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Management of Cardiovascular Risk among Moroccan Patients with Type 2 Diabetes: A Cross-Sectional Study

ABSTRACT

Objective: The aim of this study was to estimate the prevalence of cardiovascular disease and investigate cardiovascular risk management among type 2 diabetes (T2D) patients in the city of Meknes.

Materials and methods: In a non-interventional cross-sectional study, we enrolled adult outpatients (≥ 18 years old) with T2D from the endocrinology and diabetology consultation of the Military Hospital of Meknes from June 2021 to January 2022. Informed consent was signed by all participants in the study. Assessment of cardiovascular risk was based on European Society of Cardiology (ESC) Guidelines on cardiovascular disease prevention in clinical practice of 2021. Clinical, biological and therapeutic data were compared between patients with and without cardiovascular disease. Data were analyzed using SPSS version 18 statistical software.

Results: One hundred eighty T2D patients were enrolled. The mean age was 59.42 ± 8.72 years. The prevalence of cardiovascular disease was 13.3%. The prescription of statin (p < 0.001), antihypertensive treatment (p < 0.001) and platelet aggregation inhibitors (p < 0.001) was significantly higher in patients with cardiovascular disease. Overall, 5.6% patients were prescribed a blood glucose-lowering agent with demonstrated cardiovascular benefit. This prescription was higher in patients with cardiovascular disease (5 (20.8%) vs. 5 (3.2%); p = 0.004). It was found that 7.2% patients had an optimal cardiovascular risk factor management.

Conclusions: The prevalence of cardiovascular disease among T2D patients is high in the city of Meknes. Despite an optimal prescription of cardiovascular medications, comprehensive control of cardiovascular risk factors is not achieved in most patients. The use of blood glucose-lowering agents with demonstrated cardiovascular benefit was low but significantly higher among patients with cardiovascular disease. (Clin Diabetol 2023; 12; 3: 171–178

Introduction

Cardiovascular disease (CVD) is one of the leading causes of mortality among people with diabetes (PWD). The overall prevalence of CVD among PWD is 32.2% and coronary artery disease (CAD) is the most frequent [1]. Type 2 diabetes (T2D) patients have a two-fold increased risk of cardiovascular (CV) mortality compared to healthy individuals [2, 3]. Thus, management of CV risk must be a therapeutic priority in PWD. Indeed, the

treatment of the T2D patients with high CV risk has undergone a major evolution in recent years. Faced with the lack of benefit of the glucocentric approach in the prevention of cardiovascular complications, the therapeutic strategy in the T2D patient focused on the management of the associated CV risk factors as part of a multi-risk approach. This approach subsequently experienced a real evolutionary turning point following the demonstration of cardiovascular benefice with new blood glucose-lowering agents (GLAs) [4]: the glucagon-like peptide-1 receptor agonists (GLP-1 RAs) [5] and sodium-glucose co-transporter-2 inhibitors (SGLT2is) [6]. The most recent international diabetes and cardiology position statements and guidelines endorse an organ-protective therapeutic approach in T2D patients with the focus now on cardio-renal risk with a privileged place to these new agents in patients with a high CV risk or with established CVD [7, 8]. This strategy contributed to the decrease in the incidence of CVD or CV death within the last two decades [3, 9, 10]. Paradoxically, after this steady decline, there has been a recent resurgence of CAD in T2D patients, particularly among those diagnosed before the age of 65 years [11]. These disturbing statistics leads to focus on practice patterns in real life of current guidelines. Data regarding the prevalence of CVD and management of CVD and CV risk among patients with type 2 diabetes patients in Morocco are lacking. The aim of this study was to estimate prevalence of CVD and investigate CVD and CV risk management among type 2 Moroccan patient in the city of Meknes.

Methods
Population
In a non-interventional cross-sectional study, we enrolled adult outpatients ($\geq$ 18 years old) with T2D from the endocrinology and diabetology consultation of the Military Hospital of Meknes from June 2021 to January 2022.

Patients were excluded if they had other types of diabetes, a known congenital heart disease or malformation, if they were pregnant or non-resident at the city of MEKNES or patients refusing to participate to the study.

Data on patient demographics, medical history, comorbidities, laboratory and vital status measurements, micro and macrovascular complications, and blood glucose-lowering agents (GLAs), and CV medications were collected using a standardized case report form.

Assessment of cardiovascular risk factors and CVD
Anthropometric data and cardiovascular risk factors were compiled by patient response and clinical exam during a single routine health visit and from participants' paper medical records.

Hypertension was diagnosed if subjects were on drug treatment for hypertension or had a systolic blood pressure (SBP) of $\geq$ 140 mmHg and/or diastolic blood pressure of $\geq$ 90 mmHg. Obesity was diagnosed if patient had a body mass index (BMI) $\geq$ 30 kg/m^2. Smoking was defined by active smoking or smoking cessation less than 3 years.

Lipid anomalies assessment was based on enzymatic measurement of total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol after 12 hours of fasting. Non-HDL cholesterol was calculated by the difference between total cholesterol and HDL cholesterol. Dyslipidemia was defined by total cholesterol > 2 g/L [normal range (NR): < 2 g/L)], LDL cholesterol > 1.6 g/L (NR < 1.55 g/L) and/or HDL cholesterol < 0.4 g/L for men and et < 0.5 g/L for women (NR > 0.5 g/L) and/or triglycerides > 1.5 g/L (NR < 1.5 g/L) or the use of lipid lowering drugs.

Microalbuminuria was defined by an albumin: creatinine ratio (ACR) of 30–300 mg/g (NR < 30 mg/g) for a first morning void or in a spot urine sample. Macroalbuminuria was defined by an ACR greater than 300 mg/g. The estimated glomerular filtration rate (GFR) was calculated using the CKD-EPI (Chronic Kidney Disease — Epidemiology Collaboration) equation and chronic kidney failure was defined by GFR < 60 mL//min/1.73m^2. Diabetic kidney disease (DKD) was defined by macroalbuminuria and chronic kidney failure.

Assessment of cardiovascular risk was based on European Society of Cardiology (ESC) Guidelines on cardiovascular disease prevention in clinical practice of 2021 [7].

Established CVD was defined as a diagnosis of any of the following conditions in participants' medical records: cerebrovascular disease, coronary artery disease (CAD), heart failure, peripheral artery disease (PAD), or carotid artery disease. For analysis purposes, participants were stratified into two groups based on the presence (CVD group) or absence (non-CVD group) of established CVD.

Optimal CV risk factor management was defined as control of all of the following risk factors: SBP and LDL cholesterol meeting the step 2 targets of CV risk level based on ESC guidelines, glycemic control with glycated hemoglobin A1c (HbA1c) $\leq$ 8%, non-smoking status.

Statistical analysis
Data were analyzed by SPSS software. Quantitative variables were expressed as mean $\pm$ standard deviation (age, total cholesterol, LDL cholesterol, non-HDL cholesterol) or median and interquartile range (diabetes
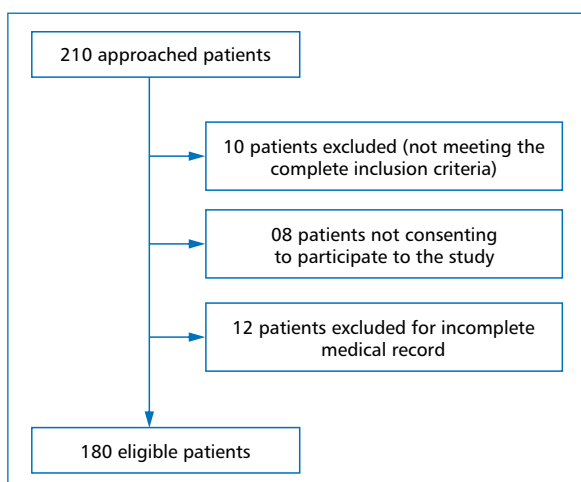
Figure 1. The Study Flow Chart

duration, HDL cholesterol, triglycerides, HbA1c, BMI). Qualitative variables were expressed as numbers and percentages. The comparison of means was made by Student's t-test, the median by the Mann-Whitney test and the proportion by Khi-deux test and Fisher's exact test. A p-value < 0.05 was considered to be statistically significant.

Ethical approval

The rights of the participants were protected by ensuring privacy during the data collection. All the data were collected in an anonymous format. There was no data collected that could be used to identify individuals. Informed consent was signed by all participants before being included in the study.

Results

Two hundred ten PWD were approached for the study. Ten patients were excluded for not meeting the complete inclusion criteria. Eight patients refused to participate to the study and 12 patients were excluded for incomplete medical record (Fig. 1). One hundred eighty T2D patients were enrolled. The mean age was 59.4 ± 8.7 years with male predominance (56.1%) and the median duration of T2D was 10 (7, 16) years. Anthropometric data and CV risk factors are summarized in Table 1.

Characteristics of the study sample by CVD status

The prevalence of CVD was 13.3% with 5.5% of CAD, 4.4% of cerebrovascular disease, 1.1% of heart failure and 2.2% of PAD. Clinical and biological data (age, sex, diabetes duration, CV risk factors, HbA1c), lipid profile (total cholesterol, LDL cholesterol, HDL

Table 1. Baseline Characteristics of Patients

Characteristics	(n = 180)
Age [years]*	59.4 ± 8.7
Sex§	
Male	101 (56.1%)
Female	79 (43.9%)
Diabetes duration°	10 (7; 16)
HbA1c°	8.1 (7.3; 9.7)
Glycemic control	
≤ 7%	31 (17.2%)
Between 7 and 8%	49 (27.2%)
Between 8 and 10%	63 (35%)
> 10%	37 (20.6%)
BMI°	26.7 (24.2; 29.3)
Weight	
Normal	58 (32.2%)
Overweight	85 (47.2%)
Obesity	37 (20.6%)
Smoking§	14 (7.8%)
Hypertension§	81 (45%)
Dyslipidemia§	145 (80.6%)
CV risk categories§	
Moderate-risk	3 (1.7%)
High-risk	59 (32.8%)
Very high-risk	118 (65.6%)
CVD§	24 (13.3%)
DKD§	35 (19.4%)
Albuminuria§	29 (16.1%)
Chronic renal failure§	
Moderate	10 (5.6%)
Severe	3 (1.7%)

*mean ± standard deviation; °median (interquartiles); §numbers (percentages); BMI — body mass index; CVD — cardiovascular disease; CV — cardiovascular; DKD — diabetic kidney disease; HbA1C — glycated hemoglobin A1c

cholesterol, non-HDL cholesterol, and triglyceride) and renal function were compared between the CVD group and non-CVD group. Results are summarized in Table 2. Factors associated with CVD were: age (64.8 ± 9.8 years vs. 58.6 ± 8.2 years, p = 0.001), hypertension [23 (95.8%) vs. 58 (37.2%); p < 0.001], obesity [10 (41.7%) vs. 27 (17.3 %); p = 0.012] and BMI [29.3 (25.1; 32.6) vs. 26.5 (24.2; 29) kg/m^2; p = 0.044] (Tab. 2).

CV medications by CVD status

Overall, 103 patients (57.2%) were receiving any CV medication and it was significantly more common in the CVD group than in the non-CVD group (24 (100%) vs.

Table 2. Comparison of Demographic and Biological Characteristic between Patients with and without CVD

	Non-CVD (n = 156)	CVD (n = 24)	p
Age*	58.6 ± 8.2	64.8 ± 9.8	0.001
Sex§			0.2
Male	85 (54.5%)	16 (66.7%)	
female	71 (45.5%)	16 (33.3%)	
Diabetes duration§			0.3
< 10 years	70 (44.9%)	8 (33.3%)	
≥ 10 years	86 (55.1%)	16 (66.7%)	
BMI (Kg/m²)	26.5 (24.2; 29)	29.3 (25.1; 32.6)	0.044
Obesity§	27 (17.3 %)	10 (41.7%)	0.012
Hypertension§	58 (37.2%)	23 (95.8%)	< 0.001
Smoking§	12 (7.7%)	2 (8.7%)	1
DKD§	31 (19.9%)	4 (16.7%)	1
Albuminuria§	25 (16%)	4 (16.7%)	1
Dyslipidemia§	122 (78.2%)	23 (95.8%)	0.051
CT (g/L)*	1.6 ± 0.4	1.5 ± 0.4	0.3
LDL CT (g/L)*	0.9 ± 0.3	0.8 ± 0.3	0.1
Non-HDL CT (g/L)*	1.2 ± 0.4	1.1 ± 0.4	0.2
HDL CT (g/L)°	0.42 (0.35; 0.52)	0.43 (0.36 ; 0.51)	0.8
TG (g/L)°	1.3 (0.9; 1.8)	1.3 (1; 1.7)	0.7
HbA1c°	8.1 (7.3; 9.9)	8.5 (7.2; 9.4)	0.8
Glycemic control§			0.2
< 8%	70 (44.9%)	9 (37.5%)	
Between 8 and 10%	52 (33.3%)	12 (50%)	
> 10	34 (21.8%)	3 (12.5%)	

*mean ± standard deviation; °median (interquartiles); §numbers (percentages); BMI — body mass index; CT — cholesterol; CVD — cardiovascular disease; DKD — diabetic kidney disease; HbA1c — glycated hemoglobin A1c, HDL — high-density lipoprotein; LDL — low-density lipoprotein; TG — triglyceride

79 (50.6%); p < 0.001. In the CVD group, statins were the most frequently utilized CV medications (95.8 %), followed by platelet aggregation inhibitors (79.2%), angiotensin converting enzyme (ACE) inhibitors (54.2%) and beta-blockers (45.8%). In the non-CVD group, statin use also predominated (35.9%) followed by ACE inhibitors (26.3%), diuretic (18.6%), and angiotensin II receptor blockers (ARBs; 10.3%). The prescription of statin (p < 0.001), platelet aggregation inhibitors (p < 0.001), ACE inhibitors (p = 0.006), ARBs (p = 0.002), beta-blockers (p < 0.001), calcium channel blockers (p = 0.004) and spironolactone (p = 0.002) was significantly higher in CVD group.
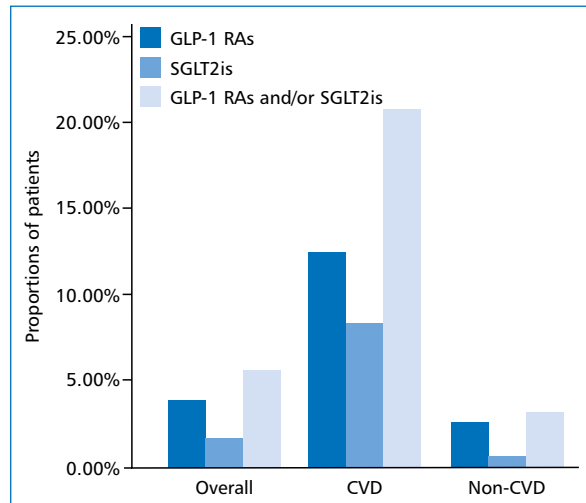

Figure 2. Prescription of GLAs with Demonstrated CV Benefit CV— cardiovascular; CVD — cardiovascular disease; GLAs — blood glucose-lowering agents; GLP-1 RAs — glucagon-like peptide-1 receptor agonists, SGLT2is — sodium-glucose co-transporter-2 inhibitors

GLAs by CVD status

Overall, metformin was the most prescribed GLAs (70%); followed by insulin (66.1%) and sulfonylurea (21.7%). Metformin was less frequently prescribed in the CVD group than the non-CVD group (62.5% vs. 71.2%). The use of sulfonylurea was significantly lower in CVD group (0 (0%) vs. 39 (25 %); p = 0.003). Whereas insulin use was more common in the CVD group than in the non-CVD group (75% vs. 64.7%).

In total, 5.6% patients were prescribed GLAs with demonstrated CV benefit. GLP-1 RAs were more frequently used than SGLT2is (3.9% vs. 1.7%) (Fig. 2). The prescription of GLA with demonstrated CV benefit was significantly higher in CVD group [5 (20.8%) vs. 5 (3.2%); p = 0.004]. The use of SGLT2is was significantly higher in CVD group (8.3% vs. 0.6%; p = 0.047) and the use of GLP-1 RAs was also higher across the CVD group (12.5% vs. 2.6%; p= 0.051).

Control of CV risk factors

Among all patients, SBP was meeting the step 1 ESC target in 85.6%, and the step 2 ESC target in 61.7%. LDL cholesterol was controlled according to step 1 ESC targets in 55% and in 25% according to step 2 ESC targets. HbA1c was ≤ 8% in 44.4% and 92.2% were not smoking.

In very high CV risk patients, SBP step 1 ESC target was achieved in 79.6% and step 2 target in 63%. LDL cholesterol was controlled according to step 1 ESC target in 40.7 % and in 22.2 % according to step 2
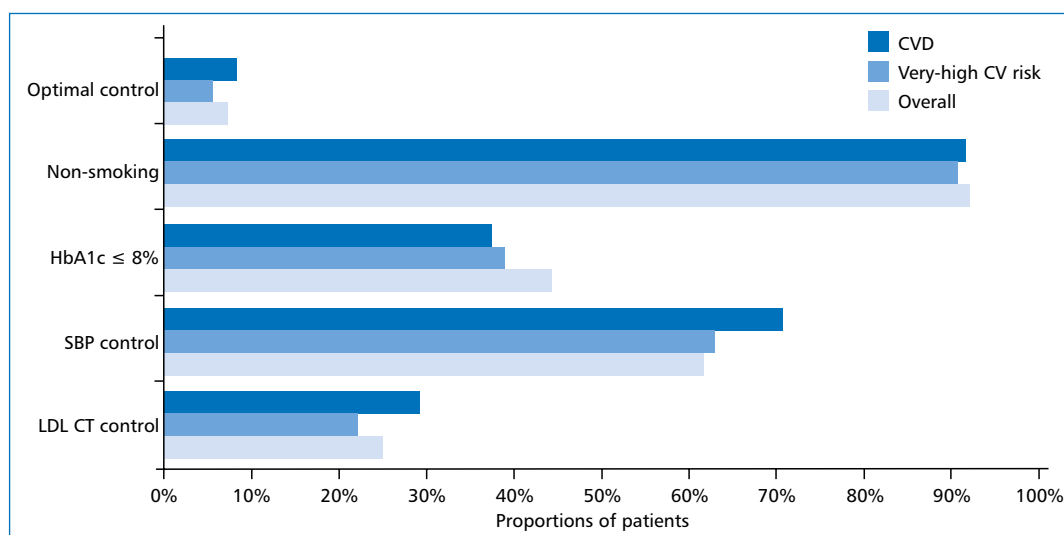
Figure 3. Cardiovascular Risk Factors Control
CV — cardiovascular; CVD — cardiovascular disease; HbA1c — glycated hemoglobin A1c, LDL-C — low-density lipoprotein cholesterol; SBP — systolic blood pressure

ESC target. HbA1c was ≤ 8% in 38.9% and 90.7% were not smoking.

In CVD group, SBP step1 ESC target was achieved in 91.7% and step 2 target in 70.8%. LDL cholesterol was controlled according to step 1 ESC target in 41.7% and in 29.2% according to step 2 ESC target. HbA1c was ≤ 8% in 37.5% and 91.7% were not smoking.

Overall, only 7.2% patients had optimal risk factor management. Optimal risk factor management was higher in CVD group (8.3% vs. 7.1%) (Fig. 3).

Discussion

The prevalence of CVD in T2D patients in the city of Meknes was 13.3%. The "DISCOVER" study is an observational study conducted over 3 years in 14,343 patients with T2D from 34 countries including African countries and the Arab Maghreb region countries (South Africa, Algeria, Tunisia) [12]. The results were similar to our study with a prevalence of atherosclerotic CVD of 11.8% [12]. However, the prevalence of CVD in T2D patients remains lower in our study compared to the majority of literature data. Indeed, in a systematic review that included the results of 57 studies worldwide over 10 years between 2007 and 2017 with more than 4 million T2D patients, the prevalence of CVD was 32.2% [1]. However, this systematic review did not include studies conducted in Africa or in the Arab Maghreb region [1]. In the multinational "CAPTURE" study, which included 9823 T2D patients from 13 countries, the prevalence of CVD was 34.8% [95% confidence interval (CI): 32.7–36.8] [13]. In the same study, the prevalence of CVD in T2D patients was 43.9% (95%

CI: 40.9–46.8) in Brazil, 38.8% (95% CI: 35.5–42.3) in Italy and 31.2% (95% CI: 28–34.4) in Turkey [13]. The CAPTURE study did not include African countries or the Arab Maghreb region. The prevalence of CVD in T2D patients was 21.4% in a Danish study including more than 17,000 T2D patients [14]. Marson et al. [15] report a prevalence of CVD in PWD in Australia of 24.9% (95% CI: 24.2–25.5). In an American cross-sectional study of 1,202,596 patients with T2D, the prevalence of CVD was 45.2% [16]. The lower prevalence in our study could be explained by the ethnic and geographical differences, lifestyle and Mediterranean dietary habits of the region. In addition, the direct comparison between the results of the different studies comes up against methodological differences in the patient's selection, the study design and the diagnosis methods of CVD.

In our study, age and hypertension were significantly associated with CVD in T2D patients, which is conform to literature data since they are well-established CV risk factors. Moreover, obesity and BMI were also significantly associated with CVD in T2D patients. Insulin resistance, which is the major pathophysiology of T2DM, has been considered a strong predictor of atherosclerotic CVD [17]. Insulin resistance is closely related to visceral adiposity and obesity, and it results in a wide range of deleterious metabolic derangements (hyperglycemia, hypertension, and dyslipidemia) that contribute to the development of atherosclerotic CVD [17]. Also, insulin resistance can be a process of physiological adaptation to protect against excess nutrient entry into cells and insulin-mediated metabolic stress [18]. According to this hypothesis, it may be prefer-

able to apply strategies of nutrient offloading, such as intensive lifestyle intervention and the use of GLP-1 RAs rather than high-dose insulin or sulfonylurea, to reduce the risk of CVD [17].

In our study, the LDL cholesterol control was suboptimal in all patients (25%) and in patients with a very high CV risk (22.2%) or with an established CVD (29.2%) despite a prescription of statins in the order of 95.8% in case of CVD. These results were also suboptimal compared to literature data. In the "DISCOVER" study, the LDL cholesterol control was achieved in 43.8% of patients [12]. In a British cohort study that included 292,170 PWD, the LDL cholesterol control was achieved in 90.4% [19]. In the Trial Evaluating Cardiovascular Outcomes With Sitagliptin (TECOS) conducted in T2D patients with CVD, the LDL cholesterol target was reached in 45.4% of patients [20]. Marson et al. [15] reported a control of LDL cholesterol in 30% (95% CI: 29–31) of patients. In the International Diabetes Management Practice Study (IDMPS), LDL cholesterol control was achieved in 33.2% [21]. This difference could be explained by the variation in the LDL threshold used in each study to define the LDL cholesterol control. In our study, LDL cholesterol control was defined by a level less than 0.7 g/L for high CV risk and less than 0.55 g/L for very high CV risk. Whereas, in the DISCOVER study [12] and the IDMPS [21], LDL cholesterol control was defined by a level less than 1 g/L and in the British cohort study [19] and the TECOS study [20] by a level less than 0.7g/L. This difference could also be explained by the suboptimal prescription of statins in all patients (43.9%), by the type of statin used since 20% of our patients were on low to moderate intensity statins and by treatment compliance.

Systolic blood pressure control was relatively better (61.7%) especially in patients with CVD (70.8%). These results are similar to the DISCOVER study results where SBP control was achieved in 67.5% of patients [12]. Furthermore, our results are better than the British cohort study [19], the TECOS study [20], the IDMPS [21] and the Marson et al. study [15] where the blood pressure control was respectively achieved in 29.8%; 57.9%; 19.2% and 44.3% of patients.

The proportion of controlled patients fell from 55% to 25% for LDL cholesterol and from 85.6% to 61.7% for SBP when proceeding to the intensified goals of STEP 2 according to the stepwise approach of the ESC guidelines [7]. This could be explained by therapeutic inertia but also by the lability of the therapeutic goals defined by the guidelines over the time.

The glycemic control defined by an HbA1c ≤ 8% was only seen in 44.4% of patients and this could be explained by the individualization of glycemic targets on the one hand and on the other hand by a selection bias since the majority of patients are referred in our consultation for a non-controlled diabetes. Our results are close to the British cohort study where glycemic control was achieved in 52% of patients [19] and better than the IDMPS, where glycemic control was achieved in 36.4% of patients [21]. Nevertheless, the HbA1c target was less than 7% in these studies.

The majority of our patients were non-smokers (92.2%). Our results were close to those reported in the literature with a proportion of non-smokers of 84.4% in the DISCOVER study [12], 86% in the British cohort study [19] and 88.6% in the TECOS study [20].

Optimal control of all CV risk factors was achieved in only 7.2% of all patients, and only in 8.3% of patients with CVD. This control was also suboptimal in the literature. Optimal control of CV risk factors was achieved in only 7.5% of patients in the British cohort study [19], and only in 3.6% in the IDMPS conducted in low- to middle-income countries [21]. The rate of optimal control of CV risk factors was relatively better in the DISCOVER study (21.5%) [12] and in the TECOS study (29.9%) [20].

The prescription OF CV medication was suboptimal in the whole studied population (57.2%). Only 43.9% of patients were on statin therapy, 43.9% on ACE inhibitors or ARBs and 11.2% on platelet aggregation inhibitors while 98.4% of patients had a high to very high CV risk. These data are comparable to those in the literature. In the DISCOVER study, the prescription of statins was in the order of 43.7% and the prescription of ACE inhibitors or ARBs in the order of 55.6% [12]. In the British cohort study, the prescription of statins was in the order of 51.9% and the prescription of ACE inhibitors or ARBs in the order of 46.8% [19]. In the CAPTURE study, the prescription of statins was in the order of 57.1% and of ACE inhibitors or ARBs in the order of 52.2% [13]. However, the prescription of platelet aggregation inhibitors was more frequent in the literature, in the order of 53.3% in the DISCOVER study [12] and 37.9% in the British cohort study [19] and 33.5% in the CAPTURE study [13].

Nevertheless, the prescription of statins, ACE inhibitors or ARBs in our study was significantly higher in patients with established CVD with higher prescription rates than those reported in the literature. Indeed, 95.8% of patients with established CVD were on statins in our study, while the proportion of patients on statins was 85.8% in the TECOS study [20], and 64.2% in the CAPTURE study [13]. Also, 91.7% of our patients were on IEC or ARBs, while the proportion of patients on IEC or ARBs was 79.5% in the TECOS study [20], and 62.3% in the CAPTURE study [13]. The prescription of platelet

aggregation inhibitors in patients with CVD was similar to the TECOS study (79.8%) [20] and superior to the CAPTURE study (57.1%) [13].

The control of CV risk factors is essential to reduce the risk of major CV events and death in T2D patients, both in primary and secondary prevention [20, 22, 23]. Despite the high level of evidence from landmark cardiovascular outcome trials and the recommendations of cardiovascular guidelines, the control of CV risk factors remains insufficient both in our study and in the literature.

In our study, despite optimal prescription of statins, ACE inhibitors or ARBs and platelet aggregation inhibitors in patients with established CVD, the rate of control of CV risk factors remains low with only 8.3% of patients having an optimal control of all CV risk factors. On the other hand, in our study as a whole, the rate of prescription of statins, ACE inhibitors or ARBs remains insufficient with regard to the large proportion of patients with a high to very high CV risk. These results could be explained by the inertia when considering proceeding to the intensified therapeutic goals, the joint patient's management with cardiologists without common consultation records, a large number of patients seen in consultation with delays in medical check-ups. In addition, treatment compliance in these patients who are often poly-medicated is not always optimal.

The prescription of GLAs with demonstrated CV benefit (GLP-1 RAs and/or SGLT2is) was also low at 5.6%. Weng et al. [16] reported a prescription of GLAs with demonstrated CV benefit < 12% in their study of prevalence of CVD in T2D patients. The prescription amounted to 21.9% of patients in the CAPTURE study [13].

In patients with CVD, the prescription of GLAs with demonstrated CV benefit in our study (20.8%) was similar to the CAPTURE study (21.5%) [13]. Marson et al. [15] reported a SGLT2is prescription of 27.7% (95% CI: 26.5–28.9) and GLP-1 RAs of 6.8% (95% CI: 6.2–7.4) in T2D patients with CVD.

The prescription of GLAs with demonstrated CV benefit in our study remains low with only one of five patients with CVD benefiting from these treatments.

Causes for this therapeutic inertia are complex, multifactorial, and can be explained by several raisons. At the system level, the cost of GLP-1 RAs and SGLT2is is high for patients living in low to middle-income countries. In Morocco the monthly cost is around 110 euros for GLP-1 RAs (liraglutide 1.2mg/day) and 45 euros for iSGLT2. GLP-1 RAs were not covered by health insurance until January 2022 and SGLT2is are still not coved by health insurance. At the patient level, fear of

side effects such as gastrointestinal disturbance and the subcutaneous route of administration of Liraglutide often discourage patients from accepting this medication. At the provider level, a large number of patients seen in each consultation do not allow the clinicians to develop and increase the patients' awareness of the benefits of these treatments. On the other hand, the lack of collaboration between cardiologist and endocrinologist and the lack of common electronic medical records to coordinate this collaboration may also contribute to this clinical inertia.

Otherwise, our study had some limitations due to the small size of the sample. The study was conducted in a single center because it is the only tertiary health care facility in the city of MEKNES and the only facility where complete medical records for patients can be provided. In addition, all of our patients benefit from health insurance coverage, which does not reflect the reality of PWD in the city of MEKNES. Also, the duration of the study was insufficient to have a greater enrollment for the group of patients in secondary prevention. Thus, these findings may not be generalizable.

Conclusions

The prevalence of CVD is high among T2D patients in the city of MEKNES. The majority of these patients have a high to very high CV risk. Our results and the literature results found that clinical inertia is a significant issue in the management of T2DM even at tertiary care teaching hospital, underlining a significant gap between the guidelines and the CV risk factors control seen in the T2D patient in real-world practice both in primary and secondary prevention. It is necessary to promote the "Treat to Target" strategy by coordinating cardiology and diabetology consultations via computerized consultation records and to define the best strategies to implement the most recent guidelines in daily clinical practice. The cost of these strategies must also be considered given that 80% of PWD live in low- to middle-income countries [21], so that they can be applied on a larger scale and will be not only cost-effective but also cost-saving for healthcare systems.

Conflict of interests

None declared.

REFERENCES

1. Einarson TR, Acs A, Ludwig C, et al. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007-2017. Cardiovasc Diabetol. 2018; 17(1): 83, doi: 10.1186/s12933-018-0728-6, indexed in Pubmed: 29884191.

2. Preis SR, Hwang SJ, Coady S, et al. Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes mellitus in the Framingham Heart Study, 1950 to 2005. Circulation. 2009; 119(13): 1728–1735, doi: 10.1161/CIRCULATIONAHA.108.829176, indexed in Pubmed: 19307472.

3. Gregg EW, Cheng YJ, Saydah S, et al. Trends in death rates among U.S. adults with and without diabetes between 1997 and 2006: findings from the National Health Interview Survey. Diabetes Care. 2012; 35(6): 1252–1257, doi: 10.2337/dc11-1162, indexed in Pubmed: 22619288.

4. Cefalu WT, Kaul S, Gerstein HC, et al. Cardiovascular Outcomes Trials in Type 2 Diabetes: Where Do We Go From Here? Reflections From a Editors' Expert Forum. Diabetes Care. 2018; 41(1): 14–31, doi: 10.2337/dci17-0057, indexed in Pubmed: 29263194.

5. Kristensen SL, Rørth R, Jhund PS, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet Diabetes Endocrinol. 2019; 7(10): 776–785, doi: 10.1016/S2213-8587(19)30249-9, indexed in Pubmed: 31422062.

6. Zelniker TA, Wiviott SD, Raz I, et al. Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus. Circulation. 2019; 139(17): 2022–2031, doi: 10.1161/CIRCULATIONAHA.118.038868, indexed in Pubmed: 30786725.

7. Visseren FLJ, Mach F, Smulders YM, et al. ESC Scientific Document Group. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021; 42(34): 3227–3337, doi: 10.1093/eurheartj/ehab484, indexed in Pubmed: 34458905.

8. American Diabetes Association, American Diabetes Association. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes — 2021. Diabetes Care. 2021; 44(Suppl 1): S125–S150, doi: 10.2337/dc21-S010, indexed in Pubmed: 33298421.

9. Gregg EW, Li Y, Wang J, et al. Changes in diabetes-related complications in the United States, 1990-2010. N Engl J Med. 2014; 370(16): 1514–1523, doi: 10.1056/NEJMoa1310799, indexed in Pubmed: 24738668.

10. Park JH, Ha KH, Kim BoY, et al. Trends in Cardiovascular Complications and Mortality among Patients with Diabetes in South Korea. Diabetes Metab J. 2021; 45(1): 120–124, doi: 10.4093/dmj.2020.0175, indexed in Pubmed: 33290647.

11. Gregg EW, Hora I, Benoit SR. Resurgence in Diabetes-Related Complications. JAMA. 2019; 321(19): 1867–1868, doi: 10.1001/jama.2019.3471, indexed in Pubmed: 30985875.

12. Patel KK, Gomes MB, Charbonnel B, et al. Global patterns of comprehensive cardiovascular risk factor control in patients with type 2 diabetes mellitus: Insights from the DISCOVER study. Diabetes Obes Metab. 2021; 23(1): 39–48, doi: 10.1111/dom.14180, indexed in Pubmed: 32845558.

13. Mosenzon O, Alguwaihes A, Leon JL, et al. CAPTURE Study Investigators. CAPTURE: a multinational, cross-sectional study of cardiovascular disease prevalence in adults with type 2 diabetes across 13 countries. Cardiovasc Diabetol. 2021; 20(1): 154, doi: 10.1186/s12933-021-01344-0, indexed in Pubmed: 34315481.

14. Rungby J, Schou M, Warrer P, et al. Prevalence of cardiovascular disease and evaluation of standard of care in type 2 diabetes: a nationwide study in primary care. Cardiovasc Endocrinol. 2017; 6(4): 145–151, doi: 10.1097/XCE.0000000000000135, indexed in Pubmed: 29276653.

15. Marson A, Raffoul N, Osman R, et al. Management of patients with type 2 diabetes and cardiovascular disease in primary care. Aust J Gen Pract. 2021; 50(4): 238–245, doi: 10.31128/AJGP-02-20-5222, indexed in Pubmed: 33786549.

16. Weng W, Tian Ye, Kong SX, et al. The prevalence of cardiovascular disease and antidiabetes treatment characteristics among a large type 2 diabetes population in the United States. Endocrinol Diabetes Metab. 2019; 2(3): e00076, doi: 10.1002/edm2.76, indexed in Pubmed: 31294089.

17. Yun JS, Ko SH. Current trends in epidemiology of cardiovascular disease and cardiovascular risk management in type 2 diabetes. Metabolism. 2021; 123: 154838, doi: 10.1016/j.metabol.2021.154838, indexed in Pubmed: 34333002.

18. Nolan CJ, Ruderman NB, Kahn SE, et al. Insulin resistance as a physiological defense against metabolic stress: implications for the management of subsets of type 2 diabetes. Diabetes. 2015; 64(3): 673–686, doi: 10.2337/db14-0694, indexed in Pubmed: 25713189.

19. Collins SÉ, Lethebe BC, Williamson T, et al. Cardiovascular risk factor control in British adults with diabetes mellitus: Retrospective cohort study. Endocrinol Diabetes Metab. 2020; 3(2): e00114, doi: 10.1002/edm2.114, indexed in Pubmed: 32318632.

20. Pagidipati NJ, Navar AM, Pieper KS, et al. TECOS Study Group. Secondary Prevention of Cardiovascular Disease in Patients With Type 2 Diabetes Mellitus: International Insights From the TECOS Trial (Trial Evaluating Cardiovascular Outcomes With Sitagliptin). Circulation. 2017; 136(13): 1193–1203, doi: 10.1161/CIRCULATIONAHA.117.027252, indexed in Pubmed: 28626088.

21. Chan JCN, Gagliardino JJ, Baik SH, et al. IDMPS Investigators. Multifaceted determinants for achieving glycemic control: the International Diabetes Management Practice Study (IDMPS). Diabetes Care. 2009; 32(2): 227–233, doi: 10.2337/dc08-0435, indexed in Pubmed: 19033410.

22. Gaede P, Lund-Andersen H, Parving HH, et al. Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med. 2008; 358(6): 580–591, doi: 10.1056/NEJMoa0706245, indexed in Pubmed: 18256393.

23. Rawshani A, Rawshani A, Franzén S, et al. Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2018; 379(7): 633–644, doi: 10.1056/NEJMoa1800256, indexed in Pubmed: 30110583.