years old or younger.[6] The global cardiovascular risk in this population tends to be underestimated.[7] Smoking,

dyslipidaemia and a family history of coronary artery disease (CAD) are considered as the most important risk factors for ischaemic heart disease.[2–6 8]

Myocarditis may be associated with serious morbidity such as dilated cardiomyopathy with heart failure and sudden cardiac death.[9–11] Myocarditis is a difficult diagnosis due to the lack of specificity of history, clinical signs, ECG changes and biomarker elevation. Endomyocardial biopsy (EMB) remains the gold standard for a definite diagnosis, but it is only recommended in specific circumstances and therefore is not widely used in clinical practice.[12] Moreover, EMB still has a suboptimal sensitivity due to sampling error and remains an invasive procedure with potentially severe complications.[12–14] Recently, cardiac MR (CMR) has emerged as a very promising technique to diagnose myocarditis in patients presenting with CP.[15 16] It is the only non-invasive, radiation-free technique capable of positively showing the myocardial damage of acute myocarditis. A recent consensus paper recommends its use for diagnosing myocarditis.[17]

Our study aimed to evaluate the prevalence of MI and myocarditis in patients younger than 40 years old presenting to the ED with CP and an elevated serum troponin I (TnI) concentration. In addition, we sought to establish the differences in clinical, angiographic and CMR features between MI and myocarditis in this cohort.

METHODS
All patients between 18 and 40 years of age admitted with CP and elevated cardiac biomarkers (TnI>0.09 μg/l, Beckman Coulter, Krefeld, Germany) to the ED of the University Hospital of Lausanne (Switzerland) between January 2009 and June 2011 were retrospectively analysed. TnI>0.09 μg/l represents the 99th percentile reference (with 10% CV). High-sensitive troponin assays have not been used in this study.[18] Forty years of age was chosen as a cut-off because only a few studies have been published in this specific age group. All data were collected from patients' clinical notes and electronic records. We analysed all cardiovascular risk factors (hypertension (>140/90), current smoking, diabetes (fasting glucose >7 mmol/l or HbA1c >6.5%), dyslipidaemia (total cholesterol >5 mmol/l or low-density lipoprotein >3 mmol/l), family history of CAD as recently defined,[19] and obesity with body mass index >30 kg/m^2). All ECGs, TnI measurements, echocardiography, coronary angiograms and CMR images were reviewed. Body temperature at admission, history of fever or of recent viral illness (<2 weeks) and cocaine abuse were noted. All medications on discharge were reviewed. Patients were classified into three groups, according to their final diagnosis. *Group 1*: Patients diagnosed with MI (ST-elevation myocardial infarction (STEMI) or non-ST-elevation myocardial infarction (NSTEMI)) based on clinical presentation, ECG, and the presence of a culprit lesion on the coronary angiogram, according to current guidelines.[20]

Group 2: Patients diagnosed with myocarditis based on at least one of three criteria: (1) presence of typical subepicardial late gadolinium enhancement (LGE) on CMR, (2) TnI elevation with normal coronary angiogram and no evidence of an alternative diagnosis and (3) clinical diagnosis in the case of typical pericarditic CP, ECG suggestive of pericarditis, elevated troponin and no evidence of an alternative diagnosis. *Group 3*: Patients with a diagnosis other than MI or myocarditis.

All the data were analysed by two independent cardiologists. Clinical follow-up was conducted by phone. Patients and/or their general practitioners were contacted to assess all cause mortality, MI[20] and rehospitalisation for CP. This study was approved by the local ethics committee.

Statistics
All analyses were performed with GraphPad Prism software, V.5.04 (GraphPad Software, La Jolla, California, USA). Statistics are reported as mean and SD, median and IQR or counts (%). Continuous variables were compared with unpaired t tests, and categorical variables with the Fisher's exact or χ^2 tests, as appropriate.
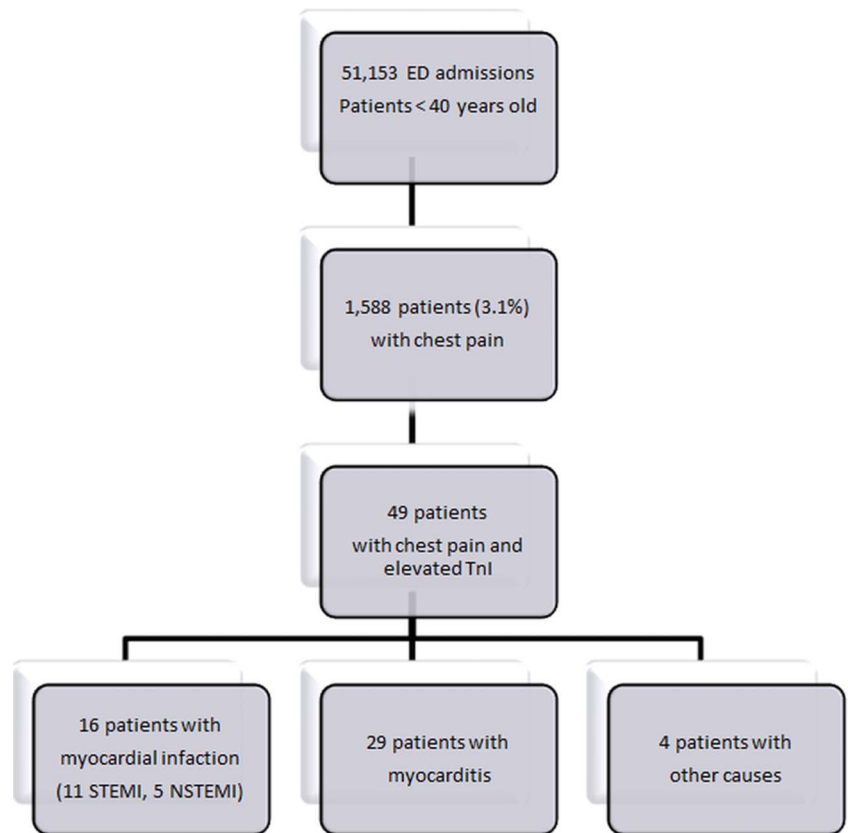
RESULTS
Patient's clinical characteristics and prevalence
From January 2009 to June 2011, 51 153 patients aged 18–40 years were admitted to our ED; 1588 patients (3.1% of all admissions, 57.9% men) were admitted for CP. In total, 505 patients had a TnI measured (31.8%) and 49 (3.1% of all patient with CP) had an elevated serum TnI concentration. These 49 patients were included for further analysis (figure 1). Baseline characteristics are summarised in table 1.

Mean age was 29.6±6.4 years old and most patients were men (n=43, 87.7%). *Group 1* included 32.7% of patients (16/49) diagnosed with MI. Eleven were STEMI (69%) and five were NSTEMI (31%). Group 1 represents 1% of all admissions for CP (16/1588). All 16 patients had coronary angiograms demonstrating a culprit coronary lesion. In patients with STEMI, seven had an occlusion of the left anterior descending artery (LAD), three of right coronary artery (RCA) and one of the left circumflex artery. Two STEMI were related to a spontaneous coronary dissection, one in a young man and one in a postpartum woman. *Group 2* included 59.2% of patients (29/49) who were diagnosed with myocarditis. Seventeen diagnoses were confirmed by CMR with the presence of typical subepicardial LGE. In these patients, six also had a normal coronary angiogram. Among the 12 other patients, 3 had a normal coronary angiogram; 3 had no signs of ischaemia on CMR and no typical LGE (considered as inconclusive CMR for myocarditis) and 6 had no complementary work-up and were diagnosed on clinical presentation only. No evidence of an alternative diagnosis was found in any patient. Only one patient in group two had an EMB.

Figure 1 Study flow chart.

Group 3 includes four patients with CP and elevated TnI attributable to other diagnoses corresponding to 8.2% (4/49). In this group, one patient with corrected transposition of the great arteries presented with right ventricular dysfunction. One patient with severe left heart failure presented with a supraventricular arrhythmia and received three inappropriate shocks by his internal cardioverter defibrillator (ICD). One patient had a hypertensive crisis after intravenous injection of adrenalin for an anaphylactic shock and one was diagnosed with a type A aortic dissection.

Differences in clinical, angiographic and CMR features between MI and myocarditis

Patients with MI (group 1) were significantly older than myocarditis patients (group 2) (mean age 34.1±3.9 vs 26.9±6.4, p=0.0002). Only two MI (1 STEMI, 1 NSTEMI) occurred in patients younger than 30 years old.

Compared with patients with myocarditis, MI patients had more cardiovascular risk factors (mean 2.06 vs 0.69). Diabetes (18.8% vs 0%, p=0.0039), dyslipidaemia (56.2% vs 3.4, p<0.0001) and family history of CAD (37.5% vs 10.3 p=0.050) were more associated with MI, compared with myocarditis, respectively. No significant association was found for smoking, hypertension and obesity. Smoking was highly prevalent in the cohort, both in MI (56.2%) and in myocarditis patients (41.4%; p=0.37). Fever on admission (>38°C) or history of recent (<2 weeks) viral illness was present in 75.9% (22/29) of patients with myocarditis, and in 0% of MI patients

(p<0.0001; table 1). No cocaine abuse was reported by any patients included in this study.

All the CMR and coronary angiograms performed in the study are summarised in table 1. All patients included in the study underwent echocardiography. No statistically significant differences were found in left ventricular ejection fraction (LVEF) between both groups (mean±SD LVEF 51±7.5 in group 1, 52.7±8.2 in group 2; p=0.48). In 12/14 patients with MI (85.7%) and in 8/29 of patients with myocarditis (27.6%), a segmental abnormality was found (p=0.0042). A CMR study was performed in 20 patients with myocarditis (median time after admission: 3.5 days, IQR 2–5 days). In comparison, 14/16 coronary angiograms were performed on the day of admission and 2/16 on day 1 after admission in patients with MI.

Typical subepicardial LGE was found in the majority of patients with myocarditis (17/20, 85%). In three patients, CMR demonstrated no LGE at all and no perfusion defect was detected after adenosine stress. In these patients, admission/peak TnI (μg/l) elevation was 0.44/1.29, 0.11/0.14 and 1.4/1.4 μg/l, peak CK activity (Ui/l) was 200, 233 and 319 and CMR scan was performed 5, 3 and 8 days after symptom onset, respectively. All three patients had a preserved ejection fraction. The absence of subepicardial LGE on CMR despite a clinical presentation that was typical for myocarditis was interpreted as a very small focus of myocarditis, below the threshold of LGE detection.

All the patients with MI were treated according to current guidelines with aspirin, clopidogrel, statins, ACE inhibitors and β-blockers.[21] The discharge

Table 1 Demographic data and characteristics of patients

	All patients included			
Number of patients	49			
Males	43 (87.7%)			
Age (mean±SD)	29.6±6.4			
	Group 1 myocardial infarction	**Group 2 myocarditis**	**Group 3 other diagnosis**	**p Value group 1 vs 2**
Patients	16 (32.7)	29 (59.2)	4	
Males	12 (75)	24 (82.8)	2	
Age (mean±SD)	34±3.8	26.9±6.4	32±5.2	0.0002
Hypertension	2 (12.5)	0	0	0.12
Diabetes	3 (18.8)	0	0	0.0039
Dyslipidaemia	9 (56.2)	1 (3.4)	0	<0.0001
Current smoking	9 (56.2)	12 (41.4)	2	0.37
Family history of CAD	6 (37.5)	3 (10.3)	0	0.050
Obesity (BMI >30 kg/m^2)	4 (25)	4 (13.8)	0	0.43
Fever or recent viral illness	0	22 (75.9)	0	<0.0001
TnI on admission (median, IQR)	1.15, IQR 0.45–17.7	3.5, IQR 0.52–8.75		0.48
Peak CK (U/l) (median, IQR)	1609, IQR 665.5–2880	437, IQR 223–999		
Left ventricular ejection fraction (%) (mean±SD)	51±7.5	52.7±8.2		
Echocardiogram performed	16 (100)	29 (100)	4	
Regional wall motion abnormality (on echocardiogram)	12 (85.7)	8 (27.6)		0.0042
Total exams performed (coronary angiogram and/or CMR)	16	23	1	
Coronary angiogram alone	12	3	0	
CMR alone	0	14	1	
CMR and coronary angiogram	4	6	0	

All values presented as N (%) unless otherwise stated.
BMI, body mass index; CAD, coronary artery disease; CMR, cardiac MRI.

treatment of patients diagnosed with myocarditis was much more heterogeneous. Only a minority (9) were prescribed ACE-inhibitors and β-blockers.

During follow-up (mean 19.9 months±8.6), only two patients from group 2 were re-admitted for CP but had no TnI elevation. No patient from group 1 was readmitted. There was no death or MI during the follow-up period.

DISCUSSION

Identification of the aetiology of CP with elevated cardiac biomarkers in young patients is a frequent and challenging issue in the ED. The clinical presentation of myocarditis can mimic MI, and neither symptoms nor ECG changes are specific for this condition. In our series MI occurs in about 1% of all admissions in patient <40 years with CP and reaches 32.7% when CP is associated with elevated TnI.

Based on our study, key clinical features may help to differentiate MI from myocarditis. Patients with MI are significantly older and have more cardiovascular risk factors. Diabetes, dyslipidaemia and family history of CAD were significantly associated with MI. Current smoking showed no significant association with MI, possibly due to the high prevalence of smoking in all

groups of our study. The prevalence of cardiovascular risk factors in our cohort is in keeping with a recently published prospective cohort of young patients presenting with ACS.[6] In our cohort, STEMI was more frequent than NSTEMI among MI patients, and the LAD was the most frequent culprit artery, which is also in accordance with previous observations.[22–25] Fever (>38°C) or a history of recent viral illness favoured myocarditis since the symptoms were present in three-quarters of patients with myocarditis, and in none of the patients with MI.

In patients presenting with CP, the first goal is to rule out ongoing MI before considering a diagnosis of myocarditis. In this regard, coronary angiography is most commonly the first exam performed. Coronary angiography is often more easily and quickly available in emergency settings than CMR, as demonstrated in our results. Nevertheless, CMR offers the possibility to non-invasively confirm the suspected diagnosis by demonstrating a typical 'myocarditic' subepicardial pattern of LGE. Although not yet mandatory in international recommendations, in the future CMR will probably have an important place in the diagnosis of myocarditis, and is already strongly recommended by some scientific societies.[17] Its use in the acute setting in stable patients is also very promising.

Typical subepicardial LGE was found in the majority of patients with suspected myocarditis. Our series shows that early CMR is a valuable diagnostic tool to confirm the diagnosis of myocarditis with a high sensitivity in the first 2 weeks after symptom onset, in accordance with another recent study.[15]

The presence of a segmental abnormality on echocardiography is very frequent in patient with MI (85.7%) and significantly associated with MI. Nevertheless, segmental abnormality is also found in about one of four patients with myocarditis, limiting its usefulness in daily practice to discriminate both diagnoses.

STEMI may occur at any age and should not be overlooked. All patients <40 years presenting with CP and typical ST elevation should undergo emergency coronary angiography, whatever their age or risk factor profile.[26] In the absence of typical ST elevation, a thorough evaluation of risk factors (especially diabetes, dyslipidaemia and family history of CAD) and clinical presentation (fever or recent symptoms of viral illness) is mandatory. Some conditions which increase the risk of MI should be considered in the risk assessment of the young patient. 'Red flags' include recent pregnancy (risk of coronary dissection), immunological diseases, prior Takayasu's arteritis, cocaine abuse, known congenital coronary abnormality, Churg-Strauss disease, Marfan disease and known coagulation disorders[22] [27–33] and should increase the suspicion of an MI.

Limitations

Our study had a retrospective design, and important information may have been missing from the charts; for example, not all patients included had a strict screening of diabetes (either repetitive glucose blood sampling or HbA1c dosage), potentially underestimating the number of patients with diabetes. This study included patients from a single centre, resulting in a small number of patients. Our observations will need confirmation from a larger prospective study. About one-third of patients with CP assessed in the ED had a TnI test performed. However, none of the 49 patients included in the study were previously admitted to our tertiary hospital for CP, limiting the number of potential previously missed diagnoses. The definitive diagnosis of myocarditis remains a difficult diagnostic challenge and was mostly diagnosed by CMR in our study. EMB is still considered as the gold standard for the diagnosis of myocarditis but was only performed in one of our patients, appropriate to the current guidelines' indications.[12]

CONCLUSION

In conclusion, MI is found in 32.7% of young patients admitted to the ED with CP and elevated serum cardiac TnI concentration. MI should therefore not be overlooked in this population. Several clinical factors may assist clinicians in differentiating patients with MI from those with myocarditis. Prospective validation of these preliminary data in a larger cohort is needed to confirm these findings.

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