

## Cardiac symptoms and yield of diagnostic tests among primary care patients with and without diabetes

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### ABSTRACT

**Aims:** To compare the symptoms, diagnostic tests used, and clinical diagnoses made among diabetic and non-diabetic patients.

**Methods:** This is a register-based study of 704 primary care patients referred electively to cardiology specialists in the city of Turku, Finland, during the year 2016. The patient's medical history, cardiovascular medication use, risk factors, cardiac symptoms, diagnostic tests applied, and diagnoses made were gathered from the medical records. The angiography data was derived from the Hospital District of Southwest Finland data pool.

**Results:** Of the cohort, 120 (17 %) patients had diabetes mellitus. They were on average older (67 vs. 63 years,  $p = 0.009$ ) and more often females (62 % vs. 38 %,  $p = 0.042$ ) than the non-diabetic patients. Chest pain or discomfort was the most prevalent symptom in the diabetic patients and a sense of arrhythmia in the non-diabetic subjects. Ischemic heart disease was diagnosed more often in the person with diabetes (15 %) than in the non-diabetic (6 %) patients ( $p = 0.004$ ). Cardiac arrhythmias were diagnosed in 26 % of the non-diabetic and 20 % of the diabetic subjects ( $p = 0.021$ ).

**Conclusions:** Symptoms that might indicate heart disease, especially chest pain/discomfort, are common in both the diabetic and the non-diabetic patients in primary care. Several diagnostic tests are applied, possibly not to miss a life-threatening disease. However, many patients do not get a specific diagnosis for their concerns.

### 1. Introduction

Coronary artery disease (CAD) is perhaps the most dreaded cardiovascular disease because it remains the leading cause of death worldwide [1]. Over the past few years, increased age-standardized death rates due to CAD have been reported in some high-income countries where the death rates were previously declining [1]. One reason for this alarming trend is the increasing global burden of diabetes since 1990 [2]. Cardiovascular diseases affect approximately 32 % of all people with type 2 diabetes [3]. Moreover, arteriosclerotic progression occurs earlier and is more severe in people with diabetes than in the non-diabetic population [4]. Thus, early recognition of CAD is essential to offer effective treatment and improve the patient's prognosis,

especially if she/he has diabetes.

Primary care physicians are usually the first point of contact for patients when they feel ill. The patient's symptoms and signs are often non-specific, posing a particular diagnostic challenge for a general practitioner (GP). Cardiac symptoms are common in the general population and are typical causes of seeking help or advice from GPs. Early signs of cardiac diseases, including CAD, may appear as chest pain/discomfort, dyspnea, effort intolerance, fatigue, and arrhythmia [5]. Atypical CAD symptoms, i.e., other than exertional chest pain/discomfort, are observed more frequently in individuals with diabetes [5,6]. Diabetic patients also tend to have silent ischemia, the prevalence of asymptomatic CAD in patients with type 2 diabetes ranges from 20 % to 60 % [6,7].

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The present study aims to compare the symptoms, diagnostic tests used, and clinical diagnoses made among diabetic and non-diabetic patients referred from primary care to cardiology specialists. We hypothesized that in the unselected patient population of primary care clinics, atypical symptoms of cardiac disease are frequent and more so in patients with diabetes than without.

## 2. Methods

The study population was gathered retrospectively from the municipal primary health care clinics of the city of Turku (185,908 inhabitants in the year 2016) [8]. Medical records of the patients (n = 1295) referred to cardiology specialists (Turku University Hospital and Turku City Hospital) during the year 2016 were evaluated. For the present analyses, we excluded patients with previously diagnosed CAD.

Medical history, cardiovascular medication use, risk factors (smoking status, family history of CAD, blood pressure, plasma lipids and glucose, estimated glomerular filtration rate, body mass index (BMI)), cardiac symptoms considered noteworthy by the GP and cardiologist, diagnostic tests applied, and diagnoses made were gathered from the medical records and the referral texts made by the GPs and from the medical records created by the cardiologists. The angiography data was collected from the Hospital District of Southwest Finland data pool. The symptoms and signs considered to be of cardiac origin were chest pain/discomfort, exertional dyspnea, sense of arrhythmia, referred pain, dizziness/syncope, symptomless pathological electrocardiogram (ECG), nausea, effort intolerance, and sweating. Diagnostic codes defined by the cardiologists were classified according to the International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10).

The institutional review board of the Hospital District of Southwest Finland and the review board of the Turku municipal health care center gave authorizations for this register-based study. As our study used routinely recorded administrative health records, informed consent was not required, nor were the participants contacted. Legal grounds for data handling are public interest and scientific research (EU General Data Protection Regulation 2016/679 (GDPR), Article 6(1)(e) and Article 9 (2)(j); Data Protection Act, Sections 4 and 6).

## 3. Statistical analysis

The descriptive statistics were presented as means with SDs or as counts with percentages. Statistical comparisons between the groups were made using the t-test, permutation test, chi-square test, or Fisher's exact test. Prevalence of symptoms and signs in patients with and without diabetes at the time of referral were analyzed using logistic regression models adjusted with age, sex, smoking, and family history of CAD. Hochberg's procedure was applied to correct levels of significance for multiple testing when appropriate. Normal distributions were evaluated graphically and with the Shapiro–Wilk W test. Stata 16.1 (Stata-Corp LP, College Station, TX, USA) was used for the analysis.

## 4. Results

### 4.1. Patient characteristics

Primary care physicians referred 704 patients without previously diagnosed CAD to cardiology specialists at cardiac clinics in the city of Turku during the year 2016. In this cohort, there were 120 (17 %) patients with diabetes mellitus who were on average older (67 vs. 63 years,  $p = 0.009$ ) and more often females (62 % vs. 38 %,  $p = 0.042$ ) than the non-diabetic patients.

Table 1 displays the comorbid conditions, risk factor levels, and the current cardiovascular medications at the time of the referral in general practice. The people with diabetes had a higher prevalence of hypertension and obstructive sleep apnea, whereas the non-diabetic patients more often had a family history of CAD. The mean BMI was higher in the

**Table 1**

Clinical characteristics of the study subjects according to the presence of diabetes mellitus. The numbers within the square brackets denote the number of patients with available data.

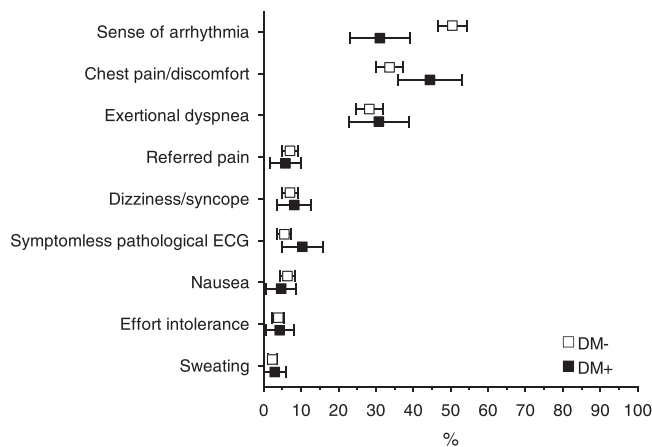
	Diabetes mellitus Not present N = 584	Diabetes mellitus Present N = 120	P-value
<b>Medical history, n (%)</b>			
Cerebrovascular disease	24 (4)	7 (6)	0.85
Hypertension	251 (43)	84 (70)	<0.001
Atrial fibrillation	99 (17)	20 (17)	0.94
Familial hypercholesterolemia	2 (0)	0 (0)	0.99
Depression	40 (7)	12 (10)	0.23
Rheumatoid arthritis	26 (4)	5 (4)	0.89
Obstructive sleep apnoea	25 (4)	15 (13)	<0.001
<b>Risk factors</b>			
Smoking status, n (%)			
Never smoked	510 (87)	98 (82)	0.15
Current smoker	39 (7)	14 (12)	
Ex-smoker	35 (6)	8 (7)	
Family history of CAD, n (%)			
Home blood pressure, mmHg, mean (SD)	115 (20)	12 (10)	0.012
	[287]	[66]	
Systolic	134 (17)	134 (14)	0.69
Diastolic	78 (10)	79 (11)	0.45
Office blood pressure, mmHg, mean (SD)			
Systolic	146 (23)	146 (18)	0.95
Diastolic	84 (12)	84 (11)	0.86
Body mass index, kg/m <sup>2</sup> , mean (SD)			
	28.6 (5.8)	32.9 (9.4)	<0.001
	[156]	[53]	
Fasting plasma lipids, mmol/l, mean (SD)			
Total cholesterol	5.24 (1.11)	4.49 (1.01)	<0.001
	[405]	[108]	
HDL cholesterol	1.66 (0.49)	1.36 (0.42)	<0.001
	[399]	[108]	
LDL cholesterol	3.01(0.99)	2.45 (0.83)	<0.001
	[393]	[108]	
Triglycerides	1.28 (0.79)	1.52 (0.66)	<0.001
	[397]	[108]	
Fasting plasma glucose, mmol/l, mean (SD)			
	5.72 (0.65)	7.72 (2.17)	0.004
	[437]	[13]	
eGFR, ml/min/1.73 m <sup>2</sup> , mean (SD)			
	73.8 (23.2)	75.4 (19.4)	0.50
	[469]	[111]	
<b>Current medication, n (%)</b>			
Statin	161 (28)	66 (55)	<0.001
Beta-blocker	225 (39)	40 (33)	0.28
Calcium-channel blocker	96 (16)	30 (25)	0.026
ACE inhibitor or Angiotensin-receptor antagonist	185 (32)	65 (54)	<0.001
Diuretics	80 (14)	34 (28)	<0.001
Nitrates	60 (10)	13 (11)	0.006
Clopidogrel	9 (2)	1 (1)	0.99
Acetylsalicylic acid	29 (5)	13 (11)	0.013
Warfarin or new oral anticoagulant	82 (14)	26 (22)	0.035

**Abbreviations:** CAD, coronary artery disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; ACE, Angiotensin-converting enzyme

diabetic subjects, who had lower HDL cholesterol and higher triglyceride concentrations than the non-diabetic subjects. The means of total and LDL cholesterol concentrations were lower in persons with diabetes than in the non-diabetic patients. The use of cardiovascular medications other than beta-blockers, clopidogrel, and oral anticoagulants was more frequent among the diabetic patients.

### 4.2. Symptoms and signs

Fig. 1 demonstrates the prevalence of symptoms and signs considered to be of cardiac origin in the diabetic and the non-diabetic patients after adjustment for age, sex, smoking, and family history of CAD. Chest pain/discomfort (43 %), exertional dyspnea (32 %), and sense of



**Fig. 1.** Prevalence of symptoms and signs in the patients with and without diabetes at the time of referral. Adjusted with age, sex, current smoking, and family history of coronary artery disease. **Abbreviation:** ECG, electrocardiogram.

arrhythmia (28 %) were the most often reported symptoms by the diabetic patients. Sense of arrhythmia was the most frequent symptom (51 %) in the non-diabetic patients, followed by chest pain/discomfort (34 %) and exertional dyspnea (28 %). There was a statistically significant difference only regarding the sense of arrhythmia ( $p < 0.001$  using Hochberg’s multiple comparison procedure) between the diabetic and the non-diabetic patients after adjustment for age, sex, current smoking, and family history of CAD. Two or more simultaneous symptoms were present in 185 (32 %) non-diabetic patients and 37 (31 %) diabetic patients ( $p = 0.86$ ). The mean number of symptoms reported by the diabetic patients was 1.2 (SD 0.7) and by the non-diabetic patients 1.4 (SD 0.7),  $p = 0.17$ .

**4.3. Diagnostic tests applied**

In the secondary care cardiac clinics, altogether 1069 diagnostic tests were performed on the 704 patients. Two or more diagnostic tests were applied to 294 (42 %) subjects. Echocardiography was the most often used diagnostic test, followed by exercise ECG and ambulatory ECG monitoring. Coronary computed tomographic angiography (CCTA) was performed on the diabetic patients more often than on the non-diabetics ( $p = 0.029$ ), whereas ambulatory ECG monitoring was applied more often to the non-diabetics ( $p = 0.040$ ). (Table 2).

Three hundred twelve non-diabetic patients were diagnosed with a specific disease, and all non-diabetics underwent a total of 949 investigations. Thus, for one diagnosis a non-diabetic patient underwent

**Table 2**  
Diagnostic tests used in the non-diabetic and diabetic patients in secondary care cardiac clinics.

	Diabetes mellitus Not present n= 584	Diabetes mellitus Present n = 120	P-value
Echocardiography, n (%)	300 (51)	61 (51)	0.91
Exercise ECG n, n (%)	244 (42)	58 (48)	0.19
Exercise ECG with isotope perfusion imaging, n (%)	3 (1)	0 (0)	0.98
Stress echocardiography, n (%)	4 (1)	0 (0)	0.95
Coronary computed tomographic angiography, n (%)	32 (5)	13 (11)	0.029
Invasive coronary angiography, n (%)	14 (2)	5 (4)	0.28
Ambulatory ECG monitoring, n (%)	274 (47)	44 (37)	0.040
None, n (%)	14 (2)	3 (3)	0.95

**Abbreviation:** ECG, electrocardiogram

approximately three diagnostic tests. Among the subjects with diabetes, 61 were given a specific diagnosis and a total of 184 diagnostic tests were carried out. Thus, three tests were conducted per a single diagnosis.

In the non-diabetic patients, sense of arrhythmia was predictive of cardiac disease, whereas chest pain/discomfort decreased the likelihood of cardiac disease. In the diabetic patients, the probability of cardiac disease increased in the patients with sense of arrhythmia or referred pain. (Table 3).

**4.4. Diagnosis**

The most common diagnostic codes applied by the cardiologists were unspecified symptoms and signs (ICD-10 codes R00–R94) in both patient groups. A specific, non-symptomatic diagnosis was defined in 44 % of the non-diabetic and 45 % of the diabetic patients ( $p = 0.90$ ). Fifteen percent of the patients did not receive any diagnosis after the cardiologist’s consultation. The distribution of diagnosis was different between the diabetic and the non-diabetic subjects ( $p = 0.036$ ). (Table 3) Ischemic heart disease was diagnosed more often in the person with diabetes (15 %) than in the non-diabetic (6 %) patients ( $p = 0.004$ ). Cardiac arrhythmias (ICD-10 codes I48–I49) were diagnosed in 26 % of the non-diabetic and 20 % of the diabetic subjects ( $p = 0.021$ ). (Table 3).

**5. Discussion**

In primary care patients referred electively to a cardiology specialist, chest pain or discomfort was the most prevalent symptom in the diabetic patients and a sense of arrhythmia in the non-diabetic subjects. However, the yield of specific diagnoses was low compared to the diagnostic tests applied. Table 4.

Contrary to our data, earlier studies have pointed out that people with diabetes have more atypical symptoms of CAD and that diabetes is a significant promoter of cardiac arrhythmias [7]. This difference may be explained by the fact that the patient population in primary care is typically healthier than in secondary care clinics. However, we cannot rule out the possibility that some patients with diabetes in our study population had autonomic neuropathy, which hindered them from recognizing arrhythmias.

In our study, chest pain/discomfort seemed to decrease the likelihood of cardiac disease in the non-diabetic patients. In Finland, CAD has

**Table 3**  
Relationships between symptoms and probability of cardiac disease diagnosis in the non-diabetic and diabetic patients.

	Diabetes mellitus Not present	P-value	Diabetes mellitus Present	P-value
	OR (95 % CI)		OR (95 % CI)	
Sense of arrhythmia	1.70 (1.04–2.77)	0.033	4.46 (1.29–15.44)	0.018
Chest pain/discomfort	0.40 (0.25–0.64)	<0.001	0.66 (0.22–2.01)	0.47
Exertional dyspnea	0.92 (0.58–1.45)	0.72	0.60 (0.18–1.94)	0.39
Referred pain	1.91 (0.92–3.98)	0.083	15.37 (1.60 to >50.0)	0.018
Dizziness/syncope	0.50 (0.22–1.10)	0.086	0.36 (0.06–2.20)	0.27
Symptomless pathological electrocardiogram	0.90 (0.38–2.14)	0.81	1.90 (0.36–10.14)	0.45
Nausea	0.85 (0.42–1.74)	0.66	0.60 (0.07–4.84)	0.63
Effort intolerance	0.61 (0.24–1.55)	0.30	0.58 (0.05–6.26)	0.66
Sweating	0.47 (0.12–1.84)	0.28	4.10 (0.35–47.34)	0.26

**Table 4**

Clinical diagnosis (ICD-10 codes) made by the cardiologists according to the presence of diabetes mellitus.

	Diabetes mellitus Not presentn= 650	Diabetes mellitus Presentn= 120
None, n (%)	90 (14)	15 (13)
Hypertension (I10-I11), n (%)	48 (7)	10 (8)
Ischemic heart disease (I20-I25), n (%)	38 (6)	18 (15)
Arrhythmias, n (%) Atrial fibrillation/flutter (I48)	170 (26)	24 (20)
Respiratory disease (J00-J99), n (%)	72 (11)	13 (11)
Other, n (%)	5 (1)	2 (2)
Nonrheumatic aortic valve disorders (I35.9)	51 (8)	12 (10)
Hypertensive heart disease (I11.0)	19 (3)	5 (4)
Atrioventricular and left bundle-branch block (I44)	10 (2)	1 (1)
Mitral (valve) insufficiency (I34.0)	7 (1)	2 (2)
Other conduction disorders (I45)	7 (1)	1 (1)
Cardiomyopathy (I42)	6 (1)	2 (2)
Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified, n (%)	5 (1)	1 (1)
R00 Abnormalities of heartbeat R07 Pain in throat and chest R06 Dyspnea R55 Syncope and collapse	182 (28)	39 (33)
	46 (7)	10 (8)
	81 (12)	18 (15)
	32 (5)	10 (8)
	12 (2)	5 (4)

been so common in the general population that even mild chest sensations may reflect fears of heart disease and increase consultation rates in primary care. In the literature, 0.7–2.7 % of all GPs consultations, home visits, and telephone contacts during office hours are related to chest pain [9].

In our data, the majority of the patients had only one symptom, although it is possible that the GPs and cardiologists reported only symptoms of primary importance. Nevertheless, the number of diagnostic tests used was relatively high, especially considering the low diagnostic yield. In a study performed in Belgium and the Netherlands, GPs referred 40 % of their patients with chest pain symptoms to secondary care clinics, and 1.8 diagnostic tests were performed when laboratory tests were taken into account [9]. In Finland, it is common that a cardiologist performs echocardiography (ECHO) bedside at the appointment. Another explanation for the high amount of ECHO examinations is that the guideline in force, the 2013 European guidelines of management of stable CAD, recommend ECHO for the first-line assessment for many cardiac symptoms [10]. In the latest 2019 European guidelines for diagnosing and managing chronic coronary syndrome, non-invasive functional imaging for myocardial ischemia or CCTA is mentioned as one of the first-line tests for diagnosing CAD in symptomatic patients [11].

In our study, CAD was diagnosed in 8 % of the referred patients, 15 % of the diabetic, and 6 % of the non-diabetic subjects. In large datasets investigating symptomatic outpatients suspected to have CAD, obstructive CAD has been diagnosed in 14–23 % of the diabetic patients and in 8–12 % of the non-diabetic patients [12–16]. In a study conducted in Belgian and Dutch primary care, chest pain was present in 1 % of all GP consultations during a two-week period, 40 % of patients were referred to secondary care, and 8 % of all chest pain cases a potentially life-threatening disease was diagnosed. In addition, 8 % of the cases were missing working or final diagnosis [9].

In this study cohort, over 40 % of the diabetic and the non-diabetic patients got no specific diagnosis for their concerns. These people are challenging to primary health care because they often return to the appointments of the GPs suffering from the same symptoms. In Turku, a GP cannot refer patients directly to diagnostic tests, which makes clinical decisions difficult. If a GP has concerns about a patient's symptoms, a referral to a cardiology specialist is justified. A Danish study conducted in primary care reported that symptoms were the predominant reason

for encounters, and in one-third of the patients with health problems, the GP could not make a specific diagnosis [16]. In our research cohort, it seems that both GPs and cardiologists order several examinations for the patients probably not to miss a life-threatening disease. This is expensive for health care and may be rough for the patient. In the 2013 published European guidelines and 2015 published Finnish national guidelines, it is recommended to estimate a patient's pre-test probability for suspected CAD to assess the need for further examinations [10,17]. By integrating a patient's age, sex, and type of chest pain, the pre-test probability allows a rational approach to referral for diagnostic testing [11,13]. However, a single GP may be concerned about atypical cardiac symptoms and give a referral to a cardiology specialist.

There are limitations to our study. This is a retrospective, registry-based dataset. We do not know the type, duration, or possible complications of diabetes. We could not utilize cardiovascular risk assessment models because of limited information on cardiovascular risk factors. Indeed, there was a considerable amount of missing data on major cardiovascular risk factors in the medical records made by both the GPs and the cardiologists (Table 1).

Further, we do not have data on all the patients who attended GPs' appointments seeking help for symptoms thought to be of cardiac origin in the city of Turku in 2016. Only the referred patients are included in our dataset. However, too little is known about the unselected patient population treated in primary care. Thus, our results may provide important information for clinicians and health care providers.

In conclusion, symptoms that might indicate heart disease, especially chest pain/discomfort, are common in both the diabetic and the non-diabetic patients in primary care. Therefore, several diagnostic tests are applied, possibly not to miss a life-threatening disease. We encourage primary care physicians to estimate patient's pre-test probability for suspected CAD when considering referral to cardiology specialist assessment. However, many patients do not get a specific diagnosis for their concerns, even though they have persistent symptoms. More research is needed on the management of patients with symptoms not related to a known disease.

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## 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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