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ESC GUIDELINES

2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

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Conceptos previos

Todo paciente con enfermedad CV establecida debe ser cribado para DM (HbA1c o glucemia capilar).

El riesgo de enfermedad coronaria comienza desde antes del diagnóstico de DM y aumenta con los niveles de glucemia.

Cuando la DM está establecida el sexo no protege frente al riesgo CV.

Ante un paciente diabético, evaluar:

- Microalbuminuria.
- ECG (si HTA o sospecha de enfermedad CV).
- Ecocardiografía (si moderado o alto riesgo de enfermedad CV).
- Controversia en estudio carotídeo en ausencia de eventos.

Estratificación del riesgo CV

MUY ALTO RIESGO:

- DM + enfermedad CV establecida.
- DM + lesión de órgano diana (ejemplo: proteinuria o FG < 30).
- DM tipo 1 con >20 años de evolución.

ALTO RIESGO:

- DM + 3 o más factores de riesgo mayores.
- DM tipo 2 con >20 años de evolución.

RIESGO MODERADO:

- DM tipo 1 <35 años con <10 años de evolución de DM.
- DM tipo 2 <50 años con <10 años de evolución de DM sin otros factores de riesgo CV.

Prevención enfermedad CV

HÁBITOS DE VIDA:

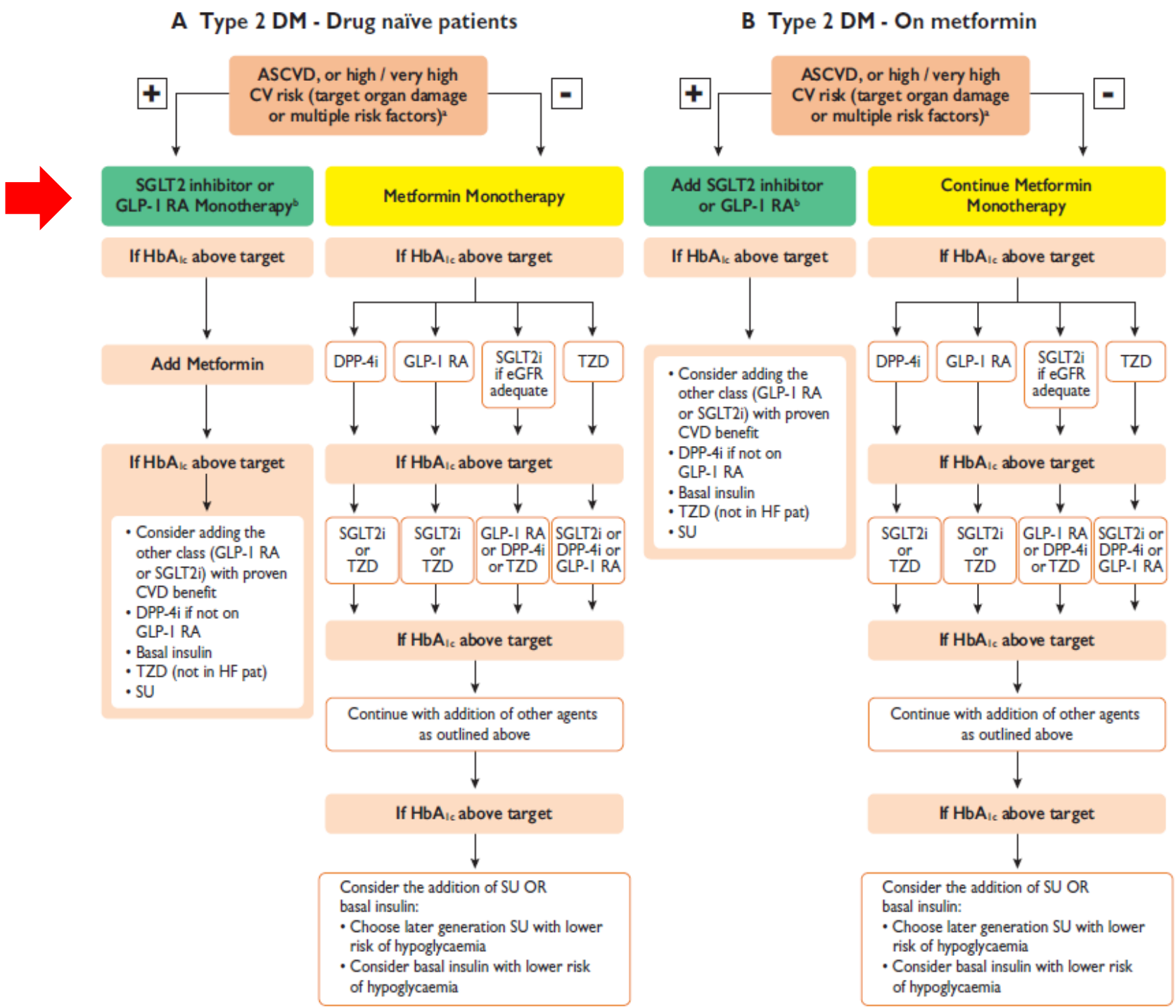
- Cambios en el hábito de vida son la clave en la prevención de la DM y sus complicaciones CV.

CONTROL GLUCÉMICO:

- HbA1c < 7% reduce las complicaciones microvasculares.
- Se deben individualizar los objetivos en población anciana.
- La hipoglucemia se ha relacionado con mayor tasa de eventos CV.

GAPS IN EVIDENCE:

- No está definido cómo personalizar los objetivos.
- Papel de nuevas tecnologías en control glucémico.


A Type 2 DM - Drug naïve patients
ASCVD, or high / very high CV risk (target organ damage or multiple risk factors)[a]
+
-
SGLT2 inhibitor or GLP-1 RA Monotherapy[b]
Metformin Monotherapy
If HbA1c above target
Add Metformin
If HbA1c above target
• Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
• DPP-4i if not on GLP-1 RA
• Basal insulin
• TZD (not in HF pat)
• SU
If HbA1c above target
DPP-4i
GLP-1 RA
SGLT2i if eGFR adequate
TZD
If HbA1c above target
SGLT2i or TZD
SGLT2i or TZD
GLP-1 RA or DPP-4i or TZD
SGLT2i or DPP-4i or GLP-1 RA
If HbA1c above target
Continue with addition of other agents as outlined above
If HbA1c above target
Consider the addition of SU OR basal insulin:
• Choose later generation SU with lower risk of hypoglycaemia
• Consider basal insulin with lower risk of hypoglycaemia
B Type 2 DM - On metformin
ASCVD, or high / very high CV risk (target organ damage or multiple risk factors)[a]
+
-
Add SGLT2 inhibitor or GLP-1 RA[b]
Continue Metformin Monotherapy
If HbA1c above target
• Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
• DPP-4i if not on GLP-1 RA
• Basal insulin
• TZD (not in HF pat)
• SU
If HbA1c above target
DPP-4i
GLP-1 RA
SGLT2i if eGFR adequate
TZD
If HbA1c above target
SGLT2i or TZD
SGLT2i or TZD
GLP-1 RA or DPP-4i or TZD
SGLT2i or DPP-4i or GLP-1 RA
If HbA1c above target
Continue with addition of other agents as outlined above
If HbA1c above target
Consider the addition of SU OR basal insulin:
• Choose later generation SU with lower risk of hypoglycaemia
• Consider basal insulin with lower risk of hypoglycaemia

iSGLT2 / GLP-1 se convierten en primera línea por delante de metformina en naïve de alto o muy alto riesgo CV o enfermedad CV establecida.

- EMPA-REG, CANVAS, DECLARE, CREDENCE -> iSGLT2
- LEADER, SUSTAIN, REWIND, PIONEER -> GLP-1

- Liraglutida y empaglifocina reducen el riesgo de muerte.
- Efectos iSGLT2 potencialmente más favorables si además el paciente presenta IC.

SGLT2 inhibitors		
Empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with T2DM and CVD, or at very high/high CV risk,[c] to reduce CV events.[306,308,309,311]	I	A
Empagliflozin is recommended in patients with T2DM and CVD to reduce the risk of death.[306]	I	B
GLP1-RAs		
Liraglutide, semaglutide, or dulaglutide are recommended in patients with T2DM and CVD, or at very high/high CV risk,[c] to reduce CV events.[176,299–300,302–303]	I	A
Liraglutide is recommended in patients with T2DM and CVD, or at very high/high CV risk,[c] to reduce the risk of death.[176]	I	B
Biguanides		
Metformin should be considered in overweight patients with T2DM without CVD and at moderate CV risk.[146,149]	IIa	C
Insulin		
Insulin-based glycaemic control should be considered in patients with ACS with significant hyperglycaemia (>10 mmol/L or >180 mg/dL), with the target adapted according to comorbidities.[260–262]	IIa	C
Thiazolidinediones		
Thiazolidinediones are not recommended in patients with HF.	III	A
DPP4 inhibitors		
Saxagliptin is not recommended in patients with T2DM and a high risk of HF.[291]	III	B

Prevención enfermedad CV

PRESIÓN ARTERIAL:

Treatment targets		
Antihypertensive drug treatment is recommended for people with DM when office BP is >140/90 mmHg.[155,178–180]	I	A
It is recommended that patients with hypertension and DM are treated 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 (aged >65 years), the SBP goal is to a range of 130 - 139 mmHg.[155,159,160,181–183]	I	A
It is recommended that target DBP is targeted to <80 mmHg, but not <70 mmHg.[160]	I	C
An on-treatment SBP of <130 mmHg may be considered in patients at particularly high risk of a cerebrovascular event, such as those with a history of stroke.[154–157,173]	IIb	C

- En preDM IECAs y ARA-II previenen la progresión a DM mejor que BB y diuréticos.

GAPS IN EVIDENCE:
- Objetivos óptimos desconocidos.
- Papel GLP1 e iSGLT2.

Prevención enfermedad CV

LÍPIDOS:

- Estatinas previenen eventos y reducen mortalidad CV.
    - Reducción de LDL 40 mg/dl se asocia a reducción del 9% de mortalidad y del 21% de eventos.
    - Reducción de LDL 40 mg/dl aumenta riesgo de DM un 10% (aumenta con la edad).
- Ezetimiba y PCSK9 nuevas oportunidades en objetivos.

GAPS IN EVIDENCE:
- Objetivos óptimos desconocidos.
- Papel PCSK9 en DM.

Prevención enfermedad CV

LÍPIDOS:

Targets		
In patients with T2DM at moderate CV risk,[c] an LDL-C target of <2.6 mmol/L (<100 mg/dL) is recommended.[210–212]	I	A
In patients with T2DM at high CV risk,[c] an LDL-C target of <1.8 mmol/L (<70 mg/dL) and LDL-C reduction of at least 50% is recommended.[d] [210–212]	I	A
In patients with T2DM at very high CV risk,[c] an LDL-C target of <1.4 mmol/L (<55 mg/dL) and LDL-C reduction of at least 50% is recommended.[d] [200,201,210]	I	B

Prevención enfermedad CV

PLAQUETAS:

- Hiperglucemia, inflamación de bajo grado, oxidación aumentada… -> activación plaquetaria.
- En pacientes de alto o muy alto riesgo CV se recomienda prevención primaria con AAS 75-100 mg.
- En riesgo moderado no está recomendada la prevención primaria con AAS.

GAPS IN EVIDENCE:
- Vacío generalizado de evidencia.

Insuficiencia cardíaca

- Pacientes con preDM o DM tienen riesgo aumentado de presentar IC.
- La presencia de IC incrementa el riesgo de DM.

- La coexistencia DM/IC aumenta el riesgo de hospitalización, muerte CV y muerte por cualquier causa.

- Primera línea de tratamiento: Metformina/iSGLT2.

GAPS IN EVIDENCE:
- ¿Cardiomiopatía diabética?
- Papel de los DPP4 en IC.
- ¿Cómo funcionan los iSGLT2 en IC?

Insuficiencia cardíaca

METFORMINA: Segura en cualquier estadio de IC.

SULFONILUREAS: No recomendadas.

TIAZOLINDIONAS: No recomendadas.

DPP4: Saxagliptina no recomendada; Sitagliptina y Linagliptina efecto neutro.

GLP-1: efecto neutro.

iSGLT2: Empaglifocina reduce hospitalización y muerte; Canaglifocina reduce riesgo de hospitalización; Dapaglifocina reduce muerte CV y hospitalización.

Fibrilación auricular

- La coexistencia DM/FA es frecuente y aumenta la mortalidad y morbilidad (ictus, IC).
    - DM es factor de riesgo independiente de FA.

- Cribado de FA a DM >65 años con palpación de pulso o ECG.

- FA identifica a DM subsidiarios de beneficiarse de control agresivo de FRCV.

Insuficiencia arterial periférica

- Manejo no difiere de pacientes sin DM.

- COMPASS: beneficio de Rivaroxaban 2.5 mg /12h + AAS 100 mg /24h en reducción de muerte CV, ictus e infarto (a costa de aumento de riesgo de sangrado mayor).

Enfermedad renal crónica

- Sólo su presencia supone alto riesgo CV.
- Se recomienda cribado anual en todo paciente diabético.
- Optimización de control glucémico frena la evolución de la ERC.
- IECA/ARA-II reducen la albuminuria -> nefroprotección.
- iSGLT2 y GLP-1 podrían conferir nefroprotección.
    - Canaglifocina reduce el riesgo relativo de ERC un 30%.

GAPS IN EVIDENCE:
- Faltan ensayos específicos para ERC en iSGLT2 y GLP-1.

Cambios en las guías de 2013

2013	2019
BP targets	
BP target <140/85 mmHg is recommended for all	Individualized BP targets are recommended SBP to 130 mmHg and, if well tolerated, <130 mmHg, but not <120 mmHg In older people (>65 years) target SBP to a range of 130 - 139 mmHg DBP to <80 mmHg but not <70 mmHg
	On-treatment SBP to <130 mmHg should be considered for patients at high risk of cerebrovascular events or diabetic kidney disease
Lipid targets	
In DM at high CV risk, an LDL-C target of <2.5 mmol/L (<100 mg/dL) In DM at very high CV risk, an LDL-C target of <1.8 mmol/L (<70 mg/dL) is recommended	In patients with T2DM at moderate CV risk, an LDL-C target of <2.6 mmol/L (<100 mg/dL) is recommended 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 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
Antiplatelet therapy	
Aspirin for primary prevention is not recommended in DM at low CVD risk	Aspirin (75 - 100 mg/day) for primary prevention may be considered in patients with DM at very high/high risk in the absence of clear contraindications
	Aspirin for primary prevention is not recommended in patients with DM at moderate CV risk

Cambios en las guías de 2013

2013	2019
Glucose-lowering treatment	
Metformin should be considered as first-line therapy in patients with DM	Metformin should be considered in overweight patients with T2DM without CVD and at moderate CV risk
Management of arrhythmias	
Oral anticoagulation in AF (paroxysmal or persistent)	
VKAs or NOACs (e.g. dabigatran, rivaroxaban, or apixaban) are recommended	It is recommended to give preference to NOACs (e.g. dabigatran, rivaroxaban, apixaban, or edoxaban)

Novedades en las guías de 2019

CV risk assessment
Resting ECG is recommended in patients with DM with hypertension or suspected CVD
Carotid or femoral ultrasound should be considered for plaque detection as CV risk modifier
Screening for CAD with coronary CT angiography and functional imaging may be considered
CAC scoring may be considered as risk modifier
ABI may be considered as risk modifier
Carotid ultrasound intima–media thickness for CV risk is not recommended
Prevention of CVD
Lifestyle intervention is recommended to delay/prevent conversion from pre-DM to T2DM
Glycaemic control
Use of self-monitoring of blood glucose should be considered to facilitate optimal glycaemic control in T2DM
It is recommended to avoid hypoglycaemia
BP management
Lifestyle changes are recommended in hypertension
RAAS blockers rather than beta-blockers/diuretics are recommended for BP control in pre-DM
It is recommended to initiate pharmacological treatment with the combination of a RAAS blocker with a calcium channel blocker or thiazide/thiazide-like diuretic
Home BP self-monitoring should be considered in patients with DM
24 h ABPM should be considered for BP assessment, and adjustment of antihypertensive treatment

Novedades en las guías de 2019

Dyslipidaemia
In patients at very high risk, with persistent high LDL-C despite treatment with maximum tolerated statin dose in combination with ezetimibe, or in patients with intolerance to statins, a PCSK9 inhibitor is recommended
Statins may be considered in asymptomatic patients with T1DM aged >30 years
Statins are not recommended in women of childbearing potential.
Antiplatelet and antithrombotic drugs
Concomitant use of a proton pump inhibitor is recommended in patients receiving aspirin monotherapy, DAPT, or oral anticoagulant monotherapy who are at high risk of gastrointestinal bleeding
Prolongation of DAPT beyond 12 months should be considered for ≤3 years in patients with DM at very high risk who have tolerated DAPT without major bleeding complications
Glucose-lowering treatment
Empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with T2DM and CVD, or at very high/high CV risk, to reduce CV events
Empagliflozin is recommended in patients with T2DM and CVD to reduce the risk of death
Liraglutide, semaglutide, or dulaglutide are recommended in patients with T2DM and CVD, or very high/high CV risk, to reduce CV events
Liraglutide is recommended in patients with T2DM and CVD, or at very high/high CV risk, to reduce the risk of death
Saxagliptin is not recommended in patients with T2DM and a high risk of HF

Novedades en las guías de 2019

Treatment of HF in DM
Device therapy with an ICD, CRT, or CRT-D is recommended
Sacubitril/valsartan instead of ACEIs is recommended in HFrEF and DM remaining symptomatic despite treatment with ACEIs, beta-blockers, and MRAs
CABG is recommended in HFrEF and DM, and two- or three-vessel CAD
Ivabradine should be considered in patients with HF and DM in sinus rhythm, and with a resting heart rate ≥70 b.p.m. if symptomatic despite full HF treatment
Aliskiren (direct renin inhibitor) in HFrEF and DM is not recommended
DM treatment to reduce HF risk
SGLT2 inhibitors (empagliflozin, canagliflozin, or dapagliflozin) are recommended to lower risk of HF hospitalization
Metformin should be considered in patients with DM and HF if eGFR >30 mL/min/1.73 m^2
GLP1-RAs and DPP4 inhibitors sitagliptin and linagliptin have a neutral effect on risk of HF and may be considered
Insulin treatment in HF may be considered
DPP4 inhibitor saxagliptin in HF is not recommended
Thiazolidinediones (pioglitazone and rosiglitazone) in HF are not recommended

Novedades en las guías de 2019

Management of arrhythmias
Attempts to diagnose structural heart disease should be considered in patients with DM with frequent premature ventricular contractions
Hypoglycaemia should be avoided as it can trigger arrhythmias
Diagnosis and management of PAD
Low-dose rivaroxaban 2.5 mg b.i.d. plus aspirin 100 mg o.d. may be considered in patients with DM and symptomatic LEAD
Management of CKD
SGLT2 inhibitors are recommended to reduce progression of diabetic kidney disease

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