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Shortness of breath as a diagnostic factor for acute coronary syndrome in male and female callers to out-of-hours primary care

Michelle Spek ,[1] Roderick P Venekamp,[1] Daphne C A Erkelens,[1] Maarten van Smeden ,[2] Loes T C M Wouters ,[1] Hester M den Ruijter ,[3] Frans H Rutten,[1] Dorien L Zwart[1]

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[1]Department of General Practice and Nursing Science, Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands
[2]Department of Epidemiology, Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands
[3]Laboratory of Experimental Cardiology, University Medical Centre Utrecht, Utrecht, The Netherlands

Correspondence to
Michelle Spek, Department of General Practice & Nursing Science, Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht 3508 GA, The Netherlands;
m.spek-3@umcutrecht.nl

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ABSTRACT

Objective Chest discomfort and shortness of breath (SOB) are key symptoms in patients with acute coronary syndrome (ACS). It is, however, unknown whether SOB is valuable for recognising ACS during telephone triage in the out-of-hours primary care (OHS-PC) setting.

Methods A cross-sectional study performed in the Netherlands. Telephone triage conversations were analysed of callers with chest discomfort who contacted the OHS-PC between 2014 and 2017, comparing patients with SOB with those who did not report SOB. We determine the relation between SOB and (1) High urgency allocation, (2) ACS and (3) ACS or other life-threatening diseases.

Results Of the 2195 callers with chest discomfort, 1096 (49.9%) reported SOB (43.7% men, 56.3% women). In total, 15.3% men (13.2% in those with SOB) and 8.4% women (9.2% in those with SOB) appeared to have ACS. SOB compared with no SOB was associated with high urgency allocation (75.9% vs 60.8%, OR: 2.03; 95% CI 1.69 to 2.44, multivariable OR (mOR): 2.03; 95% CI 1.69 to 2.44), but not with ACS (10.9% vs 12.0%; OR: 0.90; 95% CI 0.69 to 1.17, mOR: 0.91; 95% CI 0.70 to 1.19) or 'ACS or other life-threatening diseases' (15.0% vs 14.1%; OR: 1.07; 95% CI 0.85 to 1.36, mOR: 1.09; 95% CI 0.86 to 1.38). For women the relation with ACS was 9.2% vs 7.5%, OR: 1.25; 95% CI 0.83 to 1.88, and for men 13.2% vs 17.4%, OR: 0.72; 95% CI 0.51 to 1.02. For 'ACS or other life-threatening diseases', this was 13.0% vs 8.5%, OR: 1.60; 95% CI 1.10 to 2.32 for women, and 7.5% vs 20.8%, OR: 0.81; 95% CI 0.59 to 1.12 for men.

Conclusions Men and women with chest discomfort and SOB who contact the OHS-PC more often receive high urgency than those without SOB. This seems to be adequate in women, but not in men when considering the risk of ACS or other life-threatening diseases.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Shortness of breath (SOB) is considered a 'female-specific' symptom in patients with ACS.
⇒ The risk of ACS in callers contacting the out-of-hours primary care (OHS-PC) is higher among men than women.
⇒ For both sexes, chest discomfort is more common than SOB in patients with ACS.

WHAT THIS STUDY ADDS

⇒ Men and women with SOB were more likely to receive a high urgency allocation at OHS-PC than those without SOB.
⇒ In women also reporting SOB tended to be related to ACS or other life-threatening event, while this was not so for men.
⇒ Assigning higher urgency in patients with chest discomfort who also mention SOB compared with those without SOB seems adequate in women, but not in men.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ In women, but not in men with chest discomfort who also report SOB at the OHS-PC, high urgency allocation should be considered at a lower threshold than those without reporting SOB.

INTRODUCTION

Acute coronary syndrome (ACS) is an umbrella term and can be subdivided into myocardial infarction, either ST-elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI) and unstable angina. All coronary artery diseases combined, including ACS are the leading cause of death in both the USA (43.8%) and Europe (43.6%).[1 2]

Most 'classic' for ACS is retrosternal oppressive chest discomfort over a large area, spreading out to arms, jaw and/or between the shoulder blades together with autonomic nervous system (ANS)-like symptoms such as nausea/vomiting, sweating and pale face.[3 4] However, in everyday practice the clinical presentation is rather diverse. Shortness of breath (SOB) is the most common symptom after chest discomfort mentioned by patients with ACS, similarly to radiation of chest discomfort to the arms, jaw or between the shoulder blades.[3–6] Older patients, women and those with diabetes who have an ACS may present less 'classically', and symptoms such as dizziness/light-headedness, extreme fatigue and SOB have been considered as 'female-specific'.[4 7] Importantly, however, both chest discomfort and SOB may be caused by a wide

range of disorders ranging from life-threatening, for example, from ACS, to self-limiting disorders such as upper respiratory tract infection or intercostal neuralgia.[8 9]

The diagnostic dilemma is illustrated by the fact that just around 1 in 10 of cases suspected of ACS seen at the emergency department (ED) actually has an ACS.[10] In the Netherlands, the large majority (80%) of these patients are referred by the general practitioner (GP), and 20% are direct 112 (national emergency number of the Netherlands) calls. So, the majority of patients suspected of ACS in the Netherlands will contact out-of-hours primary care (OHS-PC). These OHS-PCs provide urgent primary care during evening, night and weekend hours to ensure 24/7 medical access. Telephone triage in OHS-PC is done by triage nurses.[11–13] They use a semiautomatic computer-based decision support system, the Netherlands Triage Standard (NTS).[14–16] The triage nurse selects one or more entrance complaints from a list of 56 possible entrance complaints depending on the symptoms mentioned by the caller. Based on the selected entrance complaint by the triage nurse, the NTS system displays hierarchically ordered triage questions for considering severity. Based on the answers given by the patient and entered into the system by the triage nurse, the NTS algorithm generates an urgency level to which a response time is linked which ranges from U1 to U5; U1 (immediate ambulance deployment), U2 (as soon as possible, within 1 hour), U3 (within 3 hours), U4 (within 24 hours) to U5 (telephone advice).[13 16–18] The triage nurses or supervising GP may overrule the NTS' suggested urgency level if they consider another urgency level more appropriate.[17]

Based on the urgency assessment of the NTS alone, 27% of callers with an ACS or other life-threatening event (LTE) had an urgency level that is too low (U3–U5), and with the final urgency (also including overruled cases) this was 14%.[19] Fortunately, this rate is only 0.04% (4 in 10 000 cases) of missed or delayed myocardial infarction and/or sudden cardiac death among callers with acute chest discomfort at the OHS-PC in the Netherlands.[19 20] Nevertheless, this accounts for 30.4% of all serious adverse events which is higher than the rate of serious adverse events based on all OHS-PC calls in a year which is 0.006% (6 in 100 000).[19] Large numbers of non-ACS referrals may cause an overload in the ED, which can lead to insufficient capacity for those who truly need urgent care.[17 18 21 22]

Therefore, we aimed to determine whether, among callers with chest discomfort, SOB in the OHS-PC setting was associated with high urgency allocation (U1/U2), and its potential diagnostic value for diagnosing of ACS and 'ACS or other LTE' separately. This may ultimately improve the triage by updating the NTS system accordingly.

METHODS

Study design

This study is part of the Safety First Study, a retrospective observational study with the aim of describing and improving telephone triage of callers suspected for transient ischaemic attack/stroke or ACS in Dutch OHS-PC. More detailed information about the study design and data collection is published in the study design paper of the Safety First Study.[23]

This cross-sectional study focused on SOB in callers with chest discomfort.

Study population

We included telephone triage conversations from callers who contacted the OHS-PC with chest discomfort between January 2014 and December 2017. Conversations were selected from several participating OHS-PC locations in the Utrecht region, concerning both rural and non-rural areas.[20] Eligible conversations were selected based on a combination of International Classification of Primary Care codes related to ACS (K01, K02, K03, K24, K74, K75, K76, K77, K93, L04, P74, R02, R98) and the presence of one or more keywords in the electronic patient records (chest pain, heart symptoms, heart, myocardial infarction, heart attack or common abbreviations of the aforementioned) to ensure that all callers suspected of having ACS were selected.[24] From a total number of approximately 20 000 conversations eligible for inclusion, a computer-generated random sample of more than 2000 conversations was included. Telephone triage conversations were excluded if (1) Callers were younger than 18 years of age, (2) The conversations were for callers who did not live in the OHS-PC area, (3) The caller's GP was unwilling to provide follow-up data, (4) The audio conversations were of poor quality, and (5) Telephone conversations were something other than triage (eg, a consultation with ambulance personnel).

Data collection

Patient characteristics, call characteristics, signs and symptoms were collected by listening to call recordings and examining data from the OHS-PC electronic patient record. If a characteristic, sign or symptom was not mentioned during the telephone triage conversation, it was labelled as missing. However, the 496 (22.6%) patients in whom the SOB status was unknown were considered to have 'no SOB'. For analyses they were combined with the 603 (35.5%) callers who explicitly mentioned absence of SOB during the call, either spontaneously or after being questioned about it. We conducted a sensitivity analysis in which we considered only callers who explicitly indicated to have or not have SOB.

For assessing severity of chest pain the triage nurses use a Visual Analogue Scale ranging from 0 (no pain) to 10 (the severest pain possible). Chest pain >7 was considered severe pain in the analyses.

To collect data on the final diagnosis, the caller's own GP was contacted. From the patients' primary care electronic health record, we captured data about the final diagnosis, interventions, hospitalisation and mortality within 30 days of the OHS-PC index contact. The information requested also included information from specialist letters.

Data analyses

Patient and call characteristics were compared between those with and without SOB and between women and men. Pearson's χ^2 test or Fisher's exact test (in case of groups with less than 10 people) was used to compare categorical variables and the independent sample t-test was used to compare continuous variables. Chosen entrance complaints were determined for all patients and in those with ACS. The urgency allocation was stratified into high (U1 and U2) and low (U3, U4 and U5) urgency levels.[5] ORs were calculated to analyse the relation between SOB and the final urgency allocation, between SOB and ACS, and between SOB and 'ACS or other LTE' (including a dissection of the thoracic aorta, acute heart failure and pulmonary embolism). We calculated multivariable ORs (mORs) using multivariable logistic regression with gender in the model. Finally, we added an interaction term between SOB and gender to the models to assess whether the associations were different in men and women. A value of $p<0.05$ was considered statistically significant. Data analysis was performed using IBM SPSS Statistics V.26.0.

Table 1 Baseline characteristics of 2195 callers who called the OHS-PC with chest discomfort, divided into those with and without shortness of breath

	Total n=2195	Shortness of breath n=1096 (49.9%)	No shortness of breath n=1099 (50.1%)	P value
Patient characteristics				
Mean age in years (SD)	59.1 (19.5)	60.3 (20.2)	57.9 (18.8)	**0.004**
Male sex (n=980)	980 (44.6%)	479 (43.7%)	501 (45.6%)	0.375
Female sex (n=1215)	1215 (55.4%)	617 (56.3%)	598 (54.4%)	0.375
Call characteristics				
Call duration in min:s (SD)	7:34 (3:48)	7:31 (4:02)	7:37 (3:33)	0.561
Someone else called on behalf of patient (n=2171)*	1093 (50.3%)	624 (57.5%)	469 (43.2%)	**<0.001**
GP participated in triage (n=2195)	1148 (52.3%)	574 (52.4%)	574 (52.2%)	0.947
Medical history and use of cardiovascular medication				
Any cardiac disease (n=1847)*	1195 (64.7%)	617 (68.2%)	578 (61.4%)	**0.002**
Coronary artery disease (n=1153)*	389 (33.7%)	188 (35.7%)	201 (32.1%)	0.188
Cardiac arrhythmia (n=907)*	231 (25.5%)	118 (29.0%)	113 (22.6%)	**0.028**
Valvular disease (n=767)*	77 (10.0%)	47 (13.7%)	30 (7.1%)	**0.002**
Heart failure (n=764)*	62 (8.1%)	44 (12.8%)	18 (4.3%)	**<0.001**
Cardiovascular medication use (n=1618)*	856 (52.9%)	437 (57.2%)	419 (49.1%)	**0.001**
Cardiovascular risk factors				
Hypertension (n=894)*	323 (36.1%)	153 (38.0%)	170 (34.6%)	0.301
Hypercholesterolaemia (n=825)*	212 (25.7%)	101 (27.4%)	111 (24.3%)	0.302
Diabetes mellitus (n=905)*	180 (19.9%)	110 (26.2%)	70 (14.4%)	**<0.001**
Family history of cardiovascular disease (n=293)*	212 (72.4%)	93 (75.0%)	119 (70.4%)	0.386
Symptoms mentioned during the call				
Chest pain (n=2118)*	1982 (93.6%)	953 (91.4%)	1029 (95.7%)	**<0.001**
Autonomic nervous system related symptoms† (n=2118)*	1190 (56.2%)	617 (58.8%)	573 (53.6%)	**0.016**
Chest pain characteristics				
Pain onset <12 hours (n=1919)*	1404 (73.2%)	676 (73.6%)	728 (72.8%)	0.708
Pain duration >15 min (n=1837)*	1763 (96.0%)	850 (96.5%)	913 (95.5%)	0.286
Radiation of pain (n=1676)*	1077 (64.2%)	515 (65.8%)	562 (62.9%)	0.226
Severe pain (score >7 on VAS) (n=922)*	337 (36.6%)	162 (42.9%)	175 (32.2%)	**0.001**
Urgency allocation				
High (U1 or U2)	1500 (68.3%)	832 (75.9%)	668 (60.8%)	**<0.001**
Low (U3, U4 or U5)	695 (31.7%)	264 (24.1%)	431 (39.2%)	
Final diagnosis				
ACS	252 (11.5%)	120 (10.9%)	132 (12.0%)	0.435
ACS or other LTE	319 (14.5%)	164 (15.0%)	155 (14.1%)	0.568
Non-urgent disorders	1876 (85.5%)	932 (85.0%)	944 (85.9%)	0.568

*For these variables there were missing data.
†Autonomic nervous system related symptoms consist of one or more of the following: nausea and/or vomiting, sweating, pallor/ashen skin, (near) collapse.
ACS, acute coronary syndrome; GP, general practitioner; LTE, life-threatening event; OHS-PC, out-of-hours services for primary care; VAS, Visual Analogue Scale.

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, or in developing plans for design; however, they were involved in the implementation of the study. In addition, they were asked to advise on interpretation and writing the paper. The results will be shared and discussed with the national patient community of cardiovascular diseases ('Harteraad').

RESULTS

In total 2195 callers were included, mean age 59.1 (SD: 19.5) years, 55.4% female. In total, 64.5% had SOB (56.3% women, 43.7% men). Baseline characteristics for women and men are shown in online supplemental table S1.

Baseline characteristics for callers with and without SOB are shown in table 1. Callers with SOB were slightly older than those without (60.3 years vs 57.9 years, p=0.004), more likely had someone else calling for them (57.5% vs 43.2%, p<0.001), more likely somewhat had a history of heart diseases (68.2% vs 61.4%, p=0.002). They also more likely had diabetes (26.2% vs 14.4%, p<0.001), and were more likely to have cardiovascular medication (57.2% vs 49.1%, p=0.001) than callers without SOB.

Callers with SOB were less likely to report chest pain (91.4% vs 95.7%, p<0.001), but more likely report ANS-related symptoms (58.8% vs 53.6%, p=0.016) than those without SOB. Among callers who presented with chest pain, callers also reporting SOB were more likely to report severe chest pain (42.9% vs 32.2%, p=0.001) than callers with chest pain but without reporting SOB. In total 252 (11.5%; 15.3% of the men, 8.4% of the women) callers with chest discomfort had an ACS; 29.0% an STEMI, 40.9% an NSTEMI, 23.4% unstable angina pectoris, and in 6.7% unclassified ACS. Of the 1943 callers without ACS, 3.4% had another urgent diagnosis, for example, dissection of the thoracic aorta, acute heart failure, pulmonary

Table 2 Association between SOB and urgency allocation of 2195 callers with acute chest discomfort who called the OHS-PC, divided by sex

Total calls	High urgency, n=1500 (68.3%)	Low urgency, n=695 (31.7%)	OR (95% CI)	Multivariable OR (95% CI)
SOB	832 (75.9%)	264 (24.1%)	**2.03 (1.69 to 2.44)**	**2.03 (1.69 to 2.44)***
No SOB	668 (60.8%)	431 (39.2%)		
Women	**High urgency, n=831 (68.4%)**	**Low urgency, n=384 (31.6%)**		
SOB	473 (76.7%)	144 (23.3%)	**2.20 (1.72 to 2.82)**	
No SOB	358 (59.9%)	240 (40.1%)		
Men	**High urgency, n=669 (68.3%)**	**Low urgency, n=311 (31.7%)**		
SOB	359 (74.9%)	120 (25.1%)	**1.84 (1.40 to 2.43)**	
No SOB	310 (61.9%)	191 (38.1%)		

*Multivariable analysis with sex.
OHS-PC, out-of-hours services for primary care; SOB, shortness of breath.

embolism. The remaining 96.6% had non-urgent diagnoses, for example, intercostal neuralgia, upper airways infection, anxiety and/or hyperventilation.

Among the 252 with ACS 55.9% of the women and 42.0% of the men had SOB.

Among the included 2195 callers, the entrance complaint 'chest pain' was most frequently chosen by triage nurses (in 75.5% of the cases). In 8.3% the entrance complaint 'shortness of breath' was chosen. Among the 252 with ACS, this was 82.5% ('chest pain') and 4.0% ('shortness of breath'), respectively.

Relation between presence of SOB and high urgency allocation

Callers with SOB more often received a high urgency than callers without SOB; 75.9% vs 60.8%, OR: 2.03; 95% CI 1.69 to 2.44, mOR: 2.03; 95% CI 1.69 to 2.44. This was similar for women (OR: 2.20; 95% CI 1.72 to 2.82) and men (OR: 1.84; 95% CI 1.40 to 2.43); value of p for interaction is 0.346. See table 2.

Relation between presence of SOB and the diagnosis of ACS

Those with and without SOB had a similar risk of ACS (10.9% vs 12.0%; OR: 0.90; 95% CI 0.69 to 1.17, mOR: 0.91; 95% CI 0.70 to 1.19); in women 9.2% vs 7.5%; OR: 1.25; 95% CI 0.83 to 1.88, in men 13.2% vs 17.4%; OR: 0.72; 95% CI 0.51 to 1.02. Value of p for interaction is 0.045. See table 3.

Relation between presence of SOB and the diagnosis of 'ACS or other LTE'

Fifteen per cent of those with SOB had an 'ACS or other LTE' compared with 14.1% in callers without SOB; OR: 1.07; 95% CI 0.85 to 1.36, mOR: 1.09; 95% CI 0.86 to 1.38. Among women with SOB, 13.0% had 'ACS or other LTE' compared with 8.5% in women without SOB (OR: 1.60; 95% CI 1.10 to 2.32). Among men with SOB, 17.5% had 'ACS or other LTE' compared with 20.8% in men without SOB (OR: 0.81; 95% CI 0.59 to 1.12). This was different for women and men; value of p for interaction is 0.007. See online supplemental table S2.

Relation between urgency allocation and diagnosis of 'ACS' and 'ACS or other LTE'

As shown in table 4, callers with ACS were more likely to receive a high urgency allocation than callers without ACS (88.5% vs 65.7%, p<0.001). This was the same for callers with (88.3% vs 74.4%, p=0.001) and without SOB (88.6% vs 57.0%, p<0.001). These effects were similar for women and men.

As shown in online supplemental table S3, those with an 'ACS or other LTE' had received more often a high urgency allocation than callers without an 'ACS or other LTE' (85.9% vs 65.4%, p<0.001). This was the same for callers with (87.2% vs 73.9%, p<0.001) and without (84.5% vs 56.9%, p<0.001) SOB. This was seen in all subgroups except for men with SOB; those with 'ACS or other LTE' did not receive a high urgency more often than those without 'ACS or other LTE' (82.1% vs 73.4%, p=0.094).

DISCUSSION

We assessed the relation between SOB and (1) Urgency allocation, (2) ACS and (3) 'ACS or other LTE' in callers who contacted the OHS-PC with chest discomfort. Both men and women with chest discomfort and SOB were more likely to receive a high urgency than callers without SOB. Regarding clinical outcomes, women with SOB compared with women without SOB tend to

Table 3 Association between SOB and final diagnosis ACS of 2195 callers with chest discomfort calling OHS-PC, divided by sex

Total calls	ACS n=252 (11.5%)	No ACS n=1943 (88.5%)	OR (95% CI)	Multivariable OR (95% CI)
SOB	120 (10.9)	976 (89.1)	0.90 (0.69 to 1.17)	0.91 (0.70 to 1.19)*
No SOB	132 (12.0)	967 (88.0)		
Women	**ACS n=102 (8.4%)**	**No ACS n=1113 (91.6%)**		
SOB	57 (9.2%)	560 (90.8%)	1.25 (0.83 to 1.88)	
No SOB	45 (7.5%)	553 (92.5%)		
Men	**ACS n=150 (15.3%)**	**No ACS n=830 (84.7%)**		
SOB	63 (13.2%)	416 (86.8%)	0.72 (0.51 to 1.02)	
No SOB	87 (17.4%)	414 (82.6%)		

*Multivariable analysis with sex.
ACS, acute coronary syndrome; OHS-PC, out-of-hours services for primary care; SOB, shortness of breath.

Table 4 Association between urgency allocation and final diagnosis of ACS of 2195 callers with chest discomfort calling OHS-PC, divided by those with SOB/'no SOB' and men/women

Total calls	Total	ACS n=252 (11.5%)	No ACS n=1943 (88.5%)	P value
	High urgency (U1–U2)	223 (88.5%)	1277 (65.7%)	<0.001*
	Low urgency (U3–U5)	29 (11.5%)	666 (34.3%)	
	SOB	ACS n=120 (10.9%)	No ACS n=976 (89.1%)	
	High urgency (U1–U2)	106 (88.3%)	726 (74.4%)	0.001*
	Low urgency (U3–U5)	14 (11.7%)	250 (25.6%)	
	No SOB	ACS n=132 (12.0%)	No ACS n=967 (88.0%)	
	High urgency (U1–U2)	117 (88.6%)	551 (57.0%)	<0.001*
	Low urgency (U3–U5)	15 (11.4%)	416 (43.0%)	
women	**Total**	**ACS n=102 (8.4%)**	**No ACS n=1,113 (91.6%)**	**P value**
	High urgency (U1–U2)	90 (88.2%)	741 (66.6%)	<0.001*
	Low urgency (U3–U5)	12 (11.8%)	372 (33.45)	
	SOB	ACS n=57 (9.2%)	No ACS n=560 (90.8%)	
	High urgency (U1–U2)	53 (93.0%)	420 (75.0%)	0.001*
	Low urgency (U3–U5)	4 (7.0%)	140 (25.0%)	
	No SOB	ACS n=45 (7.5%)	No ACS n=553 (92.5%)	
	High urgency (U1–U2)	37 (82.2%)	321 (58.0%)	0.001*
	Low urgency (U3–U5)	8 (17.8%)	232 (42.0%)	
men	**Total**	**ACS n=150 (15.3%)**	**No ACS n=830 (84.7%)**	**P value**
	High urgency (U1–U2)	133 (88.7%)	536 (64.6%)	<0.001*
	Low urgency (U3–U5)	17 (11.3%)	294 (35.4%)	
	SOB	ACS n=63 (13.2%)	No ACS n=416 (86.8%)	
	High urgency (U1–U2)	53 (84.1%)	306 (73.6%)	0.071*
	Low urgency (U3–U5)	10 (15.9%)	110 (26.4%)	
	No SOB	ACS n=87 (17.4%)	No ACS n=414 (82.6%)	
	High urgency (U1–U2)	80 (92.0%)	230 (55.6%)	<0.001*
	Low urgency (U3–U5)	7 (8.0%)	184 (44.4%)	

*P value for high versus low urgency.
ACS, acute coronary syndrome; OHS-PC, out-of-hours services for primary care; SOB, shortness of breath.

have an increased risk of ACS, which is significant for 'ACS or other LTE'. The difference between women and men regarding 'ACS' and 'ACS or other LTE' was significant. These findings suggest that if women with chest discomfort also mention SOB indeed more often, a high urgency should be considered than in women without SOB, while this differentiation is not useful in men.

Comparison to literature

Previous studies also reported that SOB in patients suspected of ACS was related with a worse outcome; that is, a fourfold higher quarterly and a twofold 1 year mortality.[6 25] This underlines the importance of paying special attention to women with chest discomfort and also SOB.

Previous studies also reported that SOB is a common symptom in patients with ACS.[5 8 26] In a German study 26.3% of the 5459 patients diagnosed with ACS at a chest pain unit reported SOB.[5] In an Indian study among 200 patients with acute myocardial infarction managed on the intensive cardiac care unit reported 28.5% SOB.[26] In an Irish study among 1947 patients with ACS admitted to the ED, 44.8% experienced SOB, women slightly more often than men (49.9% vs 42.9%, p=0.006).[8] In our study, SOB was mentioned similar to the last study; in 49.9% of the 2195 callers with chest discomfort (women 50.8%, men 48.9%, p=0.375), and in 47.6% of the 252 who had an ACS (women 55.9%, men 42.0%, p=0.030).

An important difference between our study and previous reports is that we assessed people who called OHS-PC, analysing both those with an ACS and without an ACS, which creates a different case mix than only assessing those seen at the ED with ACS or acute myocardial infarction.

Two previous studies also focused on the whole domain of patients suggestive of ACS.[9 27] The first study included 736 patients admitted to four US EDs. SOB was related to non-ACS (46% of patients with ACS had SOB vs 60% of patients without ACS (p<0.001)); men (41% vs 59%, p<0.001), women (58% vs 61%, p=0.754).[9] This is somewhat in contrast to our study.

The second study included 1064 patients who presented to the US ED with ACS-like symptoms, and again SOB was related to non-ACS (49.2% vs 61.7%, p=0.049).[27] Unfortunately, they did not present data separately for women and men.

Strengths and limitations

To our knowledge, this is the first study to assess the relation between SOB and (1) Urgency allocation, (2) ACS and (3) 'ACS or other LTE' in callers with chest discomfort in the OHS-PC. We were in the unique position to evaluate real-life recordings of the initial contact of callers with chest discomfort. The very first verbal symptom presentation was literally recorded, and these tape recordings were scored without knowledge of the final diagnosis, that is, without hindsight bias. Furthermore, this study includes a large population without strict exclusion criteria, resulting in a representative real-life study population. Finally, results are generalisable to callers with chest discomfort who call the OHS-PC.

As per routine practice, not all patients in our study sample were transferred to the hospital for further diagnostic assessment. This may have led to some cases having initially incorrectly received an alternative diagnosis than 'ACS or other LTE'. To reduce such misclassification as much possible, we collected data about the final diagnosis from the patient's primary care electronic health record up to 30 days after the index contact at the OHS-PC. As such, we expect that the number of 'missed' diagnoses, in particular those who are clinically relevant, is low.

Another limitation was that the clinical outcome was not available for all callers because 39.5% of GPs were not willing to share follow-up data. We could, however, show that patient and call characteristics did not differ between those with and without a final diagnosis based on follow-up information (data not shown). Thus, this selection did not cause selection bias, more so because the GPs' willingness to provide follow-up information seems not to be associated with the medical outcome of individual callers. Another limitation is that only in 77.4% of the triage calls patients were asked about presence/absence of SOB. This may have led to some misclassification; callers who had SOB but not reported it could have been labelled as not having SOB. Importantly, however, sensitivity analysis, selectively among those in whom the SOB status was known (yes or no), yielded similar point estimates but with broader CIs due to analysing a lower number of patients (online supplemental tables S4-S6). Finally, we had missing data for several variables which is inherent to use of routine care data. The triage nurse did not ask about all variables during the telephone triage.

CONCLUSIONS

Men and women with chest discomfort and SOB who contact the OHS-PC more often receive high urgency than those without SOB. This seems justified in women, as SOB increases the odds for having 'ACS or other LTE', but not in men when considering the risk of ACS or other LTEs. Therefore, triage nurses at the OHS-PC should always ask for SOB in female callers with acute chest discomfort as this helps triage given the substantial increase in risk of 'ACS or other LTE'.

In the Netherlands, we might therefore consider putting SOB as a gender-specific factor in the NTS system; asking about SOB in female callers with chest discomfort and not asking about SOB in male callers with chest discomfort.

Correction notice This article has been corrected since it was first published. Typos in the abstract and the results section have been corrected.

Twitter Hester M den Ruijter @InnovatieHester

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval Our study protocol has been reviewed by the Medical Ethics Committee (MREC) Utrecht (reference number WAG/mb/16/003208). The MREC concluded that this study is not within the scope of the Medical Research Involving Subjects Act (WMO) and granted an exemption for this study.We used a waiver for informed consent (this exception to the informed consent has been described in The Declaration of Helsinki and is further specified in the Council for International Organizations of Medical Sciences (CIOMS) guideline which contains a part about waiving informed consent.

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ORCID iDs
Michelle Spek http://orcid.org/0000-0002-5914-4231
Maarten van Smeden http://orcid.org/0000-0002-5529-1541
Loes T C M Wouters http://orcid.org/0000-0002-1525-9803
Hester M den Ruijter http://orcid.org/0000-0001-9762-014X

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Supplemental material

Appendix

Table S1. Baseline characteristics of 2,195 callers who called the OHS-PC with chest discomfort, divided in females and males.

	Total n=2,195	Females n=1,215 (55.4%)	Males n=980 (44.6%)	P-value
Patient characteristics				
Mean age in years (SD)	59.1 (19.5)	59.4 (20.2)	58.7 (18.6)	0.417
Call characteristics				
Call duration in min:sec (SD)	7:34 (3:48)	7:43 (3:53)	7:24 (3:41)	**0.047**
Someone else called on behalf of patient (n=2,171)*	1,093 (50.3%)	577 (47.8%)	516 (53.5%)	**0.009**
GP participated in triage (n=2,195)	1,148 (52.3%)	624 (51.4%)	524 (53.5%)	0.590
Medical history and use of cardiovascular medication				
Any cardiac disease (n=1,847)*	1,195 (64.7%)	624 (63.0%)	571 (66.7%)	0.094
Coronary artery disease (n=1,153)*	389 (33.7%)	154 (26.1%)	235 (41.7%)	**<0.001**
Cardiac arrhythmia (n=907)*	231 (25.5%)	130 (25.7%)	101 (25.2%)	0.862
Valvular disease (n=767)*	77 (10.0%)	44 (10.3%)	33 (9.7%)	0.784
Heart failure (n=764)*	62 (8.1%)	34 (8.0%)	28 (8.3%)	0.879
Cardiovascular medication use (n=1,618)*	856 (52.9%)	457 (51.1%)	399 (55.2%)	0.098
Cardiovascular risk factors				
Hypertension (n=894)*	323 (36.1%)	188 (36.7%)	135 (35.3%)	0.671
Hypercholesterolemia (n=825)*	212 (25.7%)	106 (23.6%)	106 (28.2%)	0.133
Diabetes mellitus (n= 905)*	180 (19.9%)	80 (16.2%)	100 (24.4%)	**0.002**
Family history of cardiovascular disease (n=293)*	212 (72.4%)	125 (78.1%)	87 (65.4%)	**0.015**
Symptoms mentioned during the call				
Shortness of breath (n=1,699)*	617 (65.8%)	479 (62.9%)	1,096 (64.5%)	0.201
Chest pain (n=2,118)*	1,982 (93.6%)	1,092 (93.4%)	890 (93.8%)	0.730

Autonomic nervous system related symptoms** (n=2,118)*	1,190 (56.2%)	691 (59.1%)	499 (52.6%)	**0.003**
Chest pain characteristics				
Pain onset <12 hours (n=1,919)*	1,404 (73.2%)	780 (73.3%)	624 (73.0%)	0.873
Pain duration >15 minutes (n=1,837)*	1763 (96.0%)	979 (96.2%)	784 (95.7%)	0.632
Radiation of pain (n=1,676)*	1,077 (64.2%)	648 (69.4%)	429 (57.8%)	**<0.001**
Severe pain (score >7 on VAS) (n=922)*	337 (36.6%)	203 (40.8%)	134 (31.6%)	**0.004**
Urgency allocation				
High (U1 or U2)	1,500 (68.3%)	831 (68.4%)	669 (68.3%)	0.948
Low (U3, U4 or U5)	695 (31.7%)	384 (31.6%)	311 (31.7%)	
Final diagnosis				
ACS	252 (11.5%)	102 (8.4%)	150 (15.3%)	**<0.001**
ACS or other LTE	319 (14.5%)	131 (10.8%)	188 (19.2%)	**<0.001**
Non-urgent disorders	1,876 (85.5%)	1,084 (89.2%)	792 (80.8%)	**<0.001**

* For these variables there were missing data, **Autonomic nervous system related symptoms consist of one or more of the following: nausea and/or vomiting, sweating, pallor/ashen skin, (near) collapse.

ACS: acute coronary syndrome, GP: general practitioner, LTE: life-threatening disease, OHS-PC: out-of-hours services for primary care, VAS: Visual Analogue Scale

Table S2. Association between SOB and final diagnosis 'ACS or other LTE' of 2,195 callers with chest discomfort calling OHS-PC, also divided by sex.

Total calls	**LTE n=319 (14.5%)**	**No LTE n=1,876 (85.5%)**	**OR (95% CI)**	**Multivariable OR (95% CI)**
SOB	164 (15.0%)	932 (85.0%)	1.07 (0.85-1.36)	1.09 (0.86-1.38)*
No SOB	155 (14.1%)	944 (85.9%)		
Females	**LTE n=131 (10.8%)**	**No LTE n=1,084 (89.2%)**		
SOB	80 (13.0%)	537 (87.0%)	**1.60 (1.10-2.32)**	
No SOB	51 (8.5%)	547 (91.5%)		
Males	**LTE n=188 (19.2%)**	**No LTE n=792 (80.8%)**		
SOB	84 (17.5%)	395 (82.5%)	0.81 (0.59-1.12)	
No SOB	104 (20.8%)	397 (79.2%)		
* Multivariable analysis with sex ACS: acute coronary syndrome, OHS-PC: out-of-hours services for primary care, SOB: shortness of breath				

Table S3. Association between urgency allocation and final diagnosis 'ACS or other LTE' of 2,195 callers with chest discomfort calling OHS-PC, divided by those with SOB/'no SOB' and males/females.

Total calls	**Total**	**LTE n=319 (14.5%)**	**No LTE n=1,876 (85.5%)**	**P-value**
	High urgency (U1-U2)	274 (85.9%)	1,226 (65.4%)	**<0.001***
	Low urgency (U3-U5)	45 (14.1%)	650 (34.6%)	
	SOB	**LTE n=164 (15.0%)**	**No LTE n=932 (85.0%)**	
	High urgency (U1-U2)	143 (87.2%)	689 (73.9%)	**<0.001***
	Low urgency (U3-U5)	21 (12.8%)	243 (26.1%)	
	No SOB	**LTE n=155 (14.1%)**	**No LTE n=944 (85.9%)**	
	High urgency (U1-U2)	131 (84.5%)	537 (56.9%)	**<0.001***
	Low urgency (U3-U5)	24 (15.5%)	407 (43.1%)	
Females	**Total**	**LTE n=131 (10.8%)**	**No LTE n=1,084 (89.2%)**	**P-value**
	High urgency (U1-U2)	114 (87.0%)	717 (66.1%)	**<0.001***
	Low urgency (U3-U5)	17 (13.0%)	367 (33.9%)	
	SOB	**LTE**	**No LTE**	

		n=80 (13.0%)	**n=537 (87.0%)**	
	High urgency (U1-U2)	74 (92.5%)	399 (74.3%)	**<0.001***
	Low urgency (U3-U5)	6 (7.5%)	138 (25.7%)	
	No SOB	**LTE n=51 (8.5%)**	**No LTE n=547 (91.5%)**	
	High urgency (U1-U2)	40 (78.4%)	318 (58.1%)	**0.005***
	Low urgency (U3-U5)	11 (21.6%)	229 (41.9%)	
Males	**Total**	**LTE n=188 (19.2%)**	**No LTE n=792 (80.8%)**	**P-value**
	High urgency (U1-U2)	160 (85.1%)	509 (64.3%)	**<0.001***
	Low urgency (U3-U5)	28 (14.9%)	283 (35.7%)	
	SOB	**LTE n=84 (18.5%)**	**No LTE n=395 (82.5%)**	
	High urgency (U1-U2)	69 (82.1%)	290 (73.4%)	0.094*
	Low urgency (U3-U5)	15 (17.9%)	105 (26.6%)	
	No SOB	**LTE n=104 (20.9%)**	**No LTE n=397 (79.2%)**	
	High urgency (U1-U2)	91 (87.%)	219 (55.2%)	**<0.001***
	Low urgency	13 (12.5%)	178 (44.8%)	

	(U3-U5)			

* P-value for high vs. low urgency; ACS: acute coronary syndrome, OHS-PC: out-of-hours services for primary care, SOB: shortness of breath

Tables sensitivity analysis

Table S4. Association between SOB and urgency allocation of 1,699 callers with acute chest discomfort who called the OHS-PC, divided by sex.

Total calls	**High urgency n=1,177 (69.3%)**	**Low urgency n=522 (30.7%)**	**OR (95% CI)**	**Multivariable OR (95% CI)**
SOB	832 (75.9%)	264 (24.1%)	**2.36 (1.91-2.92)**	**2.35 (1.90-2.91)**
No SOB	345 (57.2%)	258 (42.8%)		
Females	**High urgency n=660 (70.4%)**	**Low urgency n=277 (29.6%)**		
SOB	473 (76.7%)	144 (23.3%)	**2.34 (1.75-3.12)**	
No SOB	187 (58.4%)	133 (41.6%)		
Males	**High urgency n=517 (67.8%)**	**Low urgency n=245 (32.2%)**		
SOB	359 (74.9%)	120 (25.1%)	**2.37 (1.73-3.24)**	
No SOB	158 (55.8%)	125 (44.2%)		
* Multivariable analysis with sex OHS-PC: out-of-hours services for primary care **p-value for interaction term (gender*SOB) = 0.952**				

Table S5. Association between SOB and final diagnosis ACS of 1,699 callers with chest discomfort calling OHS-PC, also divided by sex.

Total calls	**ACS n=184 (10.8%)**	**No ACS n=1,515 (89.2%)**	**OR (95% CI)**	**Multivariable OR (95% CI)**
SOB	120 (10.9%)	976 (89.1%)	1.04 (0.75-1.43)	1.05 (0.76-1.45)
No SOB	64 (10.6%)	539 (89.4%)		
Females	**ACS n=81 (8.6%)**	**No ACS n=856 (91.4%)**		
SOB	57 (9.2%)	560 (90.8%)	1.26 (0.76-2.06)	
No SOB	24 (7.5%)	296 (92.5%)		
Males	**ACS n=103 (13.5%)**	**No ACS n=659 (86.5%)**		
SOB	63 (13.2%)	416 (86.8%)	0.92 (0.60-1.41)	
No SOB	40 (14.1%)	243 (85.9%)		
* Multivariable analysis with sex ACS: acute coronary syndrome, OHS-PC: out-of-hours services for primary care, SOB: shortness of breath **p-value for interaction term (gender*SOB) = 0.353**				

Table S6. Association between SOB and final diagnosis 'ACS or other LTE' of 1,699 callers with chest discomfort calling OHS-PC, also divided by sex.

Total calls	**LTE n=239 (14.1%)**	**No LTE n=1,460 (85.9%)**	**OR (95% CI)**	**Multivariable OR (95% CI)**
SOB	164 (15.0%)	932 (85.0%)	1.24 (0.92-1.66)	1.26 (0.94-1.70)
No SOB	75 (12.4%)	528 (87.6%)		
Females	**LTE n=105 (11.2%)**	**No LTE n=832 (88.8%)**		
SOB	80 (13.0%)	537 (87.0%)	**1.76 (1.10-2.82)**	
No SOB	25 (7.8%)	295 (92.2%)		
Males	**LTE n=134 (17.6%)**	**No LTE n=628 (82.4%)**		
SOB	84 (17.5%)	395 (82.5%)	0.99 (0.67-1.46)	
No SOB	50 (17.7%)	233 (82.3%)		
* Multivariable analysis with sex ACS: acute coronary syndrome, OHS-PC: out-of-hours services for primary care, SOB: shortness of breath **p-value for interaction term (gender*SOB) = 0.065**				