2019 ESC Guidelines on:
Diabetes, pre-diabetes, and cardiovascular disease developed in collaboration with the EASD.

Dr. Jagdeep Singh
Specialist Registrar in Cardiology and Honorary Clinical Research Fellow,
The Heart Centre, Royal Infirmary of Edinburgh.

Introduction

The European Society of Cardiology (ESC) and European Association for the Study of Diabetes (EASD) jointly published guidelines for diabetes, pre-diabetes and cardiovascular disease in August 2019, which supersedes previous guidance published in 2013. This version is less technical and more practical than its predecessor, but is also more decisive with clear recommendations and helpful visual summaries in the form of tables and algorithms. In keeping with other recent ESC guidelines, the document starts with a helpful list of all the new and updated concepts introduced. This review will focus on some key concepts.

Lifestyle advice and risk stratification

The 2019 guidance expands on and highlights the importance of lifestyle changes to delay the progression from pre-diabetes to type 2 diabetes mellitus (DM), and also to help improve HbA1c in patients already with DM.

The authors recommend a Mediterranean diet supplemented with nuts or olive oils to reduce CV events. They no longer recommend omega-3 fatty acids as they do not improve glycaemic control in DM and do not have any effect in primary or secondary prevention of CVD. Importantly, this guidance also specifies that moderate alcohol consumption to reduce CV risk should no longer be promoted.

With regard to physical activity, the authors recommend at least 150 minutes per week of moderate to vigorous activity which can be either aerobic exercise or resistance training. They also cite evidence that show regular reinforcement of the importance of exercise by healthcare workers and having a structured exercise programme result in significantly lower HbA1c levels.

While the 2013 guidance only signposted various risk models that were developed in different populations, the 2019 version provides a clear and simple clinical definition of CV risk categories. (Table 7) These categories are used consistently throughout the document and are also employed in determining treatment targets, thereby emphasising the importance of risk stratification in DM. Of note, the authors suggest aspirin (75 -100 mg/day) may be considered for primary prophylaxis in patients with DM at high / very high CV risk (Class of recommendation IIb).

SGLT2-Inhibitors and GLP-1 Receptor Agonists

Arguably the most important additions to the 2019 guidelines are around the newer generation glucose-lowering agents. The authors dedicated an entire section to discuss the evidence from CV outcome trials with particular emphasis on the implications of recently published trials involving SGLT2-inibitors and GLP-1 RAs. Notably, they recommend SGLT2-inihibitors or GLP-1RA as first line therapy for treatment-naïve DM patients with established CVD or those who are at high or very high risk of CVD. (Figure 3) It is also important to note that basal insulin and SUs have been relegated to the bottom of the treatment algorithm due to their risk of hypoglycaemia.

The recommendations around managing patients with DM and HF have also been updated to reflect recently published evidence in this area. Interestingly, SGLT2-inhibitors are the only class of glucose lowering agents that received a 1A recommendation in patients with HF. Additionally, the authors have now added saxagliptin (along with thiazolidinediones) to the 'risk of harm' (class III) category due to increased risk of HF hospitalisations.

New Targets

The new guidelines take a more individualized approach to glucose, blood pressure (BP) and lipid targets which have been summarized in Table 9 of the document.

Although the 2013 guidance already advocated individualized glycaemic targets, the current version goes further by recommending stringent HbA1c targets of 6.0-6.5% for younger patients with a shorter DM history and lower hypoglycaemia risk. On the other hand, they suggest a more lenient HbA1c target of 8-9% (previously 7-8%) for the elderly, with strong emphasis toward avoiding hypoglycaemia.

Whereas previously there was a single BP target of 140/85 mmHg, the new guidance now individualizes BP based on age and tolerability. Although the threshold for initiating therapy remains 140/90 mmHg, the on-treatment target should now be SBP <130mmHg (or <120 mmHg if tolerated) for those below age 65, and between 130-140 mmHg for patients above age 65 years. The authors recommend a DBP target of 70-80mmHg for all. They also recommend initiating anti-hypertensive therapy with at least 2 agents simultaneously with one of them being a RAAS blocker due to effects on LV remodelling, reno-protection and reduced incidence of new-onset DM in patients with pre-diabetes.

With regard to lipid targets, the 2019 guidance stratifies them based on CV risk categories. Patients with DM and moderate CV risk must aim for LDL<2.5 mmol/L, while patients with high CV risk must have an LDL reduction of at least 50% or absolute LDL < 1.8 mmol/L, and those with very high CV risk (i.e. all patients with established CVD) there must be an LDL reduction of at least 50% or absolute LDL < 1.4 mmol/L. The authors recommend adding ezetimibe to statins if targets are not reached and in patients with very high CV risk, PCSK9 inhibitors are recommended if targets are not reached despite maximal therapy. Importantly, statins are not recommended in women of childbearing potential.

Revascularisation

The authors emphasize that the indications for revascularisation (for both symptomatic and prognostic reasons) and revascularization techniques (e.g. type of stents or grafts used), are the same for patients with or without DM.

The previous iteration of this guidance leaned heavily toward coronary artery bypass grafting as the preferred revascularisation modality. However, with evidence from trials using newer-generation drug-eluting stents, the authors have now updated their recommendations based on the number and complexity of the coronary artery disease. Notably, percutaneous coronary intervention is now recommended in patients with DM and stable single or 2 vessel disease (regardless of proximal LAD involvement), as well as in patients with left main disease and low disease complexity (SYNTAX score<22).

Conclusions

The 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular disease is a timely update; particularly with the evolving evidence around CV safety (or lack thereof in some cases) of the various glucose-lowering drug classes. It represents the state-of-the-art in managing DM in the context of CV disease and will, undoubtedly, be a useful guide for both cardiologists and diabetologists alike.