Thieme

# Diabetes Mellitus and the Heart

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## Cardiovascular Risk

Patients with diabetes mellitus (DM) have a significantly increased risk of developing cardiovascular diseases with their sequelae of acute myocardial infarction, stroke and cardiovascular death. For example, even today a 60-year-old diabetic man has 6 years less life expectancy compared to a non-diabetic man of the same age, and a 60-year-old with diabetes and a previous history of a heart attack has 12 years less [1]. These data highlight the need for targeted risk stratification of patients with diabetes and the consistent treatment of diabetes, associated risk factors and cardiovascular disease.

Patients with diabetes mellitus should be categorized according to their cardiovascular risk into those with very high cardiovascular risk, high cardiovascular risk and moderate cardiovascular risk [2].

### Very high cardiovascular risk

DM and existing cardiovascular disease, or end organ damage, or ≥ 3 risk factors or diabetes duration > 20 years

### High cardiovascular risk

DM with a diabetes duration > 10 years without end organ damage, but with an additional risk factor

### Moderate cardiovascular risk

Young patients (type 1 diabetes < 35 years; type 2 diabetes < 50 years) with a diabetes duration < 10 years without other risk factors

### Further risk stratification

In addition to diagnostics for the above-mentioned risk stratification, patients with diabetes and hypertension or clinical suspicion of cardiovascular disease should receive a resting ECG. At present, no convincing data exist to use additional imaging techniques such as echocardiography, stress echocardiography, scintigraphy or MRI in asymptomatic patients with diabetes mellitus. As part of clinical routines, no determination of circulating biomarkers should be carried out as part of risk stratification.

## Cardiovascular Risk Reduction

For the recommendations on the reduction of cardiovascular risk in diabetes treatment, refer to the DDG practice recommendations on the therapy of type 2 diabetes (see p. 144) and on the treatment of lipid metabolic disorders (see p. 209). Therefore, only the basic statements are listed here:

- Patients with diabetes should receive structured advice on how to stop smoking. For patients with diabetes, a Mediterranean diet enriched with polyunsaturated and monounsaturated fatty acids is recommended. Patients with diabetes should perform moderate to strenuous physical activity for at least 150 min/week.
- In patients with type 2 diabetes and very high cardiovascular risk, a target value for LDL cholesterol of < 55 mg/dL and a minimum of 50 % reduction in LDL is recommended. For patients with a high cardiovascular risk, a target value of 70 mg/dL and a minimum of 50 % reduction in LDL is recommended. For patients with a moderate risk, a reduction in LDL cholesterol to < 100 mg/dL is recommended.
- The administration of aspirin (100 mg/day) is recommended for secondary prevention in patients with diabetes mellitus. In primary prevention administration of aspirin may be considered in patients with diabetes at very high/high risk in the absence of clear contraindications.
- The platelet aggregation inhibitor after acute coronary syndrome and/or coronary intervention (duration of dual platelet inhibition etc.) should be coordinated with the treating cardiologist.

- In accordance with the new guideline of the European Society of Cardiology, patients with diabetes mellitus should have a target blood pressure of 130–139/80–90 mmHg. A blood pressure setting < 120/70 mmHg should be avoided.
- When adjusting blood glucose levels, patients without a cardiovascular pre-existing condition should be treated according to the recommendations for type 2 diabetes; in patients with a pre-existing cardiovascular condition, hypoglycaemia should be avoided and proven therapy strategies in reducing cardiovascular risk should be used. Therefore, GLP-1 receptor agonists and/or SGLT-2 inhibitors with proven event reduction should be used for reducing cardiovascular events and mortality based on the results of large cardiovascular endpoint studies in cases of type 2 diabetes and cardiovascular diseases or a high/very high cardiovascular risk.

## Diabetes and Coronary Heart Disease

All patients with coronary heart disease should be examined for the presence of diabetes mellitus (see Diagnostics and Classification of Diabetes Mellitus, p. S1 ff). For prognostic factors, patients with diabetes mellitus and coronary heart disease should receive platelet aggregation inhibitors, ACE inhibitor therapy and lipid-lowering therapy with statins.

The first year after myocardial infarction the administration of a beta-blocker additionally leads to an improvement of the prognosis, whereby this effect decreases over the course of time. With regard to the antidiabetic therapy, the SGLT-2 inhibitors empagliflozin [3], canagliflozin [4] and dapagliflozin [5] were shown to help patients with type 2 diabetes and high cardiovascular risk benefit from a reduction in cardiovascular events and morbidity. Similarly, the administration of the GLP-1 receptor agonist liraglutide in patients with diabetes and high cardiovascular risk reduced cardiovascular events and mortality [6]. The administration of semaglutide led to a significant reduction in cardiovascular events [7]. Against the background of these data, therapy with one of these substances should be an integral part of blood glucose-lowering therapy in patients with diabetes and cardiovascular disease.

In the presence of coronary artery disease requiring intervention or surgery, the therapy of coronary revascularization in patients with diabetes does not differ from the therapy in patients without diabetes. In complex coronary findings with multi-vascular disease and low perioperative mortality, bypass surgery appears to be superior to coronary intervention. The decision on the revascularization procedure to be performed (coronary intervention or bypass surgery) should always be made by the interdisciplinary cardiac team in the case of complex coronary heart disease.

## Diabetes and Heart Failure

Epidemiological and clinical data of recent years have shown that patients with diabetes mellitus have a significantly increased risk of developing heart failure and that the prognosis of patients with diabetes and heart failure is significantly worse than that of patients with heart failure without diabetes [8, 9]. HFrEF, HFpEF and HFmrEF are categorized according to the recommendation of the European Society of Cardiology guideline (▶ **Table 1**) [10]. In principle, it can be said that half of patients with heart failure and diabetes have impaired left ventricular function.

Patients with heart failure and diabetes have limited left ventricular function. At present, clinical data only exist for patients with HFrEF that suggest an improvement in prognosis. The therapy for HFrEF in patients with diabetes does not differ from the therapy of non-diabetic patients in terms of both drug therapy and device therapy (ICD, CRT). For HFpEF and HFmrEF there are no data available that reliably prove an improvement in the prognosis of the patients, so that symptomatic therapy options -e. g. the administration of diuretics – and a treatment of comorbidity -e. g. adjustment of the arterial hypertension – are in the foreground.

With regard to blood glucose-lowering therapy, the studies with empagliflozin, canagliflozin and dapagliflozin showed a significant reduction in hospitalization for heart failure, so that these substances should be used in patients at high risk for heart failure and in patients with heart failure for blood glucose lowering and reduction of cardiovascular morbidity and mortality. Due to the increased risk of hospitalization for heart failure, glitazones and the DPP4 inhibitor saxagliptin are contraindicated in patients with heart failure.



▶ **Table 1** Definition of heart failure with preserved (HFpEF), moderately restricted (HFmrEF) and reduced ejection fraction (HFrEF).

| HF type | | HFrEF | HFmrEF | HFpEF |
|---|---|---|---|---|
| Criteria | 1 | Symptoms ± sign[1] | Symptoms ± sign[1] | Symptoms ± sign[1] |
| | 2 | LVEF < 40 % | LVEF 40–49 % | LVEF ≥ 50 % |
| | 3 | – | ▪ Increased serum concentrations of natriuretic peptides[2]<br>▪ At least 1 additional criterion:<br>– Relevant structural heart disease (LVH and/or LAE)<br>– Diastolic dysfunction[3] | ▪ Increased serum concentrations of natriuretic peptides[2]<br>▪ At least 1 additional criterion:<br>– Relevant structural heart disease (LVH and/or LAE)<br>– Diastolic dysfunction[3] |

LAE Left atrial enlargement (left atrial volume index [LAVI] > 34 ml/m$^2$); LVH left ventricular hypertrophy (left ventricular muscle mass index [LVMI] ≥ 115 g/m$^2$ for men and ≥ 95 g/m$^2$ for women). [1] Signs may be absent in early stages of heart failure (especially HFpEF) and in patients on diuretic treatment. [2] BNP > 35 pg/ml and/or NT-proBNP > 125 pg/ml. [3] E/A ratio ≥ 13, mean (septal and lateral) "E" velocity < 9 cm/s (for details see section 4.3.2 in [1]).

▶ **Table 2** Approach based on risk factors, expressed as point system with the acronym $CHA_2DS_2$-VASc score.

| Risk factor | Score |
|---|---|
| Chronic heart failure or left ventricular dysfunction | 1 |
| Hypertension | 1 |
| Age ≥ 75 years | 2 |
| Diabetes mellitus | 1 |
| Stroke/TIA/thromboembolism | 2 |
| Vascular disease history[1] | 1 |
| Age 65–74 years | 1 |
| Female | 1 |
| Maximum score | 9 |

Note: As the age can be evaluated with 0, 1 or 2 points, the maximum score is 9. [1] Condition after myocardial infarction, peripheral arterial occlusive disease, or plaque in the aorta.

## Diabetes and Atrial Fibrillation

The presence of diabetes mellitus is a separate risk factor for thromboembolic events in patients with atrial fibrillation. All patients with atrial fibrillation should be risk stratified for their risk of thromboembolism using the CHADS-VASC score (▶ **Table 2**) and accordingly receive anticoagulation with vitamin K antagonists and NOACs [11]. At this stage, no data exists that show a prognostic advantage of a rhythm restoration (cardioversion in the sinus rhythm) or frequency control in atrial fibrillation. In this respect, the procedure is comparable for patients with and without diabetes.

### German Diabetes Association: Clinical Practice Guidelines

This is a translation of the DDG clinical practice guideline published in: Diabetologie 2019; 14 (Suppl 2): S232–S234, DOI https://doi.org/10.1055/a-0898-9937

### Conflict of Interest

KS has lectured for Amgen, AstraZeneca, Bayer, OmniaMed, Lilly, Boehringer Ingelheim, NovoNordisc, Novartis and MSD and acted as consultant to AstraZeneca, Amgen and Böhringer Ingelheim. KS also carried out a research project supported by Boehringer Ingelheim. DMW has lectured and advised Amgen, AstraZeneca, Boehringer Ingelheim, MSD, NovoNordisk and Sanofi-Aventis. NM has lectured for Amgen, Boehringer Ingelheim, Sanofi-Aventis, MSD, BMS, AstraZeneca, Lilly, NovoNordisk; NM has conducted research projects supported by Boehringer Ingelheim and MSD and has acted as consultant to Amgen, Boehringer Ingelheim, Sanofi-Aventis, MSD, BMS, AstraZeneca, NovoNordisk, Lilly and Bayer. NM does not receive any personal fees for cooperation with industry.

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