

Supplementary Material

Supplementary Table 1: Search Terms and Search Strategy

Search No.	Search terms
1	acute coronary syndrome OR ACS
2	NSTEACS OR NSTEMI
3	"non ST elevation" OR "non ST segment elevation"
4	NSTEMI OR "non STEMI"
5	unstable angina OR crescendo angina
6	"ST elevation" OR "ST segment elevation"
7	STEMI
8	myocardial infarction
9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
10	atypical
11	"atypical presentation" OR "atypical signs and symptoms" OR "atypical symptomology" OR "atypical symptomatology" OR "atypical symptoms"
12	"angina equivalent" OR "anginal equivalent"
13	"absence of thoracic pain" OR "absence of thorax pain" OR "absence of thoracic discomfort" OR "absence of thorax discomfort" OR "absence of chest pain" OR "absence of chest discomfort" OR "absence of precordial pain" OR "absence of precordial discomfort" OR "absence of angina pectoris"
14	"without thoracic pain" OR "without thorax pain" OR "without thoracic discomfort" OR "without thorax discomfort" OR "without chest pain" OR "without chest discomfort" OR "without precordial pain" OR "without precordial discomfort" OR "without angina pectoris"
15	"lack of thoracic pain" OR "lack of thorax pain" OR "lack of thoracic discomfort" OR "lack of thorax discomfort" OR "lack of chest pain" OR "lack of chest discomfort" OR "lack of precordial pain" OR "lack of precordial discomfort" OR "lack of angina pectoris"
16	#9 AND #10
17	#9 AND #11
18	#9 AND #12
19	#9 AND #13
20	#9 AND #14
21	#9 AND #15

Supplementary Table 2: Mapping of reported items across studies (with regards to no cardiac chest pain status)

Author	Group	Mortality	Age	Sex (Male/Female)	Comorbidities	Medical interventions	Symptoms only
Ahmad et al. ⁵⁰	ACS		X	X*			
Andell et al. ³⁸	AMI				X (COPD)		
Borden et al. ⁴⁸	STEMI		X		X		
Bianco et al. ²⁹	STEMI			X	X		
Brieger et al. ¹¹	ACS	X	X	X	X	X	
Canto et al. ⁹	UA	X	X	X	X	X	
Chien et al. ⁴⁶	AMI	X	X				
Chien et al. ⁴⁷	NSTEMI	X	X	X	X	X	
Coronado et al. ³⁰	ACS	X	X	X	X		
Coventry et al. ³³	AMI	X	X		X	X	
Dell'Orto et al. ⁵¹	STEMI						X
Dey et al. ⁴⁹	AMI			X*			
Dorsch et al. ⁵⁴	AMI	X	X	X	X	X	
El-Menyar et al. ⁵⁷	ACS			X*			
El-Menyar et al. ²⁶	ACS	X	X	X	X		
Fujino et al. ²⁸	AMI	X	X	X	X	X	
Gajanan et al. ³¹	STEMI	X					
Goel et al. ⁵⁵	STEMI						X
Grosmaître et al. ³⁷	STEMI	X	X	X	X	X	
Gupta et al. ²⁴	AMI		X	X			
Hadi et al. ⁷⁹	ACS						X
Hadi Khafaji et al. ⁸⁰	ACS						X
Hammer et al. ⁵⁶	ACS	X	X	X	X	X	
Hwang et al. ⁵⁸	ACS	X	X	X	X		
Kayhan et al. ⁴⁵	AMI			X*			
Kinsara et al. ³⁹	NSTEMI			X*			
Lankamali and Lekamge ²⁷	ACS		X	X*			
Møller et al. ⁶⁰	AMI	X	X	X*	X	X	
Na et al. ⁴²	STEMI	X	X	X	X	X	
Nakahashi et al. ⁴³	AMI	X	X	X	X	X	
Ng et al. ³²	ACS	X					
Oliveira et al. ⁴⁰	STEMI			X*			
Ouellet et al. ⁵²	AMI						X
Pong et al. ³⁴	STEMI	X	X	X	X	X	
Rallidis et al. ³⁵	STEMI						X

<i>Roque et al.</i> ³⁶	ACS			X*		
<i>Rosell-Ortiz et al.</i> ²⁵	STEMI	X				
<i>Taylor et al.</i> ⁴¹	STEMI		X	X		
<i>Tisminetzky et al.</i> ⁵⁹	AMI		X			
<i>Woon et al.</i> ⁵³	AMI		X			
<i>Wu et al.</i> ⁴⁴	STEMI	X	X	X	X	X

*Separated into sex-specific (male/female) symptoms

Supplementary Table 3: Included study outlines

Author ref., Year	Study design, country	Participants, period of study, sample size	Symptoms reported, as considered typical	Symptoms reported, as considered atypical	Results	Outcomes [§] (atypical vs. typical)
Ahmad ⁵⁰ , 2016	Single centre observational study in the Department of Cardiology at Bahawal Victoria Hospital Bahawalpur Pakistan	Patients admitted in the Cardiology department with ACS diagnosis December, 2014 to March, 2015 Sample size: n=200	No definition given; list of clinical symptoms including chest pain	No definition given; list of clinical symptoms	Chest pain: n=132 Non-chest pain: n=68 Non-chest pain proportion: 34% (68/200)	Nil of the interested outcomes reported for atypical cohort
Andell ³⁸ , 2014	Nationwide multicentre observational study of the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART) registry Sweden	Consecutive patients diagnosed with MI admitted to Swedish coronary care units 2005 to 2010 Sample size: n=81191	No definition given; list of clinical symptoms including chest pain	No definition given; list of clinical symptoms	Chest pain: n=66334 Non-chest pain: n=14250 Non-chest pain proportion: 17.7% (14250/80584)	Nil of the interested outcomes reported for atypical cohort
Bianco ²⁹ , 2022	Multicentre prospective observational study of the Sao Paulo ST Segment Elevation Myocardial Infarction (STEMI) Registry Sao Paulo, Brazil	Consecutive patients admitted to a university hospital and diagnosed with STEMI Sample size: n=2290	Oppressive left-sided chest pain +/- radiation to the left upper limb, of great intensity and prolonged (longer than 20 minutes), with no improvement, or only partial relief with rest or sublingual nitrates. Radiation to mandible, right upper limb, back, shoulders, and epigastrium was also considered for this presentation	Atypical pain included pain in the right upper quadrant or epigastric region of the abdomen, dorsal, mandibular region, or another non-thoracic region, referred to as a twinge or burning of variable intensity, with prolonged duration (greater than 20 minutes). Dyspnoea and syncope also included in the atypical presentation cohort in the absence of chest pain within the previous hours	Typical chest pain: n=1939 Atypical: 230 (<i>Atypical chest pain: n=166</i> <i>Dyspnoea: n=38</i> <i>Syncope: n=26</i>) Atypical proportion: 10.0% (230/2290)	Nil of the interested outcomes reported for atypical cohort

<p>Borden ⁴⁸, 2012</p>	<p>Single centre database review at the University of Chicago Medical Centre – urban teaching hospital USA</p>	<p>Patients admitted through ED presenting with STEMI on ECG satisfying Centres for Medicare and Medicaid Services criteria for public STEMI reporting October 1, 2004, to October 29, 2009 Sample size: n=131</p>	<p>Chest pain considered as initial complaint if any of the following: chest pain; pressure; aching; tightness; crushing; discomfort; burning; constriction; fullness; sharpness; tingling</p>	<p>Initial complaint considered 'no chest pain' if none of the symptoms as stated under 'typical' mentioned</p>	<p>Chest pain: n=116 Non-chest pain: n=15 Non-chest pain proportion: 11.5% (15/131)</p>	<p><i>Delays</i></p> <ul style="list-style-type: none"> • Pre-program: longer DTB times, mostly due to arrival to ECG times (55 vs. 23 min, $p < 0.01$) • Post program: no differences between two groups' ECG times observed (12 vs. 11 min, $p = 0.91$), with flow on effect on DTB times (75 vs. 78 min, $p = 0.84$)
<p>Brieger et al. ¹¹, 2004</p>	<p>Multinational prospective observational study (Global Registry of Acute Coronary Events [GRACE]; 95 hospitals in 14 countries). Argentina, Australia, Austria, Belgium, Brazil, Canada, France, Germany, Italy, New Zealand, Poland, Spain, UK and US</p>	<p>Alive adult patients presenting to hospital with suspected ACS July, 1999 to June, 2002 Sample size: n=20881</p>	<p>Reported symptoms included chest pain</p>	<p>If presentation was not accompanied by chest pain</p>	<p>Typical: n=19118 Atypical: n=1763 Atypical proportion: 8.4% (1763/20881)</p>	<p><i>Mortality</i></p> <ul style="list-style-type: none"> • Higher in-hospital mortality for all atypical ACS (13.0% vs. 4.3%, $P < 0.001$, AOR 1.6, 95% CI 1.3-1.9). Trend consistent for each subtype: STEMI (18.7% vs. 6.3%, $P < 0.001$; AOR 1.7, 95% CI 1.2-2.2); NSTEMI (11.9% vs. 4.2%, $P < 0.001$; AOR NS); and UA (8.0% vs. 2.5%, $P < 0.001$; AOR 2.2, 95% CI 1.4-3.5) <p><i>Heart failure</i></p> <ul style="list-style-type: none"> • More likely to have signs of HF (Killip class II to IV: 41.8% vs. 16.1%, $P < 0.001$) <p><i>Delays</i></p> <ul style="list-style-type: none"> • Longer symptom onset to hospital arrival times (3.2 vs. 2.9 hrs, $P < 0.02$) <p><i>Diagnosis</i></p> <ul style="list-style-type: none"> • 23.8% given incorrect diagnoses, compared with 2.4% of typical presentations <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> • Atypical STEMI less likely to receive fibrinolysis (25.6% vs. 45.6%, $P < 0.001$) or PPCI (11.0% vs. 21.0%, $P < 0.001$) • Atypical NSTEMI-ACS less likely to undergo coronary angiography (39.3% vs. 50.4%, $P < 0.001$) and PCI (17.7% vs. 25.2%, $P < 0.001$) during hospitalisation • Within first 24hrs of presentation, atypical STEMI patients less likely to receive aspirin (86.3% vs. 92.8%, $P < 0.001$), or β-blocker (54.5% vs. 68.5%, $P < 0.001$). This trend extended >24hrs: aspirin (80.6% vs. 89.6%, $P < 0.001$), β-blocker (62.8% vs. 78.2%, $P < 0.001$) • No difference in administration of ACE inhibitors both ≤ 24hrs (41.7% vs. 40.3%, NS) and >24hrs (65.0% vs. 65.5%, NS) • Within first 24 hrs, atypical NSTEMI-ACS patients less likely to receive anticoagulant or antiplatelet therapy

						<p>(unfractionated heparin or LMWH 70.7% vs. 79.9%, $p < 0.001$; aspirin 81.6% vs. 88.7%, $P < 0.001$) and β-blockers (55.6% vs. 69.4%, $P < 0.001$). This trend continued beyond first 24 hrs for both anticoagulant or antiplatelet therapy (unfractionated heparin or LMWH 68.9% vs. 76.1%, $P < 0.001$; aspirin 77.4% vs. 85.3%, $P < 0.001$) as well as β-blockers (63.2% vs. 73.8%, $P < 0.001$)</p> <ul style="list-style-type: none"> At discharge, atypical STEMI and NSTEMI presentations less likely prescribed aspirin (84.3% vs. 91.5%, $P < 0.001$; 79.9% vs. 88.0%, $P < 0.001$, respectively), β-blockers (66.9% vs. 76.3%, $P < 0.001$; 63.8% vs. 71.2%, $P < 0.001$, respectively), or statins (45.9% vs. 52.2%, $P < 0.001$; 42.0% vs. 52.1%, $P < 0.001$ respectively). Atypical STEMI more likely to receive an ACE inhibitor at discharge (69.2% vs. 62.9%, $P = 0.013$)
Canto⁹, 2002	Multicentre retrospective medical record review of the Alabama Unstable Angina (UA) Study (n=22 centres) Alabama – USA	Medicare patients with confirmed diagnosis of UA hospitalised and receiving treatment January 1, 1993 to December 31, 1999 Sample size: n=4167	i) Chest pain located substernally in the left or right chest; and, ii) chest pain characterised as squeezing, tightness, aching, crushing, arm discomfort, dullness, fullness, heaviness, or pressure aggravated by exercise or relieved with rest or GTN	Absence of typical presentation. “Atypical” chest pain or discomfort reported as burning, sharp, or pleuritic in quality	Typical: n=2011 Atypical: n=2156 (Atypical chest pain n=310) Atypical proportion: 51.7% (2156/4167) Non-chest pain proportion: 45% (1946/4167)	<p><i>Diagnosis</i></p> <ul style="list-style-type: none"> Less likely to be admitted with UA diagnosis; as measured by physician documented likelihood of UA ('definite likelihood': 56.1% vs. 66.6%, $P < 0.001$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Less likely to be admitted to ICU (35.0% vs. 42.0%, $P = 0.001$) Significantly less likely to receive early aspirin or other antiplatelet agents (63.3% vs. 67.9%, $P = 0.02$) and heparin (36.2% vs. 43.2%, $P < 0.001$)
Chien⁴⁶, 2016	Single centre retrospective medical record review at Mackay Memorial Hospital Taiwan	Adult patients who presented to ED and treated for AMI January 1, 2008 to December 31, 2008 Sample size: n=329	Typical symptoms presented as chest pain, chest tightness, and any chest discomfort	Atypical symptoms included shortness of breath, nausea/vomiting/dizziness, syncope/confusion/ coma, fatigue/cold sweating, and abdominal pain	Chest pain: n=234 Atypical: n=95 Atypical proportion: 28.9% (95/329)	<p><i>Mortality</i></p> <ul style="list-style-type: none"> Significantly higher mortality rates (OR 5.75, 95% CI 2.78-11.88, $P < 0.001$)
Chien⁴⁷, 2019	Single centre retrospective medical record review at Mackay Memorial Hospital Taiwan	Adult patients who presented and were treated in the ED for NSTEMI (subset analysis from Chien et al. ⁴⁶ , 2016) January 1, 2008 to December 31, 2008 Sample size: n=194	Chest pain, chest tightness, or any chest discomfort	Other symptoms potentially considered non-chest-pain including: shortness of breath; nausea, vomiting, or dizziness; syncope or collapse; fatigue or diaphoresis; and abdominal pain	Chest pain: n=121 Non-chest pain: n=73 Non-chest pain proportion: 37% (73/194)	<p><i>Mortality</i></p> <ul style="list-style-type: none"> Significantly higher mortality rates in-hospital (30.1% vs. 7.4%, $p < 0.001$; AOR 3.09, 95% CI 1.13-8.50, $P = 0.028$), and at 1-year (38.4% vs. 13.2%, $P < 0.001$; AOR 5.37, 95% CI 2.31-12.48) <p><i>Delays</i></p> <ul style="list-style-type: none"> Longer symptom onset to ED arrival time with an average of 8h delay (19.22 vs. 11.33 hrs, $P = 0.033$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Once at ED, less likely to receive aspirin (46.6% vs. 80.2%, $P < 0.001$), clopidogrel (42.5% vs. 64.5%, $P = 0.003$), heparin (17.8% vs. 45.5%, $P < 0.001$), nitro-

						glycerine (35.6% vs. 77.7%, $P < 0.001$), and morphine (6.8% vs. 33.9%, $P < 0.001$) <ul style="list-style-type: none"> Less likely to undergo PCI (34.2% vs. 77.7%, $P < 0.001$)
Coronado ³⁰ , 2004	Subanalysis of patient data from the multicentre prospective clinical trial: Acute Cardiac Ischemia-Time Insensitive Predictive Instrument (ACI-TIPI) (n=10) USA	All consenting adults ≥ 30 years who presented to ED with symptoms suggestive of ACS May, 1993 to November, 1993 Sample size: n=2541	Painful clinical presentation included any pain reported regardless of anatomic location, severity, duration, associated symptoms, or whether pain was the primary or secondary complaint	A painless presentation defined when pain not elicited from patient's history prior to, or upon ED arrival	<i>All ACS</i> Painful: n=2379 Painless: n=158 Painless proportion: 6.2% (158/2541) <i>AMI alone</i> Painful: 807 Painless: 87 Proportion of AMI: 9.8% (87/894)	<i>Mortality</i> <ul style="list-style-type: none"> Painless ACS presentations experienced significantly higher hospital mortality rates (AOR 4.3, 95% CI 2.0-9.3) <i>Heart failure</i> <ul style="list-style-type: none"> Higher degrees of HF on admission as per Killip class (painless vs. painful) for AMI, $P = 0.001$: I) 48% v 8.8% II) 20% v 2.1% III) 41% v 9.8% IV) 6.7% v 4% <i>Delays</i> <ul style="list-style-type: none"> Of all AMI patients who died in hospital, those with painless AMI had significantly longer delays in symptom onset to ED arrival (30 vs. 12.5 hrs, $P = 0.02$) <i>Diagnosis</i> <ul style="list-style-type: none"> Patients with painless ACS more likely to be diagnosed with AMI than those with pain (9.8% vs. 4.2%, $P = 0.001$) <i>Medical interventions</i> <ul style="list-style-type: none"> Significantly fewer admitted to critical care unit compared to similar patients with pain (51% vs. 67%, $P = 0.003$)
Coventry ³³ , 2015	Retrospective cohort study – data sources used were: Emergency Department Information System, St John Ambulance Western Australia, WA Death Register, The Open Patient Admission System, and medical chart review at Sir Charles Gairdner Hospital Australia	All adult patients who arrived by ambulance to ED and received ED discharge diagnosis of MI (only first ED presentation included) January 1, 2008 and October 31, 2009 Sample size: n=382	Chest pain, including: right-sided chest pain, central chest pain, left-sided chest pain, chest tightness and chest heaviness	No definition given; list of clinical symptoms	Chest pain: n=283 Non-chest pain: n=99 Non-chest pain proportion: 26% (99/382)	<i>Mortality</i> <ul style="list-style-type: none"> Higher mortality across all time measurements: ≤ 24 hrs (6.1% v 1.4%, $P = 0.02$), ≤ 30 days (18.2% vs. 6.0%, $P < 0.001$), ≤ 1 year (37.4% vs. 17.7%, $P < 0.001$), ≤ 2 years (44.4% vs. 25.4%, $P < 0.001$) <i>Diagnosis</i> <ul style="list-style-type: none"> More likely to be diagnosed with NSTEMI (64.6% vs. 49.1%, $P < 0.001$) Less likely to be diagnosed with STEMI (15.2% vs. 38.9%, $P < 0.001$) <i>Medical interventions</i> <ul style="list-style-type: none"> Less likely to receive PPCI (5.1% vs. 33.9%, $P < 0.001$, AOR 0.19, 95% CI 0.05-0.75), angiography (2.0% vs. 13.1%, $P = 0.001$), PCI with angiography (8.1% vs. 39.9%, $P < 0.001$) or any cardiac procedure (combined angiography, PCI, CABG and CT angiography) (88.9% vs. 44.2%, $P < 0.001$; AOR 0.22, 95% CI 0.08-0.51)

<p>Dell'Orto ⁵¹, 2017</p>	<p>Prospective observational study involving six ambulances in a rural region Germany</p>	<p>Consecutive participants presenting with any outlined symptoms. ECG telemetrically transferred to ICU of PCI centre for physician interpretation April, 2010 and February, 2011 Overall sample: n=313. Subsample with confirmed STEMI: n=34, met inclusion criteria of present review</p>	<p>Not applicable as not included in study</p>	<p>Patients presenting to ambulance personnel with one or more of the following atypical symptoms: collapse or syncope, dyspnoea, nausea, atypical thorax pain (right-sided, sharp), dizziness, palpitations, or acute hypertension with systolic blood pressure higher than 180 mmHg</p>	<p>Typical: n=0 Atypical: n=34 Atypical proportion: 100% (34/34)</p>	<p>Nil of the interested outcomes reported for atypical cohort</p>
<p>Dey ⁴⁹, 2009</p>	<p>Multinational prospective observational study (Global Registry of Acute Coronary Events [GRACE]; 95 hospitals in 14 countries), Argentina, Australia, Austria, Belgium, Brazil, Canada, France, Germany, Italy, New Zealand, Poland, Spain, UK and US</p>	<p>Recruitment for GRACE occurred April, 1999 to March, 2006. Only symptoms were collected in the initial phases (not reported dates of symptoms of interest collected) Sample size: n=1026</p>	<p>Not applicable as not reported in study</p>	<p>No definition given; list of clinical symptoms</p>	<p>Chest pain: n=0 Non-chest pain: n=1026 Non-chest pain proportion: 100% (1026/1026)</p>	<p>Nil of the interested outcomes reported for atypical cohort</p>
<p>Dorsch ⁵⁴, 2001</p>	<p>Multicentre retrospective study of registry databases, biochemical reports and hospital management systems (n=20 adjacent hospitals) Yorkshire, United Kingdom</p>	<p>Consecutive patients with confirmed AMI. Only first event during recruitment period included (pts who died in ambulance or ED excluded) September 1, 1995 to November 30, 1995 Sample size: n=2082</p>	<p>Chest pain</p>	<p>Symptomatic without chest pain</p>	<p>Chest pain: n=1661 Non-chest pain: n=421 Proportion: 20.2% (421/2082)</p>	<p><i>Mortality</i></p> <ul style="list-style-type: none"> Higher mortality rates at 30-days (49.2% vs. 17.9%) as well as 365-days (61.0% vs. 26.2%). Findings remained unchanged after adjusting potential confounders (specific findings not presented) Adjusted HR for presenting without chest pain 1.60 (95% CI 1.30-1.97), <i>P</i> < 0.001 <p><i>Heart failure</i></p> <ul style="list-style-type: none"> Higher levels of LV impairment at arrival (55% vs. 46%, <i>P</i> = 0.005) <p><i>Diagnosis</i></p> <ul style="list-style-type: none"> Less likely to show ST elevation on first ECG (34% vs. 50%, <i>P</i> < 0.001) <p><i>Medical interventions</i></p>

						<ul style="list-style-type: none"> • During admission, less likely to receive revascularisation (0.7% vs. 2.1%, $P = 0.20$; AOR 0.46, 95% CI 0.13-1.52) or angiography (1.2% vs. 4.8% $P = 0.03$; AOR 0.36, 95% CI 0.14-0.90) • Less likely to be managed in CCU (39.9% vs. 77.0%, $P < 0.001$; AOR 0.27, 95% CI 0.21-0.34), enrolled in cardiac rehabilitation programme (54.2% vs. 78.8%, $P < 0.001$; AOR 0.48, 95% CI 0.33-0.70), or have cardiologist follow-up (21.5% vs. 43.2%, $P < 0.001$; AOR 0.52, 95% CI 0.36-0.77) • Despite absence of contraindication, at discharge higher proportion of non-chest pain patients not prescribed aspirin (15.8% vs. 4.6%, $P < 0.001$; AOR 2.72, 95% CI 1.65-4.51) or β-blockers (45.5% vs. 17.2% $P < 0.001$; AOR 2.66, 95% CI 1.51-4.69)
El-Menyar⁵⁷, 2009	<p>Multicentre retrospective analysis of prospectively collected patient data Gulf Registry of Acute Coronary Events (Gulf RACE); across 6 Middle Eastern countries</p> <p>Bahrain, Kuwait, Qatar, Oman, United Arab Emirates, and Yemen</p>	<p>Consecutive ACS patients from participating countries</p> <p>Over 6-month period in 2007</p> <p>Sample size: n=8169</p>	No definition given; list of clinical symptoms including ischemic chest pain	No definition given; list of clinical symptoms including atypical chest pain	<p>Typical pain: n=6484</p> <p>Atypical pain: n=537</p> <p>Dyspnoea: n=799</p> <p>Atypical proportion: 17.1% (1336/7820)</p>	Nil of the interested outcomes reported for atypical cohort
El-Menyar²⁶, 2011	<p>Multicentre retrospective analysis of prospectively collected patient data Gulf Registry of Acute Coronary Events (Gulf RACE); across 6 Middle Eastern countries</p> <p>Bahrain, Kuwait, Qatar, Oman, United Arab Emirates, and Yemen</p>	<p>Consecutive ACS patients from participating countries</p> <p>Over 5-month period in 2007</p> <p>Sample size: n=6420</p>	<p>Typical symptoms defined as including: (1) precordial chest discomfort, pain, heaviness, or fullness, possibly radiating to the arm, shoulder, back, neck, jaw, epigastrium, or other location; (2) symptoms exacerbated by exertion or stress; (3) symptoms that may be relieved by rest or use of nitro-glycerine; and (4) symptoms associated with SOB, diaphoresis, weakness, nausea or vomiting, and light-headedness</p>	<p>Atypical chest pain defined as: not severe; not prolonged; not classic in presentation; not like prior cardiac symptoms; burning, sharp, pleuritic, positional pain or discomfort reproducible on palpation of chest wall and localizable by 1 finger; or pain or discomfort in areas of the upper body other than chest, e.g., arms, epigastric, shoulder, neck.</p> <p>Dyspnoea defined as: sudden onset unexplained SOB</p>	<p>Typical pain: n=5349</p> <p>Atypical pain: n=401</p> <p>Dyspnoea: n=670</p> <p>Atypical proportion: 16.7% (1071/6420)</p>	<p><i>Mortality (dyspnoea vs. atypical pain vs. typical pain):</i></p> <ul style="list-style-type: none"> • Trend for higher in-hospital mortality (6% vs. 2.5% vs. 3%, $P < 0.001$) • This trend also observed amongst MI cohorts (STEMI: 18% vs. 6% vs. 5%; NSTEMI: 4% vs. 1.4% vs. 1.3%) • Higher GRACE scores (82% vs. 73% vs. 57%, $P < 0.001$) • Likelihood in-hospital mortality double in those with absent typical chest pain (<i>dyspnoea</i> and <i>atypical chest pain</i> combined) (AOR 2.0, 95% CI 1.29-2.75) <p><i>Heart failure and MACE (dyspnoea vs. atypical pain vs. typical pain):</i></p> <ul style="list-style-type: none"> • Higher Killip class associated with absence of typical chest pain (LVEF <40%: 53% vs. 18% vs. 18%, $P = 0.03$) • In-hospital outcomes worse when typical chest pain absent: significantly higher rates of HF (55% vs. 11% vs. 12%, $P < 0.001$), cardiogenic shock (10% vs. 3% vs. 4%, $P = 0.001$), and stroke (0.8% vs. 2.5% vs. 0.5%, $P = 0.001$). Typical chest pain patients less likely to

						<p>experience major bleeding (1% vs. 1.3% vs. 0.6%, $P = 0.001$)</p> <p><i>Diagnosis (dyspnoea vs. atypical pain vs. typical pain)</i></p> <ul style="list-style-type: none"> Atypical patients less likely to receive STEMI diagnosis (18% vs. 27% vs. 43%, $P < 0.001$) Peak troponin (ng/L), M±SD: 8±41 vs. 11±42 vs. 18±52, $P < 0.001$ First creatinine (mmol/L), Mean (SD): 130 (109) vs. 106 (81) vs. 104 (90), $P < 0.001$ <p><i>Delays</i></p> <ul style="list-style-type: none"> Delay seeking medical care >12 hrs common in dyspnoea and atypical chest pain groups compared to typical chest pain group (61% vs. 51% vs. 28%, $P < 0.001$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Those with absent typical chest pain (<i>dyspnoea</i> and <i>atypical chest pain</i> combined) experienced delayed door-to-needle time (99 vs. 55 min, $P < 0.001$) and were less likely to undergo PCI (3% vs. 5%; $P < 0.001$) Those who had an absence of typical chest pain (<i>dyspnoea vs. atypical pain vs. typical pain</i>) were less likely to: undergo coronary angiography (9% vs. 17% vs. 20%, $P < 0.001$); receive antiplatelet therapy (aspirin: 96% vs. 96% vs. 98%, $P < 0.001$; clopidogrel: 36% vs. 49% vs. 57%, $P < 0.001$; glycoprotein inhibitor: 7% v 10% vs. 11%, $P < 0.001$); β-blockers (22% vs. 64% vs. 72%, $P < 0.001$); heparin (86% vs. 91% vs. 94%, $P = 0.001$); and statins (79% vs. 83% vs. 82%, $P = 0.001$). Patients with dyspnoea more likely to receive ACE inhibitors (80% vs. 64% vs. 69%, $P < 0.001$) and experienced longer hospitalisation (6.6 (7) vs. 5.4 (4) vs. 5.5 (4), $p=0.001$)
Fujino²⁸, 2017	<p>Multicentre retrospective study of prospectively collected patient data in the Japanese registry of acute myocardial infarction J-MINUET (n=28)</p> <p>Japan</p>	<p>Consecutive patients admitted to participating institution within 48h from onset of AMI</p> <p>July, 2012 and March, 2014</p> <p>Sample size: n=3085</p> <p>(n=3283 enrolled into registry, n=198 excluded due to missing data of symptoms)</p>	<p>Chest pain or pressure due to myocardial ischemia, indifferent to the pain radiating to arm, neck or jaw</p>	<p>Specific symptoms of SOB, chest discomfort, nausea, vomiting, syncope, or none of those symptoms defined as atypical symptoms</p>	<p>Typical: n=2443</p> <p>Atypical: n=642</p> <p>Atypical proportion: 20.8% (642/3085)</p>	<p><i>Mortality (all cause)</i></p> <ul style="list-style-type: none"> In-hospital mortality significantly higher (19.5% vs. 3.3%, $P < 0.001$; AOR 3.12, 95% CI 2.19–4.47) <p><i>Heart failure and MACE</i></p> <ul style="list-style-type: none"> Higher Killip class (atypical vs. typical), $P < 0.001$: I) 51.2% v 81.9% II) 11.4% v 8.9% III) 12% v 3.7% IV) 25.4% v 5.5% Experienced significantly higher rates of MACE. Both composite (41.7% vs. 14%, $P < 0.001$; AOR 2.07, 95% CI 1.61-2.67), and individual MACE: cardiac failure (33.9% vs. 11.5%, $P < 0.001$), VT and/or fibrillation (11.1% vs.

						<p>2.3%, $P < 0.001$), and bleeding (4.6% vs. 2.1%, $P = 0.001$)</p> <p><i>Diagnosis</i></p> <ul style="list-style-type: none"> • Less likely to receive STEMI diagnosis (60.9% vs. 70.9%, $P < 0.001$) • Higher maximum CK (IU/L) (1386 (481–3540) vs. 1480 (542–3104), $P < 0.001$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> • Among STEMI patients, DTB time significantly longer when presentation was atypical (74 vs. 65 min, $P = 0.002$) • Less likely to receive urgent revascularisation (all AMI 79.5% vs. 89.5%, $P < 0.001$; STEMI 90.2% vs. 95.3%, $P < 0.001$; NSTEMI 63.0% vs. 73.4%, $P < 0.001$), including coronary angiography (All AMI 88.4% vs. 94.6%, $P < 0.001$; STEMI 95.1% vs. 97.4%, $P = 0.02$; NSTEMI 78.1% vs. 87.8%, $P < 0.001$), and PCI (all AMI 77.3% vs. 87.7%, $P < 0.001$; STEMI 88.7% vs. 94.5%, $P = 0.001$; NSTEMI 59.8% vs. 71.3%, $P < 0.001$) • CABG performed less frequently in atypical STEMI patients (1.5% vs. 0.8%, $P = 0.0239$) 	
Gajanan³¹, 2015	Single centre observational study in the Cardiac ICU of Sundaram Arulrhaj Hospitals, Tuticorin India	Female patients admitted to Cardiac ICU diagnosed with STEMI November, 2011 to November, 2013 Sample size: n=100	Chest pain or discomfort, upper body discomfort, shortness of breath	Symptoms including dyspnoea, sweating, fatigue/weakness, light headedness and stomach pain	Typical: n=43 Atypical: n=57 Atypical proportion: 57% (57/100)	<i>Mortality</i>	<ul style="list-style-type: none"> • Significantly higher mortality (29.8% vs. 11.6%, $P = 0.0495$)
Goel⁵⁵, 2012	Interviews, detailed questionnaires and medical record review of patients at Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, and three secondary care centres in UP India	Patients presenting with first STEMI admitted to Cardiology Department January, 2008 to December, 2008 Sample size: n=609	No definition given; list of clinical symptoms including chest pain	No definition given; list of clinical symptoms	Chest pain: n=510 Non-chest pain: n=99 Proportion: 16.3% (99/609)		Nil of the interested outcomes reported for atypical cohort
Grosmaître³⁷, 2013	Multicentre study Retrospective medical record review (n=4) Lyon, France	Consecutive patients aged ≥ 75 years admitted via ED with diagnosis of STEMI January, 2004 and December, 2008	Chest pain as primary presenting complaint	Atypical presentations were those not admitted to ED for chest pain	Chest pain: n=105 Atypical: n=150 Proportion: 58.8% (150/255)	<i>Mortality</i>	<ul style="list-style-type: none"> • Higher mortality rates at 1-month (42.7% vs. 21.0%, $P < 0.001$; AOR NS) <p><i>Heart failure</i></p> <ul style="list-style-type: none"> • Significantly more likely to have Killip class \geqIII (28.0% vs. 10.5%, $P < 0.001$)

		Sample size: n=255				<p><i>Delays</i></p> <ul style="list-style-type: none"> Significantly more ED wait times >1 hr (54.0% vs. 11.4%, $P < 0.001$) and decision-making times >1 hr (54.0% vs. 23.8%, $P < 0.001$) Less likely to have prehospital delays <12 hrs (32% vs. 73.3%, $P < 0.001$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Less likely to receive reperfusion therapy for all measurements of prehospital delay: <12 hrs (54.2% vs. 79.2%, $P = 0.006$); >12 hrs or unknown (34.3% vs. 71.4%, $P < 0.001$); and, regardless of prehospital delay (40.7% vs. 77.1%, $P < 0.001$) In ED, less likely to receive thrombolysis (2.0% vs. 9.5%, $P = 0.016$) or clopidogrel (32.0% vs. 45.7%, $P = 0.036$), and less likely referred to cardiology department (40.7% vs. 89.5%, $P < 0.001$)
Gupta²⁴, 2002	Single centre retrospective cross-sectional study – medical chart review at San Francisco General Hospital California, USA	Patients presenting to hospital ED admitted and diagnosed with AMI July 1, 1993, to June 30, 1998 Sample size: n=721	Chest pain including: any complaint of pain, discomfort, or pressure in the chest, left arm/shoulder, jaw, or neck	Symptoms not including chest pain; list of clinical symptoms	Typical: n=380 Atypical: n=341 Atypical proportion: 47.3% (341/721)	Nil of the interested outcomes reported for atypical cohort
Hadi⁷⁹, 2010	Multicentre Retrospective analysis of prospectively collected patient data from the Gulf Registry of Acute Coronary Events (Gulf RACE) Bahrain, Kuwait, Qatar, Oman, United Arab Emirates, and Yemen	Consecutive patients hospitalised with a final diagnosis of ACS in participating centres (n=65) February, 2007 to June, 2007 Sample size: n=8167	List of clinical symptoms including ‘ischemic-type chest pain’	No definition given; list of clinical symptoms	Ischemic-type chest pain: n=6483 Atypical: n=1771 (<i>Atypical chest pain: n=536</i>) Atypical Proportion: 21.7% (1771/8167)	Nil of the interested outcomes reported for atypical cohort
Hadi Khafaji⁸⁰, 2012	Multicentre Retrospective analysis of prospectively collected patient data from the 2 nd Gulf Registry of Acute Coronary Events (Gulf RACE-2)	Consecutive patients hospitalised with a final diagnosis of ACS in participating hospitals (n=65) October, 2008 to June, 2009 Sample size: n=5334	List of clinical symptoms including ‘typical ischemic chest pain’	No definition given; list of clinical symptoms	Typical ischemic chest pain: n=4470 Atypical: n=658 (<i>Atypical chest pain: n=263</i>) Atypical Proportion: 12.8% (658/5128)	Nil of the interested outcomes reported for atypical cohort

	Bahrain, Kuwait, Qatar, Oman, United Arab Emirates, and Yemen					
Hammer ⁵⁶ , 2019	<p>ACS Israel Survey (ACSIS) – biennial prospective national registry</p> <p>ACSIS is a biennial prospective national registry of all patients with ACS hospitalised in 25 coronary care units and cardiology departments in all general hospitals in Israel, over a 2month period (March to April)</p> <p>Israel</p>	<p>All patients hospitalised and diagnosed with ACS between March to April, and therefore enrolled in the ACSIS registry</p> <p>March to April for years: 2000, 2002, 2004, 2006, 2008, 2010, 2012, 2013, and 2016 (2000-2016)</p> <p>Sample size: n=14722</p>	'Typical chest pain' as primary complaint	Primary complaint other than typical chest pain (dyspnoea; nonspecific chest pain; other; and, palpitations) (cardiac arrest and syncope patients excluded)	<p>Typical chest pain: n=11508</p> <p>Atypical: 3214 (<i>non-specific chest pain: n=1883</i>)</p> <p>Atypical proportion: 21.0% (3214/14722)</p>	<p><i>Mortality (all cause)</i></p> <ul style="list-style-type: none"> Significantly higher mortality at 30-days (ACS: 7.7% vs. 3.6%, $P < 0.001$; STEMI: 11.8% vs. 4.9%, $P < 0.001$; NSTEMI-ACS: 5.6% vs. 2.3%, $P < 0.001$) as well as 1-year, shown via Kaplan-Meier rates (ACS 15.5% vs. 7.5%, $P < 0.001$; STEMI 18.5% vs. 8.2%, $P < 0.001$; NSTEMI-ACS 14.0% vs. 6.8%, $P < 0.001$) Typical chest pain inversely associated with 1-year mortality (aHR 0.73, 95% CI 0.65-0.82) During temporal trends analysis (2000-2006 and 2008-2016), typical patients experienced significant improvement in 1-year mortality in late period (6.2% vs 9%, $P < 0.001$). Atypical presentations showed no improvement in 1-year mortality over time (15.6% for both periods, $P < 0.001$) <p><i>Heart failure and MACE</i></p> <ul style="list-style-type: none"> Higher Killip class (III/IV) on admission (14.9% vs. 3.8%, $P < 0.001$) More likely to experience MACE within 30 days (ACS: 18.0% vs. 13.5%, $P < 0.001$; STEMI: 21.1% vs. 14.6%, $P < 0.001$; NSTEMI-ACS: 16.5% vs. 12.4%, $P < 0.001$) (MACE = Death/UA/MI/CVA/stent thrombosis/urgent revascularisation) <p><i>Delays</i></p> <ul style="list-style-type: none"> Longer symptom onset to FMC times (120 vs. 110 min, $P = 0.01$), and longer time from FMC to first ECG (51 vs. 21 min, $P < 0.001$) <p><i>Diagnosis</i></p> <ul style="list-style-type: none"> Less likely to receive STEMI diagnosis (34% vs. 48%, $P < 0.001$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Longer average times from pain onset to urgent PPCI (487 vs. 329 min, $P < 0.001$) During hospitalisation, less likely to receive PCI (48.6% vs. 64.0%, $P < 0.001$) and coronary angiography (70.8% vs. 83.0%, $P < 0.001$)
Hwang ⁵⁸ , 2009	Single centre Cross-sectional descriptive design medical record review of	Patients treated and diagnosed with first episode of ACS 2005 – 2006	Reported symptoms in the medical record (including those at ED)	Presentation not accompanied by chest pain	<p>Typical: n=841</p> <p>Atypical: n=90</p> <p>Atypical proportion: 9.7% (90/931)</p>	<p><i>Mortality</i></p> <ul style="list-style-type: none"> Significantly higher predicted mortality rates as per GRACE scoring (157.4 vs. 140.5, $P < 0.001$) <p><i>Delays</i></p>

	patients hospitalised at Chonnam National University Hospital South Korea	Sample size: n=931	presentation involving chest pain			<ul style="list-style-type: none"> Experienced longer prehospital delays >6hrs (84.4% vs. 72.1%) and less likely to arrive ≤6hrs (15.6% vs. 27.9%), $P = 0.012$ <p><i>Diagnosis</i></p> <ul style="list-style-type: none"> Less likely to be diagnosed with STEMI (43.3% vs. 59.6%), but more likely to be diagnosed with NSTEMI (21.1% vs. 17.7%) or UA (35.6% vs. 22.7%), $P = 0.007$ <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Experienced higher median hospital stay (Mean (SD): 6.6 (9.4) vs. 4.2 (4.1), $P = 0.022$), and CCU stay (15.6 (14.3) vs. 10.1 (10.4), $P = 0.011$)
Kayhan⁴⁵, 2017	Single centre retrospective medical record review at Eskişehir Osmangazi University Hospital Turkey	Adult patients (≥18 years old) admitted to ED and diagnosed with AMI January 1, to December 31, 2014 Sample size: n=285	No definition given; list of clinical symptoms including chest pain	No definition given; list of clinical symptoms	Chest pain proportion: 58.9% Non-chest pain proportion: 41.1%	Nil of the interested outcomes reported for atypical cohort
Kinsara³⁹, 2021	Multicentre retrospective analysis of prospectively collected patient data from the Saudi Acute Myocardial Infarction Registry (STARS-1) Program (n=50 participating hospitals) Saudi Arabia	Consecutive patients presenting to EDs of participating hospitals and diagnosed with NSTEMI Sample size: n=762	No definition given; list of clinical symptoms including chest pain	No definition given; list of clinical symptoms	Chest pain: n=624 Non-chest pain: n=138 Non-chest pain proportion: 18.1% (138/762)	Nil of the interested outcomes reported for non-chest pain cohort
Lankamali and Lekamge²⁷, 2010	Single centre descriptive cross-sectional study using questionnaires in the National Hospital of Sri Lanka Sri Lanka	Sample of patients diagnosed with ACS admitted to 3 randomly selected medical wards June 15, 2008, to September 15, 2008 Sample size: n=130	Symptoms included chest pain in the centre or left precordium with or without radiation to the left arm and or both sides of the neck or jaw	If presentation accompanied by chest pain in areas other than stipulated under 'typical' or not accompanied by chest pain, patient regarded as presenting with atypical symptoms	Typical Proportion: 61.5% Atypical Proportion: 38.5%	<p><i>Diagnosis</i></p> <ul style="list-style-type: none"> More likely to be diagnosed with STEMI ($P < 0.05$)
Møller⁶⁰, 2021	Multicentre retrospective cohort study utilising emergency and non-emergency medical helpline databases,	All calls made to regional medical helpline (1813) and emergency help number (112) for citizens aged ≥30 years by those who	No definition given; list of clinical symptoms including chest pain	No definition given; list of symptoms beneath banner 'atypical'	Chest pain: n=5219 Atypical: n=1713 Atypical proportion: 23.7% (1713/7222)	<p><i>Mortality</i></p> <ul style="list-style-type: none"> Higher 30-day mortality rates (19.1% vs. 3.9%) <p><i>Delays</i></p> <ul style="list-style-type: none"> Longer time from call to first troponin (median 1.9 vs. 1.4hr)

	as well as National Patient and Death Registries Copenhagen, Denmark	received a hospital diagnosis of MI or MI as cause of death within 72h after call January 31, 2014 to December 31, 2018 Sample size: n=7222 (n=8336 calls identified for n=7778 participants; information on symptom presentation available n=7222 calls)				<p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Proportionately less admitted to cardiology ward during admission (94.2% vs. 98%) Proportionately less admitted directly to cardiology ward (32.2% vs. 52.2%) Proportionately less invasive procedures performed i.e., coronary angiography, CABG or PCI, within 7 days of call (58% vs. 79.8%) Proportionately less PCIs performed within 7 days of call (31.9% vs. 54.2%) Proportionately less coronary angiography performed within 7 days of call (57.6% vs. 79%)
Na⁴², 2014	Multicentre retrospective observational cohort study (n=2 urban tertiary care hospitals) South Korea	Patients presenting to ED with suspected STEMI, and thus, activated the 'critical pathway' treatment plan January 1, 2010 and December 31, 2012 Sample size: n=513	Chief complaints of chest pain, including discomfort, tightness and pressure	No definition given; list of clinical symptoms	Chest pain: n=420 Non-chest pain: n=93 Non-chest pain proportion: 18.1% (93/513)	<p><i>Mortality</i></p> <ul style="list-style-type: none"> Higher in-hospital mortality rates (17.2% vs. 6.0%, $P < 0.001$; AOR 2.3, 95% CI 1.1-4.7) <p><i>Heart failure</i></p> <ul style="list-style-type: none"> Greater severity of HF at presentation, as per Killip class III (22.6% vs. 9.5%, $P < 0.001$) and IV (22.6% vs. 10.5%, $P < 0.001$) <p><i>Delays</i></p> <ul style="list-style-type: none"> Greater delays in symptom onset to ED arrival (4.0 vs. 0.5 hrs, $P = 0.001$) <p><i>Diagnosis</i></p> <ul style="list-style-type: none"> Higher first troponin values (mean (SD): 1.1 (2.2) vs. 0.6 (1.9), $P = 0.035$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Delayed door-to-ECG time (5.0 vs. 2.0 min, $P < 0.001$) 95.7% of chest pain patients obtained ECG ≤ 10 min, vs. 75.3% on non-chest pain patients ($P < 0.001$), and experienced 6-fold likelihood of ECG acquisition time > 10 mins (AOR 6.4, 95% CI 3.1-13.2) Longer delays in myocardial reperfusion (18.0% vs. 4.2%, $P < 0.001$) Significant delays in DTB time (65.0 vs. 57.5 min, $P < 0.001$); four-fold increase in DTB times > 90mins (AOR 4.2, 95% CI 2.0-9.0) Longer hospitalisation (6.0 vs. 5.0 days, $P = 0.020$)
Nakahashi⁴³, 2021	Multicentre retrospective analysis of prospectively collected patient data from the Rural AMI Registry study (n=41)	Patients diagnosed with AMI hospitalised within 7 days from onset January 2013 and March 2014	Any symptoms of chest pain or pressure (chest discomfort)	Specific symptoms of dyspnoea, nausea/vomiting, abdominal pain, or altered mental status	Typical: n=1187 Atypical: n=150 Atypical proportion: 11.2% (150/1337)	<p><i>Mortality</i></p> <ul style="list-style-type: none"> Higher 30-day all-cause mortality (13.3% vs. 2.9%, $P < 0.001$; aHR 2.33, 95% CI 1.20-4.38) <p><i>Heart failure</i></p> <ul style="list-style-type: none"> More likely to have signs of HF (Killip class $> I$: 46.7% vs. 20.5%, $P < 0.001$)

	participating hospitals) Japan	Sample size: n=1337				<p><i>Delays</i></p> <ul style="list-style-type: none"> • More likely to have delayed DTB time >90 min (median 101 vs. 74min, $P < 0.001$; AOR 2.76, 95% CI 1.91-4.02) with fewer achieving DTB time ≤ 90 min (40% vs. 66.3%, $P < 0.001$) <p><i>Diagnosis</i></p> <ul style="list-style-type: none"> • More likely to have multivessel disease (60% vs. 46.8%, $P < 0.05$), and have higher baseline creatinine (mg/dL) levels (median 200 vs. 157, $P < 0.05$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> • Less likely to receive drug-eluting stent (55% vs. 63.4%, $P < 0.05$) • More likely to require the use of an intra-aortic balloon pump (24% vs. 14.8%, $P < 0.05$) and mechanical ventilation (23.3% vs. 6.7%, $P < 0.001$) and temporary pacing (27.3% vs. 14.6%, $P < 0.001$) • At discharge, less likely prescribed statins (78.7% vs. 85.7%; $P < 0.05$) and ACE inhibitors or angiotensin receptor blockers (76.0% vs. 83.4%; $P < 0.05$)
Ng ³², 2020	Multicentre retrospective cohort analysis from All New Zealand Acute Coronary Syndrome Quality Improvement (ANZACS-QI) registry Midlands Region public hospitals, New Zealand	Long term renal dialysis patients diagnosed with index ACS January 1, 2010 to December 31, 2019 Sample size: n=102	At least two features of: (i) central chest pain; (ii) radiation to arm or neck; (iii) diaphoresis; (iv) associated with exertion or if it was documented to be “cardiac-sounding”	No definition given; list of symptoms beneath banner ‘atypical’	Typical: n=66 Atypical: n=27 Atypical proportion: 26.5% (27/102) 6.9% (n=7) presented in VF/VT arrest, though was not categorised as either typical or atypical by authors	<p><i>Mortality</i></p> <ul style="list-style-type: none"> • Atypical presentation independently associated with mortality at 1-year ($P = 0.0071$)
Oliveira ⁴⁰, 2023	Single centre retrospective medical record review at the Hospital de Braga Portugal	All patients diagnosed with STEMI who underwent primary PCI January 2013 and May 2016 Sample size: n=809	No definition given; list of clinical symptoms including chest pain	No definition given; list of clinical symptoms	Chest pain: n=762 Non-chest pain: n=43 Non-chest pain proportion: 5.3% (43/809)	Nil of the interested outcomes reported for non-chest pain cohort
Ouellet ⁵², 2017	Cross-sectional analysis from multicentre prospective cohort study: ComprehenSIVe Evaluation of Risk	First 2,500 individuals enrolled in SILVERAMI (≥ 75 years old) hospitalised for AMI Sample size: n=2500	Chest pain, chest discomfort	Any constellation of symptoms that did not include chest pain or chest discomfort	Typical: n=1965 Atypical: n=535 Atypical proportion: 21.4% (535/2500)	<p><i>Delays</i></p> <ul style="list-style-type: none"> • Longer prehospital delay (AOR 1.41; 95% CI 1.15–1.72) • Prehospital delays of ≥ 6 hrs more frequent (25%), than delays < 6 hrs (18.9%, $P < 0.05$ for between-group difference)

	Factors in Older Patients with Acute Myocardial Infarction (SILVER-AMI). Academic and community hospitals (n=94) USA					<ul style="list-style-type: none"> Significantly less likely to correctly ascribe symptoms to cardiac aetiology (26.6% vs. 56.4%, $P < 0.001$)
Pong³⁴, 2019	Multicentre retrospective data from Singapore Myocardial Infarction Registry (SMIR) Singapore	All cases of STEMI recorded in SMIR January, 2010 to December, 2012 Sample size: n=4667	Typical chest pain lasting ≥ 20 min	No definition given; list of clinical symptoms	Typical: n=4064 Atypical: n=603 Atypical proportion: 12.9% (603/4667)	<p><i>Mortality</i></p> <ul style="list-style-type: none"> Significantly higher 28-day mortality rates (31.2% vs. 4.5%, $P < 0.001$; AOR 3.46, 95% CI 2.64-4.52) <p><i>Heart failure and MACE</i></p> <ul style="list-style-type: none"> Significantly higher Killip class on presentation (atypical vs. typical), $P < 0.001$: I) 62.9% vs. 84.3%, AOR 1.00 (reference) II) 12.8% vs. 6.7%; AOR 1.53, 95% CI 1.08–2.16 III) 12.1% vs. 4.3%; AOR 2.41, 95% CI 1.69–3.43 IV) 12.3% vs. 4.8%; AOR 2.50, 95% CI 1.74–3.59 Significantly higher in-hospital events, including: complete heart block (4.6% vs. 2.7%, $P = 0.006$), cardiac arrhythmia (24.5% vs. 20.7%, $p=0.025$), acute renal failure (13.4% vs. 3.7%, $P < 0.001$), LV systolic dysfunction (73.7% vs. 61.7%, $P < 0.001$) <p><i>Delays</i></p> <ul style="list-style-type: none"> Shorter symptom-to-door timing (102 vs. 148 min, $P < 0.001$) <p><i>Diagnosis</i></p> <ul style="list-style-type: none"> More likely to have anterior STEMI (57.5% vs. 51.7%, $P = 0.008$; AOR NS), lateral STEMI (39.5% vs. 35.0%, $P = 0.033$; AOR NS), and LBBB (1.2% vs. 0.2%, $P < 0.001$; AOR NS) on ECG Greater increase in cardiac enzymes (peak troponin T in $\mu\text{g/L} = 1.3$ vs. 3.8, $p < 0.001$; mean CK-MB in $\mu\text{g/L} = 15.4$ vs. 70.5, $P < 0.001$); lower haemoglobin (median haemoglobin in g/dL = 12.9 vs. 14.6, $p < 0.001$), worse renal function (median creatinine in $\mu\text{mol/L} = 109.0$ vs. 87.0, $p < 0.001$) <p><i>Medical interventions</i></p> <ul style="list-style-type: none"> Significantly less likely to undergo PPCI (27.0% vs. 75.6%, $P < 0.001$), receive antiplatelet therapy (96.4% vs. 99.6%, $P < 0.001$), or aspirin within 24 hrs (98.2% vs. 99.9%, $P < 0.001$) despite no contraindications Of those who received PPCI, atypical patients experienced greater DTB time (83 vs. 63 min, $P < 0.001$) and less likely to have DTB time ≤ 60 min (22.1% vs.

						44.8%, $P < 0.001$). Trend remained when expanded to ≤ 90 min (60.1% vs. 79.7%, $P < 0.001$) <ul style="list-style-type: none"> Higher likelihood of DTB time > 60 min (AOR 2.37, 95% CI 1.59-3.53)
Rallidis³⁵, 2015	Patient interviews with questionnaires from Coronary Care Units of 2 large hospitals: University General Hospital Attikon in Athens and General Hospital of Nikea Piraeus, Greece	Consecutive patients ≤ 35 years who survived their first STEMI 1996 to 2014 Sample size: n=256	History of typical chest pain lasting > 30 min	Presentation not typical (i.e. atypical chest pain)	Typical chest pain: n=207 Atypical: n=49 (<i>Atypical chest pain: n=28</i>) Proportion of atypical: 19.1% (49/256)	Nil of the interested outcomes reported for atypical cohort
Roque³⁶, 2020	Retrospective observational study of Portuguese Registry of Acute Coronary Syndromes (ProACS) Portugal	Adult patients enrolled into ProACS registry with ACS diagnosis < 48 hrs duration (excluding MI types 2, 4 and 5) Three periods studied: 2002-2010, 2011-2015, and 2016-2019 Sample size: n=49113	No definition given; list of clinical symptoms including chest pain	No definition given; list of clinical symptoms	Typical: n=47285 Atypical: n=1828 Atypical proportion: 3.92% (1828/46621)	Nil of the interested outcomes reported for atypical cohort
Rosell-Ortiz²⁵, 2015	Retrospective observational study including EMS database and hospital medical record review Andalusia – Spain	Patients entered in register attended by out-of-hospital emergency teams January, 2006 to June, 2009 Sample size: n=2528	Central chest pain > 20 min, with or without accompanying vegetative symptoms (nausea, vomiting, sweating) and/or radiation to the jaw, left shoulder or arm	Chest pain not the predominant symptom	Typical: n=2118 Atypical: n=410 (<i>Atypical chest pain n=87</i>) Atypical proportion: 16.2% (410/2528)	<i>Mortality</i> <ul style="list-style-type: none"> More likely to die before reaching hospital (AOR 2.31, 95% CI 1.21-4.41) Of all patients who survived to hospital, 15.5% (384/2476) presented atypically. Of those who did not reach hospital alive, half (26/52) were atypical ($P < 0.001$)
Taylor⁴¹, 2022	Retrospective cohort study of consecutive patients with out-of-hospital 12-lead ECG recorded by Los Angeles Fire Department (LAFD) Los Angeles, USA	July 2011 to June 2012 Sample size: n=586	Patient presentation with chest pain, cardiac arrest, and cardiac symptoms per paramedic documentation (i.e., suspicion of cardiac aetiology)	All other patient complaints classified as "atypical"	Typical: n=469 (<i>Chest pain: n=354; cardiac arrest: n=72; cardiac symptoms: n=43</i>) Atypical: n=117 Atypical proportion: 20% (117/586)	
Tisminetzky⁵⁹, 2020	Multicentre retrospective observational study using medical record review from teaching and community	Patients presenting with first AMI 2001 to 2011 Sample size: n=2586	Patient reports of chest pain, chest pressure, chest tightness, chest discomfort, or substernal chest pain	All other symptoms of AMI (e.g., left arm pain, cough, shortness of breath, jaw pain) considered atypical	Typical: n=1861 Atypical: n=725 Atypical proportion: 28% (725/2586)	'There was a slightly increased risk of prehospital delay in those with atypical symptoms of AMI across the different age groups, with the highest risk noted in patients 85 years and older' (but I can't see that any of these are significant) <55: Referent

	hospitals in Worcester (n=11) Massachusetts, USA					55-64: AOR 1.48 (95% CI 0.72-3.03) 65-74: AOR 1.25 (95% CI 0.64-2.44) 75-84: AOR 1.63 (95% CI 0.87-3.06) >85: AOR 1.71 (95% CI 0.90-3.26)
Woon⁵³, 2003	Single centre retrospective observational study using medical record review at Changi General Hospital Singapore	Patients with discharge or death diagnosis of AMI January, 1999 to July, 1999 Sample size: n=213	Presenting symptoms of chest pain	All non-chest pain symptoms. Asymptomatic classified as 'silent'	Typical: n=167 Atypical: n=46 Atypical proportion: 21.6% (46/213)	Nil of the interested outcomes reported for atypical cohort
Wu⁴⁴, 2012	Single centre retrospective observational study using medical record review Taiwan	Patients presenting to ED and diagnosed with STEMI 2006 to 2009 Sample size: n=260	No definition given; list of clinical symptoms including chest pain	List of clinical symptoms	Chest pain: n=227 Non-chest pain: n=33 Atypical proportion: 12.7% (33/260)	<i>Mortality</i> <ul style="list-style-type: none"> Significantly higher 30-day mortality (30.3% vs. 9.7%, $P = 0.003$) <i>Heart failure</i> <ul style="list-style-type: none"> Higher rates of HF upon presentation (categorised by Killip class IV, 54.5% v 23.9%, $P < 0.001$) <i>Medical interventions</i> <ul style="list-style-type: none"> Significantly higher proportion did not receive catheterisation (PPCI) (30.3% vs. 6.2%, $P < 0.001$)

[§]only statistically significant findings reported

ACS – acute coronary syndrome; ACEI – angiotensin-converting enzyme inhibitor; AMI – acute myocardial infarction; AOR – adjusted odds ratio; CABG – coronary artery bypass grafting; CCU - coronary care unit; CK-MB – creatinine kinase myocardial band; CT – computerised tomography; DTB – door-to-balloon; ECG – electrocardiogram; ED – emergency department; FMC – first medical contact; GTN – glyceryl trinitrate; HF – heart failure; ICU – intensive care unit; LBBB – left bundle branch block; LMWH – low molecular weight heparin; LVEF – left ventricular ejection fraction; MACE – major adverse cardiovascular events; NSTEMI – non-ST elevation acute coronary syndrome; NSTEMI – non-ST elevation myocardial infarction; PPCI – Primary percutaneous intervention; SOB – shortness of breath; STEMI – ST elevation myocardial infarction; TIMI – thrombolysis in myocardial infarction; UA – unstable angina

Supplementary Table 4: Methodological quality appraisal

Quantitative non-randomised studies

Reference	Item 1	Item 2	Item 3	Item 4	Item 5	Score
<i>Ahmad et al.</i> ⁵⁰ , 2016	Yes	Yes	Yes	No	No	3/5
<i>Andell et al.</i> ³⁸ , 2014	Yes	Yes	Yes	Yes	Yes	5/5
<i>Bianco et al.</i> ²⁹ , 2022	Yes	Yes	Yes	Yes	Yes	5/5
<i>Borden et al.</i> ⁴⁸ , 2012	Yes	Yes	Yes	Yes	Yes	5/5
<i>Brieger et al.</i> ¹¹ , 2004	Yes	Yes	Yes	Yes	Yes	5/5
<i>Canto et al.</i> ⁹ , 2002	Yes	Yes	Yes	Yes	Yes	5/5
<i>Chien et al.</i> ⁴⁶ , 2016	Yes	Yes	Yes	Yes	Yes	5/5
<i>Chien et al.</i> ⁴⁷ , 2019	Yes	Yes	Yes	Yes	Yes	5/5
<i>Coronado et al.</i> ³⁰ , 2004	Yes	Yes	Yes	Yes	Yes	5/5
<i>Coventry et al.</i> ³³ , 2015	Yes	Yes	Yes	Yes	Yes	5/5
<i>Dell'Orto et al.</i> ⁵¹ , 2017	Yes	Unclear	Yes	No	No	2/5
<i>Dey et al.</i> ⁴⁹ , 2009	Yes	Yes	Yes	Yes	Yes	5/5
<i>Dorsch et al.</i> ⁵⁴ , 2001	Yes	Yes	Yes	Yes	Yes	5/5
<i>El-Menyar et al.</i> ⁵⁷ , 2009	Yes	Yes	Yes	Yes	Yes	5/5
<i>El-Menyar et al.</i> ²⁶ , 2011	Yes	Yes	Yes	Yes	Yes	5/5
<i>Fujino et al.</i> ²⁸ , 2017	Yes	Yes	Yes	Yes	Yes	5/5
<i>Gajanan et al.</i> ³¹ , 2015	Unclear	No	No	No	No	0/5
<i>Goel et al.</i> ⁵⁵ , 2012	Yes	Yes	Yes	No	No	3/5
<i>Grosmaître et al.</i> ³⁷ , 2013	Yes	Yes	Yes	Yes	Yes	5/5
<i>Gupta et al.</i> ²⁴ , 2002	Yes	Yes	Yes	Yes	Yes	5/5
<i>Hadi et al.</i> ⁷⁹ , 2010	Yes	Yes	Yes	Yes	Yes	5/5
<i>Hadi Khafaji et al.</i> ⁸⁰ , 2012	Yes	Yes	Yes	Yes	Yes	5/5
<i>Hammer et al.</i> ⁵⁶ , 2019	Yes	Yes	Yes	Yes	Yes	5/5
<i>Hwang et al.</i> ⁵⁸ , 2009	Yes	Yes	Yes	Yes	Yes	5/5
<i>Kayhan et al.</i> ⁴⁵ , 2017	Yes	Yes	Yes	No	No	3/5
<i>Kinsara et al.</i> ³⁹ , 2021	Yes	Yes	Yes	No	No	3/5
<i>Lankamali and Lekamge.</i> ²⁷ , 2010	Yes	Yes	Yes	No	No	3/5
<i>Møller et al.</i> ⁶⁰ , 2021	Yes	Yes	Yes	Yes	Yes	5/5
<i>Na et al.</i> ⁴² , 2014	Yes	Yes	Yes	Yes	Yes	5/5
<i>Nakahashi et al.</i> ⁴³ , 2021	Yes	Yes	Yes	Yes	Yes	5/5
<i>Ng et al.</i> ³² , 2020	Yes	Yes	Yes	No	No	3/5
<i>Oliveira et al.</i> ⁴⁰ , 2023	Yes	Yes	Yes	Yes	Yes	5/5
<i>Ouellet et al.</i> ⁵² , 2017	Yes	Yes	Yes	Yes	Yes	5/5
<i>Pong et al.</i> ³⁴ , 2019	Yes	Yes	Yes	Yes	Yes	5/5
<i>Rallidis et al.</i> ³⁵ , 2015	Yes	Yes	Yes	No	No	3/5
<i>Roque et al.</i> ³⁶ , 2020	Yes	Yes	Yes	Yes	Yes	5/5
<i>Rosell-Ortiz et al.</i> ²⁵ , 2015	Yes	Yes	Yes	Yes	Yes	5/5
<i>Taylor et al.</i> ⁴¹ , 2022	Yes	Yes	Yes	Yes	Yes	5/5
<i>Tisminetzky et al.</i> ⁵⁹ , 2020	Yes	Yes	Yes	Yes	Yes	5/5
<i>Woon et al.</i> ⁵³ , 2003	Yes	Yes	Yes	Yes	Yes	5/5
<i>Wu et al.</i> ⁴⁴ , 2012	Yes	Yes	Yes	Yes	Yes	5/5

Item 1: Are the participants representative of the target population?

Item 2: Are measurements appropriate regarding both the outcome and intervention (or exposure)?

Item 3: Are there complete outcome data?

Item 4: Are the confounders accounted for in the design and analysis?

Item 5: During the study period, is the intervention administered (or exposure occurred) as intended?

References

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80. Hadi Khafaji HA, Al Habib K, Asaad N, et al. Marital status and outcome of patients presenting with acute coronary syndrome: an observational report. *Clin Cardiol* 2012;35:741–8. <https://doi.org/10.1002/clc.22034>; PMID: [22740441](https://pubmed.ncbi.nlm.nih.gov/22740441/).

Supplementary Table 5: Proportion of symptoms from atypical chest pain/anginal equivalent presentations.

Author	Patient Population	Dyspnoea	Nausea Vomiting	Dizzy	Syncope	Fatigue or weakness	Diaphoresis	Palpitations	Atypical Chest Pain	Abdominal Pain	Epigastric Pain	Back pain	Miscellaneous
Ahmad et al. ⁵⁰	ACS	45.6%	Vomiting 23.5%		11.8%	Weakness 19.1%							
Andell et al. ³⁸	AMI	45.8%											Cardiac arrest 6.2%; other 48.1%
Bianco et al. ²⁹	STEMI	16.5%			11.3%				72%				
Borden et al. ⁴⁸	STEMI			Dizzy 26.7% Lightheaded 20.0%		Fatigue 40.0% Weakness 60.0% Lethargy 13.3%	Sweat 6.7%			26.7%			Hot/cold sensations 20.0%; paraesthesia 20.0%; Diarrhoea 13.3%; Cough 6.7%; hiccups 6.7%; headache 6.7%; choking sensation 6.7%; restless 6.7%
Brieger et al. ¹¹	ACS	49.3%	N or V 24.3%		(Pre)syncope 19.1%		26.2%						
Canto et al. ⁹	UA	69.4%	Nausea 37.7% Vomiting 11.4%		10.6%		25.2%		14.4%		(8.1%)		Cardiac arrest 1.0%; impending doom 0.6%; Discomfort other than chest 27.4% (arm 11.5%; epigastric 8.1%; shoulder 7.4%; neck 5.9%; jaw 1.6%; face 0.9%; ear 0.1%)
Chien et al. ⁴⁶	AMI	45.3%	Nausea/vomiting/dizziness 17.9%		Syncope/confusion/coma 15.8%	Fatigue/cold sweat 12.6%				8.4%			
Chien et al. ⁴⁷	NSTEMI (subset of above)	49.3%	Nausea/vomiting/dizziness 16.4%		Syncope/collapse 16.4%	Fatigue/diaphoresis 11%				6.8%			
Coronado et al. ³⁰	ACS	72.0%		8.2%	8.9%								Others 11.0%
Coventry et al. ³³	AMI	44.4%	Nausea 13.1% Vomiting 9.1%	12.1%	Syncope/collapse/LOC 22.2%	Fatigue/lethargy 10.1% Weakness 10.1%	Sweaty/clammy 7.1%			11.1%		3.0%	Left arm 5.1%; jaw, throat or neck pain 4.1%; confusion 18.1%; fall 14.1%; unwell 11.1%
Dell'Orto et al. ⁵¹	STEMI	50%	Nausea 17.6%	5.9%	Syncope/collapse 26.5%								
Dey et al. ⁴⁹	AMI	41.5%	N or V 25.8%		(Pre)syncope 21.4%		27.9%	4.9%					Jaw pain 6.1%
Dorsch et al. ⁵⁴	AMI	31.8%	N or V 2.1%		Collapse 16.2%		Perspire 2.4%						Upper body discomfort other than chest pain 13.1%; cardiac arrest 10.5%; generally unwell 14.0%; neuropsychiatric 5.9%; perioperative 4.0%
El-Menyar et al. ⁵⁷	ACS	59.8%							40.2%				
El-Menyar et al. ²⁶	ACS	62.6%							37.4%				Of total population (n=6704): those presenting differently (n=284) namely, LOC (1.1%), palpitation (1.1%), others (2%) (i.e., malaise, easy fatigability, or epigastric discomfort) excluded from article's analysis.

Fujino et al. ²⁸	AMI	25.9%	N or V 15.6%		19.3%					30.7%				Others 7.9%; asymptomatic 1.6%	
Gajanan et al. ³¹	STEMI	31.5%		Lightheaded 19.2%			21.3%	Sweat 22.8%				Stomach 5.2%			
Goel et al. ⁵⁵	STEMI	53.5%	N or V 11.1%										16.2%	Arm, wrist or jaw pain 15.2%; others ('including syncope') 4.0%	
Grosmaître et al. ³⁷	STEMI	26.7%	Digestive Sx/nausea 16.7%		Faint/fall 26.7%									Delirium/impaired vigilance 8.7%; impaired general condition 11.3%; others 10.0%	
Gupta et al. ²⁴	AMI	35.5%	N or V 1.8%	Dizziness/weakness/syncope 9.4%								4.1%		'Chief complaint': Cardiac arrest 14.7%; altered mental status 5.9%; trauma 5.9%; gastrointestinal bleed 2.1%; others 17.9%	
Hadi et al. ⁷⁹	ACS	45.2%			LOC 9.7%				4.7%	30.2%				Others 10.1%	
Hadi et al. ⁸⁰	ACS	60%								40%					
Hammer et al. ⁵⁶	ACS	28.1%							4.7%	Nonspecific 58.6%				Others 23.3%	
Hwang et al. ⁵⁸	ACS	36.7%			8.9%	8.9%						20.0%	4.4%	Indigestion 18.9% Diarrhoea 2.2%	
Kayhan et al. ⁴⁵	AMI	16.2%	Nausea 6.0% Vomiting 0.9%		6.8%			6.0%		Retrosternal burning 20.5%			17.1%	10.3%	Left arm pain 10.3%; distress 2.6%; headache 0.9%; shoulder pain 0.9%; right arm pain 0.9%; jaw pain 0.9%
Kinsara et al. ³⁹	NSTEMI	Dyspnoea/fatigue 65.9%					(Reported with dyspnoea)						Epigastric/shoulder/back/neck pain 22.5%	Cardiac arrest 2.2%; others 9.4%	
Lankamali and Lekamge ²⁷	ACS	44.0%		16.0%									11.0%	5.0%	
Møller et al. ⁶⁰	AMI	Breathing problems 32.5%			(*Other cardiac problem 8.1%)				*Other cardiac problem 8.1%		Abdominal/back/urinary problem 8.9%		(Reported with abdominal)	Central nervous system symptoms (including vertigo, headache, and impaired consciousness) 11.3%; other atypical symptoms; 19.9%; unclear 19.3%	
Na et al. ⁴²	STEMI	27.9%	N or V 4.3%	5.4%	14%	Weakness 4.3%						9.7%	19.4%	Mental change 7.5%; others 8.7%	
Nakahashi et al. ⁴³	AMI	28.7%	N or V 14.7%									4%		8%	Altered mental status 14.7%; others 30%
Ng et al. ³²	ACS	40.7%		14.8%							Pleuritic 11.1%				Musculoskeletal 7.4%; gastrointestinal upset 11.1%; other 14.8%; unclear 7.4%
Oliveira et al. ⁴⁰	STEMI	11.6%	Nausea 4.7%		9.3%								27.9%		Cardiac arrest 46.5%
Ouellet et al. ⁵²	AMI	49.1%	Nausea 18.9%			31.5%									Shoulder or arm pain 29.3%; indigestion 20.3%
Pong et al. ³⁴	STEMI	53.4%			6.0%			24.0%					10.6%	4.5%	Shoulder pain 2.2%; jaw pain 0.8%
Rallidis et al. ³⁵	STEMI				4.1%	Weakness 12.2%			2.0%	57.1%					Gastrointestinal symptoms 20.4%; focal neurological deficit 4.1%
Roque et al. ³⁶	ACS	46.7%			18.2%	Fatigue 7.1%									Cardiac arrest 6.0%; Others 21.9%
Rosell-Ortiz et al. ²⁵	STEMI	19.0%		5.9%	22.4%					21.2%					Unconsciousness 18.7%; non- specific malaise 12.7%

Taylor et al. 41	STEMI	29.1%	Nausea 6.8% Vomiting 1.7%	2.6%	Altered consciousness 20.5% Syncope 9.4%	Weakness 12.8%				5.1%		1.7%	Others (including: fever, seizure, CVA/stroke, headache, respiratory arrest/failure, gastrointestinal-bleed, anxiety, and unknown) 12%
Tisminetzky et al. 59	AMI	39.5%			9.5%	W/F 10.8%				5.8%			Others 34.5%
Woon et al. 53	AMI	56.3%	Nausea 6.3%		6.3%						10.4%		Confusion 6.3%; CVA 10.4%; asymptomatic 4.2%
Wu et al. 44	STEMI	36.4%	n or v 15.2%	3.0%	36.4%	Weakness 15.2%	Cold sweat 15.2%				27.3%	6.1%	
Total studies		39/41	21/41	12/41	29/41	15/41	12/41	5/41	12/41	12/41	10/41	10/41	

#'other atypical symptoms': trauma/exposure, infection/fever, musculoskeletal, complication of known disease, medication/prescription, psychiatry/abuse, bleeding, cramps, home visits, ear-nose-throat, skin, eyes, complication after treatment

*'Other cardiac' included: palpitations, pacemaker problems, and fainting

ACS – acute coronary syndrome; AMI – acute myocardial infarction; CVA – cerebrovascular accident; **LOC – loss of consciousness**; STEMI – ST elevation myocardial infarction; UA – unstable angina

Most common symptom per study in bold. Some studies report main presenting problem (mutually exclusive) others report all symptoms present across cohort with some having multiple symptoms in the one episode (see *Supplementary Table 2*).

Supplementary Table 6: Symptoms reported by each article

<i>Author</i>	<i>Symptoms reported</i>
Ahmad et al. ⁵⁰	(Chest pain); shortness of breath; syncope; vomiting; weakness alone. Mutually exclusive
Andell et al. ³⁸	(Chest pain); cardiac arrest; dyspnoea; other. Mutually exclusive
Bianco et al. ²⁹	(Chest pain); atypical chest pain; dyspnoea; syncope. Mutually exclusive
Borden et al. ⁴⁸	Abdominal pain; choking sensation; cough; diarrhoea; dizziness; fatigue; headache; hiccups; hot/cold sensations; lethargy; light-headedness; paraesthesia; restless; sweating; weakness. Not mutually exclusive
Brieger et al. ¹¹	Diaphoresis; dyspnoea; nausea and vomiting; syncope. Not mutually exclusive
Canto et al. ⁹	Atypical chest pain or discomfort; discomfort in other region: arm, epigastric region, shoulder, neck, jaw, face, ear; cardiac arrest; diaphoresis; dyspnoea; impending doom; nausea; syncope; vomiting. Not mutually exclusive
Chien et al. ⁴⁶	(Chest pain); abdominal pain; fatigue or cold sweating; nausea or vomiting or dizziness; short of breath; syncope or confusion or coma. Mutually exclusive
Chien et al. ⁴⁷	(Chest pain, chest tightness, or any chest discomfort); abdominal pain; fatigue or diaphoresis; nausea, vomiting, or dizziness; shortness of breath; syncope or collapse. Mutually exclusive
Coronado et al. ³⁰	(Chest pain); dizziness; dyspnoea; other; syncope. Mutually exclusive
Coventry et al. ³³	Abdomen or epigastric pain; back pain; confusion; dizziness; fall; fatigue or lethargy; jaw, throat or neck pain; left arm pain; nausea; shortness of breath; syncope, collapse or unconscious; sweaty & clammy; unwell; weakness; vomiting. Not mutually exclusive
Dell'Orto et al. ⁵¹	Acute hypertension; atypical chest pain; collapse/syncope; dizziness; dyspnoea; nausea; palpitations. Mutually exclusive.
Dey et al. ⁴⁹	Diaphoresis; dyspnoea; jaw pain; nausea or vomiting; palpitations; (pre)syncope. Not mutually exclusive
Dorsch et al. ⁵⁴	cardiac arrest; collapse; nausea/vomiting; neuropsychiatric presentation; non-specifically unwell; perioperative; perspiration; shortness of breath; upper body discomfort other than chest pain. Mutually exclusive
El-Menyar et al. ⁵⁷	(Ischemic chest pain); atypical chest pain, dyspnoea. Mutually exclusive
El-Menyar et al. ²⁶	(Typical pain); atypical pain; dyspnoea. Mutually exclusive
Fujino et al. ²⁸	Chest discomfort; dyspnoea; nausea or vomiting; others; syncope. Mutually exclusive
Gajanan et al. ³¹	Dyspnoea ; fatigue/weakness; light headedness; shortness of breath , stomach pain; sweating. Mutually exclusive
Goel et al. ⁵⁵	(Chest pain with or without other symptoms); dyspnoea; epigastric pain; nausea/vomiting; others; pain in arm/wrist/jaw. Mutually exclusive
Grosmaître et al. ³⁷	(Chest pain); delirium and/or impaired vigilance; digestive symptoms/nausea; dyspnoea; impaired general condition; faintness and/or fall; others. Mutually exclusive
Gupta et al. ²⁴	(Chest pain); abdominal pain; cardiac arrest; dizziness/weakness/syncope; other; shortness of breath. Mutually exclusive

<i>Hadi et al.</i> ⁷⁹	(Ischemic-type chest pain); atypical chest pain; dyspnoea; loss of consciousness; others; palpitation. Mutually exclusive
<i>Hadi Khafaji et al.</i> ⁸⁰	(Typical ischemic chest pain); atypical chest pain, dyspnoea. Mutually exclusive
<i>Hammer et al.</i> ⁵⁶	(Typical chest pain); dyspnoea; nonspecific chest pain; other; palpitations. Mutually exclusive
<i>Hwang et al.</i> ⁵⁸	Abdominal pain; back pain; diarrhoea; dyspnoea; general weakness; indigestion; syncope. Mutually exclusive
<i>Kayhan et al.</i> ⁴⁵	(Chest pain); retrosternal burning; epigastric pain; dyspnoea; left arm pain; back pain; syncope; diaphoresis; nausea; distress; headache; shoulder pain; right arm pain; vomiting; jaw pain. Mutually exclusive
<i>Kinsara et al.</i> ³⁹	(Chest pain); cardiac arrest; epigastric/shoulder/back/neck pain; others; shortness of breath/fatigue. Mutually exclusive
<i>Lankamali and Lekamge</i> ²⁷	(Chest pain); back pain; dizziness; epigastric pain; shortness of breath. Mutually exclusive.
<i>Møller et al.</i> ⁶⁰	(Chest pain; no recorded symptoms; non-informative symptoms; unconscious); abdominal/back/urinary; breathing problems; CNS symptoms; other cardiac symptoms; unclear problem. Mutually exclusive.
<i>Na et al.</i> ⁴²	(Chest pain); abdominal pain; dizziness; nausea/vomiting; dyspnoea; mental change; others; syncope; weakness. Mutually exclusive
<i>Nakahashi et al.</i> ⁴³	(Chest pain); altered mental status; abdominal pain; back pain; dyspnoea; nausea/vomiting; other. Mutually exclusive
<i>Ng et al.</i> ³²	Dizziness/syncope; dyspnoea; gastrointestinal upset; musculoskeletal; pleuritic; other; unclear; VF/VT arrest. Mutually exclusive
<i>Oliveira et al.</i> ⁴⁰	(Chest pain); cardiac arrest; dyspnoea; epigastric pain; nausea; syncope. Mutually exclusive
<i>Ouellet et al.</i> ⁵²	Indigestion; nausea; shoulder or arm pain; shortness of breath; weakness or fatigue. Not mutually exclusive
<i>Pong et al.</i> ³⁴	Back pain; diaphoresis; dyspnoea; epigastric pain; jaw pain; shoulder pain; syncope. Mutually exclusive
<i>Rallidis et al.</i> ³⁵	Atypical chest pain; focal neurological deficits; gastrointestinal symptoms; palpitations; profuse weakness; syncope. Mutually exclusive
<i>Roque et al.</i> ³⁶	(Chest pain); cardiac arrest; dyspnoea; fatigue; other; syncope. Mutually exclusive
<i>Rosell-Ortiz et al.</i> ²⁵	Atypical chest pain; dizziness; dyspnoea; syncope; non-specific malaise; unconscious. Mutually exclusive
<i>Taylor et al.</i> ⁴¹	(Cardiac arrest; cardiac symptoms; chest pain); abdominal pain; altered level of consciousness; back pain; dizziness; dyspnoea/shortness of breath; nausea; syncope/fainting; other; vomiting; weakness
<i>Tisminetzky et al.</i> ⁵⁹	(Chest pain); abdominal pain; shortness of breath; syncope; weakness/fatigue. Chief complaint. Mutually exclusive
<i>Woon et al.</i> ⁵³	(Chest pain); asymptomatic – silent; confusion; epigastric pain; nausea; shortness of breath; stroke; syncope. Mutually exclusive
<i>Wu et al.</i> ⁴⁴	Back pain; cold sweating; dizziness; dyspnoea; epigastric pain; nausea or vomiting; syncope; weakness. Not mutually exclusive

Note: Those appearing in brackets were not included in the atypical symptom reporting of this review

Supplementary Table 7: Risk factors for atypical chest pain/anginal equivalent ACS presentation, n=28 studies

Risk factor (n studies reporting on this variable)	Positive association (unadjusted)	Positive association (adjusted)	Negative association (unadjusted)	Negative association (adjusted)	No association [^]
Demographic data					
Advanced age (n=22)	11,28,42,43,46,56	9,24,30,34,41,44,47,53,54,58,59			26,27,29,37,48
Ethnicity (n=3)	34	41			9
Female sex (n=22)	11,28,34,36,37,42,44,56,57	24,26,29,54			9,27,30,33,41,43,47,48,58
Marital status (n=1)	Widowed ⁸⁰				
Nursing home (n=1)	37				
Co-morbid conditions					
Alcohol consumption (n=2)					27,29
Anaemia (n=1)	43				
COPD (n=3)	38,79				9
Dementia/age-related cognitive or communication impairment (n=2)	37	9			
Depression (n=1)					9
Diabetes (n=18)	11,28,56	26,29,34,44			9,27,30,33,37,42,43,47,48,54,58
Family history of IHD/CAD (n= 6)	27		33,56	9	26,48
Hypercholesteraemia (n= 3)				9	42,48
Hyper/dyslipidaemia (n= 11)			11,43,56,58	29,34	26,28,33,47,48
Hypertension (n=13)	11,28,34,56				9,29,30,33,42,43,47,48,58
Obesity (n=5)				29,34	26,42,56
Renal Failure/CKD (n= 9)	28,42,43,56	26,29,34			9,48
Smoker (n=14)			11,28,34,42,44,56	26	9,27,29,43,47,48,58
Previous medical events					
Previous angina (n=1)					33
Previous CABG (n=9)	28,48,56				9,11,33,34,42,48
Previous CVA/TIA/cerebrovascular disease (n=10)	28,33,42,56	44,47			9,29,43,48
Previous HF (n=9)	11,42,54,56	30		26	33,47,48
Previous IHD/CAD/CVD (n=7)	28			26,47	33,37,42,48
Previous MI (n=12)	28,34	29	43	9	11,30,33,42,47,48,56
Previous PCI (n=8)	28		11,34		9,33,42,43,48
Previous PVD (n=5)	28				9,29,43,48

[^] tested at univariate/multivariate analyses but no statistical significance found