BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

Clinical presentation in EMS patients with acute chest pain based on sex, age and medical history – prospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-054622
Article Type:	Original research
Date Submitted by the Author:	21-Jun-2021
Complete List of Authors:	Wibring, Kristoffer; University of Gothenburg; Halland County, 1Department of Ambulance and Prehospital Care Lingman, Markus; University of Gothenburg, Department of Molecular; Halland County, Halland hospital Herlitz, Johan; University of Borås Pettersson, Helena; Halland County, Department of Ambulance and Prehospital Care Lerjebo, Anette; Halland County, Department of Ambulance and Prehospital Care Bång , Angela; University of Gothenburg
Keywords:	ACCIDENT & EMERGENCY MEDICINE, Myocardial infarction < CARDIOLOGY, General diabetes < DIABETES & ENDOCRINOLOGY, Cardiology < INTERNAL MEDICINE

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Clinical presentation in EMS patients with acute chest pain based on sex, age and medical history – prospective cohort study

Authors
Kristoffer Wibring[1, 2] kristoffer.wibring@gu.se
Markus Lingman[3, 4] markus.lingman@regionhalland.se
Johan Herlitz[5] johan.herlitz@hb.se
Helena Pettersson[1] helena.pettersson@regionhalland.se
Anette Lerjebo[1] anette.lerjebo@regionhalland.se
Angela Bång[2] angela.bang@gu.se

1. Department of Ambulance and Prehospital Care, Region Halland, Sweden
2. Institute of Health and Care Sciences, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden
3. Department of Molecular and Clinical Medicine/Cardiology, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden
4. Department of Development, Halland Hospital, Halmstad, Sweden
5. The Prehospital Research Center Western Sweden, University of Borås, Borås, Sweden.

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and the interpretation discussed.

Corresponding author
Kristoffer Wibring
Ambulanssjukvården Region Halland
Varlabergsvägen 29
434 39 Kungsbacka
E-mail: kristoffer.wibring@gu.se
Phone: 0046701757679

Word count: 2 221

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

ABSTRACT

Objective: To investigate whether or not the prevalence of different chest pain-related symptoms is associated with sex, age and previous medical history of diabetes mellitus or acute coronary syndrome in patients assessed by the Emergency Medical Services (EMS) due to acute chest pain.

Design: Prospective observational cohort study.

Setting: Two-centre study in a Swedish county EMS organisation.

Participants: Unselected inclusion of 2,917 patients with chest pain who contacted the EMS during 2018 due to chest pain.

Data analysis: Multivariate analysis on the association between symptom characteristics and patients' sex, age and previous medical history.

Results: Symptomology in patients assessed by the EMS due to acute chest pain varied with sex and age, and also with previous medical history. Women suffered more often from nausea and pain in throat or back. Their pain was more often affected by palpation or movement. Older patients more often described pain onset while sleeping and that the onset of symptoms was slow, over hours rather than minutes. They were less likely to report pain in other parts of their body than their chest. They were to a lesser extent pale or nauseous. These differences were present regardless of whether the symptoms were caused by AMI or not.

Conclusions: The clinical presentation of AMI differs based on patients' sex, age and previous medical history. Similar differences appear to be present in a non-selected population of patients with acute chest pain also including those without a final diagnosis of AMI. These findings may be important in the early assessment of patients with acute chest pain with regard to suspicion of AMI in relation to sex, age and previous history of diabetes.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Unselected inclusion of a close to complete county population of patients with chest pain who contacted the emergency medical services.
- Low rates of missing data considering the prehospital nature of the data.
- Some variables involved high rates of missing data when compared with studies conducted in the hospital setting.
- A study conducted in only one county reduces generalisability.

Keywords

Chest Pain; Emergency Medical Services; Acute Myocardial Infarction; Signs and Symptoms; Clinical Presentation; Sex factors; Age factors

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

BACKGROUND

Chest pain is one of the most common complaints when contacting the emergency medical services (EMS). About 10-15 percent of all patient-related EMS missions concern patients with chest pain [1 2] out of which about 10 percent have an acute myocardial infarction (AMI) [3].

Clinical presentation is, along with ECG and biomedical markers, one cornerstone when differentiating those with AMI from those with other causes of their chest pain [4 5]. Numerous studies have investigated whether patients' sex, age, and medical history of diabetes mellitus or previous myocardial infarction are associated with differences in clinical presentation in patients diagnosed with AMI [4-7]. Even if the results vary, the general opinion is that at least age, sex and previous history of diabetes mellitus are associated with differences in symptomology at least in some patients when seeking care for AMI [4 5].

These factors are not solely associated with the type of symptoms that the patients experience but also with to what extent the patients delay seeking care [8 9]. They are also associated with patients' use of the EMS or if they use other means for transportation to hospital when suffering from chest pain [10].

The above-cited studies are mainly based on hospital data. Thus it is not possible to determine whether or not these findings also apply in the prehospital setting. Furthermore, most of these studies only included patients diagnosed with AMI. This makes it difficult to determine whether these differences in symptomology are also valid among patients with chest pain in general, including patients without AMI. This is of clinical relevance, since we need to know whether such differences in clinical presentation associated with the factors stated should be taken into account when assessing patients with chest pain in the prehospital emergency setting. Furthermore, at the time of prehospital assessment, the EMS clinician does not know with certainty whether the patient is suffering from a myocardial infarction or not.

This study therefore investigates whether or not patients with chest pain, assessed in the prehospital setting, differ in symptomology based on sex, age, previous history of diabetes mellitus or ACS (acute coronary syndrome), regardless of whether their chest pain is caused by AMI or not.

Objective

To investigate whether the prevalence of chest pain-related symptoms is associated with:

- sex
- age
- previous medical history of diabetes mellitus
- previous medical history of acute coronary syndrome.

METHODS

The study is part of the BRIAN research programme. Study population, data collection and clinical setting have been previously described and are therefore summarised briefly [11].

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Study population

In all, 3,121 EMS missions were carried out in 2018 in the county catchment area including patients ≥18 years old, with a chief complaint of chest pain. All these missions were eligible for inclusion. After excluding patients declining to participate and patients who were lost to follow-up, 2,917 EMS missions remained.

Data collection

Each patient was tracked throughout the entire healthcare chain, from EMS mission to hospital discharge. Data on symptoms were retrieved using a questionnaire filled in by the EMS personnel along with the patients' EMS medical report. Diagnosis of AMI on hospital discharge according to physician in charge was retrieved from the hospital medical record. Data collection did not affected patient care.

Endpoint

Occurrence of the following symptoms:

- Paleness or clamminess
- Nausea or vomiting
- Dyspnoea
- Pain according to the OPQRST[12] mnemonic:
  - Onset
  - Provocation/Palliation
  - Quality
  - Region and localisation
  - Severity
  - Time (behaviour over time)

Statistical analysis

The results are presented using descriptive statistics including percentage (%), number of patients (n), mean, median, standard deviation (SD) and quartiles where appropriate.

The association between patients' sex, age, previous history of diabetes or ACS and occurrence of stated symptoms was analysed using multivariate regression. The analyses were adjusted for diagnosis of AMI at hospital discharge. Patients' age was dichotomised in the analyses, using cohort median age as cut-off. No multivariate analyses were performed if the symptom of interest occurred in fewer than 100 patients. This was to ensure that the assumptions for logistic regression analyses were not violated. P-values below 0.01 were considered statistically significant (instead of 0.05 due to multiple tests). All analyses were carried out using IBM SPSS Statistics 27.

Ethical considerations

In this study, all patients eligible for inclusion were subject to an opt-out procedure. The study was approved by the Regional Ethical Review Board in Lund (Dno 2017/212).

Patient and public involvement

Patients have not been directly involved in planning or conducting this study. The design of the questionnaire was partly based on patient narratives from a previous study within this

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

research project[28] and other studies based on patient interviews. Furthermore, KW had personal contact with several patients who contacted him by phone or e-mail due to the opt-out procedure, both patients wanting to opt out and those who wanted to remain in the study. The results of the study will be presented directly to those patients who request this when contacting KW.

RESULTS

The median age of the cohort was 72 years old (Q25-Q75, 58-82). Sex was evenly distributed. Of EMS missions included, almost 30 % of patients had a previous history of ACS and 20 % of the patients had diabetes mellitus. The prevalence of AMI in terms of diagnosis on hospital discharge was 12 %. The proportion of patients with AMI on hospital discharge was associated with sex and previous history of diabetes mellitus with a higher rate among men and among patients with a history of diabetes mellitus (Table 1).

Table 1 - Incidence of diagnosis of AMI on hospital discharge

	All % (n)	Acute myocardial infarction on hospital discharge % (n)	p-value*
All	100 (2917)	12 (335)	–
Male	50 (1465)	64 (214)	<0.001
Age > 72 years	49 (1436)	55 (183)	0.036
Previous history of ACS	29 (856)	25 (84)	0.068
Previous history of diabetes mellitus	20 (578)	26 (86)	0.004

**chi2-test*
AMI = Acute myocardial infarction; ACS = Acute coronary syndrome

The most common symptom characteristics were affected breathing, time debut less than 3 hours before EMS arrival, pain debut while resting, and constant, pressuring pain located in the central chest about the size of a palm. This pattern was found regardless of patients' sex, age or previous medical history (Table 2).

Table 2 - Prevalence of symptoms based on sex, age and previous medical history of ACS or diabetes mellitus

	All % (n)	Women % (n)	Age >72 % (n)	History of ACS % (n)	History of diabetes mellitus % (n)
All (number of missing)	100 (2917)	49.8 (1452)	49.2 (1436)	29.3 (856)	19.8 (578)
Pale (565)	16.4 (386)	13.5 (157)	16.7 (196)	19.9 (140)	17.1 (81)
Clammy (565)	8.7 (204)	7.4 (86)	6.4 (75)	6.2 (44)	7.8 (37)
Nausea (576)	27.1 (635)	31.3 (363)	23.2 (270)	24.0 (169)	28.9 (137)
Vomiting (576)	7.0 (165)	6.9 (80)	6.3 (74)	5.4 (38)	7.4 (35)
Affected breathing according to patient (596)	44.6 (1040)	46.8 (537)	44.2 (514)	49.6 (347)	49.0 (229)
Pain intensity according to Numeric Rating Scale >5 (415)	32.1 (803)	33.6 (1228)	30.1 (372)	33.7 (248)	39.8 (197)
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	46.5 (442)	47.3 (445)	43.4 (245)	50.4 (195)
Debut					

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Debut during activity (752)	22.1 (479)	20.5 (217)	17.8 (191)	20.8 (132)	14.7 (64)
Debut while resting (752)	65.5 (1419)	67.4 (714)	67.6 (725)	67.8 (431)	71.3 (310)
Debut while sleeping (752)	15.8 (342)	15.6 (165)	18.1 (194)	14.2 (90)	16.6 (72)
Sudden debut, within seconds (875)	35.7 (729)	36.1 (361)	31.4 (313)	32.7 (199)	33.0 (136)
Quick debut, within minutes (875)	35.2 (718)	33.2 (332)	35.8 (357)	36.6 (223)	36.2 (149)
Slow debut, within hours (875)	29.1 (595)	30.8 (308)	32.7 (326)	30.7 (187)	30.8 (127)
Constant pain (732)	55.5 (1212)	53.3 (574)	57.1 (615)	54.9 (358)	59.8 (266)
Fluctuating pain (732)	40.4 (883)	42.3 (456)	40.0 (431)	40.0 (261)	34.8 (155)
Pain aggravating over time (732)	10.8 (237)	10.8 (116)	9.4 (101)	12.0 (78)	11.5 (51)
Pain in other parts of the body (1197)					
Head	2.5 (43)	3.3 (29)	1.8 (15)	2.0 (10)	2.3 (8)
Throat	10.3 (177)	13.3 (117)	8.6 (73)	8.8 (45)	9.1 (32)
Jaw	5.3 (92)	5.8 (51)	3.8 (32)	5.3 (27)	4.5 (16)
Neck	2.5 (43)	3.4 (30)	2.5 (21)	2.9 (15)	3.4 (12)
Between scapulars	2.2 (37)	2.7 (24)	1.5 (13)	1.6 (8)	1.4 (5)
Back	15.2 (261)	19.5 (171)	16.4 (139)	17.5 (89)	17.8 (63)
Left shoulder	8.5 (147)	9.0 (79)	7.5 (64)	9.0 (46)	9.1 (32)
Right shoulder	4.2 (72)	4.6 (40)	4.0 (34)	3.5 (18)	5.4 (19)
Left arm	24.0 (412)	23.0 (202)	23.1 (196)	29.4 (150)	28.0 (99)
Right arm	8.4 (145)	8.8 (77)	8.5 (72)	9.4 (48)	11.0 (39)
Left hand	1.0 (17)	0.7 (6)	0.4 (3)	0.2 (1)	0.8 (3)
Right hand	0.3 (6)	0.1 (1)	0.2 (2)	0.2 (1)	0.6 (2)
Stomach	7.0 (121)	7.1 (62)	7.5 (64)	6.5 (33)	8.2 (29)
Left leg	1.7 (29)	1.8 (16)	1.8 (15)	1.0 (5)	2.8 (10)
Right leg	1.4 (24)	1.4 (12)	1.4 (12)	0.6 (3)	2.8 (10)
No other pain	39.3 (676)	34.2 (301)	41.3 (351)	35.9 (183)	35.4 (125)
Pain quality (1175)					
Band-shaped	3.3 (58)	3.7 (32)	3.4 (29)	3.0 (15)	2.2 (8)
Burning	4.4 (76)	5.4 (46)	3.5 (30)	4.3 (22)	5.8 (21)
Stabbing	9.7 (169)	8.3 (71)	8.8 (75)	10.7 (54)	10.2 (37)
Cramping	8.7 (151)	9.1 (78)	6.7 (57)	6.1 (31)	8.0 (29)
Dull pain	13.9 (242)	13.6 (116)	14.6 (124)	13.6 (69)	15.7 (57)
Feels like something is on the chest	0.7 (12)	0.6 (5)	0.6 (5)	0.4 (2)	0.0 (0)
Discomfort	10.2 (178)	10.8 (92)	10.6 (90)	9.7 (49)	9.9 (36)
Tingling/Stinging	5.7 (99)	5.1 (44)	4.9 (42)	5.9 (30)	5.5 (20)
Swaying	1.7 (30)	1.6 (14)	1.5 (13)	2.0 (10)	1.4 (5)
Pressuring	57.9 (1008)	59.6 (510)	60.0 (510)	58.3 (295)	58.0 (211)
Heaviness	1.0 (17)	1.3 (11)	1.1 (9)	0.8 (4)	0.5 (2)
Aching	2.4 (41)	2.1 (18)	2.4 (20)	3.0 (15)	2.7 (10)
Chest pain localisation (640)					

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Central pain	53.4 (1215)	53.3 (599)	54.2 (613)	55.4 (377)	55.3 (255)
Left side of chest	35.5 (809)	32.0 (359)	32.7 (370)	36.0 (245)	34.3 (461)
Right side of chest	5.1 (116)	4.8 (54)	5.4 (61)	3.5 (24)	5.9 (27)
Upper part of chest	6.7 (152)	7.9 (89)	5.9 (67)	5.7 (39)	5.2 (24)
Lower part of chest	9.0 (204)	11.1 (125)	9.3 (105)	7.2 (49)	8.9 (41)
All over the chest	11.8 (269)	12.6 (141)	12.5 (141)	11.3 (77)	12.4 (57)
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.2 (107)	10.4 (109)	10.1 (63)	7.0 (30)
Size of patient's palm	58.4 (1240)	57.4 (601)	56.7 (594)	60.0 (374)	58.7 (252)
Entire chest	30.9 (655)	32.4 (339)	32.9 (344)	29.9 (186)	34.3 (147)
Palpation tenderness (655)	22.3 (505)	27.1 (302)	21.3 (239)	21.6 (146)	25.4 (115)
Pain affected by movement (719)	17.0 (373)	19.6 (211)	15.5 (169)	15.9 (105)	17.1 (76)
Pain affected by breathing (692)	25.8 (573)	26.6 (292)	21.5 (236)	20.9 (139)	24.3 (109)
ACS = Acute coronary syndrome					

Women more often suffered from nausea and pain in the throat or back. They also more commonly localised their pain to the lower part of the chest. Their pain was more often affected by palpation or movement. They were more likely to report pain in other parts of the body than their chest. They were less often pale and had a lower incidence of left-sided chest pain (Figure 1).

Older patients more often described pain onset while sleeping and that the onset of symptoms was slow, over hours rather than minutes. They were less likely to report pain in other parts of their body than the chest. They were to a lesser extent pale or nauseous. They rated their pain intensity lower and their chest pain onset occurred less often during activity. Their breathing movements more seldom affected their pain (Figure 2).

Patients with a previous history of ACS were more often pale and experienced their breathing as affected. They more often had pain in their left arm. They reported right-sided chest pain to a lesser extent, and they felt pain in any other part of their body than in the chest to a greater extent (Figure 3).

Regarding patients with a previous history of diabetes mellitus, their pain more often started while they were resting and they rated their pain intensity as higher. Their pain was less likely to start during activity (Figure 4).

In total, patients' sex was associated with the occurrence of nine different types of symptom and the same was true for patients' age. Previous history of ACS or diabetes mellitus were associated with the occurrence of five or three different symptoms respectively (Supplemental material 1-4).

DISCUSSION

Our study shows that the prevalence of numerous symptoms in prehospital patients with chest pain is associated most of all with sex and age, but also with the patient's previous medical

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

history. This is observed regardless of whether the patient's chest pain is caused by an acute myocardial infarction or not. To the best of our knowledge, this is the first study reporting results on symptomology differences in acute chest pain patients based on sex, age and previous medical history, when simultaneously adjusting for AMI incidence.

Sex, age and previous medical history seem not only to be associated with how an AMI is experienced [4 5], but also with how acute chest pain and related symptoms are perceived in general. This finding implies that previously reported differences in clinical presentation based on patients' characteristics may be a general observation in acute chest pain patients and not necessarily associated with an AMI diagnosis. This finding further complicates the already challenging task of assessing patients with acute chest pain.

For example, Sederholm et. al.[13] report that women with AMI experience pain in their back and throat more often than men and are more commonly nauseous. In our study, we also found an increased incidence of these symptoms among women, but in our material this difference was present regardless of whether their chest pain was caused by AMI or not. Thus these differences in symptomology are problematic when used for risk assessment since they are not necessarily associated with the incidence of AMI but rather with the patient's sex.

Our results strengthen the notion that the diagnostic evaluation of chest pain characteristics has limitations as a diagnostic tool and should be used with great caution [5]. Not least, clinicians should be careful not to allow patients' characteristics to influence how they evaluate patients' symptoms [6].

Strengths and limitations

This study is strengthened by the close to complete and unselected inclusion of EMS missions concerning patients with chest pain, which improves generalisability. However, the use of data from a single county negatively affects the external validity.

The results are based on sub-analyses of previously collected data and the absolute differences observed are sometimes small. Clinicians should therefore be careful not to draw over-strict conclusions on how these results should affect clinical practice.

Some of the variables included entail rather high rates of missing information. Data collection in the prehospital setting is known to be challenging and often involves higher rates of missing data than the in-hospital setting [14 15]. Considering this, the rates of missing information in this study are to be regarded as low and therefore data may be looked upon as comparatively comprehensive.

In part, the differences in clinical presentation described in this study may be explained by an uneven distribution of diagnoses other than AMI at hospital discharge. To adjust for more diagnoses than AMI at hospital discharge, a larger study sample is needed to ensure statistical robustness. However, the fact that differences in clinical presentation are explained by other diagnoses at hospital discharge does not change the implication of our results. Thus clinicians should be careful not to allow patients' characteristics to influence how they evaluate patients' symptoms in cases of acute chest pain.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

CONCLUSIONS

The clinical presentation of AMI differs based on patients' sex, age and previous medical history. Similar differences appear to be present in a non-selected population of patients with acute chest pain also including those without a final diagnosis of AMI. These findings may be important in the early assessment of patients with acute chest pain with regard to suspicion of AMI in relation to sex, age and previous history of diabetes.

List of abbreviations

ACS – acute coronary syndrome
AMI – acute myocardial infarction
EMS – emergency medical services
NRS – numeric rating scale
PEN – prehospital emergency nurse

Author contributions

KW, ML, JH, AL, HP and AB designed the study. KW, ML, JH, and AB planned the data collection. Data analysis was carried out by KW, AL and HP. KW, ML, JH, AL, HP and AB contributed in writing the manuscript. All authors read and approved the final manuscript.

Funding

This study has been funded by the Department of Ambulance and Prehospital Care, Region Halland and the Scientific Council of Region Halland (HALLAND-209901). The funding bodies had no role in the design, conduct, interpretation or writing of the report on this research.

Competing interests

The authors declare that they have no competing interests.

Patient consent for publication

Not required.

Ethics approval

The study was approved by the Regional Ethical Review Board in Lund (Dno 2017/212). All patients were given the opportunity to withdraw their participation using an opt-out procedure.

Data availability statement

The datasets generated and analysed during the current study are not publicly available due the integrity of patient privacy but are available from the corresponding author on reasonable request and if approved by the Regional Ethical Review Board in Lund.

Acknowledgements

We want to thank the following persons:

- The EMS personnel of Region Halland for their help with data collection.
- Thomas Thorsson, Vinh Norberg Nguyen and Sasa Pejicic for data extraction.
- Anders Holmén and Ulf Strömberg for statistical support.

Tables, figures and supplemental material

Figure 1 - Differences in clinical presentation based on sex

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Figure 2 - Differences in clinical presentation based on age
Figure 3 - Differences in clinical presentation based on history of ACS
Figure 4 - Differences in clinical presentation based on history of diabetes mellitus
Table 1 - Incidence of diagnosis of AMI on hospital discharge
Table 2 - Prevalence of symptoms based on sex, age and previous medical history of ACS or diabetes mellitus
Supplemental material 1 - Multivariate analyses of differences in symptoms prevalence based on sex
Supplemental material 2 - Multivariate analyses of differences in symptoms prevalence based on age
Supplemental material 3 - Multivariate analyses of differences in symptoms prevalence based on previous history of ACS
Supplemental material 4 - Multivariate analyses of differences in symptoms prevalence based on previous history of diabetes mellitus

REFERENCES

1. Clawson J, Olola C, Heward A, et al. The Medical Priority Dispatch System's ability to predict cardiac arrest outcomes and high acuity pre-hospital alerts in chest pain patients presenting to 9-9-9. *Resuscitation* 2008;78(3):298-306. doi: 10.1016/j.resuscitation.2008.03.229
2. Pedersen CK, Stengaard C, Friesgaard K, et al. Chest pain in the ambulance; prevalence, causes and outcome - a retrospective cohort study. *Scand J Trauma Resusc Emerg Med* 2019;27(1):84. doi: 10.1186/s13049-019-0659-6 [published Online First: 2019/08/29]
3. Rawshani A, Larsson A, Gelang C, et al. Characteristics and outcome among patients who dial for the EMS due to chest pain. *International Journal of Cardiology* 2014;176(3):859-65. doi: 10.1016/j.ijcard.2014.08.004
4. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39(2):119-77. doi: 10.1093/eurheartj/ehx393
5. Collet JP, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2020 doi: 10.1093/eurheartj/ehaa575 [published Online First: 2020/08/29]
6. Thuresson M, Jarlöv MB, Lindahl B, et al. Symptoms and type of symptom onset in acute coronary syndrome in relation to ST elevation, sex, age, and a history of diabetes. *Am Heart J* 2005;150(2):234-42. doi: 10.1016/j.ahj.2004.08.035
7. Strömbäck U, Engström Å, Lundqvist R, et al. The second myocardial infarction: Is there any difference in symptoms and prehospital delay compared to the first myocardial infarction? *Eur J Cardiovasc Nurs* 2018;17(7):652-59. doi: 10.1177/1474515118777391 [published Online First: 2018/05/11]
8. Moser DK, Kimble LP, Alberts MJ, et al. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Heart Association Council on cardiovascular nursing and stroke council. *Circulation* 2006;114(2):168-82. doi: 10.1161/CIRCULATIONAHA.106.176040 [published Online First: 2006/06/26]

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

9. Wechkunanukul K, Grantham H, Clark RA. Global review of delay time in seeking medical care for chest pain: An integrative literature review. *Aust Crit Care* 2017;30(1):13-20. doi: 10.1016/j.aucc.2016.04.002 [published Online First: 2016/04/23]
10. Thang ND, Karlson BW, Bergman B, et al. Characteristics of and outcome for patients with chest pain in relation to transport by the emergency medical services in a 20-year perspective. *American Journal of Emergency Medicine* 2012;30(9):1788-95. doi: 10.1016/j.ajem.2012.02.014
11. Wibring K, Lingman M, Herlitz J, et al. Prehospital stratification in acute chest pain patient into high risk and low risk by emergency medical service: a prospective cohort study. *BMJ Open* 2021;11(4):e044938. doi: 10.1136/bmjopen-2020-044938 [published Online First: 2021/04/15]
12. Eloge J, Napier TC, Dantz B. OPQRST(U): Integrating substance use disorders or "Use" into the medical history. *Subst Abus* 2018;39(4):505-08. doi: 10.1080/08897077.2018.1469104 [published Online First: 2018/08/17]
13. Sederholm Lawesson S, Isaksson RM, Ericsson M, et al. Gender disparities in first medical contact and delay in ST-elevation myocardial infarction: a prospective multicentre Swedish survey study. *BMJ Open* 2018;8(5):e020211. doi: 10.1136/bmjopen-2017-020211 [published Online First: 2018/05/03]
14. Maurin Söderholm H, Andersson H, Andersson Hagiwara M, et al. Research challenges in prehospital care: the need for a simulation-based prehospital research laboratory. *Adv Simul (Lond)* 2019;4:3. doi: 10.1186/s41077-019-0090-0 [published Online First: 2019/02/13]
15. Dickert NW, Brown J, Cairns CB, et al. Confronting Ethical and Regulatory Challenges of Emergency Care Research With Conscious Patients. *Ann Emerg Med* 2016;67(4):538-45. doi: 10.1016/j.annemergmed.2015.10.026 [published Online First: 2015/12/18]

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

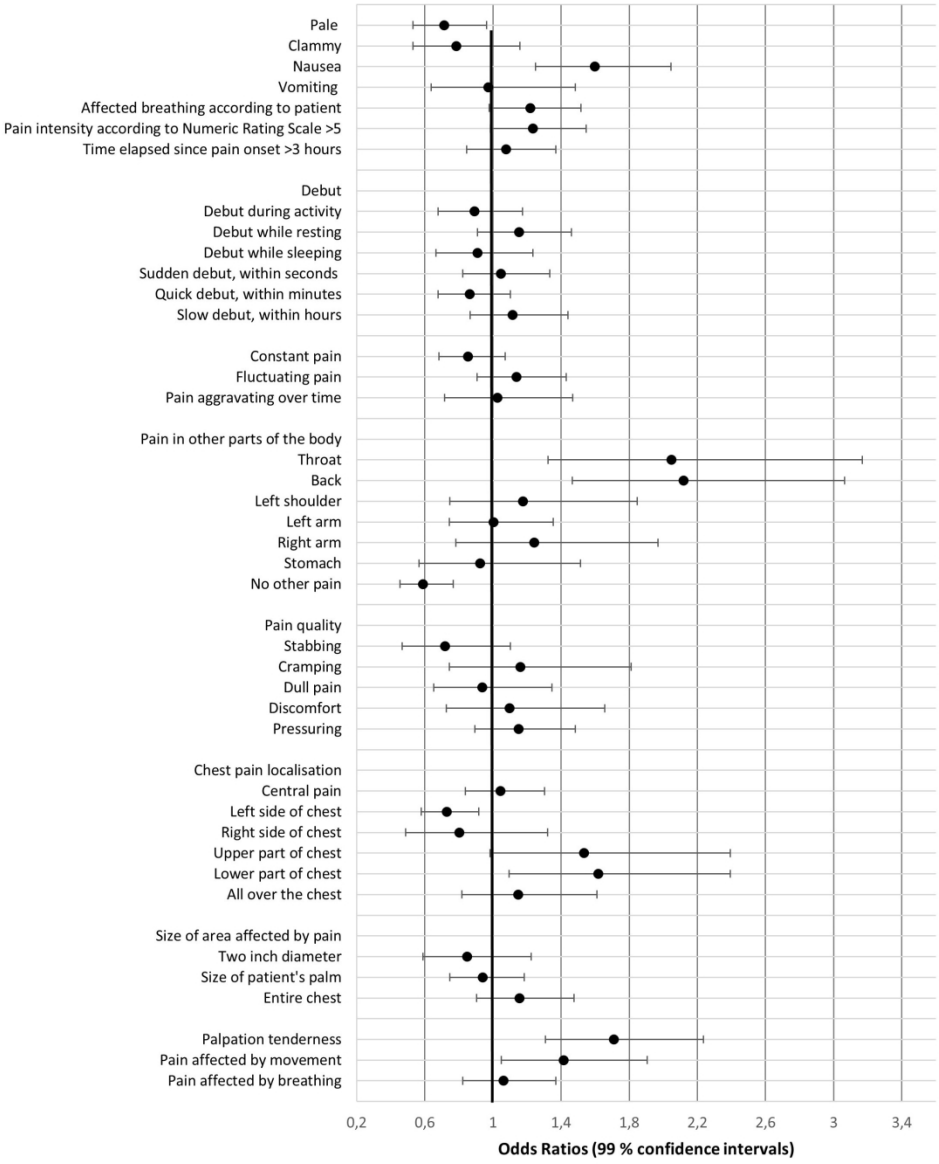

Figure 1 - Differences in clinical presentation based on sex

190x234mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

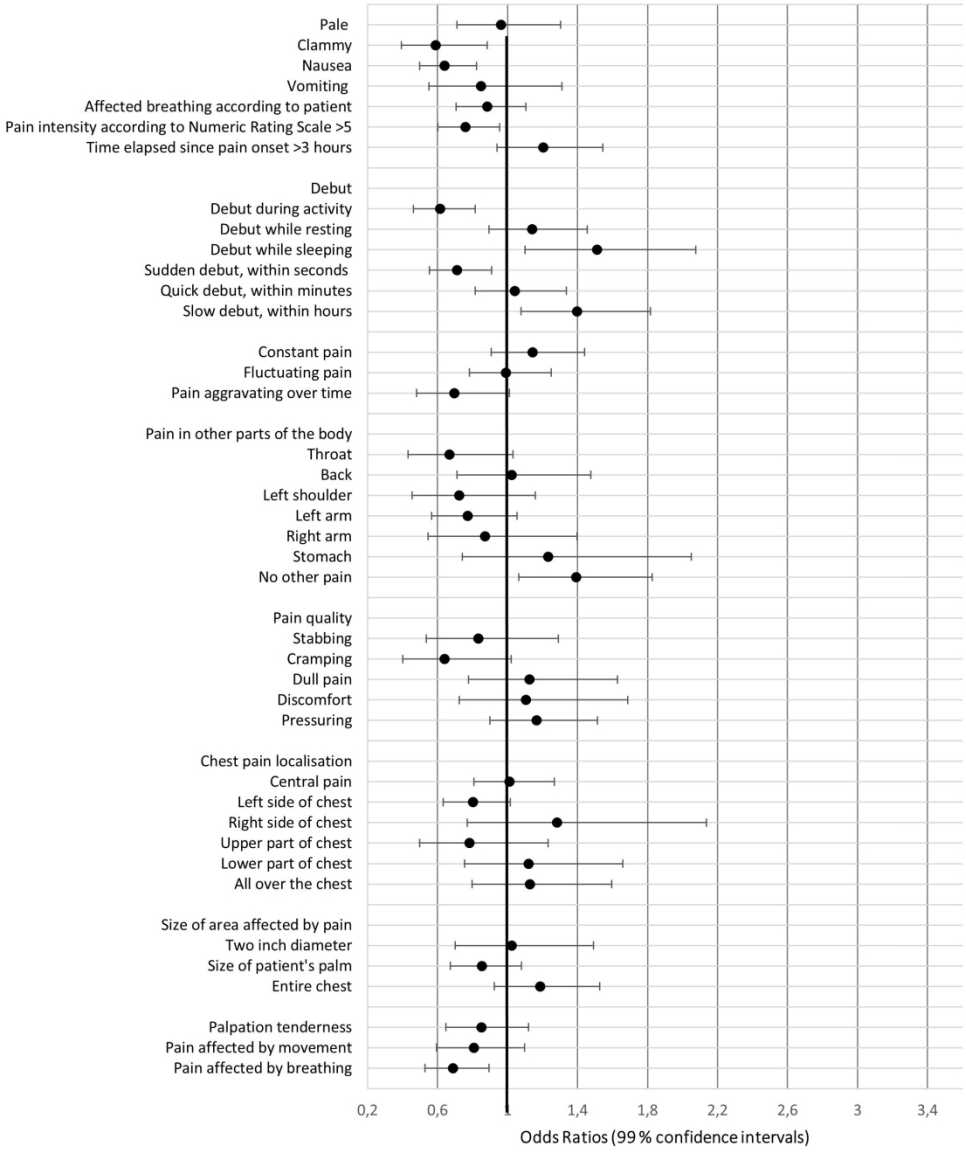

Figure 2 - Differences in clinical presentation based on age

190x223mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

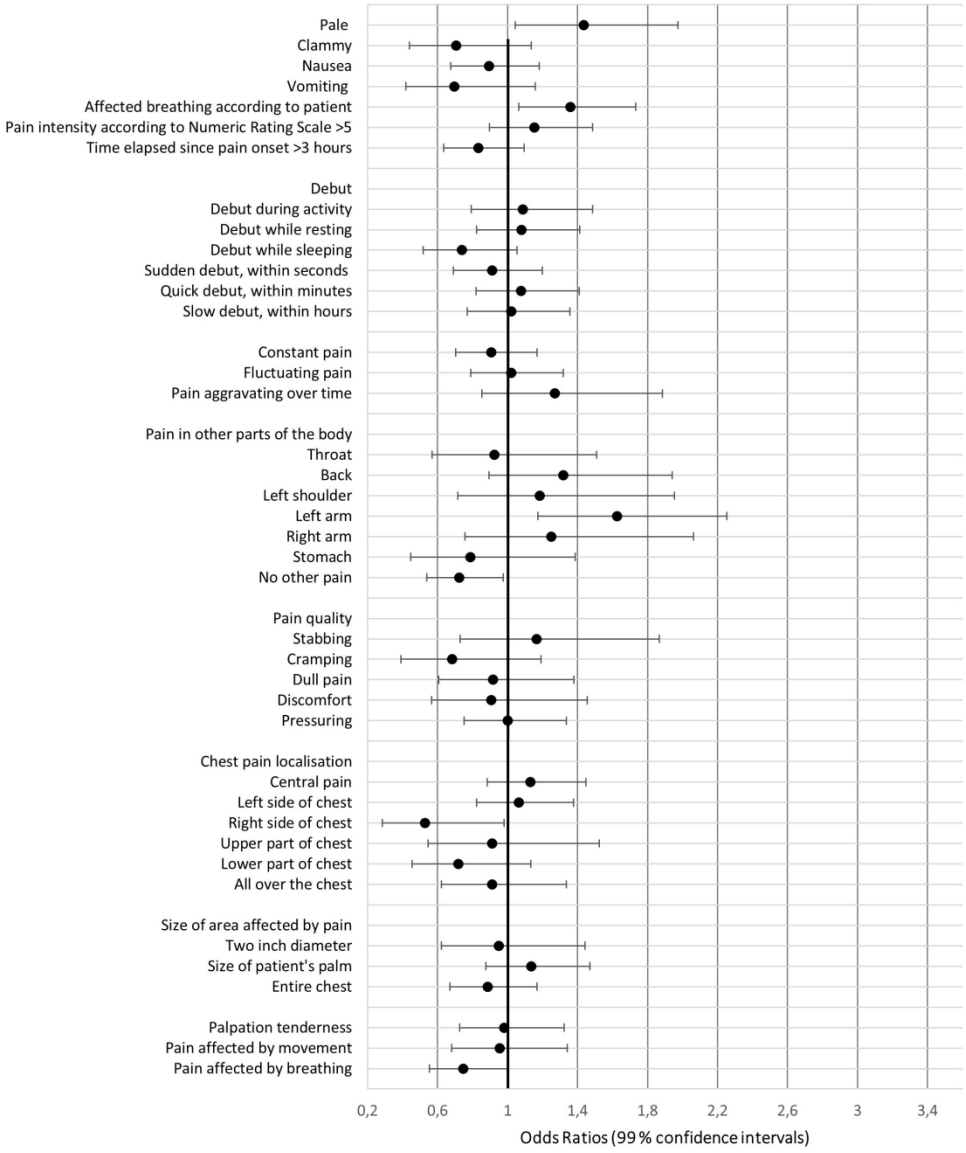

Figure 3 - Differences in clinical presentation based on history of ACS

190x221mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

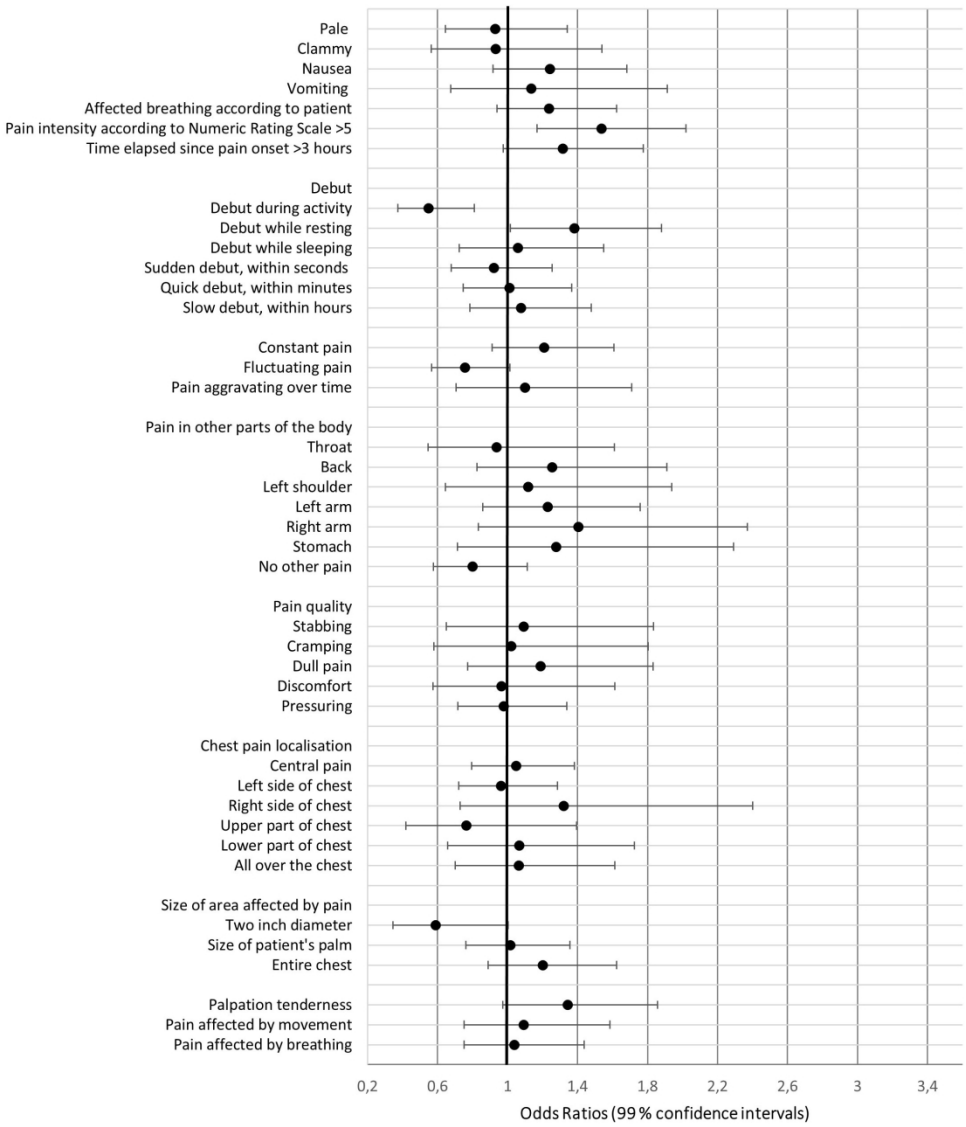

Figure 4 - Differences in clinical presentation based on history of diabetes mellitus

190x216mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Supplemental material 1 - Multivariate analyses of differences in symptoms based on sex

	All % (n)	Women % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	49.8 (1452)			
Pale (565)	16.4 (386)	13.5 (157)	0.004*	0.71	0.53-0.96
Clammy (565)	8.7 (204)	7.4 (86)	0.109	0.78	0.53-1.16
Nausea (576)	27.1 (635)	31.3 (363)	<0.001*	1.6	1.25-2.05
Vomiting (576)	7.0 (165)	6.9 (80)	0.866	0.97	0.64-1.48
Affected breathing according to patient (596)	44.6 (1040)	46.8 (537)	0.020	1.22	0.98-1.52
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	33.6 (1228)	0.016	1.23	0.99-1.55
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	46.5 (442)	0.425	1.08	0.85-1.37
Debut					
Debut during activity (752)	22.1 (479)	20.5 (217)	0.284	0.89	0.68-1.17
Debut while resting (752)	65.5 (1419)	67.4 (714)	0.125	1.15	0.91-1.46
Debut while sleeping (752)	15.8 (342)	15.6 (165)	0.411	0.91	0.67-1.23
Sudden debut, within seconds (875)	35.7 (729)	36.1 (361)	0.622	1.05	0.82-1.33
Quick debut, within minutes (875)	35.2 (718)	33.2 (332)	0.122	0.86	0.68-1.10
Slow debut, within hours (875)	29.1 (595)	30.8 (308)	0.266	1.12	0.87-1.44
Constant pain (732)	55.5 (1212)	53.3 (574)	0.072	0.85	0.68-1.07
Fluctuating pain (732)	40.4 (883)	42.3 (456)	0.145	1.14	0.91-1.43
Pain aggravating over time (732)	10.8 (237)	10.8 (116)	0.861	1.03	0.72-1.47
Pain in other parts of the body (1197)					
Head	2.5 (43)	3.3 (29)	–	–	–
Throat	10.3 (177)	13.3 (117)	<0.001*	2.05	1.32-3.17
Jaw	5.3 (92)	5.8 (51)	–	–	–
Neck	2.5 (43)	3.4 (30)	–	–	–
Between scapulars	2.2 (37)	2.7 (24)	–	–	–
Back	15.2 (261)	19.5 (171)	<0.001*	2.12	1.47-3.07
Left shoulder	8.5 (147)	9.0 (79)	0.358	1.18	0.75-1.85
Right shoulder	4.2 (72)	4.6 (40)	–	–	–
Left arm	24.0 (412)	23.0 (202)	0.974	1.00	0.74-1.35
Right arm	8.4 (145)	8.8 (77)	0.226	1.24	0.78-1.97
Left hand	1.0 (17)	0.7 (6)	–	–	–
Right hand	0.3 (6)	0.1 (1)	–	–	–
Stomach	7.0 (121)	7.1 (62)	0.685	0.93	0.57-1.52
Left leg	1.7 (29)	1.8 (16)	–	–	–
Right leg	1.4 (24)	1.4 (12)	–	–	–
No other pain	39.3 (676)	34.2 (301)	<0.001*	0.59	0.45-0.77
Pain quality (1175)					
Band-shaped	3.3 (58)	3.7 (32)	–	–	–
Burning	4.4 (76)	5.4 (46)	–	–	–
Stabbing	9.7 (169)	8.3 (71)	0.047	0.72	0.47-1.10
Cramping	8.7 (151)	9.1 (78)	0.392	1.16	0.74-1.81
Dull pain	13.9 (242)	13.6 (116)	0.646	0.94	0.65-1.35
Feels like something is on the chest	0.7 (12)	0.6 (5)	–	–	–
Discomfort	10.2 (178)	10.8 (92)	0.563	1.10	0.73-1.66
Tingling/Stinging	5.7 (99)	5.1 (44)	–	–	–
Swaying	1.7 (30)	1.6 (14)	–	–	–
Pressuring	57.9 (1008)	59.6 (510)	0.153	1.15	0.89-1.48
Heaviness	1.0 (17)	1.3 (11)	–	–	–
Aching	2.4 (41)	2.1 (18)	–	–	–

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 1 continues

	All % (n)	Women % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	53.3 (599)	0.612	1.04	0.84-1.30
Left side of chest	35.5 (809)	32.0 (359)	<0.001*	0.73	0.58-0.91
Right side of chest	5.1 (116)	4.8 (54)	0.256	0.80	0.49-1.32
Upper part of chest	6.7 (152)	7.9 (89)	0.013	1.53	0.98-2.39
Lower part of chest	9.0 (204)	11.1 (125)	0.002*	1.62	1.09-2.39
All over the chest	11.8 (269)	12.6 (141)	0.299	1.15	0.82-1.61
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.2 (107)	0.251	0.85	0.59-1.23
Size of patient's palm	58.4 (1240)	57.4 (601)	0.492	0.94	0.75-1.18
Entire chest	30.9 (655)	32.4 (339)	0.131	1.16	0.90-1.48
Palpation tenderness (655)	22.3 (505)	27.1 (302)	<0.001*	1.71	1.31-2.24
Pain affected by movement (719)	17.0 (373)	19.6 (211)	0.003*	1.41	1.05-1.91
Pain affected by breathing (692)	25.8 (573)	26.6 (292)	0.543	1.06	0.82-1.37

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 2 - Multivariate analyses of differences in symptoms based on age

	All % (n)	Age >72 % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	49.2 (1436)			
Pale (565)	16.4 (386)	16.7 (196)	0.745	0.96	0.71-1.30
Clammy (565)	8.7 (204)	6.4 (75)	0.001*	0.58	0.39-0.88
Nausea (576)	27.1 (635)	23.2 (270)	<0.001*	0.64	0.49-0.82
Vomiting (576)	7.0 (165)	6.3 (74)	0.331	0.84	0.55-1.31
Affected breathing according to patient (596)	44.6 (1040)	44.2 (514)	0.155	0.88	0.70-1.10
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	30.1 (372)	0.002*	0.75	0.60-0.95
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	47.3 (445)	0.053	1.20	0.94-1.54
Debut					
Debut during activity (752)	22.1 (479)	17.8 (191)	<0.001*	0.61	0.46-0.81
Debut while resting (752)	65.5 (1419)	67.6 (725)	0.164	1.14	0.89-1.45
Debut while sleeping (752)	15.8 (342)	18.1 (194)	0.001*	1.51	1.09-2.07
Sudden debut, within seconds (875)	35.7 (729)	31.4 (313)	<0.001*	0.71	0.55-0.91
Quick debut, within minutes (875)	35.2 (718)	35.8 (357)	0.666	1.04	0.81-1.33
Slow debut, within hours (875)	29.1 (595)	32.7 (326)	0.001*	1.39	1.07-1.81
Constant pain (732)	55.5 (1212)	57.1 (615)	0.136	1.14	0.90-1.44
Fluctuating pain (732)	40.4 (883)	40.0 (431)	0.911	0.99	0.78-1.25
Pain aggravating over time (732)	10.8 (237)	9.4 (101)	0.012	0.69	0.48-1.01
Pain in other parts of the body (1197)					
Head	2.5 (43)	1.8 (15)	–	–	–
Throat	10.3 (177)	8.6 (73)	0.016	0.66	0.43-1.03
Jaw	5.3 (92)	3.8 (32)	–	–	–
Neck	2.5 (43)	2.5 (21)	–	–	–
Between scapulars	2.2 (37)	1.5 (13)	–	–	–
Back	15.2 (261)	16.4 (139)	0.871	1.02	0.71-1.47
Left shoulder	8.5 (147)	7.5 (64)	0.077	0.72	0.45-1.15
Right shoulder	4.2 (72)	4.0 (34)	–	–	–
Left arm	24.0 (412)	23.1 (196)	0.032	0.77	0.56-1.05
Right arm	8.4 (145)	8.5 (72)	0.454	0.87	0.54-1.39
Left hand	1.0 (17)	0.4 (3)	–	–	–
Right hand	0.3 (6)	0.2 (2)	–	–	–
Stomach	7.0 (121)	7.5 (64)	0.290	1.23	0.74-2.05
Left leg	1.7 (29)	1.8 (15)	–	–	–
Right leg	1.4 (24)	1.4 (12)	–	–	–
No other pain	39.3 (676)	41.3 (351)	0.002*	1.39	1.06-1.82
Pain quality (1175)					
Band-shaped	3.3 (58)	3.4 (29)	–	–	–
Burning	4.4 (76)	3.5 (30)	–	–	–
Stabbing	9.7 (169)	8.8 (75)	0.280	0.83	0.53-1.29
Cramping	8.7 (151)	6.7 (57)	0.014	0.63	0.40-1.02
Dull pain	13.9 (242)	14.6 (124)	0.414	1.12	0.77-1.62
Feels like something is on the chest	0.7 (12)	0.6 (5)	–	–	–
Discomfort	10.2 (178)	10.6 (90)	0.547	1.10	0.72-1.68
Tingling/Stinging	5.7 (99)	4.9 (42)	–	–	–
Swaying	1.7 (30)	1.5 (13)	–	–	–
Pressuring	57.9 (1008)	60.0 (510)	0.129	1.16	0.89-1.51
Heaviness	1.0 (17)	1.1 (9)	–	–	–
Aching	2.4 (41)	2.4 (20)	–	–	–

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 2 continues

	All % (n)	Age >72 % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	54.2 (613)	0.898	1.01	0.80-1.26
Left side of chest	35.5 (809)	32.7 (370)	0.016	0.80	0.63-1.01
Right side of chest	5.1 (116)	5.4 (61)	0.208	1.28	0.77-2.13
Upper part of chest	6.7 (152)	5.9 (67)	0.163	0.78	0.49-1.23
Lower part of chest	9.0 (204)	9.3 (105)	0.462	1.11	0.75-1.65
All over the chest	11.8 (269)	12.5 (141)	0.374	1.12	0.79-1.59
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.4 (109)	0.875	1.02	0.70-1.49
Size of patient's palm	58.4 (1240)	56.7 (594)	0.082	0.85	0.67-1.07
Entire chest	30.9 (655)	32.9 (344)	0.078	1.18	0.92-1.52
Palpation tenderness (655)	22.3 (505)	21.3 (239)	0.129	0.85	0.64-1.11
Pain affected by movement (719)	17.0 (373)	15.5 (169)	0.073	0.80	0.59-1.09
Pain affected by breathing (692)	25.8 (573)	21.5 (236)	<0.001*	0.68	0.52-0.89

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 3 - Multivariate analyses of differences in symptoms based on previous history of ACS

	All % (n)	History of ACS % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	29.3 (856)			
Pale (565)	16.4 (386)	19.9 (140)	0.004*	1.43	1.04-1.97
Clammy (565)	8.7 (204)	6.2 (44)	0.059	0.70	0.44-1.13
Nausea (576)	27.1 (635)	24.0 (169)	0.298	0.89	0.67-1.18
Vomiting (576)	7.0 (165)	5.4 (38)	0.067	0.69	0.41-1.15
Affected breathing according to patient (596)	44.6 (1040)	49.6 (347)	0.001*	1.35	1.06-1.73
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	33.7 (248)	0.144	1.15	0.89-1.48
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	43.4 (245)	0.087	0.83	0.63-1.09
Debut					
Debut during activity (752)	22.1 (479)	20.8 (132)	0.501	1.08	0.79-1.48
Debut while resting (752)	65.5 (1419)	67.8 (431)	0.468	1.07	0.82-1.41
Debut while sleeping (752)	15.8 (342)	14.2 (90)	0.029	0.73	0.51-1.05
Sudden debut, within seconds (875)	35.7 (729)	32.7 (199)	0.380	0.91	0.69-1.19
Quick debut, within minutes (875)	35.2 (718)	36.6 (223)	0.483	1.07	0.82-1.41
Slow debut, within hours (875)	29.1 (595)	30.7 (187)	0.850	1.02	0.76-1.35
Constant pain (732)	55.5 (1212)	54.9 (358)	0.322	0.90	0.70-1.16
Fluctuating pain (732)	40.4 (883)	40.0 (261)	0.837	1.02	0.79-1.31
Pain aggravating over time (732)	10.8 (237)	12.0 (78)	0.122	1.26	0.85-1.88
Pain in other parts of the body (1197)					
Head	2.5 (43)	2.0 (10)	–	–	–
Throat	10.3 (177)	8.8 (45)	0.683	0.92	0.56-1.50
Jaw	5.3 (92)	5.3 (27)	–	–	–
Neck	2.5 (43)	2.9 (15)	–	–	–
Between scapulars	2.2 (37)	1.6 (8)	–	–	–
Back	15.2 (261)	17.5 (89)	0.066	1.31	0.89-1.94
Left shoulder	8.5 (147)	9.0 (46)	0.390	1.18	0.71-1.95
Right shoulder	4.2 (72)	3.5 (18)	–	–	–
Left arm	24.0 (412)	29.4 (150)	<0.001*	1.62	1.17-2.25
Right arm	8.4 (145)	9.4 (48)	0.251	1.25	0.75-2.06
Left hand	1.0 (17)	0.2 (1)	–	–	–
Right hand	0.3 (6)	0.2 (1)	–	–	–
Stomach	7.0 (121)	6.5 (33)	0.275	0.78	0.44-1.38
Left leg	1.7 (29)	1.0 (5)	–	–	–
Right leg	1.4 (24)	0.6 (3)	–	–	–
No other pain	39.3 (676)	35.9 (183)	0.005*	0.72	0.53-0.97
Pain quality (1175)					
Band-shaped	3.3 (58)	3.0 (15)	–	–	–
Burning	4.4 (76)	4.3 (22)	–	–	–
Stabbing	9.7 (169)	10.7 (54)	0.399	1.16	0.72-1.86
Cramping	8.7 (151)	6.1 (31)	0.078	0.68	0.39-1.19
Dull pain	13.9 (242)	13.6 (69)	0.582	0.91	0.60-1.38
Feels like something is on the chest	0.7 (12)	0.4 (2)	–	–	–
Discomfort	10.2 (178)	9.7 (49)	0.596	0.90	0.56-1.45
Tingling/Stinging	5.7 (99)	5.9 (30)	–	–	–
Swaying	1.7 (30)	2.0 (10)	–	–	–
Pressuring	57.9 (1008)	58.3 (295)	0.985	1.00	0.75-1.33
Heaviness	1.0 (17)	0.8 (4)	–	–	–
Aching	2.4 (41)	3.0 (15)	–	–	–

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 3 continues

	All % (n)	History of ACS % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	55.4 (377)	0.202	1.13	0.88-1.44
Left side of chest	35.5 (809)	36.0 (245)	0.532	1.06	0.82-1.37
Right side of chest	5.1 (116)	3.5 (24)	0.008*	0.52	0.28-0.98
Upper part of chest	6.7 (152)	5.7 (39)	0.639	0.91	0.54-1.52
Lower part of chest	9.0 (204)	7.2 (49)	0.061	0.71	0.45-1.13
All over the chest	11.8 (269)	11.3 (77)	0.531	0.91	0.62-1.33
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.1 (63)	0.746	0.94	0.62-1.44
Size of patient's palm	58.4 (1240)	60.0 (374)	0.207	1.13	0.87-1.47
Entire chest	30.9 (655)	29.9 (186)	0.259	0.88	0.67-1.16
Palpation tenderness (655)	22.3 (505)	21.6 (146)	0.860	0.98	0.72-1.32
Pain affected by movement (719)	17.0 (373)	15.9 (105)	0.729	0.95	0.68-1.34
Pain affected by breathing (692)	25.8 (573)	20.9 (139)	0.012	0.74	0.55-1.00

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 4 - Multivariate analyses of differences in symptoms based on previous history of diabetes mellitus

	All % (n)	History of DM % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	19.8 (578)			
Pale (565)	16.4 (386)	17.1 (81)	0.611	0.93	0.64-1.34
Clammy (565)	8.7 (204)	7.8 (37)	0.712	0.93	0.56-1.53
Nausea (576)	27.1 (635)	28.9 (137)	0.064	1.24	0.91-1.68
Vomiting (576)	7.0 (165)	7.4 (35)	0.527	1.13	0.67-1.91
Affected breathing according to patient (596)	44.6 (1040)	49.0 (229)	0.045	1.23	0.94-1.62
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	39.8 (197)	<0.001*	1.53	1.16-2.02
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	50.4 (195)	0.018	1.31	0.97-1.77
Debut					
Debut during activity (752)	22.1 (479)	14.7 (64)	<0.001*	0.54	0.37-0.81
Debut while resting (752)	65.5 (1419)	71.3 (310)	0.007*	1.38	1.01-1.88
Debut while sleeping (752)	15.8 (342)	16.6 (72)	0.702	1.05	0.72-1.54
Sudden debut, within seconds (875)	35.7 (729)	33.0 (136)	0.503	0.92	0.67-1.25
Quick debut, within minutes (875)	35.2 (718)	36.2 (149)	0.933	1.01	0.74-1.36
Slow debut, within hours (875)	29.1 (595)	30.8 (127)	0.540	1.07	0.78-1.47
Constant pain (732)	55.5 (1212)	59.8 (266)	0.084	1.21	0.91-1.60
Fluctuating pain (732)	40.4 (883)	34.8 (155)	0.014	0.75	0.56-1.01
Pain aggravating over time (732)	10.8 (237)	11.5 (51)	0.583	1.09	0.70-1.71
Pain in other parts of the body (1197)					
Head	2.5 (43)	2.3 (8)	–	–	–
Throat	10.3 (177)	9.1 (32)	0.759	0.93	0.54-1.61
Jaw	5.3 (92)	4.5 (16)	–	–	–
Neck	2.5 (43)	3.4 (12)	–	–	–
Between scapulars	2.2 (37)	1.4 (5)	–	–	–
Back	15.2 (261)	17.8 (63)	0.163	1.25	0.82-1.91
Left shoulder	8.5 (147)	9.1 (32)	0.602	1.11	0.64-1.93
Right shoulder	4.2 (72)	5.4 (19)	–	–	–
Left arm	24.0 (412)	28.0 (99)	0.137	1.23	0.85-1.75
Right arm	8.4 (145)	11.0 (39)	0.094	1.40	0.83-2.37
Left hand	1.0 (17)	0.8 (3)	–	–	–
Right hand	0.3 (6)	0.6 (2)	–	–	–
Stomach	7.0 (121)	8.2 (29)	0.280	1.27	0.71-2.29
Left leg	1.7 (29)	2.8 (10)	–	–	–
Right leg	1.4 (24)	2.8 (10)	–	–	–
No other pain	39.3 (676)	35.4 (125)	0.081	0.80	0.57-1.11
Pain quality (1175)					
Band-shaped	3.3 (58)	2.2 (8)	–	–	–
Burning	4.4 (76)	5.8 (21)	–	–	–
Stabbing	9.7 (169)	10.2 (37)	0.663	1.09	0.65-1.83
Cramping	8.7 (151)	8.0 (29)	0.926	1.02	0.57-1.80
Dull pain	13.9 (242)	15.7 (57)	0.302	1.18	0.77-1.83
Feels like something is on the chest	0.7 (12)	0.0 (0)	–	–	–
Discomfort	10.2 (178)	9.9 (36)	0.853	0.96	0.57-1.61
Tingling/Stinging	5.7 (99)	5.5 (20)	–	–	–
Swaying	1.7 (30)	1.4 (5)	–	–	–
Pressuring	57.9 (1008)	58.0 (211)	0.858	0.97	0.71-1.33
Heaviness	1.0 (17)	0.5 (2)	–	–	–
Aching	2.4 (41)	2.7 (10)	–	–	–

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 4 continues

	All % (n)	History of DM % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	55.3 (255)	0.660	1.04	0.79-1.38
Left side of chest	35.5 (809)	34.3 (461)	0.729	0.96	0.72-1.28
Right side of chest	5.1 (116)	5.9 (27)	0.229	1.32	0.72-2.40
Upper part of chest	6.7 (152)	5.2 (24)	0.250	0.76	0.42-1.39
Lower part of chest	9.0 (204)	8.9 (41)	0.734	1.06	0.65-1.72
All over the chest	11.8 (269)	12.4 (57)	0.706	1.06	0.70-1.61
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	7.0 (30)	0.010	0.58	0.34-1.00
Size of patient's palm	58.4 (1240)	58.7 (252)	0.888	1.01	0.76-1.35
Entire chest	30.9 (655)	34.3 (147)	0.119	1.20	0.88-1.62
Palpation tenderness (655)	22.3 (505)	25.4 (115)	0.019	1.34	0.97-1.85
Pain affected by movement (719)	17.0 (373)	17.1 (76)	0.540	1.09	0.75-1.58
Pain affected by breathing (692)	25.8 (573)	24.3 (109)	0.753	1.04	0.75-1.43

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

DM = Diabetes mellitus

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract		
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found		
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		
Objectives	3	State specific objectives, including any prespecified hypotheses		
Methods				
Study design	4	Present key elements of study design early in the paper		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants		
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4	Previous publication describing the cohort and data collection in detail.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Previous publication describing the cohort and data collection in detail.
Bias	9	Describe any efforts to address potential sources of bias	Previous publication describing the cohort and data collection in detail.
Study size	10	Explain how the study size was arrived at	Previous publication describing the cohort and data collection in detail.

Continued on next page

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Previous publication describing the cohort and data collection in detail.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	Previous publication describing the cohort and data collection in detail.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Previous publication describing the cohort and data collection in detail.
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Previous publication

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

			describing the cohort and data collection in detail.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	previous publication describing the cohort and data collection in detail.
		(b) Indicate number of participants with missing data for each variable of interest	Supplemental Material 1-4
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Supplemental Material 1-4 and Figure 1-
		(*b*) Report category boundaries when continuous variables were categorized	previous publication describing the cohort and data collection in detail.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-046332 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES). Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

	period

Continued on next page

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . d by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

Clinical presentation in EMS patients with acute chest pain in relation to sex, age and medical history – prospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-054622.R1
Article Type:	Original research
Date Submitted by the Author:	12-Jan-2022
Complete List of Authors:	Wibring, Kristoffer; University of Gothenburg; Halland County, 1Department of Ambulance and Prehospital Care Lingman, Markus; University of Gothenburg, Department of Molecular; Halland County, Halland hospital Herlitz, Johan; University of Borås Pettersson, Helena; Halland County, Department of Ambulance and Prehospital Care Lerjebo, Anette; Halland County, Department of Ambulance and Prehospital Care Bång , Angela; University of Gothenburg
Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	ACCIDENT & EMERGENCY MEDICINE, Myocardial infarction < CARDIOLOGY, General diabetes < DIABETES & ENDOCRINOLOGY, Cardiology < INTERNAL MEDICINE

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Clinical presentation in EMS patients with acute chest pain in relation to sex, age and medical history – prospective cohort study

Authors
Kristoffer Wibring[1, 2] kristoffer.wibring@gu.se
Markus Lingman[3, 4] markus.lingman@regionhalland.se
Johan Herlitz[5] johan.herlitz@hb.se
Helena Pettersson[1] helena.pettersson@regionhalland.se
Anette Lerjebo[1] anette.lerjebo@regionhalland.se
Angela Bång[2] angela.bang@gu.se

1. Department of Ambulance and Prehospital Care, Region Halland, Sweden
2. Institute of Health and Care Sciences, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden
3. Department of Molecular and Clinical Medicine/Cardiology, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden
4. Department of Development, Halland Hospital, Halmstad, Sweden
5. The Prehospital Research Center Western Sweden, University of Borås, Borås, Sweden.

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and the interpretation discussed.

Corresponding author
Kristoffer Wibring
Ambulanssjukvården Region Halland
Varlabergsvägen 29
434 39 Kungsbacka
E-mail: kristoffer.wibring@gu.se
Phone: 0046701757679

Word count: 2793

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

ABSTRACT

Objective: To investigate how various aspects of the symptom chest pain and associated symptoms are related to age, sex, and previous history when adjusting for a final diagnosis of acute myocardial infarction.

Design: Prospective observational cohort study.

Setting: Two-centre study in a Swedish county EMS organisation.

Participants: Unselected inclusion of 2,917 patients with chest pain cared for by the EMS during 2018 due to chest pain.

Data analysis: Multivariate analysis on the association between symptom characteristics and patients' sex, age and previous medical history.

Results: Symptomology in patients assessed by the EMS due to acute chest pain varied with sex and age, and also with previous medical history. Women suffered more often from nausea and pain in throat or back. Their pain was more often affected by palpation or movement. Older patients more often described pain onset while sleeping and that the onset of symptoms was slow, over hours rather than minutes. They were less likely to report pain in other parts of their body than their chest. They were to a lesser extent pale or nauseous. These differences were present regardless of whether the symptoms were caused by AMI or not.

Conclusions: A number of aspects of the symptom chest pain appear to differ in relation to age, sex and previous history regardless of whether the chest pain was caused by a myocardial infarction. Furthermore, some symptoms that have been shown to differ based on patient characteristics such as age, sex and previous medical history in acute myocardial infarction also appear to differ in unselected cases of chest pain regardless of the final diagnosis. This complicates the possibility to predict the underlying aetiology in the early phase of acute chest pain based on symptoms.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Unselected inclusion of a close to complete county population of patients with chest pain cared for by the emergency medical services (EMS).
- Low rates of missing data considering the use of EMS data.
- Some variables involved high rates of missing data when compared with studies conducted in the hospital setting.
- A study conducted in only one county reduces generalisability.

Keywords

Chest Pain; Emergency Medical Services; Acute Myocardial Infarction; Signs and Symptoms; Clinical Presentation; Sex factors; Age factors

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

BACKGROUND

Chest pain is one of the most common complaints among emergency medical services (EMS) patients. About 10-15 percent of all patient-related EMS missions concern patients with chest pain [1 2] out of which about 10 percent have an acute myocardial infarction (AMI) [3].

Clinical presentation is, along with ECG and biomedical markers, one cornerstone when differentiating those with AMI from those with other causes of their chest pain [4 5]. Numerous studies have investigated whether patients' sex, age, and medical history of diabetes mellitus or previous acute coronary syndrome (ACS) are associated with differences in clinical presentation in patients diagnosed with AMI [4-7]. Even if the results vary, the general opinion is that at least age, sex and previous history of diabetes mellitus are associated with differences in symptomology at least in some patients when seeking care for AMI [4 5 8].

These factors are not solely associated with the type of symptoms that the patients experience but also with to what extent the patients delay seeking care [9 10]. They are also associated with patients' use of the EMS or if they use other means for transportation to hospital when suffering from chest pain [11].

The above-cited studies are mainly based on hospital data. Thus it is not possible to determine whether or not these findings also apply in the EMS setting. Furthermore, most of these studies only included patients diagnosed with AMI. This makes it difficult to determine whether these differences in symptomology are also valid among patients with chest pain in general, including patients without AMI. This is of clinical relevance, since we need to know whether such differences in clinical presentation associated with the factors stated should be taken into account when assessing patients with chest pain in the EMS setting. Furthermore, at the time of the EMS assessment, the EMS clinician does not know with certainty whether the patient is suffering from a myocardial infarction or not.

This study therefore investigates whether patients with chest pain, assessed in the EMS setting, differ in symptomology based on sex, age, previous history of diabetes mellitus or ACS including any type of acute myocardial infarction or unstable angina, regardless of whether their chest pain is caused by AMI or not.

Objective

To investigate how various aspects of the symptom chest pain and associated symptoms are related to age, sex, and previous history when adjusting for a final diagnosis of acute myocardial infarction.

METHODS

The study is part of the BRIAN research programme. The primary objective of the BRIAN research programme is to develop a prediction model for risk stratification of EMS patients with acute chest pain. In this study collected data is analysed further to investigate associations between sex, age, medical history and clinical presentation. Study population, data collection and clinical setting have been previously described [12-14] and are therefore summarised briefly.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Study population

In all, 3,121 EMS missions were carried out in 2018 in the county catchment area including patients ≥18 years old, with a chief complaint of chest pain according to EMS personnel. All these missions were eligible for inclusion. Patients with other symptoms suggestive of AMI, for example dyspnoea, but not reporting chest pain were excluded. After excluding patients declining to participate and patients who were lost to follow-up, 2,917 EMS missions remained.

Healthcare system

The county of Halland covers an area of 5,500 km^2 and had 329,000 inhabitants in 2018. These are served by two emergency hospitals, including one with PCI capabilities. The EMS consists of eight ambulance stations with 19 ambulance vehicles. In 2018, a total of 30,672 missions were carried out by the EMS (inter-hospital site transports excluded). The EMS is staffed mainly by nurses [12].

Data collection

Each patient was tracked throughout the entire healthcare chain, from EMS mission to hospital discharge. Data on symptoms were retrieved using a novel fifteen-item questionnaire, integrated in the digital EMS medical record, filled in by the EMS personnel. The EMS medical record, and thereby also the questionnaire was available bedside and enroute by using electronic tablets. Consequently, the EMS personnel was blinded to diagnosis on hospital discharge when completing the questionnaire. The questionnaire contained items mainly focusing on the patients' pain narratives identifying onset, provocation/palliation, quality, radiation, severity etc. The questionnaire also contained items regarding nausea/vomiting, dyspnoea, paleness and clamminess.

Diagnosis of AMI on hospital discharge according to physician in charge was retrieved from the hospital medical record. AMI was defined as a diagnosis on hospital discharge including any of the following International Statistical Classification of Diseases and Related Health Problems 10-codes (ICD-10):

- I21 – Acute myocardial infarction
- I22 – Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
- I24.1 – Dressler's syndrome
- I24.8. – Other forms of acute ischemic heart disease

Diagnosis of unstable angina was not included in the definition of AMI. Data collection did not affected patient care.

Endpoint

Occurrence of the following symptoms:

- Paleness or clamminess
- Nausea or vomiting
- Dyspnoea
- Pain according to the OPQRST[15] mnemonic:
  - Onset
  - Provocation/Palliation
  - Quality
  - Region and localisation

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

- Severity
- Time (behaviour over time)

Statistical analysis

The results are presented using descriptive statistics including percentage (%), number of patients (n), mean, median, standard deviation (SD) and quartiles where appropriate.

The association between patients' sex, age, previous history of diabetes or ACS and occurrence of stated symptoms was analysed using multivariate regression. The analyses were adjusted for diagnosis of AMI at hospital discharge. Patients' age was dichotomised in the analyses, using cohort median age as cut-off. No multivariate analyses were performed if the symptom of interest occurred in fewer than 100 patients. This was to ensure that the assumptions for logistic regression analyses were not violated. P-values below 0.01 were considered statistically significant (instead of 0.05 due to multiple tests). All analyses were carried out using IBM SPSS Statistics 27.

Ethical considerations

In this study, all patients eligible for inclusion were subject to an opt-out procedure. The study was approved by the Regional Ethical Review Board in Lund (Dno 2017/212).

Patient and public involvement

Patients have not been directly involved in planning or conducting this study. The design of the questionnaire was partly based on patient narratives from a previous study within this research project[16] and other studies based on patient interviews. Furthermore, KW had personal contact with several patients who contacted him by phone or e-mail due to the opt-out procedure, both patients wanting to opt out and those who wanted to remain in the study. The results of the study will be presented directly to those patients who request this when contacting KW.

RESULTS

The median age of the cohort was 72 years old (Q25-Q75, 58-82). Sex was evenly distributed. Of EMS missions included, almost 30 % of patients had a previous history of ACS and 20 % of the patients had diabetes mellitus. The prevalence of AMI in terms of diagnosis on hospital discharge was 12 %. Diagnoses on hospital discharge varied widely. Other common diagnoses on hospital discharge were unspecified chest pain (42 %), atrial fibrillation (4 %), and heart failure (without pulmonary oedema) (2 %). The proportion of patients with AMI on hospital discharge was associated with sex and previous history of diabetes mellitus with a higher rate among men and among patients with a history of diabetes mellitus (Table 1).

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Table 1 - Incidence of diagnosis of AMI on hospital discharge			
	All % (n)	Acute myocardial infarction on hospital discharge % (n)	p-value*
All	100 (2917)	12 (335)	–
Male	50 (1465)	64 (214)	<0.001
Age > 72 years	49 (1436)	55 (183)	0.036
Previous history of ACS	29 (856)	25 (84)	0.068
Previous history of diabetes mellitus	20 (578)	26 (86)	0.004
**chi2-test* *AMI = Acute myocardial infarction; ACS = Acute coronary syndrome*			

The most common symptom characteristics were affected breathing (Table 2), pressuring pain located in the central chest about the size of a palm (Table 3) time debut less than 3 hours before EMS arrival, pain debut while resting and constant pain (Table 4), This pattern was found regardless of patients' sex, age or previous medical history (Table 2-4).

Table 2 - Clinical presentation based on sex, age and previous medical history of ACS or diabetes mellitus					
	All % (n)	Women % (n)	Age >72 % (n)	History of ACS % (n)	History of diabetes mellitus % (n)
All (number of missing)	100 (2917)	49.8 (1452)	49.2 (1436)	29.3 (856)	19.8 (578)
Pale (565)	16.4 (386)	13.5 (157)	16.7 (196)	19.9 (140)	17.1 (81)
Clammy (565)	8.7 (204)	7.4 (86)	6.4 (75)	6.2 (44)	7.8 (37)
Nausea (576)	27.1 (635)	31.3 (363)	23.2 (270)	24.0 (169)	28.9 (137)
Vomiting (576)	7.0 (165)	6.9 (80)	6.3 (74)	5.4 (38)	7.4 (35)
Affected breathing according to patient (596)	44.6 (1040)	46.8 (537)	44.2 (514)	49.6 (347)	49.0 (229)

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Table 3 - Pain narrative based on sex, age and previous medical history of ACS or diabetes mellitus					
	All % (n)	Women % (n)	Age >72 % (n)	History of ACS % (n)	History of diabetes mellitus % (n)
All (number of missing)	100 (2917)	49.8 (1452)	49.2 (1436)	29.3 (856)	19.8 (578)
Pain in other parts of the body (1197)					
Head	2.5 (43)	3.3 (29)	1.8 (15)	2.0 (10)	2.3 (8)
Throat	10.3 (177)	13.3 (117)	8.6 (73)	8.8 (45)	9.1 (32)
Jaw	5.3 (92)	5.8 (51)	3.8 (32)	5.3 (27)	4.5 (16)
Neck	2.5 (43)	3.4 (30)	2.5 (21)	2.9 (15)	3.4 (12)
Between scapulars	2.2 (37)	2.7 (24)	1.5 (13)	1.6 (8)	1.4 (5)
Back	15.2 (261)	19.5 (171)	16.4 (139)	17.5 (89)	17.8 (63)
Left shoulder	8.5 (147)	9.0 (79)	7.5 (64)	9.0 (46)	9.1 (32)
Right shoulder	4.2 (72)	4.6 (40)	4.0 (34)	3.5 (18)	5.4 (19)
Left arm	24.0 (412)	23.0 (202)	23.1 (196)	29.4 (150)	28.0 (99)
Right arm	8.4 (145)	8.8 (77)	8.5 (72)	9.4 (48)	11.0 (39)
Left hand	1.0 (17)	0.7 (6)	0.4 (3)	0.2 (1)	0.8 (3)
Right hand	0.3 (6)	0.1 (1)	0.2 (2)	0.2 (1)	0.6 (2)
Stomach	7.0 (121)	7.1 (62)	7.5 (64)	6.5 (33)	8.2 (29)
Left leg	1.7 (29)	1.8 (16)	1.8 (15)	1.0 (5)	2.8 (10)
Right leg	1.4 (24)	1.4 (12)	1.4 (12)	0.6 (3)	2.8 (10)
No other pain	39.3 (676)	34.2 (301)	41.3 (351)	35.9 (183)	35.4 (125)
Pain quality (1175)					
Band-shaped	3.3 (58)	3.7 (32)	3.4 (29)	3.0 (15)	2.2 (8)
Burning	4.4 (76)	5.4 (46)	3.5 (30)	4.3 (22)	5.8 (21)
Stabbing	9.7 (169)	8.3 (71)	8.8 (75)	10.7 (54)	10.2 (37)
Cramping	8.7 (151)	9.1 (78)	6.7 (57)	6.1 (31)	8.0 (29)
Dull pain	13.9 (242)	13.6 (116)	14.6 (124)	13.6 (69)	15.7 (57)
Fells like something is on the chest	0.7 (12)	0.6 (5)	0.6 (5)	0.4 (2)	0.0 (0)
Discomfort	10.2 (178)	10.8 (92)	10.6 (90)	9.7 (49)	9.9 (36)
Tingling/Stinging	5.7 (99)	5.1 (44)	4.9 (42)	5.9 (30)	5.5 (20)
Swaying	1.7 (30)	1.6 (14)	1.5 (13)	2.0 (10)	1.4 (5)
Pressuring	57.9 (1008)	59.6 (510)	60.0 (510)	58.3 (295)	58.0 (211)
Heaviness	1.0 (17)	1.3 (11)	1.1 (9)	0.8 (4)	0.5 (2)
Aching	2.4 (41)	2.1 (18)	2.4 (20)	3.0 (15)	2.7 (10)
Chest pain localisation (640)					

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Central pain	53.4 (1215)	53.3 (599)	54.2 (613)	55.4 (377)	55.3 (255)
Left side of chest	35.5 (809)	32.0 (359)	32.7 (370)	36.0 (245)	34.3 (461)
Right side of chest	5.1 (116)	4.8 (54)	5.4 (61)	3.5 (24)	5.9 (27)
Upper part of chest	6.7 (152)	7.9 (89)	5.9 (67)	5.7 (39)	5.2 (24)
Lower part of chest	9.0 (204)	11.1 (125)	9.3 (105)	7.2 (49)	8.9 (41)
All over the chest	11.8 (269)	12.6 (141)	12.5 (141)	11.3 (77)	12.4 (57)
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.2 (107)	10.4 (109)	10.1 (63)	7.0 (30)
Size of patient's palm	58.4 (1240)	57.4 (601)	56.7 (594)	60.0 (374)	58.7 (252)
Entire chest	30.9 (655)	32.4 (339)	32.9 (344)	29.9 (186)	34.3 (147)
Pain affected by movement (719)	17.0 (373)	19.6 (211)	15.5 (169)	15.9 (105)	17.1 (76)
Pain affected by breathing (692)	25.8 (573)	26.6 (292)	21.5 (236)	20.9 (139)	24.3 (109)
Palpation tenderness (655)	22.3 (505)	27.1 (302)	21.3 (239)	21.6 (146)	25.4 (115)
Pain intensity according to Numeric Rating Scale >5 (415)	32.1 (803)	33.6 (1228)	30.1 (372)	33.7 (248)	39.8 (197)

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Table 4 - Time aspect of pain based on sex, age and previous medical history of ACS or diabetes mellitus					
	All % (n)	Women % (n)	Age >72 % (n)	History of ACS % (n)	History of diabetes mellitus % (n)
All (number of missing)	100 (2917)	49.8 (1452)	49.2 (1436)	29.3 (856)	19.8 (578)
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	46.5 (442)	47.3 (445)	43.4 (245)	50.4 (195)
Debut					
Debut during activity (752)	22.1 (479)	20.5 (217)	17.8 (191)	20.8 (132)	14.7 (64)
Debut while resting (752)	65.5 (1419)	67.4 (714)	67.6 (725)	67.8 (431)	71.3 (310)
Debut while sleeping (752)	15.8 (342)	15.6 (165)	18.1 (194)	14.2 (90)	16.6 (72)
Sudden debut, within seconds (875)	35.7 (729)	36.1 (361)	31.4 (313)	32.7 (199)	33.0 (136)
Quick debut, within minutes (875)	35.2 (718)	33.2 (332)	35.8 (357)	36.6 (223)	36.2 (149)
Slow debut, within hours (875)	29.1 (595)	30.8 (308)	32.7 (326)	30.7 (187)	30.8 (127)
Constant pain (732)	55.5 (1212)	53.3 (574)	57.1 (615)	54.9 (358)	59.8 (266)
Fluctuating pain (732)	40.4 (883)	42.3 (456)	40.0 (431)	40.0 (261)	34.8 (155)
Pain aggravating over time (732)	10.8 (237)	10.8 (116)	9.4 (101)	12.0 (78)	11.5 (51)

Women more often suffered from nausea and pain in the throat or back. They also more commonly localised their pain to the lower part of the chest. Their pain was more often affected by palpation or movement. They were more likely to report pain in other parts of the body than their chest. They were less often pale and had a lower incidence of left-sided chest pain (Figure 1).

Older patients more often described pain onset while sleeping and that the onset of symptoms was slow, over hours rather than minutes. They were less likely to report pain in other parts of their body than the chest. They were to a lesser extent pale or nauseous. They rated their pain intensity lower and their chest pain onset occurred less often during activity. Their breathing movements more seldom affected their pain (Figure 2).

Patients with a previous history of ACS were more often pale and experienced their breathing as affected. They more often had pain in their left arm. They reported right-sided chest pain to a lesser extent, and they felt pain in any other part of their body than in the chest to a greater extent (Figure 3).

Regarding patients with a previous history of diabetes mellitus, their pain more often started while they were resting and they rated their pain intensity as higher. Their pain was less likely to start during activity (Figure 4).

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

In total, patients' sex was associated with the occurrence of nine different types of symptoms and the same was true for patients' age. Previous history of ACS or diabetes mellitus were associated with the occurrence of five or three different symptoms respectively (Supplemental material 1-4). When comparing these analyses based on age, sex and previous history to analyses of association between symptoms and AMI, i.e. AMI predictors, (Supplement 5) one can observe that several symptoms associated with sex, age and previous history are not associated with AMI and vice versa.

DISCUSSION

Our study shows that the prevalence of numerous symptoms in EMS patients with chest pain is associated most of all with sex and age, but also with the patient's previous medical history. This is observed regardless of whether the patient's chest pain is caused by an acute myocardial infarction or not. To the best of our knowledge, this is the first study reporting results on symptomology differences in acute chest pain patients based on sex, age and previous medical history, when simultaneously adjusting for AMI incidence.

Sex, age and previous medical history seem not only to be associated with how an AMI is experienced [4 5 8], but also with how acute chest pain and related symptoms are perceived in general. This finding implies that previously reported differences in clinical presentation based on patients' characteristics may be a general observation in acute chest pain patients and not necessarily associated with an AMI diagnosis. This finding further complicates the already challenging task of assessing patients with acute chest pain. Especially since these differences in clinical presentation are at hand both for symptoms associated with AMI and for symptoms with no such association.

These differences also complicate the use of symptom-based chest pain prediction tools not considering, primarily, age and sex, but also medical history. Since our findings indicate that the accuracy of a prediction tool may differ depending on these patient-related factors. This applies particularly to criteria-based assessment tools not considering patient sex or age such as Rapid Emergency Triage and Treatment System (RETTS) [17 18] or Manchester Triage System [19]. The use of more dynamic and advanced prediction models using statistical methods to adjust for these confounding factors may be one way to improve prediction accuracy and make it more valid for the complete chest pain population.

Sederholm et. al.[20] report that women with AMI experience pain in their back and throat more often than men and are more commonly nauseous. Lichtman et al. [21] and Kirherberger et al. [22] also found that women more often than men are nauseous. Araújo et al. [23] state that women with AMI are more likely to experience referred pain compared to men. Coventry et al. [24] found that women with AMI more often experience nausea and back pain. In our study, we also found an increased incidence of these symptoms among women, but in our material this difference was present regardless of whether their chest pain was caused by AMI or not. Thus these differences in symptomology are problematic when used for risk assessment since they are not necessarily associated with the incidence of AMI but rather with the patient's sex. This strengthens our notion that previous reported differences between men and women in AMI presentation are not necessarily associated with AMI but sometimes rather by sex itself.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Previous research report that older patients more often report atypical or accompanying AMI symptoms [25]. In our study older patients differed from younger ones regarding nine different aspects of their clinical presentation. For example they more often had a slower debut (hours rather than seconds or minutes), their pain was less intense and it more seldom started during activity. All these aspects can be considered atypical of AMI. On the other hand older patients less often reported accompanying or atypical symptoms such as nausea and pain affected to breathing. Altogether, the relationship between age and the clinical presentation of patients with chest pain seem to be complex both for patients with and without AMI. This strengthens the need of great humbleness when assessing older patients with chest pain, especially since age itself is a strong risk factor for AMI [8].

Kirchberger et al. [26] state that patients undergoing their second AMI more often have dyspnoea compared to patients having their first AMI. In our study, patients with a history of ACS, were more often dyspnoeic, also in cases where the chest pain were not caused by an AMI. One can reason that the higher rate of dyspnoea for patients who experience their second AMI reported by Kirchberger et al. [26] is more commonly at hand for patients with a previous history of ACS in general and is not necessarily associated with their reinfarction. Maybe this could be explained by the higher incidence of heart failure among patients with previous ACS.

Regarding patients with diabetes mellitus suffering from AMI, Manistamara et al. [27] reported that these patients tend to rate their pain as less intense compared to non-diabetic patients. In contrast, we found that patients with diabetes mellitus in general rate their chest pain as higher, regardless of AMI occurrence. This contradictory results between AMI-patients and unselected chest pain patients highlight the difficulties regarding how to value pain intensity in patients with diabetes mellitus and symptoms suggestive of AMI.

Our results strengthen the notion that the diagnostic evaluation of chest pain characteristics has limitations as a diagnostic tool and should be used with great caution [5]. The clinical presentation of patients with chest pain seems to be associated with both age, sex and previous medical history in a very complicated manner, both for patients with and without AMI as the cause of their chest pain. Altogether, clinicians should be careful when letting patients' characteristics influence how they evaluate patients' symptoms [6].

Strengths and limitations

This study is strengthened by the close to complete and unselected inclusion of EMS missions concerning patients with chest pain, which improves generalisability. However, the use of data from a single county negatively affects the external validity.

The results are based on sub-analyses of previously collected data and the absolute differences observed are sometimes small. Clinicians should therefore be careful not to draw over-strict conclusions on how these results should affect clinical practice.

Some of the variables included entail rather high rates of missing information. Data collection in the EMS setting is known to be challenging and often involves higher rates of missing data than the in-hospital setting [28 29]. Considering this, the rates of missing information in this

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

study are to be regarded as low and therefore data may be looked upon as comparatively comprehensive.

In part, the differences in clinical presentation described in this study may be explained by an uneven distribution of diagnoses other than AMI at hospital discharge. To adjust for more diagnoses than AMI at hospital discharge, a larger study sample is needed to ensure statistical robustness. However, the fact that differences in clinical presentation are explained by other diagnoses at hospital discharge does not change the implication of our results. Thus clinicians should be careful not to allow patients' characteristics to influence how they evaluate patients' symptoms in cases of acute chest pain.

CONCLUSIONS

A number of aspects of the symptom chest pain appear to differ in relation to age, sex and previous history regardless of whether the chest pain was caused by a myocardial infarction. Furthermore, some symptoms that have been shown to differ based on patient characteristics such as age, sex and previous medical history in acute myocardial infarction also appear to differ in unselected cases of chest pain regardless of the final diagnosis. This complicates the possibility to predict the underlying aetiology in the early phase of acute chest pain.

List of abbreviations

ACS – acute coronary syndrome
AMI – acute myocardial infarction
EMS – emergency medical services
NRS – numeric rating scale
RETTS – Rapid Emergency Triage and Treatment System

Author contributions

KW, ML, JH, AL, HP and AB designed the study. KW, ML, JH, and AB planned the data collection. Data analysis was carried out by KW, AL and HP. KW, ML, JH, AL, HP and AB contributed in writing the manuscript. All authors read and approved the final manuscript.

Funding

This study has been funded by the Department of Ambulance and Prehospital Care, Region Halland and the Scientific Council of Region Halland (HALLAND-209901). The funding bodies had no role in the design, conduct, interpretation or writing of the report on this research.

Competing interests

The authors declare that they have no competing interests.

Patient consent for publication

Not required.

Ethics approval

The study was approved by the Regional Ethical Review Board in Lund (Dno 2017/212). All patients were given the opportunity to withdraw their participation using an opt-out procedure.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Data availability statement

The datasets generated and analysed during the current study are not publicly available due the integrity of patient privacy but are available from the corresponding author on reasonable request and if approved by the Regional Ethical Review Board in Lund.

Acknowledgements

We want to thank the following persons:

- The EMS personnel of Region Halland for their help with data collection.
- Thomas Thorsson, Vinh Norberg Nguyen and Sasa Pejicic for data extraction.
- Anders Holmén and Ulf Strömberg for statistical support.

Tables, figures and supplemental material

Figure 1 - Differences in clinical presentation based on sex
Figure 2 - Differences in clinical presentation based on age
Figure 3 - Differences in clinical presentation based on history of ACS
Figure 4 - Differences in clinical presentation based on history of diabetes mellitus
Table 1 - Incidence of diagnosis of AMI on hospital discharge
Table 2 – Clinical presentation based on sex, age and previous medical history of ACS or diabetes mellitus
Table 3 – Pain narrative based on sex, age and previous medical history of ACS or diabetes mellitus
Table 4 – Time aspect of pain based on sex, age and previous medical history of ACS or diabetes mellitus
Supplemental material 1 - Multivariate analyses of differences in symptoms prevalence based on sex
Supplemental material 2 - Multivariate analyses of differences in symptoms prevalence based on age
Supplemental material 3 - Multivariate analyses of differences in symptoms prevalence based on previous history of ACS
Supplemental material 4 - Multivariate analyses of differences in symptoms prevalence based on previous history of diabetes mellitus
Supplement material 5 - Differences in symptoms based on diagnosis of AMI on hospital discharge

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

REFERENCES

1. Clawson J, Olola C, Heward A, et al. The Medical Priority Dispatch System's ability to predict cardiac arrest outcomes and high acuity pre-hospital alerts in chest pain patients presenting to 9-9-9. *Resuscitation* 2008;78(3):298-306. doi: 10.1016/j.resuscitation.2008.03.229
2. Pedersen CK, Stengaard C, Friesgaard K, et al. Chest pain in the ambulance; prevalence, causes and outcome - a retrospective cohort study. *Scand J Trauma Resusc Emerg Med* 2019;27(1):84. doi: 10.1186/s13049-019-0659-6 [published Online First: 2019/08/29]
3. Rawshani A, Larsson A, Gelang C, et al. Characteristics and outcome among patients who dial for the EMS due to chest pain. *International Journal of Cardiology* 2014;176(3):859-65. doi: 10.1016/j.ijcard.2014.08.004
4. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39(2):119-77. doi: 10.1093/eurheartj/ehx393
5. Collet JP, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2020 doi: 10.1093/eurheartj/ehaa575 [published Online First: 2020/08/29]
6. Thuresson M, Jarlöv MB, Lindahl B, et al. Symptoms and type of symptom onset in acute coronary syndrome in relation to ST elevation, sex, age, and a history of diabetes. *Am Heart J* 2005;150(2):234-42. doi: 10.1016/j.ahj.2004.08.035
7. Strömbäck U, Engström Å, Lundqvist R, et al. The second myocardial infarction: Is there any difference in symptoms and prehospital delay compared to the first myocardial infarction? *Eur J Cardiovasc Nurs* 2018;17(7):652-59. doi: 10.1177/1474515118777391 [published Online First: 2018/05/11]
8. Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021:CIR0000000000001030. doi: 10.1161/CIR.0000000000001030 [published Online First: 20211028]
9. Moser DK, Kimble LP, Alberts MJ, et al. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Heart Association Council on cardiovascular nursing and stroke council. *Circulation* 2006;114(2):168-82. doi: 10.1161/CIRCULATIONAHA.106.176040 [published Online First: 2006/06/26]
10. Wechkunanukul K, Grantham H, Clark RA. Global review of delay time in seeking medical care for chest pain: An integrative literature review. *Aust Crit Care* 2017;30(1):13-20. doi: 10.1016/j.aucc.2016.04.002 [published Online First: 2016/04/23]
11. Thang ND, Karlson BW, Bergman B, et al. Characteristics of and outcome for patients with chest pain in relation to transport by the emergency medical services in a 20-year perspective. *American Journal of Emergency Medicine* 2012;30(9):1788-95. doi: 10.1016/j.ajem.2012.02.014
12. Wibring K, Lingman M, Herlitz J, et al. Prehospital stratification in acute chest pain patient into high risk and low risk by emergency medical service: a prospective cohort study. *BMJ Open* 2021;11(4):e044938. doi: 10.1136/bmjopen-2020-044938 [published Online First: 2021/04/15]

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

13. Wibring K, Lingman M, Herlitz J, et al. Development of a prehospital prediction model for risk stratification of patients with chest pain. *Am J Emerg Med* 2021;51:26-31. doi: 10.1016/j.ajem.2021.09.079 [published Online First: 20211009]
14. Wibring K, Lingman M, Herlitz J, et al. Guideline adherence among prehospital emergency nurses when caring for patients with chest pain: a prospective cohort study. *Scand J Trauma Resusc Emerg Med* 2021;29(1):157. doi: 10.1186/s13049-021-00972-5 [published Online First: 20211030]
15. Eloge J, Napier TC, Dantz B. OPQRST(U): Integrating substance use disorders or "Use" into the medical history. *Subst Abus* 2018;39(4):505-08. doi: 10.1080/08897077.2018.1469104 [published Online First: 2018/08/17]
16. Wibring K, Herlitz J, Lingman M, et al. Symptom description in patients with chest pain - a qualitative analysis of emergency medical calls involving high-risk conditions. *J Clin Nurs* 2019 doi: 10.1111/jocn.14867 [published Online First: 2019/04/02]
17. Magnusson C, Herlitz J, Axelsson C. Patient characteristics, triage utilisation, level of care, and outcomes in an unselected adult patient population seen by the emergency medical services: a prospective observational study. *BMC Emerg Med* 2020;20(1):7. doi: 10.1186/s12873-020-0302-x [published Online First: 2020/01/30]
18. Widgren BR, Jourak M. Medical Emergency Triage and Treatment System (METTS): a new protocol in primary triage and secondary priority decision in emergency medicine. *J Emerg Med* 2011;40(6):623-8. doi: 10.1016/j.jemermed.2008.04.003 [published Online First: 2008/10/18]
19. Nishi FA, Polak C, Cruz DALM. Sensitivity and specificity of the Manchester Triage System in risk prioritization of patients with acute myocardial infarction who present with chest pain. *Eur J Cardiovasc Nurs* 2018;17(7):660-66. doi: 10.1177/1474515118777402 [published Online First: 2018/05/11]
20. Sederholm Lawesson S, Isaksson RM, Ericsson M, et al. Gender disparities in first medical contact and delay in ST-elevation myocardial infarction: a prospective multicentre Swedish survey study. *BMJ Open* 2018;8(5):e020211. doi: 10.1136/bmjopen-2017-020211 [published Online First: 2018/05/03]
21. Lichtman JH, Leifheit EC, Safdar B, et al. Sex Differences in the Presentation and Perception of Symptoms Among Young Patients With Myocardial Infarction: Evidence from the VIRGO Study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). *Circulation* 2018;137(8):781-90. doi: 10.1161/CIRCULATIONAHA.117.031650
22. Kirchberger I, Heier M, Kuch B, et al. Sex differences in patient-reported symptoms associated with myocardial infarction (from the population-based MONICA/KORA Myocardial Infarction Registry). *Am J Cardiol* 2011;107(11):1585-9. doi: 10.1016/j.amjcard.2011.01.040 [published Online First: 20110321]
23. Araújo C, Laszczyńska O, Viana M, et al. Sex differences in presenting symptoms of acute coronary syndrome: the EPIHeart cohort study. *BMJ Open* 2018;8(2):e018798. doi: 10.1136/bmjopen-2017-018798 [published Online First: 20180223]
24. Coventry LL, Finn J, Bremner AP. Sex differences in symptom presentation in acute myocardial infarction: a systematic review and meta-analysis. *Heart Lung* 2011;40(6):477-91. doi: 10.1016/j.hrtlng.2011.05.001
25. Tisminetzky M, Gurwitz JH, Miozzo R, et al. Age Differences in the Chief Complaint Associated With a First Acute Myocardial Infarction and Patient's Care-Seeking Behavior. *Am J Med* 2020;133(9):e501-e07. doi: 10.1016/j.amjmed.2020.02.018 [published Online First: 20200318]
26. Kirchberger I, Heier M, Golüke H, et al. Mismatch of presenting symptoms at first and recurrent acute myocardial infarction. From the MONICA/KORA Myocardial

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Infarction Registry. *Eur J Prev Cardiol* 2016;23(4):377-84. doi: 10.1177/2047487315588071 [published Online First: 20150520]
27. Manistamara H, Sella YO, Apriliawan S, et al. Chest pain symptoms differences between diabetes mellitus and non-diabetes mellitus patients with acute coronary syndrome: A pilot study. *J Public Health Res* 2021;10(2) doi: 10.4081/jphr.2021.2186 [published Online First: 20210414]
28. Maurin Söderholm H, Andersson H, Andersson Hagiwara M, et al. Research challenges in prehospital care: the need for a simulation-based prehospital research laboratory. *Adv Simul (Lond)* 2019;4:3. doi: 10.1186/s41077-019-0090-0 [published Online First: 2019/02/13]
29. Dickert NW, Brown J, Cairns CB, et al. Confronting Ethical and Regulatory Challenges of Emergency Care Research With Conscious Patients. *Ann Emerg Med* 2016;67(4):538-45. doi: 10.1016/j.annemergmed.2015.10.026 [published Online First: 2015/12/18]

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

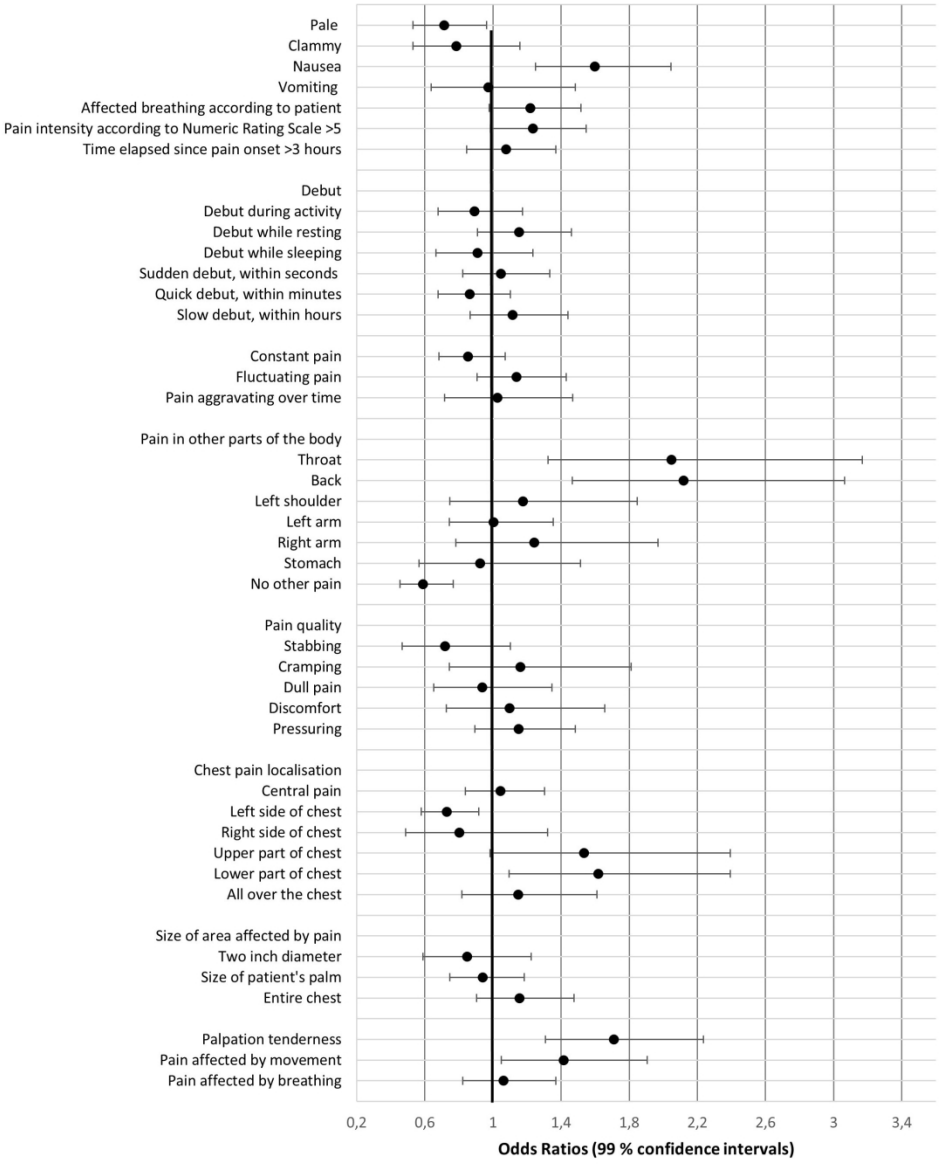

Figure 1 - Differences in clinical presentation based on sex

190x234mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

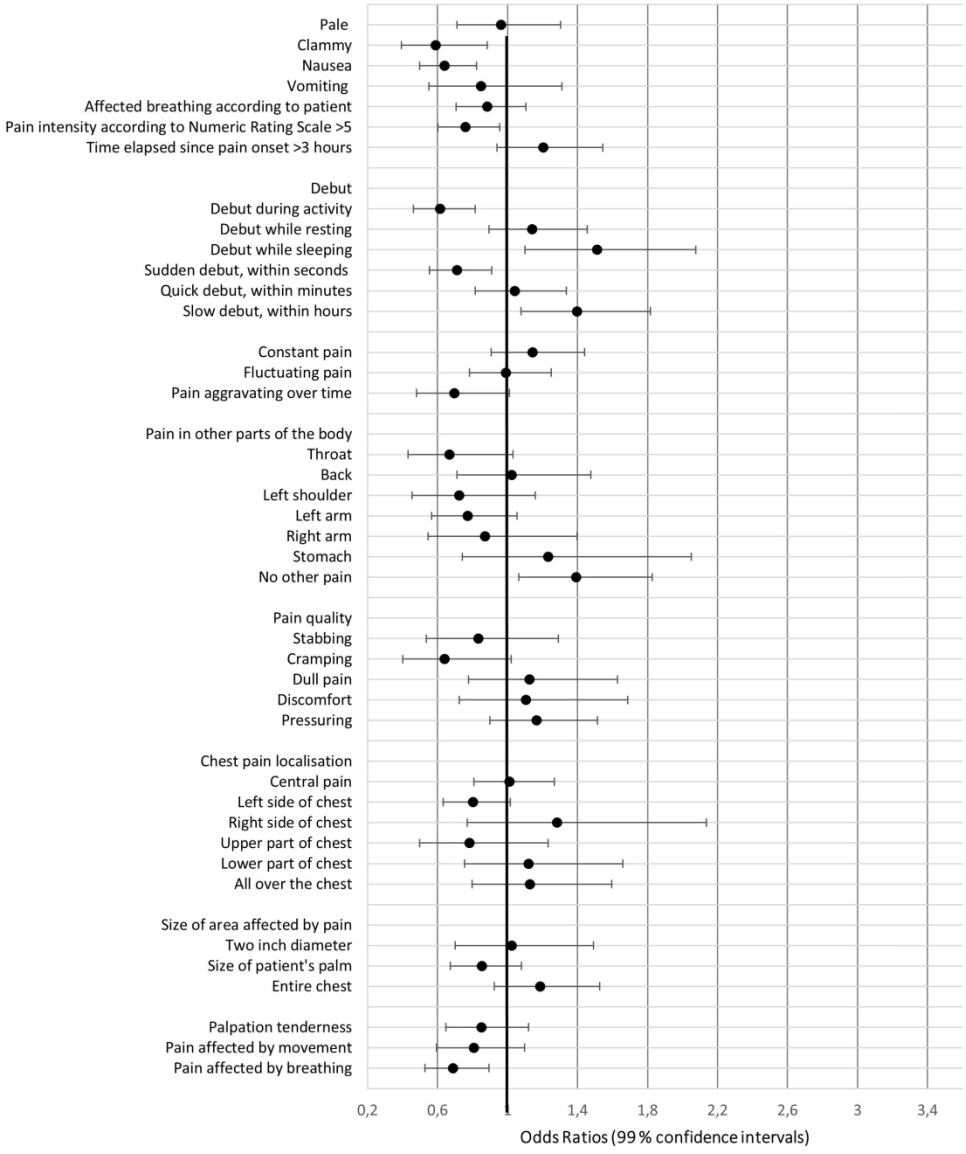

Figure 2 - Differences in clinical presentation based on age

190x223mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

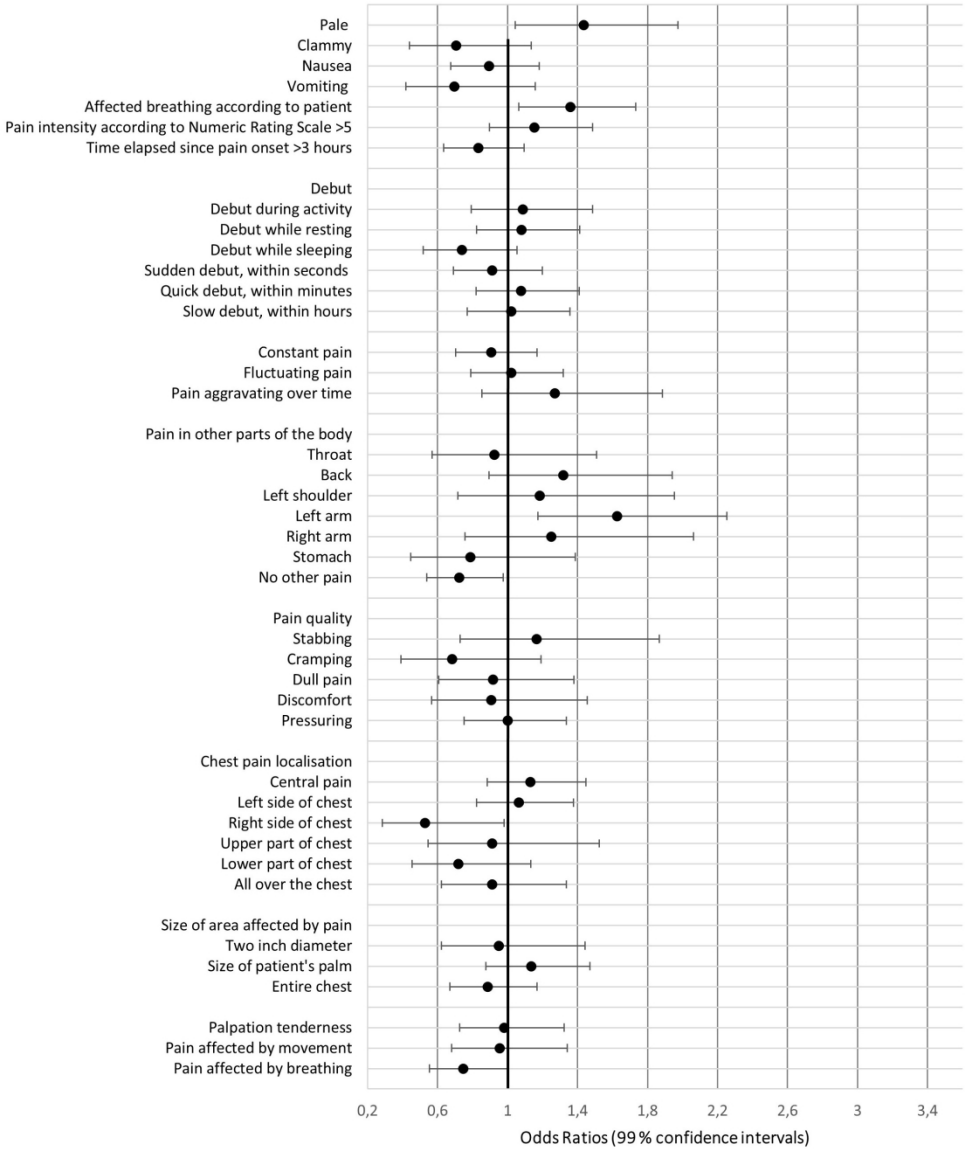

Figure 3 - Differences in clinical presentation based on history of ACS

190x221mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

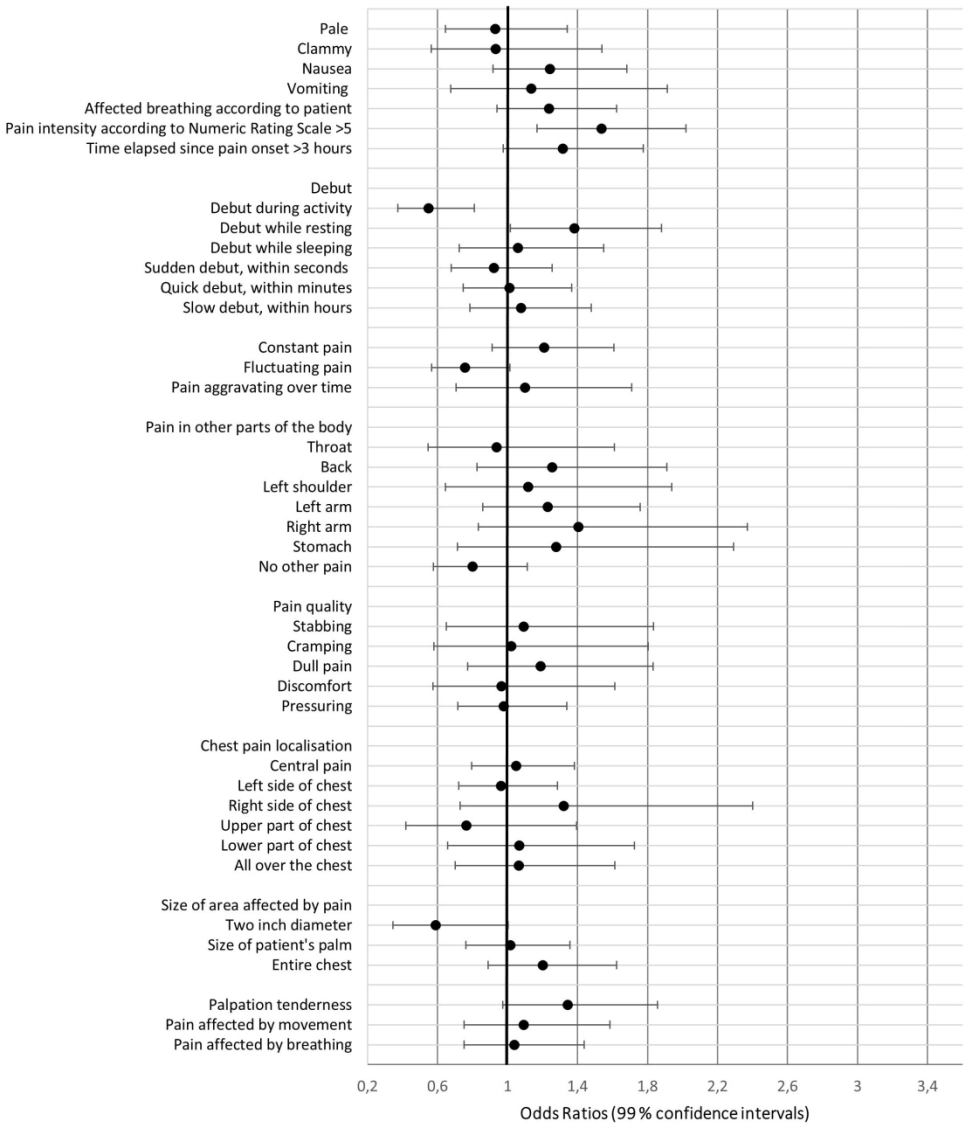

Figure 4 - Differences in clinical presentation based on history of diabetes mellitus

190x216mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Supplemental material 1 - Multivariate analyses of differences in symptoms based on sex

	All % (n)	Women % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	49.8 (1452)			
Pale (565)	16.4 (386)	13.5 (157)	0.004*	0.71	0.53-0.96
Clammy (565)	8.7 (204)	7.4 (86)	0.109	0.78	0.53-1.16
Nausea (576)	27.1 (635)	31.3 (363)	<0.001*	1.6	1.25-2.05
Vomiting (576)	7.0 (165)	6.9 (80)	0.866	0.97	0.64-1.48
Affected breathing according to patient (596)	44.6 (1040)	46.8 (537)	0.020	1.22	0.98-1.52
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	33.6 (1228)	0.016	1.23	0.99-1.55
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	46.5 (442)	0.425	1.08	0.85-1.37
Debut					
Debut during activity (752)	22.1 (479)	20.5 (217)	0.284	0.89	0.68-1.17
Debut while resting (752)	65.5 (1419)	67.4 (714)	0.125	1.15	0.91-1.46
Debut while sleeping (752)	15.8 (342)	15.6 (165)	0.411	0.91	0.67-1.23
Sudden debut, within seconds (875)	35.7 (729)	36.1 (361)	0.622	1.05	0.82-1.33
Quick debut, within minutes (875)	35.2 (718)	33.2 (332)	0.122	0.86	0.68-1.10
Slow debut, within hours (875)	29.1 (595)	30.8 (308)	0.266	1.12	0.87-1.44
Constant pain (732)	55.5 (1212)	53.3 (574)	0.072	0.85	0.68-1.07
Fluctuating pain (732)	40.4 (883)	42.3 (456)	0.145	1.14	0.91-1.43
Pain aggravating over time (732)	10.8 (237)	10.8 (116)	0.861	1.03	0.72-1.47
Pain in other parts of the body (1197)					
Head	2.5 (43)	3.3 (29)	–	–	–
Throat	10.3 (177)	13.3 (117)	<0.001*	2.05	1.32-3.17
Jaw	5.3 (92)	5.8 (51)	–	–	–
Neck	2.5 (43)	3.4 (30)	–	–	–
Between scapulars	2.2 (37)	2.7 (24)	–	–	–
Back	15.2 (261)	19.5 (171)	<0.001*	2.12	1.47-3.07
Left shoulder	8.5 (147)	9.0 (79)	0.358	1.18	0.75-1.85
Right shoulder	4.2 (72)	4.6 (40)	–	–	–
Left arm	24.0 (412)	23.0 (202)	0.974	1.00	0.74-1.35
Right arm	8.4 (145)	8.8 (77)	0.226	1.24	0.78-1.97
Left hand	1.0 (17)	0.7 (6)	–	–	–
Right hand	0.3 (6)	0.1 (1)	–	–	–
Stomach	7.0 (121)	7.1 (62)	0.685	0.93	0.57-1.52
Left leg	1.7 (29)	1.8 (16)	–	–	–
Right leg	1.4 (24)	1.4 (12)	–	–	–
No other pain	39.3 (676)	34.2 (301)	<0.001*	0.59	0.45-0.77
Pain quality (1175)					
Band-shaped	3.3 (58)	3.7 (32)	–	–	–
Burning	4.4 (76)	5.4 (46)	–	–	–
Stabbing	9.7 (169)	8.3 (71)	0.047	0.72	0.47-1.10
Cramping	8.7 (151)	9.1 (78)	0.392	1.16	0.74-1.81
Dull pain	13.9 (242)	13.6 (116)	0.646	0.94	0.65-1.35
Feels like something is on the chest	0.7 (12)	0.6 (5)	–	–	–
Discomfort	10.2 (178)	10.8 (92)	0.563	1.10	0.73-1.66
Tingling/Stinging	5.7 (99)	5.1 (44)	–	–	–
Swaying	1.7 (30)	1.6 (14)	–	–	–
Pressuring	57.9 (1008)	59.6 (510)	0.153	1.15	0.89-1.48
Heaviness	1.0 (17)	1.3 (11)	–	–	–
Aching	2.4 (41)	2.1 (18)	–	–	–

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 1 continues

	All % (n)	Women % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	53.3 (599)	0.612	1.04	0.84-1.30
Left side of chest	35.5 (809)	32.0 (359)	<0.001*	0.73	0.58-0.91
Right side of chest	5.1 (116)	4.8 (54)	0.256	0.80	0.49-1.32
Upper part of chest	6.7 (152)	7.9 (89)	0.013	1.53	0.98-2.39
Lower part of chest	9.0 (204)	11.1 (125)	0.002*	1.62	1.09-2.39
All over the chest	11.8 (269)	12.6 (141)	0.299	1.15	0.82-1.61
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.2 (107)	0.251	0.85	0.59-1.23
Size of patient's palm	58.4 (1240)	57.4 (601)	0.492	0.94	0.75-1.18
Entire chest	30.9 (655)	32.4 (339)	0.131	1.16	0.90-1.48
Palpation tenderness (655)	22.3 (505)	27.1 (302)	<0.001*	1.71	1.31-2.24
Pain affected by movement (719)	17.0 (373)	19.6 (211)	0.003*	1.41	1.05-1.91
Pain affected by breathing (692)	25.8 (573)	26.6 (292)	0.543	1.06	0.82-1.37

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Supplemental material 2 - Multivariate analyses of differences in symptoms based on age

	All % (n)	Age >72 % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	49.2 (1436)			
Pale (565)	16.4 (386)	16.7 (196)	0.745	0.96	0.71-1.30
Clammy (565)	8.7 (204)	6.4 (75)	0.001*	0.58	0.39-0.88
Nausea (576)	27.1 (635)	23.2 (270)	<0.001*	0.64	0.49-0.82
Vomiting (576)	7.0 (165)	6.3 (74)	0.331	0.84	0.55-1.31
Affected breathing according to patient (596)	44.6 (1040)	44.2 (514)	0.155	0.88	0.70-1.10
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	30.1 (372)	0.002*	0.75	0.60-0.95
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	47.3 (445)	0.053	1.20	0.94-1.54
Debut					
Debut during activity (752)	22.1 (479)	17.8 (191)	<0.001*	0.61	0.46-0.81
Debut while resting (752)	65.5 (1419)	67.6 (725)	0.164	1.14	0.89-1.45
Debut while sleeping (752)	15.8 (342)	18.1 (194)	0.001*	1.51	1.09-2.07
Sudden debut, within seconds (875)	35.7 (729)	31.4 (313)	<0.001*	0.71	0.55-0.91
Quick debut, within minutes (875)	35.2 (718)	35.8 (357)	0.666	1.04	0.81-1.33
Slow debut, within hours (875)	29.1 (595)	32.7 (326)	0.001*	1.39	1.07-1.81
Constant pain (732)	55.5 (1212)	57.1 (615)	0.136	1.14	0.90-1.44
Fluctuating pain (732)	40.4 (883)	40.0 (431)	0.911	0.99	0.78-1.25
Pain aggravating over time (732)	10.8 (237)	9.4 (101)	0.012	0.69	0.48-1.01
Pain in other parts of the body (1197)					
Head	2.5 (43)	1.8 (15)	–	–	–
Throat	10.3 (177)	8.6 (73)	0.016	0.66	0.43-1.03
Jaw	5.3 (92)	3.8 (32)	–	–	–
Neck	2.5 (43)	2.5 (21)	–	–	–
Between scapulars	2.2 (37)	1.5 (13)	–	–	–
Back	15.2 (261)	16.4 (139)	0.871	1.02	0.71-1.47
Left shoulder	8.5 (147)	7.5 (64)	0.077	0.72	0.45-1.15
Right shoulder	4.2 (72)	4.0 (34)	–	–	–
Left arm	24.0 (412)	23.1 (196)	0.032	0.77	0.56-1.05
Right arm	8.4 (145)	8.5 (72)	0.454	0.87	0.54-1.39
Left hand	1.0 (17)	0.4 (3)	–	–	–
Right hand	0.3 (6)	0.2 (2)	–	–	–
Stomach	7.0 (121)	7.5 (64)	0.290	1.23	0.74-2.05
Left leg	1.7 (29)	1.8 (15)	–	–	–
Right leg	1.4 (24)	1.4 (12)	–	–	–
No other pain	39.3 (676)	41.3 (351)	0.002*	1.39	1.06-1.82
Pain quality (1175)					
Band-shaped	3.3 (58)	3.4 (29)	–	–	–
Burning	4.4 (76)	3.5 (30)	–	–	–
Stabbing	9.7 (169)	8.8 (75)	0.280	0.83	0.53-1.29
Cramping	8.7 (151)	6.7 (57)	0.014	0.63	0.40-1.02
Dull pain	13.9 (242)	14.6 (124)	0.414	1.12	0.77-1.62
Feels like something is on the chest	0.7 (12)	0.6 (5)	–	–	–
Discomfort	10.2 (178)	10.6 (90)	0.547	1.10	0.72-1.68
Tingling/Stinging	5.7 (99)	4.9 (42)	–	–	–
Swaying	1.7 (30)	1.5 (13)	–	–	–
Pressuring	57.9 (1008)	60.0 (510)	0.129	1.16	0.89-1.51
Heaviness	1.0 (17)	1.1 (9)	–	–	–
Aching	2.4 (41)	2.4 (20)	–	–	–

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 2 continues

	All % (n)	Age >72 % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	54.2 (613)	0.898	1.01	0.80-1.26
Left side of chest	35.5 (809)	32.7 (370)	0.016	0.80	0.63-1.01
Right side of chest	5.1 (116)	5.4 (61)	0.208	1.28	0.77-2.13
Upper part of chest	6.7 (152)	5.9 (67)	0.163	0.78	0.49-1.23
Lower part of chest	9.0 (204)	9.3 (105)	0.462	1.11	0.75-1.65
All over the chest	11.8 (269)	12.5 (141)	0.374	1.12	0.79-1.59
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.4 (109)	0.875	1.02	0.70-1.49
Size of patient's palm	58.4 (1240)	56.7 (594)	0.082	0.85	0.67-1.07
Entire chest	30.9 (655)	32.9 (344)	0.078	1.18	0.92-1.52
Palpation tenderness (655)	22.3 (505)	21.3 (239)	0.129	0.85	0.64-1.11
Pain affected by movement (719)	17.0 (373)	15.5 (169)	0.073	0.80	0.59-1.09
Pain affected by breathing (692)	25.8 (573)	21.5 (236)	<0.001*	0.68	0.52-0.89

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Supplemental material 3 - Multivariate analyses of differences in symptoms based on previous history of ACS

	All % (n)	History of ACS % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	29.3 (856)			
Pale (565)	16.4 (386)	19.9 (140)	0.004*	1.43	1.04-1.97
Clammy (565)	8.7 (204)	6.2 (44)	0.059	0.70	0.44-1.13
Nausea (576)	27.1 (635)	24.0 (169)	0.298	0.89	0.67-1.18
Vomiting (576)	7.0 (165)	5.4 (38)	0.067	0.69	0.41-1.15
Affected breathing according to patient (596)	44.6 (1040)	49.6 (347)	0.001*	1.35	1.06-1.73
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	33.7 (248)	0.144	1.15	0.89-1.48
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	43.4 (245)	0.087	0.83	0.63-1.09
Debut					
Debut during activity (752)	22.1 (479)	20.8 (132)	0.501	1.08	0.79-1.48
Debut while resting (752)	65.5 (1419)	67.8 (431)	0.468	1.07	0.82-1.41
Debut while sleeping (752)	15.8 (342)	14.2 (90)	0.029	0.73	0.51-1.05
Sudden debut, within seconds (875)	35.7 (729)	32.7 (199)	0.380	0.91	0.69-1.19
Quick debut, within minutes (875)	35.2 (718)	36.6 (223)	0.483	1.07	0.82-1.41
Slow debut, within hours (875)	29.1 (595)	30.7 (187)	0.850	1.02	0.76-1.35
Constant pain (732)	55.5 (1212)	54.9 (358)	0.322	0.90	0.70-1.16
Fluctuating pain (732)	40.4 (883)	40.0 (261)	0.837	1.02	0.79-1.31
Pain aggravating over time (732)	10.8 (237)	12.0 (78)	0.122	1.26	0.85-1.88
Pain in other parts of the body (1197)					
Head	2.5 (43)	2.0 (10)	–	–	–
Throat	10.3 (177)	8.8 (45)	0.683	0.92	0.56-1.50
Jaw	5.3 (92)	5.3 (27)	–	–	–
Neck	2.5 (43)	2.9 (15)	–	–	–
Between scapulars	2.2 (37)	1.6 (8)	–	–	–
Back	15.2 (261)	17.5 (89)	0.066	1.31	0.89-1.94
Left shoulder	8.5 (147)	9.0 (46)	0.390	1.18	0.71-1.95
Right shoulder	4.2 (72)	3.5 (18)	–	–	–
Left arm	24.0 (412)	29.4 (150)	<0.001*	1.62	1.17-2.25
Right arm	8.4 (145)	9.4 (48)	0.251	1.25	0.75-2.06
Left hand	1.0 (17)	0.2 (1)	–	–	–
Right hand	0.3 (6)	0.2 (1)	–	–	–
Stomach	7.0 (121)	6.5 (33)	0.275	0.78	0.44-1.38
Left leg	1.7 (29)	1.0 (5)	–	–	–
Right leg	1.4 (24)	0.6 (3)	–	–	–
No other pain	39.3 (676)	35.9 (183)	0.005*	0.72	0.53-0.97
Pain quality (1175)					
Band-shaped	3.3 (58)	3.0 (15)	–	–	–
Burning	4.4 (76)	4.3 (22)	–	–	–
Stabbing	9.7 (169)	10.7 (54)	0.399	1.16	0.72-1.86
Cramping	8.7 (151)	6.1 (31)	0.078	0.68	0.39-1.19
Dull pain	13.9 (242)	13.6 (69)	0.582	0.91	0.60-1.38
Feels like something is on the chest	0.7 (12)	0.4 (2)	–	–	–
Discomfort	10.2 (178)	9.7 (49)	0.596	0.90	0.56-1.45
Tingling/Stinging	5.7 (99)	5.9 (30)	–	–	–
Swaying	1.7 (30)	2.0 (10)	–	–	–
Pressuring	57.9 (1008)	58.3 (295)	0.985	1.00	0.75-1.33
Heaviness	1.0 (17)	0.8 (4)	–	–	–
Aching	2.4 (41)	3.0 (15)	–	–	–

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Supplemental material 3 continues

	All % (n)	History of ACS % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	55.4 (377)	0.202	1.13	0.88-1.44
Left side of chest	35.5 (809)	36.0 (245)	0.532	1.06	0.82-1.37
Right side of chest	5.1 (116)	3.5 (24)	0.008*	0.52	0.28-0.98
Upper part of chest	6.7 (152)	5.7 (39)	0.639	0.91	0.54-1.52
Lower part of chest	9.0 (204)	7.2 (49)	0.061	0.71	0.45-1.13
All over the chest	11.8 (269)	11.3 (77)	0.531	0.91	0.62-1.33
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.1 (63)	0.746	0.94	0.62-1.44
Size of patient's palm	58.4 (1240)	60.0 (374)	0.207	1.13	0.87-1.47
Entire chest	30.9 (655)	29.9 (186)	0.259	0.88	0.67-1.16
Palpation tenderness (655)	22.3 (505)	21.6 (146)	0.860	0.98	0.72-1.32
Pain affected by movement (719)	17.0 (373)	15.9 (105)	0.729	0.95	0.68-1.34
Pain affected by breathing (692)	25.8 (573)	20.9 (139)	0.012	0.74	0.55-1.00

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Supplemental material 4 - Multivariate analyses of differences in symptoms based on previous history of diabetes mellitus

	All % (n)	History of DM % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	19.8 (578)			
Pale (565)	16.4 (386)	17.1 (81)	0.611	0.93	0.64-1.34
Clammy (565)	8.7 (204)	7.8 (37)	0.712	0.93	0.56-1.53
Nausea (576)	27.1 (635)	28.9 (137)	0.064	1.24	0.91-1.68
Vomiting (576)	7.0 (165)	7.4 (35)	0.527	1.13	0.67-1.91
Affected breathing according to patient (596)	44.6 (1040)	49.0 (229)	0.045	1.23	0.94-1.62
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	39.8 (197)	<0.001*	1.53	1.16-2.02
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	50.4 (195)	0.018	1.31	0.97-1.77
Debut					
Debut during activity (752)	22.1 (479)	14.7 (64)	<0.001*	0.54	0.37-0.81
Debut while resting (752)	65.5 (1419)	71.3 (310)	0.007*	1.38	1.01-1.88
Debut while sleeping (752)	15.8 (342)	16.6 (72)	0.702	1.05	0.72-1.54
Sudden debut, within seconds (875)	35.7 (729)	33.0 (136)	0.503	0.92	0.67-1.25
Quick debut, within minutes (875)	35.2 (718)	36.2 (149)	0.933	1.01	0.74-1.36
Slow debut, within hours (875)	29.1 (595)	30.8 (127)	0.540	1.07	0.78-1.47
Constant pain (732)	55.5 (1212)	59.8 (266)	0.084	1.21	0.91-1.60
Fluctuating pain (732)	40.4 (883)	34.8 (155)	0.014	0.75	0.56-1.01
Pain aggravating over time (732)	10.8 (237)	11.5 (51)	0.583	1.09	0.70-1.71
Pain in other parts of the body (1197)					
Head	2.5 (43)	2.3 (8)	–	–	–
Throat	10.3 (177)	9.1 (32)	0.759	0.93	0.54-1.61
Jaw	5.3 (92)	4.5 (16)	–	–	–
Neck	2.5 (43)	3.4 (12)	–	–	–
Between scapulars	2.2 (37)	1.4 (5)	–	–	–
Back	15.2 (261)	17.8 (63)	0.163	1.25	0.82-1.91
Left shoulder	8.5 (147)	9.1 (32)	0.602	1.11	0.64-1.93
Right shoulder	4.2 (72)	5.4 (19)	–	–	–
Left arm	24.0 (412)	28.0 (99)	0.137	1.23	0.85-1.75
Right arm	8.4 (145)	11.0 (39)	0.094	1.40	0.83-2.37
Left hand	1.0 (17)	0.8 (3)	–	–	–
Right hand	0.3 (6)	0.6 (2)	–	–	–
Stomach	7.0 (121)	8.2 (29)	0.280	1.27	0.71-2.29
Left leg	1.7 (29)	2.8 (10)	–	–	–
Right leg	1.4 (24)	2.8 (10)	–	–	–
No other pain	39.3 (676)	35.4 (125)	0.081	0.80	0.57-1.11
Pain quality (1175)					
Band-shaped	3.3 (58)	2.2 (8)	–	–	–
Burning	4.4 (76)	5.8 (21)	–	–	–
Stabbing	9.7 (169)	10.2 (37)	0.663	1.09	0.65-1.83
Cramping	8.7 (151)	8.0 (29)	0.926	1.02	0.57-1.80
Dull pain	13.9 (242)	15.7 (57)	0.302	1.18	0.77-1.83
Feels like something is on the chest	0.7 (12)	0.0 (0)	–	–	–
Discomfort	10.2 (178)	9.9 (36)	0.853	0.96	0.57-1.61
Tingling/Stinging	5.7 (99)	5.5 (20)	–	–	–
Swaying	1.7 (30)	1.4 (5)	–	–	–
Pressuring	57.9 (1008)	58.0 (211)	0.858	0.97	0.71-1.33
Heaviness	1.0 (17)	0.5 (2)	–	–	–
Aching	2.4 (41)	2.7 (10)	–	–	–

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 4 continues

	All % (n)	History of DM % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	55.3 (255)	0.660	1.04	0.79-1.38
Left side of chest	35.5 (809)	34.3 (461)	0.729	0.96	0.72-1.28
Right side of chest	5.1 (116)	5.9 (27)	0.229	1.32	0.72-2.40
Upper part of chest	6.7 (152)	5.2 (24)	0.250	0.76	0.42-1.39
Lower part of chest	9.0 (204)	8.9 (41)	0.734	1.06	0.65-1.72
All over the chest	11.8 (269)	12.4 (57)	0.706	1.06	0.70-1.61
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	7.0 (30)	0.010	0.58	0.34-1.00
Size of patient's palm	58.4 (1240)	58.7 (252)	0.888	1.01	0.76-1.35
Entire chest	30.9 (655)	34.3 (147)	0.119	1.20	0.88-1.62
Palpation tenderness (655)	22.3 (505)	25.4 (115)	0.019	1.34	0.97-1.85
Pain affected by movement (719)	17.0 (373)	17.1 (76)	0.540	1.09	0.75-1.58
Pain affected by breathing (692)	25.8 (573)	24.3 (109)	0.753	1.04	0.75-1.43

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

DM = Diabetes mellitus

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Supplemental material 5 - Differences in symptoms based on diagnosis of AMI on hospital discharge

	All % (n)	Diagnosis om AMI on hospital discharge % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)				
Pale (565)	16.4 (386)	30.1 (83)	<0.001*	2.26	1.80-3.82
Clammy (565)	8.7 (204)	15.6 (42)	<0.001*	2.19	1.36-3.55
Nausea (576)	27.1 (635)	27.3 (73)	0.933	1.01	0.70-1.47
Vomiting (576)	7.0 (165)	9.0 (24)	0.190	1.35	0.75-2.46
Affected breathing according to patient (596)	44.6 (1040)	38.7 (103)	0.040	0.76	0.54-1.07
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	40.5 (120)	0.001*	1.52	1.10-2.12
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	40.6 (91)	0.145	0.81	0.59-1.18
Debut					
Debut during activity (752)	22.1 (479)	33.1 (83)	<0.001*	1.89	1.30-2.76
Debut while resting (752)	65.5 (1419)	57.4 (144)	0.004*	0.67	0.48-0.96
Debut while sleeping (752)	15.8 (342)	12.7 (32)	0.160	0.76	0.45-1.26
Sudden debut, within seconds (875)	35.7 (729)	34.7 (85)	0.726	0.95	0.66-1.38
Quick debut, within minutes (875)	35.2 (718)	43.3 (106)	0.005*	1.48	1.03-2.11
Slow debut, within hours (875)	29.1 (595)	22.0 (54)	0.010	0.66	0.43-1.00
Constant pain (732)	55.5 (1212)	65.5 (165)	0.001*	1.61	1.12-2.30
Fluctuating pain (732)	40.4 (883)	32.1 (81)	0.005*	0.67	0.46-0.96
Pain aggravating over time (732)	10.8 (237)	9.9 (25)	0.615	0.89	0.50-1.59
Pain in other parts of the body (1197)					
Head	2.5 (43)	0.5 (1)	–	–	–
Throat	10.3 (177)	8.1 (17)	0.265	0.74	0.37-1.48
Jaw	5.3 (92)	9.0 (19)	–	–	–
Neck	2.5 (43)	3.3 (7)	–	–	–
Between scapulars	2.2 (37)	4.3 (9)	–	–	–
Back	15.2 (261)	18.1 (38)	0.209	1.28	0.78-2.10
Left shoulder	8.5 (147)	8.6 (18)	0.989	1.00	0.51-1.98
Right shoulder	4.2 (72)	6.2 (3)	–	–	–
Left arm	24.0 (412)	37.6 (79)	<0.001*	2.13	1.43-3.18
Right arm	8.4 (145)	17.6 (37)	<0.001*	2.78	1.63-4.73
Left hand	1.0 (17)	1.0 (2)	–	–	–
Right hand	0.3 (6)	0.5 (1)	–	–	–
Stomach	7.0 (121)	2.4 (5)	0.008*	0.29	0.09-0.97
Left leg	1.7 (29)	0.5 (1)	–	–	–
Right leg	1.4 (24)	0.0 (0)	–	–	–
No other pain	39.3 (676)	31.4 (66)	0.013	0.68	0.45-1.01
Pain quality (1175)					
Band-shaped	3.3 (58)	4.4 (9)	–	–	–
Burning	4.4 (76)	3.9 (8)	–	–	–
Stabbing	9.7 (169)	2.9 (6)	0.001*	0.27	0.09-0.76
Cramping	8.7 (151)	10.3 (21)	0.381	1.24	0.66-2.35
Dull pain	13.9 (242)	14.2 (29)	0.887	1.03	0.60-1.79
Feels like something is on the chest	0.7 (12)	1.5 (3)	–	–	–
Discomfort	10.2 (178)	8.8 (18)	0.485	0.83	0.43-1.63
Tingling/Stinging	5.7 (99)	2.0 (4)	–	–	–
Swaying	1.7 (30)	2.0 (4)	–	–	–
Pressuring	57.9 (1008)	62.7 (128)	0.134	1.26	0.85-1.88
Heaviness	1.0 (17)	1.0 (2)	–	–	–
Aching	2.4 (41)	3.4 (7)	–	–	–

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 5 continues

	All % (n)	Diagnosis om AMI on hospital discharge % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	66.4 (176)	<0.001*	1.85	1.30-2.64
Left side of chest	35.5 (809)	27.5 (73)	0.004*	0.66	0.45-0.96
Right side of chest	5.1 (116)	1.9 (5)	0.016	0.33	0.10-1.08
Upper part of chest	6.7 (152)	7.9 (21)	0.387	1.24	0.66-2.32
Lower part of chest	9.0 (204)	5.7 (15)	0.048	0.58	0.28-1.18
All over the chest	11.8 (269)	13.2 (35)	0.455	1.16	0.70-1.91
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	5.6 (14)	0.006*	0.46	0.22-0.96
Size of patient's palm	58.4 (1240)	58.8 (147)	0.893	1.02	0.72-1.45
Entire chest	30.9 (655)	35.6 (89)	0..084	1.28	0.89-1.84
Palpation tenderness (655)	22.3 (505)	13.6 (35)	<0.001*	0.51	0.32-0.83
Pain affected by movement (719)	17.0 (373)	9.9 (25)	0.002*	0.50	0.29-0.88
Pain affected by breathing (692)	25.8 (573)	14.9 (39)	<0.001*	0.47	0.30-0.75

[a]Logistic regression

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract		
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found		
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		
Objectives	3	State specific objectives, including any prespecified hypotheses		
Methods				
Study design	4	Present key elements of study design early in the paper		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants		
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4	Previous publication describing the cohort and data collection in detail.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Previous publication describing the cohort and data collection in detail.
Bias	9	Describe any efforts to address potential sources of bias	Previous publication describing the cohort and data collection in detail.
Study size	10	Explain how the study size was arrived at	Previous publication describing the cohort and data collection in detail.

Continued on next page

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Previous publication describing the cohort and data collection in detail.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	Previous publication describing the cohort and data collection in detail.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Previous publication describing the cohort and data collection in detail.
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Previous publication

For peer review only

Enseignement Supérieur (ABES) .

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l

d by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

			describing the cohort and data collection in detail.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	previous publication describing the cohort and data collection in detail.
		(b) Indicate number of participants with missing data for each variable of interest	Supplemental Material 1-4
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Supplemental Material 1-4 and Figure 1-
		(*b*) Report category boundaries when continuous variables were categorized	previous publication describing the cohort and data collection in detail.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-046332 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES). Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

	period

Continued on next page

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
d by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

Clinical presentation in EMS patients with acute chest pain in relation to sex, age and medical history – prospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-054622.R2
Article Type:	Original research
Date Submitted by the Author:	09-Jun-2022
Complete List of Authors:	Wibring, Kristoffer; University of Gothenburg; Halland County, 1Department of Ambulance and Prehospital Care Lingman, Markus; University of Gothenburg, Department of Molecular; Halland County, Halland hospital Herlitz, Johan; University of Borås Pettersson, Helena; Halland County, Department of Ambulance and Prehospital Care Lerjebo, Anette; Halland County, Department of Ambulance and Prehospital Care Bång , Angela; University of Gothenburg
Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	ACCIDENT & EMERGENCY MEDICINE, Myocardial infarction < CARDIOLOGY, General diabetes < DIABETES & ENDOCRINOLOGY, Cardiology < INTERNAL MEDICINE

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Clinical presentation in EMS patients with acute chest pain in relation to sex, age and medical history – prospective cohort study

Authors
Kristoffer Wibring[1, 2] kristoffer.wibring@gu.se
Markus Lingman[3, 4] markus.lingman@regionhalland.se
Johan Herlitz[5] johan.herlitz@hb.se
Helena Pettersson[1] helena.pettersson@regionhalland.se
Anette Lerjebo[1] anette.lerjebo@regionhalland.se
Angela Bång[2] angela.bang@gu.se

1. Department of Ambulance and Prehospital Care, Region Halland, Sweden
2. Institute of Health and Care Sciences, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden
3. Department of Molecular and Clinical Medicine/Cardiology, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden
4. Department of Development, Halland Hospital, Halmstad, Sweden
5. The Prehospital Research Center Western Sweden, University of Borås, Borås, Sweden.

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and the interpretation discussed.

Corresponding author
Kristoffer Wibring
Ambulanssjukvården Region Halland
Varlabergsvägen 29
434 39 Kungsbacka
E-mail: kristoffer.wibring@gu.se
Phone: 0046701757679

Word count: 3448

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

ABSTRACT

Objective: To assess symptom presentation related to age, sex, and previous medical history in patients with chest pain.

Design: Prospective observational cohort study.

Setting: Two-centre study in a Swedish county EMS organisation.

Participants: Unselected inclusion of 2,917 patients with chest pain cared for by the EMS during 2018.

Data analysis: Multivariate analysis on the association between symptom characteristics, patients' sex, age, previous acute coronary syndrome (ACS) or diabetes and the final outcome of acute myocardial infarction (AMI).

Results: Symptomology in patients assessed by the EMS due to acute chest pain varied with sex and age, and also with previous ACS or diabetes. Women suffered more often from nausea (odds ratio (OR) 1.6) and pain in throat (OR 2.1) or back (OR 2.1). Their pain was more often affected by palpation (1.7) or movement (OR 1.4). Older patients more often described pain onset while sleeping (OR 1.5) and that the onset of symptoms was slow, over hours rather than minutes (OR 1.4). They were less likely to report pain in other parts of their body than their chest (OR 1.4). They were to a lesser extent clammy (OR 0.6) or nauseous (OR 0.6). These differences were present regardless of whether the symptoms were caused by AMI or not.

Conclusions: A number of aspects of the symptom of chest pain appear to differ in unselected prehospital patients with chest pain in relation to age, sex and medical history, regardless of whether the chest pain was caused by a myocardial infarction or not. This complicates the possibility in prehospital care of using symptoms to predict the underlying aetiology of acute chest pain.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The unselected inclusion of a close to complete county population of patients with chest pain cared for by the emergency medical services (EMS) constitutes a strength.
- Low rates of missing data considering the use of EMS data also constitute a strength.
- Some variables involved high rates of missing data when compared with studies conducted in the hospital setting, which was a limitation.
- Another limitation was that a study conducted in only one county reduces generalisability.

Keywords

Chest Pain; Emergency Medical Services; Acute Myocardial Infarction; Signs and Symptoms; Clinical Presentation; Sex factors; Age factors

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

BACKGROUND

Chest pain is one of the most common complaints among emergency medical services (EMS) patients. About 10-15 percent of all patient-related EMS missions concern patients with chest pain [1 2] out of which about 10 percent have an acute myocardial infarction (AMI) [3].

Clinical presentation is, along with ECG and biomedical markers, one cornerstone when differentiating those with AMI from those with other causes of their chest pain [4 5]. Numerous studies have investigated whether patients' sex, age, diabetes mellitus or previous acute coronary syndrome (ACS) are associated with differences in clinical presentation in patients diagnosed with AMI [4-7]. Even if the results vary, the general opinion is that at least age, sex and diabetes mellitus are associated with differences in symptomology at least in some patients when seeking care for AMI [4 5 8].

These factors are not solely associated with the type of symptoms that the patients experience but also with to what extent the patients delay seeking care [9 10]. They are also associated with patients' use of the EMS or if they use other means for transportation to hospital when suffering from chest pain [11].

The above-cited studies are mainly based on hospital data. Thus it is not possible to determine whether or not these findings also apply in the EMS setting. Furthermore, most of these studies only included patients diagnosed with AMI. This makes it difficult to determine whether these differences in symptomology are also valid among patients with chest pain in general, including patients without AMI. This is of clinical relevance, since we need to know whether such differences in clinical presentation associated with the factors stated should be taken into account when assessing patients with chest pain in the EMS setting. Furthermore, at the time of the EMS assessment, the EMS clinician does not know with certainty whether the patient is suffering from a myocardial infarction or not.

This study therefore investigates whether patients with chest pain, assessed in the EMS setting, differ in symptomology based on sex, age, diabetes mellitus or previous ACS including any type of acute myocardial infarction or unstable angina, regardless of whether their chest pain is caused by AMI or not.

Objective

To assess symptom presentation related to age, sex, and previous medical history in patients with chest pain.

METHODS

The study is part of the BRIAN research programme. The primary objective of the BRIAN research programme is to develop a prediction model for risk stratification of EMS patients with acute chest pain. In this study collected data is analysed further to investigate associations between sex, age, medical history and clinical presentation. Study population, data collection and clinical setting have been previously described [12-14] and are therefore summarised briefly.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Study population

In all, 3,121 EMS missions were carried out in 2018 in the county catchment area including patients ≥18 years old, with a chief complaint of chest pain according to EMS personnel. All these missions were eligible for inclusion. Patients with other symptoms suggestive of AMI, for example dyspnoea, but not reporting chest pain were not included, since the objective was to investigate patients with chest pain and not patients with suspected AMI in general. This also provided clearer and more objective criteria for inclusion, improving the generalisability of the results by applying a subjective suspicion of AMI. After excluding patients declining to participate and patients who were lost to follow-up, 2,917 EMS missions remained.

Healthcare system

The county of Halland covers an area of 5,500 km^2 and had 329,000 inhabitants in 2018. These are served by two emergency hospitals, including one with PCI capabilities. The EMS consists of eight ambulance stations with 19 ambulance vehicles. In 2018, a total of 30,672 missions were carried out by the EMS (inter-hospital site transports excluded). The EMS is staffed mainly by nurses [12].

Data collection

Each patient was tracked throughout the entire healthcare chain, from EMS mission to hospital discharge. Data on symptoms were retrieved using a novel fifteen-item questionnaire, integrated in the digital EMS medical record, filled in by the EMS personnel. The EMS medical record, and thereby also the questionnaire was available bedside and enroute by using electronic tablets. Consequently, the EMS personnel was blinded to diagnosis on hospital discharge when completing the questionnaire. The questionnaire contained items mainly focusing on the patients' pain narratives identifying onset, provocation/palliation, quality, radiation, severity etc. The questionnaire also contained items regarding nausea/vomiting, dyspnoea, paleness and clamminess.

Diagnosis of AMI on hospital discharge according to physician in charge was retrieved from the hospital medical record. AMI was defined as a diagnosis on hospital discharge including any of the following International Statistical Classification of Diseases and Related Health Problems 10-codes (ICD-10):

- I21 – Acute myocardial infarction
- I22 – Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
- I24.1 – Dressler's syndrome
- I24.8. – Other forms of acute ischemic heart disease

Diagnosis of unstable angina was not included in the definition of AMI. Data collection did not affected patient care.

Previous ACS was defined as diagnosed with any of the following ICD-10 codes before the EMS mission included here, according to hospital and primary care medical records:

- I21 – Myocardial infarction
- I22 – Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
- I23 – Certain current complications following ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction (within the 28-day period)
- I24 – Other acute ischaemic heart diseases
- I252 – Old myocardial infarction

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

- I220 – Subsequent ST elevation (STEMI) myocardial infarction of anterior wall

Diabetes mellitus was defined as diagnosed with any of the following ICD-10 codes before the EMS mission included here, according to hospital and primary care medical records:

- E10 – Type 1 diabetes mellitus
- E11 – Type 2 diabetes mellitus

Endpoint

Occurrence of the following symptoms:

- Paleness or clamminess
- Nausea or vomiting
- Dyspnoea
- Pain according to the OPQRST[15] mnemonic:
  - Onset
  - Provocation/Palliation
  - Quality
  - Region and localisation
  - Severity
  - Time (behaviour over time)

Statistical analysis

The results are presented using descriptive statistics including percentage (%), number of patients (n), mean, median, standard deviation (SD) and quartiles where appropriate.

The association between patients' sex, age, diabetes or previous ACS and occurrence of stated symptoms was analysed using multivariate regression. The analyses were adjusted for diagnosis of AMI at hospital discharge. Patients' age was dichotomised in the analyses, using cohort median age as cut point. No multivariate analyses were performed if the symptom of interest occurred in fewer than 100 patients. This was to ensure that the assumptions for logistic regression analyses were not violated. P-values below 0.01 were considered statistically significant (instead of 0.05 due to multiple tests). All analyses were carried out using IBM SPSS Statistics 27.

Analyses were not carried out of associations between factors other than sex, age, diabetes or previous ACS and symptoms presentation. We thereby limited the risk of chance findings by avoiding multiple tests and too small sub-groups.

Data imputation was not performed, but cases with missing data were excluded from the analyses instead. The incidence of missing data is reported in parentheses after each variable in the tables which are included in the results.

Ethical considerations

In this study, all patients eligible for inclusion were subject to an opt-out procedure. The study was approved by the Regional Ethical Review Board in Lund (Dno 2017/212).

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Patient and public involvement

Patients have not been directly involved in planning or conducting this study. The design of the questionnaire was partly based on patient narratives from a previous study within this research project[16] and other studies based on patient interviews. Furthermore, KW had personal contact with several patients who contacted him by phone or e-mail due to the opt-out procedure, both patients wanting to opt out and those who wanted to remain in the study. The results of the study will be presented directly to those patients who request this when contacting KW.

RESULTS

The median age of the cohort was 72 years old (Q25-Q75, 58-82). Sex was evenly distributed. Of EMS missions included, almost 30 % of patients had a previous ACS and 20 % of the patients had diabetes mellitus. The prevalence of AMI in terms of diagnosis on hospital discharge was 12 %. Diagnoses on hospital discharge varied widely. Other common diagnoses on hospital discharge were unspecified chest pain (42 %), atrial fibrillation (4 %), and heart failure (without pulmonary oedema) (2 %). The proportion of patients with AMI on hospital discharge was associated with sex and diabetes mellitus with a higher rate among men and among patients with diabetes mellitus (Table 1). Eight percent had the combination of diabetes and previous history of ACS.

Table 1 - Incidence of diagnosis of AMI on hospital discharge

	All % (n)	Acute myocardial infarction on hospital discharge % (n)	p-value*
All	100 (2917)	12 (335)	–
Male	50 (1465)	64 (214)	<0.001
Age > 72 years	49 (1436)	55 (183)	0.036
Previous history of ACS	29 (856)	25 (84)	0.068
Previous history of diabetes mellitus	20 (578)	26 (86)	0.004

**chi2-test*
AMI = Acute myocardial infarction; ACS = Acute coronary syndrome

The most common symptom characteristics were affected breathing (Table 2), pressuring pain located in the central chest about the size of a palm, (Table 3) time debut less than 3 hours before EMS arrival, pain debut while resting and constant pain (Table 4), This pattern was found regardless of patients' sex, age, diabetes or previous ACS (Table 2-4).

Table 2 - Clinical presentation based on sex, age and previous medical history of ACS or diabetes mellitus

	All % (n)	Women % (n)	Age >72 % (n)	History of ACS % (n)	History of diabetes mellitus % (n)
All (number of missing)	100 (2917)	49.8 (1452)	49.2 (1436)	29.3 (856)	19.8 (578)
Pale (565)	16.4 (386)	13.5 (157)	16.7 (196)	19.9 (140)	17.1 (81)
Clammy (565)	8.7 (204)	7.4 (86)	6.4 (75)	6.2 (44)	7.8 (37)
Nausea (576)	27.1 (635)	31.3 (363)	23.2 (270)	24.0 (169)	28.9 (137)

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Vomiting (576)	7.0 (165)	6.9 (80)	6.3 (74)	5.4 (38)	7.4 (35)
Affected breathing according to patient (596)	44.6 (1040)	46.8 (537)	44.2 (514)	49.6 (347)	49.0 (229)

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Table 3 - Pain narrative based on sex, age and previous medical history of ACS or diabetes mellitus

	All % (n)	Women % (n)	Age >72 % (n)	History of ACS % (n)	History of diabetes mellitus % (n)
All (number of missing)	100 (2917)	49.8 (1452)	49.2 (1436)	29.3 (856)	19.8 (578)
Pain in other parts of the body (1197)					
Head	2.5 (43)	3.3 (29)	1.8 (15)	2.0 (10)	2.3 (8)
Throat	10.3 (177)	13.3 (117)	8.6 (73)	8.8 (45)	9.1 (32)
Jaw	5.3 (92)	5.8 (51)	3.8 (32)	5.3 (27)	4.5 (16)
Neck	2.5 (43)	3.4 (30)	2.5 (21)	2.9 (15)	3.4 (12)
Between scapulars	2.2 (37)	2.7 (24)	1.5 (13)	1.6 (8)	1.4 (5)
Back	15.2 (261)	19.5 (171)	16.4 (139)	17.5 (89)	17.8 (63)
Left shoulder	8.5 (147)	9.0 (79)	7.5 (64)	9.0 (46)	9.1 (32)
Right shoulder	4.2 (72)	4.6 (40)	4.0 (34)	3.5 (18)	5.4 (19)
Left arm	24.0 (412)	23.0 (202)	23.1 (196)	29.4 (150)	28.0 (99)
Right arm	8.4 (145)	8.8 (77)	8.5 (72)	9.4 (48)	11.0 (39)
Left hand	1.0 (17)	0.7 (6)	0.4 (3)	0.2 (1)	0.8 (3)
Right hand	0.3 (6)	0.1 (1)	0.2 (2)	0.2 (1)	0.6 (2)
Stomach	7.0 (121)	7.1 (62)	7.5 (64)	6.5 (33)	8.2 (29)
Left leg	1.7 (29)	1.8 (16)	1.8 (15)	1.0 (5)	2.8 (10)
Right leg	1.4 (24)	1.4 (12)	1.4 (12)	0.6 (3)	2.8 (10)
No other pain	39.3 (676)	34.2 (301)	41.3 (351)	35.9 (183)	35.4 (125)
Pain quality (1175)					
Band-shaped	3.3 (58)	3.7 (32)	3.4 (29)	3.0 (15)	2.2 (8)
Burning	4.4 (76)	5.4 (46)	3.5 (30)	4.3 (22)	5.8 (21)
Stabbing	9.7 (169)	8.3 (71)	8.8 (75)	10.7 (54)	10.2 (37)
Cramping	8.7 (151)	9.1 (78)	6.7 (57)	6.1 (31)	8.0 (29)
Dull pain	13.9 (242)	13.6 (116)	14.6 (124)	13.6 (69)	15.7 (57)
Fells like something is on the chest	0.7 (12)	0.6 (5)	0.6 (5)	0.4 (2)	0.0 (0)
Discomfort	10.2 (178)	10.8 (92)	10.6 (90)	9.7 (49)	9.9 (36)
Tingling/Stinging	5.7 (99)	5.1 (44)	4.9 (42)	5.9 (30)	5.5 (20)
Swaying	1.7 (30)	1.6 (14)	1.5 (13)	2.0 (10)	1.4 (5)
Pressuring	57.9 (1008)	59.6 (510)	60.0 (510)	58.3 (295)	58.0 (211)
Heaviness	1.0 (17)	1.3 (11)	1.1 (9)	0.8 (4)	0.5 (2)
Aching	2.4 (41)	2.1 (18)	2.4 (20)	3.0 (15)	2.7 (10)
Chest pain localisation (640)					

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Central pain	53.4 (1215)	53.3 (599)	54.2 (613)	55.4 (377)	55.3 (255)
Left side of chest	35.5 (809)	32.0 (359)	32.7 (370)	36.0 (245)	34.3 (461)
Right side of chest	5.1 (116)	4.8 (54)	5.4 (61)	3.5 (24)	5.9 (27)
Upper part of chest	6.7 (152)	7.9 (89)	5.9 (67)	5.7 (39)	5.2 (24)
Lower part of chest	9.0 (204)	11.1 (125)	9.3 (105)	7.2 (49)	8.9 (41)
All over the chest	11.8 (269)	12.6 (141)	12.5 (141)	11.3 (77)	12.4 (57)
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.2 (107)	10.4 (109)	10.1 (63)	7.0 (30)
Size of patient's palm	58.4 (1240)	57.4 (601)	56.7 (594)	60.0 (374)	58.7 (252)
Entire chest	30.9 (655)	32.4 (339)	32.9 (344)	29.9 (186)	34.3 (147)
Pain affected by movement (719)	17.0 (373)	19.6 (211)	15.5 (169)	15.9 (105)	17.1 (76)
Pain affected by breathing (692)	25.8 (573)	26.6 (292)	21.5 (236)	20.9 (139)	24.3 (109)
Palpation tenderness (655)	22.3 (505)	27.1 (302)	21.3 (239)	21.6 (146)	25.4 (115)
Pain intensity according to Numeric Rating Scale >5 (415)	32.1 (803)	33.6 (1228)	30.1 (372)	33.7 (248)	39.8 (197)

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Table 4 - Time aspect of pain based on sex, age and previous medical history of ACS or diabetes mellitus					
	All % (n)	Women % (n)	Age >72 % (n)	History of ACS % (n)	History of diabetes mellitus % (n)
All (number of missing)	100 (2917)	49.8 (1452)	49.2 (1436)	29.3 (856)	19.8 (578)
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	46.5 (442)	47.3 (445)	43.4 (245)	50.4 (195)
Debut					
Debut during activity (752)	22.1 (479)	20.5 (217)	17.8 (191)	20.8 (132)	14.7 (64)
Debut while resting (752)	65.5 (1419)	67.4 (714)	67.6 (725)	67.8 (431)	71.3 (310)
Debut while sleeping (752)	15.8 (342)	15.6 (165)	18.1 (194)	14.2 (90)	16.6 (72)
Sudden debut, within seconds (875)	35.7 (729)	36.1 (361)	31.4 (313)	32.7 (199)	33.0 (136)
Quick debut, within minutes (875)	35.2 (718)	33.2 (332)	35.8 (357)	36.6 (223)	36.2 (149)
Slow debut, within hours (875)	29.1 (595)	30.8 (308)	32.7 (326)	30.7 (187)	30.8 (127)
Constant pain (732)	55.5 (1212)	53.3 (574)	57.1 (615)	54.9 (358)	59.8 (266)
Fluctuating pain (732)	40.4 (883)	42.3 (456)	40.0 (431)	40.0 (261)	34.8 (155)
Pain aggravating over time (732)	10.8 (237)	10.8 (116)	9.4 (101)	12.0 (78)	11.5 (51)

Women more often suffered from nausea and pain in the throat or back. They also more commonly localised their pain to the lower part of the chest. Their pain was more often affected by palpation or movement. They were more likely to report pain in other parts of the body than their chest. They were less often pale and had a lower incidence of left-sided chest pain (Figure 1).

Older patients more often described pain onset while sleeping and that the onset of symptoms was slow, over hours rather than minutes. They were less likely to report pain in other parts of their body than the chest. They were to a lesser extent clammy or nauseous. They rated their pain intensity lower and their chest pain onset occurred less often during activity. Their breathing movements more seldom affected their pain (Figure 2).

Patients with a previous ACS were more often pale and experienced their breathing as affected. They more often had pain in their left arm. They reported right-sided chest pain to a lesser extent, and they felt pain in any other part of their body than in the chest to a greater extent (Figure 3).

Regarding patients with diabetes mellitus, their pain more often started while they were resting and they rated their pain intensity as higher. Their pain was less likely to start during activity (Figure 4).

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

In total, patients' sex was associated with the occurrence of nine different types of symptoms and the same was true for patients' age. Previous ACS or diabetes were associated with the occurrence of five or three different symptoms respectively (Supplemental material 1-4). When comparing these analyses based on age, sex and previous medical history to analyses of association between symptoms and AMI, i.e. AMI predictors, (Supplement 5) one can observe that several symptoms associated with sex, age and previous medical history are not associated with AMI and vice versa.

DISCUSSION

Our study shows that the prevalence of numerous symptoms in EMS patients with chest pain is associated most of all with sex and age, but also with the patient's previous ACS or diabetes. This is observed regardless of whether the patient's chest pain is caused by an acute myocardial infarction or not. To the best of our knowledge, this is the first study reporting results on symptomology differences in acute chest pain patients based on sex, age and previous ACS or diabetes, when simultaneously adjusting for AMI incidence.

Sex, age and previous ACS or diabetes seem not only to be associated with how an AMI is experienced [4 5 8], but also with how acute chest pain and related symptoms are perceived in general. This finding implies that previously reported differences in clinical presentation based on patients' characteristics may be a general observation in acute chest pain patients and not necessarily associated with an AMI diagnosis. This finding further complicates the already challenging task of assessing patients with acute chest pain. Especially since these differences in clinical presentation are at hand both for symptoms associated with AMI and for symptoms with no such association.

These differences also complicate the use of symptom-based chest pain prediction tools not considering, primarily, age and sex, but also medical history. Since our findings indicate that the accuracy of a prediction tool may differ depending on these patient-related factors. This applies particularly to criteria-based assessment tools not considering patient sex or age such as Rapid Emergency Triage and Treatment System (RETTS) [17 18] or Manchester Triage System [19]. The use of more dynamic and advanced prediction models using statistical methods to adjust for examined factors may be one way to improve prediction accuracy and make it more valid for the complete chest pain population.

Sederholm et. al.[20] report that women with AMI experience pain in their back and throat more often than men and are more commonly nauseous. Lichtman et al. [21] and Kirherberger et al. [22] also found that women more often than men are nauseous. Araújo et al. [23] state that women with AMI are more likely to experience referred pain compared to men. Coventry et al. [24] found that women with AMI more often experience nausea and back pain. In our study, we also found an increased incidence of these symptoms among women, but in our material this difference was present regardless of whether their chest pain was caused by AMI or not. Thus these differences in symptomology are problematic when used for risk assessment since they are not necessarily associated with the incidence of AMI but rather with the patient's sex. This strengthens our notion that previous reported differences between men and women in AMI presentation are not necessarily associated with AMI but sometimes rather by sex itself.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Previous research report that older patients more often report atypical or accompanying AMI symptoms [25]. In our study older patients differed from younger ones regarding nine different aspects of their clinical presentation. For example they more often had a slower debut (hours rather than seconds or minutes), their pain was less intense and it more seldom started during activity. All these aspects can be considered atypical of AMI. On the other hand older patients less often reported accompanying or atypical symptoms such as nausea and pain affected to breathing. Altogether, the relationship between age and the clinical presentation of patients with chest pain seem to be complex both for patients with and without AMI. This strengthens the need of great humbleness when assessing older patients with chest pain, especially since age itself is a strong risk factor for AMI [8].

The aim of this study was not to explain the physiological mechanisms behind these differences in the characteristics of chest pain. One can only speculate that changes in the nervous system related to ageing make symptoms less distinct, and that the circadian rhythm for myocardial ischaemia is not as typical among the elderly, which changes the distribution of the time of symptom onset in these patients.

Kirchberger et al. [26] state that patients undergoing their second AMI more often have dyspnoea compared to patients having their first AMI. In our study, patients with a history of ACS, were more often dyspnoeic, also in cases where the chest pain were not caused by an AMI. One can reason that the higher rate of dyspnoea for patients who experience their second AMI reported by Kirchberger et al. [26] is more commonly at hand for patients with a previous ACS in general and is not necessarily associated with their reinfarction. Maybe this could be explained by the higher incidence of heart failure among patients with previous ACS.

Regarding patients with diabetes mellitus suffering from AMI, Manistamara et al. [27] reported that these patients tend to rate their pain as less intense compared to non-diabetic patients. In contrast, we found that patients with diabetes mellitus in general rate their chest pain as higher, regardless of AMI occurrence. This contradictory results between AMI-patients and unselected chest pain patients highlight the difficulties regarding how to value pain intensity in patients with diabetes mellitus and symptoms suggestive of AMI.

Our results strengthen the idea that the diagnostic evaluation of chest pain characteristics has limitations as a diagnostic tool and should be used with great caution [5]. The clinical presentation of patients with chest pain seems to be associated with age, sex and previous ACS or diabetes in a very complicated manner, both for patients with and without AMI as the cause of their chest pain. Altogether, clinicians should be careful when allowing patients' characteristics to influence how they evaluate patients' symptoms [6]. Furthermore, perhaps risk stratification should, when possible, put more emphasis on biochemical cardiac markers, ECG, age and sex, and to a lesser extent on symptoms. This approach is also in line with the European Society of Cardiology (ESC) 0/1 hour algorithm which is solely based on cardiac troponins and time since symptoms onset [5].

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Strengths and limitations

This study is strengthened by the close to complete and unselected inclusion of EMS missions concerning patients with chest pain, which improves generalisability. However, the use of data from a single county negatively affects the external validity.

The results are based on sub-analyses of previously collected data and the absolute differences observed are sometimes small. Clinicians should therefore be careful not to draw over-strict conclusions on how these results should affect clinical practice.

Some of the variables included entail rather high rates of missing information. Data collection in the EMS setting is known to be challenging and often involves higher rates of missing data than the in-hospital setting [28 29]. Considering this, the rates of missing information in this study are to be regarded as low and therefore data may be looked upon as comparatively comprehensive. Still, missing data is always problematic as it may affect the results by introducing both type I and type II errors. As it reduces the statistical power, it may introduce bias and reduce the representativeness of the cohort studied [30]. We have no reason to suspect any substantial bias due to missing data here, as the rates of missing data mainly reflect how the data was reported by the EMS personnel. There were higher rates of missing data for symptoms reported using free text in the questionnaire (pain localisation and quality) and lower rates for symptoms reported by ticking in a box. Missing data was also more common for variables reflecting symptom onset, i.e. debut time and if pain onset was quick or slow. This probably reflects difficulties for the patients in answering such questions as symptoms onset since it is not always distinct but rather develops over time. However, the rates of missing data indicate that the results should be interpreted with care and should preferably be validated in future studies. The take home message of this study is that clinical presentation differs according to the factors examined and that less importance should be given to the exact nature of this variation.

It would be of interest to examine if factors other than age, sex and previous ACS or diabetes also affected clinical presentation. Such potential factors are for example socio-economic status, smoking, obesity, hypertension and other cardiac risk factors. However, adding more factors would increase the risk of chance findings, due to multiple analyses. Furthermore, additional factors would result in too small sub-groups, thus violating the assumptions for logistic regression analyses. Therefore, only age, sex and previous ACS or diabetes were included in this study. These factors were deemed to be of most interest; age and sex as they concern all chest pain patients and the other four factors as they have been reported to affect clinical presentation in AMI. However, this is not well described using prehospital data and when adjusting for diagnosis of AMI. Rather, differences in symptomology have been investigated using hospital data and focusing on patients with AMI regardless of their chief complaint.

In part, the differences in clinical presentation described in this study may be explained by an uneven distribution of diagnoses other than AMI at hospital discharge. To adjust for more diagnoses than AMI at hospital discharge, a larger study sample is needed to ensure statistical robustness. However, the fact that differences in clinical presentation are explained by other diagnoses at hospital discharge does not change the implication of our results. Thus clinicians

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

should be careful not to allow patients' characteristics to influence how they evaluate patients' symptoms in cases of acute chest pain.

CONCLUSIONS

A number of aspects of the symptom chest pain appear to differ in unselected prehospital patients with chest pain in relation to age, sex and previous history regardless of whether the chest pain was caused by a myocardial infarction or not. This complicates the possibility in prehospital care of predicting the underlying aetiology of acute chest pain based on symptoms.

List of abbreviations

ACS – acute coronary syndrome
AMI – acute myocardial infarction
EMS – emergency medical services
ESC – European Society of Cardiology
NRS – numeric rating scale
OR – odds ratio
RETTS – Rapid Emergency Triage and Treatment System

Author contributions

KW, ML, JH, AL, HP and AB designed the study. KW, ML, JH, and AB planned the data collection. Data analysis was carried out by KW, AL and HP. KW, ML, JH, AL, HP and AB contributed in writing the manuscript. All authors read and approved the final manuscript.

Funding

This study has been funded by the Department of Ambulance and Prehospital Care, Region Halland and the Scientific Council of Region Halland (HALLAND-209901). The funding bodies had no role in the design, conduct, interpretation or writing of the report on this research.

Competing interests

The authors declare that they have no competing interests.

Patient consent for publication

Not required.

Ethics approval

The study was approved by the Regional Ethical Review Board in Lund (Dno 2017/212). All patients were given the opportunity to withdraw their participation using an opt-out procedure.

Data availability statement

The datasets generated and analysed during the current study are not publicly available due the integrity of patient privacy but are available from the corresponding author on reasonable request and if approved by the Regional Ethical Review Board in Lund.

Acknowledgements

We want to thank the following persons:

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

- The EMS personnel of Region Halland for their help with data collection.
- Thomas Thorsson, Vinh Norberg Nguyen and Sasa Pejicic for data extraction.
- Anders Holmén and Ulf Strömberg for statistical support.

Tables, figures and supplemental material

Figure 1 - Differences in clinical presentation based on sex
Figure 2 - Differences in clinical presentation based on age
Figure 3 - Differences in clinical presentation based on history of ACS
Figure 4 - Differences in clinical presentation based on history of diabetes mellitus
Table 1 - Incidence of diagnosis of AMI on hospital discharge
Table 2 – Clinical presentation based on sex, age and previous medical history of ACS or diabetes mellitus
Table 3 – Pain narrative based on sex, age and previous medical history of ACS or diabetes mellitus
Table 4 – Time aspect of pain based on sex, age and previous medical history of ACS or diabetes mellitus
Supplemental material 1 - Multivariate analyses of differences in symptoms prevalence based on sex
Supplemental material 2 - Multivariate analyses of differences in symptoms prevalence based on age
Supplemental material 3 - Multivariate analyses of differences in symptoms prevalence based on previous history of ACS
Supplemental material 4 - Multivariate analyses of differences in symptoms prevalence based on previous history of diabetes mellitus
Supplement material 5 - Differences in symptoms based on diagnosis of AMI on hospital discharge

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

REFERENCES

1. Clawson J, Olola C, Heward A, et al. The Medical Priority Dispatch System's ability to predict cardiac arrest outcomes and high acuity pre-hospital alerts in chest pain patients presenting to 9-9-9. *Resuscitation* 2008;78(3):298-306. doi: 10.1016/j.resuscitation.2008.03.229
2. Pedersen CK, Stengaard C, Friesgaard K, et al. Chest pain in the ambulance; prevalence, causes and outcome - a retrospective cohort study. *Scand J Trauma Resusc Emerg Med* 2019;27(1):84. doi: 10.1186/s13049-019-0659-6 [published Online First: 2019/08/29]
3. Rawshani A, Larsson A, Gelang C, et al. Characteristics and outcome among patients who dial for the EMS due to chest pain. *International Journal of Cardiology* 2014;176(3):859-65. doi: 10.1016/j.ijcard.2014.08.004
4. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39(2):119-77. doi: 10.1093/eurheartj/ehx393
5. Collet JP, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2020 doi: 10.1093/eurheartj/ehaa575 [published Online First: 2020/08/29]
6. Thuresson M, Jarlöv MB, Lindahl B, et al. Symptoms and type of symptom onset in acute coronary syndrome in relation to ST elevation, sex, age, and a history of diabetes. *Am Heart J* 2005;150(2):234-42. doi: 10.1016/j.ahj.2004.08.035
7. Strömbäck U, Engström Å, Lundqvist R, et al. The second myocardial infarction: Is there any difference in symptoms and prehospital delay compared to the first myocardial infarction? *Eur J Cardiovasc Nurs* 2018;17(7):652-59. doi: 10.1177/1474515118777391 [published Online First: 2018/05/11]

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

8. Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021:CIR0000000000001030. doi: 10.1161/CIR.0000000000001030 [published Online First: 20211028]
9. Moser DK, Kimble LP, Alberts MJ, et al. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Heart Association Council on cardiovascular nursing and stroke council. *Circulation* 2006;114(2):168-82. doi: 10.1161/CIRCULATIONAHA.106.176040 [published Online First: 2006/06/26]
10. Wechkunanukul K, Grantham H, Clark RA. Global review of delay time in seeking medical care for chest pain: An integrative literature review. *Aust Crit Care* 2017;30(1):13-20. doi: 10.1016/j.aucc.2016.04.002 [published Online First: 2016/04/23]
11. Thang ND, Karlson BW, Bergman B, et al. Characteristics of and outcome for patients with chest pain in relation to transport by the emergency medical services in a 20-year perspective. *American Journal of Emergency Medicine* 2012;30(9):1788-95. doi: 10.1016/j.ajem.2012.02.014
12. Wibring K, Lingman M, Herlitz J, et al. Prehospital stratification in acute chest pain patient into high risk and low risk by emergency medical service: a prospective cohort study. *BMJ Open* 2021;11(4):e044938. doi: 10.1136/bmjopen-2020-044938 [published Online First: 2021/04/15]
13. Wibring K, Lingman M, Herlitz J, et al. Development of a prehospital prediction model for risk stratification of patients with chest pain. *Am J Emerg Med* 2021;51:26-31. doi: 10.1016/j.ajem.2021.09.079 [published Online First: 20211009]
14. Wibring K, Lingman M, Herlitz J, et al. Guideline adherence among prehospital emergency nurses when caring for patients with chest pain: a prospective cohort study. *Scand J Trauma Resusc Emerg Med* 2021;29(1):157. doi: 10.1186/s13049-021-00972-5 [published Online First: 20211030]

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

15. Eloge J, Napier TC, Dantz B. OPQRST(U): Integrating substance use disorders or "Use" into the medical history. *Subst Abus* 2018;39(4):505-08. doi: 10.1080/08897077.2018.1469104 [published Online First: 2018/08/17]
16. Wibring K, Herlitz J, Lingman M, et al. Symptom description in patients with chest pain - a qualitative analysis of emergency medical calls involving high-risk conditions. *J Clin Nurs* 2019 doi: 10.1111/jocn.14867 [published Online First: 2019/04/02]
17. Magnusson C, Herlitz J, Axelsson C. Patient characteristics, triage utilisation, level of care, and outcomes in an unselected adult patient population seen by the emergency medical services: a prospective observational study. *BMC Emerg Med* 2020;20(1):7. doi: 10.1186/s12873-020-0302-x [published Online First: 2020/01/30]
18. Widgren BR, Jourak M. Medical Emergency Triage and Treatment System (METTS): a new protocol in primary triage and secondary priority decision in emergency medicine. *J Emerg Med* 2011;40(6):623-8. doi: 10.1016/j.jemermed.2008.04.003 [published Online First: 2008/10/18]
19. Nishi FA, Polak C, Cruz DALM. Sensitivity and specificity of the Manchester Triage System in risk prioritization of patients with acute myocardial infarction who present with chest pain. *Eur J Cardiovasc Nurs* 2018;17(7):660-66. doi: 10.1177/1474515118777402 [published Online First: 2018/05/11]
20. Sederholm Lawesson S, Isaksson RM, Ericsson M, et al. Gender disparities in first medical contact and delay in ST-elevation myocardial infarction: a prospective multicentre Swedish survey study. *BMJ Open* 2018;8(5):e020211. doi: 10.1136/bmjopen-2017-020211 [published Online First: 2018/05/03]
21. Lichtman JH, Leifheit EC, Safdar B, et al. Sex Differences in the Presentation and Perception of Symptoms Among Young Patients With Myocardial Infarction: Evidence from the VIRGO Study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). *Circulation* 2018;137(8):781-90. doi: 10.1161/CIRCULATIONAHA.117.031650
22. Kirchberger I, Heier M, Kuch B, et al. Sex differences in patient-reported symptoms associated with myocardial infarction (from

For peer review only

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

the population-based MONICA/KORA Myocardial Infarction Registry). *Am J Cardiol* 2011;107(11):1585-9. doi: 10.1016/j.amjcard.2011.01.040 [published Online First: 20110321]

23. Araújo C, Laszczyńska O, Viana M, et al. Sex differences in presenting symptoms of acute coronary syndrome: the EPIHeart cohort study. *BMJ Open* 2018;8(2):e018798. doi: 10.1136/bmjopen-2017-018798 [published Online First: 20180223]
24. Coventry LL, Finn J, Bremner AP. Sex differences in symptom presentation in acute myocardial infarction: a systematic review and meta-analysis. *Heart Lung* 2011;40(6):477-91. doi: 10.1016/j.hrtlng.2011.05.001
25. Tisminetzky M, Gurwitz JH, Miozzo R, et al. Age Differences in the Chief Complaint Associated With a First Acute Myocardial Infarction and Patient's Care-Seeking Behavior. *Am J Med* 2020;133(9):e501-e07. doi: 10.1016/j.amjmed.2020.02.018 [published Online First: 20200318]
26. Kirchberger I, Heier M, Golüke H, et al. Mismatch of presenting symptoms at first and recurrent acute myocardial infarction. From the MONICA/KORA Myocardial Infarction Registry. *Eur J Prev Cardiol* 2016;23(4):377-84. doi: 10.1177/2047487315588071 [published Online First: 20150520]
27. Manistamara H, Sella YO, Apriliawan S, et al. Chest pain symptoms differences between diabetes mellitus and non-diabetes mellitus patients with acute coronary syndrome: A pilot study. *J Public Health Res* 2021;10(2) doi: 10.4081/jphr.2021.2186 [published Online First: 20210414]
28. Maurin Söderholm H, Andersson H, Andersson Hagiwara M, et al. Research challenges in prehospital care: the need for a simulation-based prehospital research laboratory. *Adv Simul (Lond)* 2019;4:3. doi: 10.1186/s41077-019-0090-0 [published Online First: 2019/02/13]
29. Dickert NW, Brown J, Cairns CB, et al. Confronting Ethical and Regulatory Challenges of Emergency Care Research With Conscious Patients. *Ann Emerg Med* 2016;67(4):538-45. doi: 10.1016/j.annemergmed.2015.10.026 [published Online First: 2015/12/18]

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

30. Kang H. The prevention and handling of the missing data. *Korean J Anesthesiol* 2013;64(5):402-6. doi: 10.4097/kjae.2013.64.5.402 [published Online First: 20130524]

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

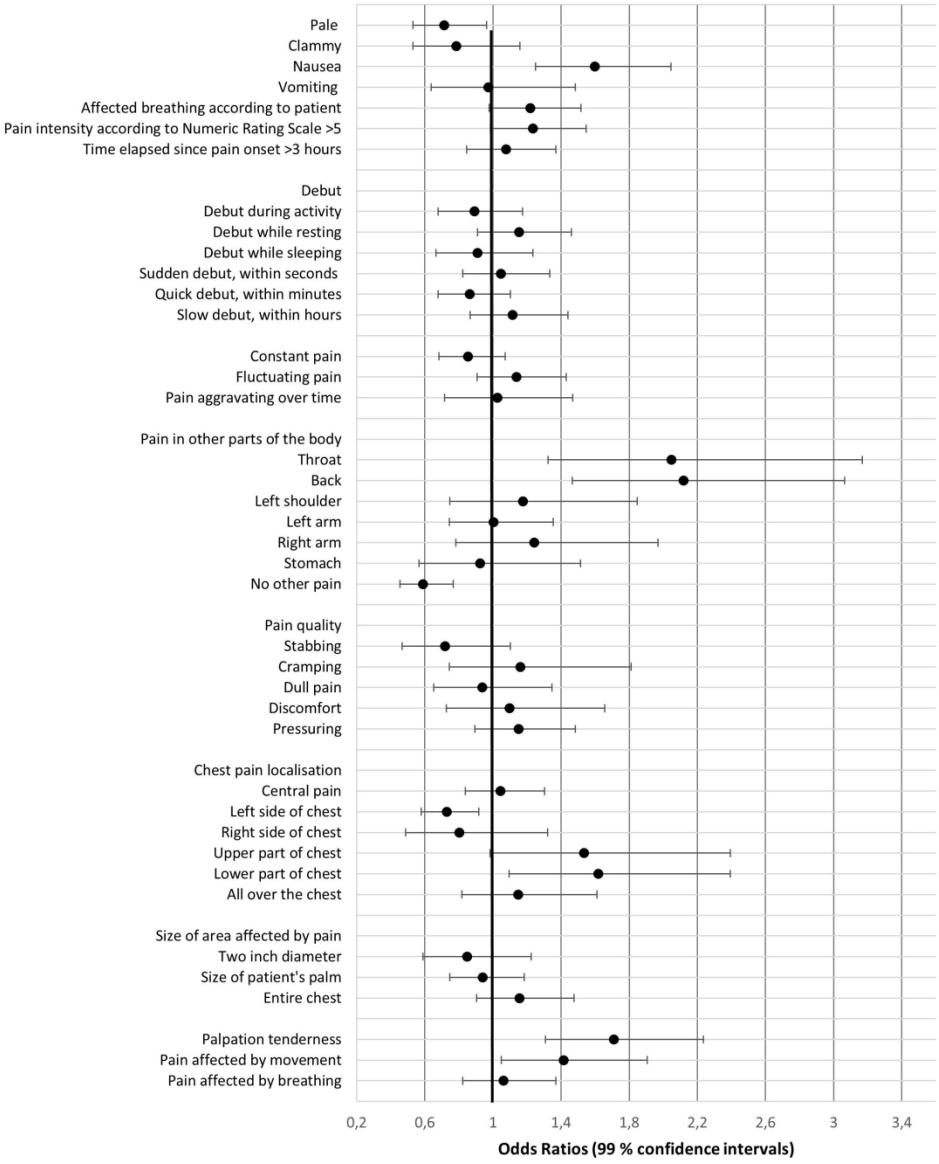

Figure 1 - Differences in clinical presentation based on sex

190x234mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

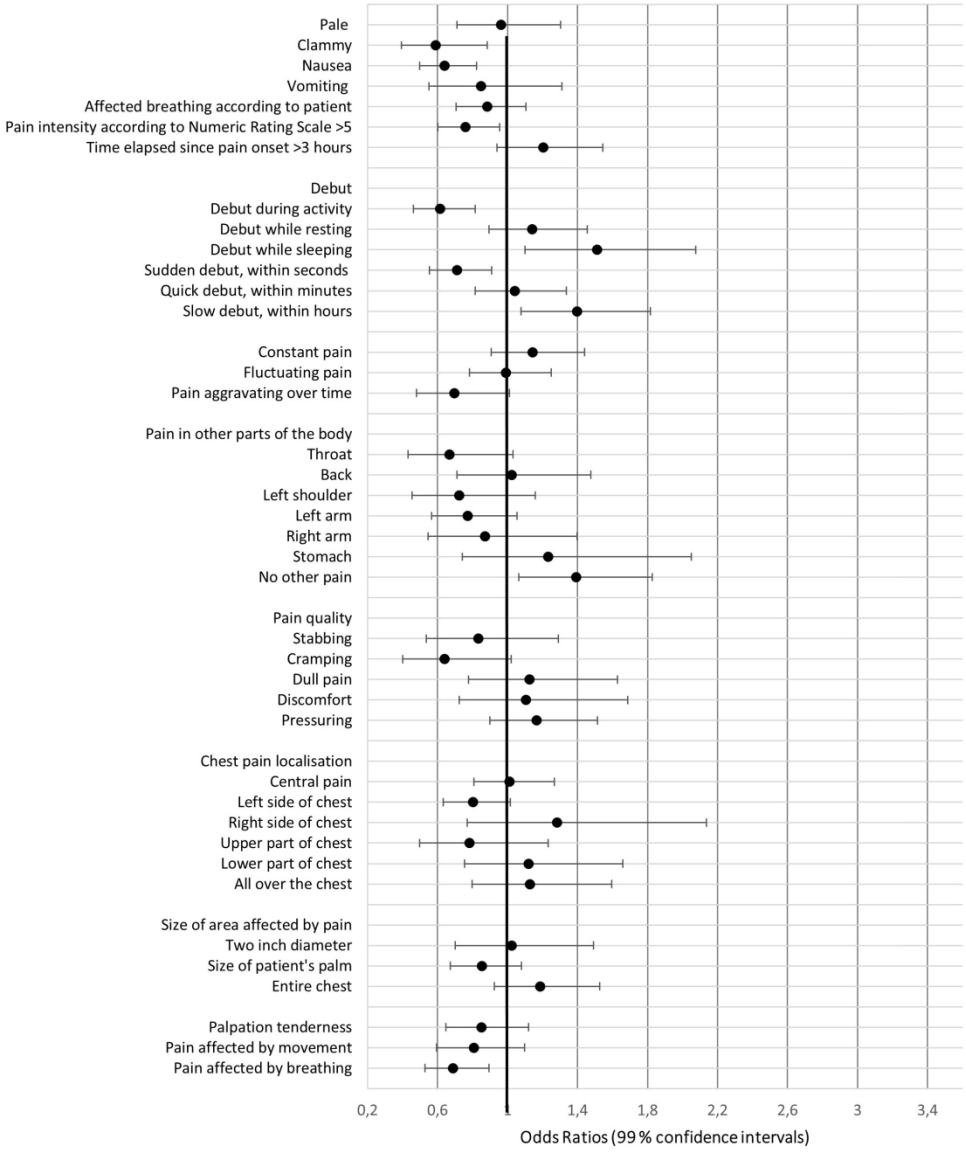

Figure 2 - Differences in clinical presentation based on age

190x223mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

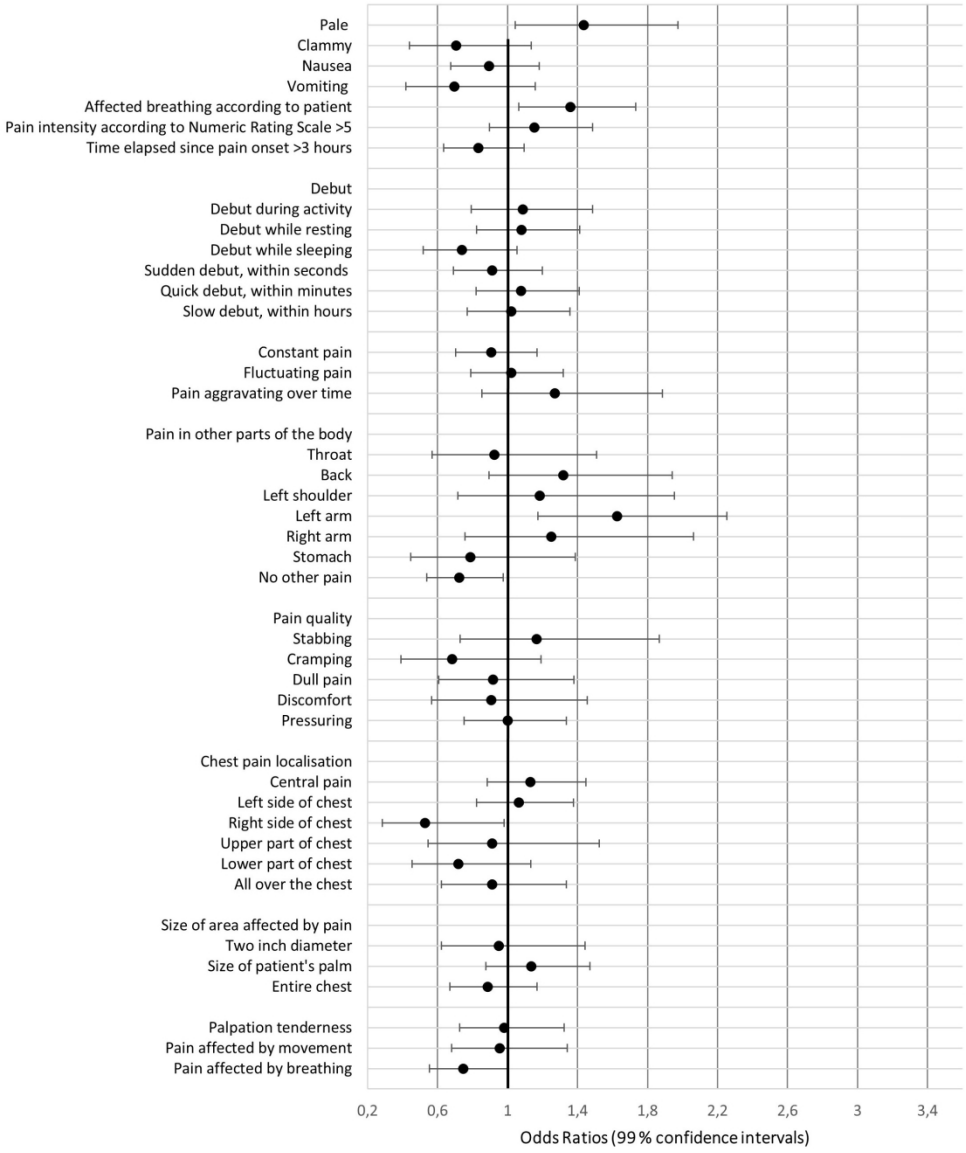

Figure 3 - Differences in clinical presentation based on history of ACS

190x221mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

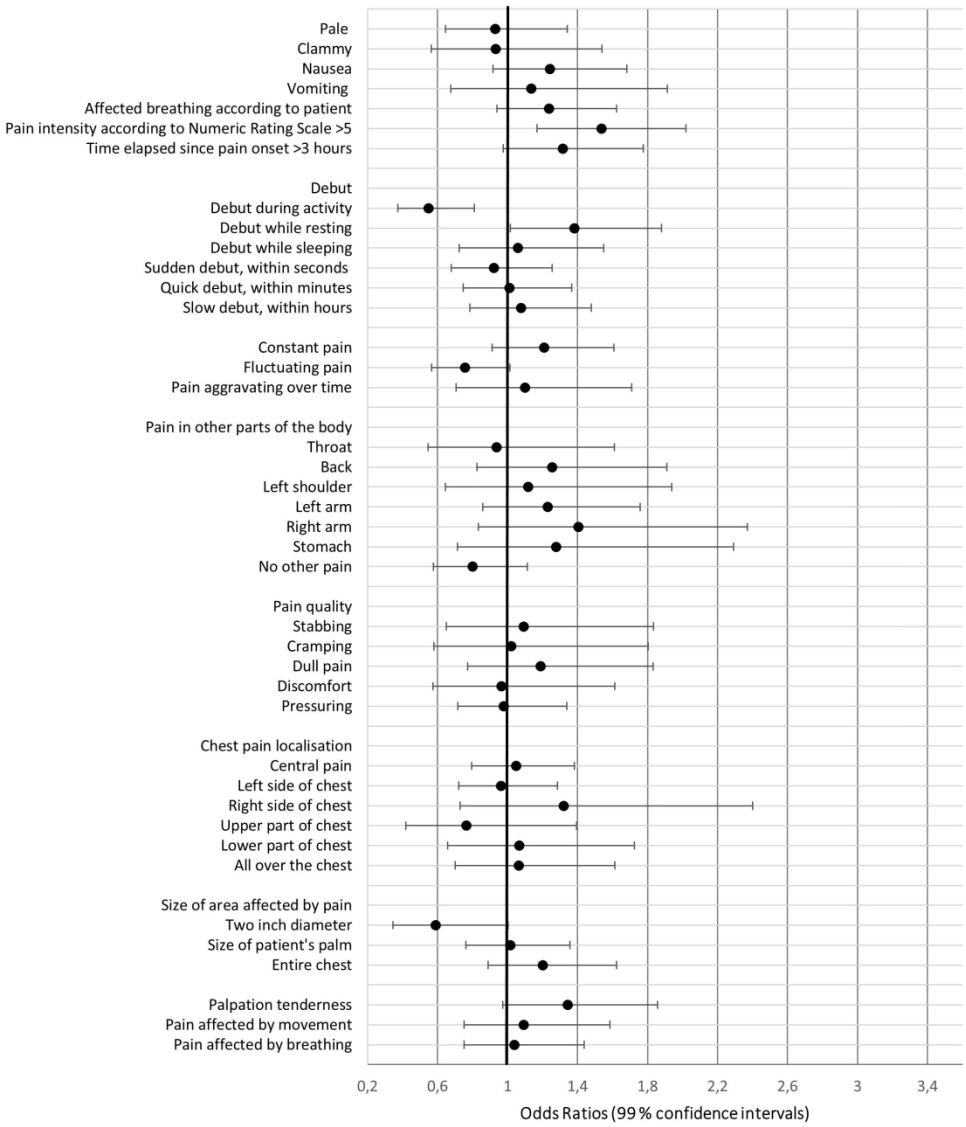

Figure 4 - Differences in clinical presentation based on history of diabetes mellitus

190x216mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Supplemental material 1 - Multivariate analyses of differences in symptoms based on sex

	All % (n)	Women % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	49.8 (1452)			
Pale (565)	16.4 (386)	13.5 (157)	0.004*	0.71	0.53-0.96
Clammy (565)	8.7 (204)	7.4 (86)	0.109	0.78	0.53-1.16
Nausea (576)	27.1 (635)	31.3 (363)	<0.001*	1.6	1.25-2.05
Vomiting (576)	7.0 (165)	6.9 (80)	0.866	0.97	0.64-1.48
Affected breathing according to patient (596)	44.6 (1040)	46.8 (537)	0.020	1.22	0.98-1.52
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	33.6 (1228)	0.016	1.23	0.99-1.55
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	46.5 (442)	0.425	1.08	0.85-1.37
Debut					
Debut during activity (752)	22.1 (479)	20.5 (217)	0.284	0.89	0.68-1.17
Debut while resting (752)	65.5 (1419)	67.4 (714)	0.125	1.15	0.91-1.46
Debut while sleeping (752)	15.8 (342)	15.6 (165)	0.411	0.91	0.67-1.23
Sudden debut, within seconds (875)	35.7 (729)	36.1 (361)	0.622	1.05	0.82-1.33
Quick debut, within minutes (875)	35.2 (718)	33.2 (332)	0.122	0.86	0.68-1.10
Slow debut, within hours (875)	29.1 (595)	30.8 (308)	0.266	1.12	0.87-1.44
Constant pain (732)	55.5 (1212)	53.3 (574)	0.072	0.85	0.68-1.07
Fluctuating pain (732)	40.4 (883)	42.3 (456)	0.145	1.14	0.91-1.43
Pain aggravating over time (732)	10.8 (237)	10.8 (116)	0.861	1.03	0.72-1.47
Pain in other parts of the body (1197)					
Head	2.5 (43)	3.3 (29)	–	–	–
Throat	10.3 (177)	13.3 (117)	<0.001*	2.05	1.32-3.17
Jaw	5.3 (92)	5.8 (51)	–	–	–
Neck	2.5 (43)	3.4 (30)	–	–	–
Between scapulars	2.2 (37)	2.7 (24)	–	–	–
Back	15.2 (261)	19.5 (171)	<0.001*	2.12	1.47-3.07
Left shoulder	8.5 (147)	9.0 (79)	0.358	1.18	0.75-1.85
Right shoulder	4.2 (72)	4.6 (40)	–	–	–
Left arm	24.0 (412)	23.0 (202)	0.974	1.00	0.74-1.35
Right arm	8.4 (145)	8.8 (77)	0.226	1.24	0.78-1.97
Left hand	1.0 (17)	0.7 (6)	–	–	–
Right hand	0.3 (6)	0.1 (1)	–	–	–
Stomach	7.0 (121)	7.1 (62)	0.685	0.93	0.57-1.52
Left leg	1.7 (29)	1.8 (16)	–	–	–
Right leg	1.4 (24)	1.4 (12)	–	–	–
No other pain	39.3 (676)	34.2 (301)	<0.001*	0.59	0.45-0.77
Pain quality (1175)					
Band-shaped	3.3 (58)	3.7 (32)	–	–	–
Burning	4.4 (76)	5.4 (46)	–	–	–
Stabbing	9.7 (169)	8.3 (71)	0.047	0.72	0.47-1.10
Cramping	8.7 (151)	9.1 (78)	0.392	1.16	0.74-1.81
Dull pain	13.9 (242)	13.6 (116)	0.646	0.94	0.65-1.35
Feels like something is on the chest	0.7 (12)	0.6 (5)	–	–	–
Discomfort	10.2 (178)	10.8 (92)	0.563	1.10	0.73-1.66
Tingling/Stinging	5.7 (99)	5.1 (44)	–	–	–
Swaying	1.7 (30)	1.6 (14)	–	–	–
Pressuring	57.9 (1008)	59.6 (510)	0.153	1.15	0.89-1.48
Heaviness	1.0 (17)	1.3 (11)	–	–	–
Aching	2.4 (41)	2.1 (18)	–	–	–

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 1 continues

	All % (n)	Women % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	53.3 (599)	0.612	1.04	0.84-1.30
Left side of chest	35.5 (809)	32.0 (359)	<0.001*	0.73	0.58-0.91
Right side of chest	5.1 (116)	4.8 (54)	0.256	0.80	0.49-1.32
Upper part of chest	6.7 (152)	7.9 (89)	0.013	1.53	0.98-2.39
Lower part of chest	9.0 (204)	11.1 (125)	0.002*	1.62	1.09-2.39
All over the chest	11.8 (269)	12.6 (141)	0.299	1.15	0.82-1.61
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.2 (107)	0.251	0.85	0.59-1.23
Size of patient's palm	58.4 (1240)	57.4 (601)	0.492	0.94	0.75-1.18
Entire chest	30.9 (655)	32.4 (339)	0.131	1.16	0.90-1.48
Palpation tenderness (655)	22.3 (505)	27.1 (302)	<0.001*	1.71	1.31-2.24
Pain affected by movement (719)	17.0 (373)	19.6 (211)	0.003*	1.41	1.05-1.91
Pain affected by breathing (692)	25.8 (573)	26.6 (292)	0.543	1.06	0.82-1.37

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Supplemental material 2 - Multivariate analyses of differences in symptoms based on age

	All % (n)	Age >72 % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	49.2 (1436)			
Pale (565)	16.4 (386)	16.7 (196)	0.745	0.96	0.71-1.30
Clammy (565)	8.7 (204)	6.4 (75)	0.001*	0.58	0.39-0.88
Nausea (576)	27.1 (635)	23.2 (270)	<0.001*	0.64	0.49-0.82
Vomiting (576)	7.0 (165)	6.3 (74)	0.331	0.84	0.55-1.31
Affected breathing according to patient (596)	44.6 (1040)	44.2 (514)	0.155	0.88	0.70-1.10
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	30.1 (372)	0.002*	0.75	0.60-0.95
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	47.3 (445)	0.053	1.20	0.94-1.54
Debut					
Debut during activity (752)	22.1 (479)	17.8 (191)	<0.001*	0.61	0.46-0.81
Debut while resting (752)	65.5 (1419)	67.6 (725)	0.164	1.14	0.89-1.45
Debut while sleeping (752)	15.8 (342)	18.1 (194)	0.001*	1.51	1.09-2.07
Sudden debut, within seconds (875)	35.7 (729)	31.4 (313)	<0.001*	0.71	0.55-0.91
Quick debut, within minutes (875)	35.2 (718)	35.8 (357)	0.666	1.04	0.81-1.33
Slow debut, within hours (875)	29.1 (595)	32.7 (326)	0.001*	1.39	1.07-1.81
Constant pain (732)	55.5 (1212)	57.1 (615)	0.136	1.14	0.90-1.44
Fluctuating pain (732)	40.4 (883)	40.0 (431)	0.911	0.99	0.78-1.25
Pain aggravating over time (732)	10.8 (237)	9.4 (101)	0.012	0.69	0.48-1.01
Pain in other parts of the body (1197)					
Head	2.5 (43)	1.8 (15)	–	–	–
Throat	10.3 (177)	8.6 (73)	0.016	0.66	0.43-1.03
Jaw	5.3 (92)	3.8 (32)	–	–	–
Neck	2.5 (43)	2.5 (21)	–	–	–
Between scapulars	2.2 (37)	1.5 (13)	–	–	–
Back	15.2 (261)	16.4 (139)	0.871	1.02	0.71-1.47
Left shoulder	8.5 (147)	7.5 (64)	0.077	0.72	0.45-1.15
Right shoulder	4.2 (72)	4.0 (34)	–	–	–
Left arm	24.0 (412)	23.1 (196)	0.032	0.77	0.56-1.05
Right arm	8.4 (145)	8.5 (72)	0.454	0.87	0.54-1.39
Left hand	1.0 (17)	0.4 (3)	–	–	–
Right hand	0.3 (6)	0.2 (2)	–	–	–
Stomach	7.0 (121)	7.5 (64)	0.290	1.23	0.74-2.05
Left leg	1.7 (29)	1.8 (15)	–	–	–
Right leg	1.4 (24)	1.4 (12)	–	–	–
No other pain	39.3 (676)	41.3 (351)	0.002*	1.39	1.06-1.82
Pain quality (1175)					
Band-shaped	3.3 (58)	3.4 (29)	–	–	–
Burning	4.4 (76)	3.5 (30)	–	–	–
Stabbing	9.7 (169)	8.8 (75)	0.280	0.83	0.53-1.29
Cramping	8.7 (151)	6.7 (57)	0.014	0.63	0.40-1.02
Dull pain	13.9 (242)	14.6 (124)	0.414	1.12	0.77-1.62
Feels like something is on the chest	0.7 (12)	0.6 (5)	–	–	–
Discomfort	10.2 (178)	10.6 (90)	0.547	1.10	0.72-1.68
Tingling/Stinging	5.7 (99)	4.9 (42)	–	–	–
Swaying	1.7 (30)	1.5 (13)	–	–	–
Pressuring	57.9 (1008)	60.0 (510)	0.129	1.16	0.89-1.51
Heaviness	1.0 (17)	1.1 (9)	–	–	–
Aching	2.4 (41)	2.4 (20)	–	–	–

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Supplemental material 2 continues

	All % (n)	Age >72 % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	54.2 (613)	0.898	1.01	0.80-1.26
Left side of chest	35.5 (809)	32.7 (370)	0.016	0.80	0.63-1.01
Right side of chest	5.1 (116)	5.4 (61)	0.208	1.28	0.77-2.13
Upper part of chest	6.7 (152)	5.9 (67)	0.163	0.78	0.49-1.23
Lower part of chest	9.0 (204)	9.3 (105)	0.462	1.11	0.75-1.65
All over the chest	11.8 (269)	12.5 (141)	0.374	1.12	0.79-1.59
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.4 (109)	0.875	1.02	0.70-1.49
Size of patient's palm	58.4 (1240)	56.7 (594)	0.082	0.85	0.67-1.07
Entire chest	30.9 (655)	32.9 (344)	0.078	1.18	0.92-1.52
Palpation tenderness (655)	22.3 (505)	21.3 (239)	0.129	0.85	0.64-1.11
Pain affected by movement (719)	17.0 (373)	15.5 (169)	0.073	0.80	0.59-1.09
Pain affected by breathing (692)	25.8 (573)	21.5 (236)	<0.001*	0.68	0.52-0.89

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Supplemental material 3 - Multivariate analyses of differences in symptoms based on previous history of ACS

	All % (n)	History of ACS % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	29.3 (856)			
Pale (565)	16.4 (386)	19.9 (140)	0.004*	1.43	1.04-1.97
Clammy (565)	8.7 (204)	6.2 (44)	0.059	0.70	0.44-1.13
Nausea (576)	27.1 (635)	24.0 (169)	0.298	0.89	0.67-1.18
Vomiting (576)	7.0 (165)	5.4 (38)	0.067	0.69	0.41-1.15
Affected breathing according to patient (596)	44.6 (1040)	49.6 (347)	0.001*	1.35	1.06-1.73
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	33.7 (248)	0.144	1.15	0.89-1.48
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	43.4 (245)	0.087	0.83	0.63-1.09
Debut					
Debut during activity (752)	22.1 (479)	20.8 (132)	0.501	1.08	0.79-1.48
Debut while resting (752)	65.5 (1419)	67.8 (431)	0.468	1.07	0.82-1.41
Debut while sleeping (752)	15.8 (342)	14.2 (90)	0.029	0.73	0.51-1.05
Sudden debut, within seconds (875)	35.7 (729)	32.7 (199)	0.380	0.91	0.69-1.19
Quick debut, within minutes (875)	35.2 (718)	36.6 (223)	0.483	1.07	0.82-1.41
Slow debut, within hours (875)	29.1 (595)	30.7 (187)	0.850	1.02	0.76-1.35
Constant pain (732)	55.5 (1212)	54.9 (358)	0.322	0.90	0.70-1.16
Fluctuating pain (732)	40.4 (883)	40.0 (261)	0.837	1.02	0.79-1.31
Pain aggravating over time (732)	10.8 (237)	12.0 (78)	0.122	1.26	0.85-1.88
Pain in other parts of the body (1197)					
Head	2.5 (43)	2.0 (10)	–	–	–
Throat	10.3 (177)	8.8 (45)	0.683	0.92	0.56-1.50
Jaw	5.3 (92)	5.3 (27)	–	–	–
Neck	2.5 (43)	2.9 (15)	–	–	–
Between scapulars	2.2 (37)	1.6 (8)	–	–	–
Back	15.2 (261)	17.5 (89)	0.066	1.31	0.89-1.94
Left shoulder	8.5 (147)	9.0 (46)	0.390	1.18	0.71-1.95
Right shoulder	4.2 (72)	3.5 (18)	–	–	–
Left arm	24.0 (412)	29.4 (150)	<0.001*	1.62	1.17-2.25
Right arm	8.4 (145)	9.4 (48)	0.251	1.25	0.75-2.06
Left hand	1.0 (17)	0.2 (1)	–	–	–
Right hand	0.3 (6)	0.2 (1)	–	–	–
Stomach	7.0 (121)	6.5 (33)	0.275	0.78	0.44-1.38
Left leg	1.7 (29)	1.0 (5)	–	–	–
Right leg	1.4 (24)	0.6 (3)	–	–	–
No other pain	39.3 (676)	35.9 (183)	0.005*	0.72	0.53-0.97
Pain quality (1175)					
Band-shaped	3.3 (58)	3.0 (15)	–	–	–
Burning	4.4 (76)	4.3 (22)	–	–	–
Stabbing	9.7 (169)	10.7 (54)	0.399	1.16	0.72-1.86
Cramping	8.7 (151)	6.1 (31)	0.078	0.68	0.39-1.19
Dull pain	13.9 (242)	13.6 (69)	0.582	0.91	0.60-1.38
Feels like something is on the chest	0.7 (12)	0.4 (2)	–	–	–
Discomfort	10.2 (178)	9.7 (49)	0.596	0.90	0.56-1.45
Tingling/Stinging	5.7 (99)	5.9 (30)	–	–	–
Swaying	1.7 (30)	2.0 (10)	–	–	–
Pressuring	57.9 (1008)	58.3 (295)	0.985	1.00	0.75-1.33
Heaviness	1.0 (17)	0.8 (4)	–	–	–
Aching	2.4 (41)	3.0 (15)	–	–	–

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 3 continues

	All % (n)	History of ACS % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	55.4 (377)	0.202	1.13	0.88-1.44
Left side of chest	35.5 (809)	36.0 (245)	0.532	1.06	0.82-1.37
Right side of chest	5.1 (116)	3.5 (24)	0.008*	0.52	0.28-0.98
Upper part of chest	6.7 (152)	5.7 (39)	0.639	0.91	0.54-1.52
Lower part of chest	9.0 (204)	7.2 (49)	0.061	0.71	0.45-1.13
All over the chest	11.8 (269)	11.3 (77)	0.531	0.91	0.62-1.33
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	10.1 (63)	0.746	0.94	0.62-1.44
Size of patient's palm	58.4 (1240)	60.0 (374)	0.207	1.13	0.87-1.47
Entire chest	30.9 (655)	29.9 (186)	0.259	0.88	0.67-1.16
Palpation tenderness (655)	22.3 (505)	21.6 (146)	0.860	0.98	0.72-1.32
Pain affected by movement (719)	17.0 (373)	15.9 (105)	0.729	0.95	0.68-1.34
Pain affected by breathing (692)	25.8 (573)	20.9 (139)	0.012	0.74	0.55-1.00

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Supplemental material 4 - Multivariate analyses of differences in symptoms based on previous history of diabetes mellitus

	All % (n)	History of DM % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)	19.8 (578)			
Pale (565)	16.4 (386)	17.1 (81)	0.611	0.93	0.64-1.34
Clammy (565)	8.7 (204)	7.8 (37)	0.712	0.93	0.56-1.53
Nausea (576)	27.1 (635)	28.9 (137)	0.064	1.24	0.91-1.68
Vomiting (576)	7.0 (165)	7.4 (35)	0.527	1.13	0.67-1.91
Affected breathing according to patient (596)	44.6 (1040)	49.0 (229)	0.045	1.23	0.94-1.62
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	39.8 (197)	<0.001*	1.53	1.16-2.02
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	50.4 (195)	0.018	1.31	0.97-1.77
Debut					
Debut during activity (752)	22.1 (479)	14.7 (64)	<0.001*	0.54	0.37-0.81
Debut while resting (752)	65.5 (1419)	71.3 (310)	0.007*	1.38	1.01-1.88
Debut while sleeping (752)	15.8 (342)	16.6 (72)	0.702	1.05	0.72-1.54
Sudden debut, within seconds (875)	35.7 (729)	33.0 (136)	0.503	0.92	0.67-1.25
Quick debut, within minutes (875)	35.2 (718)	36.2 (149)	0.933	1.01	0.74-1.36
Slow debut, within hours (875)	29.1 (595)	30.8 (127)	0.540	1.07	0.78-1.47
Constant pain (732)	55.5 (1212)	59.8 (266)	0.084	1.21	0.91-1.60
Fluctuating pain (732)	40.4 (883)	34.8 (155)	0.014	0.75	0.56-1.01
Pain aggravating over time (732)	10.8 (237)	11.5 (51)	0.583	1.09	0.70-1.71
Pain in other parts of the body (1197)					
Head	2.5 (43)	2.3 (8)	–	–	–
Throat	10.3 (177)	9.1 (32)	0.759	0.93	0.54-1.61
Jaw	5.3 (92)	4.5 (16)	–	–	–
Neck	2.5 (43)	3.4 (12)	–	–	–
Between scapulars	2.2 (37)	1.4 (5)	–	–	–
Back	15.2 (261)	17.8 (63)	0.163	1.25	0.82-1.91
Left shoulder	8.5 (147)	9.1 (32)	0.602	1.11	0.64-1.93
Right shoulder	4.2 (72)	5.4 (19)	–	–	–
Left arm	24.0 (412)	28.0 (99)	0.137	1.23	0.85-1.75
Right arm	8.4 (145)	11.0 (39)	0.094	1.40	0.83-2.37
Left hand	1.0 (17)	0.8 (3)	–	–	–
Right hand	0.3 (6)	0.6 (2)	–	–	–
Stomach	7.0 (121)	8.2 (29)	0.280	1.27	0.71-2.29
Left leg	1.7 (29)	2.8 (10)	–	–	–
Right leg	1.4 (24)	2.8 (10)	–	–	–
No other pain	39.3 (676)	35.4 (125)	0.081	0.80	0.57-1.11
Pain quality (1175)					
Band-shaped	3.3 (58)	2.2 (8)	–	–	–
Burning	4.4 (76)	5.8 (21)	–	–	–
Stabbing	9.7 (169)	10.2 (37)	0.663	1.09	0.65-1.83
Cramping	8.7 (151)	8.0 (29)	0.926	1.02	0.57-1.80
Dull pain	13.9 (242)	15.7 (57)	0.302	1.18	0.77-1.83
Feels like something is on the chest	0.7 (12)	0.0 (0)	–	–	–
Discomfort	10.2 (178)	9.9 (36)	0.853	0.96	0.57-1.61
Tingling/Stinging	5.7 (99)	5.5 (20)	–	–	–
Swaying	1.7 (30)	1.4 (5)	–	–	–
Pressuring	57.9 (1008)	58.0 (211)	0.858	0.97	0.71-1.33
Heaviness	1.0 (17)	0.5 (2)	–	–	–
Aching	2.4 (41)	2.7 (10)	–	–	–

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 4 continues

	All % (n)	History of DM % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	55.3 (255)	0.660	1.04	0.79-1.38
Left side of chest	35.5 (809)	34.3 (461)	0.729	0.96	0.72-1.28
Right side of chest	5.1 (116)	5.9 (27)	0.229	1.32	0.72-2.40
Upper part of chest	6.7 (152)	5.2 (24)	0.250	0.76	0.42-1.39
Lower part of chest	9.0 (204)	8.9 (41)	0.734	1.06	0.65-1.72
All over the chest	11.8 (269)	12.4 (57)	0.706	1.06	0.70-1.61
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	7.0 (30)	0.010	0.58	0.34-1.00
Size of patient's palm	58.4 (1240)	58.7 (252)	0.888	1.01	0.76-1.35
Entire chest	30.9 (655)	34.3 (147)	0.119	1.20	0.88-1.62
Palpation tenderness (655)	22.3 (505)	25.4 (115)	0.019	1.34	0.97-1.85
Pain affected by movement (719)	17.0 (373)	17.1 (76)	0.540	1.09	0.75-1.58
Pain affected by breathing (692)	25.8 (573)	24.3 (109)	0.753	1.04	0.75-1.43

[a]Multivariate regression analyses including sex, age, previous history of ACS or diabetes mellitus and diagnosis of AMI on hospital discharge

*p-value <0.01 i.e. statistically significant

DM = Diabetes mellitus

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Supplemental material 5 - Differences in symptoms based on diagnosis of AMI on hospital discharge

	All % (n)	Diagnosis om AMI on hospital discharge % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
All (number of missing)	100 (2917)				
Pale (565)	16.4 (386)	30.1 (83)	<0.001*	2.26	1.80-3.82
Clammy (565)	8.7 (204)	15.6 (42)	<0.001*	2.19	1.36-3.55
Nausea (576)	27.1 (635)	27.3 (73)	0.933	1.01	0.70-1.47
Vomiting (576)	7.0 (165)	9.0 (24)	0.190	1.35	0.75-2.46
Affected breathing according to patient (596)	44.6 (1040)	38.7 (103)	0.040	0.76	0.54-1.07
Pain intensity according to Numeric Rating Scale >5	32.1 (803)	40.5 (120)	0.001*	1.52	1.10-2.12
Time elapsed since pain onset >3 hours (1007)	45.2 (863)	40.6 (91)	0.145	0.81	0.59-1.18
Debut					
Debut during activity (752)	22.1 (479)	33.1 (83)	<0.001*	1.89	1.30-2.76
Debut while resting (752)	65.5 (1419)	57.4 (144)	0.004*	0.67	0.48-0.96
Debut while sleeping (752)	15.8 (342)	12.7 (32)	0.160	0.76	0.45-1.26
Sudden debut, within seconds (875)	35.7 (729)	34.7 (85)	0.726	0.95	0.66-1.38
Quick debut, within minutes (875)	35.2 (718)	43.3 (106)	0.005*	1.48	1.03-2.11
Slow debut, within hours (875)	29.1 (595)	22.0 (54)	0.010	0.66	0.43-1.00
Constant pain (732)	55.5 (1212)	65.5 (165)	0.001*	1.61	1.12-2.30
Fluctuating pain (732)	40.4 (883)	32.1 (81)	0.005*	0.67	0.46-0.96
Pain aggravating over time (732)	10.8 (237)	9.9 (25)	0.615	0.89	0.50-1.59
Pain in other parts of the body (1197)					
Head	2.5 (43)	0.5 (1)	–	–	–
Throat	10.3 (177)	8.1 (17)	0.265	0.74	0.37-1.48
Jaw	5.3 (92)	9.0 (19)	–	–	–
Neck	2.5 (43)	3.3 (7)	–	–	–
Between scapulars	2.2 (37)	4.3 (9)	–	–	–
Back	15.2 (261)	18.1 (38)	0.209	1.28	0.78-2.10
Left shoulder	8.5 (147)	8.6 (18)	0.989	1.00	0.51-1.98
Right shoulder	4.2 (72)	6.2 (3)	–	–	–
Left arm	24.0 (412)	37.6 (79)	<0.001*	2.13	1.43-3.18
Right arm	8.4 (145)	17.6 (37)	<0.001*	2.78	1.63-4.73
Left hand	1.0 (17)	1.0 (2)	–	–	–
Right hand	0.3 (6)	0.5 (1)	–	–	–
Stomach	7.0 (121)	2.4 (5)	0.008*	0.29	0.09-0.97
Left leg	1.7 (29)	0.5 (1)	–	–	–
Right leg	1.4 (24)	0.0 (0)	–	–	–
No other pain	39.3 (676)	31.4 (66)	0.013	0.68	0.45-1.01
Pain quality (1175)					
Band-shaped	3.3 (58)	4.4 (9)	–	–	–
Burning	4.4 (76)	3.9 (8)	–	–	–
Stabbing	9.7 (169)	2.9 (6)	0.001*	0.27	0.09-0.76
Cramping	8.7 (151)	10.3 (21)	0.381	1.24	0.66-2.35
Dull pain	13.9 (242)	14.2 (29)	0.887	1.03	0.60-1.79
Feels like something is on the chest	0.7 (12)	1.5 (3)	–	–	–
Discomfort	10.2 (178)	8.8 (18)	0.485	0.83	0.43-1.63
Tingling/Stinging	5.7 (99)	2.0 (4)	–	–	–
Swaying	1.7 (30)	2.0 (4)	–	–	–
Pressuring	57.9 (1008)	62.7 (128)	0.134	1.26	0.85-1.88
Heaviness	1.0 (17)	1.0 (2)	–	–	–
Aching	2.4 (41)	3.4 (7)	–	–	–

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Supplemental material 5 continues

	All % (n)	Diagnosis om AMI on hospital discharge % (n)	p-value[a]	Odds Ratio	Confidence Interval, 99 %
Chest pain localisation (640)					
Central pain	53.4 (1215)	66.4 (176)	<0.001*	1.85	1.30-2.64
Left side of chest	35.5 (809)	27.5 (73)	0.004*	0.66	0.45-0.96
Right side of chest	5.1 (116)	1.9 (5)	0.016	0.33	0.10-1.08
Upper part of chest	6.7 (152)	7.9 (21)	0.387	1.24	0.66-2.32
Lower part of chest	9.0 (204)	5.7 (15)	0.048	0.58	0.28-1.18
All over the chest	11.8 (269)	13.2 (35)	0.455	1.16	0.70-1.91
Size of area affected by pain (794)					
Two inch diameter	10.7 (228)	5.6 (14)	0.006*	0.46	0.22-0.96
Size of patient's palm	58.4 (1240)	58.8 (147)	0.893	1.02	0.72-1.45
Entire chest	30.9 (655)	35.6 (89)	0..084	1.28	0.89-1.84
Palpation tenderness (655)	22.3 (505)	13.6 (35)	<0.001*	0.51	0.32-0.83
Pain affected by movement (719)	17.0 (373)	9.9 (25)	0.002*	0.50	0.29-0.88
Pain affected by breathing (692)	25.8 (573)	14.9 (39)	<0.001*	0.47	0.30-0.75

[a]Logistic regression

*p-value <0.01 i.e. statistically significant

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract		
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found		
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		
Objectives	3	State specific objectives, including any prespecified hypotheses		
Methods				
Study design	4	Present key elements of study design early in the paper		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants		
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4	Previous publication describing the cohort and data collection in detail.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Previous publication describing the cohort and data collection in detail.
Bias	9	Describe any efforts to address potential sources of bias	Previous publication describing the cohort and data collection in detail.
Study size	10	Explain how the study size was arrived at	Previous publication describing the cohort and data collection in detail.

Continued on next page

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Previous publication describing the cohort and data collection in detail.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	Previous publication describing the cohort and data collection in detail.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Previous publication describing the cohort and data collection in detail.
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Previous publication

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

			describing the cohort and data collection in detail.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	previous publication describing the cohort and data collection in detail.
		(b) Indicate number of participants with missing data for each variable of interest	Supplemental Material 1-4
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Supplemental Material 1-4 and Figure 1-
		(*b*) Report category boundaries when continuous variables were categorized	previous publication describing the cohort and data collection in detail.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-046332 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES). Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

	period

Continued on next page

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
d by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

bmjopen-2021-054622 on 8 August 2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l'Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.