Diabetes & Cardiovascular Disease

Reference:

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

12 Edition Braunwald's Heart Disease

Table 6 Biochemical diagnostic criteria for diabetes and pre-diabetes according to the World Health Organization and the American Diabetes Association

Glycaemic marker	WHO criteria (2011, 2019)[5,6]	ADA criteria (2021)[7]
	Diabetes	
FPG	≥7.0 mmol/L (≥126 mg/dL)	
2hPG (OGTT)	≥11.1 mmol/L (≥200 mg/dL)	
HbA1c	≥6.5% (≥48 mmol/mol)	
RPG	≥11.1 mmol/L (≥200 mg/dL)	
	Pre-diabetes	
FPG	6.1–6.9 mmol/L (110–125 mg/dL)	5.6–6.9 mmol/L (100–125 mg/dL)
2hPG (OGTT)	7.8–11.0 mmol/L (140–199 mg/dL)	
HbA1c	6.0–6.4% (42–47 mmol/mol)	5.7–6.4% (39–47 mmol/mol)

ADA, American Diabetes Association; 2hPG, 2 h plasma glucose; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; RPG, random plasma glucose; OGTT, oral glucose tolerance test; WHO, World Health Organization.

Table 7 Cardiovascular risk categories in type 2 diabetes

Very high CV risk	Patients with T2DM with: • Clinically established ASCVD or • Severe TOD or • 10-year CVD risk ≥20% using SCORE2-Diabetes
High CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk 10 to <20% using SCORE2-Diabetes
Moderate CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk 5 to <10% using SCORE2-Diabetes
Low CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk <5% using SCORE2-Diabetes

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; SCORE2-Diabetes, type 2 diabetes-specific 10-year CVD risk score; T2DM, type 2 diabetes mellitus; TOD, target-organ damage; UACR, urinary albumin-to-creatinine ratio.
Severe TOD defined as eGFR <45 mL/min/1.73 m^2 irrespective of albuminuria; or eGFR 45–59 mL/min/1.73 m^2 and microalbuminuria (UACR 30–300 mg/g; stage A2); or proteinuria (UACR >300 mg/g; stage A3); or presence of microvascular disease in at least three different sites [e.g. microalbuminuria (stage A2) plus retinopathy plus neuropathy].[43–45]

Table 7 Cardiovascular risk categories in patients with diabetes[a]

Very high risk	Patients with DM **and** established CVD **or** other target organ damage[b] **or** three or more major risk factors[c] **or** early onset T1DM of long duration (>20 years)
High risk	Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor
Moderate risk	Young patients (T1DM aged <35 years or T2DM aged <50 years) with DM duration <10 years, without other risk factors

CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.

[a]Modified from the 2016 European Guidelines on cardiovascular disease prevention in clinical practice.[27]

[b]Proteinuria, renal impairment defined as eGFR <30 mL/min/1.73 m^2, left ventricular hypertrophy, or retinopathy.

[c]Age, hypertension, dyslipidemia, smoking, obesity.

Recommendation Table 3 — Recommendations for reducing weight in patients with type 2 diabetes with or without cardiovascular disease

Recommendations	Class[a]	Level[b]
It is recommended that individuals living with overweight or obesity aim to reduce weight and increase physical exercise to improve metabolic control and overall CVD risk profile.[56,79]	I	A
Glucose-lowering medications with effects on weight loss (e.g. GLP-1 RAs) should be considered in patients with overweight or obesity to reduce weight.[67]	IIa	B
Bariatric surgery should be considered for high and very high risk patients with BMI ≥35 kg/m^2 (≥Class II[c]) when repetitive and structured efforts of lifestyle changes combined with weight-reducing medications do not result in maintained weight loss.[73–77]	IIa	B

BMI, body mass index; CVD, cardiovascular disease; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

Recommendation Table 5 — Recommendations for physical activity/exercise in patients with type 2 diabetes with or without cardiovascular disease

Recommendation	Class[a]	Level[b]
It is recommended to increase any physical activity (e.g. 10 min daily walking) in all patients with T2DM with and without CVD. Optimal is a weekly activity of 150 min of moderate intensity or 75 min of vigorous endurance intensity.[97,98]	I	A
It is recommended to adapt exercise interventions to T2DM-associated comorbidities, e.g. frailty, neuropathy, or retinopathy.[108,115]	I	B
It is recommended to introduce structured exercise training in patients with T2DM and established CVD, e.g. CAD, HFpEF, HFmrEF, HFrEF, or AF to improve metabolic control, exercise capacity and quality of life, and to reduce CV events.[108,115,116]	I	B
It is recommended to perform resistance exercise in addition to endurance exercise at least twice a week.[115,117]	I	B

Recommendation Table 8 — Recommendations for glucose-lowering treatment for patients with type 2 diabetes and atherosclerotic cardiovascular disease to reduce cardiovascular risk

Recommendations	Class[a]	Level[b]
It is recommended to prioritize the use of glucose-lowering agents with proven CV benefits[c,d] followed by agents with proven CV safety[e] over agents without proven CV benefit or proven CV safety.	I	C
Sodium–glucose co-transporter-2 inhibitors		
SGLT2 inhibitors with proven CV benefit[c] are recommended in patients with T2DM and ASCVD to reduce CV events, independent of baseline or target HbA1c and independent of concomitant glucose-lowering medication.[71,150–152,155,189]	I	A
Glucagon-like peptide-1 receptor agonists		
GLP-1 RAs with proven CV benefit[d] are recommended in patients with T2DM and ASCVD to reduce CV events, independent of baseline or target HbA1c and independent of concomitant glucose-lowering medication.[70,72,161,163,164]	I	A
Other glucose-lowering medications to reduce cardiovascular risk		
If additional glucose control is needed, metformin should be considered in patients with T2DM and ASCVD.	IIa	C

Recommendation Table 9 — Recommendation for glucose-lowering treatment for patients with type 2 diabetes without atherosclerotic cardiovascular disease or severe target-organ damage to reduce cardiovascular risk

Recommendations	Class[a]	Level[b]
In patients with T2DM without ASCVD or severe TOD[c] at low or moderate risk, treatment with metformin should be considered to reduce CV risk.[183]	IIa	C
In patients with T2DM without ASCVD or severe TOD[c] at high or very high risk, treatment with metformin may be considered to reduce CV risk.	IIb	C
In patients with T2DM without ASCVD or severe TOD[c] but with a calculated 10-year CVD risk[d] ≥10%, treatment with a SGLT2 inhibitor or GLP-1 RA may be considered to reduce CV risk.[155,164]	IIb	C

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT2, sodium–glucose co-transporter-2; T2DM, type 2 diabetes mellitus; TOD, target-organ damage; UACR, urinary albumin-to-creatinine ratio.

[a]Class of recommendation.

[b]Level of evidence.

[c]Severe TOD defined as eGFR <45 mL/min/1.73 m^2 irrespective of albuminuria; or eGFR 45–59 mL/min/1.73 m^2 and microalbuminuria (UACR 30–300 mg/g; stage A2); or proteinuria (UACR >300 mg/g; stage A3); or presence of microvascular disease in at least three different sites [e.g. microalbuminuria (stage A2) plus retinopathy plus neuropathy].

[d]Using SCORE2-Diabetes.

Weight gain	Weight loss	Hypoglycemia
Sulfonylureas	**Metformin**	**Sulfonylureas**
Thiazolidinediones	**SGLT2 Inh**	Insulin
Insulin	**GLP-1 RA**	

Recommendation Table 10 — Recommendations for blood pressure management in patients with diabetes

Recommendations	Class[a]	Level[b]
Screening for hypertension		
Regular BP measurements[c] are recommended in all patients with diabetes to detect and treat hypertension to reduce CV risk.[193,232,233]	I	A
Treatment targets		
Anti-hypertensive drug treatment is recommended for people with diabetes when office BP is ≥140/90 mmHg.[196,202,234,235]	I	A
It is recommended to treat hypertension in patients with diabetes in an individualized manner. The BP goal is to target SBP to 130 mmHg and <130 mmHg if tolerated, but not <120 mmHg. In older people (age >65 years), it is recommended to target SBP to 130–139 mmHg.[196,236–238]	I	A
An on-treatment SBP target of <130 mmHg may be considered in patients with diabetes at particularly high risk of a cerebrovascular event to further reduce their risk of stroke.[194–198,239,240]	IIb	B

Treatment and evaluation		
Lifestyle changes (weight loss if overweight, physical activity, alcohol restriction, sodium restriction, increased consumption of vegetables, using low-fat dairy products) are recommended in patients with diabetes and hypertension.[205–207,210]	I	A
It is recommended to initiate treatment with a combination of a RAS inhibitor and a CCB or thiazide/thiazide-like diuretic.[196,213–216,218,241]	I	A
Home BP self-monitoring should be considered in patients with diabetes on anti-hypertensive treatments to check that BP is appropriately controlled.[242]	IIa	B
24 h ambulatory blood pressure monitoring should be considered to assess abnormal 24 h BP patterns, including nocturnal hypertension and reduced or reversed nocturnal BP dipping, and to adjust anti-hypertensive treatment.[243]	IIa	B

BP, blood pressure; CCB, calcium channel blocker; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; RAS, renin–angiotensin system; SBP, systolic blood pressure.

BP Control in Diabetes

➢ *First line:*

- ACEI or ARB (Drug of choice)
- CCB
- Thiazide like Diuretics (Chlorthalidone- Indapamide)

➢ *Second line:*

- Beta Blocker (Carvedilol & Labetalol: better glycemic effect)
- MRAs
- Alpha Blocker
- Centrally acting agents

Dyslipidemia in Diabetes

- **Increased Apo B**
- **Increased Triglyceride**
- **Increased LDL**
- **Decreased HDL**

Recommendation Table 11 — Recommendations for the management of dyslipidaemia in patients with diabetes

Recommendations	Class[a]	Level[b]
Lipid targets		
In patients with T2DM at moderate CV risk, an LDL-C target of <2.6 mmol/L (<100 mg/dL) is recommended.[248,249]	I	A
In patients with T2DM at high CV risk, an LDL-C target of <1.8 mmol/L (<70 mg/dL) and LDL-C reduction of at least 50% is recommended.[248,249]	I	A
In patients with T2DM at very high CV risk, an LDL-C target of <1.4 mmol/L (<55 mg/dL) and LDL-C reduction of at least 50% is recommended.[248,249]	I	B
In patients with T2DM, a secondary goal of a non-HDL-C target of <2.2 mmol/L (<85 mg/dL) in very high CV risk patients and <2.6 mmol/L (<100 mg/dL) in high CV risk patients is recommended.[283–285]	I	B

Lipid-lowering treatment		
Statins are recommended as the first-choice LDL-C-lowering treatment in patients with diabetes and above-target LDL-C levels. Administration of statins is defined based on the CV risk profile of the patients and the recommended LDL-C (or non-HDL-C) target levels.[247–249]	I	A
A PCSK9 inhibitor is recommended in patients at very high CV risk, with persistently high LDL-C levels above target despite treatment with a maximum tolerated statin dose, in combination with ezetimibe, or in patients with statin intolerance.[267,286]	I	A
If the target LDL-C is not reached with statins, combination therapy with ezetimibe is recommended.[259,260]	I	B
If a statin-based regimen is not tolerated at any dosage (even after re-challenge), a PCSK9 inhibitor added to ezetimibe should be considered.[287,288]	IIa	B
If a statin-based regimen is not tolerated at any dosage (even after re-challenge), ezetimibe should be considered.[259,260]	IIa	C
High-dose icosapent ethyl (2 g b.i.d.) may be considered in combination with a statin in patients with hypertriglyceridaemia[c].[274]	IIb	B

b.i.d., twice a day; CV, cardiovascular; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9;

Recommendation Table 13 — Recommendations for antithrombotic therapy in patients with diabetes and acute or chronic coronary syndrome without indications for long-term oral anticoagulation

Recommendations	Class[a]	Level[b]
ASA at a dose of 75–100 mg o.d. is recommended in patients with diabetes and previous MI or revascularization (CABG or stenting).[291,325,326]	I	A
In patients with ACS and diabetes who undergo PCI, a $P2Y_{12}$ receptor inhibitor (ticagrelor or prasugrel) is recommended in addition to ASA (75–100 mg o.d.), maintained over 12 months.[310–312,314]	I	A
Clopidogrel 75 mg o.d. following appropriate loading (e.g. 600 mg or at least 5 days already on maintenance therapy) is recommended in addition to ASA for 6 months following coronary stenting in patients with CCS, irrespective of stent type, unless a shorter duration is indicated due to the risk or occurrence of life-threatening bleeding.[327–332]	I	A
Clopidogrel is recommended as an alternative in case of ASA intolerance.[333]	I	B
In patients with diabetes and ACS treated with DAPT who are undergoing CABG and do not require long-term OAC therapy, resuming a $P2Y_{12}$ receptor inhibitor as soon as deemed safe after surgery and continuing it up to 12 months is recommended.[315,334,335]	I	C
Prolonging DAPT beyond 12 months after ACS should be considered for up to 3 years in patients with diabetes who have tolerated DAPT without major bleeding complications.[c,317,318,336]	IIa	A
Adding very low-dose rivaroxaban[d] to low-dose ASA for long-term prevention of serious vascular events should be considered in patients with diabetes and CCS or symptomatic PAD without high bleeding risk.[304,305]	IIa	B

ACS, acute coronary syndrome; ASA, acetylsalicylic acid; b.i.d., twice a day; CABG, coronary artery bypass graft; CCS, chronic coronary syndrome; DAPT, dual antiplatelet therapy; MI, myocardial infarction; OAC, oral anticoagulant; o.d., once daily; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention.

[a]Class of recommendation.

[b]Level of evidence.

[c]In case of ticagrelor, a reduced dose (60 mg b.i.d.) should be used.[317]

[d]Rivaroxaban 2.5 mg b.i.d.

Recommendation Table 14 — Recommendations for antithrombotic therapy in patients with diabetes and acute or chronic coronary syndrome and/or post-percutaneous coronary intervention requiring long-term oral anticoagulation

Recommendations	Class[a]	Level[b]
In patients with AF and receiving antiplatelet therapy, eligible for anticoagulation, and without a contraindication,[c] NOACs are recommended in preference to a VKA.[339,340,343]	I	A
In patients with ACS or CCS and diabetes undergoing coronary stent implantation and having an indication for anticoagulation, triple therapy with low-dose ASA, clopidogrel, and an OAC is recommended for at least 1 week, followed by dual therapy with an OAC and a single, oral, antiplatelet agent.[339–342,344,345]	I	A
In patients with ACS or CCS and diabetes undergoing coronary stent implantation and having an indication for anticoagulation, prolonging triple therapy with low-dose ASA, clopidogrel, and an OAC should be considered up to 1 month if the thrombotic risk outweighs the bleeding risk in the individual patient.[341–344]	IIa	C

Recommendation Table 15 — Recommendations for gastric protection in patients with diabetes taking antithrombotic drugs

Recommendations	Class[a]	Level[b]
When antithrombotic drugs are used in combination, proton pump inhibitors are recommended to prevent gastrointestinal bleeding.[337,347,348,351–353,355]	I	A
When a single antiplatelet or anticoagulant drug is used, proton pump inhibitors should be considered to prevent gastrointestinal bleeding, considering the bleeding risk of the individual patient.[338,347,348,351,352]	IIa	A
When clopidogrel is used, omeprazole and esomeprazole are not recommended for gastric protection.[356]	III	B

Recommendation Table 17 — Recommendations for revascularization in patients with diabetes

Recommendations	Class[a]	Level[b]
It is recommended that similar revascularization techniques are implemented (e.g. the use of DES and the radial approach for PCI, and the use of the left internal mammary artery as the graft for CABG) in patients with and without diabetes.[400]	I	A
Myocardial revascularization in CCS is recommended when angina persists despite treatment with anti-anginal drugs or in patients with a documented large area of ischaemia (>10% LV).[382,401,402,402a]	I	A
Complete revascularization is recommended in patients with STEMI without cardiogenic shock and with multivessel CAD.[403–405]	I	A
Complete revascularization should be considered in patients with NSTE-ACS without cardiogenic shock and with multivessel CAD.[406,407]	IIa	C
Routine immediate revascularization of non-culprit lesions in patients with MI and multivessel disease presenting with cardiogenic shock is not recommended.[408]	III	B

CABG, coronary artery bypass graft; CAD, coronary artery disease; CCS, chronic coronary syndrome; DES, drug-eluting stents; LV, left ventricle; MI, myocardial infarction; NSTE-ACS, non-ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

Heart Failure and Diabetes

- CAD (most common cause)
- HTN
- AF
- Cardiomyopathy (LVH)
- Cardio neuropathy
- Microangiopathy
- Fluid expansion
- Renal Hyper filtration
- SNS overdrive

Recommendation Table 20 — Recommendations for heart failure treatments in patients with heart failure with reduced ejection fraction and diabetes

Recommendations	Class[a]	Level[b]
Recommendations for the pharmacological treatment indicated in patients with HFrEF (NYHA class II–IV) and diabetes		
SGLT2 inhibitors (dapagliflozin, empagliflozin, or sotagliflozin[c]) are recommended in all patients with HFrEF and T2DM to reduce the risk of HF hospitalization and CV death.[189,491,494,497]	I	A
Sacubitril/valsartan or an ACE-I is recommended in all patients with HFrEF and diabetes to reduce the risk of HF hospitalization and death.[471,501,502,527]	I	A
Beta-blockers[d] are recommended in patients with HFrEF and diabetes to reduce the risk of HF hospitalization and death.[509–512,528]	I	A

MRAs[e] are recommended in patients with HFrEF and diabetes to reduce the risk of HF hospitalization and death.[507,529]	I	A
An intensive strategy of early initiation of evidence-based treatment (SGLT2 inhibitors, ARNI/ ACE-Is, beta-blockers, and MRAs), with rapid up-titration to trial-defined target doses starting before discharge and with frequent follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce re-admissions or mortality.[490]	I	B

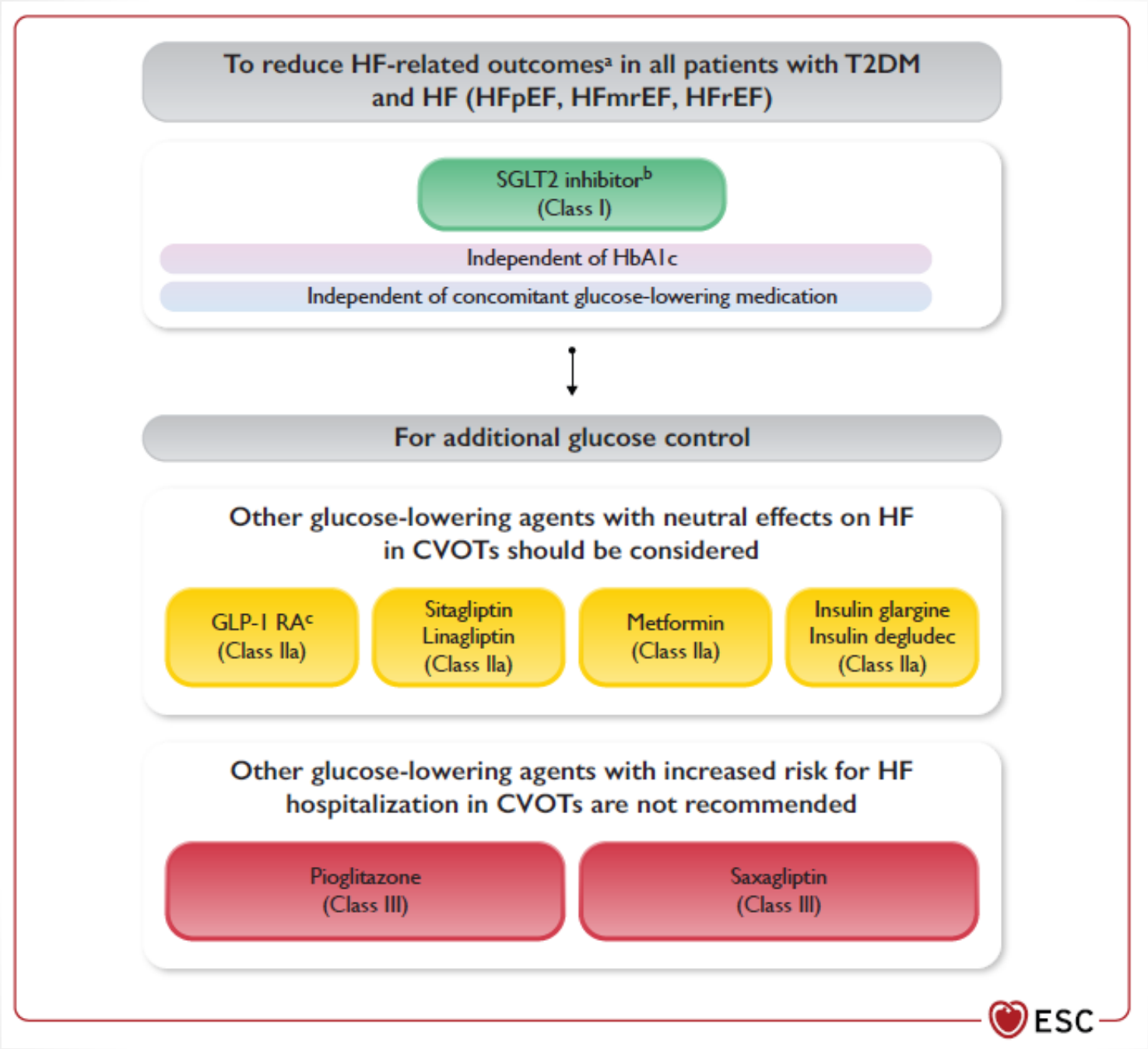
Sustained-released metoprolol succinate

Carvedilol - Bisoprolol - Nebivolol

Recommendation Table 21 — Recommendations for heart failure treatments in patients with diabetes and left ventricular ejection fraction over 40%

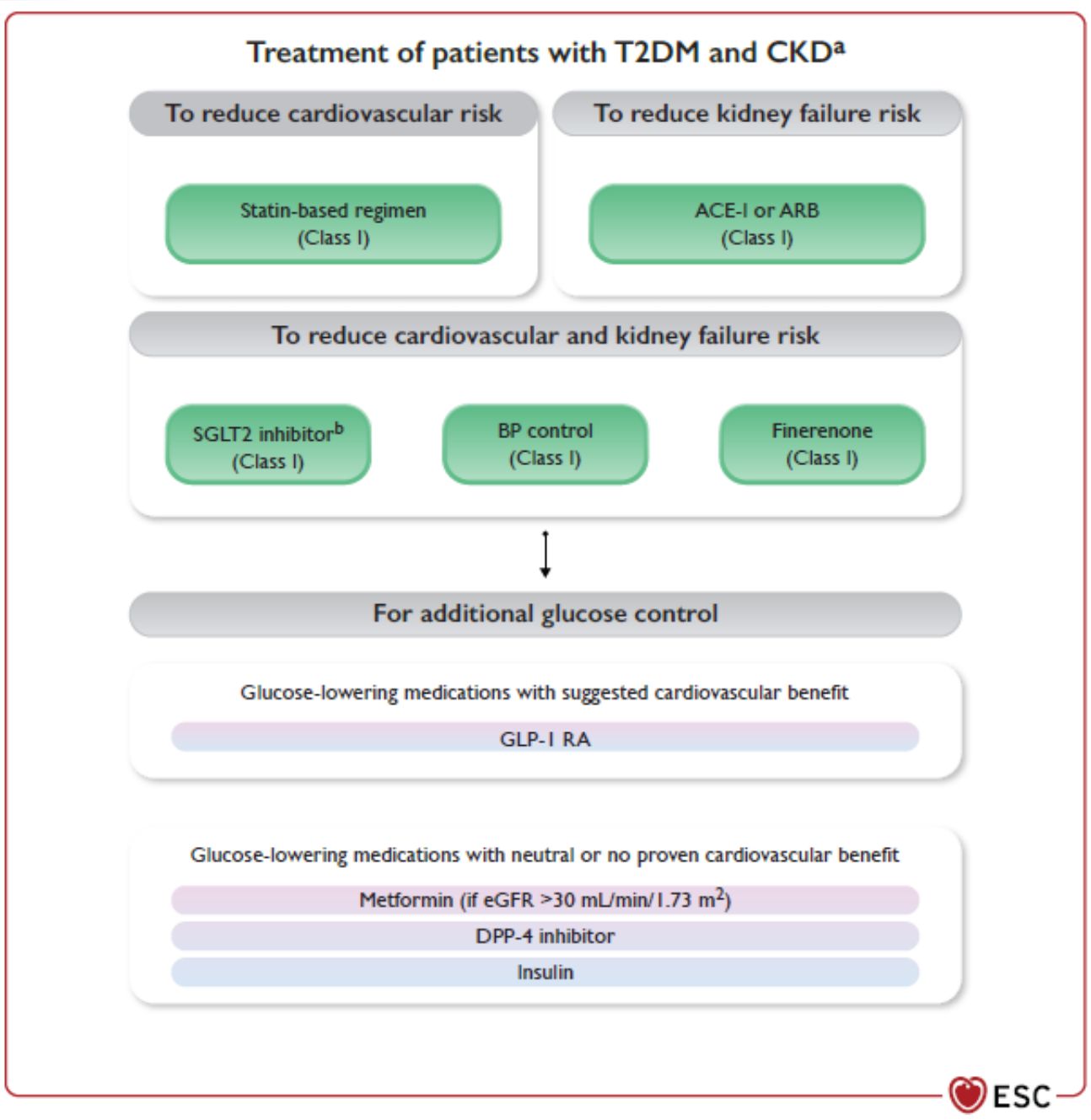
Recommendations	Class[a]	Level[b]
Empagliflozin or dapagliflozin are recommended in patients with T2DM and LVEF >40% (HFmrEF and HFpEF) to reduce the risk of HF hospitalization or CV death.[530–533]	I	A
Diuretics are recommended in patients with HFpEF or HFmrEF and diabetes with signs and/or symptoms of fluid congestion to improve symptoms, exercise capacity, and HF hospitalization.[520]	I	C

CV, cardiovascular disease; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; LVEF, left ventricular ejection fraction; T2DM, type 2 diabetes mellitus.


To reduce HF-related outcomes[a] in all patients with T2DM and HF (HFpEF, HFmrEF, HFrEF)
SGLT2 inhibitor[b] (Class I)
Independent of HbA1c
Independent of concomitant glucose-lowering medication
For additional glucose control
Other glucose-lowering agents with neutral effects on HF in CVOTs should be considered
GLP-1 RA[c] (Class IIa)
Sitagliptin Linagliptin (Class IIa)
Metformin (Class IIa)
Insulin glargine Insulin degludec (Class IIa)
Other glucose-lowering agents with increased risk for HF hospitalization in CVOTs are not recommended
Pioglitazone (Class III)
Saxagliptin (Class III)
ESC

AF and Diabetes

Anticoagulation		
Oral anticoagulation is recommended for preventing stroke in patients with AF and diabetes and with at least one additional (CHA_2DS_2-VASc) risk factor for stroke.[636]	I	A
For preventing stroke in AF, NOACs are recommended in preference to VKAs, with the exception of patients with mechanical valve prostheses or moderate to severe mitral stenosis.[637]	I	A
Oral anticoagulation should be considered for preventing stroke in patients with AF and diabetes but no other CHA_2DS_2-VASc risk factor for stroke. This includes patients with T1DM or T2DM <65 years old.[638–640]	IIa	B


Treatment of patients with T2DM and CKD[a]
To reduce cardiovascular risk
To reduce kidney failure risk
Statin-based regimen (Class I)
ACE-I or ARB (Class I)
To reduce cardiovascular and kidney failure risk
SGLT2 inhibitor[b] (Class I)
BP control (Class I)
Finerenone (Class I)
For additional glucose control
Glucose-lowering medications with suggested cardiovascular benefit
GLP-1 RA
Glucose-lowering medications with neutral or no proven cardiovascular benefit
Metformin (if eGFR >30 mL/min/1.73 m2)
DPP-4 inhibitor
Insulin
ESC

Thanks for your attention