



BMJ Open Predictors of long-term symptom burden and quality of life in patients hospitalised with chest pain: a prospective observational study

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ABSTRACT

Objective To describe the magnitude and predictors of symptom burden (SB) and quality of life (QoL) 3 months after hospital admission for acute chest pain.

Design Prospective observational study.

Setting Single centre, outpatient follow-up.

Participants 1506 patients.

Outcomes Scores reported for general health (RAND-12), angina-related health (Seattle Angina Questionnaire 7 (SAQ-7)) and dyspnoea (Rose Dyspnea Scale) 3 months after hospital admission for chest pain.

Methods A total of 1506 patients received questionnaires assessing general health (RAND-12), angina-related health (SAQ-7) and dyspnoea (Rose Dyspnea Scale) 3 months after discharge. Univariable and multivariable regression models identified predictors of SB and QoL scores. A mediator analysis identified factors mediating the effect of an unstable angina pectoris (UAP) diagnosis.

Results 774 (52%) responded. Discharge diagnoses were non-ST elevation myocardial infarction (NSTEMI) (14.2%), UAP (17.1%), non-coronary cardiac disease (6.6%), non-cardiac disease (6.3%) and non-cardiac chest pain (NCCP) (55.6%). NSTEMI had the most favourable, and UAP patients the least favourable SAQ-7 scores (median SAQ-7-summary; 88 vs 75, $p < 0.001$). NCCP patients reported persisting chest pain in 50% and dyspnoea in 33% of cases. After adjusting for confounders, revascularisation predicted better QoL scores, while UAP, current smoking and hypertension predicted worse outcome. NSTEMI and UAP patients who were revascularised reported higher scores ($p < 0.05$) in SAQ-7-QL, SAQ7-PL, SAQ7-summary (NSTEMI) and all SAQ-7 domains (UAP). Revascularisation altered the unstandardised beta value ($> \pm 10\%$) of an UAP diagnosis for all SAQ-7 and RAND-12 outcomes.

Conclusions Patients with NSTEMI reported the most favourable outcome 3 months after hospitalisation for chest pain. Patients with other diseases, in particular UAP patients, reported lower scores. Revascularised NSTEMI and UAP patients reported higher QoL scores compared with patients receiving conservative treatment. Revascularisation mediated all outcomes in UAP patients.

Trial registration number NCT02620202.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The study includes a large group of well-characterised patients admitted with chest pain, including both cardiac and non-cardiac causes of chest pain.
- ⇒ Both disease specific and generic quality of life data are reported, and the generic data are compared with measures from the general population.
- ⇒ There was a substantial proportion of missing data dominated by younger patients with overall less risk factors.
- ⇒ Detailed information on ethnicity, socioeconomic status and detailed angiographic data was not registered, and accordingly, these possible confounders could not be adjusted for.
- ⇒ Baseline scores was not available; thus, the study lacks ability to attribute the direct effect of revascularisation in improving scores between hospitalisations and 3-month phase.

INTRODUCTION

Acute chest pain is a common presenting symptom in the emergency department, accounting for approximately 10% of all non-trauma or non-surgery visits.^{1 2} Implementation of the European Society of Cardiology (ESC) algorithms may lead to early discharge of up to half of patients presenting with chest pain.^{2 3} As turnaround times in the hospitals decrease, two patient groups may receive less focus and consequently are at risk of undertreatment.

The first group is the large proportion suffering from non-cardiac conditions with musculoskeletal, gastrointestinal, pulmonary and other miscellaneous aetiologies.⁴ Previous quality of life research have mostly focused on non-ST-elevation myocardial infarction (NSTEMI) patients, and less is known about the challenges of patients with

non-cardiac chest pain (NCCP).⁵⁻⁸ These patients impose a risk of future unnecessary healthcare investigations and surplus readmissions, if symptoms persist, and no medical rationale or treatment is provided.⁴

The second group includes patients with ischaemic heart disease who are not identified as NSTEMI, commonly diagnosed as unstable angina pectoris (UAP). UAP patients may differ from NSTEMI patients and typically have ischaemic cardiac disease being less available for revascularisation.⁹⁻¹⁰ They are typically 'ruled-out' by the ESC algorithms for non-ST segment elevation acute coronary syndrome (NSTEMI-ACS).¹¹⁻¹² There is an ongoing debate on how this condition should be defined and what is the optimal treatment options after the implementation of high sensitivity troponin assays.¹³ Data describing symptom burden or the effect of revascularisation in UAP patients as measured with validated quality of life instruments are scarce¹⁴⁻¹⁸ and should be further elaborated.

The aim of this study was to describe the magnitude and predictors of symptom burden and quality of life 3 months after discharge in different groups of chest pain patients. Furthermore, we performed an in-depth analysis investigating symptom burden and quality of life in UAP patients.

METHODS

Study design

This article reports data from the *Aiming Towards Evidence Based Interpretation of Cardiac Biomarkers in Patients With Chest Pain* (WESTCOR) study, a prospective observational study recruiting patients with chest pain and suspected NSTEMI-ACS (Clinical Trials number NCT02620202).¹⁹ A total of 1506 patients were included using the following criteria: ≥ 18 years, admission due to chest pain, an ECG excluding ST segment elevation (STEMI) and able to provide written informed consent. Patient-reported outcomes were assessed at a 3-month follow-up using self-administered disease-specific and generic questionnaires administered by postal mail.

Approximately half of the included patients ($n=779$ (51.7%)) responded. Five patients were excluded due to a stable angina pectoris diagnosis. Thus, this left our final analytical sample at 774 patients (figure 1).

Data collection

High sensitivity cTnT (Roche Diagnostics) and cTnI (Abbott Diagnostics), creatinine and lipid analysis were performed on admission. Details are provided in online supplemental material. The diagnosis in all patients were adjudicated by two independent cardiologists based on all available clinical data, routine laboratory results (hs-cTnT), ECG, ultrasound and imaging findings. A third adjudicator resolved disagreements. Details are described earlier¹⁹ and provided in the online supplemental material. NSTEMI and UAP were defined according to the third universal definition for Myocardial infarction.²⁰ Revascularisation was defined as either percutaneous

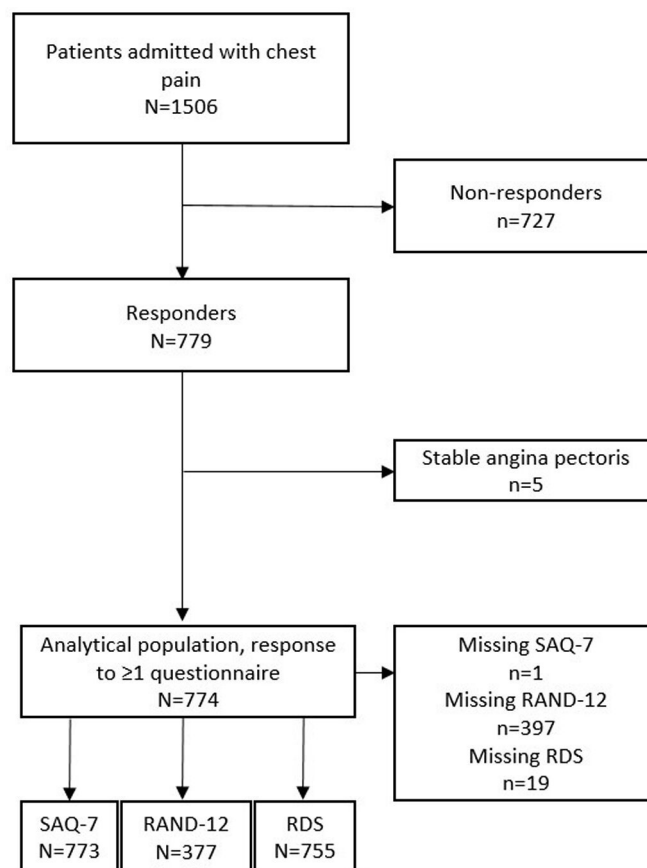


Figure 1 Flow chart of the study population. RDS, Rose Dyspnea Scale; SAQ-7, Seattle Angina Questionnaire 7.

coronary intervention (PCI) or coronary artery bypass graft (CABG) during hospitalisation or in close association with the hospitalisation (decided during hospitalisation but performed after discharge).

Quality of life instruments

Disease-specific health status related to angina was determined using a validated shortened version of the Seattle Angina Questionnaire (SAQ-7)²¹ consisting of a seven-item questionnaire evaluating four key domains (angina frequency (SAQ7-AF), physical limitation (SAQ7-PL), quality of life (SAQ7-QL) and summary score (SAQ7)). The scoring ranged from 0 to 100 (best). A score of 100 on the SAQ7-AF domain was defined as angina free.²²

The patient's level of dyspnoea with activity was assessed using the Rose Dyspnea Scale (RDS), which is a four-item questionnaire with a score range from 0 to 4, where 0 indicates no dyspnoea and 4 indicates dyspnoea with minimal activity.²³ We considered a score of 0 or 1 as 'no dyspnoea or minor dyspnoea', while a score of 2 or more was considered pronounced dyspnoea.

Generic health status was assessed using the 12-item questionnaire RAND-12, which is a truncated version of the Short Form Health Survey-36. RAND-12 ranges from 0 to 100 (best) and can be summarised in two domains: a physical component Physical Component Score (PCS-12) and a Mental Component Score (MCS-12).²⁴

Missing data

SAQ-7 and RDS were distributed to all participants, while RAND-12 was included on a later time point with approximately half of the patients receiving it. Patients with complete response in at least one of the three were included in the applicable data analysis (figure 1). In the SAQ-7, missing values in one of the questions would result in taking the average of the non-missing values, as suggested by the SAQ-7 guidelines.

Normative population

The physical and mental component scores attained from the RAND-12 questionnaire were compared with scores from a normal population obtained from the Norwegian Centre for Research Data. The data stems from a large study (NorLAG) conducted in three rounds from 2002 to 2017.²⁵ The participants were contacted by phone, followed by questionnaires via postal mail, which they could fill in on paper or online. To match the median age in the analytical population, we excluded patients with an age below and above the 25th and 75th quartile, resulting in the inclusion of 6240 individuals.

Statistical analyses

Baseline characteristics are presented as frequencies and proportions for categorical variables and median with 25th–75th percentiles (IQR) for continuous variables. Normality was checked using the Kolmogorov-Smirnov normality test, and overall, the data were skewed. Kruskal-Wallis test was used to compare continuous variables between the five diagnostic groups, and χ^2 test or Fisher's exact test (as applicable) for comparing proportions. Mann-Whitney U test was used for comparing two groups (responders and non-responders, the patient data to the general population and revascularised vs non-revascularised).

Univariable linear regression was used to identify the association between independent explanatory variables (patient characteristics including baseline troponin concentrations, revascularisation and adjudicated diagnosis) and dependent outcome variables (the six different quality of life scores in SAQ-7 and RAND-12). Candidate predictor variables with p value ≤ 0.10 in univariable regression analysis were adjusted for in the multivariable linear regression models. The revascularisation variable was included in the multivariable model if p value was < 0.15 because of its clinical importance. Collinearity between the predictor variables was inspected by using Spearman's rank correlation, where a limit of correlation coefficient (ρ) > 0.4 was set. If predictor variables had an intercorrelation exceeding this value, the variable with the most significant correlation with the outcome variable was selected. Goodness of fit was expressed as the adjusted R^2 .

As the UAP patients overall had lower scores compared with others, we performed a subgroup analysis. A series of trivariable regression models were undertaken in order to evaluate which factors could mediate the effect of

quality of life in patients with UAP. Quality of life scores were assigned as the dependent variables, while UAP and potential mediators were assigned as the independent variables. The effect of the potential mediator was defined significant if it changed the unstandardised coefficient of the UAP diagnosis $> \pm 10\%$.

A two-tailed p value < 0.05 was considered statistically significant throughout all analyses. The p value in tables 1 and 2 represents comparison across all five groups, using Kruskal-Wallis test, χ^2 test or Fisher's exact test, as applicable. Data analyses were performed using IBM SPSS software, V.25 (IBM Corp) and R software V.1.2.5001.

RESULTS

Baseline characteristics

A total of 305 women and 469 men were included in the analytical population, with a median age of 66 (57–73) years. The prevalence of NSTEMI and UAP was 14.2% and 17.1%, respectively, while non-coronary cardiac disease was 6.6%, non-cardiac disease was 6.3% and NCCP was 55.6% (table 1).

Patients with NSTEMI and UAP were more likely to be male and older compared with patients with NCCP. A subset of risk factors (hypertension, hyperlipidaemia, family history of MI and previous smoking) and prior cardiovascular disease was more frequent in patients with UAP. Patients with NSTEMI underwent revascularisation more frequently (74.5%) compared with patients with UAP (40.6%). Demographic and clinical characteristics stratified by diagnosis are provided in table 1.

When comparing patients who responded to at least one questionnaire to patients who did not respond, we found no difference as regarding sex, but the response group was older (66 years vs 58 years, $p < 0.001$), more likely to have hypertension, known hyperlipidaemia ($p < 0.001$ for both) and prior and currently treated with PCI ($p = 0.036$ and $p < 0.001$) (online supplemental table S1).

Differences in quality of life scores and symptom burden among diagnostic groups

Symptom and quality of life scores 3 months after discharge are summarised in table 2.

Patients with NSTEMI had the most favourable score in all domains except SAQ7-PL. Regarding angina frequency, patients with NSTEMI, non-cardiac disease and NCCP all had a median SAQ7-AF score of 100, whereas patients with UAP or non-coronary cardiac disease had median scores of 90 ($p = 0.003$ across all patient groups). The latter two groups also had the lowest scores on quality of life (SAQ7-QL, $p = 0.009$ across all patient groups), physical limitation (SAQ7-PL, $p = 0.001$ across all patient groups) and summary SAQ7-score ($p < 0.001$ across all patient groups). Three months after hospitalisation for chest pain, more patients with NSTEMI and non-cardiac disease were totally free of chest pain compared with remaining groups (figure 2). Patients with UAP had the highest prevalence of angina, with nearly 60% reporting

Table 1 Baseline characteristics stratified by diagnosis groups

Demographic and clinical characteristics (total=774)	NSTEMI (n=110)	UAP (n=133)	Non-coronary cardiac disease (n=51)	Non-cardiac disease (n=49)	NCCP (n=431)	P value
Age, median (25th–75th percentile)	67 (57–75)	68 (60–75)	70 (61–79)	70 (59–77)	63 (53–72)	<0.001
Gender, female, n (%)	30 (27.3)	35 (26.7)	15 (29.4)	23 (46.9)	202 (46.7)	<0.001
Risk factors, n (%)						
Hypertension	49 (44.5)	75 (56.4)	21 (41.2)	23 (46.9)	183 (42.5)	0.119
Hyperlipidaemia	34 (30.9)	88 (66.2)	26 (51.0)	18 (36.7)	176 (40.9)	<0.001
Diabetes mellitus	14 (12.7)	26 (19.5)	4 (7.8)	5 (10.2)	46 (10.6)	0.069
Insulin dependent	3 (2.7)	11 (8.4)	1 (2.0)	0 (0)	10 (2.3)	
Obesity (BMI >30)	12 (22.2)	18 (24.3)	4 (16.7)	7 (29.2)	50 (22.1)	0.876
Family history (MI)	16 (14.5)	28 (21.1)	7 (13.7)	7 (14.3)	84 (19.5)	0.501
Unknown	12 (10.9)	11 (8.4)	5 (9.8)	2 (4.1)	36 (8.3)	0.707
Current smoker	25 (22.7)	20 (15.3)	7 (13.7)	9 (18.4)	74 (17.1)	0.539
Previous smoker	44 (40.0)	64 (47.3)	24 (47.1)	21 (42.9)	202 (47.1)	0.853
Medical history, n (%)						
Prior myocardial infarction	20 (18.2)	39 (29.3)	10 (19.6)	7 (14.3)	71 (16.6)	0.019
Prior PCI	22 (20.0)	55 (41.4)	11 (21.6)	7 (14.3)	72 (16.9)	<0.001
Prior CABG	9 (8.2)	26 (19.8)	2 (3.9)	5 (10.2)	16 (3.7)	<0.001
Prior heart failure	4 (3.6)	3 (2.3)	6 (11.8)	0 (0)	13 (3.0)	0.033
Prior stroke	5 (4.5)	8 (6.1)	3 (5.9)	1 (2.0)	8 (1.8)	0.128
Peripheral vascular disease	3 (2.7)	9 (6.9)	0 (0)	0 (0)	5 (1.2)	0.006
Reduced renal function*	9 (10.7)	13 (17.8)	6 (16.2)	7 (19.4)	30 (11.3)	0.337
Vital parameters at admission, median (25th–75th percentile)						
Systolic BP, mm Hg	149 (136–176)	148 (136–160)	140 (124–155)	139 (125–158)	145 (133–161)	0.016
Diastolic BP, mm Hg	85 (75–93)	84 (76–91)	88 (76–96)	80 (73–90)	83 (75–91)	0.619
Heart rate, bpm	74 (62–82)	70 (62–80)	94 (66–130)	72 (65–87)	69 (62–80)	<0.001
BMI	26.4 (24.2–28.7)	26.1 (24.7–29.9)	27.2 (26.1–29.1)	27.3 (24.8–30.3)	26.7 (24.2–29.7)	0.879
Biomarkers, median (25th–75th percentile)						
cTnT, ng/L	50.5 (22–160.5)	9.0 (6.0–18.0)	16.0 (9.0–23.0)	8.0 (4.0–13.0)	6.0 (3.0–10.0)	<0.001
cTnI, ng/L	121.7 (26.2–462.8)	4.1 (2.6–9.4)	9.6 (4.2–24.4)	3.7 (1.8–8.3)	2.6 (1.5–4.8)	<0.001
Investigations and intervention, n (%)						
Coronary CT angiography	7 (6.4)	44 (33.1)	10 (19.6)	12 (24.5)	220 (51.0)	<0.001
Coronary angiography	100 (90.9%)	102 (76.7%)	14 (27.5%)	8 (16.3%)	84 (19.5%)	<0.001
PCI during hospitalisation	72 (65.5)	50 (37.6)	2 (3.9)	1 (2.0)	2 (0.7)	<0.001
Revascularisation	82 (74.5)	54 (40.6)	3 (5.9)	1 (2.0)	6 (1.4)	<0.001
Medications at admission, n (%)						
Statins	34 (30.9)	87 (65.4)	25 (49.0)	18 (36.7)	174 (40.4)	<0.001
Warfarin	2 (1.8)	10 (7.5)	5 (9.8)	2 (4.1)	19 (4.4)	<0.001
ASA	38 (34.5)	79 (59.4)	20 (39.2)	12 (24.5)	129 (29.9)	<0.001
Clopidogrel	5 (4.5)	15 (11.3)	2 (3.9)	1 (2.0)	16 (3.7)	0.021
Ticagrelor	3 (2.7)	10 (7.5)	2 (3.9)	0 (0.0)	11 (2.6)	0.063
ACEI	5 (4.5)	7 (5.3)	2 (3.9)	0 (0.0)	4 (0.9)	0.007
Beta blockers	11 (10.0)	5 (3.8)	8 (15.7)	0 (0.0)	3 (0.7)	<0.001
Diuretics	18 (16.4)	34 (25.6)	13 (25.5)	8 (16.3)	78 (18.1)	0.212

*eGFR < 60 mL/min/1.73m².

ACEI, ACE inhibitors; ASA, acetylsalicylic acid; BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; cTnI, cardiac troponin I; cTnT, cardiac troponin T; eGFR, estimated glomerular filtration rate; NCCP, non-cardiac chest pain; NSTEMI, non-ST segment elevation myocardial infarction; PCI, percutaneous coronary intervention; UAP, unstable angina pectoris.

Table 2 Quality of life indices 3 months after discharge stratified by diagnosis group

Questionnaire, median (25th–75th percentile)	NSTEMI n=110	UAP n=133	Non-coronary cardiac disease n=51	Non-cardiac disease n=49	NCCP n=431	P value
SAQ-7	n=110	n=133	n=51	n=49	n=431	
Angina frequency (SAQ7-AF)	100 (80–100)	90 (60–100)	90 (80–100)	100 (80–100)	100 (80–100)	0.003
Quality of life (SAQ7-QL)	88 (50–100)	63 (38–100)	63 (38–100)	75 (50–100)	75 (50–100)	0.009
Physical limitation (SAQ7-PL)	92 (67–100)	75 (58–100)	75 (50–100)	83 (52–100)	100 (59–100)	0.001
Summary score (SAQ7)	88 (70–100)	75 (52–100)	75 (55–94)	83 (68–100)	84 (70–100)	<0.001
RAND-12	n=42	n=77	n=21	n=22	n=215	
PCS-12 median	54 (41–60)	46 (35–55)	50 (36–55)	44 (35–57)	52 (38–57)	0.079
MCS-12 median	54 (45–60)	50 (41–56)	48 (35–60)	48 (39–57)	51 (41–58)	0.455

NCCP, non-cardiac chest pain; NSTEMI, non-ST segment elevation myocardial infarction; SAQ-7, Seattle Angina Questionnaire 7; UAP, unstable angina pectoris.

either weekly or daily episodes (figure 2). Similarly, patients with NSTEMI had the largest proportion of individuals with absence of or minor dyspnoea (71%), while patients with UAP had the largest proportion (44%) who were hindered in their daily activities by pronounced dyspnoea (figure 3).

Regarding overall health status, both components of the RAND-12 were more favourable among patients with NSTEMI, with a score of 54 (41–60) and 54 (45–60) for the physical and mental domain (PSC-12 and MCS-12), respectively (table 2). Patients with non-cardiac disease had the lowest scores, 44 (45–57) for the PSC-12 and 48 (39–57) for the MSC-12 component. However, these differences did not reach statistical significance.

Comparison between responders and the general population

The median values of the two components of RAND-12 were compared with data from a normative population with the same age in order to investigate any differences in general health between this group and responders included in the analyses. The general population showed a higher median value for MCS-12 (58 vs 51, $p<0.001$) but not PCS-12 (52 vs 50, $p=0.383$) (see online supplemental table S2).

Effect of revascularisation

A total of 74.5% of NSTEMI and 40.6% of UAP patients were revascularised. NSTEMI patients who were revascularised demonstrated better quality of life in three

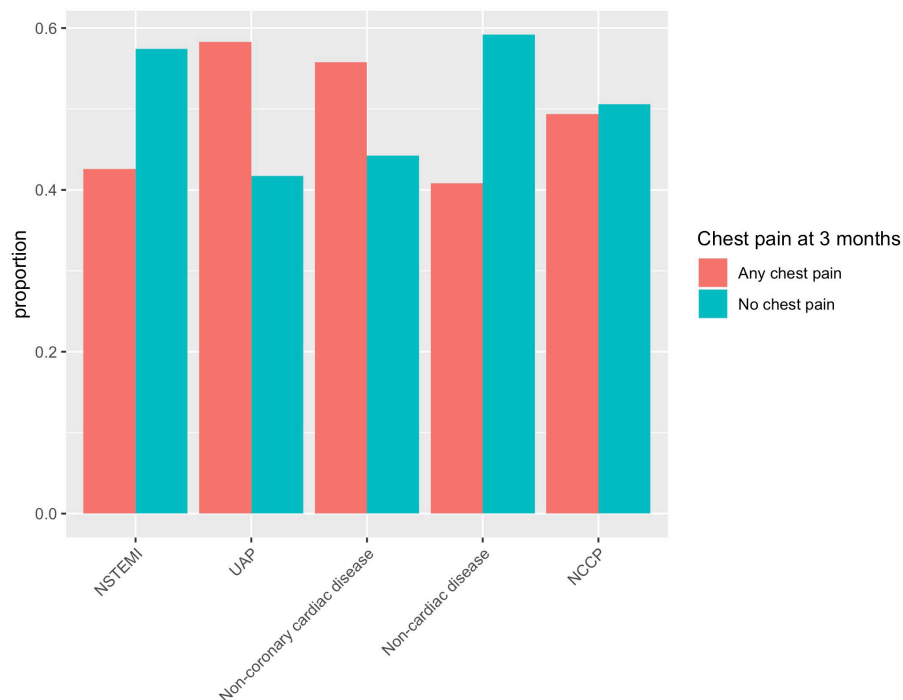


Figure 2 Proportion of patients who reported angina (chest pain) freedom at 3 months, as assessed by SAQ7-AF. NCCP, non-cardiac chest pain; NSTEMI, non-ST elevation myocardial infarction; SAQ7-AF, Seattle Angina Questionnaire 7 angina frequency; UAP, unstable angina pectoris.

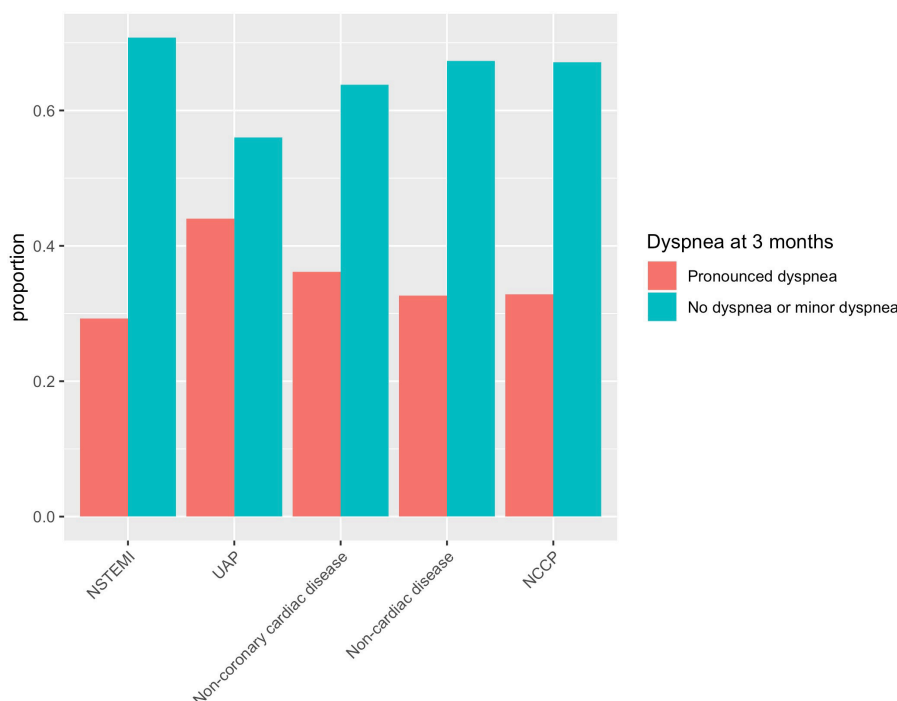


Figure 3 Proportion of patients reporting dyspnoea at 3 months, assessed by Rose Dyspnea Scale. NCCP, non-cardiac chest pain; NSTEMI, non-ST elevation myocardial infarction; UAP, unstable angina pectoris.

domains: SAQ7-QL, SAQ7-PL and SAQ7-summary (all $p < 0.05$) compared with those treated conservatively (non-revascularised) (figure 4). Similar findings were observed in the UAP group; patients who were revascularised had significantly higher scores in all domains of the SAQ-7 questionnaire (all $p < 0.05$).

Predictors of quality of life and symptom burden

The results of the univariable regression analyses are provided in the online supplemental table S3. Adjusted multivariable analysis demonstrated that revascularisation and a diagnosis of UAP were the most prominent predictors of angina frequency (SAQ7-AF) (table 3).

Patients who underwent revascularisation were associated with higher quality of life (SAQ7-QL) 3 months after admission ($\beta = 0.10$ (95% CI 0.02 to 0.17), $p = 0.012$), while those diagnosed with UAP ($\beta = -0.14$ (95% CI -0.21 to 0.06), $p < 0.001$), hypertension ($\beta = -0.10$ (95% CI -0.17 to 0.02), $p = 0.009$) and current smoking ($\beta = -0.10$ (95% CI -0.18 to 0.03), $p = 0.005$) were associated with lower quality of life. Regarding physical limitation (SAQ7-PL), age, prior CABG, reduced renal function and current smoking were associated with a lower score (all $p < 0.05$). Revascularisation ($\beta = 0.15$ (95% CI 0.06 to 0.23), $p = 0.001$), a diagnosis of UAP ($\beta = -0.18$ (95% CI -0.29 to 0.09), $p < 0.001$) or non-coronary cardiac disease ($\beta = -0.11$ (95% CI -0.19 to 0.02), $p = 0.013$) were significant in predicting a summary score of SAQ-7.

Regarding general health, we found hypertension, current smoking, increased BMI and a diagnosis of UAP to be associated with worse general health as measured by the PCS-12 domain of the RAND-12 instrument. A history of prior MI ($\beta = -0.11$ (95% CI -0.23 to 0.01), $p = 0.041$)

and current smoking ($\beta = -0.13$ (95% CI -0.23 to 0.03), $p = 0.015$) were associated with worse mental health as measured by MCS-12.

Factors mediating the effect of an UAP diagnosis on quality of life and symptom burden

The mediator analysis, presented in the online supplemental table S4, showed that revascularisation was the most dominant mediator of quality of life in patients with UAP as it managed to alter the unstandardised beta coefficient of the UAP variable more than the 10% threshold in all subdomains, both in the angina-related SAQ-7 instrument and the generic RAND-12 instrument. Adding to that, prior PCI or CABG significantly mediated the effect of an UAP diagnosis on angina-related quality of life and physical limitation.

DISCUSSION

The current study has several important findings. First, NSTEMI patients report more favourable scores for angina frequency, dyspnoea and physical and mental quality of life compared with other patient groups 3 months after hospitalisation for acute chest pain. UAP patients and patients with other cardiac diseases report the lowest scores. Even though the NCCP group was heterogeneous with the upper quartile reporting excellent outcomes half of NCCP patients reported persisting chest pain and one in three reported pronounced dyspnoea. Second, patients who had been admitted for acute chest pain showed overall lower mental health indices compared with the general population. Third, the most important overall predictor for favourable scores

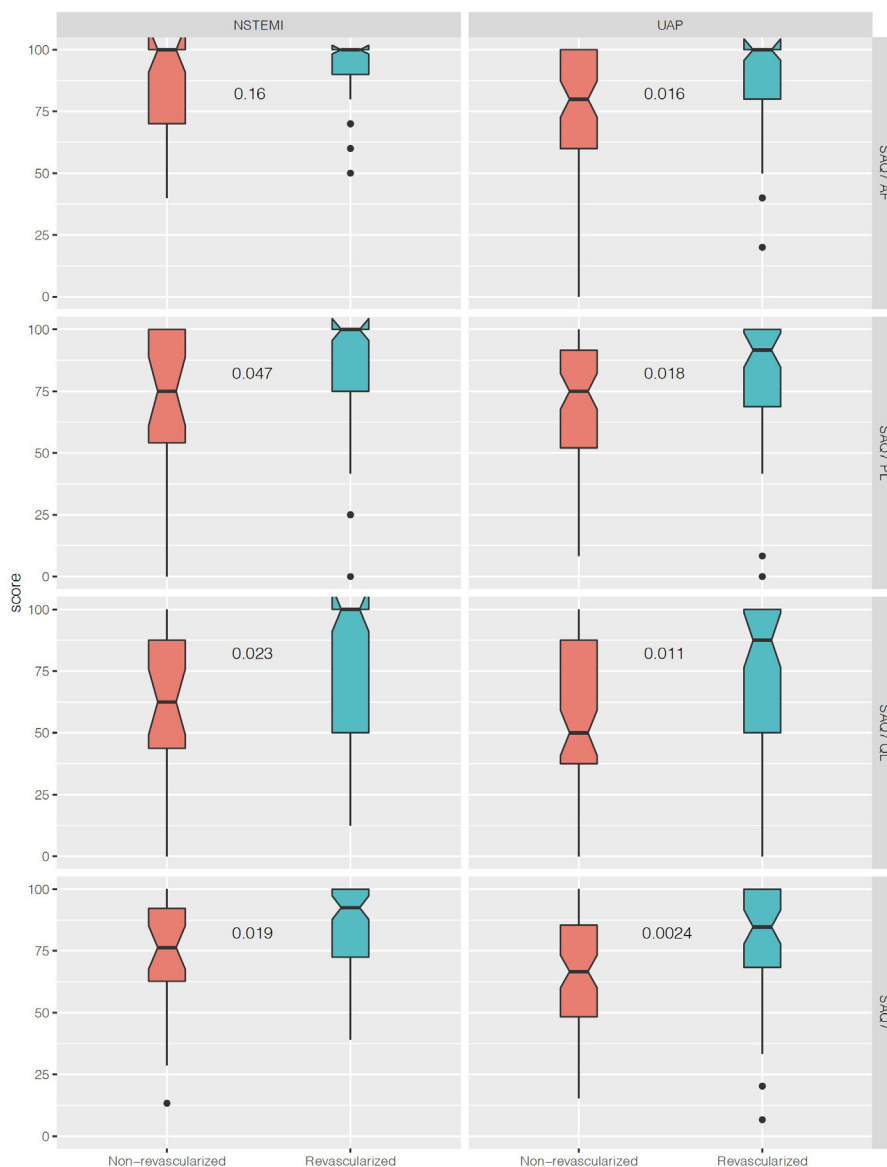


Figure 4 Boxplots of median values of four subdomain of the SAQ-7 questionnaire in revascularised and non-revascularised patients (with p values between the groups), both among NSTEMI and UAP patients. NSTEMI, non-ST elevation myocardial infarction; SAQ-7, Seattle Angina Questionnaire 7; UAP, unstable angina pectoris.

was revascularisation, while the most important predictor of unfavourable scores was a diagnosis of UAP. Finally, revascularisation appeared to mediate the unfavourable scores reported in the UAP group beneficially.

Large proportions of patients diagnosed with NCCP reported chest pain and dyspnoea 3 months after discharge. Compared with the NSTEMI population, we observed an overall higher symptom burden and lower quality of life in NCCP patients, in addition to the mental component score of RAND-12 being lower than community norms.⁴ Other studies report that these patients experience a persistence of symptoms that may lead to overinvestigations if they are rehospitalised.^{26 27} Wielgosz and colleagues²⁸ followed 821 patients with normal coronary arteries over a period of 1 year, the majority of these patients continued to suffer from chest pain, despite the observation that NCCP possessed a good prognosis. The

high symptom burden indicates that different supportive and multifaceted follow-up strategies should be investigated in NCCP patients.

The UAP patients had among the worst outcomes. This could be related to a higher prevalence of risk factors, more comorbidities⁷ and treatment with revascularisation being less frequent than the NSTEMI group. One previous report by Rumsfeld *et al* also found that a discharge diagnosis of UAP was significantly associated with worse SF-36 physical component score.¹⁷ Our study supplement the findings of Rumsfeld and colleagues by also including a disease-specific instrument (SAQ-7).

Revascularisation was an important predictor of quality of life in our data, for both NSTEMI and UAP patients. The effect on AMI have been observed earlier. The PREMIER study and TRIUMPH registry (similar PCI rate as us) reported angina at 30 days in 26.9% and 29.1%

Table 3 Multivariable regression models of the association between predictors and scores of SAQ-7 and RAND-12 instruments

	SAQ7-AF β (95% CI)	P value	SAQ7-QL β (95% CI)	P value	SAQ7-PL β (95% CI)	P value	SAQ7-summary β (95% CI)	P value	PCS-12 β (95% CI)	P value	MCS-12 β (95% CI)	P value
Age	NS		NS		-0.22 (-0.44 to 0.17)	<0.001	NS		NS		NS	
Female gender	NS		NS		NS	NS	NS		NS		NS	
Prior MI	NS		NS		NS	NS	NS		NS		-0.11 (-0.23 to 0.01)	0.041
Prior CABG	NS		-0.08 (-0.16 to 0.01)	0.036	-0.11 (-0.20 to 0.02)	0.022	NS		NS		NS	
Hypertension	NS		-0.10 (-0.17 to 0.02)	0.009	NS	NS			-0.24 (-0.38 to 0.11)	0.001	NS	
Current smoking	NS		-0.10 (-0.18 to 0.03)	0.005	-0.09 (-0.18 to 0.004)	0.041	NS		-0.127 (-0.26 to 0.01)	0.060	-0.13 (-0.23 to 0.03)	0.015
Reduced renal function	NS		NS		-0.11 (-0.21 to 0.02)	0.025	NS		-0.18 (-0.33 to 0.04)	0.011	NS	
BMI	NS		NS		NS	NS			NS		NS	
Revascularisation	0.15 (0.05 to 0.23)	0.002	0.10 (0.02 to 0.17)	0.012	NS	NS	0.15 (0.06 to 0.23)	0.001	NS		NS	
UAP	-0.19 (-0.31 to 0.10)	<0.001	-0.14 (-0.21 to 0.06)	<0.001	NS	NS	-0.18 (-0.29 to 0.09)	<0.001	-0.17 (-0.29 to 0.02)	0.028	NS	
Non-coronary cardiac disease	NS		NS		-0.09 (-0.17 to 0.001)	0.047	-0.11 (-0.19 to 0.02)	0.013	NS		NS	
	R ² =0.069 p<0.001		R ² =0.061 p<0.001		R ² =0.125 p<0.001		R ² =0.070 p<0.001		R ² =0.157 p<0.001		R ² =0.037 p=0.014	

Standardised β-coefficients are provided with 95% CIs.
The empty cells denote variables that were tested in the univariable regression analysis showing no significant correlation (p value <0.10) with the applicable dependent variable and accordingly are not included in the applicable multivariable linear regression models (see Methods section).
BMI, body mass index; CABG, coronary artery bypass graft; NS, not significant; SAQ7-AF, Seattle Angina Questionnaire 7 angina frequency; SAQ7-PL, Seattle Angina Questionnaire 7 physical limitation; SAQ7-QL, Seattle Angina Questionnaire 7 quality of life; UAP, unstable angina pectoris.

of myocardial infarction patients, compared with 42.6% of NSTEMI patients in our data.^{29 30} Our study adds to previous research within this field by showing that revascularisation was a strong predictor for higher SAQ7-AF score (angina freedom), SAQ7-QL and SAQ7-summary score also in patients with UAP and would clearly mediate the outcome of the scorings in this patient group. This is interesting given that the randomised CorMicA trial showed a favourable outcome in stable angina patients without significant coronary stenosis who were randomised to assessment of coronary flow reserves, microcirculation and vasoactive testing followed by targeted treatment,^{31 32} as opposed to standard care. Given the lower revascularisation rate and higher symptom burden seen in UAP patients, such novel investigation and treatment protocols are highly warranted and should be further investigated in this group.^{31 32}

Strengths and limitations

One of the key strengths in this study is that we include a large heterogeneous group of patients with chest pain, including both cardiac and non-cardiac causes, thereby collecting data from all relevant groups, except STEMI. Furthermore, we compare the generic quality of life data to available comparators from the general population. Another strength is the use of comprehensive measurement by use of standardised disease-specific and generic health instruments.³³ Generally, a disease-specific measure is more sensitive (in this case for cardiovascular outcomes), while a generic measure taps the patient's overall health.³⁴

Our study should be viewed in the light of several limitations. First, there was a substantial proportion of missing data. These patients were younger and with overall less risk factors. This introduces a possible bias as different scores could have been reported if all patients had responded. However, we found similar physical capacity (PCS-12 score) in chest pain patients and the age-adjusted general population, strengthening the assumption that reduction in scores are due to disease-specific symptoms. Second, we did not register information on ethnicity (the western Norwegian population is mainly Caucasian) or socioeconomic status, and accordingly, could not adjust for these possible confounders. Third, the characteristics of NSTEMI and UAP groups tend to differ in both clinical and demographic components; a logistic regression model was used to compensate for this, but we could not exclude non-recognised confounders to be present. Detailed angiographic data or non-invasive ischaemia investigations were not registered so the basis for different revascularisations rates between NSTEMI and UAP patients could not be elucidated in detail.^{9 10} Angiography was done on clinical indication, and patients were treated and received revascularisation in accordance with current guidelines. This means that patients received revascularisation if the operator identified a significant stenosis that was available for PCI (or CABG as applicable). A few patients (n=10) underwent revascularisation due to identification of a coronary artery stenosis during angiography, but still were not given

a final adjudicated diagnosis of acute coronary syndrome by the adjudicators who had all clinical information available including symptom development and results of investigations performed after PCI. This imposes uncertainty to our data analyses but is unlikely to impact the overall findings. Fourth, the disease-specific SAQ-7 instrument measures 'angina' but do not differentiate between chest pain of anginal aetiologies and NCCP that stem from the thorax cavity or psychogenic origins. Also, we did not measure follow-up data on intensity of medications so this could not be attributed to angina episodes and symptom burden at 3 month investigation. Finally, we did not measure baseline scores for the quality of life questionnaires and thus lack the ability to attribute the direct effect of revascularisation in improving scores between hospitalisations and 3-month phase.

Conclusion

NSTEMI patients have favourable disease-specific symptom and quality of life outcomes 3 months after the event, while the opposite may be expected in UAP and to some extent also NCCP patients. Symptom burden in UAP patients is large and should not be neglected. Revascularisation was associated with better quality of life and less symptom burden in both NSTEMI and UAP patients. Future studies should investigate if treatment (revascularisation or medical) may be expanded in UAP patients and if improved outpatient follow-up is beneficial for NCCP patients.

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REFERENCES

- Ayerbe L, González E, Gallo V, *et al.* Clinical assessment of patients with chest pain; a systematic review of predictive tools. *BMC Cardiovasc Disord* 2016;16:18.
- Stepinska J, Lettino M, Ahrens I, *et al.* Diagnosis and risk stratification of chest pain patients in the emergency department: focus on acute coronary syndromes. A position paper of the acute cardiovascular care association. *Eur Heart J Acute Cardiovasc Care* 2020;9:76–89.
- Mockel M, Searle J, Muller R, *et al.* Chief complaints in medical emergencies: do they relate to underlying disease and outcome? The Charité emergency medicine study (CHARITEM). *Eur J Emerg Med* 2013;20:103–8.
- Fass R, Achem SR. Noncardiac chest pain: epidemiology, natural course and pathogenesis. *J Neurogastroenterol Motil* 2011;17:110–23.
- Maddox TM, Reid KJ, Rumsfeld JS, *et al.* One-year health status outcomes of unstable angina versus myocardial infarction: a prospective, observational cohort study of ACS survivors. *BMC Cardiovasc Disord* 2007;7:28.
- Munyombwe T, Hall M, Dondo TB, *et al.* Quality of life trajectories in survivors of acute myocardial infarction: a national longitudinal study. *Heart* 2020;106:33–9.
- Kim M-J, Jeon DS, Gwon H-C, *et al.* Health-related quality-of-life after percutaneous coronary intervention in patients with UA/NSTEMI and STEMI: the Korean multicenter registry. *J Korean Med Sci* 2013;28:848–54.
- Brink E, Grankvist G, Karlson BW, *et al.* Health-related quality of life in women and men one year after acute myocardial infarction. *Qual Life Res* 2005;14:749–57.
- Kvisvik B, Mørkrid L, Røsjø H, *et al.* High-sensitivity troponin T vs I in acute coronary syndrome: prediction of significant coronary lesions and long-term prognosis. *Clin Chem* 2017;63:552–62.
- Ellis C, Gamble G, Hamer A, *et al.* Patients admitted with an acute coronary syndrome (ACS) in New Zealand in 2007: results of a second comprehensive nationwide audit and a comparison with the first audit from 2002. *N Z Med J* 2010;123:25–43.
- Collet J-P, 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* 2021;42:1289–367.
- Tjora HL, Steiro O-T, Langørgen J, *et al.* Diagnostic performance of novel troponin algorithms for the Rule-Out of non-ST-elevation acute coronary syndrome. *Clin Chem* 2022;68:291–302.
- Braunwald E, Morrow DA. Unstable angina: is it time for a reequiem? *Circulation* 2013;127:2452–7.
- Arnold SV, Smolderen KG, Kennedy KF, *et al.* Risk factors for rehospitalization for acute coronary syndromes and unplanned revascularization following acute myocardial infarction. *J Am Heart Assoc* 2015;4:1352. doi:10.1161/JAHA.114.001352
- Fanaroff AC, Kaltenbach LA, Peterson ED, *et al.* Management of persistent angina after myocardial infarction treated with percutaneous coronary intervention: insights from the TRANSLATE-ACS study. *J Am Heart Assoc* 2017;6:e007007.
- Cohen DJ, Van Hout B, Serruys PW, *et al.* Quality of life after PCI with drug-eluting stents or coronary-artery bypass surgery. *N Engl J Med* 2011;364:1016–26.
- Rumsfeld JS, Magid DJ, Plomondon ME, *et al.* Predictors of quality of life following acute coronary syndromes. *Am J Cardiol* 2001;88:781–4.
- De Smedt D, Clays E, De Bacquer D. Measuring health-related quality of life in cardiac patients. *Eur Heart J Qual Care Clin Outcomes* 2016;2:149–50.
- Tjora HL, Steiro O-T, Langørgen J, *et al.* Aiming toWards evidence baSed inTerpretation of cardiac biOmArkers in patients pResenting with chest pain-the WESTCOR study: study design. *Scand Cardiovasc J* 2019;53:280–5.
- Thygesen K, Alpert JS, Jaffe AS, *et al.* Third universal definition of myocardial infarction. *Eur Heart J* 2012;33:2551–67.
- Chan PS, Jones PG, Arnold SA, *et al.* Development and validation of a short version of the Seattle angina questionnaire. *Circ Cardiovasc Qual Outcomes* 2014;7:640–7.
- Weintraub WS, Spertus JA, Kolm P, *et al.* Effect of PCI on quality of life in patients with stable coronary disease. *N Engl J Med* 2008;359:677–87.
- Baron SJ, Chinnakondepalli K, Magnuson EA, *et al.* Quality-of-Life After Everolimus-Eluting Stents or Bypass Surgery for Left-Main Disease: Results From the EXCEL Trial. *J Am Coll Cardiol* 2017;70:3113–22.
- Ware J, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220–33.
- Veenstra M, Herlofson K, Aartsen M, *et al.* Cohort profile: the Norwegian life course, ageing and generation study (NorLAG). *Int J Epidemiol* 2021;50:728–9.
- Moi KA, Smoczyńska A, Rahel BM, *et al.* Non-cardiac chest pain: prognosis and secondary healthcare utilisation. *Open Heart* 2018;5:e000859.
- Ruddox V, Mathisen M, Otterstad JE. Prevalence and prognosis of non-specific chest pain among patients hospitalized for suspected acute coronary syndrome - a systematic literature search. *BMC Med* 2012;10:58.
- Wielgosz AT, Fletcher RH, McCants CB, *et al.* Unimproved chest pain in patients with minimal or no coronary disease: a behavioral phenomenon. *Am Heart J* 1984;108:67–72.
- Longmore RB, Spertus JA, Alexander KP, *et al.* Angina frequency after myocardial infarction and quality of life in older versus younger adults: the prospective registry evaluating myocardial infarction: event and recovery study. *Am Heart J* 2011;161:631–8.
- Doll JA, Tang F, Cresci S, *et al.* Change in angina symptom status after acute myocardial infarction and its association with readmission risk: an analysis of the translational research investigating underlying disparities in acute myocardial infarction patients' health status (triumph) registry. *J Am Heart Assoc* 2016;5:3205. doi:10.1161/JAHA.116.003205
- Ford TJ, Stanley B, Good R, *et al.* Stratified medical therapy using invasive coronary function testing in angina: the CorMicA trial. *J Am Coll Cardiol* 2018;72:2841–55.
- Ford TJ, Yie E, Sidik N, *et al.* Ischemia and NO obstructive coronary artery disease: prevalence and correlates of coronary vasomotion disorders. *Circ Cardiovasc Interv* 2019;12:e008126.
- Kornowski R. Patient reported outcomes measures (PROMs) in cardiovascular disease. *Eur Heart J Qual Care Clin Outcomes* 2021:qcab051.
- Brazier JE, Yang Y, Tsuchiya A, *et al.* A review of studies mapping (or cross walking) non-preference based measures of health to generic preference-based measures. *Eur J Health Econ* 2010;11:215–25.