Recommendations for early identification of heart failure in patients with diabetes: Consensus statement of the Swiss Society of Endocrinology and Diabetology and the Heart Failure Working Group of the Swiss Society of Cardiology

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Summary

Diabetes is a well-recognised risk factor for the development of heart failure, with a prevalence higher than 30% in patients with diabetes aged over 60 years. Heart failure often emerges as the primary cardiovascular manifestation in patients with type 2 diabetes and appears to be even more prevalent in type 1 diabetes. In Switzerland, there are approximately 500,000 individuals with diabetes, and the number of affected people has been steadily rising in recent years. Therefore, the consequences of heart failure will affect an increasing number of patients, further straining the Swiss healthcare system. Early lifestyle modification and initiation of appropriate treatment can prevent or at least significantly delay the onset of symptomatic heart failure by several years. These facts underscore the urgent need for early detection of individuals with subclinical heart failure, which often remains undiagnosed until the first episode of acute heart failure requiring hospital admission occurs. To address this issue, the European Society of Cardiology, the American Diabetes Association (ADA) and other international professional societies have published recommendations on heart failure screening, diagnosis and management. To address this issue in Switzerland, experts from the Swiss Society of Endocrinology and Diabetology, the Swiss Society of Cardiology and the General Internal Medicine specialty met and prepared a consensus report including a simple diagnostic algorithm for use in everyday practice.

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Introduction

Heart failure epidemiology

Diabetes is a significant risk factor for heart failure, along with hypertension, atherosclerotic cardiovascular disease, obesity, cardiotoxins (e.g. cardiotoxic anti-cancer therapies, alcohol) and familial predisposition [1–5]. This increased risk of heart failure in diabetes is also evident in the prevalence rates. In the general population, heart failure prevalence is estimated to be between 1.5% and 2%. However, this rate can increase to as high as 30% in individuals over the age of 60 who have diabetes [6, 7], with higher prevalence observed in those with type 1 diabetes compared to type 2 diabetes [8]. In cases of type 2 diabetes, heart failure often manifests as the first cardiovascular condition, preceding stroke, myocardial infarction or peripheral arterial disease [9]. The risk of developing heart failure correlates with the degree of deviation from normal blood glucose levels [8].

In Switzerland, the number of individuals with diabetes is increasing, currently estimated at around 500,000 people [10]. Out of these, approximately 40,000 individuals are affected by type 1 diabetes [10, 11]. The exact number of individuals with both diabetes and heart failure is not yet

known. However, recent data from the SwissDiab study reveal that at least one in ten diabetes outpatients receiving tertiary care is affected by heart failure [12]. Within this group, three out of five cases of heart failure are newly diagnosed [12].

Pathophysiology and risk factors

The pathophysiological processes in heart failure and diabetes are based on the interplay of various mechanisms [8]. This interaction may result in left ventricular systolic or diastolic dysfunction, occurring independently of other established heart failure aetiologies, such as coronary artery disease or hypertension [8]. Responsible factors include the activation of the renin-angiotensin-aldosterone system (RAAS), mitochondrial dysfunction, oxidative stress, inflammation and accumulation of advanced glycation endproducts [8].

Women with diabetes often display more severe endothelial, coronary microvascular and diastolic abnormalities than men, which leads to an increased risk of heart failure in women with diabetes [8]. Moreover, individuals with type 1 diabetes often exhibit structural features of early heart failure with the preserved ejection fraction phenotype and increased left ventricular stiffness, which explains the higher prevalence of heart failure in type 1 diabetes compared to type 2 diabetes [8]. Furthermore, other major risk factors in addition to diabetes itself contribute to the development of heart failure in patients with diabetes, such as obesity, long-term and/or suboptimal diabetes management, insulin therapy, hypertension, hyperlipidaemia and present micro- and/or macrovascular complications (e.g. diabetic kidney disease, coronary artery disease) [8].

Definition of heart failure and classification

The European Society of Cardiology (ESC) Guidelines for the diagnosis and treatment of acute and chronic heart failure define heart failure as follows [4]:

Heart failure is not a single pathological diagnosis, but a clinical syndrome consisting of cardinal symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by other physical signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema). It is due to a structural and/or functional abnormality of the heart that results in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise.

The classification of heart failure into three phenotypes based on the measurement of left ventricular ejection fraction (LVEF) has become widely accepted in clinical practice (figure 1) [4]:

Figure 1: Heart failure (HF) categories according to European Society of Cardiology (ESC) Guidelines 2021 [4]. EF: ejection fraction; LVEF: left ventricular ejection fraction.

HFrEF	HFmrEF	HFpEF
HF with reduced EF LVEF ≤40%	HF with mildly reduced EF LVEF 41–49%	HF with preserved EF LVEF ≥50%

Heart failure is a progressive disease and structural as well as functional changes start long before symptoms develop and hence before the definition of heart failure is fulfilled. The two asymptomatic stages before the development of overt heart failure have been named "at risk for heart failure" and "pre-heart failure" [1]. The presence of established diabetes alone indicates that an individual is at risk of heart failure. Additional risk factors (e.g. obesity) increase the likelihood for progression to symptomatic (overt) heart failure. If structural or functional cardiac changes occur in the absence of symptoms or signs, the "pre-heart failure" stage has been reached [1].

It is essential in general practice to identify these early, subclinical stages so that treatment can be started or intensified early, helping to prevent or delay heart failure [13, 14]. Various recommendations, including those from the German Society of Cardiology, the Austrian Diabetes Society, the Austrian Cardiology Society as well as the American Diabetes Association (ADA), emphasise the importance of early heart failure detection in individuals with diabetes [8, 15, 16].

However, these proposals lack a clearly defined algorithm for the early identification of heart failure in patients with diabetes that can be easily implemented in primary care settings. Thus, members of the Swiss Society of Endocrinology and Diabetology and the Swiss Society of Cardiology joined with general practitioners (GPs) to form a consensus group dedicated to developing a straightforward and effective recommendation for the early detection and prevention of heart failure in diabetes. A further goal was to raise awareness about the increased risk of heart failure in individuals with diabetes and to facilitate implementation of these recommendations.

Methodology

A structured approach was chosen for the development of this consensus paper, based on established recommendations from organisations such as the European Society of Cardiology and the American Diabetes Association (ADA), and aimed to achieve an algorithm adapted to Switzerland. Where available, the class of recommendation and level of evidence are provided according to the guidelines. In addition, we clearly distinguish between evidence-based recommendations and expert opinions by appending "Swiss C" to statements that are based on the consensus of the expert group.

Natriuretic peptides for early diagnosis of heart failure and detection of patients with subclinical heart failure

The natriuretic peptides (NPs) NT-proBNP and BNP are part of the diagnostic algorithm of the ESC in patients with suspected heart failure (Class I level of evidence B) [4]. If typical signs or symptoms are present, measuring natriuretic peptides as the initial diagnostic test is recommended [4]. In the non-acute setting, an NT-proBNP <125 ng/l and BNP <35 ng/l rules out heart failure hence other diagnoses must be considered. If the natriuretic peptides are higher than these cut-offs, heart failure is likely and needs to be confirmed by echocardiography [4].

As cardiomyocytes produce natriuretic peptides under stress due to volume or pressure overload of the heart,

these markers serve as indicators of the molecular stress to which the heart is exposed [5]. Thus, natriuretic peptides are valuable for the detection of patients at increased risk of developing heart failure, which includes patients with asymptomatic cardiac dysfunction [1]. In patients at risk of developing heart failure, the American Heart Association (AHA) / American College of Cardiology (ACC) / Heart Failure Society of America (HFSA) Guidelines recommend the NT-proBNP- or BNP-based screening followed by team-based care, including a cardiovascular specialist (Class IIa, level of evidence B) [13].

The STOP-HF Randomized Trial demonstrated that natriuretic peptide screening in patients at risk of heart failure, followed by collaborative care, diagnostic evaluation and treatment for those with elevated levels, can reduce the combined rates of left ventricular systolic dysfunction, diastolic dysfunction and heart failure [17]. This approach has a high probability of being cost-effective [18]. Furthermore, the PONTIAC study showed that for individuals with diabetes without heart disease but with high NT-proBNP levels, quickly increasing the doses of renin-angiotensin-aldosterone system antagonists and beta-blockers to the highest tolerable amount is both safe and effective in preventing heart-related events [14].

Consequently, the two natriuretic peptides BNP and NT-proBNP are considered suitable candidates for the early identification of heart failure in patients with diabetes [19].

Discussion

Recommendations for early identification and prevention of heart failure in patients with diabetes

Patients with diabetes are more likely to develop heart failure, particularly if they have additional risk factors, and will progress to symptomatic disease earlier than the general population. Therefore, patients should be proactively questioned at every encounter regarding typical heart failure symptoms such as breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea, reduced exercise tolerance, fatigue, tiredness, prolonged time to recover after exercise and swollen ankles.

If the patient does not report any of these typical heart failure symptoms, the Swiss consensus group recommends the following step-by-step algorithm (figure 2) based on age and natriuretic peptide levels.

Asymptomatic patients with diabetes *younger than 60 years* with no additional risk factors are unlikely to develop heart failure in the near future, as the incidence of heart failure rises with age. No specific measures need to

Figure 2: Swiss recommendations 2024 with step-by-step algorithm for heart failure (HF) identification in diabetes patients. *If a patient has several additional heart failure risk factors such as obesity[#], long-term and/or suboptimally managed diabetes therapy [##], hypertension [#], hyperlipidaemia or micro- and/or macrovascular complications (diabetic kidney disease [DKD], coronary artery disease [CAD]) [#], being female [#], a determination of NT-proBNP or BNP may be considered individually for patients <60 years. [#]according to the Consensus Report of the American Diabetes Association; [##]according to the consensus group Swiss Recommendations for Early Identification of Heart Failure in Patients with Diabetes.
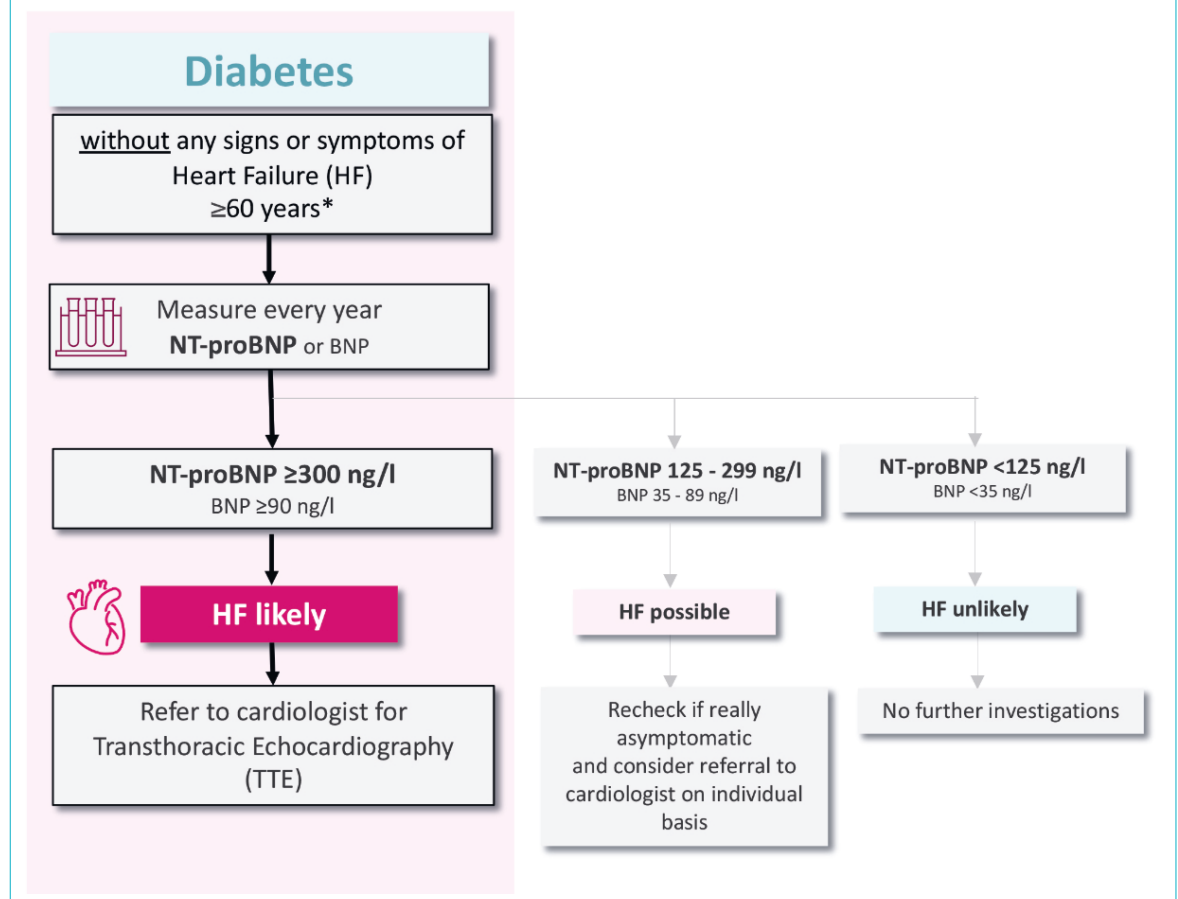
be taken in this group apart from regular clinical checks for symptoms and signs of heart failure [20] (Swiss C).

Asymptomatic diabetes patients *older than 60 years* have a higher risk of undetected heart failure. In this second group, the Swiss Consensus Group recommends measuring natriuretic peptides once a year. According to the level of the natriuretic peptides, heart failure is deemed likely (NT-proBNP ≥300 ng/l, BNP ≥90 ng/l), possible (NT-proBNP 125–299 ng/l, BNP 35–89 ng/l) or unlikely (NT-proBNP <125 ng/l, BNP <35 ng/l) (Swiss C).

– Increased natriuretic peptide levels are associated with a heightened risk of developing heart failure and of mortality, even if imaging shows no structural or functional abnormalities [5]. In asymptomatic patients, a referral to a cardiologist is recommended when subclinical heart failure is likely, i.e. if NT-proBNP ≥300 ng/l or BNP ≥90 ng/l [5]. The Swiss Consensus group has consciously chosen a higher cut-off value for natriuretic peptides than the one typically recommended for diagnosing heart failure in symptomatic patients or in the recent ESC clinical consensus statement for early diagnosis of heart failure, aiming to minimise false positive results that could lead to unnecessary investigations [4, 5] (Swiss C).

– In patients with only mildly elevated levels of natriuretic peptides (NT-proBNP 125–299 ng/l, BNP 35–89 ng), a reassessment for signs or symptoms of heart failure is recommended. For those who are truly asymptomatic, a decision should be made on an individual basis, taking into account age and the number and types of risk factors present. The patient may either be directly referred to a cardiologist or scheduled for a follow-up measurement in six months. An increase in natriuretic peptide levels during this period suggests a higher risk of developing heart failure, triggering a referral to a cardiologist. Atrial fibrillation and chronic kidney disease increase natriuretic peptide levels whereas levels are lower in obese individuals. This needs to be considered if natriuretic peptide levels are in the grey zone [8] (figure 3) (Swiss C).

– If no elevated natriuretic peptides are found (NT-proBNP <125 ng/l, BNP <35 ng/l), heart failure is unlikely and no further investigations are required. The annual measurements should be continued as part of routine management for patients with diabetes over 60 years of age (Swiss C).

The ADA Consensus group recommends annual determination of natriuretic peptides in individuals with diabetes regardless of age [8]. The Swiss consensus group recommends regular natriuretic peptide measurements for asymptomatic patients with diabetes aged 60 years or older, as the prevalence of heart failure increases significantly from this age onward [6, 7] (Swiss C). The discussions around the age cut-off also focused on practical implementation in daily practice and minimisation of unnecessary investigations. Nevertheless, regular natriuretic peptide measurements should be considered at a younger age if several additional risk factors other than diabetes are present, since this increases the likelihood of developing heart failure earlier in life.

For *asymptomatic patients with diabetes under 60 with multiple heart failure risk factors* – including obesity, prolonged poor diabetes control (evidenced by continuous HbA1c elevation), insulin therapy, hypertension, hyperlipidaemia, micro- or macrovascular complications (chronic kidney disease [CKD], diabetic kidney disease [DKD] or coronary artery disease [CAD]) and being female – individual consideration for heart failure screening using natriuretic peptides is advised [8]. In patients *with newly diagnosed diabetes*, a single measurement of natriuretic peptides may be considered for the purpose of heart failure risk assessment and as a reference value for subsequent measurements depending on age and the presence of other heart failure risk factors (Swiss C).

If heart failure symptoms are evident, a NT-proBNP level of ≥125 ng/l or a BNP level of ≥35 ng/l suggests – but does not confirm – the presence of heart failure. Patients exhibiting elevated natriuretic peptides should be evaluated by a cardiologist using echocardiography, and classified and treated based on left ventricular ejection fraction as heart failure with reduced ejection fraction (HFrEF), heart failure with mildly reduced ejection fraction (HFmrEF) or heart failure with preserved ejection fraction (HFpEF) according to the ESC Guidelines 2021 [4] (Swiss C).

Early heart failure management in patients with diabetes

The primary aim of this consensus paper is to promote the early detection of heart failure in patients with diabetes. In addition, the following section provides a summary of key therapeutic principles for patients with diabetes at high risk of heart failure.

Risk factor management, including encouragement to engage in regular physical activity, should be the standard of care (figure 4). According to the Swiss Society for Endocrinology and Diabetes (SSED) Guidelines, a combination of metformin and a sodium-glucose co-transport 2 (SGLT2) inhibitor is generally advised for patients with type 2 diabetes to provide cardiovascular and renal protection [21]. For obese patients, a combination of metformin and a glucagon-like peptide-1 receptor agonist (GLP-1 RA) should be considered initially [21]. The use of SGLT2 inhibitors is discouraged in type 1 diabetes due to the increased risk of diabetic ketoacidosis [22].

For asymptomatic patients with elevated natriuretic peptide levels, it is recommended to intensify risk factor management, encourage further lifestyle changes and review the pharmacological treatment of diabetes [21]. Thiazolidinediones, dipeptidyl peptidase 4 (DPP-4) inhibitors (especially saxagliptin and alogliptin) and sulphonylureas should be avoided in these patients [8, 21]. While definitive scientific evidence is pending, the Swiss Consensus group suggests – in line with the ADA recommendation

Figure 3: Comorbidities and level of natriuretic peptides (NPs) (according to European Society of Cardiology heart failure guidelines 2021).
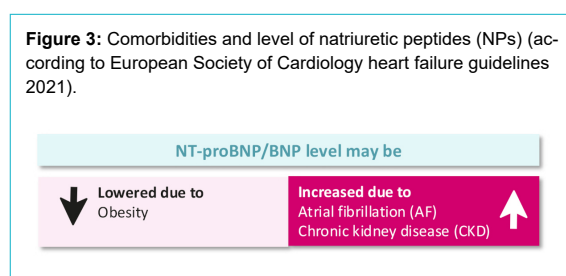

NT-proBNP/BNP level may be

Lowered due to
Obesity

Increased due to
Atrial fibrillation (AF)
Chronic kidney disease (CKD)

Figure 4: Swiss recommendations 2024 on early heart failure (HF) management in patients with diabetes. [a] Recommendation of the consensus group Swiss Recommendations for Early Identification of Heart Failure in Patients with Diabetes; no clear scientific data available yet; [b] According to the Swiss recommendations of the Society for Endocrinology and Diabetes (SGED/SSED) for the treatment of type 2 diabetes mellitus (2023) [23]. DPP-4: Dipeptidyl peptidase 4; GLP-1 RA: Glucagon-like peptide-1 receptor agonist; SGLT2-I: dapagliflozin or empagliflozin as sodium-glucose transport protein 2 (SGLT2) inhibitor.
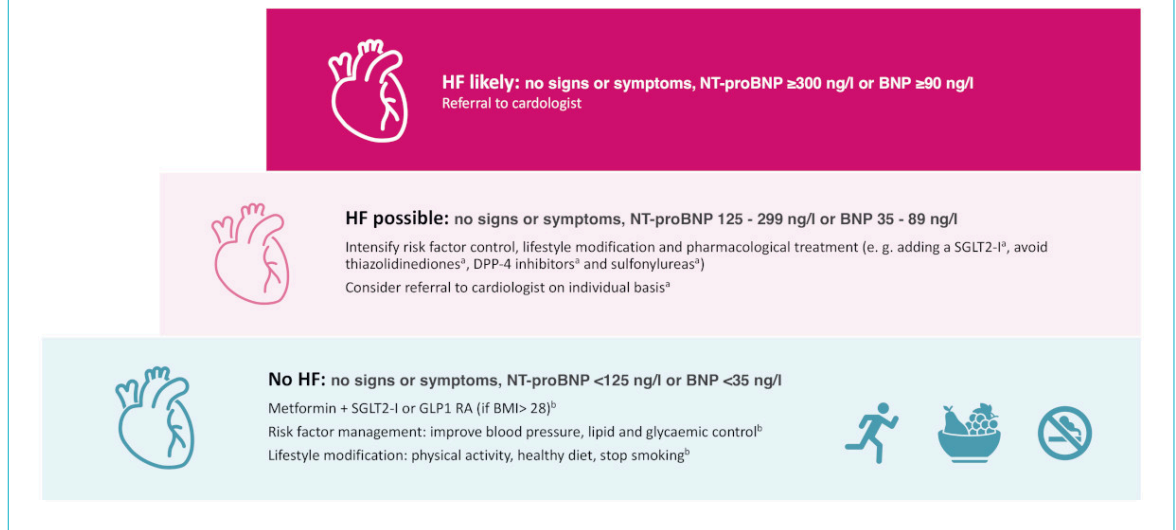
– adding an SGLT2 inhibitor for cardioprotection at this stage if not established yet [8]. Depending on the degree of natriuretic peptide elevation and other factors, a referral to a cardiologist is recommended as described above.

Figure 4 provides a summary of the main treatment standards, but for more comprehensive information, the ESC heart failure guidelines 2021 (including the 2023 update), the ADA consensus report and the recent ESC clinical consensus statement with practical algorithms for early diagnosis of heart failure should be consulted [4, 5, 8, 23].

Concluding remarks

Active monitoring for heart failure in diabetic care is strongly recommended to detect heart failure early. In addition to questioning about typical symptoms and examining for signs of heart failure at every encounter, the annual measurement of natriuretic peptides in patients older than 60 (or earlier if multiple risk factors for heart failure are present) should be a standard part of diabetes management. Early detection of patients at high risk of heart failure will delay or may even prevent progression to overt heart failure. Such a strategy can be expected to improve care before patients become symptomatic and to reduce the number of patients being diagnosed when admitted to hospital for acute heart failure, thereby reducing morbidity and mortality. The European Society of Cardiology promotes early diagnosis of heart failure not only in patients with diabetes but also in patients with other cardiovascular risk factors [5]. Further research is needed to better guide treatment of patients in stages preceding heart failure as well as to confirm the cost-effectiveness of such strategies.

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