

Contents

Foreword: Diabetes and Atherosclerotic Cardiovascular Disease xiii

Adriana G. Ioachimescu

Preface: Diabetes and Atherosclerotic Cardiovascular Disease: Novel Insights and Therapeutic Strategies xv

Guillermo E. Umpierrez

The Evolving Epidemiology of Atherosclerotic Cardiovascular Disease in People with Diabetes 1

Francisco J. Pasquel, Edward W. Gregg, and Mohammed K. Ali

Atherosclerotic cardiovascular disease (ASCVD) is a leading global cause of death and accounts for most deaths among individuals with diabetes. This article reviews the latest observational and trial data on changes in the relationship between diabetes and ASCVD risk, remaining gaps in how the role of each risk factor is understood, and current knowledge about specific interventions. Differences between high-income countries and low-income and middle-income countries are examined, barriers and facilitators are discussed, and a discussion around the concept of ideal cardiovascular health factors (Life's Simple 7) is focused on.

Prediabetes and Cardiovascular Disease: Pathophysiology and Interventions for Prevention and Risk Reduction 33

Ben Brannick and Sam Dagogo-Jack

Prediabetes is a state characterized by impaired fasting glucose or impaired glucose tolerance. This article discusses the pathophysiology and macrovascular complications of prediabetes. The pathophysiologic defects underlying prediabetes include insulin resistance, alpha- and beta-cell dysfunction, increased lipolysis, inflammation, and suboptimal incretin effect. Recent studies have revealed that the long-term complications of diabetes manifest in some people with prediabetes; these complications include microvascular and macrovascular disorders. Finally, the authors present an overview of randomized control trials aimed at preventing progression from prediabetes to type 2 diabetes and discuss their implications for macrovascular risk reduction.

Pathogenesis of Cardiovascular Disease in Diabetes 51

Andrea V. Haas and Marie E. McDonnell

The most common cause of death among adults with diabetes is cardiovascular disease (CVD). In this concise review on pathogenesis of CVD in diabetes, the 4 common conditions, atherosclerosis, microangiopathy, diabetic cardiomyopathy, and cardiac autonomic neuropathy, are explored and illustrated to be caused by interrelated pathogenetic factors. Each of these diagnoses can present alone or, commonly, along with others owing to overlapping pathophysiology. Although the spectrum of

physiologic abnormalities that characterize the diabetes milieu is broad and goes beyond hyperglycemia, the authors highlight the most relevant evidence supporting the current knowledge of potent factors that contribute to CVD in diabetes.

Intensive Diabetes Treatment and Cardiovascular Outcomes in Type 1 Diabetes Mellitus: Implications of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study 30-Year Follow-up

65

Savitha Subramanian and Irl B. Hirsch

Type 1 diabetes mellitus, an autoimmune disorder characterized by beta-cell destruction and absolute insulin deficiency, is associated with significantly increased cardiovascular disease risk, but the mechanisms underlying this enhanced risk are unclear. Results of the pivotal Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications study have shown that compared with conventional therapy, intensive glycemic control results in decreased cardiovascular morbidity and mortality. Evidence from this study also revealed contributions of blood pressure, renal disease, body weight, and lipids to cardiovascular disease in type 1 diabetes mellitus. Extrapolating from existing evidence, this article addresses clinical strategies to mitigate cardiovascular risks.

Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes Mellitus

81

Marian Sue Kirkman, Hussain Mahmud, and Mary T. Korytkowski

People with type 2 diabetes mellitus are at high risk of morbidity and mortality from cardiovascular disease (CVD). Based on observed relationships between hyperglycemia and CVD, several large clinical trials have investigated the ability of treatment strategies to achieve hemoglobin A_{1c} less than 7% (53 mmol/mol) as a way of reducing this risk. These studies demonstrate that intensified glycemic therapy may reduce CVD risk in younger patients with recent-onset type 2 diabetes mellitus but not in high-risk older individuals with established disease. Attention to blood pressure and lipid-lowering therapies with modified glycemic goals for older high-risk individuals is recommended.

Cardiovascular Outcomes Trials of Glucose-Lowering Drugs or Strategies in Type 2 Diabetes

97

Hertzel C. Gerstein and Reema Shah

As recently as 20 years ago there were no randomized controlled trials of potentially cardiovascular protective therapies in people with type 2 diabetes. The ongoing cardiovascular trials bring the needed evidence. Both primary and subsidiary analyses have transformed diabetes from a largely eminence-based specialty to one that is firmly evidence based. These studies have provided evidence supporting glucose-lowering drugs for patients with cardiovascular risk factors. Randomized controlled trials such as those described here will continue to challenge assumptions and create new approaches and paradigms that can be pursued to reduce and hopefully eliminate serious cardiovascular and other consequences of diabetes.

Heart Failure: Epidemiology, Pathophysiology, and Management of Heart Failure in Diabetes Mellitus 117

Anders Jorsal, Henrik Wiggers, and John J.V. McMurray

This article briefly discusses the epidemiology of heart failure and diabetes and summarizes the key findings from the recent cardiovascular outcome trials in patients with type 2 diabetes, with a focus on heart failure as an end point.

Personalizing Glucose-Lowering Therapy in Patients with Type 2 Diabetes and Cardiovascular Disease 137

Silvio E. Inzucchi

Twelve drug categories are marketed in the United States to lower blood glucose concentrations in type 2 diabetes mellitus (T2DM). After metformin, there is disagreement about the optimal next choice for combination therapy. Guidelines advise balancing potency, risks, benefits, and costs. For T2DM and cardiovascular disease (CVD), emerging evidence suggests that certain options may have specific advantages. Specific members of the thiazolidinedione, sodium-glucose cotransporter-2 inhibitor, and glucagon-like peptide-1 receptor agonist classes have been associated with significant reductions in major adverse cardiovascular events, generally in those with established CVD. A personalized approach should consider these evidence-based therapies to optimize clinical outcomes.

Managing Dyslipidemia in Type 2 Diabetes 153

Adam J. Nelson, Simon K. Rochelau, and Stephen J. Nicholls

Cardiovascular disease is the most frequent cause of morbidity and mortality among individuals with diabetes, and although there has been significant reduction in excess risk, these individuals remain at least twice as likely to sustain atherosclerotic events. Aggressive management of traditional factors, such as dyslipidemia, remains the cornerstone of risk mitigation. Diabetes and its associated insulin resistance generate qualitative and quantitative changes in lipid profile, which complicate effective treatment. This article summarizes the background to diabetic dyslipidemia and provides a précis of the available management options.

Blood Pressure Control and Cardiovascular/Renal Outcomes 175

Farheen K. Dojki and George L. Bakris

Hypertension is an important and modifiable risk factor for the macrovascular and microvascular complications of diabetes. The prior literature outlines the significance of lowering blood pressure and subsequent cardiovascular and microvascular benefits. Blood pressure targets of less than 140/90 mm Hg are recommended in all adults with diabetes, with lower blood pressure targets of less than 130/80 mm Hg beneficial for those with higher cardiovascular disease risk. Treatment to lower blood pressure is primarily based on a foundation of lifestyle modifications, low sodium diet, exercise, and good sleep hygiene coupled with multiple medication classes such as renin angiotensin system inhibitors.

Hyperglycemia in Acute Coronary Syndromes: From Mechanisms to Prognostic Implications

185

Mikhail Kosiborod

Numerous studies have documented that hyperglycemia is frequent in patients hospitalized with acute coronary syndromes, affects patients with and without established diabetes, and is associated with adverse outcomes, with incremental increase in the risk of mortality and complications observed across the spectrum of glucose elevations. This article reviews present knowledge about the association between glucose levels and outcomes of patients hospitalized with acute coronary syndromes, describes available data regarding inpatient glucose management in this patient group and comparative data across the spectrum of critically ill hospitalized patients, addresses some controversies in this field; and offers practical recommendations for patient management based on existing data.

Perioperative Management of Hyperglycemia and Diabetes in Cardiac Surgery Patients

203

Rodolfo J. Galindo, Maya Fayfman, and Guillermo E. Umpierrez

Perioperative hyperglycemia is common after cardiac surgery, reported in 60% to 90% of patients with diabetes and in approximately 60% of patients without a history of diabetes. Many observational and prospective randomized trials in critically ill cardiac surgery patients support a strong association between hyperglycemia and poor clinical outcome. Despite ongoing debate about the optimal glucose target, there is strong agreement that improved glycemic control reduces perioperative complications.

Antiplatelet Therapy in Diabetes

223

Arjun Majithia and Deepak L. Bhatt

Cardiovascular disease (CVD) is a significant cause of morbidity and mortality among patients with diabetes mellitus (DM). Increased platelet reactivity among patients with DM contributes to disproportionately high levels of atherothrombotic CVD. Consequently, there has been tremendous interest in exploring the role of antiplatelet therapies in DM to reduce the development of and frequency of future cardiovascular events.

Managing Diabetes and Cardiovascular Risk in Chronic Kidney Disease Patients

237

Dragana Lovre, Sulay Shah, Aanu Sihota, and Vivian A. Fonseca

The authors discuss mechanisms of increased cardiovascular disease (CVD) in patients with chronic kidney disease (CKD) and strategies for managing cardiovascular (CV) risk in these patients. Their focus was mainly on decreasing CV events and progression of microvascular complications by reducing levels of glucose and lipids. The authors searched PubMed with no limit on the date of the article. All articles were discussed among all authors. They chose pertinent articles and searched their references in turn for additional relevant publications.