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ORIGINAL SCIENTIFIC PAPER

Incidence, clinical presentation, management, and outcome of acute pericarditis and myopericarditis

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Aims Little is known about the epidemiology, clinical presentation, management, and outcome of acute pericarditis and myopericarditis.

Methods and results The final diagnoses of acute pericarditis, myopericarditis, and non-ST-segment elevation myocardial infarction (NSTEMI) of patients presenting to seven emergency departments in Switzerland with acute chest pain were centrally adjudicated by two independent cardiologists using all information including serial measurements of high-sensitivity cardiac troponin T. The overall incidence of pericarditis and myopericarditis was estimated relative to the established incidence of NSTEMI. Current management and long-term outcome of both conditions were also assessed. Among 2533 chest pain patients, the incidence of pericarditis, myopericarditis, and NSTEMI were 1.9% ($n = 48$), 1.1% ($n = 29$), and 21.6% ($n = 548$), respectively. Accordingly, the estimated incidence of pericarditis and myopericarditis in Switzerland was 10.1 [95% confidence interval (95% CI) 9.3–10.9] and 6.1 (95% CI 5.6–6.7) cases per 100 000 population per year, respectively, vs. 115.0 (95% CI 112.3–117.6) cases per 100 000 population per year for NSTEMI. Pericarditis (85% male, median age 46 years) and myopericarditis (62% male, median age 56 years) had male predominance, and commonly (50% and 97%, respectively) resulted in hospitalization. No patient with pericarditis or myopericarditis died or had life-threatening arrhythmias within 30 days [incidence 0% (95% CI 0.0–4.8%)]. Compared with NSTEMI, the 2-year all-cause mortality adjusted hazard ratio of pericarditis and myopericarditis was 0.40 (95% CI 0.05–2.96), being 0.59 (95% CI 0.40–0.88) for non-cardiac causes of chest pain.

Conclusion Pericarditis and myopericarditis are substantially less common than NSTEMI and have an excellent short- and long-term outcome.

Clinical trial registration ClinicalTrial.gov, number NCT00470587, https://clinicaltrials.gov/ct2/show/NCT00470587.

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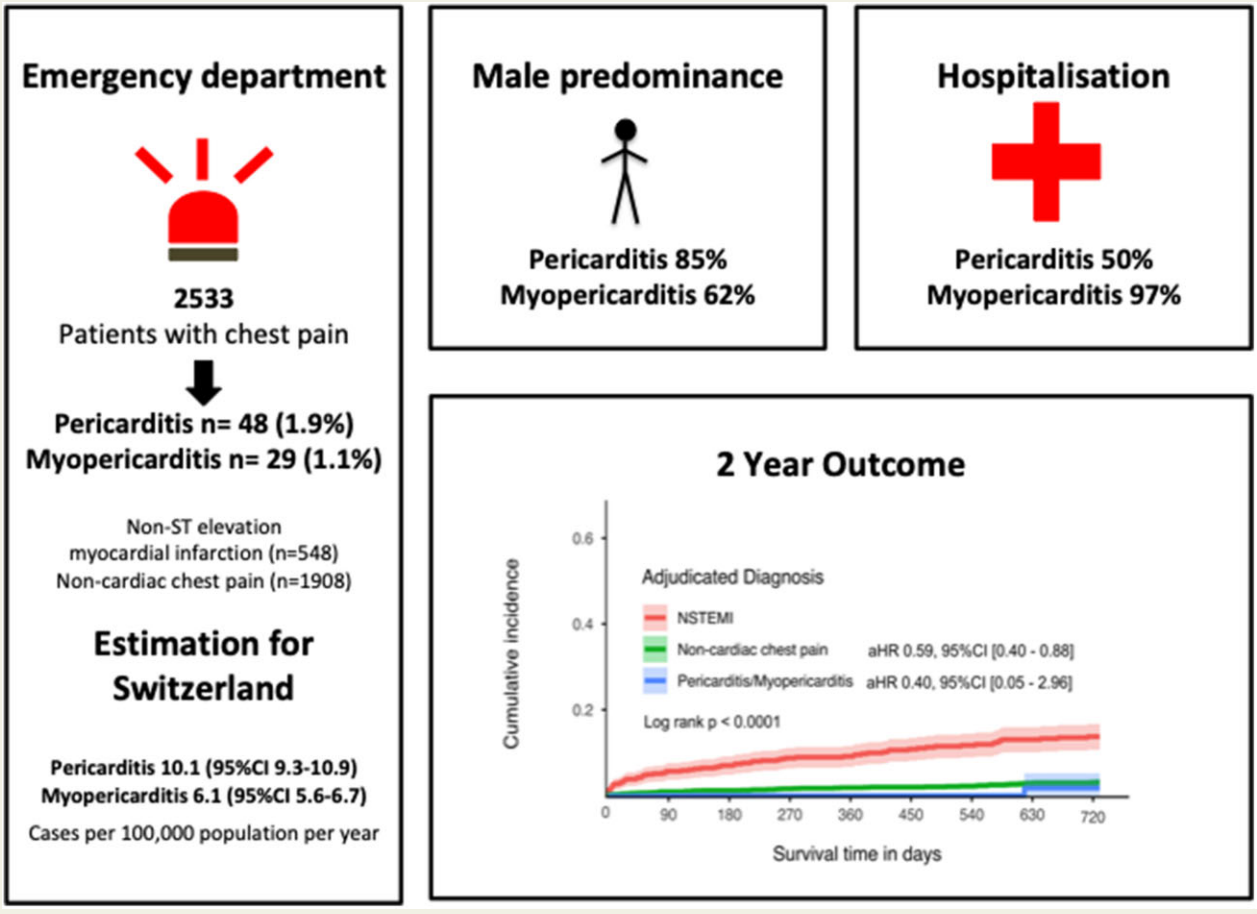
Graphical Abstract



Keywords Pericarditis • Myopericarditis • NSTEMI • Incidence • Presentation • Outcome

Introduction

Acute pericarditis and myopericarditis are important differential diagnoses of acute myocardial infarction (AMI) among patients presenting to the emergency department (ED) with acute chest pain.[1–4] Unfortunately, in contrast to AMI, there are enormous uncertainties regarding the incidence, clinical presentation, management, and long-term outcome of acute pericarditis and myopericarditis.[1–3,5–7] For example, the incidence of acute pericarditis was estimated at 27.7 cases per 100 000 population per year based on data in an Italian urban area, but only 3.3 cases per 100 000 population per year based on data from a Finnish national registry.[3,8] Similarly, there are relevant uncertainties regarding the disposition of patients with myopericarditis.[9] While current clinical practice guidelines recommend hospitalization,[1] the majority of patients with myopericarditis were directly discharged from the ED in a large single-centre registry from Spain.[10]

As chest pain seems present in more than 90% of patients with acute pericarditis and myopericarditis,[1] we used data from a large prospective multicentre study enrolling unselected patients presenting with acute chest pain to the ED with central adjudication of final diagnoses to address these major gaps in clinical knowledge. The incidence of acute pericarditis and myopericarditis in the overall population was estimated relative to the established incidence of non-ST-segment elevation myocardial infarction (NSTEMI).

Objectives

The primary aim of this study was to describe the incidence of pericarditis and myopericarditis among patients presenting to the ED with chest pain and to estimate the overall incidence and long-term outcome of pericarditis and myopericarditis in Switzerland.

Materials and methods

Study design and population

This is a secondary analysis of the prospective, international, multicentre Advantageous Predictors of Acute Coronary Syndromes Evaluation

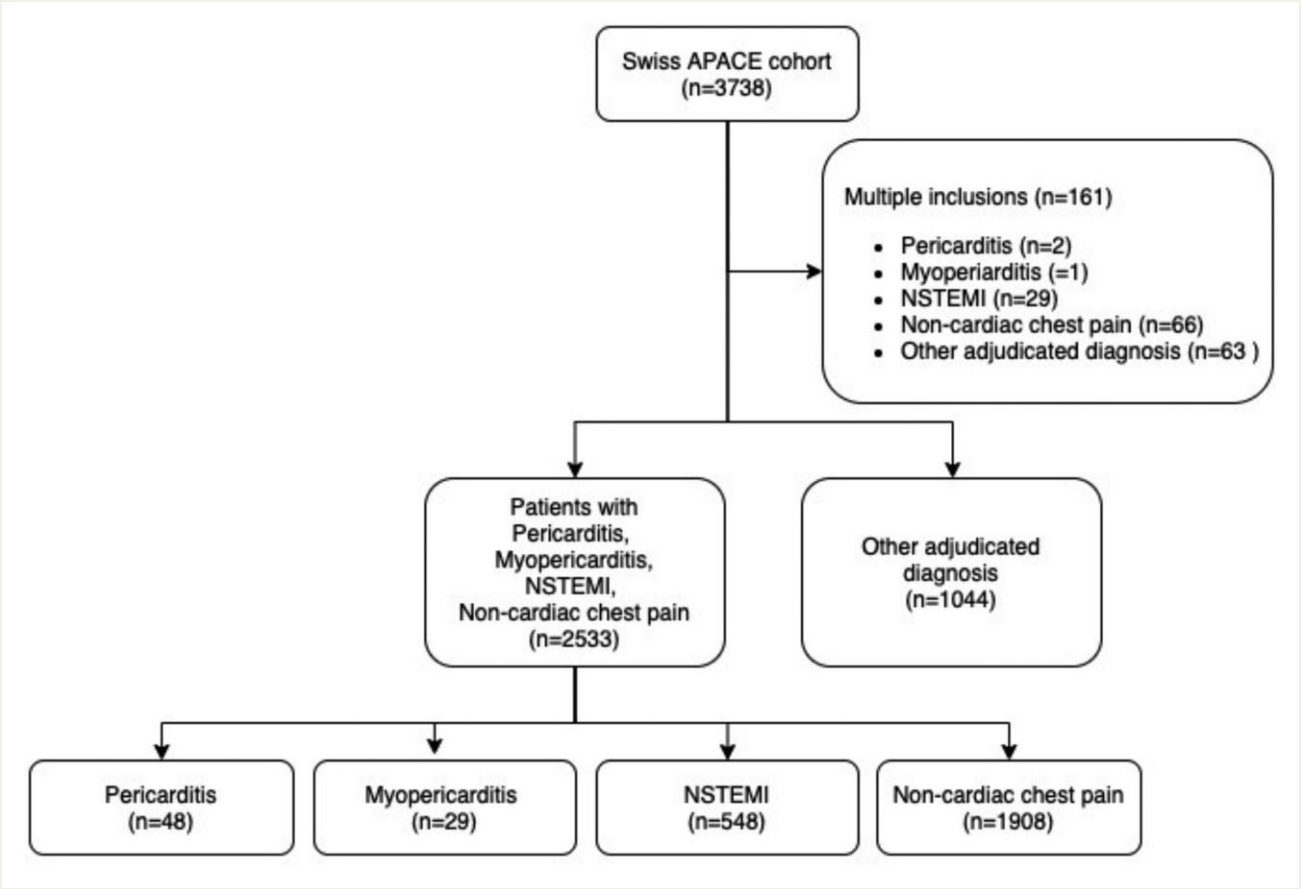


Figure 1 Flow chart of patient inclusion. APACE, Advantageous Predictors of Acute Coronary Syndromes Evaluation study; NSTEMI, non ST-segmental elevation myocardial infarction.

(APACE) study (NCT00470587) enrolling adult patients presenting with acute chest pain (onset or peak of symptoms within the last 12 h) to the ED.[11–14] For this analysis, patients were eligible if presenting to one of the seven EDs in Switzerland participating in APACE (*Figure 1*). Patients were included irrespective of renal function, while patients with terminal kidney failure on chronic haemodialysis were excluded. Patients with ST-segment elevation myocardial infarction were excluded as they often bypass the ED and are triaged directly from the ambulance to the catheterization laboratory. The study was conducted according to the principles of the Declaration of Helsinki and was approved by the local ethics committee. Written informed consent was obtained from all patients. The data were analysed according to the STROBE guidelines for observational studies.[15]

Routine clinical assessment

Patients underwent clinical assessment that included detailed patient history, physical examination, 12-lead electrocardiogram (ECG), continuous 12-lead ECG monitoring, pulse oximetry, standard blood tests including cardiac troponin (cTn), and cardiac imaging as indicated in clinical practice guidelines.[1,16,17] The decision to perform echocardiography, coronary angiography, cardiac magnetic resonance imaging (MRI), and other cardiac imaging modalities was taken by the treating physician in the ED in conjunction with the attending cardiologist taking into account pre-test probability and local availability.

Adjudication of final diagnosis

Adjudication of the final diagnosis was performed centrally by two independent cardiologists at the core laboratory (University Hospital Basel) applying the fourth universal definition of AMI and current guidelines for the diagnosis of pericarditis/myopericarditis using two sets of data[1,16,18]: first, all available medical records obtained during clinical care including medical history, physical examination, and results of laboratory tests including serial clinical high-sensitivity (hs)-cTn levels, ECG, radiologic tests, transthoracic echocardiography, cardiac MRI, cardiac exercise test, lesion severity, and morphology in coronary angiography—pertaining to the patient from the time of ED presentation to 90-day follow-up; second, study-specific assessments, including detailed chest pain characteristics using 34 predefined criteria, serial hs-cardiac troponin T (hs-cTnT) blood concentrations obtained from study samples, and clinical follow-up by telephone and/or mail. In situations of disagreement about the diagnosis, cases were reviewed and adjudicated in conjunction with a third cardiologist.[11–14] As recommended, the diagnosis of acute pericarditis was made with two of the following criteria: (i) chest pain, particularly if sharp and pleuritic, improved by sitting up and leaning forward; (ii) pericardial friction rub; (iii) new widespread ST-segment elevation or PR-segment depression in the ECG, and (iv) pericardial effusion.[1] Myopericarditis was diagnosed in the presence of elevated hs-cTn concentrations above the 99th percentile of the respective assay in addition to the criteria for pericarditis. For the differential diagnosis of myopericarditis vs. NSTEMI, all clinical and imaging findings were evaluated in conjunction. For example,

patients with e.g. a 60% coronary stenosis could still be adjudicated to have myopericarditis, if the cardiac MRI showed clear mid- or epicardial late gadolinium enhancement.[16,17] Signs of systemic inflammation such as fever, leucocytosis, and elevated C-reactive protein concentration were additionally considered during adjudication.[1]

Aetiologies

The aetiologies of both pericarditis and myopericarditis were classified into idiopathic, viral, purulent/bacterial, autoimmune, and post-cardiac intervention.[1,19] The aetiology was considered idiopathic, if despite extensive clinical and diagnostic work-up no other triggering agent could be identified.

Estimation of incidence

The incidence of pericarditis, myopericarditis, and NSTEMI in the prospective multicentre chest pain cohort was calculated. The ratio of absolute NSTEMI cases in the cohort to the absolute number of NSTEMI (code ICD-10 I214) as main diagnoses among all hospitalizations in Switzerland during the years 2006–2015 was assessed using the 'Medical hospital statistics of Switzerland' published online for each year (Source Swiss Federal Statistical Office).[20] With this approach, the number of pericarditis and myopericarditis cases per 100 000 population per year was estimated using the mean adult standard population living in Switzerland during 2006 and 2015 (Source Swiss Federal Statistical Office).[21] This approach relies on the assumption that the likelihood of presenting to the ED is similar for patients with acute pericarditis and myopericarditis vs. patients with NSTEMI. The reliability of this assumption was tested by quantifying the severity of chest pain in all patients. Finding comparable pain severity in patients with pericarditis and myopericarditis vs. NSTEMI would support this assumption.

Management, follow-up, and outcome

To compare the differences in diagnostic work-up between pericarditis and myopericarditis, we analysed cardiac procedures including ECG, echocardiography, coronary angiography, and cardiac MRI. After hospital discharge, patients were followed by trained researchers at 3, 12, and 24 months by telephone or in written form. Additionally, all available medical records were reviewed. Death and life-threatening arrhythmias within 30 days and 2-year all-cause mortality, adjusted for age, sex, history of hypertension, history of dyslipidaemia, history of known coronary artery disease, history of diabetes, history of cancer, history of myocardial infarction, and history of stroke were analysed in patients with the adjudicated diagnosis of pericarditis, myopericarditis, and compared with patients with NSTEMI and non-cardiac causes of chest pain.

Statistical analysis

Incidence calculations were made using proportions relative to NSTEMI (Supplementary material online, *Figure S1*) and 95% confidence intervals (95% CIs) were calculated based on Poisson distribution. The plausibility of the assumption of similar presentation to the ED in patients with pericarditis/myopericarditis vs. patients with NSTEMI was examined by comparing the maximal intensity of acute chest pain quantified in the ED for these conditions.

Continuous variables were described as median and interquartile range (IQR) and categorical variables by numbers and percentages of cases. The Mann–Whitney *U* test or the Kruskal–Wallis test was used for continuous variables and the Pearson χ^2 or the Fisher's exact test for categorical variables. All hypothesis testing was two-tailed and *P*-values <0.05 were considered statistically significant. The Cochran–Armitage test was used to test for linear temporal trends. Confidence intervals for proportions were calculated using Wilson's method. Kaplan–Meier curves were used to estimate the 2-year all-cause mortality rate, and the log-rank test was used to compare NSTEMI vs. pericarditis/myocarditis and non-cardiac chest pain. Considering the total number of deaths in our cohort and to avoid overfitting in the model, nine independent variables were chosen for adjustment, based on relevant previous findings and clinical knowledge. The Cox proportional hazard model was used to calculate the hazard ratios for 2-year all-cause mortality. Cox models were adjusted for age, sex, history of hypertension, history of dyslipidaemia, history of known coronary artery disease, history of diabetes, history of cancer, history of myocardial infarction, and history of stroke. The proportional hazard assumption was assessed using the Schoenfield residuals test. For this analysis, multiple inclusions were excluded. Statistical analyses were performed using IBM SPSS Statistics for Windows and Macintosh V 26.0 (Chicago, IL, USA) and R version 3.6.2 (Vienna, Austria).

Results

Study cohort

From April 2006 to August 2015, 3738 patients were prospectively enrolled in Switzerland. Of these, 2533 had an adjudicated diagnosis either of pericarditis, myopericarditis, NSTEMI, or non-cardiac chest pain (*Figure 1*). Over the study period of 10 years, there was no trend regarding the inclusion of patients with pericarditis or myopericarditis in relation to the total number of enrolled patients. *P*-values for trend analysis were 0.64 for pericarditis and 0.81 for myopericarditis (*Figure 2*).

Incidence

The incidence of pericarditis, myopericarditis, and NSTEMI in the cohort was 1.9%, 1.1%, and 21.6%, with 48, 29, and 548 cases, respectively. Thus, the relative incidence of pericarditis to NSTEMI was 1:11, myopericarditis to NSTEMI 1:19, and pericarditis/myopericarditis to NSTEMI 1:7. The plausibility of the assumption of similar presentation to the ED in patients with pericarditis/myopericarditis vs. patients with NSTEMI was confirmed by comparable maximal intensity of acute chest pain quantified in the ED for these conditions [median visual analogue scale 6/10 (IQR 5.0–8.0) vs. 7/10 (IQR 5.0–8.0), $P = 0.309$] (Supplementary material online, *Table S3*).

During the study period (2006–2015), NSTEMI was the main diagnosis of 72 076 hospitalizations in Switzerland and the mean adult (>19 years) population living in Switzerland during this period was on average 6 270 440 inhabitants (Supplementary material online, *Tables S1* and *S2*). Using the ratio of pericarditis, myopericarditis and NSTEMI in our cohort and NSTEMI in Switzerland, the overall incidence of pericarditis and myopericarditis in Switzerland was estimated to be 10.1 (95% CI 9.3–10.9) and 6.1 (95% CI 5.6–6.7) cases per 100 000 population per year, respectively, vs. 115.0 (95% CI 112.3–117.6) cases per 100 000 population per year for NSTEMI. The combined incidence of pericarditis/myopericarditis was estimated at 16.1 (95% CI 15.2–17.2) cases per 100 000 population per year.

Baseline characteristics and patient disposition

There were no significant differences between patients with pericarditis and myopericarditis in relation to age, vital signs, cardiovascular

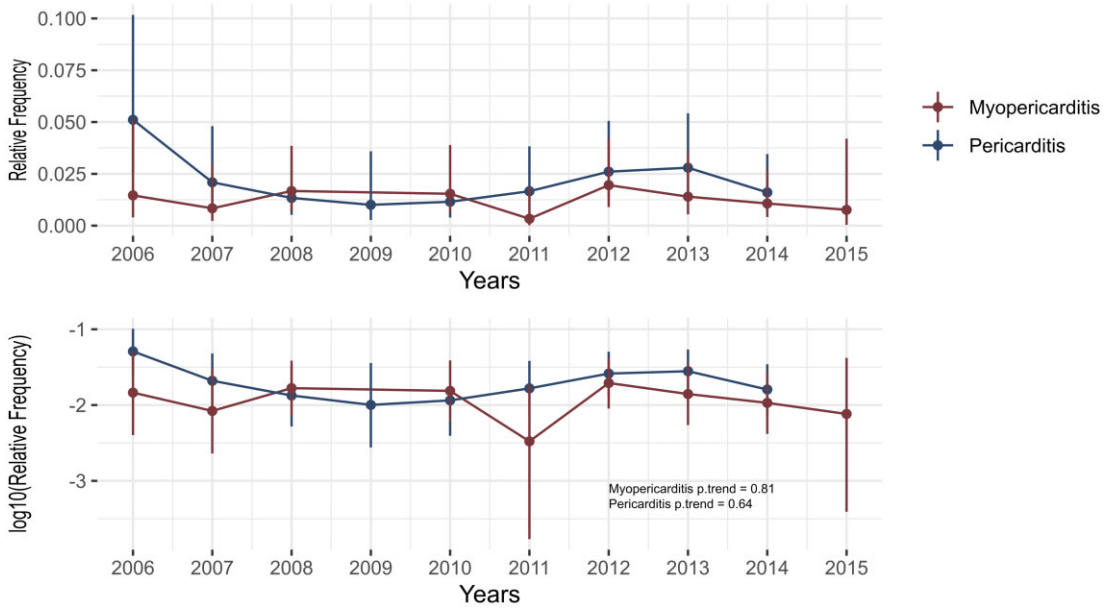


Figure 2 Inclusion of patients with pericarditis or myopericarditis over the study period of 10 years. *Top*: Relative frequencies of pericarditis and myopericarditis over the study period of 10 years (2006–2015) with 95% confidence intervals. *Bottom*: Logarithmized relative frequencies of pericarditis and perimyocarditis over the same study period to compare relative changes (same slopes = same relative change) with 95% confidence intervals. *P*-values for temporal trend were non-significant (*P*-value for temporal trend in pericarditis = 0.64 vs. 0.81 in myopericarditis). In 2009, no patient with myopericarditis and in 2015, no patient with pericarditis was enrolled.

risk factors, or chronic medication at baseline (*Table 1*). Pericarditis (85% male, median age 46 years) and myopericarditis (62% male, median age 56 years) showed male predominance, and commonly (50% and 97%, respectively) resulted in hospitalization. A pericardial friction rub could be auscultated in the ED in 18% ($n = 7$) of patients with pericarditis and in 4% ($n = 1$) with myopericarditis (*Table 2*).

Electrocardiogram changes including PR-segment depression, ST-segment elevation, and ST-segment depression were present in 57% of patients with pericarditis/myopericarditis. Of the hospitalized patients, 4% ($n = 2$) with pericarditis vs. 59% ($n = 17$) with myopericarditis were admitted to an intensive care unit ($P < 0.001$). The median length of stay in the ED/hospital in patients with pericarditis was 0.5 days (IQR 0.0–1.0) and 5 days (IQR 4.0–8.0) in patients with myopericarditis ($P < 0.001$) (*Table 3*). The baseline characteristics of NSTEMI and non-cardiac chest pain patients are described in Supplementary material online, *Table S3*.

Aetiologies

The aetiologies were comparable among patients with pericarditis and myopericarditis, with viral infection being the most common cause in both groups: 54% in pericarditis vs. 48% in myopericarditis (*Figure 3*).

Management and outcome

Non-steroidal anti-inflammatory drugs (NSAIDs) were given to 88% ($n = 42$) of patients with pericarditis and 45% ($n = 13$) of patients with myopericarditis, colchicine to 6% and 3%, respectively (*Table 3*).

Clinical follow-up among patients with pericarditis, myopericarditis, NSTEMI, and non-cardiac chest pain was completed at 3 months in 97%, at 12 months in 84%, and at 24 months in 67%. Within 30 days, there were no life-threatening arrhythmias and/or death in a single patient with pericarditis or myopericarditis. The hazard ratio for all-cause mortality at 2 years was 0.40 (95% CI 0.05–2.96) for pericarditis/myopericarditis vs. NSTEMI compared to a hazard ratio of 0.59 (95% CI 0.40–0.88) for non-cardiac chest pain vs. NSTEMI (*Figure 4*). The adjusted hazard ratio for all-cause mortality was 0.60 (95% CI 0.08–4.38) for pericarditis/myopericarditis vs. non-cardiac chest pain.

Discussion

We used data from a large prospective multicentre study of patients presenting with acute chest pain to an ED, centrally adjudicating the final diagnosis to address remaining uncertainties regarding the incidence, characteristics, management, and outcome of patients with pericarditis and myopericarditis. We report eight major findings.

First, the incidence of pericarditis, myopericarditis, and NSTEMI was 1.9%, 1.1%, and 21.6%, respectively. Thus, pericarditis/myopericarditis was substantially less common vs. NSTEMI (about 1:7). There was no trend regarding the inclusion of patients with pericarditis or myopericarditis over time. Knowledge about this relative incidence and the associated pretest probabilities among patients presenting with acute chest pain to the ED will help clinicians in their assessment of these patients. *Second*, combining the ED-specific data obtained in

Table 1 Baseline characteristics

	Pericarditis/myopericarditis ($n = 77$)	Pericarditis ($n = 48$)	Myopericarditis ($n = 29$)	*P*-value
Age, years	47 (34.0–67.0)	46.0 (35.8–63.2)	56.0 (33.0–69.0)	0.581
Female sex	18 (23)	7 (15)	11 (38)	0.027
Vital signs				
Heart rate, /min	87 (74–98)	89 (77–98)	84 (72–97)	0.452
Systolic blood pressure, mmHg	139 (127–148)	140 (132–148)	130 (123–147)	0.291
Diastolic blood pressure, mmHg	82 (76–92)	84 (79–92)	79 (68–93)	0.083
Temperature, °C	37.3 (36.9–37.6)	37.3 (36.9–37.5)	37.2 (36.9–37.8)	0.862
Oxygen saturation, %	98 (96–100)	98 (97–100)	98 (96–100)	0.910
Maximum of chest pain, VAS	6 (5–8)	6 (5–8)	6 (5–8)	0.686
BMI, kg/m^2	26.2 (23.4–28.4)	26.0 (23.1–28.4)	26.6 (23.5–28.1)	0.667
Cardiovascular risk factors				
Hypertension	27 (35)	13 (27)	14 (48)	0.084
Hypercholesterolaemia	16 (21)	9 (19)	7 (24)	0.576
Diabetes mellitus	7 (9)	5 (10)	2 (7)	0.704
Current smoking	23 (30)	13 (27)	10 (34)	0.609
History of smoking	21 (27)	14 (29)	7 (24)	0.793
eGFR, mL/min/1.73 m^2	95.5 (83.1–108.8)	102.3 (89.9–109.2)	90.2 (81.1–107.7)	0.073
Chronic prior medication				
Aspirin (prophylactic dose)	11 (14)	5 (10)	6 (21)	0.314
Vitamin K antagonists	3 (4)	2 (4)	1 (3)	1.000
New oral anticoagulants	0 (0)	0 (0)	0 (0)	—
Beta-blocker	12 (16)	6 (12)	6 (21)	0.351
Calcium antagonists	5 (6)	3 (6)	2 (7)	1.000
ACE-inhibitors/AT-II-antagonists	13 (17)	7 (15)	6 (21)	0.539
NSAIDs	5 (6)	3 (6)	2 (7)	1.000
Steroids	0 (0)	0 (0)	0 (0)	—
Colchicine	0 (0)	0 (0)	0 (0)	—

Categorical data are presented as no (%) of cases and continuous data as median (IQR).
The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration formula.
ACE, angiotensin converting enzyme; ATII, angiotensin-II; BMI, body mass index; NSAID, non-steroidal anti-inflammatory drugs; VAS, visual analogue scale, range 0–10.

this multicentre study with national data on the incidence of NSTEMI in the years of enrolment the incidence of pericarditis/myopericarditis with symptoms leading to an ED presentation in Switzerland was calculated to be 16.1 (95% CI 15.2–17.2) cases per 100 000 inhabitants per year. This rate is comparable to the incidence estimated for Denmark based on national data (14.5 cases per 100 000 inhabitants in 2016).[22] The lower rate estimated for Finland seems well explained by the fact that it was based only on hospitalized patients (3.3 cases per 100 000 population per year person-years).[8] The higher rate estimated in an Italian urban area (27.7 cases per 100 000 population per year)[3] may be explained in that it was derived from a referral centre for pericarditis inducing an associated referral bias. In addition, there may be regional differences. *Third*, pericarditis (85%) and myopericarditis (62%) had a strong male predominance.[2,8,23] While this finding is confirmed by prior observations,[2,8,23] it is largely unexplained. Sex hormones, as well as sex-specific susceptibility and/or exposure to certain viral pathogens may at least, in part, explain the different incidences in men and women.[23] *Fourth*, the median age in this cohort recruited from the ED with pericarditis or myopericarditis was 47 years, largely consistent with observations from the Finish national registry, where median age was 52 years.[8] In contrast, patients were slightly younger (mean age 39 years) in the cohort recruited in Italy from three reference centres for pericardial diseases.[2] This difference could at least partly be explained by younger and less complex patients, who may have been managed by general practitioner and who therefore did not present to the ED. *Fifth*, C-reactive protein concentration was only mildly elevated (median 15 mg/L) at ED presentation, with more than a quarter of patients even having normal concentrations. This finding is consistent with prior observations, including one study showing that 22% of patients had normal high-sensitivity C-reactive protein concentration at presentation.[24,25] In 34% of these cases, the cause of normal concentrations was early presentation.[25] Early presentation may also have contributed to lower than expected C-reactive protein concentrations in this study, as it included only patients presenting within 12 h after the onset or peak of chest pain, and thereby rather early in the disease course, and at times prior to the rise of C-reactive protein. *Sixth*, NSAID were given to 88% of patients with pericarditis and 45% of patients with myopericarditis, which is consistent with prior series and current recommendations.[1,24–27] In contrast, the use of colchicine was low. Two

Table 2 History, clinical, and diagnostic characteristics

	Pericarditis/myopericarditis (*n* = 77)	Pericarditis (*n* = 48)	Myopericarditis (*n* = 29)	*P*-value
History				
Previous (myo)pericardial disease	10 (13)	8 (17)	2 (7)	0.304
Autoimmune/connective tissue disease	5(6)	3(6)	2(7)	1.000
Heart failure	2 (3)	0 (0)	2 (7)	0.139
Tuberculosis	0 (0)	0 (0)	0 (0)	—
Cocaine use	1 (1)	0 (0)	1 (3)	0.377
Viral episode within the last 15 days	29 (38)	20 (42)	9 (31)	0.467
Chest pain characteristics				
Stabbing/sharp	29 (38)	23 (48)	6 (21)	0.028
Changes with postural or respiratory movements	44 (83)	36 (88)	8 (67)	0.183
Syncope prior presentation	2 (3)	2 (4)	0 (0)	0.524
Clinical findings[d]				
Peripheral oedema	6 (8)	1 (2)	5 (17)	0.026
Pericardial rub	8 (12)	7 (18)	1 (4)	0.128
Laboratory findings				
hs-cTnT, Elecsys, ng/L[a]	8.0 (4.5–40.0)	5.0 (2.9–7.0)	81.0 (32.4–252.5)	<0.001
hs-cTnI, Architect, ng/L[a]	4.8 (2.0–131.5)	2.8 (1.8–4.5)	242.3(17.5–959.5)	<0.001
Peak hs-cTnT, Elecsys, ng/L[b]	9.0 (5.0–53.3)	5.1 (4.0–8.1)	100.0 (32.4–301.8)	<0.001
Peak hs-cTnI, Architect, ng/L[b]	7.0 (3.0–203.2)	3.6 (2.1–7.0)	260.0 (38.0–3296.5)	<0.001
CRP, mg/L	15.0 (3.0–68.0)	14.5(3.2–65.8)	26.0 (3.0–78.0)	0.821
Electrocardiogram changes	44 (57)	33 (69)	11 (38)	0.010
PR-segment depression[c]	27 (35)	21 (44)	6 (21)	0.050
Significant ST-segment elevation	14 (18)	11 (23)	3 (10)	0.228
Significant ST-segment depression	3 (4)	1 (2)	2 (7)	0.553
Transthoracic echocardiography[d]	67 (87)	42 (88)	25 (86)	1.000
Wall motion abnormalities				
Global	5 (7)	1 (2)	4 (16)	0.061
Segmental	8 (12)	4 (10)	4 (16)	0.459
Pericardial effusion				
Mild	15 (22)	10 (24)	5 (20)	0.772
Moderate	3 (4)	2 (5)	1 (4)	1.000
Severe	2 (3)	1 (2)	1 (4)	1.000
Coronary angiography[d]	17 (22)	3 (6)	14 (48)	<0.001
Low coronary sclerosis	2 (12)	1 (33)	1 (7)	0.331
1 vessel coronary artery disease	2 (12)	0 (0)	2 (14)	1.000
2 vessel coronary artery disease	1 (6)	0 (0)	1 (7)	1.000
Cardiac magnetic resonance imaging[d]	21 (27)	3 (6)	18 (62)	<0.001
Late gadolinium enhancement	16 (76)	3 (100)	13 (72)	0.549
Endomyocardial biopsy	0 (0)	0 (0)	0 (0)	—

Categorical data are presented as no (%) of cases, continuous variables as median (interquartile range).
[a]At presentation.
[b]Peak-concentrations of 0, 1, 2, 3, 6 h serial study measurements.
[c]The PR-segment was not assessable in three patients because the initial heart rhythm was no sinus rhythm.
[d]Findings presented as no (%) of cases undergoing the examination.

factors may at least in part explain the infrequent use of colchicine. First, in the vast majority (87%) of patients, this was the first episode of pericarditis/myopericarditis, while the evidence supporting the use of colchicine is strongest in patients with recurrent pericarditis.[1] Second, during the study period colchicine was not commercially available in Switzerland. It had to be imported from one of its neighbouring countries, thereby requiring substantial administrative efforts and time. *Seventh*, about 50% of patients with pericarditis and nearly all (97%) patients with myopericarditis were hospitalized. This observation is in agreement with current European Society of Cardiology

Table 3 Treatment characteristics

	Pericarditis/myopericarditis ($n = 77$)	Pericarditis ($n = 48$)	Myopericarditis ($n = 29$)	*P*-value
Intervention				
Pericardiocentesis	1 (1)	1 (2)	0 (0)	1.000
Medication for the acute episode[a]				
NSAID	55 (71)	42 (88)	13 (45)	<0.001
Aspirin (therapeutic dose)	0 (0)	0 (0)	0 (0)	—
Colchicine	4 (5)	3 (6)	1 (3)	1.000
Corticoids	1 (1)	0 (0)	1 (3)	0.377
ACE-inhibitors	15 (19)	2 (4)	13 (45)	<0.001
Calcium antagonist	3 (4)	0 (0)	3 (10)	0.050
Beta-blocker	13 (17)	3 (6)	10 (34)	0.003
Antiarrhythmics	3 (4)	2 (4)	1 (3)	1.000
Oral anticoagulants	6 (8)	1 (2)	5 (17)	0.026
Hospitalizations				
Hospitalizations	52 (68)	24 (50)	28 (97)	<0.001
ICU admission	19 (25)	2 (4)	17 (59)	<0.001
Length of ED/hospital stay (days)	2.0 (0.0–6.0)	0.5 (0.0–1.0)	5.0 (4.0–8.0)	<0.001

Data are presented as no (%) of cases.
ACE, angiotensin converting enzyme; ED, emergency department; ICU, intensive care unit; NSAID, non-steroidal anti-inflammatory drugs.
[a]New treatment started for the current episode of peri- or myopericarditis; oral anticoagulants includes vitamin K antagonists or novel oral anticoagulants.

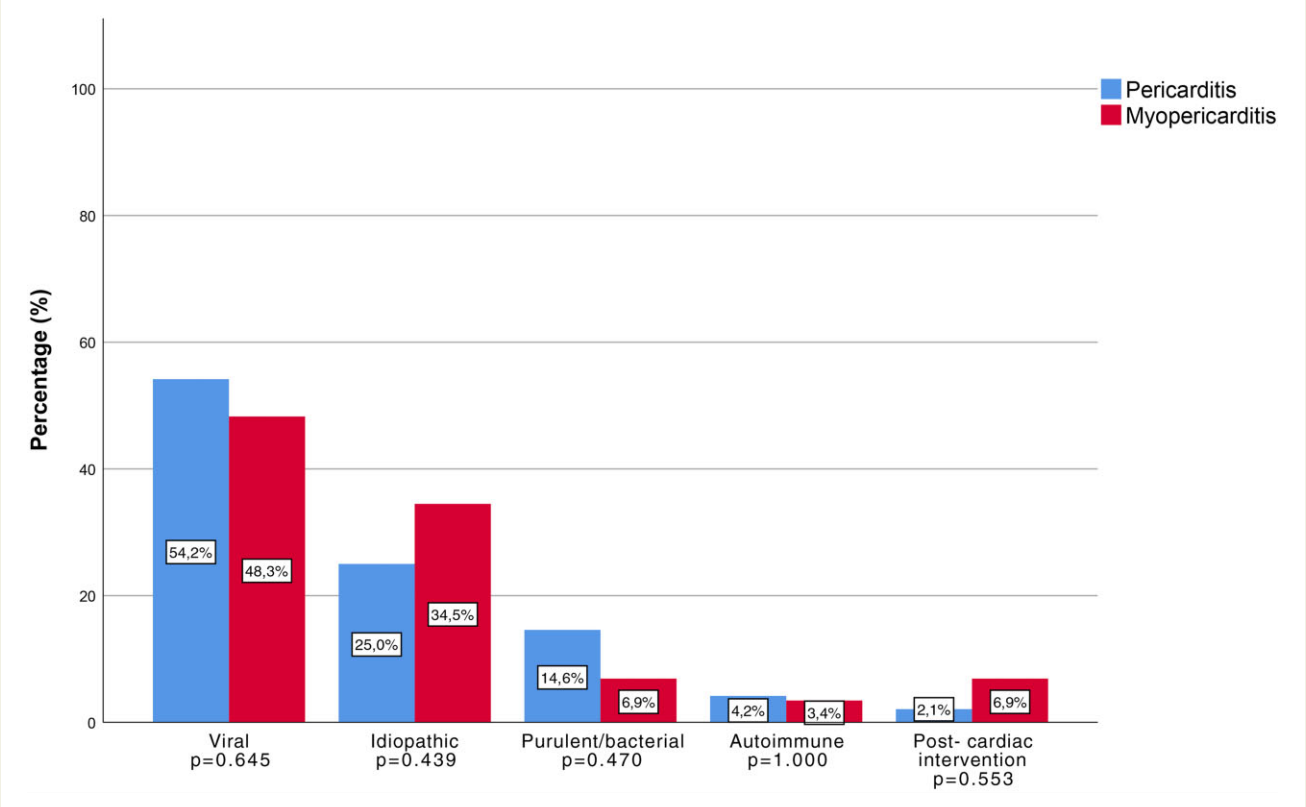


Figure 3 Aetiologies. Data are presented as percentage (%) of cases. The aetiology was classified as idiopathic, if despite extensive work-up no other aetiology could be confirmed. Purulent/bacterial includes either evidence of pus in the pericardium in the course of a confirmed bacterial infection. Viral was defined as virus detection in the blood or anamnestic reference to a previous viral infection within the last 15 days prior admission.

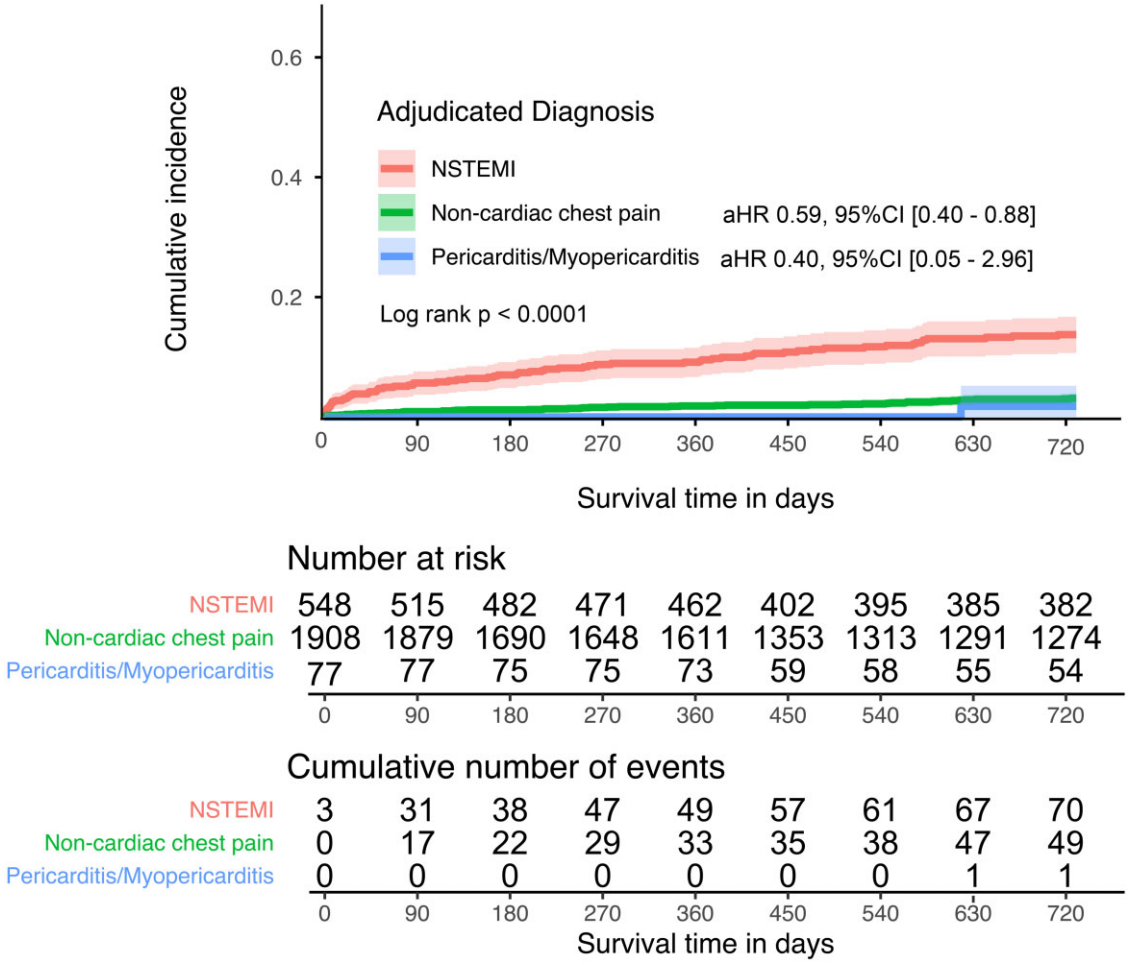


Figure 4 Kaplan–Meier curve and Cox regression for all-cause mortality in non-ST-elevation myocardial infarction vs. pericarditis and myopericarditis and vs. non-cardiac chest pain. Kaplan–Meier curve with log-rank test (*P*-value) and Cox regression with adjusted hazard ratio for 2-year all-cause mortality of patients stratified according to final adjudicated diagnosis of non-ST-elevation myocardial infarction compared to patients with non-cardiac chest pain and patients with either pericarditis or myopericarditis adjusted for age, sex, history of hypertension, history of dyslipidaemia, history of known coronary artery disease, history of diabetes, history of cancer, history of myocardial infarction, and history of stroke.

clinical practice guidelines recommending hospitalization in patients with myopericarditis.[1] However, it is in contrast with a recent single-centre study from Barcelona reporting that only 33% of patients with myopericarditis were hospitalized.[10] Similarly, patient disposition seems to be highly variable in pericarditis. *Eighth*, life-threatening arrhythmias and/or death did not occur within 30 days in a single patient with pericarditis or myopericarditis. Similarly, 2-year long-term follow-up showed a very good long-term prognosis. These findings extend and corroborate observations made in dedicated pericarditis/myopericarditis referral centres.[2,7,28–33] Apparently, the pattern and/or the mechanism of cardiomyocyte injury in myopericarditis is less prone to ventricular arrhythmias as compared to that in NSTEMI and may well justify outpatient management in some patients.

Study limitations

Some limitations merit consideration when interpreting these findings. *First*, this was a secondary analysis of a large, ongoing multicentre study enrolling patients presenting with acute chest pain to the ED. Therefore, the calculated pericarditis/myopericarditis to NSTEMI ratio is likely valid and generalizable to all EDs. However, since in some patients pericarditis/myopericarditis may cause only mild symptoms not resulting in ED presentation, we might possibly have underestimated their incidence overall. In addition, pericarditis following cardiac surgery may occur while patients are still hospitalized and would, therefore, also not result in ED presentation, again leading to underestimation of the incidence. *Second*, despite the use of a very stringent methodology including central adjudication by two independent cardiologists including serial measurements of hs-cTnT, we may have missed a small number of patients with pericarditis/myopericarditis. We also may have misclassified a small number of patients as pericarditis/myopericarditis as the extent of cardiac work-up and the choice of the cardiac imaging modality was determined by the clinical team according to pre-test probabilities and current clinical practice guidelines. *Third*, we cannot comment on the incidence,

characteristics, and outcome of pericarditis/myopericarditis in patients with terminal renal failure on chronic dialysis, as these patients were excluded. *Fourth*, no specific sample size calculation was performed for this secondary analysis, and our sample size of patients with (myo-) pericardial inflammatory syndromes was modest.

Conclusion

Pericarditis and myopericarditis are substantially less common compared to NSTEMI. The estimated incidence was 16.1 (95% CI 15.2–17.2) cases per 100 000 persons in Switzerland per year. Both, pericarditis and myopericarditis have excellent short- and long-term outcome, suggesting that outpatient management should be considered for both disorders.

Supplementary material

Supplementary material is available at *European Heart Journal: Acute Cardiovascular Care* online.

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References

1. Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J, Brucato A, Gueret P, Klingel K, Lionis C, Maisch B, Mayosi B, Pavie A, Ristic AD, Sabaté Tenas M, Seferovic P, Swedberg K, Tomkowski W; ESC Scientific Document Group. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases. *Eur Heart J* 2015;**36**:2921–2964.
2. Imazio M, Brucato A, Barbieri A, Ferroni F, Maestroni S, Ligabue G, Chinaglia A, Cumetti D, Casa GD, Bonomi F, Mantovani F, Di Corato P, Lugli R, Faletti R, Leuzzi S, Bonamini R, Modena MG, Belli R. Good prognosis for pericarditis with and without myocardial involvement: results from a multicenter, prospective cohort study. *Circulation* 2013;**128**:42–49.
3. Imazio M, Cecchi E, Demichelis B, Chinaglia A, Ierna S, Demarie D, Ghisio A, Pomari F, Belli R, Trinchero R. Myopericarditis versus viral or idiopathic acute pericarditis. *Heart* 2007;**94**:498–501.
4. Bhatia S, Anstine C, Jaffe AS, Gersh BJ, Chandrasekaran K, Foley TA, Hodge D, Anavekar NS. Cardiac magnetic resonance in patients with elevated troponin and normal coronary angiography. *Heart* 2019;**105**:1231–1236.
5. Imazio M. Contemporary management of pericardial diseases. *Curr Opin Cardiol* 2012;**27**:308–317.
6. Bonnefoy E, Godon P, Kirkorian G, Fatemi M, Chevalier P, Touboul P. Serum cardiac troponin I and ST-segment elevation in patients with acute pericarditis. *Eur Heart J* 2000;**21**:832–836.
7. Imazio M, Spodick DH, Brucato A, Trinchero R, Adler Y. Controversial issues in the management of pericardial diseases. *Circulation* 2010;**121**:916–928.
8. Kytö V, Sipilä J, Rautava P. Clinical profile and influences on outcomes in patients hospitalized for acute pericarditis. *Circulation* 2014;**130**:1601–1606.
9. Imazio M, Cecchi E, Demichelis B, Ierna S, Demarie D, Ghisio A, Pomari F, Coda L, Belli R, Trinchero R. Indicators of poor prognosis of acute pericarditis. *Circulation* 2007;**115**:2739–2744.
10. Martínez-Nadal G, Prepoudis A, Miró Ò, Matas A, Cepas P, Aldea A, Izquierdo M, Alonso Viladot JR, Flores D, Gualandro DM, Müller C, López-Barbeito B. Características clínicas de las pericarditis y miopericarditis diagnosticadas en urgencias y factores asociados con la necesidad de hospitalización. *Emergencias* 2020;**32**:97–104.
11. Reichlin T, Hochholzer W, Bassetti S, Steuer S, Stelzig C, Hartwiger S, Biedert S, Schaub N, Buerge C, Potocki M, Noveanu M, Breidthardt T, Twerenbold R, Winkler K, Bingisser R, Mueller C. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. *N Engl J Med* 2009;**361**:858–867.
12. Neumann JT, Twerenbold R, Ojeda F, Sörensen NA, Chapman AR, Shah ASV, Anand A, Boeddinghaus J, Nestelberger T, Badertscher P, Mokhtari A, Pickering JW, Troughton RW, Greenslade J, Parsonage W, Mueller-Hennessen M, Gori T, Jernberg T, Morris N, Liebetrau C, Hamm C, Katus HA, Münzel T, Landmesser U, Salomaa V, Iacoviello L, Ferrario MM, Giampaoli S, Kee F, Thorand B, Peters A, Borchini R, Jørgensen T, Söderberg S, Sans S, Tunstall-Pedoe H, Kuulasmaa K,

Renné T, Lackner KJ, Worster A, Body R, Ekelund U, Kavsak PA, Keller T, Lindahl B, Wild P, Giannitsis E, Than M, Cullen LA, Mills NL, Mueller C, Zeller T, Westermann D, Blankenberg S. Application of high-sensitivity troponin in suspected myocardial infarction. *N Engl J Med* 2019;**380**:2529–2540.
13. Puelacher C, Gugala M, Adamson PD, Shah A, Chapman AR, Anand A, Sabti Z, Boeddinghaus J, Nestelberger T, Twerenbold R, Wildi K, Badertscher P, Rubini Gimenez M, Shrestha S, Sazgary L, Mueller D, Schumacher L, Kozhuharov N, Flores D, Du Fay de Lavallaz J, Miro O, Martín-Sánchez FJ, Morawiec B, Fahrni G, Osswald S, Reichlin T, Mills NL, Mueller C. Incidence and outcomes of unstable angina compared with non-ST-elevation myocardial infarction. *Heart* 2019;**105**:1423–1431.
14. Reichlin T, Irfan A, Twerenbold R, Reiter M, Hochholzer W, Burkhalter H, Bassetti S, Steuer S, Winkler K, Peter F, Meissner J, Haaf P, Potocki M, Drexler B, Osswald S, Mueller C. Utility of absolute and relative changes in cardiac troponin concentrations in the early diagnosis of acute myocardial infarction. *Circulation* 2011;**124**:136–145.
15. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;**61**:344–349.
16. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD, Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD; ESC Scientific Document Group. Fourth universal definition of myocardial infarction (2018). *Eur Heart J* 2019;**40**:237–269.
17. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T, Gale CP, Gilard M, Jobs A, Jüni P, Lambrinou E, Lewis BS, Mehilli J, Meliga E, Merkely B, Mueller C, Roffi M, Rutten FH, Sibbing D, Siontis GCM; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 29;**42**:2020–2021.
18. Roffi M, Patrono C, Collet J-P, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen K, Lancellotti P, Landmesser U, Mehilli J, Mukherjee D, Storey RF, Windecker S; ESC Scientific Document Group. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of. *Eur Heart J* 2016;**37**:267–315.
19. Lewinter MM. Acute pericarditis. *N Engl J Med* 2014;**371**:2410–2416.
20. BFS. Medizinische Statistik der Krankenhäuser 2006-2016. 2006. https://bfs.admin.ch/bfs/de/home/statistiken/katalogedatenbanken/ (6 February 2020).
21. BFS. Altersmasszahlen der ständigen Wohnbevölkerung nach Staatsangehörigkeitskategorie und Geschlecht, 1999-2018. 2019. https://www.bfs.admin.ch/bfs/de/home/statistiken/bevoelkerung/stand-entwicklung/alter-zivilstand-staatsangehoerigkeit.assetdetail.9466622.html (8 February 2020).
22. Skajaa N, Horváth-Puhó E, Adelborg K, Bøtker HE, Rothman KR, Sørensen HT. Lack of seasonality in occurrence of pericarditis, myocarditis, and endocarditis. *Ann Epidemiol* 2019;**37**:77–80.
23. Fairweather DL, Cooper LT, Blauwet LA. Sex and gender differences in myocarditis and dilated cardiomyopathy. *Curr Probl Cardiol* 2013;**38**:7–46.
24. Meisel SR, Nashed H, Natour R, Abu Fanne R, Saada M, Amsalem N, Levin C, Kobo O, Frimerman A, Levi Y, Mohsen J, Shotan A, Roguin A, Kleiner-Shochat M. Differentiation between myopericarditis and acute myocardial infarction on presentation in the emergency department using the admission C-reactive protein to troponin ratio. *PLoS One* 2021;**16**:e0248365.
25. Imazio M, Brucato A, Maestroni S, Cumetti D, Dominelli A, Natale G, Trinchero R. Prevalence of C-reactive protein elevation and time course of normalization in acute pericarditis implications for the diagnosis, therapy, and prognosis of pericarditis. *Circulation* 2011;**123**:1092–1097.
26. Caforio ALP, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, Fu M, Heliö T, Heymans S, Jahns R, Klingel K, Linhart A, Maisch B, McKenna W, Mogensen J, Pinto YM, Ristic A, Schultheiss H-P, Seggewiss H, Tavazzi L, Thiene G, Yilmaz A, Charron P, Elliott PM; European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J* 2013;**34**:2636–2648.
27. Berg J, Lovrinovic M, Baltensperger N, Kissel CK, Kottwitz J, Manka R, Patriki D, Scherff F, Schmied C, Landmesser U, Lüscher TF, Heidecker B. Non-steroidal anti-inflammatory drug use in acute myopericarditis: 12-month clinical follow-up. *Open Heart* 2019;**6**:e000990.
28. Imazio M, Demichelis B, Parrini I, Giuggia M, Cecchi E, Gaschino G, Demarie D, Ghisio A, Trinchero R. Day-hospital treatment of acute pericarditis: a management program for outpatient therapy. *J Am Coll Cardiol* 2004;**43**:1042–1046.
29. Imazio M, Brucato A, Cemin R, Ferrua S, Maggiolini S, Beqaraj F, Demarie D, Forno D, Ferro S, Maestroni S, Belli R, Trinchero R, Spodick DH, Adler Y. A randomized trial of colchicine for acute pericarditis. *N Engl J Med* 2013;**369**:1522–1528.
30. Imazio M, Gaita F, LeWinter M. Evaluation and treatment of pericarditis: a systematic review. *JAMA* 2015;**314**:1498–1506.
31. Imazio M, Brucato A, Spodick DH, Adler Y. Prognosis of myopericarditis as determined from previously published reports. *J Cardiovasc Med* 2014;**15**:835–839.
32. Lotrionte M, Biondi-Zoccai G, Imazio M, Castagno D, Moretti C, Abbate A, Agostoni P, Brucato AL, Di Pasquale P, Raatikka M, Sangiorgi G, Laudito A, Sheiban I, Gaita F. International collaborative systematic review of controlled clinical trials on pharmacologic treatments for acute pericarditis and its recurrences. *Am Heart J* 2010;**160**:662–670.
33. Imazio M, Brucato A, Cemin R, Ferrua S, Belli R, Maestroni S, Trinchero R, Spodick DH, Adler Y; CORP (COlchicine for Recurrent Pericarditis) Investigators. Colchicine for recurrent pericarditis (CORP): a randomized trial. *Ann Intern Med* 2011;**155**:409–414.