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DEVELOPMENT OF DIAGNOSTIC APPROACHES AND IMPROVEMENT OF PREVENTION OF NEPHROCARDIAL SYNDROME IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract: This thesis is devoted to the development of diagnostic approaches and improvement of prevention of nephrocardial syndrome in patients with type 2 diabetes mellitus. Type 2 diabetes is associated with a high burden of renal and cardiovascular complications, and modern evidence shows that kidney and heart dysfunction in these patients should be considered as interconnected pathological processes rather than separate clinical problems. Early markers of kidney injury, particularly albuminuria and reduced estimated glomerular filtration rate, are closely associated with increased cardiovascular risk and may serve as key indicators for early diagnosis of nephrocardial syndrome. The study is based on analysis of contemporary guidelines and scientific publications devoted to diabetic kidney disease, chronic kidney disease risk management, cardiovascular–kidney–metabolic syndrome, and biomarker-based prediction of cardiorenal complications. Particular attention is given to routine diagnostic indicators such as UACR, eGFR, blood pressure, glycemic control, and lipid profile, as well as to additional tools including echocardiography and NT-proBNP. Recent data suggest that NT-proBNP may improve prediction of cardiovascular and renal complications in patients with type 2 diabetes and may therefore strengthen early diagnostic algorithms. The thesis concludes that effective diagnosis and prevention of nephrocardial syndrome require a complex and integrated approach. Early screening, risk stratification, and timely initiation of cardiorenal-protective treatment can reduce progression of kidney disease, lower cardiovascular risk, and improve long-term outcomes in patients with type 2 diabetes.

Keywords: type 2 diabetes mellitus, nephrocardial syndrome, diabetic kidney disease, cardiovascular risk, albuminuria, eGFR, NT-proBNP, early diagnosis, prevention, cardiorenal protection

Introduction

Currently, type 2 diabetes mellitus is one of the most widespread chronic diseases worldwide, characterized not only by impaired glucose metabolism but also by the development of multi-organ complications. According to the World Health Organization, diabetes significantly increases the risk of cardiovascular diseases, stroke, kidney failure, and premature disability, and diabetes-related complications continue to impose a substantial burden on global healthcare systems [1]. In this context, early identification of combined heart and kidney dysfunction in patients with type 2 diabetes has become one of the key priorities of modern medicine. In patients with type 2 diabetes, kidney and cardiovascular damage often develop simultaneously. Diabetic kidney disease is one of the leading causes of chronic kidney disease and is strongly associated with an increased risk of cardiovascular complications, including heart failure, atherosclerotic disease, and cardiovascular mortality [2,3]. In recent medical literature, this interaction is often described as a cardiorenal or cardiovascular–kidney–metabolic (CKM)

syndrome. The American Heart Association emphasizes that heart, kidney, and metabolic disorders should not be considered separately but rather as components of a unified pathophysiological continuum [4]. Therefore, the concept of nephrocardial syndrome in this thesis refers to the clinically significant and mutually aggravating dysfunction of the kidneys and heart in patients with type 2 diabetes [4,5].

The clinical relevance of this syndrome lies in the fact that early markers of kidney damage, such as albuminuria and reduced glomerular filtration rate (GFR), are closely associated with an increased risk of heart failure and adverse cardiovascular outcomes [3,6]. The American Diabetes Association recommends routine assessment of the urine albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) in all patients with type 2 diabetes, as these indicators play a crucial role in early detection of diabetic kidney disease and cardiovascular risk stratification [2]. Moreover, albuminuria is now considered not only a marker of kidney damage but also an independent predictor of cardiovascular mortality and heart failure [6]. However, relying solely on traditional laboratory parameters is insufficient. In recent years, increasing attention has been given to additional biomarkers and diagnostic tools, including NT-proBNP, high-sensitivity troponins, inflammatory markers, kidney-specific biomarkers, and echocardiographic parameters, for a more comprehensive assessment of cardiorenal risk in patients with type 2 diabetes [5,7]. Several studies have demonstrated that NT-proBNP provides additional prognostic value in predicting cardiovascular and renal complications in such patients [7]. This highlights the need for a multi-component diagnostic approach that evaluates both renal and cardiac function simultaneously, rather than focusing solely on glycemic control or serum creatinine levels [4,7].

In current clinical practice, one of the major challenges is that both renal and cardiac impairments in patients with type 2 diabetes are often diagnosed at advanced stages. Early screening, accurate risk stratification, and timely preventive interventions could significantly reduce the burden of complications [2,3]. According to ADA and KDIGO guidelines, therapies such as renin–angiotensin system blockers, SGLT2 inhibitors, GLP-1 receptor agonists, and non-steroidal mineralocorticoid receptor antagonists play an essential role in reducing both renal and cardiovascular risks [2,3,8]. This further supports the concept that diagnosis and prevention should be integrated into a single comprehensive strategy [8]. Thus, the relevance of this thesis lies in the need to develop effective diagnostic approaches for early detection of nephrocardial syndrome in patients with type 2 diabetes and to improve preventive strategies. The development of a diagnostic algorithm based on UACR, eGFR, blood pressure, glycemic indicators, lipid profile, cardiac biomarkers, and instrumental examinations can enhance early identification of high-risk patients and enable timely intervention [2,4,7]. Therefore, this thesis aims to analyze and improve approaches to the diagnosis and prevention of nephrocardial syndrome in patients with type 2 diabetes based on modern scientific evidence.

Main Part

In patients with type 2 diabetes mellitus (T2DM), the interaction between renal and cardiovascular injury is no longer viewed as an accidental coexistence of two common complications. Contemporary evidence shows that metabolic dysfunction, chronic inflammation, endothelial injury, activation of the renin–angiotensin–aldosterone system, oxidative stress, and hemodynamic overload create a shared pathophysiological background in which kidney damage accelerates cardiac dysfunction and cardiac impairment, in turn, worsens renal perfusion and

kidney outcomes [4]. This interconnected process is now widely interpreted within the broader cardiovascular–kidney–metabolic framework proposed by the American Heart Association, which emphasizes that diabetes, chronic kidney disease, and cardiovascular disease should be assessed as one continuum rather than isolated disorders [4]. From a clinical perspective, nephrocardial syndrome in T2DM may be understood as a condition in which diabetic kidney injury and cardiovascular dysfunction develop in parallel, reinforce one another, and increase the probability of adverse outcomes such as heart failure, progressive chronic kidney disease, hospitalization, and cardiovascular death [2,3,5]. The problem is especially important because diabetic kidney disease is one of the leading causes of chronic kidney disease worldwide, and patients with albuminuria or reduced eGFR have substantially higher cardiovascular risk than diabetic patients without renal involvement [2,3]. The ADA Standards of Care recommend that all people with T2DM undergo regular assessment of urinary albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR), since these measures are central both for detecting kidney disease and for stratifying cardiorenal risk [2].

The first practical task in developing diagnostic approaches for nephrocardial syndrome is therefore the identification of patients at increased risk. In routine practice, this begins with traditional indicators: diabetes duration, blood pressure, glycemic control, body mass index, smoking, dyslipidemia, history of cardiovascular disease, albuminuria, and decline in eGFR [2,3]. These parameters remain essential because they are accessible and clinically interpretable. ADA guidance specifically identifies UACR and eGFR as the key screening tests for kidney involvement in diabetes, while KDIGO continues to rely on the cause–GFR–albuminuria framework for staging CKD and estimating prognosis [2,3]. In T2DM, even moderately elevated albuminuria may be clinically meaningful, because albuminuria reflects not only glomerular injury but also generalized vascular dysfunction [2,6]. However, reliance on creatinine and albuminuria alone may delay recognition of the full nephrocardial burden. Some patients show progressive cardiovascular risk before advanced reductions in eGFR become obvious, while others may have declining renal reserve without overt heart failure symptoms [4,7]. For that reason, current literature increasingly supports a multidimensional diagnostic model. Beyond kidney screening, evaluation should include careful cardiovascular assessment: office and, where possible, ambulatory blood pressure monitoring, electrocardiography, echocardiographic assessment of left ventricular structure and diastolic function, and identification of subclinical fluid overload or left ventricular hypertrophy [4]. The rationale for such an expanded approach is consistent with the AHA advisory, which calls for integrated screening algorithms that identify risk at earlier stages of the cardiovascular–kidney–metabolic syndrome [4].

Among emerging markers, NT-proBNP deserves special attention. Although traditionally associated with heart failure, recent evidence suggests that NT-proBNP also improves prediction of cardiorenal complications in T2DM [7]. A 2024 *Diabetologia* study from the Hong Kong Diabetes Biobank found that NT-proBNP improved risk prediction for coronary heart disease, congestive heart failure, and kidney failure beyond clinical risk factors alone, suggesting that this biomarker may help identify diabetic patients who require more intensive surveillance and preventive therapy [7]. This is clinically relevant because nephrocardial syndrome often develops silently, and a marker that reflects myocardial stress may reveal high-risk patients before overt decompensation occurs. At the same time, NT-proBNP should be interpreted cautiously, since renal dysfunction itself may increase natriuretic peptide levels [7]. Even so, when interpreted together with eGFR, albuminuria, and imaging findings, NT-proBNP appears to add meaningful prognostic value [7]. Another important principle in diagnosis is risk

stratification rather than simple binary classification. It is not enough to state that a patient has or does not have nephrocardial syndrome; clinicians need to determine the level of risk and likely trajectory [3,4]. A patient with persistent albuminuria, moderately reduced eGFR, poorly controlled blood pressure, elevated NT-proBNP, and echocardiographic evidence of left ventricular diastolic dysfunction should be considered at much higher risk than a patient with isolated mild albuminuria and stable hemodynamics. This staged approach is in line with both CKD and CKM frameworks, which emphasize that prognosis depends on the cumulative burden of metabolic, renal, and cardiovascular abnormalities [3,4]. Such stratification is also valuable for organizing follow-up frequency, specialist referral, and therapeutic intensity [2,3].

Preventive improvement is the second core component of this thesis topic. Once nephrocardial risk is identified, the goal is not only to describe it but to intervene early enough to slow its progression. Current standards indicate that prevention in T2DM must go beyond glycemic lowering alone [2,3]. Blood pressure control, reduction of albuminuria, preservation of kidney function, and prevention of heart failure hospitalization should all be treatment targets [2,3]. ADA and KDIGO documents support the use of renin–angiotensin system blockade in appropriate patients with albuminuria and hypertension, because these agents reduce intraglomerular pressure and lower albumin excretion [2,3]. More recently, SGLT2 inhibitors have emerged as a cornerstone of cardiorenal protection in T2DM, with benefits that extend beyond glucose lowering to kidney protection and heart failure risk reduction [2,3]. GLP-1 receptor agonists also contribute to cardiovascular risk reduction in selected high-risk patients [2]. In addition, non-steroidal mineralocorticoid receptor antagonists such as finerenone have added a new dimension to prevention in diabetic kidney disease. Clinical trial data showed that finerenone reduced kidney and cardiovascular outcomes in patients with T2DM and chronic kidney disease, making it particularly relevant for those with persistent albuminuria despite standard care [8]. This is important for nephrocardial prevention because residual risk remains high even after glucose and blood pressure are treated. Therefore, prevention should be viewed as layered therapy: lifestyle modification, glycemic optimization, blood pressure control, RAAS blockade where indicated, SGLT2 inhibition, and selected use of additional protective drugs based on risk profile [2,3,8].

A practical diagnostic-preventive algorithm for nephrocardial syndrome in T2DM may therefore include several consecutive stages. First, all patients should undergo baseline annual screening with UACR and eGFR, as well as assessment of blood pressure, HbA1c, lipid profile, and cardiovascular history [2]. Second, those with albuminuria, eGFR decline, resistant hypertension, dyspnea, edema, previous cardiovascular disease, or prolonged diabetes duration should undergo expanded assessment including ECG, echocardiography, and, where available, biomarkers such as NT-proBNP and high-sensitivity troponin [4,7]. Third, patients identified as high risk should be referred for intensified cardiorenal prevention, which may include nephrology or cardiology consultation, more frequent follow-up, optimization of antihyperglycemic therapy toward cardiorenal-protective agents, and close monitoring of kidney function and fluid status [2,3]. This algorithmic model reflects current guideline trends favoring earlier and more integrated intervention [2,4]. It should also be emphasized that prevention is not limited to drugs. Lifestyle factors remain highly relevant. WHO notes that healthy diet, maintenance of normal body weight, physical activity, and avoidance of tobacco can prevent or delay T2DM and reduce downstream complications [1]. In patients who already have T2DM, these same factors influence progression of hypertension, obesity, and vascular dysfunction, all of which contribute to cardiorenal injury [1,4]. Thus, early diagnosis of nephrocardial syndrome

should also trigger structured counseling on sodium intake, weight control, exercise, and adherence. Without such measures, even the best pharmacologic strategy may remain incomplete [1,2].

Overall, the most rational approach to nephrocardial syndrome in T2DM is a combined one: early screening, layered diagnosis, biomarker-supported risk stratification, and proactive prevention [2,3,4,7]. The central idea is that kidney and heart injury in diabetes should be looked for before overt organ failure develops. If clinicians combine classical markers such as UACR and eGFR with cardiovascular evaluation and selected biomarkers such as NT-proBNP, they can identify high-risk patients earlier and tailor interventions more effectively [2,7]. In this sense, improvement of diagnosis and prevention is not merely a technical task but a change in clinical thinking—from isolated complication management to integrated cardiorenal-metabolic care [4].

Table 1. Proposed approach to diagnosing and improving prevention of nephrocardial syndrome in patients with type 2 diabetes

Component	What should be assessed	Clinical purpose	Practical significance
Baseline renal screening	UACR, eGFR	Detect diabetic kidney disease early	Identifies patients entering cardiorenal risk pathway
Baseline metabolic evaluation	HbA1c, lipid profile, BMI, blood pressure	Define overall metabolic and vascular risk	Helps stratify progression risk and treatment intensity
Cardiovascular assessment	ECG, echocardiography, heart failure symptoms, prior CVD	Detect structural/functional cardiac involvement	Supports recognition of silent or early nephrocardial changes
Biomarker expansion	NT-proBNP, selected cardiac biomarkers	Improve prognostic precision	Useful for identifying high-risk patients beyond routine factors
Risk stratification	Combine albuminuria, eGFR, BP, biomarkers, echo findings	Separate low-, moderate-, and high-risk groups	Enables personalized monitoring and referral decisions
Preventive pharmacotherapy	RAAS blockers, SGLT2 inhibitors, GLP-1 receptor agonists,	Reduce kidney progression and cardiovascular events	Integrates diagnosis with early intervention

Component	What should be assessed	Clinical purpose	Practical significance
	finerenone where indicated		
Lifestyle prevention	Diet, exercise, weight control, smoking avoidance	Lower modifiable drivers of CKM progression	Essential background therapy for long-term prevention

Conclusion

In conclusion, nephrocardial syndrome in patients with type 2 diabetes mellitus should be regarded as a clinically important manifestation of the broader cardiovascular–kidney–metabolic continuum, in which renal and cardiac dysfunction develop in parallel and worsen each other's course. The reviewed evidence shows that early renal markers such as albuminuria and reduced eGFR are closely linked with adverse cardiovascular outcomes, while integrated assessment of kidney and heart status provides a more accurate understanding of patient risk than isolated evaluation of glycemic control alone. The analysis also indicates that improvement of diagnostic approaches requires a combined strategy based on routine assessment of UACR and eGFR, clinical evaluation of cardiovascular status, and the use of additional biomarkers such as NT-proBNP in selected patients. Such an approach makes it possible to identify high-risk patients earlier, stratify prognosis more precisely, and initiate timely preventive measures before advanced renal or cardiac failure develops. At the same time, prevention should be understood as a continuous and multifactorial process. Current standards support not only glycemic control, but also blood pressure management, reduction of albuminuria, lifestyle modification, and the use of cardiorenal-protective therapies such as RAAS inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, and, in appropriate cases, finerenone. Therefore, improving prevention of nephrocardial syndrome in type 2 diabetes depends on early diagnosis, regular monitoring, and integrated treatment strategies aimed at preserving both renal and cardiovascular function.

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