Clinical features of myocardial infarction and myocarditis in young adults

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Clinical features of myocardial infarction and myocarditis in young adults

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ABSTRACT

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

Design: Retrospective, observational, single center study.

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

Primary outcome measures: Prevalence of myocardial infarction and myocarditis and characterisation of clinical presentation.

Results: 1588 patients 18-40 years old were admitted to the ED with CP. 49 (3.1%) patients with an elevated TnI (> 0.09 ug/l) were included. 32.7% (16/49) were diagnosed with myocardial infarction (11 STEMI and 5 NSTEMI) and 59.2% (29/49) with myocarditis. Compared to 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), dyslipidemia (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, 2 patients with myocarditis were re-admitted for chest pain.

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, dyslipidemia, family history of CAD, and fever or recent viral illness.

Article focus

Myocardial infarction in young adults has been few studied and only scarce epidemiological data is available.

To differentiate myocardial infarction and myocarditis is a difficult diagnostic challenge.

Key messages

Myocardial infarction is found in about one third of patients <40 years old admitted to the emergency department with chest pain and elevated serum cardiac TnI concentration. Myocardial infarction should therefore not be overlooked in young adults.

Key clinical factors may help to differentiate MI from myocarditis

Strengths and limitations

This study provides an estimate of the prevalence of myocardial infarction in young adults admitted with chest pain in a single centre.

This study shows the usefulness of clinical factors in differentiating myocardial infarction from myocarditis and the role of early cardiac magnetic resonance.

Limitations of this study include the small number of patient and retrospective design.

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 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 need for coronary angiography and its timing is a recurrent question in young patients who usually present with fewer coronary risk factors, and therefore a lower pre-test probability of MI. Only a few small epidemiological studies are 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, dyslipidemia and family history of coronary artery disease (CAD) are considered as the most important risk factors for ischemic 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 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] In recent years, cardiac magnetic resonance (CMR) has emerged as a very promising technique to diagnose myocarditis in patients presenting with CP.[15, 16] It is the only non-invasive 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 elevated serum 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 18-40 years old admitted with CP and elevated cardiac biomarkers (TnI > 0.09 ug/l, Beckman Coulter, Germany) to the ED of the University Hospital of Lausanne (Switzerland) between January 2009 and June 2011 were retrospectively analyzed. 40 years old was chosen as a cut-off because only few studies have been published in this specific age group. All data were collected from patients' clinical notes and electronic records. We analyzed all cardiovascular risk factors (active smoking, diabetes, dyslipidemia, family history of CAD as recently defined [18], and obesity with BMI >30 Kg/m^2). All ECGs, TnI measurements, echocardiography, coronary angiograms and CMR results were reviewed. Body temperature at admission, history of fever or of recent viral illness (< 2 weeks), and cocaine abuse were noted. Patients were classified into 3 groups, according to their final diagnosis. **Group 1**: Included patients diagnosed with myocardial infarction (STEMI or NSTEMI) based on clinical presentation, ECG, and the presence of a culprit lesion on the coronary angiogram, according to current guidelines.[19] **Group 2**: Included patients with myocarditis. The diagnosis of myocarditis was based on at least one of three definite criteria: 1) presence of typical sub-epicardial late gadolinium enhancement (LGE) on CMR, 2) TnI elevation with normal coronary angiogram and no evidence of an alternative diagnosis, 3)

clinical diagnosis in case of typical pleuritic chest pain, suggestive ECG of pericarditis, elevated troponin, and no evidence of an alternative diagnosis**. Group 3:** Included 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, myocardial infarction [19] and re-hospitalisation for CP. This study was approved by the local ethics committee.

Statistics

All analyses were performed with GraphPad Prism software, version 5.04 (GraphPad Software, La Jolla, California). Statistics are reported as mean and standard deviation (SD), median and interquartile range (IQR), or counts (%). Continuous variables were compared with unpaired *t* tests, and categorical variables with the Fisher exact or chi-square tests, as appropriate.

RESULTS

Patient's clinical characteristics and prevalence

From January 2009 to June 2011, 51,153 patients aged 18 - 40 years old were admitted to our ED; 1,588 patients (3.1% of all admissions, 57.9% males) were admitted for CP. 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. (see **figure 1**) Baseline characteristics are summarized in **table 1**.

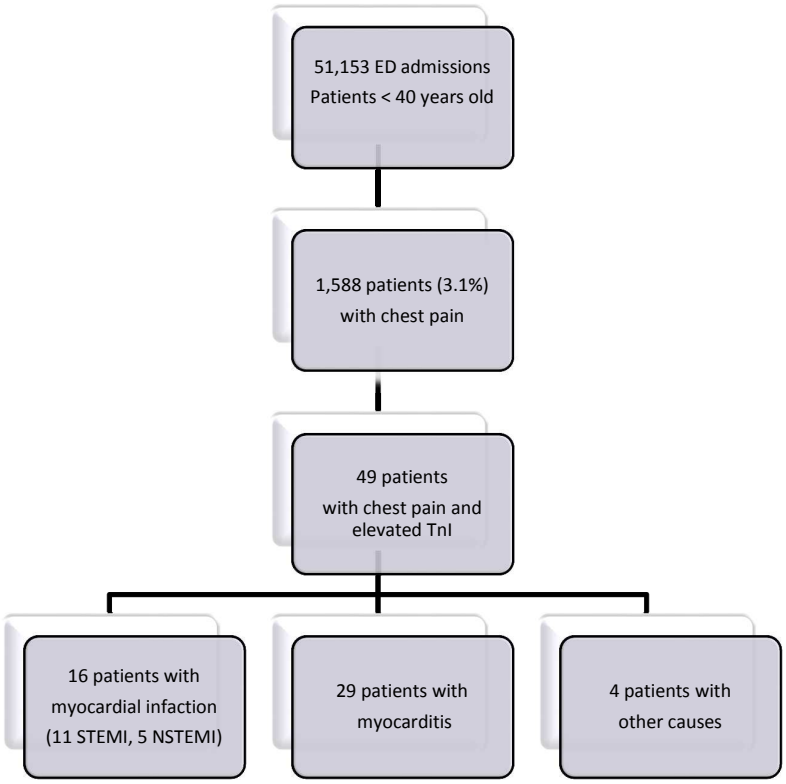

Figure1. Flow chart of the study

	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
Dyslipidemia	9 (56.2)	1 (3.4)	0	<0.0001
Active 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/m2)	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		
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		0.48
Segmental abnormality	12 (85.7)	8 (27.6)		0.0042
Total exams realized	16	23	1	
Coronary angiogram alone	12	3	0	
CMR alone	0	14	1	
CMR and coronary angiogram	4	6	0	
No exams	0	6	3	

Table 1. Demographic data and characteristics of patients. All values presented as N (%) unless otherwise stated.

Mean age was 29.6 ± 6.4 years old and most patients were male (n=43, 87.7%). **Group 1** included 32.7 % of patients (16/49) diagnosed with myocardial infarction. 11 were STEMI (69%) and 5 were NSTEMI (31%). Group 1 represents 1% of all admissions for chest pain (16/1588). All 16 patients had coronary angiograms demonstrating a culprit coronary lesion. In patients with STEMI, 7 had an occlusion of the left anterior descending artery (LAD), 3 of right coronary artery (RCA) and 1 of the left circumflex artery (LCx). Two STEMI were related to a spontaneous coronary dissection, one in a young man and one in a post-partum woman. **Group 2** included 59.2 % of patients (29/49) diagnosed with myocarditis. 17 diagnoses were confirmed by CMR with the presence of typical sub-epicardial LGE. In these patients, 6 also had a normal coronary angiogram. Among the 12 other patients, 3 had a normal coronary angiogram; 3 had no signs of ischemia 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 2 had a EMB. **Group 3** includes 4 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 3 inappropriate shocks by his 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 to patients with myocarditis, MI patients had more cardiovascular risk factors (mean 2.06 vs 0.69). Diabetes (18.8% vs 0%, p=0.0039), dyslipidemia (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 to myocarditis, respectively. No significant association was found for smoking, hypertension and obesity. Active 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 myocardial infarction patients (P<0.0001). (**see 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 summarized in **table 1.** All patients included in the study had an 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 3 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 ug/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.

During follow-up (mean 19.9 months ± 8.6), only 2 patients from Group 2 were re-admitted for chest pain but had no TnI elevation. No patient from Group 1 was readmitted. There was no death or myocardial infarction 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 factors may help to differentiate MI from myocarditis. Patients with MI are significantly older and have more cardiovascular risk factors. Diabetes, dyslipidemia and family history of CAD were significantly associated with MI. Active smoking showed no significant association with MI, due to high prevalence of smoking in all groups. The prevalence of cardiovascular risk factors in our cohort is in accordance 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 LAD was the most frequent culprit artery, which is in accordance with previous observations.[20-23] Fever (>38°C) or a history of recent viral illness favoured myocarditis since the symptoms were present in three quarter 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. Coronary angiography is in this view most of the time the first exam performed. Coronary angiogram is also 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” sub-epicardial pattern of LGE. Although not yet mandatory in international recommendations, CMR will probably have in the future an important place in the diagnosis, and it is already strongly recommended by some scientific societies.[17] Its use already in emergency setting is 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 two 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 patient out of four 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 chest pain and typical ST elevation should undergo emergent coronary angiography, whatever their age and risk factor profile.[24] In absence of typical ST elevation, a thorough evaluation of risk factors (especially diabetes, dyslipidemia and family history of CAD) and clinical presentation (fever or recent symptoms of viral illness) is mandatory. Some conditions increasing the risk of MI should be included in the risk assessment in young patient. These "red flags” including recent pregnancy (risk of coronary dissection), immunological diseases, prior Takayasu's arteritis, cocaine abuse, known congenital coronary abnormality, Marfan disease and known coagulation disorder [20, 25-30] 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 chest pain assessed in the emergency department had a TnI test performed. However, none of the 49 patients included in the study were previously admitted to our tertiary hospital for chest pain, 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 chest pain 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 myocardial infarction from those with myocarditis. Prospective validation of these preliminary data in a larger cohort is needed to confirm these findings.

Contributorship Cyril Pellaton (CP) and Olivier Muller (OM) have reviewed all the patients' notes (clnical history, ECG, exam performed). CP, OM and Eric Eckhout have reviewed all the coronary angiogram performed. CP, Pierre Monney, Juerg Schwitter have reviewed all the cardiac magnetic resonances performed. Olivier Hugli provided all the data of the patients admitted in the emergency department. All authors contributed to the concept of the paper and have read the final manuscript.

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Data Sharing No additional unpublished data.

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ABSTRACT

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

Design: Retrospective, observational, single center 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 myocardial infarction, myocarditis and the characterisation of clinical presentation.

Results: 1588 patients between 18-40 years old were admitted to the ED with CP during 30 consecutive months. 49 (3.1%) patients with an elevated TnI (> 0.09 ug/l) were included. 32.7% (16/49) were diagnosed with myocardial infarction (11 STEMI and 5 NSTEMI) and 59.2% (29/49) with myocarditis. Compared to 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), dyslipidemia (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, 2 patients with myocarditis were re-admitted for chest pain.

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, dyslipidemia, family history of CAD, and fever or recent viral illness.

Article focus

Myocardial infarction in young adults has rarely been studied and limited epidemiological data is available.

Differentiating between myocardial infarction and myocarditis is a difficult diagnostic challenge.

Key messages

Myocardial infarction is found in approximately one third of patients <40 years old admitted to the emergency department with chest pain and elevated serum cardiac TnI concentration. The possibility of myocardial infarction should not be overlooked in young adults.

Key clinical features may help differentiate MI from myocarditis.

Strengths and limitations

This study provides an estimate of the prevalence of myocardial infarction in young adults admitted with chest pain to a single centre.

This study demonstrates the usefulness of clinical features in differentiating myocardial infarction from myocarditis and the role of early cardiac magnetic resonance imaging.

Limitations of this study include the relatively small number of patients and the retrospective design.

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 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 pre-test 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, dyslipidemia and a family history of coronary artery disease (CAD) are considered as the most important risk factors for ischemic 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 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 magnetic resonance (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

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 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 18-40 years old admitted with CP and elevated cardiac biomarkers (TnI > 0.09 ug/l, Beckman Coulter, Germany) to the ED of the University Hospital of Lausanne (Switzerland) between January 2009 and June 2011 were retrospectively analyzed. TnI > 0.09 ug/l represents the 99th percentile reference (with 10% CV). High-sensitive troponin assays have not been used in this study[18]. 40 years old 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 analyzed all cardiovascular risk factors (hypertension (>140/90), current smoking, diabetes (fasting glucose >7mmol/l or Hb1ac >6.5%), dyslipidemia (total cholesterol > 5mmol/l or LDL > 3mmol/l), family history of CAD as recently defined [19], and obesity with BMI >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 3 groups, according to their final diagnosis. **Group 1**: Patients diagnosed with myocardial infarction (STEMI or 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 sub-epicardial late gadolinium enhancement (LGE) on CMR, 2) TnI elevation with normal coronary angiogram and no evidence of an alternative diagnosis, 3) clinical diagnosis in case of typical pleuritic chest pain, 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, myocardial infarction [20] and re-hospitalisation for CP. This study was approved by the local ethics committee.

Statistics

All analyses were performed with GraphPad Prism software, version 5.04 (GraphPad Software, La Jolla, California). Statistics are reported as mean and standard deviation (SD), median and interquartile range (IQR), or counts (%). Continuous variables were compared with unpaired *t* tests, and categorical variables with the Fisher exact or chi-square tests, as appropriate.

RESULTS

Patient's clinical characteristics and prevalence

From January 2009 to June 2011, 51,153 patients aged 18 - 40 years old were admitted to our ED; 1,588 patients (3.1% of all admissions, 57.9% males) were admitted for CP. 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 summarized in **table 1**.

	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
Dyslipidemia	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/m2)	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	

Table 1: Demographic data and characteristics of patients. All values presented as N (%) unless otherwise stated.

Mean age was 29.6 ± 6.4 years old and most patients were male (n=43, 87.7%). **Group 1** included 32.7 % of patients (16/49) diagnosed with myocardial infarction. 11 were STEMI (69%) and 5 were NSTEMI (31%). Group 1 represents 1% of all admissions for chest pain (16/1588). All 16 patients had coronary angiograms demonstrating a culprit coronary lesion. In patients with STEMI, 7 had an occlusion of the left anterior descending artery (LAD), 3 of right coronary artery (RCA) and 1 of the left circumflex artery (LCx). Two STEMI were related to a spontaneous coronary dissection, one in a young man and one in a post-partum woman. **Group 2** included 59.2 % of patients (29/49) who were diagnosed with myocarditis. 17 diagnoses were confirmed by CMR with the presence of typical sub-epicardial LGE. In these patients, 6 also had a normal coronary angiogram. Among the 12 other patients, 3 had a normal coronary angiogram; 3 had no signs of ischemia 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 2 had an EMB. **Group 3** includes 4 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 3 inappropriate shocks by his 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 to patients with myocarditis, MI patients had more cardiovascular risk factors (mean 2.06 vs 0.69). Diabetes (18.8% vs 0%, p=0.0039), dyslipidemia (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 to 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 myocardial infarction 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 summarized 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 3 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 ug/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 of the patients with myocardial infarction were treated according to current guidelines with aspirin, clopidogrel, statins, ACE-inhibitors and beta-blockers[21]. The discharge treatment of patients diagnosed with myocarditis was much more heterogeneous. Only a minority (9) were prescribed ACE-inhibitors and beta-blockers.

During follow-up (mean 19.9 months ± 8.6), only 2 patients from Group 2 were re-admitted for chest pain but had no TnI elevation. No patient from Group 1 was readmitted. There was no death or myocardial infarction 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, dyslipidemia 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" sub-epicardial 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 two 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 patient out of four 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 chest pain 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, dyslipidemia 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 a 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 chest pain assessed in the emergency department had a TnI test performed. However, none of the 49 patients included in the study were previously admitted to our tertiary hospital for chest pain, 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 chest pain 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 myocardial infarction from those with myocarditis. Prospective validation of these preliminary data in a larger cohort is needed to confirm these findings.

Authorship: CP and OM reviewed all the patients' clinical data. CP, OM and EE reviewed all the coronary angiograms performed. CP, PM and JS have reviewed all the cardiac magnetic resonance scans performed. OH provided all the data of the patients admitted in the emergency department, contributed to study design and data analysis. AL contributed to study design, data analysis and critical appraisal of the manuscript. All authors contributed to the concept of the study and have read the final manuscript.

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Competing interests None

Data Sharing No additional unpublished data.

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Clinical features of myocardial infarction and myocarditis in young adults

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ABSTRACT

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

Design: Retrospective, observational, single center 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 myocardial infarction, myocarditis and the characterisation of clinical presentation.

Results: 1588 patients between 18-40 years old were admitted to the ED with CP during 30 consecutive months. 49 (3.1%) patients with an elevated TnI (> 0.09 ug/l) were included. 32.7% (16/49) were diagnosed with myocardial infarction (11 STEMI and 5 NSTEMI) and 59.2% (29/49) with myocarditis. Compared to 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), dyslipidemia (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, 2 patients with myocarditis were re-admitted for chest pain.

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, dyslipidemia, family history of CAD, and fever or recent viral illness.

Article focus

Myocardial infarction in young adults has rarely been studied and limited epidemiological data is available.

Differentiating between myocardial infarction and myocarditis is a difficult diagnostic challenge.

Key messages

Myocardial infarction is found in approximately one third of patients <40 years old admitted to the emergency department with chest pain and elevated serum cardiac TnI concentration. The possibility of myocardial infarction should not be overlooked in young adults.

Key clinical features may help differentiate MI from myocarditis.

Strengths and limitations

This study provides an estimate of the prevalence of myocardial infarction in young adults admitted with chest pain to a single centre.

This study demonstrates the usefulness of clinical features in differentiating myocardial infarction from myocarditis and the role of early cardiac magnetic resonance imaging.

Limitations of this study include the relatively small number of patients and the retrospective design.

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 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 pre-test 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, dyslipidemia and a family history of coronary artery disease (CAD) are considered as the most important risk factors for ischemic 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 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 magnetic resonance (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

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 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 18-40 years old admitted with CP and elevated cardiac biomarkers (TnI > 0.09 ug/l, Beckman Coulter, Germany) to the ED of the University Hospital of Lausanne (Switzerland) between January 2009 and June 2011 were retrospectively analyzed. TnI > 0.09 ug/l represents the 99th percentile reference (with 10% CV). High-sensitive troponin assays have not been used in this study[18]. 40 years old 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 analyzed all cardiovascular risk factors (hypertension (>140/90), current smoking, diabetes (fasting glucose >7mmol/l or Hb1ac >6.5%), dyslipidemia (total cholesterol > 5mmol/l or LDL > 3mmol/l), family history of CAD as recently defined [19], and obesity with BMI >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 3 groups, according to their final diagnosis. **Group 1**: Patients diagnosed with myocardial infarction (STEMI or 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

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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, myocardial infarction [20] and re-hospitalisation for CP. This study was approved by the local ethics committee.

Statistics

All analyses were performed with GraphPad Prism software, version 5.04 (GraphPad Software, La Jolla, California). Statistics are reported as mean and standard deviation (SD), median and interquartile range (IQR), or counts (%). Continuous variables were compared with unpaired *t* tests, and categorical variables with the Fisher exact or chi-square tests, as appropriate.

RESULTS

Patient's clinical characteristics and prevalence

From January 2009 to June 2011, 51,153 patients aged 18 - 40 years old were admitted to our ED; 1,588 patients (3.1% of all admissions, 57.9% males) were admitted for CP. 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 summarized in **table 1**.

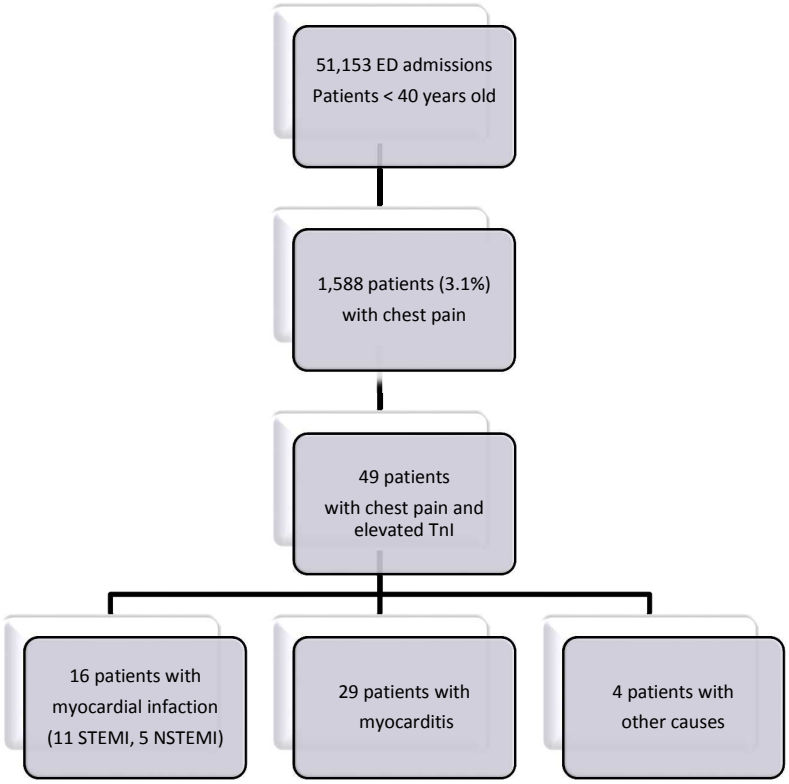

Figure1: Study flow chart

	Patients included			
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Diabetes	3 (18.8)	0	0	0.0039
Dyslipidemia	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/m2)	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		
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CMR and coronary angiogram	4	6	0	

Table 1: Demographic data and characteristics of patients. All values presented as N (%) unless otherwise stated.

Mean age was 29.6 ± 6.4 years old and most patients were male (n=43, 87.7%). **Group 1** included 32.7 % of patients (16/49) diagnosed with myocardial infarction. 11 were STEMI (69%) and 5 were NSTEMI (31%). Group 1 represents 1% of all admissions for chest pain (16/1588). All 16 patients had coronary angiograms demonstrating a culprit coronary lesion. In patients with STEMI, 7 had an occlusion of the left anterior descending artery (LAD), 3 of right coronary artery (RCA) and 1 of the left circumflex artery (LCx). Two STEMI were related to a spontaneous coronary dissection, one in a young man and one in a post-partum woman. **Group 2** included 59.2 % of patients (29/49) who were diagnosed with myocarditis. 17 diagnoses were confirmed by CMR with the presence of typical sub-epicardial LGE. In these patients, 6 also had a normal coronary angiogram. Among the 12 other patients, 3 had a normal coronary angiogram; 3 had no signs of ischemia 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 2 had an EMB. **Group 3** includes 4 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 3 inappropriate shocks by his 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 to patients with myocarditis, MI patients had more cardiovascular risk factors (mean 2.06 vs 0.69). Diabetes (18.8% vs 0%, p=0.0039), dyslipidemia (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 to 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 myocardial infarction 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 summarized 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 3 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 ug/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 of the patients with myocardial infarction were treated according to current guidelines with aspirin, clopidogrel, statins, ACE-inhibitors and beta-blockers[21]. The discharge treatment of patients diagnosed with myocarditis was much more heterogeneous. Only a minority (9) were prescribed ACE-inhibitors and beta-blockers.

During follow-up (mean 19.9 months ± 8.6), only 2 patients from Group 2 were re-admitted for chest pain but had no TnI elevation. No patient from Group 1 was readmitted. There was no death or myocardial infarction 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, dyslipidemia 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" sub-epicardial 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 two 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 patient out of four 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 chest pain 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, dyslipidemia 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 a 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 chest pain assessed in the emergency department had a TnI test performed. However, none of the 49 patients included in the study were previously admitted to our tertiary hospital for chest pain, 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 chest pain 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 myocardial infarction from those with myocarditis. Prospective validation of these preliminary data in a larger cohort is needed to confirm these findings.

Authorship: CP and OM reviewed all the patients' clinical data. CP, OM and EE reviewed all the coronary angiograms performed. CP, PM and JS have reviewed all the cardiac magnetic resonance scans performed. OH provided all the data of the patients admitted in the emergency department, contributed to study design and data analysis. AL contributed to study design, data analysis and critical appraisal of the manuscript. All authors contributed to the concept of the study and have read the final manuscript.

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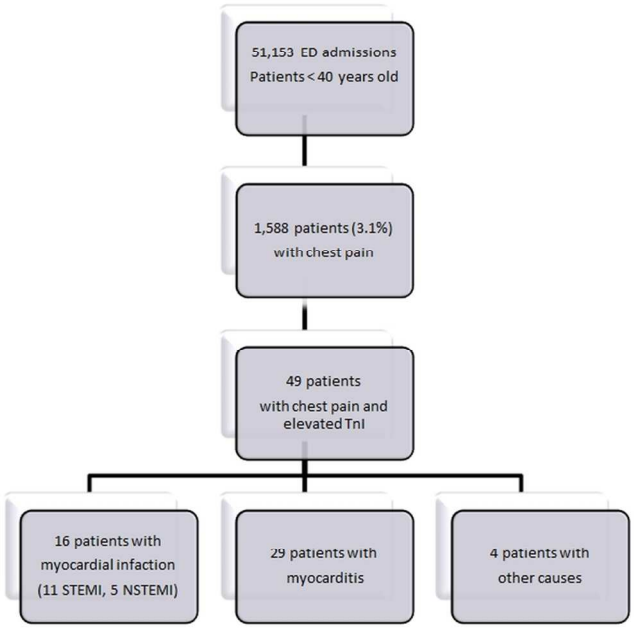

Figure1: Study flow chart

113x90mm (300 x 300 DPI)