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Prediction of Chronic Heart Failure Developmentin Patients with Diabetes and Atherosclerotic Complications: A Narrative Review

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Abstract
Heart failure (HF) is one of the most frequent and prognostically important cardiovascular complications of type 2 diabetes mellitus (T2DM), and it often develops alongside coronary, cerebrovascular, and peripheral atherosclerosis. Because effective preventive therapy now exists, identifying which patients with diabetes and atherosclerotic disease will develop HF has become a practical clinical priority. This narrative review summarises the epidemiological link between diabetes, atherosclerotic disease, and HF, and critically appraises the main prediction tools: clinical risk scores (WATCH-DM and TRS-HFDM), biomarker-based scores using natriuretic peptides and cardiac troponins, and models developed after acute coronary syndrome. Clinical scores achieve moderate discrimination (C-indices of roughly 0.70–0.76) and use routinely available data, whereas adding NT-proBNP and high-sensitivity troponin raises discrimination to 0.84–0.87 for HF hospitalisation. Performance varies with baseline risk, and few models were derived specifically in patients with established atherosclerotic disease. We outline a stepwise approach that combines a clinical score with selective biomarker testing and link risk stratification to preventive therapy with sodium-glucose cotransporter 2 (SGLT2) inhibitors. Key gaps include harmonised outcome definitions, prospective impact studies, and validation in more diverse populations.

Keywords: *Type 2 Diabetes Mellitus; Heart Failure; Atherosclerotic Cardiovascular Disease; Risk Prediction; Risk Score; Natriuretic Peptides; SGLT2 Inhibitors*

I. INTRODUCTION

Heart failure is among the most common first cardiovascular presentations of type 2 diabetes. In a cohort of 1.9 million people in England, heart failure and peripheral arterial disease were the most frequent initial manifestations of cardiovascular disease in people with T2DM, accounting for 14.1% and 16.2% of first presentations, respectively (1). Observational studies consistently show a two- to four-fold higher risk of HF in people with diabetes than in those without, and poor glycaemic control further increases that risk (2, 16). Importantly, the high prevalence of HF has persisted despite effective glucose-lowering therapy, which suggests that factors beyond hyperglycaemia drive the risk (3).

Atherosclerotic disease compounds this burden. In the international REACH registry of patients with established atherothrombosis or at high risk for it, 43.6% of the 45,227 patients followed for four years had diabetes. Diabetes was associated with a 33% higher risk of hospitalisation for HF (9.4% vs 5.9%; adjusted odds ratio 1.33), and in patients with diabetes, HF at baseline was strongly associated with subsequent cardiovascular death (adjusted hazard ratio 2.45) (4). Patients with diabetes and atherosclerotic complications therefore face two interacting threats, ischaemic events and HF, and the second is easier to overlook.

Prediction matters because the treatment landscape has changed. SGLT2 inhibitors reduce cardiovascular death and heart failure hospitalisation in patients with T2DM at high cardiovascular risk (5, 6, 17, 18), and current guidelines recommend their use to prevent HF hospitalisation in such patients (7). The clinical question is shifting from whether to treat to whom to prioritise for HF-directed prevention and monitoring. This narrative review examines how development of chronic HF can be predicted in patients with diabetes and atherosclerotic complications, what each tool contributes, and where the evidence is weakest.

II. SCOPE AND APPROCH

This is a narrative rather than a systematic review. It is deliberately restricted to 20 PubMed-indexed publications selected for their relevance to HF risk in diabetes: large epidemiological studies, scientific statements and guidelines, landmark trials, and the principal risk-prediction models with their external validations. The conclusions should therefore be read as a focused synthesis of key evidence, not an exhaustive survey. Where the evidence refers to incident HF or to hospitalisation for HF rather than to established chronic HF, we state this explicitly, because the definition of the outcome differs across tools.

III. WHY ATHEROSCLEROTIC DISEASE AND DIABETES LEAD TO HEART FAILURE

Diabetes is an independent risk factor for HF even after adjustment for coronary artery disease and its risk factors. Unlike myocardial infarction and stroke, the risk of HF in T2DM persists even when conventional risk factors such as smoking, hypertension, and LDL cholesterol are well controlled (9, 19). The pathophysiology is complex and extends beyond the structural

and functional changes of diabetic cardiomyopathy (3), and diabetes and HF share pathophysiological mechanisms that interact (2). In patients with atherosclerotic complications, ischaemic myocardial injury, prior infarction, and revascularisation add a substantial ischaemic contribution on top of diabetic myocardial disease. Kidney disease is a second major contributor. The components of the TIMI risk score, namely prior HF, atrial fibrillation, coronary artery disease, reduced estimated glomerular filtration rate, and albuminuria, highlight that underlying cardiac and renal disease are key drivers of HF hospitalisation in T2DM (9).

IV. CLINICAL RISK SCORES

4.1 WATCH-DM

The WATCH-DM score was derived with machine learning from 8,756 participants with T2DM and no HF at baseline in the ACCORD trial, who were at high cardiovascular risk. It combines nine routinely available variables: weight (BMI), age, hypertension, creatinine, HDL cholesterol, fasting plasma glucose, QRS duration, myocardial infarction, and coronary artery bypass grafting. Each one-point increment was associated with a 24% higher relative risk of HF over five years, and five-year HF incidence rose from 1.1% in the lowest quintile to 17.4% in the highest. In an external validation cohort (ALLHAT), the machine-learning model and the integer score showed good discrimination (C-index 0.74 and 0.70) and acceptable calibration (8). Because prior myocardial infarction and coronary revascularisation are score components, WATCH-DM directly incorporates atherosclerotic complications, and it requires no biomarkers or imaging.

4.2 TRS-HFDM

The TIMI Risk Score for Heart Failure in Diabetes (TRS-HFDM) was developed in 8,212 placebo-treated patients with T2DM in SAVOR-TIMI 53 (20) and validated in DECLARE-TIMI 58 (18). Five variables independently predicted HF hospitalisation: prior HF, atrial fibrillation, coronary artery disease, eGFR below 60 mL/min/1.73 m², and urine albumin-to-creatinine ratio. Together they give an integer score from 0 to 7, with prior HF and severe albuminuria weighted most heavily (9). Unlike WATCH-DM, TRS-HFDM predicts HF hospitalisation in patients with or without prior HF, which broadens its use but blurs the line between prediction of new HF and prognosis in established HF.

4.3 External validation across settings

A multicohort validation tested both scores in the TECOS trial (n = 12,028), the Look AHEAD trial (n = 4,867), and an electronic health record cohort (n = 7,475). In Look AHEAD, both scores had similar discrimination and calibration for five-year HF (C-index 0.70). Both performed worse and underpredicted risk in TECOS (C-indices 0.65 and 0.62), a trial population with established cardiovascular disease and a higher baseline risk. In the electronic health record cohort, WATCH-DM achieved a C-index of 0.73 with good calibration, whereas TRS-HFDM could not be validated there because urinary albumin-to-creatinine ratio was missing for most patients (10). Two lessons follow. First, performance depends on the baseline risk of the population, and recalibration may be needed in higher-risk atherosclerotic cohorts. Second, a score is only useful if its inputs are measured in routine practice, and albuminuria testing remains incomplete.

V. BIOMARKER-ENHANCED PREDICTION

Biomarkers of myocardial stress and injury refine risk beyond clinical variables. In pooled data from three community cohorts (ARIC, the Dallas Heart Study, and MESA), a simple integer score using high-sensitivity troponin T, NT-proBNP, high-sensitivity C-reactive protein, and ECG-based left ventricular hypertrophy stratified five- and ten-year HF risk in 6,799 participants with diabetes or prediabetes. Among people with diabetes, the five-year HF risk was 12.0% for a score of 3 or higher, whereas a score of 0 or 1 carried a risk comparable to that of people with normal glycaemia (11). A separate analysis showed that adding natriuretic peptides to the WATCH-DM score improved prediction, and the gain was greatest among patients with low or

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intermediate clinical risk; the WATCH-DM scores reached C-indices of 0.80 (machine learning) and 0.71 (integer score) in individuals with dysglycaemia (12).

In trial populations, a score built from NT-proBNP, prior HF, and high-sensitivity troponin T predicted HF hospitalisation more accurately than clinical variables alone, with C-indices of 0.87 in the derivation cohort (SAVOR-TIMI 53) and 0.84 in the validation cohort (DECLARE-TIMI 58) (13). The same score identified patients with a greater absolute benefit from the SGLT2 inhibitor dapagliflozin (13). A caveat is that the community biomarker score was derived in participants free of cardiovascular disease (11), so its performance in patients with established atherosclerotic complications is less certain.

VI. PREDICTION AFTER ACUTE CORONARY SYNDROME

Patients with diabetes who have had a recent acute coronary syndrome are a distinct high-risk group. In the EXAMINE trial of 5,380 such patients, clinical variables combined with biomarkers (chiefly NT-proBNP) enabled risk prediction for an expanded set of HF outcomes, including cardiovascular death, HF hospitalisation, rising NT-proBNP during follow-up, and initiation of loop diuretics, with a C-statistic of 0.72 (14). This is among the few analyses that address the atherosclerotic population directly, and it supports routine measurement of natriuretic peptides in this setting.

Table 1. Principal models for predicting heart failure in diabetes

Model (reference)	Derivation population	Main predictors	Outcome	Reported discrimination
WATCH-DM (8)	ACCORD trial, T2DM without HF at baseline (n = 8,756); validated in ALLHAT	BMI, age, hypertension, creatinine, HDL-C, fasting glucose, QRS duration, prior MI, prior CABG	5-year incident HF	C-index 0.74 (machine-learning model) and 0.70 (integer score) in external validation
TRS-HFDM (9)	Placebo arm of SAVOR-TIMI 53 (n = 8,212); validated in DECLARE-TIMI 58	Prior HF, atrial fibrillation, coronary artery disease, eGFR <60, urine albumin-to-creatinine ratio	Hospitalisation for HF	Gradient of risk in derivation and validation cohorts; C-index 0.70 in Look AHEAD (10)
Biomarker score (11)	Pooled ARIC, Dallas Heart Study, MESA; participants free of CVD (n = 6,799 with dysglycaemia)	hs-cTnT, NT-proBNP, hs-CRP, ECG left ventricular hypertrophy	5- and 10-year incident HF	Good discrimination and calibration reported
WATCH-DM plus natriuretic peptides (12)	Community-based individuals with dysglycaemia	WATCH-DM score with natriuretic peptide levels	5-year incident HF	C-index 0.80 (machine-learning) and 0.71 (integer score); gain from natriuretic peptides greatest at low or intermediate risk
NT-proBNP/hsTnT score (13)	Placebo arm of SAVOR-TIMI 53 (n = 6,106); validated in DECLARE-TIMI 58 (n = 7,251)	NT-proBNP, prior HF, hsTnT	Hospitalisation for HF	C-index 0.87 (derivation), 0.84 (validation)
EXAMINE model (14)	T2DM after recent acute coronary syndrome (n = 5,380)	Clinical variables plus biomarkers, chiefly NT-proBNP	Expanded HF outcomes	C-statistic 0.72

C-index, concordance index; HF, heart failure; hs-cTnT, high-sensitivity cardiac troponin T; hs-CRP, high-sensitivity C-reactive protein; MI, myocardial infarction; CABG, coronary artery bypass grafting; UACR, urine albumin-to-creatinine ratio. Values are those reported in the cited studies and are not directly comparable because populations and outcomes differ.

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VII. FROM PREDICTION TO PREVENTION

In the EMPA-REG OUTCOME trial of patients with T2DM at high cardiovascular risk, empagliflozin lowered the primary composite cardiovascular outcome and all-cause mortality compared with placebo (5). A meta-analysis of three cardiovascular outcome trials with 34,322 patients, 60.2% of whom had established atherosclerotic cardiovascular disease, examined cardiovascular and renal outcomes by baseline atherosclerotic disease, HF, and renal function (6). Its principal conclusion for this review is that the HF benefit of SGLT2 inhibitors is not restricted to patients with prior HF.

Risk scores help decide where preventive effort yields the most. In the TRS-HFDM analysis, dapagliflozin lowered the relative risk of HF hospitalisation across risk categories, but absolute reductions were larger in higher-risk patients (9). In the CANVAS programme, WATCH-DM risk category did not modify the relative effect of canagliflozin on HF hospitalisation among participants without baseline HF, and both scores identified the patients at highest risk who were most likely to benefit (15). The 2022 AHA/ACC/HFSA guideline recommends SGLT2 inhibitors to prevent HF hospitalisation in patients with T2DM and established cardiovascular disease or high cardiovascular risk, and it supports natriuretic peptide–based screening for patients at risk of HF (7).

VIII. A PRACTICAL STEPWISE APPROACH

The evidence summarised above suggests a pragmatic, two-step approach, which represents our interpretation and has not been tested prospectively in patients with atherosclerotic complications. Step one is to apply a clinical score (WATCH-DM where laboratory data are available; TRS-HFDM when albuminuria is measured) to every patient with diabetes and atherosclerotic disease who has no HF diagnosis (8–10). Step two is to measure NT-proBNP, with or without high-sensitivity troponin, selectively in patients with low or intermediate clinical risk, where biomarkers add the most information (11–13). Patients classified as high risk by either step are candidates for SGLT2 inhibitor therapy if not already prescribed, for echocardiographic assessment, and for closer follow-up. Because absolute benefit is greatest at higher baseline risk, this approach concentrates attention where it matters most (9, 13, 15). After an acute coronary syndrome, natriuretic peptide testing is particularly relevant (14).

IX. LIMITATIONS OF THE CURRENT EVIDENCE AND RESEARCH GAPS

Several limitations temper these conclusions. First, most scores were derived from clinical trial populations, which are selected and may not represent routine practice. Second, discrimination is moderate for clinical scores and falls in higher-risk cohorts (10), so scores identify risk gradients rather than individual outcomes. Third, outcome definitions differ: some tools predict incident HF, others HF hospitalisation, and few separate HF with reduced from preserved ejection fraction. Fourth, few models were developed specifically in patients with established atherosclerotic disease (14), and some key inputs, such as albuminuria, are often unavailable (10). Fifth, evidence on whether score-guided prevention improves clinical outcomes is largely indirect, derived from post hoc analyses of trials. Finally, performance in more diverse populations and in low- and middle-income settings remains to be demonstrated. Priorities include prospective impact studies, recalibration in atherosclerotic cohorts, standardised outcome definitions, and evaluation of imaging markers alongside biomarkers.

X. CONCLUSION

Heart failure is a frequent and often early complication in patients with diabetes and atherosclerotic disease. Validated clinical scores such as WATCH-DM and TRS-HFDM offer a low-cost first step, and natriuretic peptides and troponin materially improve discrimination, particularly in patients at low or intermediate clinical risk. Because SGLT2 inhibitors can reduce HF hospitalisation, risk stratification should be linked to treatment decisions. Future work should test integrated clinical-biomarker pathways in atherosclerotic populations and show that score-guided prevention improves outcomes.

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