



ELSEVIER

Contents available at [ScienceDirect](#)

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International
Diabetes
Federation



Current management and screening of peripheral and coronary artery disease in people with diabetes mellitus in Europe. The PADDIA/CADDIA survey

Guillaume Mahe ^{a,b,*}, Marianne Brodmann ^c, Davide Capodanno ^d, Antonio Ceriello ^e, Thomas Cuisset ^f, Victoria Delgado ^g, Christine Espinola-Klein ^h, Thomas W. Johnson ⁱ, Muriel Sprynger ^j, Naveed Sattar ^k, Oliver Schnell ^l, Paul Valensi ^m

^a Vascular Medicine and Investigation Department, INSERM CIC-1414, University of Rennes 2, M2S – EA 7470, F-35000 Rennes, France

^b Pôle imagerie médicale et explorations fonctionnelles, Hôpital Pontchaillou, 2 rue Henri Le Guilloux, Rennes F-35033, France

^c Division of Angiology, Department of Internal Medicine, Medical University Graz, Auenbruggerplatz 27, 8036 Graz, Austria

^d Division of Cardiology, Azienda Ospedaliero Universitaria Policlinico “G. Rodolico-San Marco”, University of Catania, Catania, Italy

^e IRCCS MultiMedica, Via Milanese, 300, 20099 Sesto San Giovanni, Milan, Italy

^f Département of Cardiology, Chu Timone, 264 Rue Saint-Pierre, 13005 Marseille, France

^g Department of Cardiology, Leiden University Medical Center, Albinusdreef 2, 2300 RC Leiden, the Netherlands

^h Department of Cardiology, University Medical Centre of the Johannes Gutenberg University, Mainz, Germany

ⁱ Bristol Heart Institute, University Hospitals Bristol & Weston NHS Foundation Trust, Bristol BS2 8HW, United Kingdom

^j Cardiology Department, University Hospital Sart Tilman, Bd de l'Hôpital, B4000 Liege, Belgium

^k Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, United Kingdom

^l Forschergruppe Diabetes e.V., Helmholtz Center, Munich Ingolstädter Landstr. 1, 85764 Munich – Neuherberg, Germany

^m AP-HP, Unit of Endocrinology-Diabetology-Nutrition, CRNH-IdF, CINFO, Paris 13 University, Jean Verdier Hospital, Bondy, France

ARTICLE INFO

Article history:

Received 30 September 2021

Received in revised form

9 January 2022

Accepted 18 January 2022

Available online 24 January 2022

ABSTRACT

Aims: This survey aimed to evaluate the current management and screening of coronary artery disease and peripheral artery disease in people with type 2 diabetes mellitus (T2DM) in Europe, utilizing the 2013 ESC/EASD (European Society of Cardiology/European Association for the Study of Diabetes) guidelines as a benchmark.

Methods: The PADDIA/CADDIA survey is a European medical research collaboration targeting cardiologists, vascular physicians, diabetologists and general practitioners from Austria, Belgium, France, Germany, Italy, Netherlands and United Kingdom.

Results: The questionnaire was completed by sixty-three physicians, of whom 75% declared assessing the cardiovascular risk of people with T2DM mostly without using a risk score (59%). More than 90% of the panel, check HbA1c, blood pressure and low-density lipoprotein cholesterol targets in their patients with T2DM and coronary or peripheral artery disease. For 94% the presence of T2DM influence their patients' management, by optimizing blood glucose, blood pressure and low-density lipoprotein cholesterol control. Only 37% considered screening for lower extremity peripheral artery disease among their T2DM

Keywords:

Diabetes

Coronary artery disease

Peripheral artery disease

Treatment

Atherosclerosis

* Corresponding author at: Vascular Medicine and Investigation Department, INSERM CIC-1414, University of Rennes 2, M2S – EA 7470, F-35000 Rennes, France. Pôle imagerie médicale et explorations fonctionnelles, Hôpital Pontchaillou, 2 rue Henri Le Guilloux, Rennes F-35033, France.

E-mail address: maheguillaume@yahoo.fr (G. Mahe).

<https://doi.org/10.1016/j.diabres.2022.109214>

0168-8227/© 2022 Elsevier B.V. All rights reserved.



patients and 35% among those with cardiovascular disease.

Conclusions: Physicians mostly follow the ESC/EASD 2013 guidelines, but when it comes to screening for additional conditions including coronary artery disease or peripheral artery disease, or intensifying the antithrombotic regimen there is need for better guidance.

© 2022 Elsevier B.V. All rights reserved.

1. Introduction

In 2019, the prevalence of diabetes worldwide was estimated at 463 million of people, with 90% having type 2 diabetes mellitus (T2DM), and concerningly half of individuals (50.1%) being unaware of their condition [1]. Cardiovascular disease (CVD) is one of the most important causes of morbidity and mortality in people with T2DM [2,3]. It is linked to accelerated atherosclerosis (i.e. coronary artery disease [CAD], carotid artery disease, lower extremity artery disease [LEAD] [4,5]) and people with T2DM are more likely to be hospitalized for conditions including heart failure, ischemic stroke, chronic kidney disease and lower limb amputation, compared with people without T2DM [6].

To limit the progression of CVD in people with T2DM, management of glucose control, as well as control of atherosclerotic risk factors with lifestyle modifications and drugs are required [1,4]. Furthermore, detection of CVD such as CAD, LEAD and carotid artery disease is important in people with T2DM [6–8].

To improve the management of those patients, recommendations have been proposed and updated by several international societies [4,9,10] – for example by updating targets in terms of blood pressure (BP) control or lipid levels in the latest 2019 ESC-EASD Guidelines [4].

Considering the higher risk of CVD associated with T2DM and aiming at promoting advancement of knowledge on all aspects of CVD and T2DM, the hypothesis that there may be a gap in the provision of screening and treatment of CAD and PAD (i.e. carotid artery disease and LEAD) in people with T2DM across different countries was worthy of exploration [24]. The aim of the PADDIA (Peripheral Artery Disease in DIAbetic patients)/CADDIA (Coronary Artery Disease in DIAbetic patients) survey was to evaluate physician awareness of the 2013 ESC/EASD guidelines [9] regarding the management of CVD in people with T2DM across Europe, and to put these practices in perspective of the newest ESC/EASD guidelines, which were published in 2019.

2. Materials & methods

A Steering Committee (SC) was constituted to lead the PAD-DIA/CADDIA project, with at least one representative per nation involved (Austria, Belgium, France, Germany, Italy, Netherlands and United Kingdom). Members of the SC were selected based on their publication track and expertise in the cardiovascular and diabetes fields.

This project consisted of establishing a snapshot, in patients with T2DM, of contemporary clinical practices in the management of their respective CVD risk, and based on

this observational data, to propose ways of improvement, in the light of the most recent ESC-EASD Guidelines published in 2019 [4]. In order to assess current clinical practices, an online survey was conducted in spring 2019. The survey was designed using Delphi method involving six stages [25]:

- (1) identifying a need for further research – Can we improve CVD prevention in people with T2DM?;
- (2) completing a literature search on PAD and CAD management in people with T2DM. Selection of the papers was made by location of the study (Europe and United States), date of publication (only articles published in the last 5 years). PubMed and Cochrane database have been used to perform this literature review;
- (3) developing a questionnaire of statements. Based on relevant literature reviews and clinical expertise of the SC members, a questionnaire was elaborated to analyze current practice in PAD and CAD management in patients with T2DM. Each SC member was asked to propose 10 questions. After compiling these questions by topic, the SC agreed on 28 questions. These questions, grouped in 5 sections (physician's profile, risk evaluation, analyses, treatment, procedures & follow-up, see Supplementary material) were submitted to European physicians, including cardiologists, vascular physicians, diabetologists and GPs from the 6 involved countries: Austria, Belgium, France, Germany, Italy, and United Kingdom;
- (4) conducting anonymous iterative mail or e-mail questionnaire rounds; a link for the survey was sent to the Diabetes and CardioVascular Disease (D&CVD) EASD study group members (approximately 200 people), and we bought an e-mail list address of European specialists (cardiologists, diabetologists, vascular physicians) containing around 2000 e-mails,
- (5) providing individual and/or group feedback between questionnaire rounds;
- (6) summarizing the findings without meeting nor direct interaction of the voting participants . [15,16]

The questionnaire was available online, in English, from 18 April to 19 August 2019 for the round of voting.

Data analysis: The results were anonymous and analyzed in aggregate only. Results are expressed in percent. Consensus agreement was based on a 2/3 majority responders.

3. Results

The online survey was open for 4 months. We excluded questionnaires not fulfilling at least the “risk evaluation” section.

Our analysis is therefore based on 63 physicians, from France (35%), Austria (25%), Italy (17%), Germany (8%), United Kingdom (8%) and Belgium (6%). The physicians' specialties were cardiology in the majority (46%), vascular medicine (14%), cardiology and vascular medicine (17%), diabetology (13%) and general practice with a subspecialty in vascular medicine (10%).

3.1. Cardiovascular risk evaluation and management of risk factors

Among this panel, 84% of the physicians reported using the 2013 ESC/EASD guidelines on diabetes, prediabetes and CVD in their daily practice, and 75% routinely evaluated cardiovascular (CV) risk for people with diabetes. Even though no specific risk score among Framingham (16%), SCORE (27%), UKPDS (11%), QRISK 1 (8%), ADVANCE (2%), CAC (11%) was preferred. Fifty-nine percent of physicians answered that no risk score was used. In the questionnaire, most physicians reported they check HbA1c levels (93%), systolic blood pressure (BP) (95%), LDL-c levels (92%), total cholesterol (85%), triglycerides (81%), HDL-c (76%), body mass index (78%), and microalbuminuria (73%) in their population with diabetes. Of interest, 94% of the physicians answered they modify their cardiovascular disease management for people with known or with newly diagnosed T2DM. Changes included: optimizing T2DM therapies (79%), considering lower LDL-c targets (74%) and lower BP targets (65%). Forty-eight percent of the physicians considered changing the antiplatelet regimens. Eleven percent of the physicians considered the non-HDL-c goal; and in case of proteinuria (routinely checked by 79%), 82% began Angiotensin-Converting Enzyme Inhibitor (ACEi) or Angiotensin Receptor Blocker (ARB), 42% referred the patient to diabetes team, 44% to a nephrologist (i.e. Table 1).

3.2. T2DM and Peripheral Artery Diseases (carotid artery disease and lower extremity peripheral artery disease) assessment

In people with T2DM, most (70%) physicians consider screening for lower extremity PAD mainly in patients with typical symptoms (e.g. claudication, wounds...), but some (37%), screen all patients with diabetes. In other potential responses, 25% would screen every patient with T2DM and older than 50 years, 35% every patient with known CVD and T2DM, 22% in patients with T2DM and a family history of early CVD and 22% in patients with T2DM duration > 10 years (i.e. Table 2). There is no single preferred screening method to detect PAD. Fifty seven percent check the pulses, 58% measure the ankle-brachial index (ABI), 58% perform a Doppler Ultrasound (DUS) examination and 15% measure the toe-brachial index (TBI) (Fig. 1). Fifty-five percent of the physicians declared checking for lower extremity PAD once a year, 20% every two years and 23% only in patients with symptoms.

Physicians reported they screen for carotid artery disease mainly in people with typical symptoms (e.g. suspected neurological symptoms, patient with cervical systolic murmur...) (58%), and many of them screen for atherosclerotic carotid disease in all patients with T2DM (32%), all patients older than 50 years (37%), all patients with CVD (47%), all patients

with a family history of premature CVD (43%), and people with >10 years of T2DM (31%) (i.e. Table 2).

3.3. T2DM and CAD assessment

Responding physicians reported they screen for significant CAD patients with T2DM and other forms of CVD (84%), typical chest pain (79%), 2 or more risk factors like hypertension and hypercholesterolemia (71%), proteinuria or renal failure (65%), T2DM for >20 years (56%), microalbuminuria (42%) and some physicians also reported they assess for CAD patients without symptoms (29%) (i.e. Table 3). In a patient with T2DM and elevated CV risk, as depicted by systolic BP at 155 mmHg and total cholesterol level at 6.4 mmol/L (115.3 mg/dl), 70% of responding physicians would screen for CAD. In that case, they are more likely to perform an exercise stress electrocardiogram test (70%). In patients with lower extremity PAD, 88% of physicians said they also screen for CAD, but there is no preferred method here (i.e. Table 3).

3.4. Treatment management and follow-up for CAD and PAD

As above mentioned, 94% of the physicians would modify their CVD management in a patient with diabetes, but in CAD or PAD patients under 80 years of age, the objectives of HbA1c, BP and LDL-cholesterol appear heterogeneous (i.e. Fig. 1).

Before coronary angiography, 70% of the responding physicians would routinely stop metformin if their diabetic patients were on this drug. After coronary angiography, 82% of the physicians said they monitor the renal function in patients on glucose-lowering drugs.

In patients with CAD undergoing coronary angiography with or without revascularization, physicians routinely prescribe statins (89%), single antiplatelet therapy using aspirin (74%), renin-angiotensin-aldosterone system inhibitors (72%), beta-blockers (47%), dual antiplatelet therapy with aspirin and a P2Y12 inhibitor (16%).

In the case of acute coronary syndrome, the preferred duration of treatment with dual antiplatelet therapy is ≥ 12 months (44% of the responders).

In patients with symptomatic PAD and low bleeding risk, the preferred antiplatelet/ antiplatelet + anticoagulant drugs were said to be aspirin 80 – 100 mg once daily (43%), clopidogrel 75 mg once daily (32%), and aspirin 100 mg once daily + rivaroxaban 2.5 mg twice daily (26%).

In patients with CAD (asymptomatic for at least 12 months, with no atrial fibrillation and low bleeding risk), the preferred antiplatelet treatment is aspirin 80 – 100 mg once daily (68%), clopidogrel 75 mg once daily (19%) (i.e. Table 4).

The algorithm proposed in Fig. 2 represents the current management and screening of PAD and CAD in people with T2DM in Europe.

4. Discussion

To the best of our knowledge, this is the first survey that asks about the management of PAD and CAD in T2DM patients by

Table 1 – Cardiovascular risk evaluation and management of risk factors.

Questions	Answers	%
Do you use the ESC/EASD guidelines on diabetes, prediabetes and cardiovascular disease in your daily practice?	Yes No	84% 16%
Do you routinely evaluate cardiovascular risk for your patients with diabetes?	No Yes	25% 75%
How do you evaluate this cardiovascular risk?	Framingham score SCORE UKPDS QRISK 1 ADVANCE CAC Score No score needed	16% 27% 11% 8% 2% 11% 59%
Do you alter the management of CV disease/Lower extremity PAD if your patients have known or have newly-diagnosed T2DM?	No Yes	6% 94%
If you have to alter the management of your CV disease/ Lower extremity PAD patients, in which way will you do it?	Consider optimising T2DM therapies Consider stricter LDL-C targets Consider non-HDL-C goal Consider stricter BP targets Consider altering anti-platelets regimens	79% 74% 11% 65% 48%
In CAD-PAD patients, what do you check?	HbA1c Blood Glucose Systolic BP Triglycerides Total Cholesterol HDL-C LDL-C Non-HDL-C Apo B Proteinuria BMI Microalbuminuria	93% 69% 95% 81% 85% 76% 92% 32% 12% 64% 78% 73%
Do you routinely check for proteinuria in your diabetic patients?	Yes No	79 % 21 %
In the presence of proteinuria, you would consider:	Starting ACEi/ARB Lowering systolic BP under 130 mmHg Referral to diabetic team Referral to nephrologist No further action Don't know	82% 68% 42% 44% 2% 0%

ESC = European society of Cardiology; EASD = European Association for the Study of Diabetes; SCORE = Systematic coronary risk evaluation; UKPDS = United Kingdom Prospective Diabetes Study; QRISK 1 = cardiovascular disease risk algorithm; ADVANCE = Action in Diabetes and Vascular disease: preterAx and diamicroN mr Controlled Evaluation; CAC score = Coronary Artery Calcium score; CV = Cardiovascular; PAD = Peripheral Artery Disease; T2DM = Type 2 Diabetes Mellitus; LDLc = low-density lipoprotein cholesterol; HDLc = High-density lipoprotein cholesterol; BP = Blood Pressure; CAD = Coronary Arterial Disease; HbA1c = Glycated Hemoglobin Type A1C; BP = Blood Pressure; Apo B = apolipoprotein B; BMI = Body Mass Index; ACEi = Angiotensin Converting Enzyme Inhibitor; ARB = Angiotensin Receptor Blocker; mmHg = millimeter of mercury.

The numbers in bold correspond to a consensus agreement based on a 2/3 majority responders.

Table 2 – T2DM and Peripheral Artery Diseases assessment.

Questions	Answers (not mutually exclusive)	%
For which T2DM patients would you consider screening for lower extremity PAD?	In patients with typical symptoms (claudication, wounds...) All patients Every patient with T2DM and age of > 50yrs Every patient with CVD and T2DM In patients with T2DM and a positive family history of PAD In patients with > 10 years of diabetes	70% 37% 25% 35% 22% 22%
What is your screening method for lower extremity PAD in diabetic patients?	Checking the pulses Ankle-brachial index (ABI) Duplex ultrasound (DUS) Toe-brachial index (TBI)	57% 58% 58% 15%
How often do you check for lower extremity PAD in your patients with DM?	Once a year Every 2 years Only in patients with symptoms	55% 20% 23%
For which T2DM patients would you consider screening for atherosclerotic carotid disease?	In patients with neurological symptoms All patients Every patient with T2DM and age of > 50yrs Every patient with CVD and T2DM In patients with T2DM and a positive family history of atherosclerosis carotid disease In patients with > 10 years of diabetes	58% 32% 37% 47% 47% 31%

T2DM = Type 2 Diabetes Mellitus; PAD = Peripheral Artery Disease; CVD = Cardiovascular Disease.

The numbers in bold correspond to a consensus agreement based on a 2/3 majority responders.

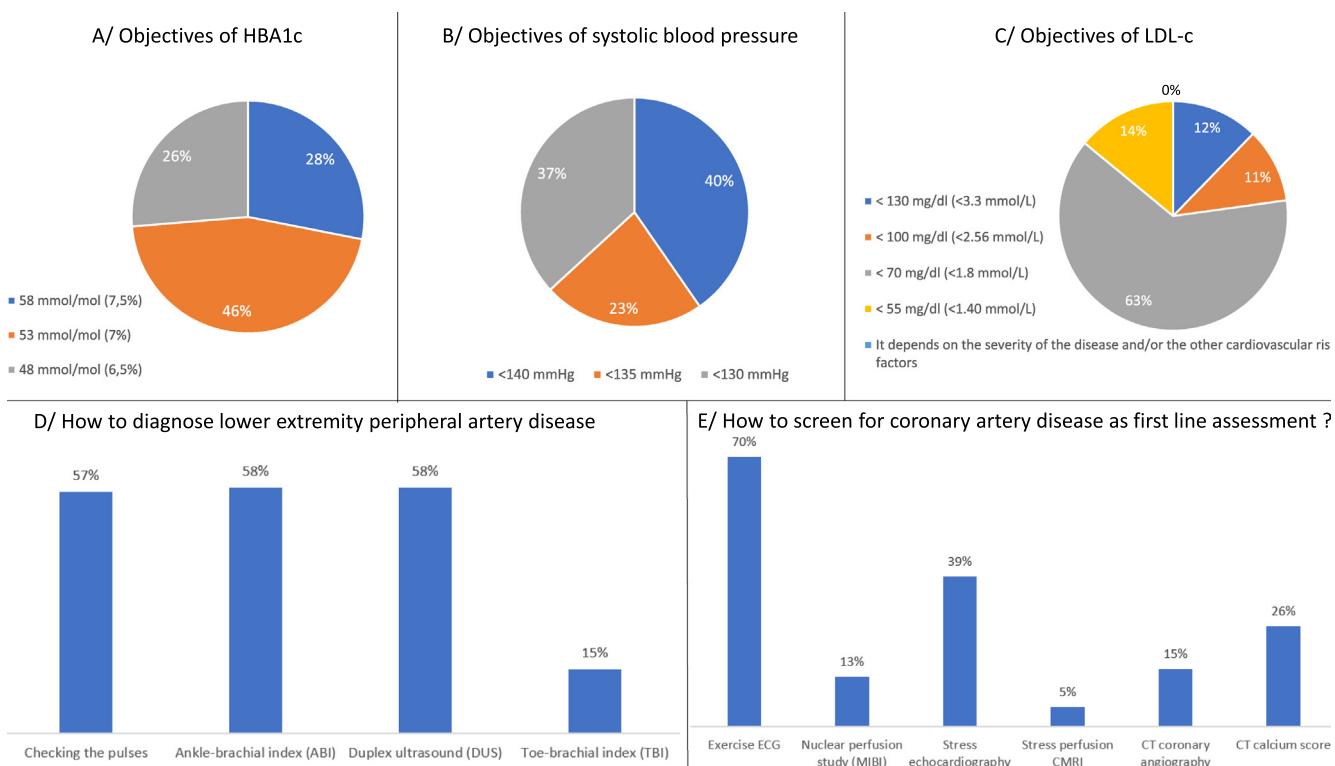


Fig. 1 – Results of the survey about the objectives of HbA1c, systolic blood pressure and LDLc and diagnosis methods in patients with Coronary Artery Disease/ Peripheral Artery Disease under 80 years-old AND diabetes.

physicians from different countries and specialties. This point is very interesting since it reflects the real-life management of those patients in European countries. We show that the management of some points is homogeneous. For other points there are discrepancies among physicians' choice, even though several guidelines exist [4,9,10].

A large majority (84%) of this panel uses the ESC/EASD guidelines published in 2013 [9]. This is not surprising because all the physicians come from European countries and this survey was performed before the release of the new ESC/EASD guidelines published in 2019 [4]. Thus, responses obtained in this survey must be analyzed according to the 2013 ESC/EASD guidelines [9].

The concept of CV risk assessment in patients with T2DM, recommended by all scientific societies, is well-acknowledged by this European panel, since 75% of them perform such assessment [9,10]. A majority of physicians answered that no score is needed for the CV risk assessment [11]. Indeed, the recommendations proposed to classify T2DM patients as high or very high-risk patients depending on the presence of concomitant risk factors or target organ damage without the need for any score. More precisely the new 2019 guidelines have introduced a class of moderate risk for some patients with diabetes: young patients (Type 1 diabetes under <35 years of age or T2DM under <50 years of age) with a disease duration shorter than 10 years and without any other risk factors [4]. So, these guidelines stratify the CV risk in 3 classes (moderate, high, or very high) but again without using any score [4]. According to the ESC, SCORE must not be used for diabetic patients.

Furthermore, our study suggests that physicians are aware of the morbidity and mortality in patients with T2DM and CVD. Almost all of them (94%) answered that the presence of T2DM in a patient with CVD modifies their management. Indeed, in case of T2DM, physicians considered optimizing the glucose-lowering therapies, in line with current guidelines [4,9]. However, the HbA1c target appears to be less clear to this panel of physicians even if most of them (74%) considered the HbA1c target equal to 7.0% or 7.5% (Fig. 1) whereas the guidelines said $\leq 7\%$ for most patients. This target aims at decreasing the risk of microvascular complications. To assess the deleterious effect of T2DM, most physicians paid attention to target organ damage by measuring microalbuminuria (73%) and proteinuria (79%) [12,13]. This has been emphasized in the latest 2019 ESD-EASD Guidelines specifying that routine assessment of microalbuminuria is indicated to identify patients at risk of developing renal dysfunction or at high risk of future CV disease [4]. The presence of microalbuminuria is associated with the start of ACEi/ ARB therapies which is in line with the guidelines [4,9]. In addition, physicians consider also stricter LDL-c and BP targets in patients with CVD and T2DM. LDL-c targets have been lowered in the 2019 ESC-EASD guidelines with a new target ≤ 1.40 mmol/l (≤ 55 mg/dl) in very high-risk patients whereas the target was <1.8 mmol/L (<70 mg/dl) in 2013. The 2013 LDL-c target was the choice of 63% physicians. The systolic BP target has been reduced from <140 mmHg to <130 mmHg if well tolerated and the diastolic BP from <85 mmHg to <80 mmHg [4,9]. Furthermore, this management in T2DM patients is confirmed by the parameters checked by the physicians that are

Table 3 – T2DM and CAD assessment.

Questions	Answers	%
When do you evaluate the presence of significant coronary artery disease (CAD) in your T2DM patients?	An asymptomatic patient without target organ damage Patients with T2DM and typical chest pain Patient with T2DM and other forms of CV disease Proteinuria or renal failure Microalbuminuria Two risk factors like hypertension and hypercholesterolemia T2DM duration over 20 years	29% 79% 84% 65% 42% 71% 56%
In a patient with T2DM and elevated CV risk (systolic BP 155 mmHg & total cholesterol 6.4 mmol/L (e.g 250 mg/dL)) would you routinely screen for CAD?	No Yes	30% 70%
How would you screen for CAD as first line assessment?	Exercise ECG Nuclear perfusion study (MIBI) Stress echocardiography Stress perfusion CMRI CT coronary angiography CT calcium score	70% 13% 39% 5% 15% 26%
In T2DM patients with lower extremity PAD, do you screen your patients for CAD?	No, if they are asymptomatic	12%
How do you screen CAD in T2DM patients with lower extremity PAD?	Yes with stress ECG (1st line) with stress echo or stress myocardial nuclear imaging (1st line) with coronary CT-scan (1st line) with CT calcium score with coronary angiography (1st line) I send the patient to the cardiologist (I'm not a cardiologist)	88% 37% 47% 14% 14% 5% 24%

T2DM = Type 2 Diabetes Mellitus; CAD = Coronary Arterial Disease; CV = Cardiovascular; ECG = Electrocardiogram; CT = computerized tomography; PAD = Peripheral Artery Disease.

The numbers in bold correspond to a consensus agreement based on a 2/3 majority responders.

Table 4 – Treatment management and follow-up for CAD and PAD with TDM2.

Questions	Answers	%
In CAD-PAD patients under 80 years of age, what is your objective of HbA1c?	58 mmol/mol (7.5%) 53 mmol/mol (7%) 48 mmol/mol (6.5%)	28% 46% 26%
In CAD-PAD patients under 80 years of age, what is your objective of systolic BP?	<140 mmHg <135 mmHg <130 mmHg <130 mg/dl (<3.3 mmol/L) <100 mg/dl (<2.56 mmol/L) <70 mg/dl (<1.8 mmol/L) <55 mg/dl (<1.40 mmol/L)	40% 23% 37% 12% 11% 63% 14%
In CAD-PAD patients, what is your optimal LDL-c goal?	It depends on the severity of the disease and/or the other CV risk factors	0%
Do you routinely stop biguanides (e.g., metformin...) in T2DM patients before coronary angiography?	No Yes	30% 70%
To your patients with T2DM with CAD undergoing coronary angiography with or without revascularization, do you routinely prescribe?	Beta-blockers ACEi or ARB Statins Single antiplatelet therapy with aspirin Dual antiplatelet therapy with aspirin and a P2Y12 inhibitor None of these	47% 72% 89% 74% 16% 5%
Do you routinely monitor the renal function after coronary angiography in diabetic patients on glucose-lowering drugs?	No Yes	18% 82%
What is the optimal duration of dual therapy (antiplatelet + antiplatelet or anticoagulant therapy) for T2DM in patients after acute coronary syndrome (ACS)?	≤3months 3–6 months 6–12 months ≥12 months Aspirin 80–100 mg OD Aspirin 80 mg BID Clopidogrel 75 mg OD Aspirin 80 mg OD + Clopidogrel 75 mg OD Aspirin 100 mg OD + Rivaroxaban 2.5 mg BID I would ask the cardiologist (I am not a cardiologist)	7% 18% 32% 44% 61% 7% 19% 7% 12% 9%
In T2DM patients with CAD (asymptomatic for > 12 months, no atrial fibrillation and low bleeding risk), which antiplatelet drug(s) do you prefer?	Aspirin 80–100 mg OD Aspirin 80 mg BID Clopidogrel 75 mg OD Aspirin 80 mg OD + Clopidogrel 75 mg OD Aspirin 100 mg OD + Rivaroxaban 2.5 mg BID I would ask the cardiologist (I am not a cardiologist)	39% 4% 32% 14% 26% 9%
In T2DM patients with symptomatic PAD and low bleeding risk, which antiplatelet drug(s) do you prefer to use?	Aspirin 80–100 mg OD Aspirin 80 mg BID Clopidogrel 75 mg OD Aspirin 80 mg OD + Clopidogrel 75 mg OD Aspirin 100 mg OD + Rivaroxaban 2.5 mg BID I would ask the cardiologist (I am not a cardiologist)	39% 4% 32% 14% 26% 9%

CAD = Coronary Arterial Disease; PAD = Peripheral Artery Disease; BP = Blood Pressure; LDL-c = Low-Density Lipoprotein Cholesterol; CV = Cardiovascular; T2DM = Type 2 Diabetes Mellitus; ACEi = Angiotensin-Converting Enzyme inhibitor; ARB = Angiotensin Receptor Blocker. OD : Once a day; BID : Twice a day

The numbers in bold correspond to a consensus agreement based on a 2/3 majority responders.

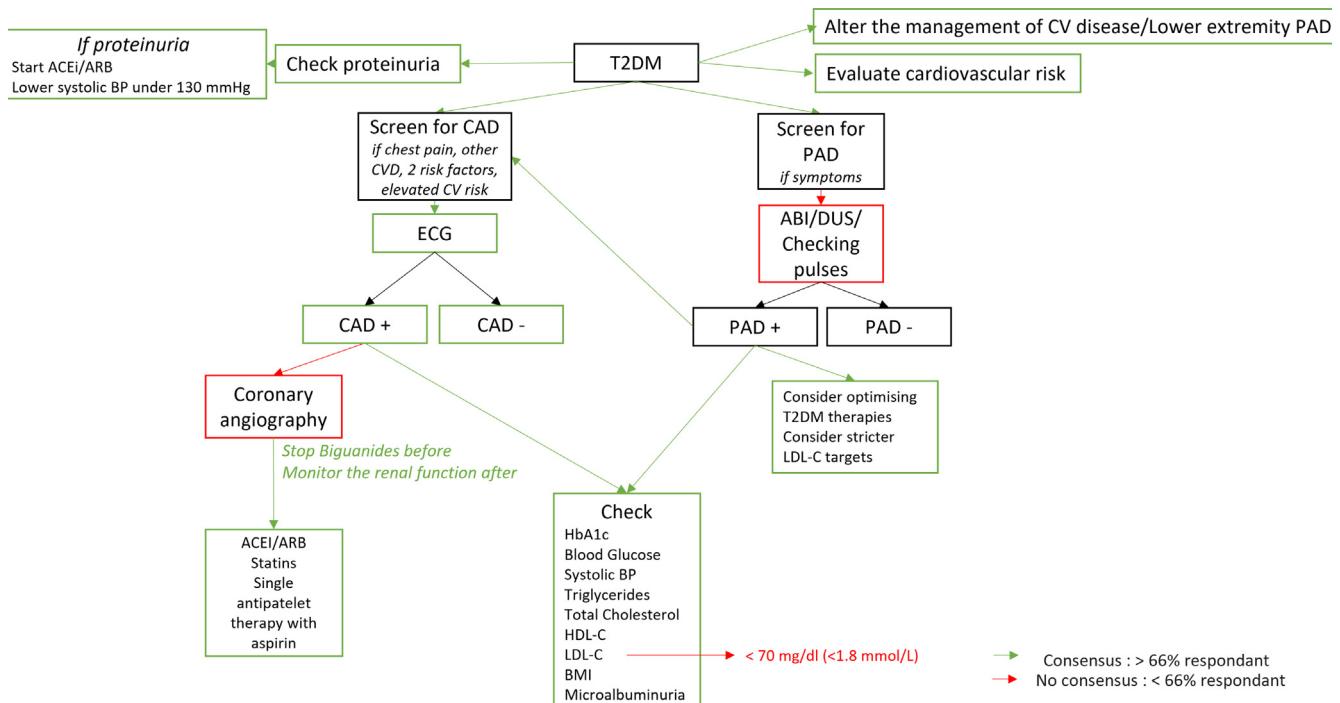


Fig. 2 – Current management and screening of PAD and CAD in people with T2DM in Europe. **Fig. 2 legend:** T2DM = Type 2 Diabetes Mellitus; CAD = Coronary Artery Disease; PAD = Peripheral Artery Disease (i.e. carotid artery disease and lower extremity artery disease); ECG = Electrocardiogram; ACEi = Angiotensin-Converting Enzyme Inhibitors; ARB = Angiotensin Receptor Blockers, ACS = Acute Coronary Syndrome, CCTA = Coronary Computed Tomography Angiography, HDL-c = High Density Lipoprotein cholesterol, LDLc = Low-Density Lipoprotein cholesterol, UKPDS = United Kingdom Prospective Diabetes Study.

for the most important systolic BP (95%), HbA1c (93%), and LDL-c (92%) (i.e. Table 1).

A majority of physicians also prescribed the appropriate treatment in patients with diabetes and CAD undergoing coronary angiography with or without revascularization [4,9]. They also monitored the renal function after angiography because of a high risk of contrast-induced nephropathy [14]. Other points of management were less consensual. The first issue is when physicians should screen for CAD, carotid artery disease or LEAD. Among the six possible answers for each question, the majority of physicians (58 to 79%) answered they assessed for CVD in the case of symptoms suggesting CVD. A lower proportion of physicians would consider exploring every patient with T2DM for CAD, carotid artery disease and LEAD in 29%, 32% and 37% respectively. The 2013 guidelines recommended clinical screening to detect LEAD every year whereas the frequency of the assessment was less clear for carotid artery disease in 2019 [4]. Regarding screening for CAD the effectiveness and the method to detect silent CAD are controversial [15,16]. Some practitioners may refer their patients to a cardiologist for screening and the cardiologist chooses the method. Anyway the method of screening must be adapted to the patient and the local situation. Screening for CAD was mentioned in the 2013 guidelines to be considered in selected high-risk patients. This point was confirmed in the 2019 guidelines which stipulates first to stratify the CV risk, using risk modifiers like Coronary Artery Calcium score, Coronary Computed Tomography Angiogra-

phy (CCTA) or Ankle-Brachial Index (ABI), and then to screen for CAD only very high-risk patients (LEAD, high CAC score, proteinuria or renal failure) [4]. In addition our panel (70%) was more likely to propose an exercise electrocardiogram as the first-line tool whereas a study showed that sensitivity and specificity of this test are not optimal (47% and 81%, respectively) when compared to coronary angiography in asymptomatic patients with T2DM [17]. In line with that, according to the latest 2019 ESC-EASD guidelines, stress testing including functional imaging or Coronary computed tomography angiography (CCTA) may be indicated for screening CAD. How to screen for LEAD is another issue. Checking the arterial pulses and measuring ABI were proposed by the majority of physicians and are in agreement with the guidelines even if the choice of the ABI instead of TBI is debatable in this specific population with a high risk of calcified arteries [18,19].

The last issue is the antithrombotic therapy. For the T2DM patients with PAD, physicians are broadly equally split between the use of aspirin alone, clopidogrel alone or the association rivaroxaban-aspirin. This can be explained by the results of the CAPRIE trial for the use of clopidogrel alone whereas the association rivaroxaban-aspirin is supported by the results of the COMPASS trial [20,21]. A subgroup analysis of T2DM patients in the COMPASS trial that was prespecified in the protocol strengthens this interest for the use of this association [22]. The duration of dual therapy (i.e. antiplatelet + antiplatelet or anticoagulant therapy) remains controversial

since only 44% would have maintained the treatment over 12 months as recommended in T2DM in patients after acute coronary syndrome (ACS) [23] (i.e. Table 4).

Limitations: The main limitation of this study is the small number of participating physicians. This can be explained by the way of distributing the survey by email and within a short period. However, even with this small number of participants the survey shows that there appears to be some disparities in the management of T2DM patients. The small number of responders precluded the possibility to analyze the results according to specialties. A second limitation was the limited number ($n = 28$) of questions that were asked. This was a choice of the steering committee to try to obtain a maximal number of responders. The last limitation was the quite small number of countries involved in this survey. Only six countries from Europe participated. Therefore, the results of the present study cannot be extrapolated to the whole Europe countries. The study strengthens the importance of doing such study in a larger number of countries to assess whether or not management of patients with cardiovascular diseases and diabetes might be improved.

To conclude, despite all the relevant caveats in the conduct of this survey, this study suggests that the management of people with diabetes appears broadly consistent with relevant guidelines. Discrepancies in the management remain largely in areas of clinical uncertainty for which more evidence is needed.

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.

Acknowledgements

Medical writing assistance with the preparation of this manuscript was provided by KPL.

Funding

The authors received no funding from an external source.

REFERENCES

- [1] Williams R, Karuranga S, Malanda B, Saeedi P, Basit A, Besançon S, et al. Global and regional estimates and projections of diabetes-related health expenditure: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Practice*. 2020;162.
- [2] Preis SR, Hwang S-J, Coady S, Pencina MJ, D'Agostino RB, Savage PJ, et al. Trends in All-Cause and Cardiovascular Disease Mortality among Women and Men with and without Diabetes in the Framingham Heart Study, 1950–2005. *Circulation* 2009;119(13):1728–35.
- [3] Leon BM. Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations and future research. *WJD* 2015;6(13):1246. <https://doi.org/10.4239/wjd.v6.i13.1246>.
- [4] Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J* 2020;41(2):255–323.
- [5] The Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet*. 2010;375(9733):2215–22.
- [6] Hoke M, Schillinger M, Minar E, Goliasch G, Binder CJ, Mayer FJ. Carotid ultrasound investigation as a prognostic tool for patients with diabetes mellitus. *Cardiovasc Diabetol* 2019;18:90.
- [7] Association AD. Peripheral Arterial Disease in People With Diabetes. *Diabetes Care* 2003;26(12):3333–41.
- [8] Bax JJ, Young LH, Frye RL, Bonow RO, Steinberg HO, Barrett EJ. Screening for Coronary Artery Disease in Patients With Diabetes. *Diabetes Care* 2007;30(10):2729–36.
- [9] ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. The Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *Revista Española de Cardiología (English Edition)*. 67(2):2014;136.
- [10] Association AD. 7. Diabetes Technology: Standards of Medical Care in Diabetes—2020. *Diabetes Care*. 43(Supplement 1):2020;S77–88.
- [11] Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016;37(29):2315–81.
- [12] Mogensen CE. Microalbuminuria Predicts Clinical Proteinuria and Early Mortality in Maturity-Onset Diabetes. *N Engl J Med* 1984;310(6):356–60.
- [13] Pontremoli R. Microalbuminuria Is an Early Marker of Target Organ Damage in Essential Hypertension. *Ame J Hypertens* 1998;11(4):430–8.
- [14] Gami AS, Garovic VD. Contrast Nephropathy After Coronary Angiography. *Mayo Clinic Proc* 2004;79(2):211–9.
- [15] Young LH, Wackers FJT, Chyun DA, Davey JA, Barrett EJ, Taillefer R, et al. Cardiac Outcomes After Screening for Asymptomatic Coronary Artery Disease in Patients With Type 2 Diabetes: The DIAD Study: A Randomized Controlled Trial. *JAMA* 2009;301(15):1547. <https://doi.org/10.1001/jama.2009.476>.
- [16] Cosson E, Nguyen MT, Chanu B, Banu I, Chiheb S, Balta C, et al. Cardiovascular risk prediction is improved by adding asymptomatic coronary status to routine risk assessment in type 2 diabetic patients. *Diabetes Care* 2011;34(9):2101–7.
- [17] Valensi P, Henry P, Boccardo F, Cosson E, Prevost G, Emmerich J, et al. Risk stratification and screening for coronary artery disease in asymptomatic patients with diabetes mellitus: Position paper of the French Society of Cardiology and the French-speaking Society of Diabetology. *Diabetes Metabol* 2021;47(2).
- [18] Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: Executive Summary. *Circulation* 2017;135(12):e686–725.
- [19] Aboyans V, Ricco J-B, Bartelink M-LEL, Björck M, Brodmann M, Cohnert T, et al. 2017 ESC Guidelines on the Diagnosis and

Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). *Eur Heart J* 2018;39(9):763–816.

[20] A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *The Lancet*. 348 (9038):1996;1329–39.

[21] Eikelboom JW, Connolly SJ, Bosch J, Dagenais GR, Hart RG, Shestakova O, et al. Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease. *N Engl J Med* 2017;377 (14):1319–30.

[22] Bhatt DL, Eikelboom JW, Connolly SJ, Steg PG, Anand SS, Verma S, et al. Role of Combination Antiplatelet and Anticoagulation Therapy in Diabetes Mellitus and Cardiovascular Disease: Insights From the COMPASS Trial. *Circulation* 2020;141(23):1841–54.

[23] Roffi M, Patrono C, Collet J-P, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2016;37 (3):267–315.

[24] Khunti K, Ceriello A, Cos X, De Block C. Achievement of guideline targets for blood pressure, lipid, and glycaemic control in type 2 diabetes: A meta-analysis. *Diabetes Res Clin Practice* 2018;137:137–48.

[25] Okoli C, Pawlowski SD. The Delphi method as a research tool: an example, design considerations and applications. *Informat Manage* 2004;42(1):15–29.