BMJ Open

Diagnostic performance of reproducible chest wall tenderness to rule out acute coronary syndrome in acute chest pain: a prospective diagnostic study

Christoph Gräni,[1] Oliver Senn,[2] Manuel Bischof,[1] Pietro E Cippà,[3] Till Hauffe,[1] Lukas Zimmerli,[1,4] Edouard Battegay,[1,4] Daniel Franzen[1,5]

To cite: Gräni C, Senn O, Bischof M, *et al*. Diagnostic performance of reproducible chest wall tenderness to rule out acute coronary syndrome in acute chest pain: a prospective diagnostic study. *BMJ Open* 2015;**5**:e007442. doi:10.1136/bmjopen-2014-007442

▸ Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2014-007442).

Received 12 December 2014
Accepted 30 December 2014

[1]Division of Internal Medicine, University Hospital Zurich, Zurich, Switzerland
[2]Institute of General Practice and Health Services Research, University of Zurich, Zurich, Switzerland
[3]Division of Nephrology, University Hospital Zurich, Zurich, Switzerland
[4]Center of Competence Multimorbidity and University Research Priority Program Dynamics of Healthy Aging, University of Zurich, Zurich, Switzerland
[5]Pulmonary Division, University Hospital Zurich, Zurich, Switzerland

Correspondence to
Dr Christoph Gräni;
christoph.graeni@usz.ch

ABSTRACT

Objectives: Acute chest pain (ACP) is a leading cause of hospital emergency unit consultation. As there are various underlying conditions, ranging from musculoskeletal disorders to acute coronary syndrome (ACS), thorough clinical diagnostics are warranted. The aim of this prospective study was to assess whether reproducible chest wall tenderness (CWT) on palpation in patients with ACP can help to rule out ACS.

Methods: In this prospective, double-blinded diagnostic study, all consecutive patients assessed in the emergency unit at the University Hospital Zurich because of ACP between July 2012 and December 2013 were included when a member of the study team was present. Reproducible CWT on palpation was the initial step and was recorded before further examinations were initiated. The final diagnosis was adjudicated by a study-independent physician.

Results: 121 patients (60.3% male, median age 47 years, IQR 34–66.5 years) were included. The prevalence of ACS was 11.6%. Non-reproducible CWT had a high sensitivity of 92.9% (95% CI 66.1% to 98.8%) for ACS and the presence of reproducible CWT ruled out ACS (p=0.003) with a high negative predictive value (98.1%, 95% CI 89.9% to 99.7%). Conversely non-reproducible CWT ruled in ACS with low specificity (48.6%, 95% CI 38.8% to 58.5%) and low positive predictive value (19.1%, 95% CI 10.6% to 30.5%).

Conclusions: This prospective diagnostic study supports the concept that reproducible CWT helps to rule out ACS in patients with ACP in an early stage of the evaluation process. However, ACS and other diagnoses should be considered in patients with a negative CWT test.

Trial registration number: ClinicalTrial.gov: NCT01724996.

Strengths and limitations of this study

- This is the first study to our knowledge with a prospective, double-blinded design for the evaluation of chest wall tenderness on palpation in acute chest pain patients for ruling out acute coronary syndrome.
- Our study supports data from previous studies that reproducible chest wall tenderness helps to rule out acute coronary syndrome in acute chest pain admissions.
- Among the limitations are the small sample size and the possible interobserver and intraobserver variability due to multiple study members and difficulty of standardising the index test.

INTRODUCTION

Acute chest pain (ACP) accounts for approximately up to 10% of all medical emergency room admissions.[1–7] The estimated life time prevalence of ACP in the general population is 20–40%.[8] The spectrum of underlying conditions is broad and ranges from harmless musculoskeletal causes, gastro-oesophageal reflux disease, pneumonia, psychosomatic disorders to life-threatening conditions like pulmonary embolism, pneumothorax, aortic dissection and acute coronary syndrome (ACS). The reported incidence of ACS or angina pectoris in patients with ACP ranges between 4.8% and 12% in those seeking their general practitioners,[9–12] compared with up to 24% in patients presenting to University Hospital emergency units.[10]

In the diagnostic work-up of ACP, the medical history, clinical examination, laboratory tests, ECG and radiographic imaging are crucial to rapidly identify potentially life-threatening conditions such as ACS.[13–16] For example, ECG has a reported sensitivity between 20% and 60% for the diagnosis of ACS.[17] Laboratory results indicating myocardial ischaemia (troponin-I, troponin-T creatine kinase) may not be conclusive in the first hours after initiation of pain. This, therefore, mandates time-consuming serial laboratory tests.[17] Patients at low-to-intermediate risk with negative troponin, and normal or unclear ECG might have to undergo further testing like non-invasive cardiac imaging with radiation exposure.[18 19] Such patients show more downstream testing like expensive invasive coronary

angiography with additional radiation exposure and use of nephrotoxic radiographic contrast medium.[18 20 21]

Hence, it is desirable to have an early, fast and reliable bedside test to rule out ACS in patients presenting with ACP. Reproducible chest wall tenderness (CWT) on palpation of the thorax, where the maximum pain sensation is referred, is generally considered to be associated with a benign musculoskeletal cause and may help to rule out ACS in absence of additional examinations (ECG, laboratory tests, radiographic testing). Most of these studies were retrospective, in general practitioner settings, or the test was not clearly defined as one of the initial steps in the ACP evaluation process.[22–25] The exact diagnostic value of this sign has never been investigated in prospective and appropriately blinded clinical studies. To fill this lack of knowledge we aimed to evaluate, with a strict prospective and blinded design, the diagnostic performance of reproducible CWT as an easy bedside test to rule out early suspected ACS in emergency admissions presenting with ACP.

METHODS

Participants

Between July 2012 and December 2013, all consecutive patients referred by a third party or self-referred patients ≥18 years presenting with self-reported ACP (first or recurrent episode) at the emergency unit of the University Hospital Zurich were prospectively included in this study when a member of the study team was present. Exclusion criteria were recent thoracic surgery within 1 year, any chronic inflammatory joint or connective tissue disease, fibromyalgia and unstable haemodynamic condition with systolic blood pressure ≤90 mm Hg or tachyarrhythmia. Furthermore, patients referred directly to the cardiac chest pain unit by a third party or for whom laboratory results, ECG or chest X-ray were already available at the time of enrolment were excluded.

Written informed consent was obtained from all patients. The study was registered at http://www.clinicaltrials.gov (NCT01724996).

Index test

The index test is reproducible CWT on palpation. Patients were brought into supine position with 30° elevated upper body. Flat digital index with moderate pressure was applied, where the maximum pain was pointed by the patient. 'Reproducible CWT' or 'non-reproducible CWT' was noted.

Presence of reproducible CWT was defined as the following: the self-reported pain could be provoked in the same quality and intensity by digital palpation over the region of complaints over the chest. If no pain or any other pain than the self-reported pain by palpation could be elicited, the test result was defined as non-reproducible CWT.

Reference test

ACS was defined according to the universal definition of acute myocardial infarction in the ESC Guidelines from 2012.[26] The gold standard reference tests to rule out ACS in patients with ACP are serial troponin measurements and/or ECG.[27]

Study course in the emergency unit

After admission to the emergency unit, the first assessment and triage of patients with ACP was conducted by an attending physician or nurse not related to the study team to check for haemodynamic stability and for the need of urgent medical care. After enrolment, an investigator of the study performed the index test. Index test of CWT was noted before completing the standardised questionnaire (see below), and further initial routine clinical diagnostics, including medical history, physical examination, ECG, laboratory testing and chest X-ray, were initiated by a study-independent emergency physician. At the time of chest palpation, the investigator was blinded for the final diagnosis, which was made by another emergency physician independent of the study team, based on the initial diagnostic work-up and possible further examinations (eg, coronary angiography, CT).

Questionnaire and data collection

Intensity of ACP was graded with the visual analogue scale (VAS) ranging from 0 (no pain) to 10 (worst pain). Localisation of maximum pain (retrosternal, left or right chest side), pain radiation (right arm, left arm, neck, back or epigastric), quality of pain (stabbing, pressure, burning or squeezing), pain aggravating and relieving factors (respiration, movements or rest), and additional symptoms (dyspnoea, nausea, vertigo, sweating) were asked. Moreover, it was noted whether ACP was a first episode or recurrent episode, and if the patient was self-referred or referred by a third party. Previous coronary artery disease (CAD), cardiovascular risk factors (arterial hypertension, dyslipidaemia, obesity, family history, diabetes mellitus, smoking status), illicit drug use, alcohol consumption, medication and demographic data were registered.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, V.22 (IBM Corporation, Armonk, New York, USA). Data are reported as median±IQR from 25th to 75th centile or mean±SD or percentages, as appropriate. Continuous variables were analysed using the Student t test or Mann-Whitney U test, as appropriate. Categorical data were analysed with χ^2 test or Fisher's exact test, respectively. p Values of all outcomes were two-sided; a value less than 0.05 was considered to indicate statistical significance. CI was defined as 95%. Furthermore, diagnostic sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio (LR) and OR of reproducible CWT for ruling in or ruling out ACS were analysed. Multivariable logistic regression analysis was applied to investigate the independent association between ACS and CWT, controlling for established

cardiovascular risk factors (known CAD, age, sex, arterial hypertension, dyslipidaemia, family history of CAD, smoking and diabetes). Goodness-of-fit of the model was tested using Hosmer-Lemeshow χ^2 test.

RESULTS

Participants

A total of 121 patients (median age 47 years, IQR 34–66.5 years, 60.3% male) were included in the study. In total, 71.1% of patients were self-referrals. In 52.9% of patients, the ACP was the first episode. Demographic data and cardiovascular risk profile of all emergency admissions with ACP and categorised as ACS and non-ACS are summarised in table 1. Patients in the ACS group were significantly older and cardiovascular risk factors (dyslipidaemia and hypertension) were more prevalent. In figure 1 the self-reported localisation of the maximum ACP sensation is shown.

The characterisation of symptoms on emergency room admission is displayed in table 2. The self-reported chest pain in the ACS group was localised mainly retrosternal, and described as pressure compared with patients without ACS who had stabbing pain on the left side with aggravation on deep inspiration.

Final diagnosis

The leading cause of ACP was a musculoskeletal disorder (62, 51.2%) after other diagnoses had been excluded (table 3). In 14 (11.6%) patients, of whom the large majority were men, based on troponin and/or ECG changes the final diagnosis of ACS could be made. Thirteen patients were treated with percutaneous coronary intervention using drug-eluting stents while one was referred for urgent coronary artery bypass surgery (figure 2).

In figure 2 the flow chart of enrolment and outcomes of CWT test in ACP admissions is shown.

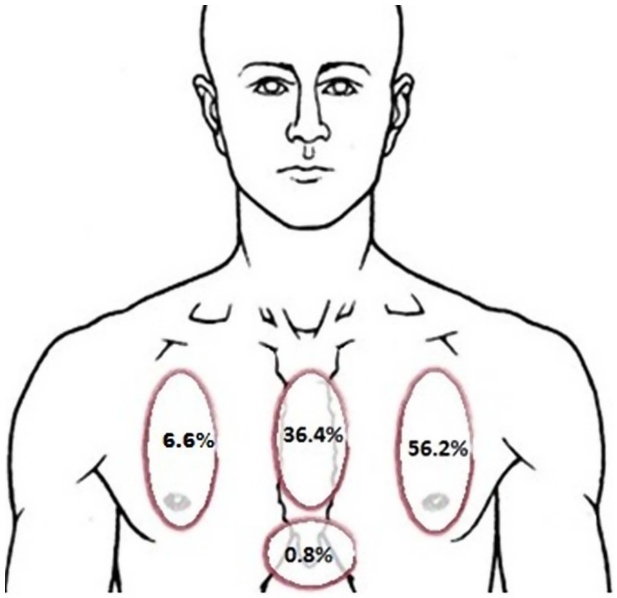

Figure 1 Localisation and percentage distribution of self-reported acute chest pain in all patients.

Table 1 Baseline characteristics of all emergency admissions with ACP

	All emergency admissions with ACP	ACS	Non-ACS	p Value
N	121	14 (11.6%)	107 (88.4%)	
Gender (male)	73 (60.3%)	10 (71.4%)	63 (58.87%)	0.56
Age [years]	47 [34–66.5]	61.0 [54.5–66.3]	45.0 [34.0–68]	**0.011**
BMI (kg/m^2)	27.0 [24.4–29.7]	27.0 [25.7–30.0]	27.0 [23.9–29.6]	0.268
Systolic blood pressure [mm Hg]	132.5 [122.0–143.50]	144.5 [133.0–154.8]	130.5 [121.0–141.0]	**0.014**
Diastolic blood pressure [mm Hg]	81 [76.0–90]	90 [80.0–100.0]	80 [75.0–89.3]	**0.031**
Heart rate (*/min)	75 [66.0–88.0]	76 [63.8–85.0]	75 [66–88]	0.784
VAS (0–10)	5.0 [4.0–7.0]	5 [2.0–7.3]	5 [4–7]	1.0
Previous medication:				
Antihypertensive medication	36 (29.8%)	6 (42.9%)	28 (28.0%)	0.35
Analgesic medication	25 (20.7%)	3 (21.4%)	22 (20.6%)	1.00
Anticoagulants	31 (25.6%)	6 (42.9%)	25 (23.4%)	0.19
Alcohol abuse	33 (27.5%)	8 (57.1%)	25 (23.4%)	**0.021**
Illicit drug abuse	8 (6.6%)	0	8 (7.5%)	0.59
Smoker	43 (35.5%)	5 (35.7%)	38 (35.5%)	1.0
Cigarettes consumption [PY]	7.21 (±14.9)	10.0 (±16.1)	6.9 (±14.8)	0.67
Hypertension	47 (38.8%)	11 (78.6%)	36 (33.6%)	**0.002**
Known CAD	18 (14.9%)	2 (14.3%)	16 (15.0%)	1.0
Dyslipidaemia	33 (27.3%)	8 (57.1%)	25 (23.4%)	**0.021**
Family history positive for CAD	37 (30.6%)	7 (50.0%)	30 (28.0%)	0.123
Diabetes mellitus	6 (5.0%)	0	6 (5.6%)	1.0

Bold typeface indicates significant results.
(±), SD; [], IQR; ACP, acute chest pain; ACS, acute coronary syndrome; BMI, body mass index; CAD, coronary artery disease; PY, pack years; VAS, visual analogue scale.

Table 2 Characterisation of symptoms on emergency room admission

	ACS (n=14)	Non-ACS (n=107)	p Value
Pain localisation			
Retrosternal	11 (78.6%)	33 (30.8%)	<0.001
Left chest	3 (21.4%)	65 (60.8%)	0.008
Right chest	0	8 (7.5%)	0.59
Epigastric	0	1 (0.9%)	1.0
Pain character			
Stabbing	3 (21.4%)	61 (57.0%)	0.02
Pressure	9 (64.3%)	33 (30.8%)	0.01
Burning	2 (14.3%)	6 (5.6%)	0.23
Squeezing	0	7 (6.5%)	1.0
Pain radiation			
No radiation	4 (28.6%)	52 (48.6%)	0.25
Left arm	5 (35.7%)	24 (22.4%)	0.31
Right arm	3 (21.4%)	9 (8.4%)	0.14
Jaw	1 (7.1%)	5 (4.7%)	0.52
Back	1 (7.1%)	13 (12.1%)	1.0
Epigastric	0	4 (3.7%)	1.0
Pain alleviating factors			
No	9 (64.3%)	51 (49.0%)	0.24
Respiration	0	3 (2.9%)	1.0
Movement	0	7 (6.7%)	1.0
Rest	5 (35.7%)	46 (44.2%)	0.78
Pain aggravating factors			
No	6 (42.9%)	40 (37.37%)	0.77
Respiration	1 (7.1%)	41 (38.38%)	0.03
Movement	6 (42.9%)	25 (23.23%)	0.19
Rest	1 (7.1%)	1 (1.01%)	0.22
Additional symptoms			
No	6 (42.9%)	60 (57.7%)	0.40
Dyspnoea	5 (35.7%)	24 (23.1%)	0.32
Nausea	0	7 (6.7%)	1.0
Dizziness	2 (14.2%)	9 (8.7%)	0.61
Sweating	1 (7.1%)	7 (6.7%)	1.0

ACS, acute coronary syndrome.

Table 3 Final diagnosis after emergency unit admission with acute chest pain

Diagnosis	Total (N=121)
Musculoskeletal disorder	62 (51.2%)
Acute coronary syndrome	14 (11.6%)
Gastro-oesophageal reflux disease	6 (5.0%)
Pneumonia	6 (5.0%)
Tachyarrhythmia	7 (5.8%)
Perimyocarditis	6 (5.0%)
Pulmonary embolism	5 (4.1%)
Stable angina pectoris	5 (4.1%)
Pleuritis	3 (2.5%)
Hypertensive emergency	3 (2.5%)
Psychosomatic disorder	3 (2.5%)
Aortic dissection	1 (0.8%)

Index test 'CWT' versus reference test 'troponin and/or ECG' versus 'troponin'

Based on the reference test of troponin and/or ECG, 14 out of 121 were classified as patients with ACS. Fifty-three of the 121 patients had reproducible CWT. In 13 of the 14 patients with ACS, CWT was non-reproducible resulting in a sensitivity of 92.9%; 52 out of 107 patients without ACS had reproducible CWT resulting in a specificity of 48.6%. Only 1 out of 53 patients with reproducible CWT suffered from ACS resulting in a NPV of 98.1%. In contrast, 13 out of the 68 patients with non-reproducible CWT suffered from ACS resulting in a PPV of 19.1%. Serial troponin measurements showed a sensitivity of 85.7% and specificity of 86.9%, PPV of 46.2% and NPV for 97.9% for ACS (tables 4 and 5) compared with the reference test of troponin and/or ECG.

Non-reproducible CWT remained independently associated with ACS after correction for known CAD, age, gender, family history of CAD, arterial hypertension, smoking, diabetes and dyslipidaemia resulting in an adjusted OR of 7.5 (95% CI 1.4 to 40.1; p=0.018). The model showed no evidence of lack of fit based on the Hosmer-Lemeshow χ^2 statistic.

DISCUSSION

Clinical examination, including palpation of the chest wall, is part of the routine evaluation of patients with ACP. Reproducible CWT in patients presenting with ACP may be associated with a benign cause like musculoskeletal disorders and may help to rule out ACS.[22 23] In our prospective study in the emergency department of the University Hospital Zurich, we evaluated the diagnostic performance of CWT on palpation to rule out ACS in patients presenting with ACP. Non-reproducible CWT had a high sensitivity, low specificity and low PPV for the diagnosis of ACS. However, the presence of reproducible CWT helped to rule out ACS with a high NPV. The results of this prospective, double-blinded study are consistent with other findings in retrospective analyses with different patient cohorts and settings. A recent cross-sectional study carried out by general physicians showed that reproducible CWT in patients presenting with chest pain had an adjusted OR in a multivariate model of 0.27 for the diagnosis of CAD. Corresponding positive LR and negative LR for the presence of CWT for excluding and including CAD were 0.25 and 1.71, respectively.[8] According to meta-analysis data, reproducible CWT had, compared with our study, a similar sensitivity (3–15%) and specificity (64–83%) for the diagnosis of ACS. In reproducible CWT, positive LR was 0.3, and in non-reproducible CWT, negative LR increases to 1.3 suggesting that reproducible CWT is negatively associated with ACS.[24] Similar results were published in the meta-analysis by Bruyninckx *et al* who reported a 94% sensitivity of non-reproducible CWT for the diagnosis of ACS. Negative LR in the setting of non-reproducible CWT was 0.17.[25] In another cross-sectional study, a prediction score in patients with ACP and underlying possible

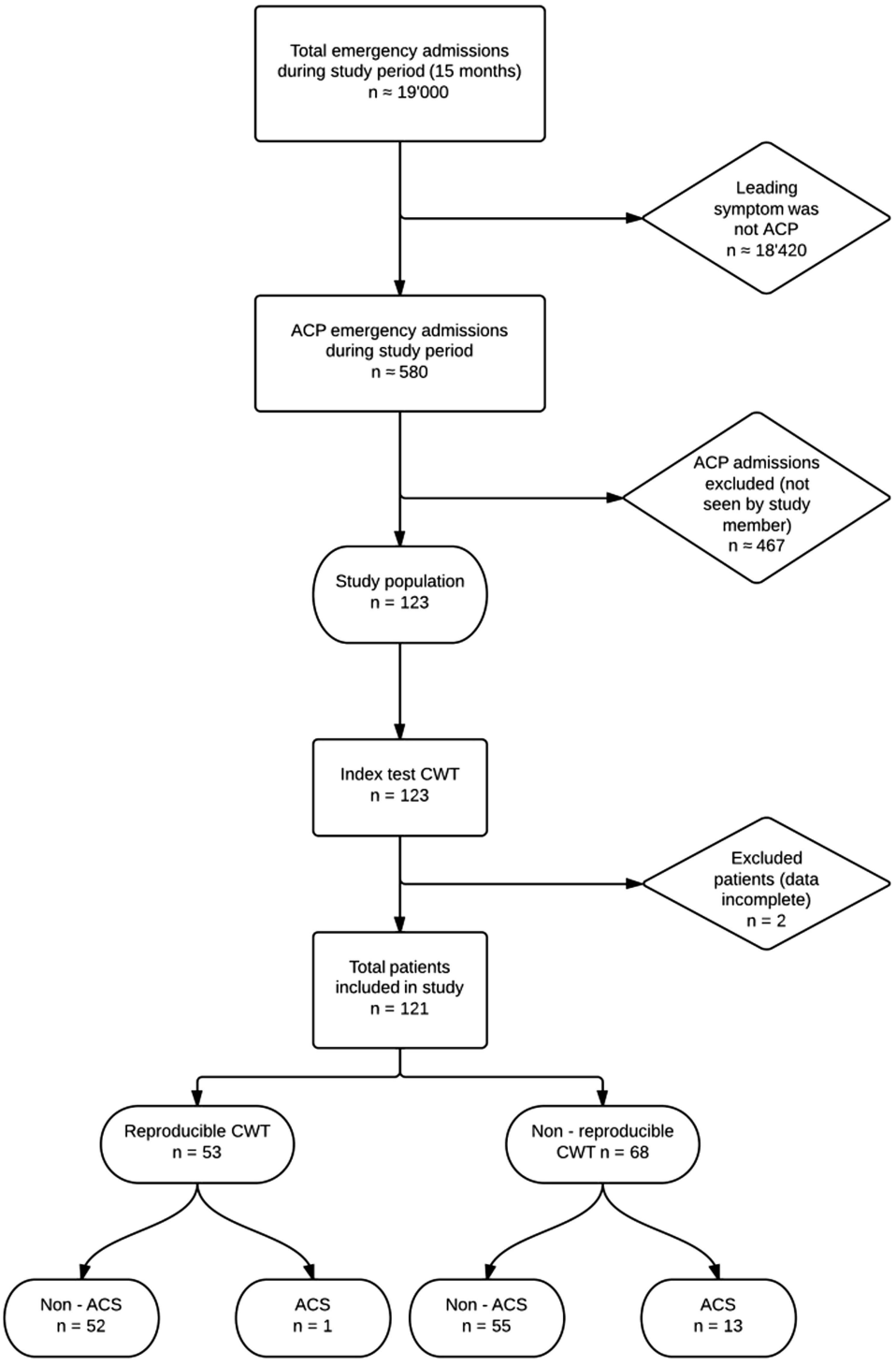

Figure 2 Enrolment and outcomes of ACP admissions and CWT test. ACP, acute chest pain; ACS, acute coronary syndrome; CWT, chest wall tenderness.

Table 4 Reproducible chest wall tenderness in patients with and without ACS

	ACS (n=14)	Non-ACS (n=107)	p Value
Non-reproducible CWT	13 (92.8%)	55 (51.4%)	0.003
Reproducible CWT	1 (7.1%)	52 (48.6%)	

ACS, acute coronary syndrome; CWT, chest wall tenderness.

CAD was proposed for general practitioners. Aside from other five variables (age, gender, known vascular disease, 'patient thinks heart is causing the pain', exercise-dependent pain), 'pain not reproducible on palpation' was an independent determinant for the prediction of a CAD. Non-reproducible CWT on palpation had an adjusted OR of 3.15.[28] In our study sample, we could detect reproducible CWT as an independent determinant to rule out ACS after correction for the established

Table 5 Diagnostic performance of 'non-reproducible CWT' and 'troponin' for the diagnosis of acute coronary syndrome

	Non-reproducible CWT			Serial troponin		
		95% CI	p Value		95% CI	p Value
Sensitivity	92.9%	66.1% to 98.8%	0.003	85.7%	57.2 to 97.8%	0.000
Specificity	48.6%	38.8% to 58.5%		86.9%	79.0% to 92.65%	
PPV	19.1%	10.6% to 30.5%		46.2%	26.61% to 66.1%	
NPV	98.1%	89.9% to 99.7%		97.9%	92.6% to 99.7%	
Positive LR	1.8	1.4 to 2.3		6.6	3.8 to 11.2	
Negative LR	0.15	0.02 to 2.3		0.16	0.05 to 0.6	
OR		1.6 to 97.3	0.017	39.9	8.1 to 197.2	0.000

CWT, chest wall tenderness; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

cardiovascular risk factors in a multivariate model with an OR of 7.5, which is consistent with the data from Chun and McGee.[24] Our study results also confirm the data analysed by Goodacre *et al*[17] who stated that non-reproducible CWT had a sensitivity of 91.7%, low specificity of 27.8%, PPV of 4.2%, NPV of 99.0%, positive LR of 1.27 and negative LR of 0.30 for the diagnosis of ACS. However, in most of the publications, the quality of CWT was not clearly defined. Furthermore, the sequence of the clinical evaluation was not clearly defined and it is not evident if the investigator or patient was already informed about further test results or differential diagnoses.[22–25] To address these issues, we designed our study as strictly prospective enabling the blinding of patient and investigator for the primary end point. We conducted CWT as an initial step showing that reproducible CWT as a fast bedside test helped to rule out ACS in a very early stage. Moreover, we only considered reproducible CWT (ie, pain triggered by palpation corresponds exactly to the self-reported ACP). CWT of alternative quality was excluded and registered as non-reproducible CWT. The important new finding of our study is that only reproducible CWT helps to rule out ACS and not any CWT. Interestingly our index test 'non-reproducible CWT' had a similar sensitivity and NPV compared with the reference test of serial troponin measurements for ruling out ACS in ACP. However, serial troponin analysis is time consuming compared with the fast and easy CWT test. Nevertheless, troponin is highly specific, thus resulting in better PPV for the diagnosis of ACS.[29] Regarding the secondary end points, ACP in ACS group was mainly reported retrosternal, pressure-like and less stabbing like that which is consistent with previous studies.[23 30] Deep inspiration as pain aggravating factor was significantly more reported in the non-ACS group, most probably due to underlying musculoskeletal disorder, pleuritis or perimyocarditis.

LIMITATIONS

Albeit the members of the study team were blinded for the final diagnosis, the physical appearance of the patients (eg, body mass index, gender, age) could have biased the physician. Furthermore, the applied pressure for testing of CWT is not standardised, which may have led to interobserver and intraobserver variability. Using a dolorimeter[31] could help to minimise this bias. However, the aim of the study was to investigate a simple bedside test and a dolorimeter is not applicable in daily clinical practice. Another limitation was that patient enrolment was only carried out when a member of the study team was present. Also of note is that the ACS group in our study population was too small to evaluate other predictive factors for the diagnosis of ACS, including aspects of the patient's history and pain characteristics in multivariate analysis. The subgroup analysis considering age, gender, socioeconomic status, pre-existing conditions would also require a greater sample size. Nevertheless, a subgroup analysis concerning the impact of these factors on CWT would be of great interest as there is evidence for differences in pain perception in different age groups, gender, socioeconomic status and in patients with comorbidities.[32–34] These subgroup studies might have implications for clinicians in dealing with patients presenting with ACP.

CONCLUSION

This first prospective, double-blinded diagnostic study shows that palpation of the chest wall is a fast and easy feasible bedside test in patients presenting with ACP. If reproducible CWT is present, the test helps to rule out ACS at an early stage of the diagnostic process. However, ACS or other diagnoses should be considered in patients with non-reproducible CWT. It goes without saying that testing of CWT does not replace a thorough history taking, and clinical and further diagnostic evaluation. However, this study demonstrates that palpation of the chest wall should be performed *as a first step* in ACP admissions to improve early triage and decision-making until ECG and troponin tests are available. Larger studies are needed to confirm these findings.

Contributors CG and DF were responsible for the conception, design, analysis, interpretation of the data and drafting of the manuscript. OS, LZ and EB were involved in the analysis, interpretation of the data and drafting of the manuscript. MB, PEC and TH were involved in acquisition of data and drafting of the manuscript. All authors read and approved the final manuscript.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None.

Patient consent Obtained.

Ethics approval This study was approved by the Ethics Committee of the Canton of Zurich, Switzerland (KEK-ZH 2012-0391).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

REFERENCES

1. Burt CW. Summary statistics for acute cardiac ischemia and chest pain visits to United States EDs, 1995–1996. *Am J Emerg Med* 1999;17:552–9.
2. Qamar A, McPherson C, Babb J, *et al*. The Goldman algorithm revisited: prospective evaluation of a computer-derived algorithm versus unaided physician judgment in suspected acute myocardial infarction. *Am Heart J* 1999;138(4 Pt 1):705–9.
3. Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. *Am J Med* 1989;86:262–6.
4. Goodacre S, Cross E, Arnold J, *et al*. The health care burden of acute chest pain. *Heart* 2005;91:229–30.
5. Solinas L, Raucci R, Terrazzino S, *et al*. Prevalence, clinical characteristics, resource utilization and outcome of patients with acute chest pain in the emergency department. A multicenter, prospective, observational study in north-eastern Italy. *Italian Heart J* 2003;4:318–24.
6. Goodacre S, Cross E, Lewis C, *et al*. Effectiveness and safety of chest pain assessment to prevent emergency admissions: ESCAPE cluster randomised trial. *BMJ* 2007;335:659.
7. Knockaert DC, Buntinx F, Stoens N, *et al*. Chest pain in the emergency department: the broad spectrum of causes. *Eur J Emerg Med* 2002;9:25–30.
8. Bosner S, Becker A, Abu Hani M, *et al*. Accuracy of symptoms and signs for coronary heart disease assessed in primary care. *Br J Gen Pract* 2010;60:e246–57.
9. Verdon F, Herzig L, Burnand B, *et al*. Chest pain in daily practice: occurrence, causes and management. *Swiss Med Wkly* 2008;138:340–7.
10. Erhardt L, Herlitz J, Bossaert L, *et al*. Task force on the management of chest pain. *Eur Heart J* 2002;23:1153–76.
11. Ruigomez A, Rodriguez LA, Wallander MA, *et al*. Chest pain in general practice: incidence, comorbidity and mortality. *Fam Pract* 2006;23:167–74.
12. Diethelm M. Brustschmerz—nicht vom Herz. *Schweiz Med Forum* 2005(5):51–8.
13. Than M, Aldous S, Lord SJ, *et al*. A 2-hour diagnostic protocol for possible cardiac chest pain in the emergency department: a randomized clinical trial. *JAMA Intern Med* 2014;174:51–8.
14. Raff GL, Chinnaiyan KM, Cury RC, *et al*. SCCT guidelines on the use of coronary computed tomographic angiography for patients presenting with acute chest pain to the emergency department: a report of the Society of Cardiovascular Computed Tomography Guidelines Committee. *J Cardiovasc Comput Tomogr* 2014;8:254–71.
15. Diercks DB, Peacock WF IV, Hollander JE, *et al*. Diagnostic accuracy of a point-of-care troponin I assay for acute myocardial infarction within 3 hours after presentation in early presenters to the emergency department with chest pain. *Am Heart J* 2012;163:74–80.e4.
16. Hollander JE. Risk stratification of emergency department patients with chest pain: the need for standardized reporting guidelines. *Ann Emerg Med* 2004;43:68–70.
17. Goodacre S, Locker T, Morris F, *et al*. How useful are clinical features in the diagnosis of acute, undifferentiated chest pain? *Acad Emerg Med* 2002;9:203–8.
18. Amsterdam EA, Aman E. The patient with chest pain: low risk, high stakes. *JAMA Intern Med* 2014;174:553–4.
19. Gruettner J, Haghi D, Henzler T, *et al*. Cardiac computed tomographic angiography in patients with acute chest pain and moderately-increased troponin. *In Vivo* 2012;26:1035–9.
20. Redberg RF. Priorities in the evaluation of patients with chest pain. *JAMA Intern Med* 2014;174:554.
21. Safavi KC, Li SX, Dharmarajan K, *et al*. Hospital variation in the use of noninvasive cardiac imaging and its association with downstream testing, interventions, and outcomes. *JAMA Intern Med* 2014;174:546–53.
22. Goodacre SW, Angelini K, Arnold J, *et al*. Clinical predictors of acute coronary syndromes in patients with undifferentiated chest pain. *QJM* 2003;96:893–8.
23. Lee TH, Cook EF, Weisberg M, *et al*. Acute chest pain in the emergency room. Identification and examination of low-risk patients. *Arch Intern Med* 1985;145:65–9.
24. Chun AA, McGee SR. Bedside diagnosis of coronary artery disease: a systematic review. *Am J Med* 2004;117:334–43.
25. Bruyninckx R, Aertgeerts B, Bruyninckx P, *et al*. Signs and symptoms in diagnosing acute myocardial infarction and acute coronary syndrome: a diagnostic meta-analysis. *Br J Gen Pract* 2008;58:105–11.
26. Thygesen K, Alpert JS, Jaffe AS, *et al*. Third universal definition of myocardial infarction. *Eur Heart J* 2012;33:2551–67.
27. Mueller C. Biomarkers and acute coronary syndromes: an update. *Eur Heart J* 2014;35:552–6.
28. Bosner S, Haasenritter J, Becker A, *et al*. Ruling out coronary artery disease in primary care: development and validation of a simple prediction rule. *CMAJ* 2010;182:1295–300.
29. Guo X, Feng J, Guo H. The predictive value of the bedside troponin T test for patients with acute chest pain. *Exp Clin Cardiol* 2006;11:298–301.
30. Edmondstone WM. Cardiac chest pain: does body language help the diagnosis? *BMJ* 1995;311:1660–1.
31. Simms RW, Goldenberg DL, Felson DT, *et al*. Tenderness in 75 anatomic sites. Distinguishing fibromyalgia patients from controls. *Arthritis Rheum* 1988;31:182–7.
32. Arslanian-Engoren C, Patel A, Fang J, *et al*. Symptoms of men and women presenting with acute coronary syndromes. *Am J Cardiol* 2006;98:1177–81.
33. Kyker KA, Limacher MC. Gender differences in the presentation and symptoms of coronary artery disease. *Curr Womens Health Rep* 2002;2:115–19.
34. Dorner TE, Muckenhuber J, Stronegger WJ, *et al*. The impact of socio-economic status on pain and the perception of disability due to pain. *Eur J Pain* 2011;15:103–9.