Turk J Endocrinol Metab. 2022;26:1-12

A Cross-Sectional Study of the Prevalence of Cardiovascular Disease in Adults with Type 2 Diabetes in Türkiye: The CAPTURE Study

Türkiye'de Erişkin Tip 2 Diabetes Mellituslularda Güncel Kardiyovasküler Hastalık Prevalansının Kesitsel Bir Çalışması: CAPTURE Türkiye Çalışması

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Abstract

Objective: The primary objective of the CAPTURE study was to estimate the prevalence of cardiovascular disease (CVD) in adults with Type 2 diabetes mellitus (T2DM) across 13 countries from 5 continents. Here, we present the findings from Türkiye. **Material and Methods:** The non-interventional, cross-sectional CAPTURE study (NCT03811288; NCT03786406) was conducted across 15 centers in Türkiye. Standardized demographic and clinical data were collected from adults with T2DM who were treated by primary or specialist care physicians. The prevalences of CVD and its 7 subtypes were estimated. Descriptive statistics were used for data analysis. **Results:** Amongst the 801 participants (n=200 from primary care, n=601 from specialist care) with T2DM enrolled, 250 had established CVD, an estimated weighted prevalence of 31.2% (28.0-34.4) 95% confidence interval. Atherosclerotic CVD contributed to the majority (85.6%) of the CVD cases. An estimated 24.0% of the Türkiye sample had coronary heart disease (CHD). Heart failure was the second most predominant CVD subtype in Türkiye is correct sample (5.4%), followed by cardiac arrhythmia and conduction abnormalities (4.7%). Sodium-glucose co-transporter 2 inhibitors and glucagon-like peptide-1 receptor agonists with cardiovascular (CV) benefits were prescribed to 17.5% and 0.1% of the patients, respectively. **Conclusion:** Approximately 30% of participants with T2DM had established CVD in the CAPTURE Türkiye population, comparable to the global pooled prevalence. CHD was the major contributor and encompassed approximately 75% of the CVD cases. The use of glucose-lowering medication with CV benefits was low compared to the global pooled population, which may be due to the lack of reimbursement of these medications in Türkiye.

Keywords: Cross-sectional study; prevalence; cardiovascular disease; Type 2 diabetes mellitus; Türkiye

Özet

Amaç: CAPTURE çalışmasında, 5 kıtadan 13 ülkede erişkin Tip 2 diabetes mellituslu (T2DM) bireylerde kardiyovasküler hastalık (KVH) prevalansını ortaya çıkarmak amaçlanmıştır. Burada, Türk kohortundan elde edilen bilgiler sunulmaktadır. **Gereç ve Yöntemler:** Girişimsel olmayan kesitsel bir çalışma olan CAPTURE (NCT03811288; NCT03786406), Türkiye'de 15 merkezde tamamlandı. Birinci basamak hekimleri* ve uzman hekimler** tarafından tedavi edilen erişkin T2DM'lilere ait standardize demografik ve klinik veriler toplandı. Elde edilen verilerden KVH ve 7 alt tipinin prevalans tahminleri hesaplandı. Veriler tanımlayıcı istatistiksel yöntemlerle analiz edildi. **Bulgular:** Çalışmaya, T2DM'li 801 (birinci basamak* n=200, uzman** n=601) hasta kaydedildi. Çalışmaya katılan hastaların 250'sine KVH tanısı konmuştur ve KVH'nin tahmini ağırlıklı prevalansı %31,2'dir (%95 güven aralığı, 28,0-34,4). KVH vakalarının çoğunluğu aterosklerotik KVH (%85,6) idi. Türkiye örnekleminin %24'ünde koroner kalp hastalığı (KKH) olduğu ölçüldü. Kalp yetersizliği (%5,4) en sık saptanan 2. KVH alt tipiyken, kardiyak aritmi ve ileti anormalliklerini (%4,7) kalp yetersizliği takip etmektedir. Kardiyovasküler yararı kanıtlanmış ilaçlardan sodyum glukoz transport-2 inhibitörleri ve glukagon benzeri peptid-1 reseptör agonistlerinin reçete edilme oranları sırasıyla %17,5 ve %0,1 olarak saptanmıştır. **Sonuç:** Türkiye'deki T2DM hastalarında KVH, küresel CAPTURE popülasyonunda bulunan prevalansa benzer şekilde hastaların yaklaşık %30'unda saptanmıştır. KKKH en sık saptanan hastalık olurken, KVH vakalarının %75'ini oluşturmuştur. Kardiyovasküler yararı olan glukoz düşürücü ilaçların kullanımı, muhtemelen bu ilaçların Türkiye'de geri ödenmemesi nedeniyle küresel havuzdaki nüfusa kıyasla düşüktü.

Anahtar kelimeler: Kesitsel çalışma; prevalans; kardiyovasküler hastalık; Tip 2 diabetes mellitus; Türkiye

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Peer review under responsibility of Turkish Journal of Endocrinology and Metabolism.

Received: 27 Oct 2021 **Accepted:** 10 Jan 2022 **Available online:** 22 Feb 2022

DOI: 10.25179/tjem.2021-86803

Introduction

Type 2 diabetes mellitus (T2DM) is closely associated with microvascular and macrovascular complications (1), particularly cardiovascular disease (CVD), with a two-to four-fold increased risk of developing CVD in patients diagnosed with T2DM relative to those without a diabetes diagnosis (2). According to 2017 data, the proportion of patients in Türkiye that have CVD is 17.5% (14% for men and 21% for women) (3). Another study conducted in 2017 reported that 24.2% of patients in Türkiye with T2DM and poor metabolic control [glycated hemoglobin (HbA1c) ≥7%, low-density lipoprotein cholesterol ≥100 mg/dL, and arterial blood pressure ≥135/85 mmHg] had macrovascular complications, and 23% of this population had coronary artery disease (4). In Türkiye, CVD accounts for almost half of the overall deaths, and projections indicate the numbers might double by 2030 (5). Diabetes is recognized as an important risk factor for the development of CVD; among the T2DM population, CVD causes almost 50% of deaths (6,7). Hence, many diabetes treatment guidelines highlight the importance of synergistically managing T2DM and CVD (8,9). These guidelines were also driven by the requirement from the US Food and Drug Administration for pharmaceutical companies to perform additional cardiovascular outcome trials (CVOTs) to demonstrate cardiovascular (CV) safety and efficacy of treatments used in T2DM (8,10). The demonstrated superiority of glucose-lowering agents, such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose co-transporter-2 (SGLT2) inhibitors, in such CVOTs led to the revision of treatment guidelines to include GLP-1 RAs and SGLT2 inhibitors as first-line (11) or second-line (8,12,13) treatments for patients with T2DM and established CVD, or those at a high risk of developing CVD.

Türkiye has the highest prevalence of T2DM in Europe, where approximately 6.6 million adults are affected (14). In Türkiye, the age-adjusted comparative prevalence rate is 11.1% and is projected to increase rapidly, with almost 10.4 million adults estimated to be diagnosed with T2DM in 2045, making Türkiye one of the 10 countries with the highest estimated rates of diabetes (14). T2DM has a significant impact on the Turkish health service and accounts for approximately 23.8% of the total health expenditure (14). The economic burden on health service resources is estimated to be three-fold higher for the treatment of complications of diabetes than for the resources used to control diabetes prior to the onset of such complications (15). Due to the close association between T2DM and CVD and the burden placed on health resources, it is essential to determine the contemporary prevalence of CV risk and systemically assess the CV risk factors in people with T2DM (4,16).

Multinational, cross-sectional data on the estimation of the prevalence of CVD in people with T2DM based on standardized methodologies are lacking (17), particularly since the introduction of glucose-lowering agents with demonstrated CV efficacy. The primary objective of CAPTURE was to estimate the prevalence of CVD in adults with T2DM across 13 countries from 5 continents using standardized methodology (18). This article reports the results from the CAPTURE study conducted in Türkiye.

Material and Methods

Study Design

The non-interventional, cross-sectional CAPTURE study was conducted across 214 centers in 13 countries. The study design was described in the primary study (18), which reported the global findings; here, we present the country-specific data for Türkiye.

CAPTURE was registered with ClinicalTrials.gov (NCT03786406 and NCT03811288) and was conducted in accordance with the Declaration of Helsinki (19), International Society for Pharmacoepidemiology Good Pharmacoepidemiology Practices (20), and the local Turkish regulations for clinical research. The study protocol was approved by the appropriate clinical research ethics committees and the relevant institutional review boards at each participating site in Türkiye; a list of the participating sites is provided in Table 1 in the supplementary materials. The initial protocol was approved by the Clinical Studies Ethics Committee of the Erciyes University on November 21 2018 (approval number: 2018/614); the updated protocol

Table 1. List of the sites in Türkiye that participated in the CAPTURE study and provided ethical approval.

Site	Study investigators
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Ankara University Faculty of Medicine	Özgür Demir
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(including 11 additional sites) was approved on January 9 2019 by the same committee (approval number: 2019/42). All participants provided informed consent prior to study participation.

Site Selection

Information regarding routine T2DM management in Türkiye was provided by the local medical affairs personnel. Details of the types of physicians who typically manage T2DM (primary care practitioners, diabetologists, endocrinologists, cardiologists, and other specialists) and the types of treatment sites (primary care centers and specialist settings, including different types of hospitals) were provided. Based on the data provided and extensive literature reviews, the sites that offered the most accurate representation of T2DM management in Türkiye were selected for the study.

Participants

Participants (aged ≥18 years) who had been admitted to the relevant clinics in each center within a specified 90-day period, and were diagnosed with T2DM ≥180 days prior were included. Full inclusion and exclusion criteria were detailed by Mosenzon and colleagues (18).

Data Collection

Participants were invited, informed consent was obtained, and data collection was performed by the treating physician or a qualified delegate during a single healthcare visit. The medical records of the participants were the primary source of data, which were collected via standardized electronic case report forms and transferred to a central database via a web-based data capture system. The medication used by the patients (including those that were discontinued within the last 3 months) was also noted. The study protocol did not require screening or evaluation of the presence of complications.

Objectives/Endpoints of the Study

A part of the primary objective of the CAPTURE study was to estimate the prevalence of CVD in adults with T2DM in primary and specialist care settings in each country, including the 15 centers in Türkiye (see Table S1 for a list of participating sites). The diagnosis of CVD was based on one of the following conditions: aortic disease, cardiac arrhythmia or conduction abnormalities, carotid artery disease, cerebrovascular disease, coronary heart disease (CHD), heart failure, or peripheral artery disease (PAD). Moreover, the presence of any of the following conditions was categorized as atherosclerotic CVD (ASCVD): cerebrovascular disease, CHD, PAD, or carotid artery disease. The diagnostic criteria for CVD conditions recorded in the study are presented in Table 2.

Table 2. The definitions of CVD diagnoses used in the CAPTURE study (18).

		CVD subtype	Diagnoses used
CVD	Atherosclerotic CVD	Cerebrovascular disease	Ischemic stroke
			Hemorrhagic stroke
			Stroke, unspecified
			Transient ischemic attack
		Carotid artery disease	N/A
		Coronary heart disease	Myocardial infarction
			Stable coronary artery disease/angina pectoris
			Other ischemic heart disease
			Past revascularization procedure
		Peripheral artery disease	Asymptomatic peripheral artery disease that is defined as low ankle-branchial index (<0.90) or pulse abolition
			Claudication
			Limb ischemia
			Non-traumatic amputation
		Heart failure	Symptomatic (NYHA Group II-IV or unknown, LVEF ≥50%, LVEF 40-49%, LVEF <40% or LVEF unknown)
			Asymptomatic (NYHA Group I, LVEF ≥50%, LVEF 40-49%, LVEF <40% or LVEF unknown)
			Hospitalization due to heart failure
		Cardiac arrhythmia	Atrial fibrillation, atrial flutter
			Supraventricular tachycardia
			Ventricular tachycardia
			Ventricular fibrillation
			Bradyarrhythmia, sinus node dysfunction
			Bradyarrhythmia, atrioventricular block
		Aortic disease	Aortic dissection
			Aortic aneurysm
			Thromboembolic aortic disease

CVD: Cardiovascular disease; N/A: Not applicable; NYHA: New York Heart Association functional classification; LVEF: Left ventricular ejection fraction.

Additionally, the study population was characterized by demographics, medical records, clinical and laboratory data, usage of glucose-lowering agents, and CVD medications. The usage of glucose-lowering agents with demonstrated CV benefit, including GLP-1RAs (dulaglutide, liraglutide, and semaglutide) and SGLT2 inhibitors (canagliflozin, dapagliflozin, and empagliflozin), were of particular interest. Participants were grouped according to the presence or absence of CVD (CVD versus no CVD subgroups).

Statistical Analysis

The prevalence [95% confidence interval (CI)] of CVD and its subtypes were calculated. The estimates were weighted according to the proportion of patients managed in primary versus secondary specialist care settings in Türkiye, as estimated by the sponsor (i.e. 25% versus 75%). Descriptive data on sample characteristics were not weighted and are presented for the overall Türkiye study sample the CVD group, and the no CVD group. The differences in characteristics between groups (CVD group versus the no CVD group, primary care setting versus secondary care setting) were not compared statistically due to the descriptive study design. Statistical testing was not planned because the large sample size in the global CAPTURE study provides a risk of such analyses identifying statistically significant differences with no clinical relevance.

Results

Between December 2018 and September 2019, 801 participants with T2DM (n=200 from primary care, n=601 from specialist care) were enrolled across 15 centers in Türkiye. The characteristics of the participants were as follows: 58.6% were female, the median (interquartile range) age was

59.0 years (53.0-66.0), the median diabetes duration was 9.9 years (4.9-15.9), and median body mass index (BMI) was 30.4 kg/m^2 (27.0-34.7) (Table 3).

Prevalence of CVD

Amongst the Türkiye study sample, 250 participants had established CVD with an estimated weighted prevalence (95% CI) of 31.2% (28.0; 34.4) (Table 4). ASCVD contributed to the majority of the CVD cases, accounting for approximately 85.6% of the reported cases, and its weighted estimated prevalence was 26.7%. CHD had the highest weighted estimate for the prevalence of the CVD subtype at 24%, and heart failure was

Table 3. The demographic and clinical characteristics of the CAPTURE study population in Türkiye, grouped by the CVD status.

			CVD status			
	Study population (n=801)		CVD (n=250)		No CVD (n=551)	
Characteristic	**n**	**Data**	**n**	**Data**	**n**	**Data**
Female	801	469 (58.6)	250	131 (52.4)	551	338 (61.3)
Age, years	801	59.0 (53.0-66.0)	250	64.0 (57.0-70.0)	551	57.0 (52.0-64.0)
Diabetes duration, years	799	9.9 (4.9-15.9)	249	11.8 (6.8-19.9)	550	9.8 (4.8-14.9)
HbA1c,%	783	7.7 (6.7-9.3)	243	8.0 (6.7-9.6)	540	7.6 (6.6-9.1)
FPG, mg/dL	737	148 (119-193)	230	155 (121-215)	507	147 (118-186)
BMI, kg/m^2	794	30.4 (27.0-34.7)	249	30.0 (26.9-34.5)	545	30.5 (27.0-34.8)
Systolic blood pressure, mmHg	692	130 (120-140)	227	130 (120-140)	465	128 (120-140)
Diastolic blood pressure, mmHg	692	80 (70-84)	227	80 (70-85)	465	80 (70-84)
Total cholesterol, mg/dL	684	193.0 (164.4-226.0)	211	183.0 (155.0-221.0)	473	197.0 (170.0-227.0)
LDL cholesterol, mg/dL	755	116.2 (91.8-145.0)	236	107.0 (82.5-135.0)	519	119.0 (94.9-147.9)
HDL cholesterol, mg/dL	730	43.0 (37.0-51.0)	220	41.0 (36.0-48.5)	510	44.0 (38.0-52.0)
Non-HDL cholesterol, mg/dL	424	157.0 (101.5-208.0)	121	144.0 (80.0-197.6)	303	161.0 (112.0-215.1)
Triglyceride, mg/dL	762	149.0 (108.0-216.0)	235	144.0 (105.0-214.0)	527	150.0 (109.0-216.0)
eGFR, mL/min/1.73 m^2						
>89	730	343 (47.0)	226	69 (30.5)	504	274 (54.4)
>59-89		290 (39.7)		104 (46.0)		186 (36.9)
>29-59		89 (12.2)		49 (21.7)		40 (7.9)
≤29		8 (1.1)		4 (1.8)		4 (0.8)
Albuminuria	563		183		380	
Microalbuminuria		96 (17.1)		35 (19.1)		61 (16.1)
Macroalbuminuria		38 (6.7)		20 (10.9)		18 (4.7)
Hypertension	750	449 (59.9)	240	182 (75.8)	510	267 (52.4)
Familial hypercholesterolemia	679	93 (13.7)	208	32 (15.4)	471	61 (13.0)
Retinopathy,	801		250		551	
Yes[†]		134 (16.7)		71 (28.4)		63 (11.4)
Nephropathy,	801		250		551	
Yes[†]		104 (13.0)		53 (21.2)		51 (9.3)
Neuropathy,	801		250		551	
Yes[†]		186 (23.2)		78 (31.2)		108 (19.6)
Current smoker	801	158 (19.7)	250	45 (18.0)	551	113 (20.5)
Physical activity[‡], days per week	647		193		454	
0-1		297 (45.9)		103 (53.4)		194 (42.7)
2-3		151 (23.3)		40 (20.7)		111 (24.4)
4-5		68 (10.5)		16 (8.3)		52 (11.5)
6-7		131 (20.2)		34 (17.6)		97 (21.4)

Data are n (%) or median (interquartile range). Differences between CVD and no CVD groups were not compared statistically.
[†]These complications were recorded within the participants' medical records. Data that has been confirmed only by the participant has not been included in this table; [‡]Days with ≥30 min of moderate activity; CVD: Cardiovascular disease; HbA1c: Glycated hemoglobin; FPG: Fasting plasma glucose; BMI: Body mass index; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; eGFR: Estimated glomerular filtration rate.

Table 4. The overall prevalence estimates of CVD in adults with Type 2 diabetes mellitus in Türkiye (n=801).

CVD diagnosis	Definition of CVD diagnosis	Number of patients	Prevalence (95% CI), %
CVD	Cerebrovascular disease; carotid artery disease; CHD; peripheral artery disease; heart failure; cardiac arrhythmia; aortic disease	250	31.2 (28.0; 34.4)
Atherosclerotic CVD	Cerebrovascular disease; carotid artery disease; CHD; peripheral artery disease	214	26.7 (23.7; 29.7)
CHD	Myocardial infarction; stable coronary artery disease; other ischemic heart disease; past revascularization procedure	192	24.0 (21.1; 26.9)
Carotid artery disease	-	9	1.1(0.4; 1.9)
Cerebrovascular disease	Ischemic, hemorrhagic, or unspecified stroke; transient ischemic attack	14	1.7 (0.8; 2.7)
Cardiac arrhythmia and conduction abnormalities	Atrial fibrillation; atrial flutter; supraventricular or ventricular tachycardia; ventricular fibrillation, bradyarrhythmia: sinus node dysfunction or AV block	38	4.7 (3.3; 6.2)
Peripheral artery disease	Asymptomatic peripheral artery disease [low-ankle branchial index (<0.90) or pulse abolition]; claudication; limb ischemia; non-traumatic amputation	16	2.0 (1.0; 3.0)
Heart failure	Symptomatic or asymptomatic heart failure; hospitalization for heart failure	43	5.4 (3.8; 6.9)
Aortic disease	Aortic dissection or aneurysm; thromboembolic aortic disease	5	0.6 (0.1; 1.2)

CVD: Cardiovascular disease; CI: Confidence interval; CHD: Coronary heart disease; AV: Atrioventricular.

the second most predominant (5.4%). Cardiac arrhythmia and conduction abnormalities were the third most common subtype of CVD (4.7%), followed by peripheral arterial disease (2.0%), cerebrovascular disease (1.7%), carotid artery disease (1.1%), and aortic disease (0.6%) (Figure 1).

The prevalence of CVD in specialist care was 32.9% and in primary care was 26.0%; the prevalence of ASCVD was similar to the prevalence of CVD in both settings (29.5% versus 18.5%, respectively) (Figure 2). The prevalence of CHD was 26.6% in specialist care and 16.0% in primary care. Although

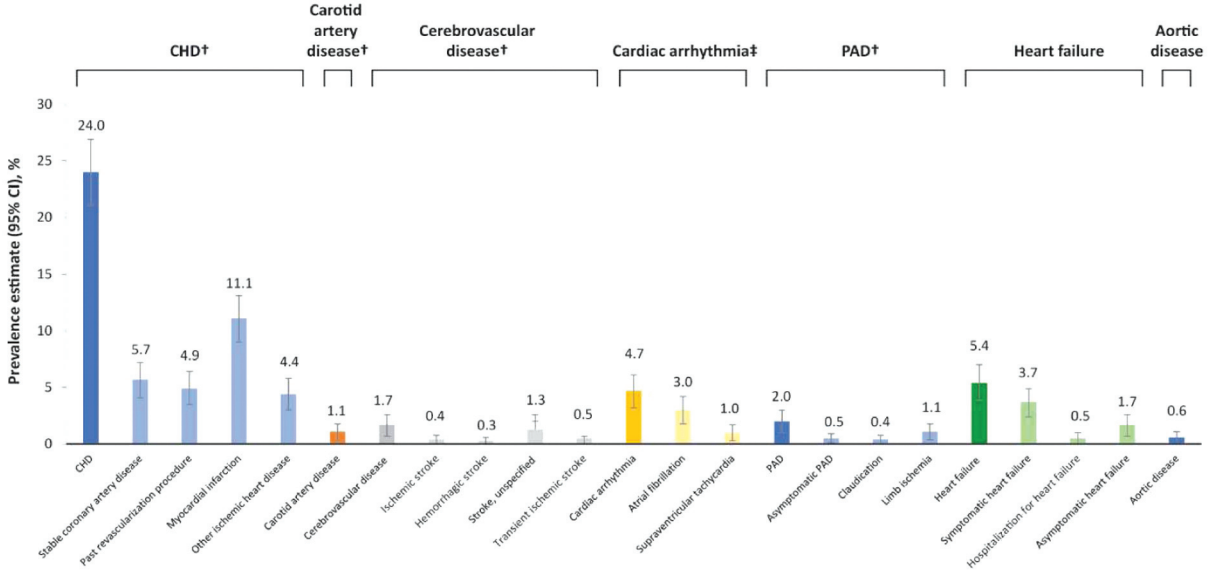

Figure 1. The prevalence of cardiovascular disease in participants with Type 2 diabetes mellitus in Türkiye according to disease subtype and diagnoses.
The data are overall prevalence estimates (95% CI) weighted according to care setting. Diagnoses are not mutually exclusive; one participant may have multiple diagnoses. The differences between disease subtypes and diagnoses were not compared statistically.
†Categorized as atherosclerotic cardiovascular disease; ‡Included conduction abnormalities; CI: Confidence interval; CHD: Coronary heart disease; PAD: Peripheral artery disease.

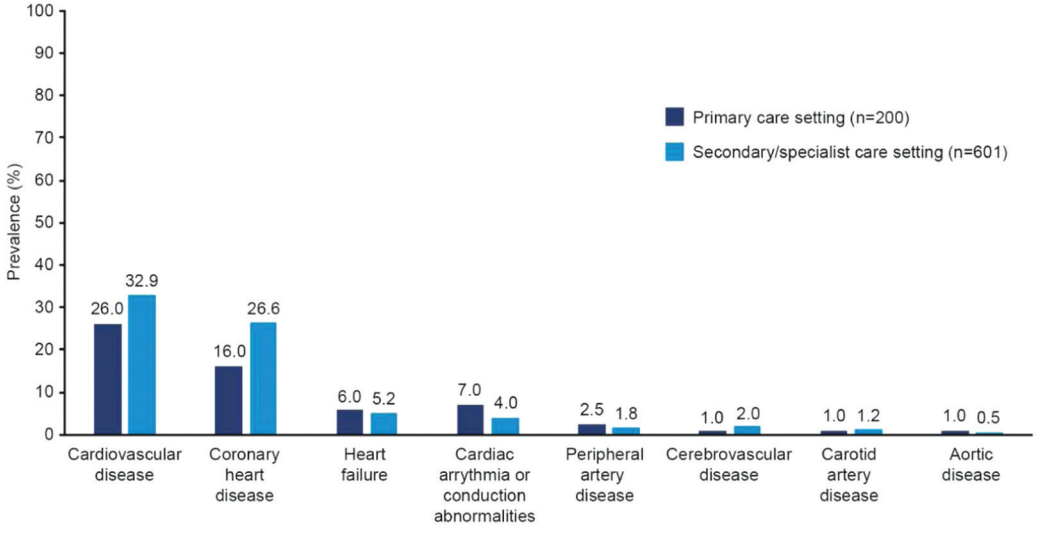

Figure 2. Cardiovascular disease prevalence in participants with Type 2 diabetes mellitus by disease subtype in Türkiye, according to primary and specialist care settings.
The differences between patients in primary care settings and secondary care settings were not compared statistically.

the prevalence estimates of PAD, heart failure, and cardiac arrhythmia and conduction abnormalities appeared to be higher in primary care than in specialist care (2.5% versus 1.8%, 6.0% versus 5.2%, and 7.0% versus 4.0%, respectively), the differences were not statistically analyzed as per the descriptive study design (Figure 2).

Characteristics of the Study Population According to CVD Status

Assessment of clinical and demographic characteristics in the Türkiye study population according to CVD stratification revealed that participants in the CVD group tended to be older than the no CVD group (median age, 64.0 years versus 57.0 years, respectively) (Table 3). In the no CVD group, the proportion of patients with an estimated glomerular filtration rate of >89 mL/min/1.73 m^2 (54.4%) was higher than the CVD group (30.5%), similarly the proportion of female participants was also higher (61.3% versus 52.4%).

Differences were observed between the CVD group and the no CVD group. For example, 75.8% of the participants in the CVD group and 52.4% in the no CVD group had hypertension, the median duration of diabetes was 11.8 and 9.8 years, respectively, and their median HbA1c was 8.0% versus 7.6%, respectively. The proportion of patients with comorbidities varied between groups and, in general, appeared higher in the CVD group than in the no CVD group (neuropathy: 31.2% versus 19.6%; retinopathy: 28.4% versus 11.4%; nephropathy: 21.2% versus 9.3%, respectively) (Table 3).

Glucose-Lowering Medication

A total of 781 participants (97.5%) in the CAPTURE Türkiye study population received glucose-lowering agents (Table 5). The most prescribed oral antidiabetic (OAD) treatment was metformin, which accounted for 75.4% of OAD usage; biguanide use was higher in the no CVD (79.7%) group than in the CVD (66.0%) group. Similarly, the administration of thiazolidinediones was 7.8% in the no CVD group and 2.8% in the CVD group. In contrast, insulin administration and treatment using alpha-glucosidase inhibitor were reportedly higher in the CVD group than in the no CVD group (49.6% versus 37.0% and 4.4% versus 2.9%, respectively) (Table 5).

The administration of glucose-lowering agents with proven CV benefits was higher in the overall population than in the CVD group (17.6% versus 16.4%, respectively). The use of SGLT2 inhibitors with CV benefits was considerably higher than the use of GLP-1 RAs with CV benefits (17.5% versus 0.1%, respectively) in the Türkiye study sample. This was observed consistent regardless of the CVD status (Figure 3).

Table 5. The use of glucose-lowering agents in the CAPTURE study population in Türkiye, stratified by CVD status.

		CVD status	
Glucose-lowering agents	**Study population (n=801)**	**CVD (n=250)**	**No CVD (n=551)**
Any glucose-lowering agent,			
Yes	781 (97.5)	243 (97.2)	538 (97.6)
No	20 (2.5)	7 (2.8)	13 (2.4)
Oral antidiabetic drug,			
Any	703 (87.8)	208 (83.2)	495 (89.8)
Biguanide	604 (75.4)	165 (66.0)	439 (79.7)
DPP-4 inhibitor	260 (32.5)	76 (30.4)	184 (33.4)
Sulfonylurea	116 (14.5)	36 (14.4)	80 (14.5)
SGLT2 inhibitor	140 (17.5)	40 (16.0)	100 (18.1)
Alpha glucosidase inhibitor	27 (3.4)	11 (4.4)	16 (2.9)
Thiazolidinedione	50 (6.2)	7 (2.8)	43 (7.8)
Glinide	8 (1.0)	4 (1.6)	4 (0.7)
Insulin,			
Any	328 (40.9)	124 (49.6)	204 (37.0)
Basal	249 (31.1)	95 (38.0)	154 (27.9)
Bolus	216 (27.0)	93 (37.2)	123 (22.3)
GLP-1 RA	67 (8.4)	18 (7.2)	49 (8.9)
Monotherapy,			
Any	274 (34.2)	91 (36.4)	183 (33.2)
Biguanide	169 (21.1)	44 (17.6)	125 (22.7)
Insulin (any)	77 (9.6)	35 (14.0)	42 (7.6)
DPP-4 inhibitor	10 (1.2)	5 (2.0)	5 (0.9)
Sulfonylurea	7 (0.9)	3 (1.2)	4 (0.7)
SGLT2 inhibitor	3 (0.4)	1 (0.4)	2 (0.4)
GLP-1 RA	1 (0.1)	-	1 (0.2)
Dual therapy,			
Any	266 (33.2)	79 (31.6)	187 (33.9)
Biguanide and insulin (any)	73 (9.1)	24 (9.6)	49 (8.9)
Biguanide and alpha glucose inhibitor	2 (0.2)	-	2 (0.4)
Biguanide and DPP-4 inhibitor	58 (7.2)	11 (4.4)	47 (8.5)
Biguanide and sulfonylurea	31 (3.9)	10 (4.0)	21 (3.8)
Biguanide and SGLT2 inhibitor	10 (1.2)	2 (0.8)	8 (1.5)
Biguanide and glinides	1 (0.1)	-	1 (0.2)
Biguanide and thiazolidinediones	13 (1.6)	2 (0.8)	11 (2.0)
Biguanide and GLP-1 RA	15 (1.9)	4 (1.6)	11 (2.0)
SGLT2 inhibitor and insulin (any)	7 (0.9)	2 (0.8)	5 (0.9)
GLP-1 RA and sulfonylurea	1 (0.1)	1 (0.4)	-
Triple therapy,			
Any	175 (21.8)	60 (24.0)	115 (20.9)
Biguanide and sulfonylurea and DPP-4 inhibitor	30 (3.7)	11 (4.4)	19 (3.4)
Biguanide and DPP-4 inhibitor and insulin (any)	44 (5.5)	15 (6.0)	29 (5.3)
Biguanide and GLP-1 RA and insulin (any)	9 (1.1)	3 (1.2)	6 (1.1)
Biguanide and SGLT2 inhibitor and insulin (any)	19 (2.4)	9 (3.6)	10 (1.8)
Biguanide and sulfonylurea and insulin (any)	2 (0.2)	1 (0.4)	1 (0.2)
Biguanide and DPP-4 inhibitor and SGLT2 inhibitor	13 (1.6)	5 (2.0)	8 (1.5)
Biguanide and sulfonylureas+SGLT2 inhibitor	2 (0.2)	-	2 (0.4)
Biguanide and sulfonylureas+GLP-1 RA	1 (0.1)	-	1 (0.2)
Biguanide and GLP-1 RA+SGLT2 inhibitor	22 (2.7)	5 (2.0)	17 (3.1)
Therapy with ≥4 glucose-lowering agents,			
Any	66 (8.2)	13 (5.2)	53 (9.6)
Use of glucose-lowering medication with CV benefit			
GLP-1 RA	1 (0.1)	1 (0.4)	-
SGLT2 inhibitor	140 (17.5)	40 (16.0)	100 (18.1)

CVD: Cardiovascular disease; CI: Confidence interval; CHD: Coronary heart disease; AV: Atrioventricular.
Data are n (%). Differences between CVD and no CVD groups were not compared statistically.

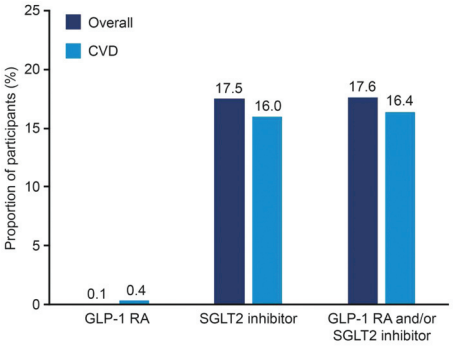

Figure 3. The use of glucose-lowering agents with proven CV benefits in the CAPTURE Türkiye population, stratified by CVD status.
CV: Cardiovascular; CVD: Cardiovascular disease; GLP-1 RA: Glucagon-like peptide-1 receptor agonist; SGLT2: Sodium-glucose co-transporter 2.
The data are proportion of participants using a glucose-lowering agent with proven CV protection as per the guidelines of American Diabetes Association (GLP-1 RAs: Dulaglutide, liraglutide, and semaglutide; SGLT2 inhibitors: Canagliflozin, dapagliflozin, and empagliflozin) (24). The differences between the overall and CVD populations were not compared statistically.

Discussion

In this study, the weighted prevalence of CVD in patients with T2DM in Türkiye (31.2%) was found to be similar to the overall pooled estimate (34.8%); however, the mean prevalence in the TEMD study was lower (24.2%) (4,18). This was the first study to use standardized methodology to measure the prevalence of CVD across 13 countries. ASCVD accounted for the majority of the disease burden in both the overall pooled sample and the study sample from Türkiye (31.8% versus 26.7%, respectively), along with CHD (17.7% versus 24.0%, respectively), heart failure (2.4% versus 5.4%, respectively), and cardiac arrhythmia and conduction abnormalities (4.2% versus 4.7%, respectively). However, the major components of stroke, coronary artery disease, and carotid artery disease, which greatly contributed to the overall CVD burden, were relatively unsubstantial in the Turkish CAPTURE population.

The low estimated prevalence of coronary artery disease in the study sample was consistent with the findings of a previously published nationwide survey of metabolic parameters of patients with diabetes (TEMD; 24.0% versus 22.9%, respectively) in Türkiye (4). The small discrepancy between the data may be attributable to the differences in CV risk factors in the patient population between the 2 studies; patient demographics consisted of a higher BMI and rate of hypertension and a longer duration of diabetes in the patients of the TEMD study (21) compared to the patients in the CAPTURE Türkiye study sample.

The prevalence of CVD was higher in patients in the specialist care setting than in the primary care setting; this could be because those receiving specialist care may have a greater burden of comorbidities. Furthermore, patients without significant illness might be less inclined to seek primary care, and consequently, this could have contributed to the lower CVD prevalence in the primary care setting (22). Despite this, the prevalences of some CVD subtypes such as heart failure, PAD, and cardiac arrhythmia and conduction abnormalities were higher in the primary care setting.

A relatively high percentage of participants in the Türkiye study population received SGLT2 inhibitors with proven CV benefits (17.5%) comparable to the overall pooled sample (15.0%) (18). This difference between the global and Türkiye study samples may be the result of Turkish treatment guidelines and regulatory agencies (8) recommending the use of SGLT2 inhibitors with proven CV safety in patients with a history of CV events. The utilization rate of GLP-1 RAs was 8.4%, whilst the utilization rate of GLP-1 RAs with demonstrated CV benefits, which are an endorsed treatment option as per the Turkish diabetes treatment guidelines (8), was <1%. Unlike other antidiabetic medications, most GLP-1 RAs are not commonly reimbursed by the Turkish healthcare system for the treatment of T2DM or obesity (BMI >30 kg/m^2) unless prescribed by endocrinologists working in tertiary healthcare facilities (8). Exenatide is the most commonly prescribed and reimbursed GLP-1 RA in Türkiye; however, as it has previously shown no CV benefits (23) and it was not defined as a GLP-1 RA with CV benefit in this study. It is likely that the low utilization rate of GLP-1 RA with CV benefits observed in this study might be associated with the high treatment costs and lack of reimbursement of these medications in Türkiye.

Limitations of the Study

The CAPTURE study has many strengths, predominantly the large sample size generated as a result of the multinational, cross-sectional study design (18). This delivered the advantage of increasing generalizability of the results, and also provided the opportunity to stratify the data according to CVD status. Our findings could facilitate and inform the design and entry criteria of future outcome trials in Türkiye enhancing the generalizability of their results to other populations.

In the absence of available medical records, clinical data were collected through patient-reported measures. Thus, results obtained from this data could be biased, considering no corrective measures were in place for preventing this bias. Another limitation was the absence of statistical analyses of group differences due to the study design. The design of the study also meant that ascertainment bias may have led to an overestimation in CVD prevalence data, as patients with complications might consult their healthcare provider more frequently than the general T2DM population.

Conclusion

The CAPTURE study identified that approximately 30% of the participants with T2DM in the Türkiye population were suffering from established CVD, which was comparable to the global pooled prevalence rate. Approximately 75% of the CVD cases were attributable to CHD. The findings from the study population in Türkiye were similar to the local and global treatment guidelines at the time of the study. Similarly, the use of SGLT2 inhibitors, which have been shown to have CV benefits, was comparable to the overall pooled sample. However, GLP-1 RAs, which also have CV benefits, were prescribed to fewer patients with T2DM in Türkiye compared to the overall pooled sample, most likely because these medications are generally not reimbursed in Türkiye.

Previous Publication

Some of the analyses presented in this manuscript have been published previously as an abstract and subsequently presented as an oral presentation at the Congresses of Endocrinology and Metabolic Diseases of Türkiye (CEMDT), held by TEMD on 19-23 May 2021 in the Sueno Congress Center, Antalya. Prof Fahri Bayram was the presenting author and the abstract/presentation title was 'A cross-sectional study of the contemporary prevalence of cardiovascular disease in adults with type 2 diabetes mellitus in Türkiye: CAPTURE Türkiye.

Source of Finance

The funding source (Novo Nordisk A/S) of the CAPTURE study participated in the study design, site selection (in collaboration with a contract research organization), study coordination, data management, data analysis (including the country-level data analysis), and study report preparation.

Acknowledgements

The authors would like to thank the CAPTURE study participants, investigators, and coordinators. Medical writing support was provided by Raman Dehil, BSc, and Brendan Deeney, BSc, and editorial assistance was provided by Rosalind Perrett, BA, all of Ashfield MedComms, an Ashfield Health company, funded by Novo Nordisk A/S.

Conflict of Interest

Fahri Bayram: Speaker honoraria and travel sponsorship from Bilim İlaç, Abbott, Novo Nordisk, Sanofi Genzyme, Pfizer, and Eczacıbaşı İlaç; advisory board and consultancy for Novo Nordisk, Sanofi Genzyme, Abbott, Pfizer, and Bilim İlaç; and participation in clinical trials for Novo Nordisk, Lilly, Sanofi, and Abbott. Taner Bayraktaroğlu: Speaker honoraria from Bilim İlaç, Sanofi Genzyme, Boehringer Ingelheim, Merck Sharp & Dohme (MSD); advisory board and consultancy for Novo Nordisk; and participation in clinical trials for Novo Nordisk, Sanofi, and Novartis Pharmaceuticals. Mehmet Sargın: No conflict of interest to declare. İbrahim Şahin: No conflict of interest to declare. Sibel Güldiken: No conflict of interest to declare. Ayşegül Dalbeler: Employee of Novo Nordisk. Alper Sönmez: No conflict of interest to declare.

Author Contributions

The authors confirm that they meet the International Committee of Medical Journal Editors (ICJME) requirements for author-

ship. All authors have contributed to the analysis and interpretation of the data, drafted and/or critically reviewed the article, and share the final responsibility for the content of the manuscript, as well as the decision to submit it for publication. Author contributions are as follows: conceptualization of this article: Fahri Bayram, Taner Bayraktaroğlu, Mehmet Sargın, İbrahim Şahin, Sibel Güldiken, Ayşegül Dalbeler, Alper Sönmez; investigation: Fahri Bayram, Taner Bayraktaroğlu, Mehmet Sargın, İbrahim Şahin, Sibel Güldiken, Alper Sönmez; writing/original draft preparation: Fahri Bayram, Taner Bayraktaroğlu, Mehmet Sargın, İbrahim Şahin, Sibel Güldiken, Ayşegül Dalbeler, Alper Sönmez; writing/review and editing: Fahri Bayram, Taner Bayraktaroğlu, Mehmet Sargın, İbrahim Şahin, Sibel Güldiken, Ayşegül Dalbeler, Alper Sönmez; supervision: Fahri Bayram, Ayşegül Dalbeler (Note that as this was a secondary manuscript from the CAPTURE study, the study methodology, formal analysis, and data curation were completed by Novo Nordisk and authors on the primary manuscript).

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