Article published online: 2024-05-13

Review Article

Review of the Diagnostic and Prognostic Values of Cardiac Markers in Diabetes

Tabarak Haamid Elbo-Iswadi[1] Hind Mazen Hasan Alsharayri[1] Rahaf Wardeh[1] AlaaEldin Bashier[1] Fauzia Rashid[1] Elamin Ibrahim Abdelgadir[1]

[1] Endocrinology Department, Dubai Health Authority, Dubai, United Arab Emirates

J Diabetes Endocrine Practice

Address for correspondence Tabarak Haamid Elbo-Iswadi, MD, Endocrinology Department, Dubai Health Authority, Dubai 7272, United Arab Emirates (e-mail: t.samarrai@gmail.com).

Hind Mazen Hasan Alsharayri, Dubai Health Authority, U.A.E (e-mail: hind_mhs@hotmail.com).

Abstract

Introduction Cardiovascular disease is a leading cause of mortality in people with diabetes (PWD). We aimed to explore the role of troponin T (TnT) and probrain natriuretic peptide (proBNP) as screening and prognostic indicators of cardiovascular morbidity and mortality in PWD in the existing literature.

Methods This review paper is a focused narrative nonsystematic review of the literature which examined relevant publications pertinent to the significance of cardiac biomarkers. We aimed to investigate the diagnostic value of cardiac TnT (cTnT) and cTnI in addition to proBNP in diabetes and the prognostic value of cTnT and proBNP in diabetic and nondiabetic patients. The process of searching through literature was conducted from December 2022 to April 2023. Searches were done across PubMed and Google Scholar databases to identify relevant articles published from January 2001 to April 2023. The selected were entered into EndNote 20 software to extract the title and abstract.

Results A total of 75 articles were identified in Google Scholar in addition to 32 articles from PubMed. After a thorough review, only a total of 22 articles were selected, pointing out those which discussed the pathophysiology and diagnostic, prognostic, and screening values of the types of Tn and proBNP markers. The value of TnT in PWD, specifically T2D, is threefold higher than in healthy patients. Individuals with high levels of high-sensitivity (hs) cTnI or cTnT were at the highest mortality risk. Nonetheless, N-terminal (NT)-proBNP and TnT function independently as predictors of unfavorable outcomes.

Conclusions TnT is an important early screening tool prognostic indicator. Elevated TnT was associated with an increased risk of cardiovascular events in PWD. hs-cTn may help diabetes-related clinical care for older persons by identifying those at high mortality risk; furthermore, in diabetic individuals, NT-pro-BNP appears to be 92% sensitive and 90% specific for the diagnosis of heart failure.

Keywords

- cardiovascular
- diabetes
- mortality
- proBNP
- troponin

DOI https://doi.org/10.1055/s-0044-1786014.
ISSN 2772-7653.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Hyperglycemia, the hallmark of type 2 diabetes mellitus, is strongly related to microvascular and macrovascular complications. One of the notable complications is cardiovascular disease, the leading cause of death in persons with type 2 diabetes mellitus. Through examining the published literature, this review discusses the role of troponin T (TnT) and probrain natriuretic peptide (proBNP) as screening and prognostic markers of cardiovascular morbidity and mortality in diabetic patients. Recent international guidelines have recommended routine screening for subclinical cardiac insults, including thorough history critique, electrophysiology cardiac recordings, as well as biochemical screening, specifically for heart failure screening.

This review article aimed to elaborate on the pathophysiology between diabetes and clinical or subclinical cardiac events. We shall focus on the landmark biomarkers such as Tn, proBNP, their subtypes, and association with hemoglobin A1c in addition to their diagnostic and prognostic values in people with diabetes (PWD). Moreover, this article will summarize the diagnostic differences between diabetic and nondiabetic patients.

The comprehensiveness and thoroughness of this review make it novel compared with previous reviews, which do not orient the reader about the molecular biology, pathophysiology, and mechanism of action of these molecules. Moreover, previously published reviews only focused on highlighting the diagnostic value of the biomarkers and did not discuss the prognostic or screening values discussed in this review article.

Methodology

This review paper is a focused narrative nonsystematic review of the literature which examined relevant publications pertinent to the significance of cardiac biomarkers.

Objectives: We aimed to investigate the diagnostic value of cardiac TnT (cTnT) and cTnI in addition to proBNP in diabetes and the prognostic value of cTnT and proBNP in diabetic and nondiabetic patients.

Search methods: The process of searching through literature was done from December 2022 to April 2023. Searches were done across Google Scholar and PubMed databases to identify relevant articles published from January 2001 to April 2023 without language restrictions. Then, the selected studies from this search strategy were entered into EndNote 20 software to extract the title and abstract.

Selection criteria: All trials assessing the link between diabetes and the cardiac markers, as well as the observational data, systematic reviews were included to aid in the summary of this review.

Data extraction: Two authors have independently extracted and reviewed the available studies in the abovementioned search engines. No language, country of conduct, funding, and study duration restrictions were applied. A third author have reviewed the merged summary of the two authors and modified the manuscript, when necessary, the other authors reviewed the final version and concurred on the final article and the conclusions. Throughout the review process, four research questions were identified as shown in ►**Table 1**, and we attempted to answer them in this article.

Results

A total of 75 articles was identified in Google Scholar in addition to 32 articles from PubMed. After thorough review, only a total of 22 articles, which discussed the pathophysiology and diagnostic, prognostic, and screening values of the types of Tns and proBNP markers, in addition to two books have been selected.

Narrative Summary and Discussion

Overview of Troponin and Probrain Natriuretic Peptide

A calcium-regulatory protein known as Tn controls the calcium-dependent contraction of skeletal and cardiac muscles. Tn is uniformly distributed along the whole length of thin filaments and joins with tropomyosin and actin to form an ordered complex. Tn and tropomyosin reduce the contractile connection between myosin and actin at low intracellular Ca^{2+} concentrations. Once the Ca^{2+} concentration rises, this suppression is released by the binding of Ca^{2+} to Tn. Tn is a complex comprising three subunits which are TnC, TnI, and TnT; these subunits perform the same basic tasks of Tn, including binding to tropomyosin, inhibiting the interaction between actomyosin and Ca^{2+}, and binding to Ca^{2+}.[1]

Myocardial TnI and TnT are two myocardium-specific proteins which get released into the serum before creatine kinase (CK-MB). The location of these proteins within the cell affects the biokinetics of Tn release. Following injury, there is a biphasic rise in serum Tn levels, which is associated with the early release of free cytoplasmic proteins and the subsequent slower, more gradual rise, which coincides with the disintegration of the real cardiac muscle fiber. As early as 2 to 3 hours following the initiation of rises in the CK-MB level, Tn levels start to rise substantially in the serum. The release and elevation of Tns is sustained for 5 to 7 days due to the gradual degradation of the contractile proteins in cardiac cells.[2]

Myocardial wall stress is the primary trigger for elevated BNP and NT-proBNP production and secretion. Myocardial ischemia and endocrine regulation by cytokines and neurohormones are other factors that might be significant stimuli.[3] The interaction between BNP and the natriuretic peptide receptor type A, which generates intracellular cGMP, mediates several biological effects in the systemic circulation. BNP has various physiological effects, including natriuresis and diuresis, peripheral vasodilatation, and suppressing the sympathetic nervous and renin-angiotensin systems. BNP is excreted from plasma by interacting with the natriuretic peptide receptor type C (NPR-C) and proteolyzed by neutral endopeptidases. NT-proBNP, on the other hand, is primarily excreted by the kidneys. Recent research,

Table 1 Summary of major trials that linked the diabetes with higher cardiac markers level

Research question	Study	Study subjects	Result
What is the screening value of high-sensitivity troponin T in diabetic patients without a known cardiovascular disease?	Troponin in diabetic patients with and without chronic coronary artery disease (Observational longitudinal case-control single-center study)	• Total of 95 patients • 50 were diabetic with cardiovascular disease. • 45 were diabetic with angiographically normal coronary arteries	• 94.9% of diabetic patients without CAD had detectable troponin values. • 20.7% of diabetic patients without CAD had values higher than 14 pg/mL
What is the prognostic value of high-sensitivity troponins in diabetic patients?	The prognostic value of troponin T and N-terminal pro-B-type natriuretic peptide, alone and in combination, in heart failure patients with and without diabetes (Randomized Controlled Trial)	• Total of 1,907 patients • 1,148 (60%) were nondiabetic with heart failure • 759 (40%) were diabetic with heart failure	• Patients with both a high hs-cTnI or hs-cTnT and high comorbidity were at highest mortality risk. • Patients with high hs-cTnI or hs-cTnT, even with mild comorbidities, were linked to higher mortality
What is the diagnostic value of NT-proBNP in diabetic patients?	Prospective Comparison of ARNI (angiotensin receptor/neprilysin inhibitor) with ACEI (Angiotensin-converting enzyme inhibitors) to Determine the Impact on Global Mortality and Morbidity in Heart Failure trial (PARADIGM-HF	• Total of 1,907 patients • 1,148 (60%) were nondiabetic with heart failure • 759 (40%) were diabetic with heart failure	• There is no difference in NT-proBNP levels between patients with and without diabetes
What is the prognostic value of NT-proBNP in diabetic patients?	Usefulness of aminoterminal pro-brain natriuretic peptide testing for the diagnostic and prognostic evaluation of dyspneic patients with diabetes mellitus seen in the emergency department (from the PRIDE Study)	• Total of 599 subjects • 157 (26.2%) were diabetic • 442 were nondiabetic (74%)	• NT-pro-BNP level of 986 pg/mL is independently related to an increased risk of mortality at 1 y in diabetic patients

Abbreviations: CAD, coronary artery disease; hs-cTnI; high-sensitivity cardiac troponin I; NT-proBNP, N-terminal probrain natriuretic peptide; PRIDE, Pro-BNP Investigation of Dyspnea in the Emergency.

however, raises the possibility of additional significant clearance mechanisms for NT-proBNP. BNP has a half-life of 20 minutes, but NT-proBNP possesses a half-life of 120 minutes, which explains why the serum levels of NT-proBNP are about six times higher than those of BNP.[4]

A dynamic increase of high-sensitivity cardiac TnT and TnI (hs-cTnI or hs-cTnT) above the 99th percentile of healthy individuals signals MI (myocardial infarction) if the clinical presentation is consistent with myocardial ischemia. When high-sensitivity assays are used, cTn levels in MI patients rise quickly (often within 1 hour of symptom start) and stay elevated for a variable duration of time (which may last up to several days).[5] Although considerably below the diagnostic threshold, low-grade increases in Tn in the general population are also linked to future cardiovascular disease events and might be used to screen people for CVD risk.[6] Overall, hs-cTnI or hs-cTnT tests offer similar, not superior, diagnostic precision in the early detection of MI.[7] Furthermore, hs-cTnI or hs-cTnT assays provide an equivalent diagnostic accuracy[8] for the sharp distinction between type one MIs (which occur as a result of rupture of atherothrombotic plaques or erosion) and type 2 myocardial infarctions (which occur as a result of an imbalance and acute mismatch between the oxygen supply of the myocardium and the oxygen demand).[9]

A rise in cTnI is increasingly linked to outcomes related to CVD, whereas cTnT is more strongly linked to the probability of mortality from causes other than CVD.[1] There is no apparent difference in clearance between cTnI and cTnT once released into the bloodstream. However, cTnI is broken down and released from necrotic cardiac tissue more quickly than cTnT. In patients with MI, cTnI reaches greater peak concentrations and reverts to average concentrations more quickly due to quicker breakdown and release.[10]

Diagnostic Efficiency of Troponin T and Probrain Natriuretic Peptide

hs-Tn assays show a more significant negative predictive value for acute myocardial infarction (AMI) than conventional cTn assays. They shorten the "Tn-blind" window, allowing for faster AMI identification. They lead to an absolute increase of 4% and a relative increase of 20% in type 1 MI detection (which happens due to plaque rupture). Moreover, they are linked to a twofold increase in type 2 MI detection (which happens due to supply–demand mismatch).[5] hs-cTnI performed at 0/1 and 0/2 hours had a high negative predictive value and sensitivity for acute MI, particularly when combined with a thorough evaluation of the characteristics of the chest pain, a physical examination, an

electrocardiogram, and a repeat test at a 3-hour interval. These will aid in identifying the uncommon but possible occurrence of hs-delayed Tn release into the bloodstream, especially in patients who present early.[11] A single sensitive TnI assay exhibited a negative predictive value of 84.1% and a positive predictive value of 86.7% in individuals who presented within 3 hours following the onset of chest pain. TnI reflected a 90.7% sensitivity and 90% specificity. Regardless of when the chest pain started, the diagnostic accuracy in baseline and serial samples was essentially the same.[12]

The median values of NT-proBNP increased as left ventricular (LV) dysfunction deteriorated and New York Heart Association class rose. NT-proBNP tends to be more accurate than BNP at detecting milder forms of LV dysfunction. As a community screening test for LV dysfunction, NT-proBNP is not recommended. However, due to its high negative predictive value, NT-proBNP may be a simple and efficient method for high-risk individuals to rule out severe systolic LV dysfunction.[13] Therefore, it can be a valuable screening tool for diabetic patients as they are a high-risk group which requires early identification and exclusion of systolic LV dysfunction.

Troponin T and Diabetes

Incidence, mortality, and morbidity of illnesses including acute coronary syndrome, arrhythmias, stroke, pulmonary embolism, and other conditions that cause Tn elevation via its release in circulation have all been demonstrated to be positively predicted by hemoglobin A1c. Chronic hyperglycemia reduces glomerular filtration, which reduces Tn clearance. It also affects heart microcirculation, which causes microvascular damage and, in turn, ischemia, which contributes to increased Tn concentration.[14,15]

With modern assays, T2DM increases the levels of cTnT in the general population. In a population of T2DM patients, almost one in five had TnT values above the 99th percentile of a reference population when measured by a highly sensitive assay. Levels of TnT were stable over time, associated with conventional risk factors, and displayed a graded relationship with hospitalizations, although this trend was not statistically significant.[16]

Troponin T and Diabetic Kidney Disease

Although there were few differences between patients with and without a history of cardiovascular disease, the estimated increases in the studied cardiac biomarkers at a glomerular filtration rate (GFR) of 15 mL/min/1.73 m^2 ranged from 2-fold to 15-fold. Hs-cTnT levels correlated more strongly to measured GFR and increased more at low GFR compared with hs-cTnI. As a result, hs-cTnI can be more reliable in monitoring the cardiovascular prognosis of diabetic patients. For NT-proBNP, the rise correlating with low kidney function was more correctly predicted by a local cystatin C-based eGFR formula compared with creatinine-based eGFR (using the modification of diet in renal disease [MDRD] or chronic kidney disease collaboration equation [CKD-EPI]). To conclude, the extent of the elevation of cardiac markers at low renal function is highly variable. For NT-proBNP, cystatin C-based eGFR provides better predictions of the extent of elevation compared with the MDRD or CKD-EPI equation.[17,18]

Patients with CKD frequently have higher cTn values even when they do not have acute coronary syndrome. According to reports, cTnT concentration is elevated more frequently than cTnI. Similar to what was seen for cTnT, patients with CKD frequently have elevated cTnI values. cTnT concentration was independently related to death, while cTnI were not.[19] As a result, cTnT can be used as a biomarker tool of mortality specifically in the diabetic CKD population.

Cardiac Markers and Cardiovascular Mortality

Tn elevation is an established predictor of coronary artery disease (CAD) and diabetes mellitus. However, it is unknown if diabetic patients with CAD and diabetic patients with healthy coronary arteries have varying Tn levels. A study was conducted to examine the distribution and prognostic value of high-sensitive TnT measurement in patients with type 2 diabetes who did not have cardiovascular disease. The study's findings revealed that 94.9% of the patients had detectable Tn values, and 20.7% had values higher than the upper reference limit for the healthy population (14 pg/mL). For this patient population, the 99th percentile result was 48 pg/mL. When Tn levels were greater than 14 pg/mL, age, sex, glomerular filtration rate, and hypertension were all present. Between patients with hs-TnT >14 pg/mL and those with <hs-TnT 14pg/mL, the incidence of MACE was 3.96 per 100 patients/year (p/y) and 1.07 per 100 p/y, respectively (hazard ratio [HR] = 3.78; 95% confidence interval [CI]: 1.49–9.58; $p = 0.005$). The study concluded that the 99th percentile value of TnT in a population of patients with type 2 diabetes is threefold higher than the value proposed by the manufacturer for a healthy population. The distribution of TnT readings between men and women was also shown to be significantly different, according to the study. Since TnT readings over the reference upper threshold were linked to an increase in the risk of cardiovascular events in these individuals, this biomarker may be an important early screening tool and prognostic indicator.[20]

Moreover, increases in either Tn (9.4 ng/L for hs-cTnI and 25 ng/L for hs-cTnT) were found to be linked to coronary heart disease, heart failure, chronic renal disease, pulmonary illness, dementia, hypertension hypoglycemia, and frailty. High hs-cTnI and high hs-cTnT further stratified mortality risk beyond comorbidity levels across a median follow-up of 6.2 years (418 fatalities); individuals with a high hs-cTnI or hs-cTnT and high comorbidity were at highest mortality risk. High hs-cTnI (HR: 3.0 [95% CI: 1.7, 5.4]) or hs-cTnT (HR: 3.3 [95% CI: 1.8, 6.2]) were linked to higher mortality, even in patients with mild comorbidities. This reflects how both hs-cTnI and hs-cTnT represented a variety of comorbidities. Therefore, high-sensitivity cTn may help diabetes-related clinical care for older persons by identifying those at high mortality risk.[21]

Furthermore, it has been seen that diabetic patients with CAD had higher levels of Tn than did controls (median values, 12.0 pg/mL [95% CI:10–16] vs. 7.0 pg/mL [95% CI: 5.9–8.5], respectively; $p = 0.0001$). The diagnosis of CAD has an area under the receiver operating characteristic curve of 0.712, with a sensitivity of 70% and a specificity of 66%. The two

groups did not vary in plasma BNP levels or oxidative stress markers (myeloperoxidase, nitrotyrosine, and oxidized LDL). Gender ($p = 0.04$), serum glucose ($p = 0.03$), and TnI ($p = 0.01$) all showed independent statistical significance in a multivariate analysis. In conclusion, chronic CAD is associated with Tn increase, in diabetic patients with several concomitant cardiovascular risk factors.[20]

NT-proBNP and TnT were measured in the biomarker substudy of the "Prospective Comparison of ARNI (angiotensin receptor/neprilysin inhibitor) with ACEI (Angiotensin-converting enzyme inhibitors) to Determine the Impact on Global Mortality and Morbidity in Heart Failure trial (PARADIGM-HF)." Compared with individuals without diabetes, heart failure patients with diabetes have a higher level of TnT elevation but not a higher NT-proBNP. When utilized together, TnT and NT-proBNP can be used to identify diabetic patients who have a very high absolute risk of developing complications. Comparatively to patients without diabetes, the TnT frequency-distribution showed a higher frequency of elevated Tn in the diabetic population. Contrarily, there was no difference in NT-proBNP levels between patients with and without diabetes; this result could be limited due to the sample size of 1907 out of which only 40% had diabetes. Compared with 34% of patients without diabetes, 50% of diabetes patients had higher TnT levels. The more frequent rise of TnT in diabetic patients is likely due to the higher prevalence of MI in this population.

Nonetheless, TnT levels were also higher in nonischemic HFrEF diabetic patients, not just those with an ischemic etiology; this raises the possibility of diabetes-related microvascular cardiomyocyte injury in the absence of macrovascular myocardial infarction. Each biomarker and diabetes were indicators of poorer outcomes. Thus, patients with diabetes portrayed an elevated TnT and an NT-proBNP level in the highest percentile (9% of all patients). Diabetic patients also had a TnT value of 18 ng/L in addition to a NT-proBNP value in the lowest percentile (16% of all patients). Moreover, diabetic patients portrayed an absolute risk of cardiovascular death or heart failure hospitalization of 265 per 1,000 person-years, as opposed to a rate of 42 per 1,000 person-years in those without diabetes. In multivariable studies that included NT-proBNP and TnT values, these values were demonstrated to function independently as a predictor of unfavorable outcomes.[22] Furthermore, it is important to note that diabetes appears to have no effect on the diagnostic accuracy of natriuretic peptides.[23] In diabetic individuals, NT-pro-BNP has been shown to be 92% sensitive and 90% specific for the diagnosis of HF. From a prognostic perspective, NT-pro-BNP level of 986 pg/mL has been shown to be independently related to an increased risk of mortality at 1 year in diabetic individuals.[24]

Knowledge Gaps and Scope for Future Research

It is recommended that further studies should be done to examine the prevalence, causes, and prognostic consequences of cTnT elevations detected by a high-sensitivity assay in PWD. Second, it is recommended to study whether aggressive CV risk-factor modification, in this patients' population, lowers Tn levels. Third, it is recommended to study the prognostic role of ProBNP in diabetic patients with cardiovascular events through follow-up and cohort studies. Fourthly, it is recommended to perform a prospective comparison which examines the screening and prognostic value differences between diabetic and nondiabetic patients using a bigger sample size than that utilized in the earlier trials. Finally, although the latest Consensus Report of the American Diabetes Association recommends annual screening of diabetic patients for heart failure with a cut-off natriuretic peptide value that is more than 125 pg/m,[24] it is recommended that diabetic individuals with a NT-pro-BNP value which is higher than 986 pg/mL are given more frequent shorter interval multidisciplinary outpatient monitoring and follow-ups with cardiologists and diabetologists as they are likely to have a higher mortality rate than other diabetic patients.

Conclusions

TnT is an important early screening tool prognostic indicator since TnT readings over the reference upper threshold were linked to an increased risk of cardiovascular events in diabetes. hs-cTn may help diabetes-related clinical care for older persons by identifying those at high mortality risk; furthermore, in diabetic individuals, NT-pro-BNP appears to be 92% sensitive and 90% specific for the diagnosis of HF. From a prognostic perspective, an NT-pro-BNP level of 986 pg/mL is independently related to an increased risk of mortality at 1 year in diabetic patients.

Authors' Contributions

A.B. suggested the topic of the study and coordinated its design. The literature search, identification of relevant articles, drafting the literature review article, and editing were done by T.E., H.A., and R.W.

A.B., F.R, and E.A critically reviewed the manuscript and edited it. Meetings were done in person in addition to through the Zoom online platform. All authors revised, read, and approved the final article.

Compliance with Ethical Principles

No ethical approval is required.

Funding

None.

Conflict of Interest

None declared.

References

1 Lennarz WJ, Lane MD. Calcium Signalling: Motility (Actomyosin–Troponin System). Encyclopedia of biological chemistry. London:: Academic Press; 2013:250–251

2 Walls RM, Hockberger RS, Gausche-Hill M, et al. Chapter 78: Acute Coronary Syndrome. Rosen's Emergency Medicine: Concepts and Clinical Practice. Philadelphia:: Elsevier; 2013:1016–1021

3 Weber M, Hamm C. Role of B-type natriuretic peptide (BNP) and NT-proBNP in clinical routine. Heart 2006;92(06):843–849
4 Lugnier C, Meyer A, Charloux A, Andrès E, Gény B, Talha S. The endocrine function of the heart: physiology and involvements of natriuretic peptides and cyclic nucleotide phosphodiesterases in heart failure. J Clin Med 2019;8(10):1746
5 Collet JP, Thiele H, Barbato E, et al; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2021;42(14):1289–1367
6 Welsh P, Preiss D, Hayward C, et al. Cardiac troponin T and troponin I in the general population. Circulation 2019;139(24): 2754–2764
7 Boeddinghaus J, Twerenbold R, Nestelberger T, et al; APACE investigators. Clinical use of a new high-sensitivity cardiac troponin I assay in patients with suspected myocardial infarction. Clin Chem 2019;65(11):1426–1436
8 Nestelberger T, Boeddinghaus J, Giménez MR, et al; APACE investigators. Direct comparison of high-sensitivity cardiac troponin T and I in the early differentiation of type 1 vs. type 2 myocardial infarction. Eur Heart J Acute Cardiovasc Care 2022;11(01):62–74
9 DeFilippis AP, Chapman AR, Mills NL, et al. Assessment and treatment of patients with type 2 myocardial infarction and acute nonischemic myocardial injury. Circulation 2019;140(20): 1661–1678
10 Starnberg K, Fridén V, Muslimovic A, et al. A possible mechanism behind faster clearance and higher peak concentrations of cardiac troponin I compared with troponin T in acute myocardial infarction. Clin Chem 2020;66(02):333–341
11 Boeddinghaus J, Twerenbold R, Nestelberger T, et al; APACE Investigators. Clinical validation of a novel high-sensitivity cardiac troponin I assay for early diagnosis of acute myocardial infarction. Clin Chem 2018;64(09):1347–1360
12 Keller T, Zeller T, Peetz D, et al. Sensitive troponin I assay in early diagnosis of acute myocardial infarction. N Engl J Med 2009;361 (09):868–877
13 Pfister R, Scholz M, Wielckens K, Erdmann E, Schneider CA. Use of NT-proBNP in routine testing and comparison to BNP. Eur J Heart Fail 2004;6(03):289–293
14 Šimić S, Svaguša T, Prkačin I, Bulum T. Relationship between hemoglobin A1c and serum troponin in patients with diabetes and cardiovascular events. J Diabetes Metab Disord 2019;18(02): 693–704
15 Lazzeri C, Valente S, Chiostri M, Picariello C, Gensini GF. Microalbuminuria in hypertensive nondiabetic patients with ST elevation myocardial infarction. J Cardiovasc Med (Hagerstown) 2010; 11(10):748–753
16 Hallén J, Johansen OE, Birkeland KI, et al. Determinants and prognostic implications of cardiac troponin T measured by a sensitive assay in type 2 diabetes mellitus. Cardiovasc Diabetol 2010;9:52
17 National Kidney Foundation. National Kidney Foundation. Cystatin C-Based Equation (2012). Accessed March 21, 2024 at: https://www.kidney.org [cited 2024 Jan 17].
18 Bjurman C, Petzold M, Venge P, Farbemo J, Fu ML, Hammarsten O. High-sensitive cardiac troponin, NT-proBNP, hFABP and copeptin levels in relation to glomerular filtration rates and a medical record of cardiovascular disease. Clin Biochem 2015;48(4-5):302–307
19 Lamb EJ, Kenny C, Abbas NA, et al. Cardiac troponin I concentration is commonly increased in nondialysis patients with CKD: experience with a sensitive assay. Am J Kidney Dis 2007;49(04): 507–516
20 Segre CA, Hueb W, Garcia RM, et al. Troponin in diabetic patients with and without chronic coronary artery disease. BMC Cardiovasc Disord 2015;15:72
21 Tang O, Daya N, Matsushita K, et al. Performance of high-sensitivity cardiac troponin assays to reflect comorbidity burden and improve mortality risk stratification in older adults with diabetes. Diabetes Care 2020;43(06):1200–1208
22 Rørth R, Jhund PS, Kristensen SL, et al. The prognostic value of troponin T and N-terminal pro B-type natriuretic peptide, alone and in combination, in heart failure patients with and without diabetes. Eur J Heart Fail 2019;21(01):40–49
23 Pop-Busui R, Januzzi JL, Bruemmer D, et al. Heart failure: an underappreciated complication of diabetes. a consensus report of the American Diabetes Association. Diabetes Care 2022;45(07): 1670–1690
24 O'Donoghue M, Kenney P, Oestreicher E, et al. Usefulness of aminoterminal pro-brain natriuretic peptide testing for the diagnostic and prognostic evaluation of dyspneic patients with diabetes mellitus seen in the emergency department (from the PRIDE Study). Am J Cardiol 2007;100(09):1336–1340

