Current management of diabetes and cardiovascular risk in primary care

Take home messages

Introduction

Traditional HbA1c-lowering therapies

- Decrease microvascular complications
- Do not improve CV mortality substantially

Newer T2DM treatments

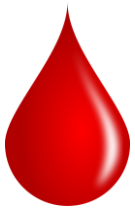
- Resulted in significant CV benefits in some CV outcome studies

Guidelines

- Assume that patients with diabetes are at higher CV risk
- Recommend full CVD prevention interventions

Progression of pre-diabetes to type 2 diabetes (1/2)

Prediabetes



Refers to impaired glucose tolerance (IGT)

For diagnosing IGT, an OGTT is recommended*

- 2hPG ≥7.8 and <11.1 mmol/L

Progression from prediabetes to T2DM

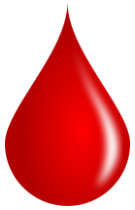
Lifestyle counselling should be provided in those at risk for T2DM and in those with IGT

Lifestyle counselling leading to healthy diet, modest weight loss and increased physical activity can prevent or delay progression

*By the ESC/EASD guidelines
OGTT: oral glucose tolerance test; 2hPG: 2-hour post-load plasma glucose

Progression of pre-diabetes to type 2 diabetes (2/2)

Type 2 diabetes mellitus



Is characterised by insulin resistance

Usually does not cause symptoms for several years

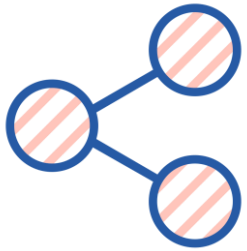
Diagnosis is based on HbA1c and FPG combined

- *HbA1c of >6.5% and FPG of >6.5 mmol/L*

FPG: fasting plasma glucose

Type 2 diabetes-related CV risk (1/2)

Microvascular and macrovascular complications



HbA1c is a good biomarker for risk of microvascular complications

- *Risk becomes evident above HbA1c of 6.5%*

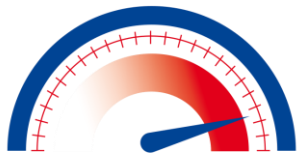
Diabetic patients are at higher risk for CVD

Diabetes is a CV mortality risk factor

The presence of microvascular complications in T2DM is an independent risk factor for macrovascular CV events

Type 2 diabetes-related CV risk (2/2)

Risk assessment



Patients with DM and ≥1 other CV risk factor or target organ damage should be considered at very high risk

All other patients with T2DM should be considered at high risk

DM: diabetes mellitus

Therapeutic considerations (1/2)

Tight glycaemic control

Can reduce microvascular complications of T2DM, but does not lower CV risk sufficiently

Rapid and strict HbA1c control can do harm

Ideal treatment for T2DM

Multifactorial intervention has been shown to reduce vascular complications and mortality

- Lipid lowering, BP lowering, and possibly use of aspirin

BP: blood pressure

Therapeutic considerations (2/2)

New anti-diabetes agents and CV outcomes

Some GLP-1RAs and SGLT2 inhibitors have shown CV benefit in CV outcome trials

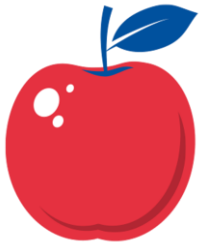
- *Benefits vary among drug classes and individual agents*

Diabetes should be considered a state of enhanced CV risk

- *Should be targeted with therapy, as opposed to only treating hyperglycaemia.*

Management options for hyperglycaemia and CV risk (1/5)

Non-pharmacological control of hyperglycaemia



Lifestyle management is the first measure for the prevention and/or management of T2DM

- *Healthy diet, physical activity and cessation of smoking*

Diabetes can be reversed by weight loss

- *This can be achieved by structured weight management programme delivered in primary care*

Management options for hyperglycaemia and CV risk (2/5)

Pharmacotherapy

Metformin

- First-line oral antiglycaemic therapy
- Does not cause weight gain and hypoglycaemia
- May reduce the risk of CV mortality, especially in obese patients

SU, α-glucosidase inhibitors and PPAR-γ agonists

- Additional oral antiglycaemic therapies
- SU and PPAR-γ agonists cause weight gain
- α-glucosidase inhibitors do not cause weight gain
- SU confer a risk of hypoglycaemia

SU: sulphonylureas; PPAR-γ: Peroxisome proliferator-activated receptor gamma

Management options for hyperglycaemia and CV risk (3/5)

Novel anti-diabetes drugs: Weight

DPP-4 inhibitors are weight neutral

GLP-1RAs and SGLT2 inhibitors induce weight loss

Novel anti-diabetes drugs: Hypoglycaemia

DPP-4 inhibitors, injectable GLP-1RAs and SGLT2 inhibitors do not cause hypoglycaemia

DPP-4: dipeptidylpeptidase-4; GLP-1RAs: glucagon-like peptide-1 receptor agonists;
SGLT2: sodium-glucose-cotransporter 2

Management options for hyperglycaemia and CV risk (4/5)

Novel anti-diabetes drugs: CV safety/ benefit

DPP-4 inhibitors	CV safety has been demonstrated for sitagliptin and linagliptin
	Higher risk of HHF was found with saxagliptin or alogliptin
GLP-1RAs	Liraglutide, semaglutide and albiglutide have shown CV safety
	Liraglutide, semaglutide and albiglutide reduce CV events
	Lixisenatide and exenatide are CV neutral

DPP-4: dipeptidylpeptidase-4; HHF: hospitalisation for heart failure;
GLP-1RAs: glucagon-like peptide-1 receptor agonists

Management options for hyperglycaemia and CV risk (5/5)

Novel anti-diabetes drugs: CV safety/ benefit

SGLT2 inhibitors

Empagliflozin and canagliflozin have been shown to lower MACE

- *With specific benefit for HF endpoints*

Dapagliflozin, tested in a lower risk population, reduced HHF

- *Without lowering MACE*

In primary prevention patients, dapagliflozin lowered HHF

- *But this SGLT2 inhibitor class does not appear to lower MACE*

SGLT2: sodium-glucose-cotransporter 2; HF: heart failure; HHF: hospitalisation for heart failure; MACE: major adverse cardiovascular events

Suggested mechanisms of new antidiabetes agents

SGLT2 inhibitors

Rapid separation of CV event curves and benefit on HF outcomes are seen with SGLT2 inhibitors

Beneficial CV effects of these drugs may therefore involve reduced circulatory volume

GLP-1RAs

The separation of CV event curves takes longer with GLP-1RAs

This drug class may therefore impact atherogenic processes

Recommendations and guidelines

Recommendations T2DM patients with CVD

Lifestyle management and metformin therapy

Additional therapy with demonstrated CVD benefit in a relevant patient population

Challenges faced in clinical reality

Personalised T2DM management

- Balancing benefits and risks
- Taking individual treatment objectives into account
- Taking specific benefits of new anti-diabetes agents in subgroups into account

Prediction of future complications

Using six variables, five subgroups of adults with new-onset diabetes have been identified with predictive value for future complications

- *Severe autoimmune diabetes, severe insulin-deficient diabetes, severe insulin-resistant diabetes, mild obesity-related diabetes and mild age-related diabetes*