BG Pulse Journal USA
ISSN:1947-2536 http://www.bgpulseusa.com/index.php/bg
BG PULSE JOURNAL

UDC 616.12-008.46-036.12-07-037(575.162)

PROGNOSTIC SIGNIFICANCE OF CLINICAL AND LABORATORY INDICATORS IN PATIENTS WITH CHRONIC HEART FAILURE

Yuldasheva Gulnora Bakhtiyarovna
Associate Professor of the Department of Internal Medicine,
Andijan State Medical Institute, Uzbekistan, Andijan
Doi: https://doi.org/10.5281/zenodo.21766362

Abstract: Chronic heart failure remains a progressive and ultimately fatal syndrome, representing a massive burden on the healthcare system of the Republic of Uzbekistan. This prospective observational study investigates the specific prognostic value of clinical, echocardiographic, and laboratory indicators in predicting adverse cardiovascular outcomes among patients with chronic heart failure residing in the Andijan region. A cohort of 420 patients with established chronic heart failure (NYHA functional classes II-IV) was continuously monitored over an 18-month period at regional cardiological centers. The study evaluated conventional clinical metrics alongside advanced biomarkers, specifically N-terminal pro-B-type natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hs-CRP), and the estimated glomerular filtration rate. The empirical results demonstrated that while traditional symptoms and the six-minute walk test provided foundational functional data, they lacked sufficient sensitivity for predicting imminent decompensation. Conversely, elevated baseline NT-proBNP levels (exceeding 1200 pg/mL), reduced left ventricular ejection fraction (below 35%), and the presence of subclinical renal dysfunction emerged as the most potent, independent predictors of hospital readmission and cardiovascular mortality. The discussion contextualizes these findings within the local epidemiological landscape of the Fergana Valley, emphasizing issues such as medication adherence and the late clinical presentation of ischemic heart disease. The study concludes that the routine integration of molecular biomarkers, specifically NT-proBNP, into standard regional cardiological protocols is imperative for accurately stratifying risk, optimizing guideline-directed medical therapy, and ultimately reducing the high rates of re-hospitalization among the vulnerable heart failure population in Andijan.

Keywords: Chronic heart failure, prognostic markers, NT-proBNP, cardiovascular mortality, clinical cardiology, Andijan region, left ventricular ejection fraction, disease progression.

SURUNKALI YURAK YETISHMOVCHILIGI BO'LGAN BEMORLARDA KLINIK-LABORATOR KO'RSATKICHLARNING PROGNOSTIK AHAMIYATI

Annotatsiya: Surunkali yurak yetishmovchiligi O'zbekiston Respublikasi sog'liqni saqlash tizimi uchun ulkan yuk bo'lib qolayotgan progressiv va oxir-oqibat o'limga olib keluvchi sindromdir. Ushbu istiqbolli kuzatuv tadqiqoti Andijon viloyatida istiqomat qiluvchi surunkali yurak yetishmovchiligi bo'lgan bemorlarda noxush yurak-qon tomir oqibatlarini bashorat qilishda klinik, exokardiografik va laboratoriya ko'rsatkichlarining o'ziga xos prognostik qiymatini o'rganadi. Surunkali yurak yetishmovchiligi (NYHA bo'yicha II-IV funksional sinflari) tasdiqlangan 420 nafar bemordan iborat guruh viloyat kardiologiya markazlarida 18 oy davomida uzluksiz kuzatib borildi. Tadqiqot an'anaviy klinik o'lchovlar bilan bir qatorda ilg'or biomarkerlarni, xususan, N-terminal

pro-B-tipli natriyuretik peptid (NT-proBNP), yuqori sezuvchanlikka ega C-reaktiv oqsil (hs-CRP) va hisoblangan koptokchalar filtratsiya tezligini baholadi. Empirik natijalar shuni ko'rsatdiki, an'anaviy simptomlar va olti daqiqalik yurish testi asosiy funksional ma'lumotlarni taqdim etsa-da, ular yaqinlashib kelayotgan dekompensatsiyani prognoz qilish uchun yetarli sezuvchanlikka ega emas. Aksincha, bazal NT-proBNP darajasining yuqoriligi (1200 pg/ml dan ortiq), chap qorincha otib berish fraksiyasining pasayishi (35% dan past) va subklinik buyrak disfunksiyasining mavjudligi shifoxonaga qayta yotqizish va yurak-qon tomir kasalliklaridan o'limning eng kuchli, mustaqil prediktorlari sifatida namoyon bo'ldi. Muhokama qismi ushbu topilmalarni Farg'ona vodiysining mahalliy epidemiologik manzarasi doirasida tahlil qilib, dori-darmonlarni qabul qilish tartibiga rioya qilmaslik va ishemik kasallikning kech aniqlanishi kabi muammolarni ta'kidlaydi. Tadqiqot xulosa qiladiki, xavfni to'g'ri tabaqalash, ko'rsatmalarga asoslangan tibbiy davolanishni optimallashtirish va oxir-oqibat Andijondagi yurak yetishmovchiligi bo'lgan zaif aholi o'rtasida qayta kasalxonaga yotqizishning yuqori ko'rsatkichlarini kamaytirish uchun molekulyar biomarkerlarni, xususan, NT-proBNPni standart hududiy kardiologik protokollarga muntazam ravishda kiritish shart.

Kalit so'zlar: Surunkali yurak yetishmovchiligi, prognostik markerlar, NT-proBNP, yurak-qon tomir kasalliklaridan o'lim, klinik kardiologiya, Andijon viloyati, chap qorincha otib berish fraksiyasi, kasallikning kuchayishi.

ПРОГНОСТИЧЕСКАЯ ЗНАЧИМОСТЬ КЛИНИКО-ЛАБОРАТОРНЫХ ПОКАЗАТЕЛЕЙ У ПАЦИЕНТОВ С ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ

Аннотация. Хроническая сердечная недостаточность остается прогрессирующим и в конечном итоге фатальным синдромом, представляющим огромную нагрузку на систему здравоохранения Республики Узбекистан. Данное проспективное наблюдательное исследование изучает специфическую прогностическую ценность клинических, эхокардиографических и лабораторных показателей в прогнозировании неблагоприятных сердечно-сосудистых исходов среди пациентов с хронической сердечной недостаточностью, проживающих в Андижанской области. Когорта из 420 пациентов с установленной хронической сердечной недостаточностью (II-IV функциональные классы по NYHA) непрерывно наблюдалась в течение 18 месяцев в региональных кардиологических центрах. В исследовании оценивались традиционные клинические метрики наряду с передовыми биомаркерами, в частности, N-концевым про-B-типом натрийуретического пептида (NT-proBNP), высокочувствительным C-реактивным белком (hs-CRP) и расчетной скоростью клубочковой фильтрации. Эмпирические результаты продемонстрировали, что, хотя традиционные симптомы и тест шестиминутной ходьбы предоставляли базовые функциональные данные, им не хватало достаточной чувствительности для прогнозирования надвигающейся декомпенсации. Напротив, повышенный базовый уровень NT-proBNP (более 1200 пг/мл), сниженная фракция выброса левого желудочка (ниже 35%) и наличие субклинической дисфункции почек оказались наиболее мощными независимыми предикторами повторной госпитализации и сердечно-сосудистой смертности. В обсуждении эти результаты рассматриваются в контексте местной эпидемиологической ситуации Ферганской долины, подчеркивая такие проблемы, как несоблюдение режима приема лекарств и позднее клиническое проявление ишемической болезни сердца. В заключении

исследования утверждается, что рутинная интеграция молекулярных биомаркеров, в частности NT-proBNP, в стандартные региональные кардиологические протоколы крайне важна для точной стратификации риска, оптимизации медикаментозной терапии, основанной на руководствах, и в конечном итоге для снижения высоких показателей повторной госпитализации среди уязвимой популяции с сердечной недостаточностью в Андижане.

Ключевые слова: Хроническая сердечная недостаточность, прогностические маркеры, NT-proBNP, сердечно-сосудистая смертность, клиническая кардиология, Андижанская область, фракция выброса левого желудочка, прогрессирование заболевания.

Introduction

Chronic heart failure is an intricate clinical syndrome that represents the common, final, and irreversible pathway for a multitude of cardiovascular diseases. Despite the continuous evolution of Guideline-Directed Medical Therapy (GDMT), which includes the widespread use of beta-blockers, angiotensin receptor-neprilysin inhibitors, and mineralocorticoid receptor antagonists, chronic heart failure remains a dominant cause of hospitalization, severely diminished quality of life, and premature mortality on a global scale. In the Republic of Uzbekistan, the demographic transition toward an older population, combined with a high regional prevalence of poorly controlled arterial hypertension and ischemic heart disease, has led to a dramatic escalation in heart failure cases. The Andijan region, possessing one of the highest population densities in the country, acutely experiences the socioeconomic and clinical impact of this epidemic.

The primary challenge in managing chronic heart failure within regional outpatient and inpatient settings is the extreme unpredictability of its clinical course. Patients frequently experience periods of apparent clinical stability that are suddenly interrupted by episodes of severe acute decompensation, requiring emergency hospitalization. Historically, cardiologists have relied heavily on the New York Heart Association (NYHA) functional classification and subjective symptom reporting (such as the degree of dyspnea or peripheral edema) to estimate disease severity and guide therapeutic decisions. However, contemporary cardiovascular literature definitively proves that clinical symptoms are late indicators of disease progression. Symptoms only manifest after massive, underlying neurohormonal activation and continuous myocardial remodeling have already occurred.

To transition from a reactive to a highly proactive, predictive model of care, modern cardiology has increasingly integrated objective laboratory and echocardiographic biomarkers into routine risk stratification. The natriuretic peptide system, specifically NT-proBNP, has emerged as the absolute gold standard in this regard. Released by the ventricular myocardium in direct response to excessive wall stretch and volume overload, NT-proBNP provides a real-time, quantitative molecular snapshot of myocardial stress. Furthermore, the role of systemic inflammation, indicated by high-sensitivity C-reactive protein (hs-CRP), and the concept of cardio-renal syndrome, evaluated through the estimated Glomerular Filtration Rate (eGFR), are now recognized as critical determinants of survival in these patients.

Despite international consensus on the utility of these markers, their systematic prognostic application in the specific clinical and epidemiological context of the Fergana Valley remains under-researched. Variations in genetic profiles, local dietary habits (such as high sodium intake), and delayed patient presentation to specialized cardiological centers in Andijan may uniquely influence the predictive thresholds of these markers. Therefore, the primary objective of this prospective scientific study is to evaluate and precisely quantify the prognostic significance of

specific clinical and laboratory indicators in predicting adverse cardiovascular events (re-hospitalization and mortality) among a large, representative cohort of patients with chronic heart failure residing in the Andijan region.

Materials and methods

To achieve the research objectives, a robust, prospective, and observational cohort study was carefully designed and executed over an 18-month period. The clinical investigation was conducted at the Andijan Regional Cardiological Dispensary and affiliated multidisciplinary medical centers across the region. The study protocol was subjected to rigorous review and formally approved by the local Institutional Bioethics Committee. Written, informed consent was systematically obtained from all participating patients or their legal representatives prior to enrollment in the clinical trial.

Study Population - The cohort comprised 420 adult patients of both genders, aged between 45 and 80 years, who had a confirmed clinical and echocardiographic diagnosis of chronic heart failure of ischemic or hypertensive etiology, corresponding to NYHA functional classes II, III, and IV.

Exclusion Criteria - To ensure that the prognostic evaluation was not confounded by acute, non-heart-failure related mortality risks, stringent exclusion criteria were applied. Patients who had experienced an acute myocardial infarction or stroke within the preceding three months, individuals with severe end-stage renal disease requiring hemodialysis, patients with active malignant neoplasms, acute infectious diseases, or severe chronic obstructive pulmonary disease were explicitly excluded from the study.

Clinical and Instrumental Assessment - Upon initial enrollment (baseline), all patients underwent a comprehensive clinical assessment. This included a detailed medical history, physical examination, assessment of the NYHA functional class, and the execution of a standardized Six-Minute Walk Test (6MWT) to objectively measure exercise tolerance. Transthoracic echocardiography was performed by certified specialists using standard protocols to determine the Left Ventricular Ejection Fraction (LVEF), left ventricular end-diastolic volume, and indices of diastolic dysfunction.

Laboratory Analysis - Venous blood samples were collected from all patients in the morning, following a 12-hour fasting period. The laboratory panel included:

NT-proBNP levels, quantified using an automated electrochemiluminescence immunoassay.

High-sensitivity C-reactive protein (hs-CRP), measured utilizing immunoturbidimetry.

Serum creatinine levels, from which the estimated Glomerular Filtration Rate (eGFR) was calculated using the CKD-EPI formula to assess renal function.

Complete blood count to identify anemia (hemoglobin levels).

Follow-up and Endpoints

The patients were continuously followed for a period of 18 months through scheduled outpatient clinic visits and structured telephone interviews. The primary combined clinical endpoint was defined as cardiovascular mortality or emergency re-hospitalization directly due to acute decompensation of heart failure.

Statistical Analysis - All collected clinical, instrumental, and laboratory data were processed utilizing advanced biostatistical software (SPSS version 26.0). Continuous variables were expressed as means and standard deviations, while categorical variables were presented as absolute numbers and percentages. The comparison between the group that reached the primary endpoint and the stable group was performed using the Student's t-test and the Chi-square test. Univariate and multivariate Cox proportional hazards regression analyses were conducted to determine the independent prognostic value of the assessed variables. Receiver Operating Characteristic (ROC)

curve analysis was used to determine the optimal predictive cut-off values for the biomarkers. Statistical significance was declared at a p-value of less than 0.05.

Results

During the 18-month follow-up period, the clinical trajectory of the 420 enrolled patients clearly bifurcated. A total of 118 patients (28.1%) reached the primary combined endpoint (experiencing either cardiovascular mortality or emergency re-hospitalization for acute decompensated heart failure). This group was designated as the "Adverse Outcome Cohort." The remaining 302 patients (71.9%) remained clinically stable without requiring emergency inpatient interventions and were designated as the "Stable Cohort."

The baseline demographic data indicated that the mean age of the overall cohort was 62.4 years, with a slight male predominance (55%). The primary etiologies of heart failure in this regional cohort were ischemic heart disease (64%) and long-standing, poorly controlled arterial hypertension (36%).

A comparative analysis of the baseline clinical and laboratory parameters between the two cohorts revealed highly significant differences, serving as clear prognostic indicators.

Comparison of Baseline Parameters (Stable Cohort vs. Adverse Outcome Cohort):

- NYHA Class III-IV prevalence: Stable Cohort = 38%; Adverse Outcome Cohort = 72% ($p < 0.001$)
- Six-Minute Walk Test distance (meters): Stable Cohort = 345 ± 45; Adverse Outcome Cohort = 210 ± 35 ($p < 0.001$)
- Left Ventricular Ejection Fraction (%): Stable Cohort = 42.5 ± 6.2; Adverse Outcome Cohort = 31.4 ± 5.8 ($p < 0.001$)
- NT-proBNP (pg/mL): Stable Cohort = 650 ± 210; Adverse Outcome Cohort = 1850 ± 430 ($p < 0.001$)
- hs-CRP (mg/L): Stable Cohort = 3.2 ± 1.1; Adverse Outcome Cohort = 8.5 ± 2.4 ($p < 0.001$)
- eGFR (mL/min/1.73m2): Stable Cohort = 68.4 ± 12.5; Adverse Outcome Cohort = 45.2 ± 10.1 ($p < 0.001$)
- Hemoglobin (g/L): Stable Cohort = 128 ± 12; Adverse Outcome Cohort = 112 ± 10 ($p = 0.003$)

The data definitively demonstrate that patients who eventually required re-hospitalization or succumbed to the disease possessed a vastly different molecular and hemodynamic profile at baseline, despite appearing relatively similar in general outpatient consultations.

The ROC curve analysis identified that an NT-proBNP level exceeding 1200 pg/mL upon admission was the most sensitive and specific threshold for predicting adverse events in this regional demographic (Sensitivity: 86%, Specificity: 82%). Similarly, an LVEF below 35% and an eGFR below 60 mL/min/1.73m2 served as powerful prognostic cut-offs.

When subjected to multivariate Cox regression analysis to adjust for confounding variables such as age, gender, and underlying etiology, three parameters emerged as the most potent, independent predictors of the primary endpoint:

- NT-proBNP greater than 1200 pg/mL (Hazard Ratio: 3.4, 95% Confidence Interval: 2.1 - 5.5, $p < 0.001$).
- LVEF less than 35% (Hazard Ratio: 2.8, 95% Confidence Interval: 1.8 - 4.4, $p < 0.001$).
- eGFR less than 60 mL/min/1.73m2, indicating cardio-renal syndrome (Hazard Ratio: 2.1, 95% Confidence Interval: 1.4 - 3.2, $p = 0.002$).

Discussion

The empirical evidence generated by this prospective study in the Andijan region strongly validates the absolute necessity of transitioning from symptom-based management to biomarker-guided risk stratification in patients with chronic heart failure. The alarmingly high rate of adverse outcomes (28.1% over 18 months) underscores the aggressive nature of the disease within the local population. This high incidence is likely exacerbated by specific regional factors, including a traditional diet high in sodium which complicates volume management, delayed presentation to specialized cardiologists, and inconsistent adherence to complex, multi-drug regimens.

The exceptional predictive superiority of NT-proBNP observed in this cohort aligns perfectly with global cardiological paradigms. NT-proBNP is not merely a diagnostic tool; it is a dynamic, continuous gauge of ventricular wall stress. The massive elevations documented in the adverse outcome cohort accurately reflect a myocardium that is failing to compensate for hemodynamic overload. For cardiologists operating in the polyclinics of Andijan, a baseline NT-proBNP level exceeding the identified threshold of 1200 pg/mL must be interpreted as a critical "red flag." It dictates that the patient is on a rapid trajectory toward pulmonary edema or cardiogenic shock, mandating the immediate up-titration of diuretics and disease-modifying agents, even if the patient currently denies severe shortness of breath.

Furthermore, the identification of reduced eGFR as a major independent predictor highlights the devastating impact of cardio-renal syndrome. As the failing heart provides inadequate forward perfusion to the kidneys, and elevated central venous pressure causes renal venous congestion, renal function inevitably declines. This creates a vicious cycle: worsening renal function leads to fluid retention, which further overloads the failing heart. Identifying this subclinical renal decline through routine eGFR calculations is a highly cost-effective prognostic strategy that must be universally adopted in local clinics.

The role of systemic inflammation, indicated by elevated hs-CRP, and the presence of anemia also emerged as significant contributors to disease progression. Chronic heart failure is now recognized as a state of prolonged, low-grade systemic inflammation that accelerates endothelial dysfunction and promotes myocardial fibrosis. The presence of anemia further starves the peripheral tissues and the myocardium of oxygen, forcing the heart to increase its chronotropic effort, thereby accelerating its own exhaustion.

The practical implementation of these findings requires a structural update to regional heart failure management protocols. Relying solely on the NYHA class and the patient's subjective complaints frequently results in clinical inertia. By formally integrating NT-proBNP, eGFR, and echocardiographic LVEF into a unified prognostic algorithm, healthcare providers in the Andijan region can objectively identify the hidden, high-risk patient. This precision-medicine approach ensures that intensive outpatient monitoring, specialized heart failure clinic referrals, and aggressive pharmacological interventions are directed precisely toward the patients who need them the most, ultimately preventing catastrophic decompensation and rationalizing the use of regional inpatient resources.

Conclusion

This comprehensive regional investigation unequivocally demonstrates that the clinical trajectory of chronic heart failure can be accurately predicted through the strategic evaluation of specific laboratory and instrumental markers. The study definitively proves that while traditional clinical symptoms provide necessary baseline context, they fundamentally lack the predictive sensitivity required to foresee rapid physiological decompensation. In the population of the Andijan region, an NT-proBNP concentration exceeding 1200 pg/mL, a left ventricular ejection fraction

below 35%, and the presence of diminished renal function (eGFR < 60) serve as the most potent, independent predictors of imminent hospital readmission and cardiovascular mortality. To alter the devastating natural history of this disease and reduce the severe burden on local emergency departments, regional health ministries must urgently mandate the integration of these objective biomarkers into routine clinical practice. Utilizing a predictor-guided management algorithm will empower cardiologists to transition from reactive crisis management to proactive, life-saving, and highly targeted medical therapy.

References

1. Ponikowski, P., Voors, A. A., Anker, S. D., Bueno, H., Cleland, J. G., Coats, A. J., ... & van der Meer, P. (2016). 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal, 37(27), 2129-2200.
2. McMurray, J. J., Adamopoulos, S., Anker, S. D., Auricchio, A., Böhm, M., Dickstein, K., ... & Ponikowski, P. (2012). ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. European Heart Journal, 33(14), 1787-1847.
3. Januzzi, J. L., van Kimmenade, R., Lainchbury, J., Bayes-Genis, A., Ordonez-Llanos, J., Santalo-Bel, M., ... & Richards, M. (2006). NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients. European Heart Journal, 27(3), 330-337.
4. Fonarow, G. C., Adams, K. F., Abraham, W. T., Yancy, C. W., & Boscardin, W. J. (2005). Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis. JAMA, 293(5), 572-580.
5. Heywood, J. T., Fonarow, G. C., Costanzo, M. R., Mathur, V. S., Wigneswaran, J. R., & Wynne, J. (2007). High prevalence of renal dysfunction and its impact on outcome in 118,465 patients hospitalized with acute decompensated heart failure: a report from the ADHERE database. Journal of Cardiac Failure, 13(6), 422-430.
6. Anand, I. S., Latini, R., Florea, V. G., Kuskowski, M. A., Rector, T., Masson, S., ... & Cohn, J. N. (2005). C-reactive protein in heart failure: prognostic value and the effect of valsartan. Circulation, 112(12), 1428-1434.
7. O'Meara, E., Clayton, T., McEntegart, D. J., McMurray, J. J., Piña, I. L., Granger, C. B., ... & Pocock, S. J. (2006). Clinical correlates and consequences of anemia in a broad spectrum of patients with heart failure: results of the Candesartan in Heart Failure: Assessment of Reduction in Mortality and morbidity (CHARM) Program. Circulation, 113(7), 986-994.
8. Khodjaeva, D. T. (2020). Epidemiology of cardiovascular diseases in Uzbekistan: Current status and the impact of urbanization. Central Asian Journal of Medical Sciences, 6(2), 45-52.
9. Yancy, C. W., Jessup, M., Bozkurt, B., Butler, J., Casey, D. E., Drazner, M. H., ... & Wilkoff, C. E. (2013). 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology, 62(16), e147-e239.
10. Felker, G. M., Leimberger, J. D., Califf, R. M., Cuffe, M. S., Massie, B. M., Adams, K. F., ... & O'Connor, C. M. (2004). Risk stratification after hospitalization for decompensated heart failure. Journal of Cardiac Failure, 10(6), 460-466.