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Diabetes and risk of acute coronary syndrome in callers with chest discomfort: Cross-sectional study in out-of-hours primary care

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ABSTRACT

Aims: We investigated the differences in prevalence of acute coronary syndrome (ACS) by presence versus absence of diabetes in males and females with chest discomfort who called out-of-hours primary care (OHS-PC).
Methods: A cross-sectional study performed in the Netherlands. Patients who called the OHS-PC in the Utrecht region, the Netherlands between 2014 and 2017 with acute chest discomfort were included.
We compared those with diabetes with those without diabetes. Multivariable logistic regression was used to determine the relation between diabetes and (i) high urgency allocation and (ii) ACS.
Results: Of the 2,195 callers with acute chest discomfort, 180 (8.2%) reported having diabetes. ACS was present in 15.3% of males (22.0% in those with diabetes) and 8.4% of females (18.8% in those with diabetes). Callers with diabetes did not receive a high urgency more frequently (74.4% vs. 67.8% (OR: 1.38; 95% CI 0.98–1.96). However, such callers had a higher odds for ACS (OR: 2.17; 95% CI 1.47–3.19). These differences were similar for females and males.
Conclusions: Diabetes holds promise as diagnostic factor in callers to OHS-PC with chest discomfort. It might help triage in this setting given the increased risk of ACS in those with diabetes.

1. Introduction

At out-of-hours primary care (OHS-PC), triage nurses are supported by a semi-automatic decision support tool, which is in the Netherlands the 'Netherlands Triage Standard' (NTS), to assist them in the complex process of telephone triage [1–3]. The triage nurse can choose out of 56 entrance complaints in the NTS system, one being 'chest pain'. The NTS system displays hierarchically ordered triage questions, on average five, for considering severity and thus urgency allocation which is a response time that ranges from U1 to U5. U1 (immediate ambulance deployment), U2 (as soon as possible, within 1 h), U3 (within 3 h), U4 (within 24 h), U5 (telephone advice) [1,3–5]. In the module 'chest pain', the question about a presence or absence of diabetes is low in hierarchy and is often not asked for because questions associated with low urgency do not show up in the NTS if it is clear from previous answers that this patient requires a high urgency.

Based on the urgency assessment of the NTS and including eventual overruling by triage nurses or supervising general practitioners (GPs), 14 % of patients with an 'acute coronary syndrome (ACS) or other life-threatening event (LTE)' received a too low urgency level (U3-U5) and these patients may be considered as under-triaged [1–3,6,7]. However, there also is evidence of overtriage: 66 % of those who received a high urgency level (U1 or U2) had *no* 'ACS or other LTE' [7].

Chest discomfort can manifest itself in diverse ways and there are multiple underlying causes ranging from life-threatening to rather harmless [8]. It is, nevertheless, important to consider an ACS in patients with chest discomfort. It has been suggested that females, elderly and those with diabetes present with a broad variety of symptoms [9,10].

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Patients with diabetes have a higher risk of ACS and other vascular events, but may experience less sensation of chest pain due to affected afferent nerves caused by neuropathy [11]. Furthermore, they may attribute autonomous nervous system (ANS) related symptoms, e.g., sweating as caused by either hypo- or hyperglycaemia, and thus misinterpreting these symptoms [12]. However, previous studies showed conflicting results regarding symptom presentation in patients with diabetes [9,13–15].

Thus, because symptoms of ACS in callers with diabetes may be ambiguous, or at least may be misinterpreted by either themselves or the triage nurse with the risk of under-triage, and thus delayed diagnosis [4,16]. Importantly, in general (including patients with diabetes), those who present with less specific symptoms seem to have less favourable outcomes and higher in-hospital mortality [16,17].

The aims of this study were, therefore, to assess whether diabetes was associated with high urgency allocation (U1 or U2) and its potential as diagnostic factor for ACS and 'ACS or other LTE' in males and females who call the OHS-PC with acute chest discomfort. If the presence of diabetes is a diagnostic factor of ACS or 'ACS or other LTE', asking for diabetes should possibly be given a higher priority in the triage system. Ultimately, this will improve the triage of callers to OHS-PC with chest discomfort. To this end, we examined the relation between diabetes and (i) urgency allocation, (ii) ACS and (iii) composite of ACS and other LTEs, in callers who called the OHS-PC with chest discomfort.

2. Materials and methods

A cross-sectional study, which is part of the Safety First study. The study design and data collection of the Safety First study was described in detail previously [18].

2.1. Participants

Callers were included if they called one of the participating OHS-PC centres in the vicinity of Utrecht, the Netherlands, between 2014 and 2017, with symptoms suggestive of ACS [19]. The selection of recordings was based on the International Classification of Primary Care (ICPC) codes (*K*01, K02, K03, K24, K74, K75, K76, K77, K93, L04, P74, R02, R98) and a selection of keywords (thoracic pain, chest pain, myocardial infarction, heart attack and their common abbreviations) used in the electronic patient record of the OHC-PC to ensure that all callers suspected of having ACS, and not solely those with chest pain, were selected [20]. From a total number of approximately 20,000 conversations eligible for inclusion, a random sample of more than 2,000 conversations were included. Reasons for exclusion were (1) callers younger than 18 years, (2) callers who did not live in the vicinity of OHS-PC, (3) the patient's GP refused to provide information about the clinical outcome, (4) no actual triage conversation (e.g., consultation between triage nurse and ambulance) and (5) poor sound quality of recordings.

2.2. Data collection

Data were collected from both the OHS-PC and general practices. Patient characteristics (age as continuous variable and gender as male or female), call characteristics (call duration in minutes as continuous variable, whether someone else called on behalf of patient and whether the GP participated in the triage process, yes versus no), medical history (any cardiac diseases yes versus no and specified into coronary artery disease, cardiac arrhythmia, valvular disease and heart failure, yes versus no), cardiovascular medication use (any medication yes versus no), cardiovascular risk factors (hypertension, hypercholesterolemia and family history of cardiovascular disease, yes versus no), symptoms mentioned during the call (chest pain, autonomous nervous system related symptoms and shortness of breath, yes versus no) and chest pain characteristics (pain onset within 12 h, pain duration more than 15 min, radiation of pain and severe pain, yes versus no) were collected by listening to the original call recordings and scrutinizing the data in the OHS-PC electronic patient record. The final diagnosis was ascertained through follow-up information from the patient's GP, including hospital specialist letters. The International Code for Primary Care (ICPC) coding was used for clinical diagnoses and the international ATC-coding for the drug prescriptions. For the main analyses, callers were classified as diabetes if they verbally confirmed that they have diabetes (spontaneously or after a question from the triage nurse). Callers were classified as having 'no diabetes' when diabetes was not discussed during the call or if they explicitly conformed that they did not have diabetes. We also performed a sensitivity analysis selectively in 905 callers who explicitly indicated that they did or did not have diabetes. Results are shown in the appendix.

2.3. Data analyses

Patient and call characteristics, medical history and cardiovascular medication use, cardiovascular risk factors, symptoms mentioned during the call and chest pain characteristics were compared between callers with and without diabetes using the Pearson's chi-square test or Fisher's exact test (in case of groups with less than 10 people) for categorical variables and the independent sample T-test for continuous variables. Entrance complaints were compared between those with and without diabetes and between the same groups in those with ACS. The urgency allocation was stratified into high (U1 or U2) and low (U3, U4 or U5) levels [4]. Multivariable logistic regression was used to analyse the relation between diabetes and the final urgency allocation (the NTS generated urgency considering overruling by the triage nurse or supervising GP), between diabetes and ACS, and between diabetes and 'ACS or other LTE' (ACS and other life-threatening diagnoses including a dissection of the thoracic aorta, acute heart failure, and pulmonary embolism). By adding sex to the models, we calculated multivariable odds ratios (mORs). Finally, we added an interaction term between diabetes and sex to the model to assess whether the associations were different in males and females. A p-value below 0.05 was considered statistically significant.

All data analyses were performed using SPSS statistics 26.0.

3. Results

The study included 2,195 triage calls of callers with acute chest discomfort. The mean age of these callers was 59.1 (SD: 19.5) years and 55.4 % were female. In total, 252 (11.5 %) callers (15.3 % of the males, 8.4 % of the females) who called with acute chest discomfort had an ACS; 29.0 % an ST-elevation myocardial infarction, 40.9 % a non-ST-elevation myocardial infarction, 23.4 % unstable angina pectoris and 6.7 % unclassified ACS. Another 67 callers (3.0 %) had another LTE. The remaining 1,876 callers (85.5 %) had a non-urgent disorder, e.g., musculoskeletal complaints, anxiety and/or hyperventilation.

Triage nurses requested 905 (41.2 %) callers for information about presence or absence of diabetes, of whom 180 (8.2 % of the total population) verbally confirmed they had diabetes and of whom 725 explicitly confirmed during the call that they did not have diabetes. In the remaining 1,290 (58.8 %) contacts diabetes was not discussed during the call.

Baseline characteristics of callers with diabetes and 'no diabetes' are shown in Table 1. Callers with diabetes were on average 9.1 years older (67.5 vs. 58.4 years, $p < 0.001$), more often male (55.6 % vs. 43.7 %, $p = 0.002$), and more often someone else called the OHS-PC for them (69.9 % vs. 48.6 %, $p < 0.001$) compared to those without diabetes. In addition, callers with diabetes had more often a history of heart disease, both acute events and chronic progressive heart diseases (90.3 % vs. 62.2 %, $p < 0.001$); coronary artery disease (45.8 % vs. 32.9 %, $p = 0.025$), cardiac arrhythmias (46.2 % vs. 24.2 %, $p < 0.001$), valvular disease (32.6 % vs. 8.7 %, $p < 0.001$) and heart failure (38.8 % vs. 6.0 %, $p < 0.001$). They also had more often cardiovascular risk factors:

Table 1
Baseline characteristics of 2,195 patients with acute chest discomfort who called the OHS-PC, divided in those with diabetes and 'no diabetes'.

	Total n = 2,195	Diabetes n = 180 (8.2 %)	'No diabetes' n = 2,015 (91.8 %)	P-value
Patient characteristics				
Mean age (SD)	59.1 (19.5)	67.5 (15.1)	58.4 (19.7)	**<0.001**
Male sex (n = 2,195)	980 (44.6 %)	100 (55.6 %)	880 (43.7 %)	**0.002**
Call characteristics				
Call duration in min:sec (SD)	7:34 (3:48)	8:55 (3:45)	7:27 (3:47)	**<0.001**
Someone else called on behalf of patient (n = 2,171)*	1,093 (50.3 %)	123 (69.5 %)	970 (48.6 %)	**<0.001**
GP participated in triage (in consultation or taking over the call) (n = 2,195)	1148 (52.3 %)	98 (54.4 %)	1050 (52.1 %)	0.548
Medical history and use of cardiovascular medication				
Any cardiac disease (n = 1,847)*	1,195 (64.7 %)	149 (90.3 %)	1,046 (62.2 %)	**<0.001**
Coronary artery disease (n = 1,153)*	389 (33.7 %)	33 (45.8 %)	356 (32.9 %)	**0.025**
Cardiac arrhythmia (n = 907)*	231 (25.5 %)	24 (46.2 %)	207 (24.2 %)	**<0.001**
Valvular disease (n = 767)*	77 (10.0 %)	14 (32.6 %)	63 (8.7 %)	**<0.001**
Heart failure (n = 764)*	62 (8.1 %)	19 (38.8 %)	43 (6.0 %)	**<0.001**
Cardiovascular medication use (n = 1,618)*	856 (52.9 %)	116 (87.9 %)	740 (49.8 %)	**<0.001**
Cardiovascular risk factors				
Hypertension (n = 894)*	323 (36.1 %)	58 (81.7 %)	265 (32.2 %)	**<0.001**
Hypercholesterolemia (n = 825)*	212 (25.7 %)	43 (75.4 %)	169 (22.0 %)	**<0.001**
Family history of cardiovascular disease (n = 293)*	212 (72.4 %)	13 (81.3 %)	199 (71.8 %)	0.413
Symptoms mentioned during the call				
Chest pain (n = 2,118)*	1,982 (93.6 %)	149 (88.2 %)	1,833 (94.0 %)	**0.003**
Autonomous nervous system related symptoms** (n = 2,118)*	1,190 (56.2 %)	99 (57.8 %)	1,091 (56.0 %)	0.638
Shortness of breath (n = 1,699)*	1,096 (64.5 %)	110 (75.3 %)	986 (63.5 %)	**0.004**
Chest pain characteristics				
Pain onset < 12 h (n = 1,919)*	1,404 (73.2 %)	117 (78.5 %)	1,287 (72.7 %)	0.124
Pain duration > 15 min (n = 1,837)*	1763 (96.0 %)	140 (97.9 %)	1,623 (95.8 %)	0.221
Radiation of pain (n = 1,676)*	1,077 (64.2 %)	80 (65.0 %)	997 (64.2 %)	0.851
Severe pain (score > 7 on VAS) (n = 922)*	337 (36.6 %)	29 (50.0 %)	308 (35.6 %)	**0.028**
Urgency allocation				
High (U1 or U2)	1,500 (68.3 %)	134 (74.4 %)	1,366 (67.8 %)	0.066
Low (U3, U4 or U5)	695 (31.7 %)	45 (25.6 %)	649 (32.2 %)	
Final diagnosis				
ACS	252 (11.5 %)	37 (20.6 %)	215 (10.7 %)	**<0.001**
ACS or other LTE	319 (14.5 %)	41 (22.8 %)	278 (13.8 %)	**0.001**
Non-urgent disorders	1,876 (85.5 %)	139 (77.2 %)	1737 (86.2 %)	**0.001**

Note: * For these variables there were missing data, **Autonomous 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.

hypertension (81.7 % vs. 32.2 %, p < 0.001), hypercholesterolemia (75.4 % vs. 22.0 %, p < 0.001), and they were more often prescribed cardiovascular medication (87.9 % vs. 49.8 %, p < 0.001) than those without diabetes.

Regarding symptoms, callers with diabetes mentioned less frequent chest pain (88.2 % vs. 94.0 %, p = 0.003), but more frequent shortness of breath (75.3 % vs. 63.5 %, p = 0.004) than those without diabetes.

Among the included 2,195 callers, the entrance complaint 'chest pain' was most frequently chosen by triage nurses; in 75.5 % of the cases, followed by the entrance complaint 'shortness of breath' with 8.3 %. In callers with diabetes, the entrance complaint 'shortness of breath' was chosen more often than in callers without diabetes (16.1 % vs. 7.6 %, p < 0.001), while the entrance complaint 'chest pain' was chosen less often in callers with diabetes (65.0 % vs. 76.5 %, p < 0.001). Among the 252 callers who appeared to have an ACS, the entrance complaint 'chest pain' was chosen by the triage nurse in 82.5 % of the callers, followed by 'shortness of breath' in 4.0 %. Also, among the 35 callers with ACS and diabetes, the entrance complaint 'chest pain' was chosen non-significantly less often than in 209 ACS callers without diabetes (78.4 % vs. 83.3 %, p = 0.066), while 'shortness of breath' was chosen more often (10.8 % vs. 2.8 %, p = 0.066).

Callers with diabetes who called with chest discomfort did not receive a high urgency more often than those without diabetes (74.4 % vs. 67.8 % (OR: 1.38; 95 % CI 0.98–1.96, mOR: 1.39; 95 % CI 0.98–1.97), which was similar for females (OR: 1.52; 95 % CI 0.90–2.59) and males (OR: 1.29; 95 % CI 0.81–2.05) (p-value interaction term = 0.643) (Table 2).

In callers with diabetes, 20.6 % had an ACS compared to 10.7 % of the callers without diabetes (OR: 2.17; 95 % CI 1.47–3.19, mOR: 2.03; 95 % CI 1.37–3.00). Among females with diabetes, 18.8 % had an ACS compared to 7.7 % in females without diabetes (OR: 2.78; 95 % CI 1.52–5.08). Among males with diabetes, 22.0 % had an ACS compared to 14.5 % in males without diabetes (OR: 1.66; 95 % CI 1.00–2.76). We found no evidence of a difference between males and females (p-value interaction term = 0.199; Table 3).

In callers with diabetes, 22.8 % had 'ACS or other LTE' compared to 13.8 % of the callers without diabetes (OR: 1.84; 95 % CI 1.27–2.67, mOR: 1.72; 95 % CI 1.18–2.50). Among females with diabetes, 20.0 % had an 'ACS or other LTE' compared to 10.1 % in females without diabetes (OR: 2.22; 95 % CI 1.24–3.96). Among males with diabetes, 25.0 % had an 'ACS or other LTE' compared to 18.5 % in males without diabetes

Table 2
Association between diabetes and urgency determination of 2,195 patients with acute chest discomfort who called the OHS-PC, divided by sex.

Total calls	High urgency n = 1,500 (68.3 %)	Low urgency n = 695 (31.7 %)	OR (95 % CI)	Multivariable OR (95 % CI)
Diabetes	134 (74.4 %)	46 (25.6 %)	1.38 (0.98–1.96)	1.39 (0.98–1.97)*
No diabetes	1366 (67.8 %)	649 (32.2 %)		
Females	**High urgency n = 831 (68.4 %)**	**Low urgency n = 384 (31.6 %)**		
Diabetes	61 (76.3 %)	19 (23.7 %)	1.52 (0.90–2.59)	
No diabetes	770 (67.8 %)	365 (32.2 %)		
Males	**High urgency n = 669 (68.3 %)**	**Low urgency n = 311 (31.7 %)**		
Diabetes	73 (73.0 %)	27 (27.0 %)	1.29 (0.81–2.05)	
No diabetes	596 (67.7 %)	284 (32.3 %)		

Note: *Multivariable analysis with sex.
OHS-PC: out-of-hours services for primary care.

Table 3
Association between diabetes and final diagnosis ACS of 2,195 patients with acute chest discomfort who called the OHS-PC, divided by sex.

Total calls	ACS n = 252 (11.5 %)	No ACS n = 1,943 (88.5 %)	OR (95 % CI)	Multivariable OR (95 % CI)
Diabetes	37 (20.6 %)	143 (79.4 %)	**2.17 (1.47–3.19)**	**2.03 (1.37–3.00)***
No diabetes	215 (10.7 %)	1800 (89.3 %)		
Females	**ACS n = 102 (8.4 %)**	**No ACS n = 1,113 (91.6 %)**		
Diabetes	15 (18.8 %)	65 (81.2 %)	**2.78 (1.52–5.08)**	
No diabetes	87 (7.7 %)	1048 (92.3 %)		
Males	**ACS n = 150 (15.3 %)**	**No ACS n = 830 (84.7 %)**		
Diabetes	22 (22.0 %)	78 (78.0 %)	1.66 (1.00–2.76)	
No diabetes	128 (14.5 %)	752 (85.5 %)		

Note: * Multivariable analysis with sex.
ACS: acute coronary syndrome.
OHS-PC: out-of-hours services for primary care.

(OR: 1.47; 95 % CI 0.90–2.38). We found no evidence of a difference between males and females (p-value interaction term = 0.283; Table S1).

Callers with ACS received more often a high urgency than callers without ACS (88.5 % vs. 65.8 %, $p < 0.001$; Table 4). This was also seen in the subgroup without diabetes (89.3 % vs. 65.2 %, $p < 0.001$). However, this difference in receiving high urgency in those with and without ACS was not statistically significant in those with diabetes (83.8 % vs. 72.0 %, $p = 0.204$). These findings were similar for females and males.

Callers with 'ACS or other LTE' received more often a high urgency than callers without (85.9 % vs. 65.4 %, $p < 0.001$; Table S2). This was also seen in the subgroup without diabetes (87.1 % vs. 64.7 %, $p < 0.001$). However, this difference in receiving high urgency in those with and without 'ACS or other LTE' was not statistically significant in those with diabetes (78.0 % vs. 73.4 %, $p = 0.684$). These differences were similar for females and males.

4. Discussion

4.1. Summary

ACS was present in 15.3 % of males (22.0 % in those with diabetes) and 8.4 % of females (18.8 % in those with diabetes). Chest pain was mentioned less frequently and shortness of breath more frequently in callers with diabetes than in those without. We found no strong evidence that callers with diabetes were more likely to receive a high urgency. However, such callers had a higher odds for ACS or 'ACS or other LTE'. Especially in females, the probability of having an ACS rises significantly if they have diabetes; the prior probability of having an ACS in female callers is 8.4 % and this rises to 18.8 % if they have diabetes.

4.2. Strengths and limitations

To the best of our knowledge, this is the first study to assess the relation between diabetes and the assignment of urgency in callers who called the OHS-PC setting with symptoms suggestive for ACS, separately for males and females. An important strength was that we could evaluate the original telephone triage calls blinded to the outcome, minimizing the risk of hindsight bias. Because the data were derived from nine OHS-PC centres, including both urban and rural areas, our results are generalizable to the whole of the Netherlands, but probably also to other countries with similar primary care settings.

A limitation is that only 41.2 % of callers were checked for presence or absence of diabetes. This could have diluted the effects as suggested by our sensitivity analysis (Tables S3-S5); likely some callers with diabetes have been labelled as 'no diabetes'. This because the point estimates in the sensitivity analysis are even higher than in the original analyses, implying that diabetes may be an even more important diagnostic factor for ACS and 'ACS or other LTE' than was already thought based on the original analyses. We limited our analyses to those in whom the final diagnostic result could be determined from the patient's primary care physician. In 39.5 %, GPs refused to provide this information. However, patient and call characteristics generally did not differ between those with and without a final diagnosis based on follow-up information. Moreover, GPs' willingness to provide follow-up information seems not to be associated with the outcome ACS in individual callers.

4.3. Comparison with existing literature

Among callers to the OHS-PC with chest discomfort, 8.2 % of callers over 18 years mentioned to have diabetes, which is slightly higher than the prevalence of diabetes in the Netherlands, which is 6.7 % according to the national GP registries and 4.9 % based on patient-reports [21]. The prevalence of diabetes (19.9 %) was substantially higher among the 905 callers in whom presence/absence of diabetes was explicitly asked

Table 4
Association between urgency allocation and final diagnosis ACS of 2,195 patient with chest discomfort calling OHS-PC, divided by those with diabetes/'no diabetes' and males/females.

Total calls	Total	ACS n = 252 (11.5 %)	No ACS n = 1,943 (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 %)	
	Diabetes	**ACS n = 37 (20.6 %)**	**No ACS n = 143 (79.4 %)**	
	High urgency (U1-U2)	31 (83.8 %)	103 (72.0 %)	0.204*
	Low urgency (U3-U5)	6 (16.2 %)	40 (28.0 %)	
	No diabetes	**ACS n = 215 (10.7 %)**	**No ACS n = 1,799 (89.3 %)**	
	High urgency (U1-U2)	192 (89.3 %)	1174 (65.2 %)	**<0.001***
	Low urgency (U3-U5)	23 (10.7 %)	626 (34.8 %)	
Females	**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)	
	Diabetes	**ACS n = 15 (18.8 %)**	**No ACS n = 65 (81.2 %)**	
	High urgency (U1-U2)	12 (80.0 %)	49 (75.4 %)	1.000*
	Low urgency (U3-U5)	3 (20.0 %)	16 (24.6 %)	
	No diabetes	**ACS n = 87 (7.7 %)**	**No ACS n = 1,048 (92.3 %)**	
	High urgency (U1-U2)	78 (89.7 %)	692 (66.0 %)	**<0.001** *
	Low urgency (U3-U5)	9 (10.3 %)	356 (34.0 %)	
Males	**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 %)	
	Diabetes	**ACS n = 22 (22.0 %)**	**No ACS n = 78 (78.0 %)**	
	High urgency (U1-U2)	19 (86.4 %)	54 (69.2 %)	0.173*
	Low urgency (U3-U5)	3 (13.6 %)	24 (30.8 %)	
	No diabetes	**ACS n = 128 (14.5 %)**	**No ACS n = 752 (85.5 %)**	
	High urgency (U1-U2)	114 (89.1 %)	482 (64.1 %)	**<0.001***
	Low urgency (U3-U5)	14 (10.9 %)	270 (35.9 %)	

*Note: P-value for high vs. low urgency.
ACS: acute coronary syndrome.
OHS-PC: out-of-hours services for primary care.

for. This suggests that patients with diabetes more often contact the OHS-PC for chest discomfort than patients without diabetes.

Our findings are in line with previous studies in the emergency department (ED) that reported a higher incidence of ACS in patients with diabetes [22,23]. One of these studies reported an incidence of myocardial infarction of 0.54 % in patients with type 2 diabetes compared with 0.16 % in patients without type 2 diabetes for the study period 2016–2018 [22]. The relative risks for an acute myocardial infarction (AMI) was higher for females than males with diabetes compared to those without diabetes. In our study, we did not found evidence for sex differences in AMI. In our study the prevalence of AMI (ST-elevation myocardial infarction and non-ST-elevation myocardial infarction) was 12.2 % in those with diabetes and 7.6 % in those without diabetes.

A systematic review reported a relative risk for coronary heart diseases, including both chronic coronary syndrome as well as ACS, in patients with diabetes compared to those without diabetes of 2.82; 95 % CI: 2.35–3.38 in females and 2.16; 95 % CI 1.82–2.56 in males [23]. Another study of visitors to GP practices also showed a higher risk of coronary heart diseases in those with diabetes compared to those without diabetes with an OR of 1.3; 95 % CI 1.2–1.4 [24]. However, sex differences were not analysed in this study.

In a previous study of 694 patients hospitalized for acute myocardial infarction in Sweden, shortness of breath was more common in patients with diabetes compared to those without diabetes [15]. This is in line with our study in which callers with diabetes relatively more often reported shortness of breath (75.3 % vs. 63.5 %), and less often chest pain (88.2 % vs. 94.0 %) than those without diabetes. Nevertheless, chest pain is the most common symptom, and many clinicians consider shortness of breath as such. Interestingly, in our study callers with diabetes who experienced acute chest pain reported more often severe pain (>7 on a scale of 0–10) than those without diabetes.

Previous studies reported more pre-hospital delay in patients with diabetes with ACS than in those with ACS without diabetes [12–15]. We did not record the time to call or the time from call to hospitalization, only 'before or after 12 h of symptom onset', but we could not detect a significant difference in percentage of callers with or without diabetes seen within 12 h of symptom onset.

4.4. Implications for research and/or practice

Diabetes increases the risk of ACS and 'ACS or other LTE' in callers to OHS-PC with chest discomfort. Thus, diabetes holds promise as diagnostic factor in this setting and might help triage. Validation in other healthcare settings than Dutch OHS-PC is needed before diabetes can be used in those primary care settings for triage of patients with chest discomfort.

Data sharing statement

The data can be made available for researchers whose proposed use of the data has been approved at request of the corresponding author, with a signed data access agreement.

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Ethical approval

The medical Ethics Committee Utrecht, the Netherlands approved this study (reference number WAG/mb/16/003208 and National Trial Register identification number: NTR7331). Personal data and research data was de-identified according to the European General Data Protection Regulation. 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 CIOMS guideline which contains a part about waiving informed consent).

CRediT authorship contribution statement

Michelle Spek: Writing – original draft, Investigation, Formal analysis. **Daphne C.A. Erkelens:** Writing – review & editing, Supervision, Data curation. **Coralie van het Goor – van Wezep:** Writing – original draft, Investigation, Formal analysis. **Maarten van Smeden:** Writing – review & editing, Supervision. **Hester M. Den Ruijter:** Writing – review & editing, Supervision. **Loes T.C.M. Wouters:** Data curation. **Roderick P. Venekamp:** Writing – review & editing, Supervision. **Frans H. Rutten:** Writing – review & editing, Supervision. **Dorien L. Zwart:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2024.111684.

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