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2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes

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PREFACE

The American College of Cardiology (ACC) has a long history of developing documents (e.g., decision pathways, health policy statements, appropriate use criteria) to provide members with guidance on both clinical and nonclinical topics relevant to cardiovascular (CV) care. In most circumstances, these documents have been created to complement clinical practice guidelines and to inform clinicians about areas where evidence may be new and evolving or where sufficient data may be more limited. In spite of this, numerous care gaps continue to exist, highlighting the need for more streamlined and efficient processes to implement best practices in service to improved patient care.

Central to the ACC's strategic plan is the generation of "actionable knowledge"–a concept that places emphasis on making clinical information easier to consume, share, integrate, and update. To this end, the ACC has evolved from developing isolated documents to the development of integrated "solution sets." Solution sets are groups of closely related activities, policy, mobile applications, decision support, and other tools necessary to transform care and/or improve heart health. Solution sets address key questions facing care teams and attempt to provide practical guidance to be applied at the point of care. They use both established and emerging methods to disseminate information for CV conditions and their related management. The success of the solution sets rests firmly on their ability to have a measurable impact on the delivery of care. Because solution sets reflect current evidence and ongoing gaps in care, the associated content will be refined over time to best match changing evidence and member needs.

Expert consensus decision pathways (ECDPs) represent a key component of solution sets. The methodology for ECDPs is grounded in assembling a group of clinical experts to develop content that addresses key questions facing our members across a range of high-value clinical topics (1). This content is used to inform the development of various tools that accelerate real time use of clinical policy at the point of care. They are not intended to provide a single correct answer; rather, they encourage clinicians to ask questions and consider important factors as they define a treatment plan for their patients. Whenever appropriate, ECDPs seek to provide unified articulation of clinical practice guidelines, appropriate use criteria, and other related ACC clinical policy. In some cases, covered topics will be addressed in subsequent clinical practice guidelines as the evidence base evolves. In other cases, these will serve as stand-alone policy.

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1. INTRODUCTION

Despite major therapeutic advances leading to improved outcomes over the past 2 decades, CV disease remains the leading cause of morbidity and mortality in patients with type 2 diabetes (T2D) (2–4). Over this time, the prevalence of T2D has increased, while the excess risk of adverse CV events in patients with T2D (compared with patients without diabetes) has remained largely unchanged (5,6). Accordingly, the development of treatment strategies to improve CV outcomes in this vulnerable patient population remains a major priority. Diabetes is typically thought of as a disease of elevated blood glucose (7). Although large clinical trials have consistently demonstrated an improvement in microvascular outcomes in patients with T2D with intensive versus conservative glucose control, similar results have not been demonstrated for CV outcomes in patients with T2D, despite the clinically important differences in hemoglobin A1c (HbA1c) achieved between treatment groups in glucose-lowering trials (8–11). The opportunities for improving clinical outcomes in patients with T2D and CV disease have recently expanded.

Many sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide 1 receptor agonists (GLP-1RAs) have been demonstrated to significantly reduce the risk of major adverse cardiovascular events (MACE) (12–19). SGLT2 inhibitors also substantially diminish the risks of heart failure (HF) hospitalization and progression of diabetic kidney disease (DKD). Although the exact mechanisms of CV and renal benefits remain uncertain, they appear to exceed the direct glucose-lowering effects of these agents and may be related to additional mechanisms of action of each class of medications (20,21). Data proving that SGLT2 inhibitors and GLP-1RAs improve outcomes in patients with T2D and CV disease have triggered a major paradigm shift beyond glucose control to a broader strategy of comprehensive CV risk reduction (2,22,23). The potential of these compounds has also stimulated re-examination of the traditional roles of various medical specialties in the management of T2D, compelling CV specialists to adopt a more active role in prescribing drugs that may previously have been seen primarily as glucose-lowering therapies. This evolving role has created a need for novel clinical care delivery models that are collaborative, interprofessional, and multidisciplinary in their approach to managing this high-risk patient group with multiple comorbidities. The purpose of this ECDP is to update the 2018 ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease (ASCVD) (24) with data from emerging studies, and continue to provide succinct, practical guidance on the use of specific agents for reducing CV risk in patients with T2D.

1.1. A Focus on Comprehensive CV Risk Reduction in T2D

Although the primary focus of patients, clinicians, and healthcare systems should be the prevention of T2D (25), a significant proportion of patients cared for by CV clinicians have known T2D, undiagnosed diabetes, or prediabetes (26). Because most morbidity and mortality in T2D comes from CV events (27), the CV specialist has a key role in optimizing these patients' care and is well-positioned to address 3 key areas in the management of patients with T2D:

1. Screening for T2D in their patients with or at high risk of CV disease;
2. Aggressively treating CV risk factors; and
3. Incorporating newer glucose-lowering agents with evidence for improving CV outcomes into routine practice.

Data from the NCDR PINNACLE registry from 2008 through 2009 show that only 13% of outpatients in the United States with coronary artery disease cared for primarily by cardiologists are screened for T2D (28). While the proportion screened is likely to have improved in the decade since that report was published, there remains a need for improvement in comprehensive CV risk factor control among patients with T2D (29,30), as current care delivery is often fragmented, episodic, and focused on treating acute events. Comprehensive CV risk factor control reduces events and improves survival in patients with T2D (31,32). This includes encouraging a healthy diet, regular physical activity, weight loss, smoking cessation, assiduous control of blood pressure (33), lowering of atherogenic blood lipids (34,35), and use of antiplatelet agents in accordance with current treatment guidelines (2,35,36). Only a minority of patients with diabetes achieve these key benchmarks (37).

Beyond these core recommendations, CV specialists should be aware of the strong clinical evidence regarding specific glucose-lowering therapies proven to lower CV risk. Given that patients with T2D and CV disease frequently follow up with their CV specialists, a firm understanding of the efficacy and safety profiles and net clinical benefits of these agents is important. Such encounters are an ideal time to review the patient's overall management and consider the initiation of these novel agents to favorably impact patient care and outcomes.

2. METHODS

The ACC created the Heart House Roundtables, a structured format of interactive discussion among a broad group of stakeholders, to address high-value topics and issues that clinicians and patients face daily, such as the treatment of CV disease in patients with T2D (38). The planning committee for the Managing CV Disease Risk in Diabetes roundtable was led by Mikhail Kosiborod, MD, FACC, and Larry Sperling, MD, FACC. To accommodate the multiple perspectives concerning new therapeutic options for patients with T2D, the roundtable included several experts in diverse medical specialties, such as cardiology, family medicine, internal medicine, and endocrinology, and included physicians, nurses, advanced practice providers, and pharmacists. Recognizing the significant impact of recently available CV outcomes trial data, discussions focused on the real-world challenges faced in working toward comanaging T2D and CV disease for improved patient outcomes. As a result, the ACC saw an opportunity to provide guidance to fill the current gap between CV clinicians and diabetes care providers who jointly manage patients with T2D and ASCVD, HF, and/or DKD. To support this effort, a writing committee of multidisciplinary experts was convened in 2017 to develop an ECDP providing guidance on the use of antidiabetic agents proven to reduce CV risk in patients with T2D (24). For this update, the writing committee convened in late 2019 via conference call attended only by writing committee members and ACC staff. Differences were resolved by consensus among the group, and no portions of the ECDP required administrative decision overrides. The work of the writing committee was supported only by the ACC and did not have any commercial support. Writing committee members were all unpaid volunteers.

The ACC and the Solution Set Oversight Committee (SSOC) recognize the importance of avoiding real or perceived relationships with industry (RWI) or other entities that may affect clinical policy. The ACC maintains a database that tracks all relevant relationships for ACC members and persons who participate in ACC activities, including those involved in the development of ECDPs. ECDPs follow ACC RWI Policy in determining what constitutes a relevant relationship, with additional vetting by the SSOC.

ECDP writing groups must be chaired or co-chaired by an individual with no relevant RWI. While vice chairs and writing group members may have relevant RWI, this must constitute less than 50% of the writing group. Relevant disclosures for the writing group, external reviewers, and SSOC members can be found in Appendixes 1 **and** 2. Participants are discouraged from acquiring relevant RWI throughout the writing process.

3. ASSUMPTIONS AND DEFINITIONS

To facilitate interpretation of the recommendations provided in this ECDP, specific assumptions were made by the writing committee as specified in Section 3.1.

3.1. General Clinical Assumptions

1. The principal focus of this effort, including ECDP considerations, applies to patients with T2D and CV disease or who are at high risk for CV disease.
2. The writing committee endorses the evidence-based approaches to CV disease risk reduction recommended in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (33), the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (34), and the 2019 ACC/AHA Guidelines on the Primary Prevention of Cardiovascular Disease (39).
3. The writing committee endorses the evidence-based approaches to diabetes management outlined in the American Diabetes Association (ADA) Standards of Medical Care in Diabetes: Chapter 10. Cardiovascular Disease and Risk Management (2).
4. The writing committee endorses the evidence-based approaches to HF therapy and management enumerated in the 2013 ACCF/AHA Guideline for the Management of Heart Failure, the 2016 ACC/AHA/HFSA Focused Update on the New Pharmacological Therapy for Heart Failure: an Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure, and the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction (40–42). It is important to note that the 2013 and 2017 HF guidelines as well as the 2017 ECDP do not include major trials that are described in this ECDP because of the timing of those publications.
5. Optimal patient care decisions should properly reflect the patient's preferences and priorities as well as those of the managing clinician.
6. This ECDP is not intended to supersede good clinical judgement. The treating clinician should seek input as needed from relevant experts (e.g., pharmacists, cardiologists, endocrinologists).
7. This ECDP is based on the best data currently available. New information is being generated rapidly (e.g., CV outcomes trials of additional agents and including other patient populations), and as these data become available, they will impact the considerations made here. Clinicians should be careful to incorporate relevant information published after this ECDP.
8. A background effort aimed at comprehensive CV risk reduction is essential, using the full complement of diet, exercise, and lifestyle recommendations, as

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