

Contents

Part I Diagnosis and Mechanisms of Disease

| | |
|-----------------------------------------------------------------------------------|----|
| 1 Epidemiology, Definition, and Diagnosis of Diabetes Mellitus | 3 |
| 1.1 Global Burden of Diabetes. | 3 |
| 1.2 Definition | 7 |
| 1.3 Diagnosis. | 9 |
| References | 10 |
| 2 Diabetes and Cardiovascular Disease. | 13 |
| 2.1 Blood Glucose Levels and Vascular Events | 13 |
| 2.2 High Cardiovascular Risk Despite Multifactorial Intervention. | 14 |
| 2.3 Impaired Glucose Tolerance in Patients with Coronary Artery Disease | 16 |
| References | 19 |
| 3 Mechanisms of Diabetic Atherosclerosis | 23 |
| 3.1 Hyperglycemia, Oxidative Stress, and Endothelial Dysfunction | 23 |
| 3.2 Insulin Resistance. | 26 |
| 3.3 Molecular Targets to Improve Insulin Sensitivity in Type 2 Diabetes. | 28 |
| 3.4 Thrombosis and Coagulation | 30 |
| References | 31 |

| | |
|------------------------------------------------------------------------------------|----|
| 4 Environment, Epigenetic Changes, and Cardiovascular Damage | 35 |
| 4.1 Epigenetic Changes | 35 |
| 4.2 DNA Methylation and Histone Modifications | 36 |
| 4.3 Chromatin Remodeling and Diabetic Atherosclerosis | 37 |
| 4.4 Epigenetic Inheritance..... | 41 |
| 4.5 MicroRNAs..... | 42 |
| References | 44 |
| 5 Diabetic Cardiomyopathy | 49 |
| 5.1 Heart Failure in Patients with Diabetes | 49 |
| 5.2 Diastolic Dysfunction | 50 |
| 5.3 Lipotoxicity..... | 52 |
| 5.4 Glucotoxicity..... | 53 |
| References | 55 |
| 6 Cerebrovascular Disease | 59 |
| 6.1 Prevalence and Prognosis of Cerebrovascular Disease in Diabetic Patients | 59 |
| 6.2 Pathophysiology..... | 61 |
| 6.3 Clinical Evidence | 62 |
| References | 63 |

Part II Management of Cardiovascular Risk Factors

| | |
|------------------------------------------|----|
| 7 Risk Stratification | 69 |
| 7.1 Risk Engines | 69 |
| 7.2 Application of Risk Calculators..... | 70 |
| 7.3 Biomarkers | 72 |
| 7.3.1 DNA Methylation..... | 73 |
| 7.3.2 MicroRNAs | 74 |

| | |
|----------------------------------------------------------------------|------------|
| Contents | xi |
| | |
| 7.3.3 Inflammatory Cytokines | 74 |
| 7.3.4 Vascular Calcification Markers.... | 75 |
| 7.3.5 Advanced Glycation End-Products (AGEs) | 76 |
| 7.4 Role of Vascular Imaging | 77 |
| 7.5 Detection of Coronary Artery Disease... | 78 |
| References | 80 |
| 8 Hyperglycemia..... | 85 |
| 8.1 Glycemic Control and Microvascular Complications..... | 85 |
| 8.2 Glycemic Control and Macrovascular Complications..... | 88 |
| 8.3 Hypoglycemia..... | 90 |
| 8.4 Recommended Glycemic Targets..... | 92 |
| 8.5 Cardiovascular Effects of Glucose-Lowering Drugs | 94 |
| References | 98 |
| 9 Diabetic Dyslipidemia | 101 |
| 9.1 Definition and Pathophysiology of Diabetic Dyslipidemia | 101 |
| 9.2 LDL Cholesterol Lowering Therapies.... | 103 |
| 9.3 TGL, HDL, and Residual Vascular Risk | 107 |
| 9.4 Therapeutic Targets | 108 |
| References | 110 |
| 10 Arterial Hypertension..... | 115 |
| 10.1 Prevalence and Pathophysiology | 115 |
| 10.2 Clinical Evidence | 116 |
| 10.3 Blood Pressure Targets in People with Diabetes | 122 |
| 10.4 Antihypertensive Drugs | 122 |
| 10.4.1 RAAS Inhibitors | 124 |
| 10.4.2 RAAS and Renal Outcomes in Type 2 Diabetes | 125 |

| | |
|------------------------------------------------------------------------------------|------------|
| 10.4.3 ACEs/ARBs Treatment and New-Onset Diabetes..... | 125 |
| 10.4.4 Calcium Channel Blockers, Beta Blockers, Diuretics | 126 |
| 10.5 Resistant Hypertension and Renal Sympathetic Denervation..... | 127 |
| References | 128 |
| 11 Antiplatelet Therapy..... | 133 |
| 11.1 Enhanced Platelet Reactivity in Diabetes | 133 |
| 11.2 Aspirin..... | 134 |
| 11.3 Clopidogrel | 136 |
| 11.4 Prasugrel | 137 |
| 11.5 Ticagrelor..... | 138 |
| References | 142 |
| Part III Treatment of Cardiovascular Diseases in Patients with Diabetes | |
| 12 Coronary Artery Disease | 147 |
| 12.1 Medical Therapy vs. Myocardial Revascularization..... | 147 |
| 12.2 PCI vs. CABG..... | 150 |
| 12.3 Bare-Metal vs. Drug-Eluting Stents..... | 154 |
| 12.4 First vs. Second Generation DES..... | 156 |
| References | 159 |
| 13 Acute Coronary Syndromes..... | 163 |
| 13.1 Prevalence and Prognosis | 163 |
| 13.2 Glycemic Control in Acute Coronary Syndromes..... | 165 |
| 13.3 Antithrombotic Therapy | 166 |
| 13.4 Anticoagulants | 168 |
| References | 169 |

| | |
|------------------------------------------------------------------------------|------------|
| Contents | xiii |
| 14 Heart Failure | 173 |
| 14.1 Prognosis of Heart Failure in Patients with Diabetes | 173 |
| 14.2 Pharmacological Therapy | 174 |
| 14.2.1 RAAS Blockade..... | 174 |
| 14.2.2 Neprilysin Inhibition | 180 |
| 14.2.3 Beta-blockers..... | 180 |
| 14.2.4 Diuretics..... | 181 |
| 14.3 Glycemic Control and Risk of Heart Failure | 182 |
| References | 185 |
| 15 Ischemic Stroke | 189 |
| 15.1 Diabetes, Atrial fibrillation, and Stroke | 189 |
| 15.2 Pharmacological Approaches to Prevent Stroke in DM..... | 190 |
| 15.2.1 Antihypertensive Treatment | 190 |
| 15.2.2 Lipid-Lowering Therapies | 192 |
| 15.2.3 Antidiabetic Medications..... | 193 |
| 15.3 Stroke Prevention in Diabetic Patients With Atrial Fibrillation..... | 194 |
| 15.3.1 Warfarin | 194 |
| 15.3.2 Dabigatran..... | 195 |
| 15.3.3 Apixaban | 195 |
| 15.3.4 Rivaroxaban | 199 |
| References | 199 |
| 16 Peripheral Artery Disease | 203 |
| 16.1 Prevalence and Prognosis | 203 |
| 16.2 Diagnosis | 205 |
| 16.3 Pharmacological and Nonpharmacological Treatment..... | 209 |
| 16.4 Endovascular and Surgical Management | 211 |
| References | 212 |