



2023 European Society of Cardiology (ESC) Guidelines for the Management of Cardiovascular Disease in Patients with Diabetes

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Citation: EMJ Cardiol. 2023;11[1]:20-23. DOI/10.33590/emjcardiol/10301135.
<https://doi.org/10.33590/emjcardiol/10301135>.



The 2023 update of the European Society of Cardiology (ESC) guidelines for the management of cardiovascular disease (CVD) in patients with diabetes was presented in a symposium session at the ESC Congress 2023, held in Amsterdam, the Netherlands, from the 25th–28th of August. The updates redefined the 2019 guidelines, acknowledging recent findings from cardiovascular outcome trials (CVOT) on the safety and efficacy of glucose-lowering medications to provide practice-changing recommendations. The session also introduced a novel tool in predicting CVD risk, SCORE2-Diabetes, an innovative model that accounts for conventional and diabetes-related risk factors, stratified by geographical location.

INTRODUCTION

Patients with diabetes have an increased risk of CVD. The presence of two comorbidities, diabetes and CVD, can have a major impact on patient prognosis, and affect treatment strategy. Diabetes diagnosis can result in an increased risk of developing chronic kidney disease which, in turn, can impact prognosis and act as a driver of CVD. Nikolaus Marx, University Hospital Aachen, Germany, and symposium Co-Chair, highlighted the importance of identifying individuals with these comorbidities through screening, an essential aspect of the new guidelines. Due to the high levels of undetected diabetes in patients with CVD, it is recommended that all patients with CVD be screened for diabetes using fasting glucose and/or HbA1c, tools that are readily available to cardiologists. In turn, patients with diabetes must also be screened for CVD and the presence of kidney disease through assessing estimated glomerular filtration rate, defined by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), and urine albumin creatinine ratio, assessing albuminuria in the spot urine.

The 2023 guidelines also focus on the management of CVD in patients with Type 2 diabetes (T2D), focusing on clinical approaches and key recommendations. Special attention is given to the proven cardiovascular (CV) benefit of, and safety of, glucose-lowering medications. The experts also highlight the importance of identifying and effectively treating heart failure (HF) in patients with diabetes, to reduce HF-related hospitalisation and all-cause mortality.

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PREDICTING CARDIOVASCULAR RISK WITH SCORE2-DIABETES

The first presenter, Emanuele Di Angelantonio, University of Cambridge, UK, focused their discussion on the novel CV risk assessment tool for patients with diabetes, SCORE2-Diabetes. Patients with diabetes have an average two-fold increase in developing CVD, including



coronary heart disease, stroke, and other CV events. Diabetes is also associated with multiple CVD risk factors, such as dyslipidaemia and hypertension, each of which mediates an increased risk of disease. Di Angelantonio highlighted that this increased risk is directly reflected in years of life lost by both males and females with T2D, who have a reduced life expectancy of approximately 6 years.

Over recent years, a special emphasis has been placed on developing diabetes-specific CV risk prediction models that can identify those most at risk, as well as those who would benefit most from intervention. Models developed so far have combined conventional risk factors, including age, sex, and lifestyle factors, and diabetes-specific factors, such as HbA1c, diabetes duration, and target organ damage (TOD). Current models include ADVANCE, which can predict 4-year CV risk; UKPDS, which predicts CVD risk in the UK; and DIAL, which can predict lifetime risk. Di Angelantonio highlighted that, although useful, these tools have many limitations, including a basis on older patient cohorts and a lack of geographical calibration.

For the presentation of the novel 2023 ESC Guidelines, the Society developed a new risk prediction tool, SCORE2-Diabetes. SCORE2-Diabetes was developed and tested in external cohorts, and has extended features above previously used predictions tools. The SCORE2-Diabetes prediction model was calibrated to different regions in Europe, based on their associated level of risk.

Different regions of Europe are classified as low, moderate, high, and very high risk. Di Angelantonio presented an example of a model patient with a specific risk profile, and demonstrated how, by using the SCORE2-Diabetes system, CVD can be predicted according to the region of Europe where they reside. SCORE2-Diabetes can estimate 10-year CVD risk for patients with T2D, and can discriminate risk based on both conventional risk factors and those related to T2D. Concluding the presentation, Di Angelantonio underlined that the new guidelines recommend that for patients with atherosclerotic CVD (ASCVD) or severe TOD, SCORE2-Diabetes should always be used to classify patients into either low, moderate, or high-risk categories.

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GLUCOSE-LOWERING MEDICATIONS FOR THE REDUCTION OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE RISK

The second presentation delved into guideline updates surrounding the recommended indications for first- and second-line glucose-lowering medications. Darren Keith McGuire, University of Texas Southwestern Medical Center, Dallas, USA, presented a series of updates on the 2019 guidelines, changed due to the results of meta-analysis and CVOT. McGuire highlighted the importance of the different recommendations for patients with or without ASCVD and TOD, and drew special attention to the totality of evidence now supporting the proven CV benefit and safety of glucose-lowering medications.

First-line recommendations for reducing CV risk independent of glucose control is treatment using both GLP-1 receptor agonists (RA) and SGLT2 inhibitors. This is an update from previous guidelines, which encouraged the use of GLP-1 RA and/or SGLT2 inhibitors. This change is based on the clinical indications for simultaneous use and meta-analysis of CVOTs with GLP-1 RA. Data presented demonstrated a 15% fatal risk reduction for CV death, a 12% fatal risk reduction for non-fatal or fatal myocardial infarction, and what McGuire described as a “robust” observation of 19% fatal risk reduction for stroke. Additional stratification of these results revealed a significant improvement in patients with established ASCVD compared to patients without. SGLT2 inhibitors showed less consistency in efficacy, but still maintained a statistically significant decrease in CV death, myocardial infarction, and stroke. When stratified by the presence or absence of ASCVD, there was an 11% relative risk reduction for those with ASCVD, and no demonstrated benefit for those without. McGuire concluded that the ESC updated recommendations were that both classes of drug had the same indications, with proven efficacy and proven CV benefit for those with T2D.

McGuire then spoke about second-line medications, explaining that the broad clinical consensus is the use of a glucose-lowering agent with suggested CV benefits, such as metformin or pioglitazone. Meta-analysis of the CV effects demonstrated safety and plausible CVD efficacy of metformin; however, it did not conclusively

show CVD efficacy. Analysis of pioglitazone demonstrated nominal significance; however, this again demonstrated no conclusive CVD efficacy, though data did support a 17% risk reduction in CVD death. McGuire also acknowledged the concern about HF, with meta-analysis data for pioglitazone showing a 32% statistically significant risk of heart failure; however, they highlighted that this represented a very small absolute risk difference of approximately 0.4%. McGuire additionally underlined that most of this additional risk appeared to be driven by plasma volume expansion, and therefore that the risks should be manageable.

Summarising the updated recommendations in the guidelines, McGuire explained that for patients with T2D, without ASCVD or severe TOD, but with a calculated 10-year CVD risk $\geq 10\%$, treatment with an SGLT2 inhibitor or GLP-1 RA should be considered to reduce CV risk. Additionally, patients with T2D, without ASCVD or severe TOD, and with a SCORE2-Diabetes of high to very high risk, metformin and/or an SGLT2 inhibitor and/or GLP-1 RA is recommended. Finally, for patients with ASCVD, SGLT2 inhibitors and GLP-1RA are recommended.

HEART FAILURE AND DIABETES

Patients with T2D have a higher incidence of HF compared to controls, resulting in an accelerated time to first cardiac event. It is therefore essential that patients with T2D undergo regular systematic screening for HF symptoms at every clinical encounter, explained Katharina Schütt, University Hospital Aachen. The 2023 guidelines provide clear recommendations on how to screen and diagnose HF in patients with T2D, according to the HF guidelines. Patients are at high risk, and therefore a systematic survey is recommended at each clinical encounter. If HF is suspected due to symptoms or abnormal ECG, the ESC recommends physicians measure B-type natriuretic peptide or N-terminal-pro B-type natriuretic peptide. In addition to this, the diagnostic tests recommended in patients with suspected HF include 12 lead ECG; transthoracic echocardiography; chest radiography (X-ray); and routine blood tests for comorbidities, such as full blood count, urea, creatine, electrolytes, thyroid function, lipids, and iron status.

If these tests are negative, then the guidelines recommend regular repetition. However, if they are positive, HF is defined through left ventricular (LV) measurements, in accordance with HF guidelines.

Schütt then discussed updates to the guidelines surrounding the treatment of HF in patients with T2D. All patients with HF and T2D are recommended SGLT2 inhibitors to reduce HF-related outcomes, such as CV death and HF hospitalisation. This is recommended irrespective of left ventricle ejection fraction, and independent of HbA1c and concomitant glucose-lowering medication. For all patients with HF with reduced ejection fraction (HFrEF; New York Heart Association [NYHA] Class II–IV) and T2D, the SGLT2 inhibitors dapagliflozin, empagliflozin, or sotagliflozin are recommended to reduce the risk of hospitalisation.

This recommendation is based on evidence from the DAPA-HF, EMPEROR-Reduced, and SOLOIST-WHF trials, where the three SGLT2 inhibitors demonstrated significantly reduced total CV death and HF hospitalisation. In addition to this, regardless of the presence or absence of T2D, the three SGLT2 inhibitors are recommended in all patients with HFrEF.

Concluding their presentation, Schütt touched on novel recommendations in the 2023 guidelines regarding the initiation and up-titration of HFrEF medications, based on the findings of the STRONG-HR trial, which included patients on a higher dose than standard care. The trial allowed for a defined dose prior to discharge, with subsequent frequent follow-up visits in the first 6 weeks following an HF hospitalisation. This resulted in a significant reduction in 100-day re-admission for HF and all-cause death. ESC guidelines recommend this strategy to reduce readmission and all-cause mortality.

CONCLUSION

The 2023 updated guidelines provided a clear overview of changing recommended practices surrounding the screening, diagnosis, and management of patients with diabetes, who are at risk of CVD. Marx also highlighted a series of additional updates to the guidelines that were not covered in the symposium, including CV risk reduction in patients with diabetes; management of coronary artery disease and diabetes; arrhythmias; T1D and CVD; and person-centred care.

