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Short Communication

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The 2019 ESC Guidelines for the Management of Diabetes and Dyslipidaemias – What is New from the Hypertensive Patient's Perspective?

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Abstract:

While the previous ESC guidelines on diabetes [1] and dyslipidaemias [2] had been published relatively recently, new emerging evidence regarding the effect and management of diabetes and dyslipidaemias in cardiovascular (CV) patients have warranted an update of these guidelines. On one hand, studies have confirmed the key role of low-density-lipoprotein (LDL) cholesterol in atherogenesis [3] and thus in CV disease, therefore justifying the proposal of new LDL-C goals and a revised CV risk classification. On the other hand, new studies on therapies for diabetes mellitus (DM) have shown CV benefit, requiring their incorporation into clinical practice guidelines.

Keywords: cardiovascular risk, low density lipoprotein-cholesterol, SGLT2

The 2019 ESC guidelines on dyslipidaemias:

As far as risk assessment is concerned, the SCORE (systematic coronary risk estimation) risk charts have been updated (Figure 1), by extending the age from 65 to 70 and by removing the cholesterol band of 8 mmol/l, since these patients are already considered at high risk. Hypertensive patients don't represent a separate population in the 2019 guidelines. The SCORE charts incorporate the interaction between blood pressure (BP) and each of the other risk factors.

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The CV risk classification has been slightly modified (Table 1):

Most hypertensive patients will thus fall in the moderate-, high- or very high-risk category. For patients with high BP, the new guidelines maintain the previous recommendations with respect to cessation of smoking, having a body mass index of 20-25 kg/m^2, performing 30-60 minutes of physical activity daily and having a blood pressure target <140/90 mm Hg (with lower treatment targets in most patients provided that treatment is well tolerated). However, lipid levels targets changed significantly in the new guidelines:

- LDL-C: treatment goals for LDL-C are summarised in Table 2
- Non-HDL-C (high-density lipoprotein cholesterol) goals are <2.2, 2.6, and 3.4 mmol/L (<85,

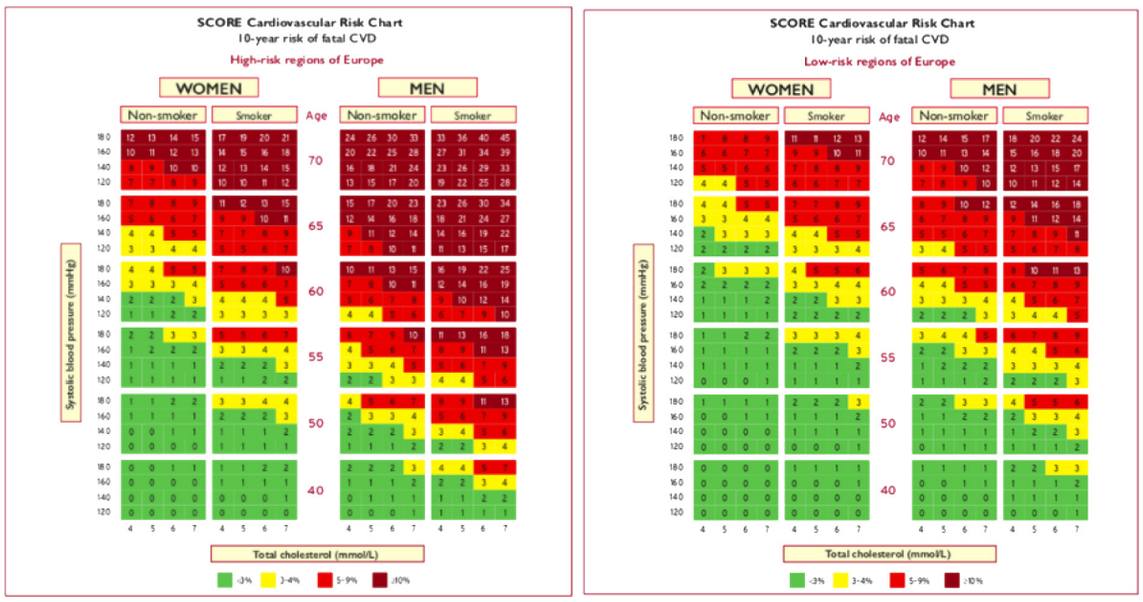

Figure 1. SCORE risk chart calculator among regions of Europe with high (left panel) and low CV risk (right panel)

Table 1. Cardiovascular risk categories in the general population (adapted from [4])

Very-high risk	People with any of the following: • Documented ASCVD (previous ACS, stable angina, coronary revascularization, stroke, TIA, peripheral artery disease or significant plaque on coronary angiography or CT scan or on carotid ultrasound) • DM with target organ damage,a or at least three major risk factors, or early onset of T1DM of long duration (>20 years) • Severe CKD (eGFR <30 mL/min/1.73 m^2) • A calculated SCORE >10% • FH with ASCVD or with another major risk factor
High-risk	People with:• Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP>180/110 mmHg• Patients with FH without other major risk factors • Patients with DM without target organ damage,a with DM duration >10 years or another additional risk factor • Moderate CKD (eGFR 30-59 mL/min/1.73 m2)• A calculated SCORE between 5% and 10%
Moderate-risk	Young patients (T1DM<35 years; T2DM<50 years) with DM duration<10 years, without other risk factors. Calculated SCORE between 1% and 5%
Low-risk	Calculated SCORE<1%

ASCVD = atherosclerotic cardiovascular disease; ACS = acute coronary syndrome; BP = blood pressure; CKD = chronic kidney disease; CT = computed tomography; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; FH = familial hypercholesterolaemia; LDL-C = low-density lipoprotein cholesterol; T1DM = type 1 DM; T2DM = type 2 DM; TC = total cholesterol; TIA = transient ischaemic attack. aTarget organ damage is defined as microalbuminuria, retinopathy, or neuropathy.

100, and 130 mg/dL) for very-high-, high-, and moderate-risk people, respectively

- Apolipoprotein B goals are <65, 80, and 100 mg/dL for very-high-, high-, and moderate-risk people, respectively
- Triglycerides: no goal defined, but <1.7 mmol/L (<150 mg/dL) indicates lower risk

In order to reach the LDL-C goals for the specific level of risk, the guidelines recommend

Table 2. Recommendations for treatment goals for LDL-C [4]

	Class	Level
In secondary prevention for patients at very-high risk, an LDL-C reduction of >50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended	**I**	**A**
In primary prevention for individuals at very-high risk but without FH, an LDL-C reduction of >50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended	**I**	**C**
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of >50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered	**IIa**	**C**
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered	**IIb**	**B**
In patients at high risk, an LDL-C reduction of >50% from baseline and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended	**I**	**A**
In individuals at moderate risk, an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered	**IIa**	**A**
In individuals at low risk, an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered	**IIb**	**A**

Table 3. Cardiovascular risk categories in patients with DM [5]

Very-high risk	Patients with DM **and** established CV disease **or** target organ damage,[a] **or** at least three major risk factors,[b] **or** early onset of T1DM of long duration (>20 years)
High-risk	Patients with DM duration>10 years without target organ damage plus any other additional risk factor
Moderate-risk	Young patients (T1DM<35 years; T2DM<50 years) with DM duration<10 years, without other risk factors

CV=cardiovascular; DM=diabetes mellitus; T1DM=type 1 diabetes mellitus; T2DM=type 2 diabetes mellitus; [a]Proteinuria, renal impairment defined as eGFR>30 ml/min/1.73 m^2, left ventricular hypertrophy, retinopathy; [b]Age, smoking, high BP, raised lipid levels, obesity

begining with a high-intensity statin at highest tolerated dose *(class I, level of evidence A)*, with the addition of ezetimibe if the goal is not reached *(class I, level of evidence B)*. In the case that LDL-C goals are not met with the above-mentioned combination, the addition of a PCSK9 inhibitor is recommended for very-high risk patients in secondary prevention *(class I, level of evidence A)* or in primary prevention for patients with familial hypercholesterolaemia (FH) and another major risk factor *(class I, level of evidence C)*. The addition of a PCSK9 inhibitor may be considered for primary prevention in patients at very-high risk but without FH *(class IIb, level of evidence C)*. If a statin-based regimen is not tolerated at any dosage, ezetimibe should be considered *(class IIa, level of evidence C)*.

In high-risk patients with hypertriglyceridaemia >2.3 mmol/l (>200 mg/dl), statins are recommended as first-line drugs *(class I, level of evidence B)*. The combination of n-3 polyunsaturated fatty acids with statin should be considered in patients with triglycerides level >1.5 mmol/l (>135 mg/dl) despite statin treatment *(class IIa, level of evidence B)*. Fibrates may be added to statins for primary prevention if triglycerides level > 2.3 mmol/l (>200 mg/dl) *(class IIb, level of evidence B)*.

Trials and meta-analyses have consistently shown a reduction in CV risk in response to lowering LDL-C levels [6-7]. The 2019 guidelines emphasize the need for lifestyle changes together with adequate lipid-lowering therapy and adherence to medication in order to reach the LDL-C goal tailored for the specific CV risk category.

The 2019 ESC guidelines on diabetes, pre-diabetes and CV disease:

The 2019 guidelines propose several CV risk categories among patients with DM (Table 3). Hypertensive patients fall into either the high-risk or the very-high risk category, depending on the coexistence of other risk factors, target organ damage or established CV disease.

There are new recommendations for BP control in patients with DM [5]:

- Individualized BP targets are recommended:
  - systolic BP (SBP) to 130 mm Hg and, if well tolerated, <130 mm Hg, but not <120 mm Hg *(class I, level of evidence A)*
  - in people >65 years target SBP to a range of 130-139 mm Hg *(class I, level of evidence A)*
  - diastolic BP (DBP) to <80 mm Hg but not <70 mm Hg *(class I, level of evidence C)*
  - on-treatment SBP to <130 mm Hg should be considered for patients at high risk of cerebrovascular events or diabetic kidney disease *(class IIb, level of evidence C)*
- Lifestyle changes (weight loss, physical activity, alcohol and sodium restriction) are recommended in hypertensive patients with DM/ pre-DM *(class I, level of evidence A)*
- A renin-angiotensin-aldosterone system (RAAS) blocker is recommended in the treatment of hypertension in DM, particularly in the presence of target organ damage *(class I, level of evidence A)*
- It is recommended to initiate treatment of hypertension with a combination of a RAAS blocker and a calcium channel blocker or thiazide/thiazide-like diuretic *(class I, level of evidence A)*
- RAAS blockers rather than beta-blockers/diuretics are recommended for BP control in pre-DM *(class IIa, level of evidence A)*
- The effect of new glucose-lowering agents on BP should be considered *(class IIa, level of evidence C)*
- Home BP self-monitoring should be considered in DM patients *(class IIa, level of evidence C)*
- 24-hour ambulatory BP monitoring (ABPM) should be considered in order to adjust antihypertensive treatment *(class IIa, level of evidence C)*

New recommendations concern antiplatelet therapy for primary prevention. The 2019 guidelines state that aspirin may be used for primary prevention in patients with DM at high/very high risk in the absence of clear contraindications *(class IIb, level of evidence A).*

A separate chapter in the new guidelines focuses on new oral glucose-lowering drugs, such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose co-transporter 2 (SGLT2) inhibitors. Several cardiovascular outcome trials haven proven the cardiovascular benefit of these glucose lowering drugs for patients with high/very high CV risk [8-13]. The guidelines highlight that the choice of glucose-lowering agent should be made taking into account the presence of CV disease and the total CV risk.

For hypertensive patients with high or very-high risk, the 2019 recommendations include new glucose-lowering agents:

- SGLT 2 inhibitors (empagliflozin, canagliflozin, or dapagliflozin) are recommended in patients with T2DM and CVD, or at very high/high CV risk, to reduce CV events *(class I, level of evidence A)*
- Empagliflozin is recommended in patients with T2DM and CVD to reduce the risk of death *(class I, level of evidence B)*
- GLP-1 RAs (liraglutide, semaglutide or dulaglutide) are recommended in patients with T2DM and CVD, or at very high/high CV risk, to reduce CV events *(class I, level of evidence A)*
- Liraglutide is recommended in patients with T2DM and CVD, or at very high/high CV risk, to reduce the risk of death *(class I, level of evidence B)*

Furthermore, SGLT2 inhibitors are associated with a lower risk of heart failure (HF) hospitalization among patients with DM and are recommended in order to reduce HF risk if eGFR>30 ml/min/1.73m^2 *(class I, level of evidence A).* They are also associated

with a lower risk of renal endpoints in patients with DM and are recommended for the prevention of chronic kidney disease if eGFR is between 30 and 90 ml/min/1.73m^2 *(class I, level of evidence B).*

Conclusion

Hypertension, diabetes and dyslipidaemia are elements of the atherosclerosis continuum and CV disease remains the leading cause of morbidity and mortality in the western world [14]. The importance of CV prevention remains unquestionable and it can be achieved by promoting a healthy lifestyle and by reducing risk factors for CV disease, such as LDL-C levels, BP and glucose levels. Deeper insights into the pathogenic mechanisms of CV disease, emerging therapies and increasing body of evidence from clinical trials warrant the continuous update of clinical practice guidelines. These guidelines provide new recommendations which allow clinicians to apply therapeutic strategies tailored to the patients' risk, thus reducing the global burden of CV disease.

Conflict of intereset

The author declare no conflict of interest.

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