

Higher In-Hospital Mortality in Patients with Nonspecific Complaints Presenting to the Emergency Department

JJH Wachelder, PM Stassen, RS Fourmanov, CH Nickel & HR Haak

Abstract

Background: Nonspecific complaints (NSC) at the Emergency Department (ED) are not well researched yet.

Objective: To investigate the number of patients who could be classified as having NSC early after arrival in the ED using an algorithm.

Method: Retrospective cohort study was conducted among all hemodynamically stable non-trauma adult patients with MTS category orange/yellow visiting the ED. Patients who had no specific complaints/signs, predefined on a list, were categorized as NSC.

Results: In total, 2419 patients, of whom 102 (4.2%) presented with NSC. Hospitalization was more prevalent (85.3% vs. 69.0%, $p < 0.001$) and in-hospital mortality was higher in the NSC-group (11.8% vs. 3.5%, adjusted OR 2.0, 95% CI 1.0-3.9, $p = 0.04$).

Conclusion: Using an algorithm it is possible to identify NSC patients who have (worse) outcomes than those classified as SC.

Keywords

Nonspecific Complaints; Emergency Medicine; Emergency Department; Mortality.

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Introduction

Complaints, such as ‘not feeling well’ and ‘feeling exhausted’, are often labelled as ‘Nonspecific Complaints’ (NSC). The prevalence of NSC in patients visiting the Emergency Department (ED) ranges from 13.0 to 21.5%.^{1,2} These patients are often undertriaged at the ED despite the high prevalence of serious underlying conditions, for example myocardial infarction.² It is challenging to correctly diagnose the specific underlying disease in patients with NSC, which is complicated further by comorbidity, polypharmacy and cognitive impairment or social circumstances.³ All these factors contribute to the higher risk of both hospitalization and mortality these NSC patients have compared to patients with Specific Complaints (SC).^{2,4}

So far, there is no clear definition of NSC, which makes it difficult to investigate this problem.^{5,6} One study, the BANC study, proposed a definition for NSC, using an algorithm that can be completed during work-up in the ED, after history taking, physical examination and making an ECG.² Using the BANC definition, 13.5% of non-trauma patients could be labelled as having NSC. This selected group was seriously ill, as illustrated by the finding that 59% of these patients turned out to

have a serious condition and 6% died within 30-day follow up.² The timing of differentiating NSC from SC is important in the ED, because early in the process, diagnostic and therapeutic decisions have to be made.² We hypothesize that NSC patients can indeed be identified early during work up in the ED using items that become available early after arrival in the ED.

The objective of our large retrospective cohort study in adult medical patients was to investigate the number of patients who could be classified as having NSC early after arrival in the ED using an algorithm comparable to the one used in the BANC study, and to compare their characteristics and outcome with patients classified as having SC.

Methods

Study design, setting and population

A retrospective cohort study was performed at Máxima Medical Centre (MMC), the Netherlands, which is a 550-bed teaching hospital with more than 31,000 ED visits yearly. Patients are mostly referred by general practitioners (51.8%), who provide health care service 24 hours per day.⁷ After arrival at the ED, all patients are first triaged by an ED nurse, using the Manchester Triage System

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(MTS).⁷ Patients with cardiac or gynaecological problems are assessed and treated in departments outside the ED, and therefore not included.

All adult (≥ 18 years old) non-trauma patients who visited the ED in an eight-month period (September 2010 and May 2011) with triage code yellow or orange using the Manchester Triage System (MTS) with normal vital signs were evaluated for inclusion. Another inclusion criteria was normal vital signs during initial presentation (systolic blood pressure (SBP) >90 mmHg, heart rate (HR) <120 beats/min, temperature (between 35.6 and 38.4). Exclusion criteria were: abnormal vital signs (vital signs out of normal range), ST-segment elevated myocardial infarction, moribund patients with end-stage malignancy, available recent (one week) laboratory findings before ED arrival, referrals from other hospitals and more than one missing vital sign.

The included patients were then further categorized into the NSC or the SC group. Patients were categorized as having NSC if 1) their complaint was not on the list of SC (supplementary data) and 2) no working diagnosis could be made after history taking, physical examination and ECG analysis. All others were categorized as SC.

We used the same algorithm to categorize complaints as the BANC study did (Figure 1),² except for: 1) triage classification (we used the MTS triage categories orange and yellow, the BANC study used the Emergency Severity Index (ESI) category two and three), and 2) we did not include the respiratory rate in the list of vital signs as this vital sign was not systematically recorded in our ED, and 3) gynaecology and cardiology patients were excluded, because they presented at another emergency department of their own specialty. We considered these differences to be not very significant as the triage categories of ESI and MTS both aim to select urgent patients who should be assessed and treated within the hour^{17,18} and a respiratory rate is not the most reliable vital sign as the interobserver agreement was found to be low in some studies.⁸⁻¹⁰

This study was approved by the Institutional Review Board of MMC and confirmed that the Medical Research Involving Human Subject Act (WMO) was not applicable (METC 15.091).

Data collection & definitions

Data of all adult patients were collected from the electronic patient records by one researcher (JW) who used a standardized abstraction form. Two independent medical abstractors (JW and RF) reviewed the medical charts. During the data retrieval phase, several meetings took place during

which cases with disagreement on inclusion and categorization were discussed and agreed upon. The STROBE checklist was used to check the criteria for chart review.¹¹

Data on premorbid status were retrieved from the electronic ED files: age, sex, comorbidity, number of medications, ED visits during the preceding 90 days. Comorbidity was quantified using the Charlson Comorbidity Index (CCI).¹² All electronic patient (both ED and hospital) records were assessed to retrieve comorbidity. Polypharmacy was defined as the use of six or more medications.¹³

Medical data we retrieved included triage category, triage pathway and laboratory tests (C-reactive protein, haemoglobin, sodium, potassium and creatinine). The triage category was assessed by the five-category MTS score, which was categorized as follows: high urgency (red and orange), moderate urgency (yellow) and low urgency (green); the colour blue is not used in our ED.¹⁴ The triage pathways at the ED were categorized following the MTS pathways that are chosen by the triage nurse. The laboratory findings were categorized as abnormal using the following (reference) values: Leukocytes $>12.0 \times 10^9/l$, Haemoglobin <6.0 mmol/l, Sodium <135 or >145 mmol/l, Potassium <3.5 or >5.0 mmol/l and Creatinine >100 $\mu\text{mol/l}$.

Organizational data retrieved were date of visit (weekend visits were ED visits on Saturday and Sunday), mode of patient referral (which was categorized as self-referral, referral by general practitioner, by medical specialist or by ambulance), the number of diagnostic tests (sum of radiological tests, ECG, arterial blood gas analysis, laboratory tests, urinalysis, urine and blood culture) performed at the ED, number of consultations in the ED and ED-Length of Stay (LOS). ED-LOS was defined as the time between arrival at the ED and discharge from the ED in minutes.⁷ The dates of admission, discharge, death and ED-revisit were retrieved, when applicable. All-cause in-hospital mortality was retrieved from the electronic patient records.

Data analysis

The statistical analyses were conducted using SPSS (IBM SPSS Statistics for MacBook, version 22.0, Armonk, New York). For evaluation of differences between NSC- and SC-patients the unpaired-t-test, (for continuous data with normal distribution), the Mann-Whitney U test (for continuous nonparametric data) and the Chi square test were used (for categorical data). Missing data were categorized as 'unknown' and included in the analysis of categorical

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parameters in order to explore the influence of missing data. Confounders were included in the multivariate logistic regression analysis in order to measure the independent effect of NSC on in-hospital mortality. Confounders used were age, comorbidity, medication and triage category. Cox regression analysis was performed to calculate Odds Ratios (OR) for mortality, which and these was adjusted for confounders. The Odds Ratio (OR) and corresponding 95% confidence interval (CI) were calculated. A two-sided p-value lower than 0.05 was considered significant.

Results

Characteristics of study population

In total, 4462 adult non-trauma patients who were triaged as orange/yellow visited the ED within the 8-month study period (Figure 1). Of these, 2043 were excluded because their vital signs were abnormal, or pre-hospital lab results were available. In total, 2419 patients (14.3%) were included in our analysis, of whom 102 patients (4.2%) were classified as having NSC and 2317 (95.8%) patients as having SC.

Comparison of NSC- with SC-patients

Patients with NSC were older than SC-patients (76 vs. 62 years, $p < 0.001$) (Table 1). Patients with NSC had a higher CCI (mean 2 vs. 1, $p = 0.002$) and more often had a malignancy. In addition, they used more medications than patients with SC (mean 5.8

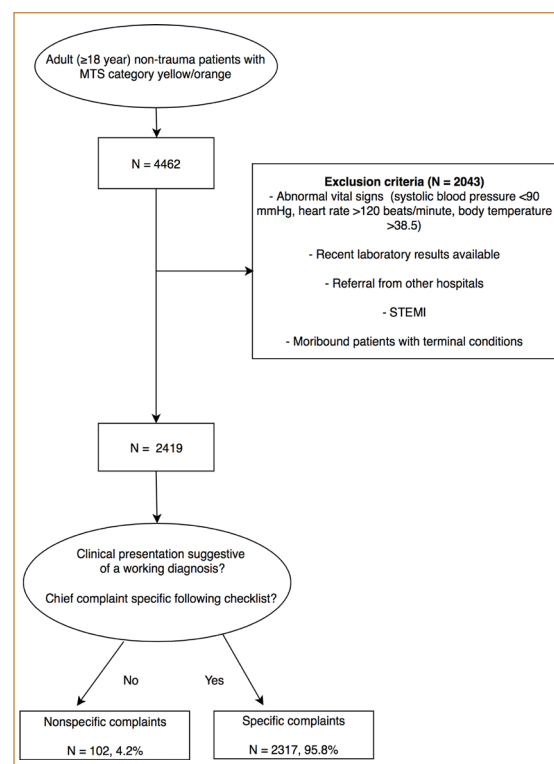


Figure 1. Flow chart of patient classification.

MTS = Manchester Triage System. STEMI = ST-segment elevated myocardial infarction. GCS = Glasgow Coma Scale.

vs. 3.3, $p < 0.001$). Patients presenting with NSC more often had visited the ED 30 days before the index visit compared to SC patients (26.5 vs 15.0%, $p = 0.003$).

Table 1. Premorbid condition of NSC and SC-patients.

	Nonspecific complaints (N = 102, 4.2%)	Specific complaints (N = 2137, 95.8%)	P-value
Age (mean, SD)*	76 (12.7)	62 (18.5)	<0.001
Male (%)	48 (47.1%)	1137 (49.1%)	0.762
CCI (mean, SD)*	2.0 (2.1)	1.2 (1.7)	0.002
Malignancy (%)*	31 (30.4%)	337 (14.5%)	<0.001
Diabetes Mellitus (%)	21 (20.6%)	287 (13.3%)	0.06
Cardiovascular (%)	15 (14.7%)	221 (9.5%)	0.178
Cerebrovascular (%)	14 (13.7%)	222 (9.6%)	0.124
Pulmonary (%)	9 (8.8%)	393 (17.0%)	0.021
Dementia (%)	2 (2.0%)	32 (1.4%)	0.656
Missing (%)	4 (3.9%)	135 (5.8%)	
Prior ED visits (%)*	27 (26.5%)	348 (15.0%)	0.003
Number of medications (%)*	6.7 (3.6)	4.7 (4.0)	<0.001
Missing	12 (11.8%)	572 (24.7%)	

CCI = Charlson Comorbidity Index. ED= Emergency Department. SD= Standard Deviation. P-values for NSC-patients vs. SC-patients; calculated using the unpaired T-test and the Chi-square test. * Significant P-value (<0.05).

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Table 2. Organizational and clinical factors

	Nonspecific complaints (N = 102, 4.2%)	Specific complaints (N = 2137, 95.8%)	P-value
Mode of referral (%)[*]			0.004
General practitioner	83 (81.4%)	1512 (65.3%)	
Self-referral	9 (8.8%)	516 (22.3%)	
Ambulance	6 (5.9%)	215 (9.3%)	
Specialist	4 (3.9%)	74 (3.2%)	
Weekend (%)	21 (20.6%)	531 (22.9%)	0.632
Specialties involved at ED (%)			0.128
1	12 (11.8%)	276 (11.9%)	
≥2	3 (2.9%)	21 (0.9%)	
Diagnostic procedures, mean (SD)[*]	3.0 (1.5)	2.7 (1.3)	0.001
Laboratory findings			
Leukocytes>12.0 10 ⁹ /l	24 (23.5%)	586 (25.3%)	0.643
Haemoglobin<6.0 mmol/l	21 (20.6%)	255 (11.0%)	0.007
Sodium<135 mmol/l	30 (29.4%)	230 (9.9%)	<0.001
Sodium>145 mmol/l	6 (5.9%)	50 (2.2%)	0.032
Potassium<3.5 mmol/l	13 (12.7%)	165 (7.1%)	0.047
Potassium>5.0 mmol/l	13 (12.7%)	84 (3.6%)	<0.001
Creatinine>100 μmol/l	45 (44.1%)	476 (20.6%)	<0.001
No laboratory assessment (%)	5 (4.9%)	130 (5.6%)	1.000
ED-LOS, minutes, mean (SD)[*]	171 (63)	153 (68)	0.010
Outcomes			
Hospitalization (%)[*]	87 (85.3%)	1596 (69.0%)	<0.001
LOS-hospital days, median (IQR)[*]	7 (0 – 63)	4 (0 – 212)	<0.001
In-hospital mortality (%)	12 (11.8%)	82 (3.5%)	0.001

MTS = Manchester Triage System. ED = Emergency Department. IQR = Interquartile Range. P-values for NSC-patients vs. SC-patients; calculated using the Chi-square test and the Mann-Whitney-U-test. * Significant P-value (<0.05)

Patients with NSC more often had been referred by the GP than those with SC (81.4% vs. 65.2%, $p=0.004$) (Table 2). Abnormal laboratory values were more prevalent in patients with NSC than in patients with SC, most specifically sodium levels (more often lower than 135 mmol/l and higher than 145 mmol/l) and creatinine levels (more often higher than 100 μmol/l).

The number of diagnostic tests performed at the ED was higher (mean 3.0 vs. 2.6, $p=0.001$) and the ED-LOS was longer for patients with NSC than for SC patients (median 171 vs. 153 minutes, $p=0.010$). Hospitalization occurred more often in patients with NSC (85.3%) than in SC-patients (69.0%, $p<0.001$), and the hospital-LOS was longer in the NSC-group than in the SC-group (median 7 vs. 4 days, $p<0.001$). The number of patients who

revisited the ED within 90 days after the initial ED visit was comparable in both groups (20.0% vs. 15.7%, $p=0.341$).

Patients with NSC had a higher in-hospital mortality rate than patients with SC (11.8% vs. 3.5%, $p<0.001$, unadjusted OR 3.6; 95% CI 1.9 – 6.9). After controlling for the confounders age, comorbidity, medication and triage category, patients with NSC still had a higher in-hospital mortality than patients with SC (adjusted HR 2.0; 95% CI 1.0 – 3.9, $p=0.04$).

Discussion

Patients with NSC in our cohort were selected using an algorithm including data obtained early in the ED process. The selected patients with NSC were mostly older with more comorbidity

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and polypharmacy than those with SC. They had a longer ED-LOS, were more often hospitalized, had a longer hospital-LOS and had substantially higher (11.8 vs. 3.5%) in-hospital mortality in comparison with SC-patients.

So far, only a few studies have investigated the prevalence, characteristics and outcomes of patients presenting with NSC in the ED. However, lack of a uniform definition impedes research on this matter and explains divergent results on characteristics and outcomes.¹⁵⁻¹⁷ In the literature, patients with NSC are also referred as 'general disability',⁵ 'decreased general condition'¹ and 'weakness'.¹⁸ We applied most of the criteria used in the BANC study.² The observed prevalence of NSC was low (4.2%), and lower than in the BANC study (13.5%) and in other studies (13-21.5%).^{16,19,20} This difference may be due to the two small adjustments of the algorithm. We, like many other hospitals, use the triage system (MTS instead of ESI), but the categories of both systems aim to select comparably urgent patients who should be assessed and treated within the hour.^{21,22} We were unfortunately not able to retrieve the respiratory rate in all patients, but this vital sign is not the most reliable vital sign when assessed by a health care professional and the interobserver agreement is found to be low in some studies.⁸⁻¹⁰ Other explanations for the difference in prevalence are differences in the study population (teaching hospital vs. university hospital and our patients were on average 5 years younger than in the BANC study). In addition, the health care system varies between countries. In the Netherlands, patients are mostly referred to the ED by a GP. It is possible that patients with NSC are less often referred to the ED by GPs, mostly the GPs know their older adult patients and a nonspecific presentation is better recognized by their GP and they are treated in the home situation. This might explain the lower prevalence of NSC in our study. Additionally, despite definition and setting differences between studies the outcomes did not differ between NSC and SC patients.^{1,2,5,20,23} Nevertheless, the algorithm is able to differentiate NSC from SC.

Our study found that patients presenting with NSC were old, often had polypharmacy and many comorbidities, which is in accordance with the BANC study.² In addition, these patients have a poor prognosis, and most (not all) studies observed identical conclusions on this matter.^{1,2,17,24,25} although our study found a higher in-hospital mortality (11.8%) than other studies did (5.5-7.5%).^{2,5,20,26} This is probably due to the using other definitions for NSC and ways of patient

selection. The finding of the higher mortality in NSC-patients warrants valid risk stratification tools that identify these patients. Indeed, it has been shown that especially older patients (highly prevalent in our NSC population) who present with 'normal' vital parameters can have serious underlying conditions.²² We believe our study confirms that patients who visit the ED with NSC are particularly vulnerable. The observed number of adverse outcomes in patients with NSC is alarming.

Recognition of patients with NSC in the ED and acknowledging their high risk of adverse health outcomes is essential. Except for the BANC study, all other studies on patients presenting with NSC did not include specific complaints and findings of the physical examination and a normal ECG as exclusion criteria: they defined NSC based on presenting complaint.^{15,16} This could be important regarding the diagnostic process of these patients, as it is hard to initiate a management protocol when no specific complaints or signs are observed. We found that patients with NSC underwent slightly more diagnostic procedures at the ED and that the median ED-LOS was longer compared to patients with SC. These findings illustrate that the diagnostic process of patients with NSC is complex as has been conformed in earlier studies^{23,27} and it is possible that physicians lack specific experience in managing patients with NSC.^{3,17,19} This indicates that identification of patients with NSC – especially those at high risk of adverse outcomes – is a first step. Design of care pathways to further diagnose and treat these patients is needed.

Our study has some limitations. The retrospective design may have led to coding errors and missing values in our database. These missing data could have influenced patient selection because missing data on complaints, vital signs, ECGs may have led to under- or overestimation of the prevalence and the outcome. Furthermore, recording bias could have occurred due to the retrospective chart analyses of the medical patient records. However, we tried to minimize this bias by performing record review by two independent medical abstractors following the STROBE guidelines. Lastly, we used logistic regression analyses to determine differences in mortality risk between NSC and SC-patients. Due to our focus on in-hospital mortality, vulnerable patients who were sent home to die in their own environment were missed. However, this probably will be a small group, because we excluded moribund patients.

Our study shows that it is feasible to identify NSC patients using an algorithm early in the

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work-up in the ED and that these identified NSC patients have a poor prognosis. This illustrates even more the need for a standardized care pathway in order to maintain a high quality of care of these mostly frail older patients. We propose that diagnostic algorithms that are feasible for use

in the ED will be externally tested for commonly used triage systems in future studies on the topic of NSC.

Conflicts of Interest

The authors have no conflicts of interest to declare

Supplementary data

Table 1. Checklist of specific chief complaints following the Banc criteria

Pain (chest, abdominal, head, leg, joint, back)	GCS score <14, confusion, intoxication, seizure
Dyspnoea, cough	Bleeding (e.g. GI, lung)
Weakness localized, stroke-like symptoms	Syncope
Swollen extremity (leg, arm)	Anxiety, psychotic symptoms, suicidal ideation
Diarrhoea	Skin lesion, allergic skin reaction
Dysuria	Fever
Vertigo	Palpitations
Nausea with vomiting	Trauma

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