

Optimizing Post-Discharge Heart Failure Care: The Role of Natriuretic Peptides

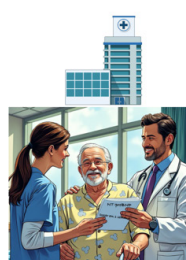
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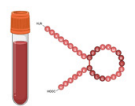
Central Illustration: Optimizing Post-Discharge Heart Failure Care: The Role of Natriuretic Peptides



ABC Heart Failure & Cardiomyopathy

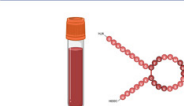


Hospital discharge



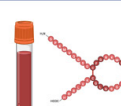
Discharge NP

One-week
 • Prediction of events
 • Adjust medications according to NP trajectory



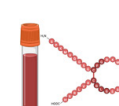
One-week NP measurement

Three months
 • Prediction of events
 • Adjust medications according to NP trajectory



Three-month NP measurement

Consider serial measurement (every 3-4 months)



Serial measurement

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A proposed post-discharge strategy for patients with heart failure using natriuretic peptides at different timepoints. Natriuretic peptides concentrations and trajectories provide prognostic information and may add information to clinical decision-making. NP: natriuretic peptides.

Abstract

Heart failure (HF) remains a leading cause of hospitalization, mortality, and health-care burden worldwide. The post-discharge period following acute decompensated heart failure (ADHF) is characterized by a heightened risk of rehospitalization and death, particularly during the first 90 days, known as the “vulnerable phase.” Effective strategies for risk stratification and therapy optimization during this phase are crucial to improve outcomes.

Keywords

Natriuretic Peptides; Heart Failure; Emergency Medical Services; Dyspnea; Diagnosis

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Natriuretic peptides (NPs), including B-type natriuretic peptide (BNP) and its N-terminal fragment (NT-proBNP), are well-established biomarkers of myocardial stress. Beyond their diagnostic role, NPs have emerged as powerful prognostic tools for post-discharge risk assessment and as potential guides for therapy titration. Elevated NP levels at discharge and persistently high concentrations one week post-discharge strongly predict adverse outcomes. Evidence from the STRONG-HF trial demonstrated that early, intensive follow-up incorporating NP monitoring and rapid guideline-directed medical therapy (GDMT) up-titration significantly reduced mortality and rehospitalization. Serial NP measurements further enhance risk stratification by capturing dynamic changes over time. Although trials such as GUIDE-IT showed mixed results for NP-guided therapy using fixed targets, patients achieving lower NP levels consistently demonstrated better outcomes.

In conclusion, NPs provide incremental prognostic value beyond clinical assessment in the vulnerable post-discharge phase and throughout long-term management. Early and serial NP monitoring can identify high-risk patients and support GDMT optimization. Future research should refine

timing, thresholds, and integration of NP-guided strategies into multimodal risk models to enhance personalized HF care and improve global patient outcomes.

Introduction

Heart failure (HF) is a prevalent and serious condition, affecting over 64 million individuals globally and imposing substantial morbidity, mortality, and health-care costs.¹ Hospitalization for acute decompensated heart failure (ADHF) is a sentinel event, marking a period of heightened vulnerability. Patients discharged after ADHF are at elevated risk of adverse outcomes, particularly during the first 90 days, a phase often termed the “vulnerable phase”.^{2–4} Event rates in this period remain significant; in one study, 22% of patients experienced death or readmission within 90 days post-discharge,² whereas other reports indicate rates approaching 30%.⁴ Effective post-discharge risk stratification and optimization of therapy remain critical to improving outcomes.

Natriuretic peptides (NPs), especially B-type natriuretic peptide (BNP) and its N-terminal prohormone fragment (NT-proBNP), are established biomarkers of myocardial stress and volume overload. Beyond their diagnostic utility in acute decompensation, NP measurement has emerged as a potentially valuable tool for prognostication and for guiding guideline-directed medical therapy (GDMT) in the post-discharge setting. This narrative review examines the biology of NP, the evidence supporting their prognostic role after hospital discharge, and the evolving literature on NP-guided therapy titration, emphasizing both global applicability and remaining uncertainties.⁵

The natriuretic peptide biology

BNP and NT-proBNP are cardiac-derived hormones released in response to myocardial wall stress.^{6,7} In the hospitalized HF population, the primary driver of NP secretion is acute volume overload and increased intracardiac pressures, manifesting as pulmonary or systemic congestion. In contrast, in ambulatory patients or in individuals who have undergone effective decongestion, NP levels predominantly reflect chronic alterations in cardiac structure and function, including ventricular dilation, hypertrophy, and systolic or diastolic dysfunction.^{6,7}

This distinction has practical implications. The concept of “wet” versus “dry” BNP/NT-proBNP underscores the dynamic nature of these biomarkers: “wet” levels indicate active congestion and acute hemodynamic stress, while “dry” levels in compensated patients are indicative of residual myocardial pathology rather than overt fluid overload. Recognizing this physiological gradient is essential for interpreting NP measurements in post-discharge care.

Natriuretic peptides during hospitalization

At admission for ADHF, NP values are typically markedly elevated. These levels correlate with hemodynamic severity, pulmonary capillary wedge pressure, and overall congestion.^{8,9} Effective in-hospital decongestion through diuretics and GDMT generally leads to substantial reductions in NP values, reflecting relief of myocardial wall stress and decreased intracardiac pressures.¹⁰

The NP level at discharge, while lower than admission, remains a strong prognostic marker. Several studies have demonstrated that higher discharge BNP or NT-proBNP levels predict short-term rehospitalization and mortality.^{11–13} These observations highlight that NP values provide risk information above and beyond traditional clinical assessment and underscore the potential utility of post-discharge NP monitoring.

Role of NP measurement one week after discharge

Early post-discharge assessment of NP levels has garnered interest as a method to identify patients at persistent risk. The STRONG-HF trial, a randomized multicenter study, evaluated high-intensity post-discharge follow-up with early outpatient visits, uptitration of GDMT, and clinical and laboratory assessment, including NT-proBNP measurements.¹⁴ This intensive treatment strategy of rapid up-titration of GDMT after an acute HF admission reduced symptoms, improved quality of life, and reduced the risk of 180-day all-cause death or HF readmission compared with usual care.¹⁴ A subanalysis of the STRONG-HF trial demonstrated that NT-proBNP levels measured approximately one week after discharge were strongly predictive of adverse events within three months. Patients with persistently elevated NT-proBNP at one week experienced higher rates of readmission and mortality compared with those whose levels declined.^{15,16}

These findings support a model in which early biomarker assessment can identify residual risk not captured by conventional clinical evaluation.¹⁵ Collectively, these data suggest that measuring NP within the first week post-discharge may refine short-term risk stratification and provide actionable information for timely therapy adjustments.

Role of NP measurement beyond the vulnerable phase

In the STRONG-HF trial, the prediction power of NT-proBNP was limited to three months after discharge. This suggests that a new NP measurement should be done after three months. In fact, longer-term post-discharge NP measurements provide complementary prognostic information. In the PARADIGM-HF trial,¹⁷ 63% of patients had been hospitalized for ADHF in the last year. Serial NT-proBNP measurements were evaluated in the ambulatory setting in patients receiving sacubitril/valsartan or enalapril.¹⁸ Higher NP levels were consistently associated with increased risk of HF hospitalization and cardiovascular death, even after adjustment for established clinical predictors.¹⁸

The incremental value of NP relative to clinical risk scores is exemplified by studies comparing NT-proBNP with the MAGGIC risk score. The MAGGIC risk score is derived by combining 13 clinical variables used in routine practice, including age, sex, ejection fraction, systolic blood pressure, BMI, and creatinine level, into a proportional hazards model.^{19,20} Rohen et al. demonstrated that NP measurement improved risk reclassification beyond the MAGGIC score, suggesting that dynamic biomarker assessment can enhance prognostic precision in ambulatory HF patients (most of them had been hospitalized in the last year).²¹ These findings highlight that NP levels retain prognostic significance beyond the immediate post-discharge period, supporting their use in medium-term risk monitoring.

Role of serial NP measurement

Serial NP measurements provide additional insights beyond single time-point assessments. Repeated measures allow quantification of biomarker trajectories, capturing both relative and absolute changes from baseline. Studies have demonstrated that a decline in NP levels over time correlates with improved outcomes, whereas persistently elevated or rising NP levels signal ongoing risk.²²⁻²⁴

Recent evidence further supports the use of serial NP for patient reclassification. A subanalysis of the GUIDE-IT trial showed that incorporating NP changes over multiple time points reclassified risk in a substantial subset of patients compared with baseline values alone.²⁵ Serial NP monitoring, therefore, represents a promising strategy to refine risk stratification and potentially guide therapy titration after discharge, although interventional studies targeting therapy adjustments based on NP trajectories remain limited.

NP-guided therapy titration

As discussed before, NP can be used to assess response to treatment, and as such may be useful to progress or withhold GDMT. However, the role of NP to guide GDMT titration with a specific NP value as a target to reach is not clear. Early studies, such as the PROTECT trial, suggested that NP-guided titration could improve medication optimization and reduce adverse events.²⁶ More recently, the GUIDE-IT trial, a multicenter randomized study, compared NT-proBNP-guided therapy with usual care in high-risk HFrEF patients.²⁷ Although GUIDE-IT was neutral for its primary endpoint, post-hoc analyses indicated that patients achieving lower NT-proBNP levels had superior outcomes, supporting the role of natriuretic peptide to assess response to treatment, regardless of whether you use an NP target or just use clinical information.²⁸

STRONG-HF provides a complementary perspective. In this pragmatic-positive framing, the trial demonstrated that early, intensive post-discharge follow-up combined with GDMT optimization, in which NP measurement was a key component, significantly reduced HF rehospitalization and mortality at three months.¹⁴ The trial suggests that monitoring NP trajectories, rather than an NP target, can inform safe and effective up-titration of GDMT, particularly in the early vulnerable phase. Collectively, these studies underscore that NP-guided therapy remains a promising approach, although variability in trial design and patient populations has contributed to heterogeneous findings. The Central Illustration demonstrates a proposed post-discharge strategy for patients with HF using NPs, and Figure 1 illustrates possible clinical decisions according to NP trajectories.

Unresolved gaps and controversies

Despite robust evidence for the prognostic value of NP post-discharge, several unresolved questions persist. First, the optimal timing and frequency of NP measurements remain unclear. While early post-discharge measurement (e.g., one week) identifies high-risk patients,¹⁴ whether repeated measurements at three months, six months, or longer intervals improve outcomes is uncertain.

Second, thresholds for clinical action remain debated. Different studies have used absolute NP cutoffs, percentage

change from baseline, or trajectories to guide interventions.^{29,30} Lack of standardization limits comparability and may explain variable trial results.

Third, although NP-guided therapy titration is biologically plausible and supported by exploratory analyses, randomized evidence demonstrating consistent outcome benefits is limited. Heterogeneity in patient adherence, comorbidities, and clinician behavior likely contributes to these inconsistencies.

Finally, integrating NP into broader risk models is an ongoing challenge. While NP improves risk stratification relative to clinical scores alone, combining biomarkers with imaging, hemodynamics, and patient-reported outcomes to develop holistic, actionable models remains an unmet need.

Conclusions

NPs are powerful biomarkers that reflect both acute congestion and chronic myocardial pathology. Elevated NP at hospital discharge, as well as trajectories measured early post-discharge, provide valuable prognostic information for HF patients. Evidence from STRONG-HF and other studies suggests that early NP assessment may facilitate identification of patients at high risk for rehospitalization or death within the vulnerable post-discharge period. Serial NP monitoring further refines risk stratification and offers a potential strategy to guide GDMT titration.

While randomized trials of NP-guided therapy have yielded mixed results, the cumulative evidence supports the clinical utility of NP for risk assessment and therapy optimization, particularly when integrated with comprehensive clinical evaluation. Remaining gaps include standardization of measurement timing, actionable thresholds, and integration with multi-dimensional risk models. Future research should focus on refining NP-guided approaches and clarifying their role in improving patient-centered outcomes globally.

Author Contributions

Conception and design of the research and Writing of the manuscript: Villacorta H; Analysis and interpretation of the data and Critical revision of the manuscript for content: Villacorta AS.

Potential conflict of interest

Humberto Villacorta - Speaker fees and study support from Roche Diagnostics and QuidelOrtho.

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Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

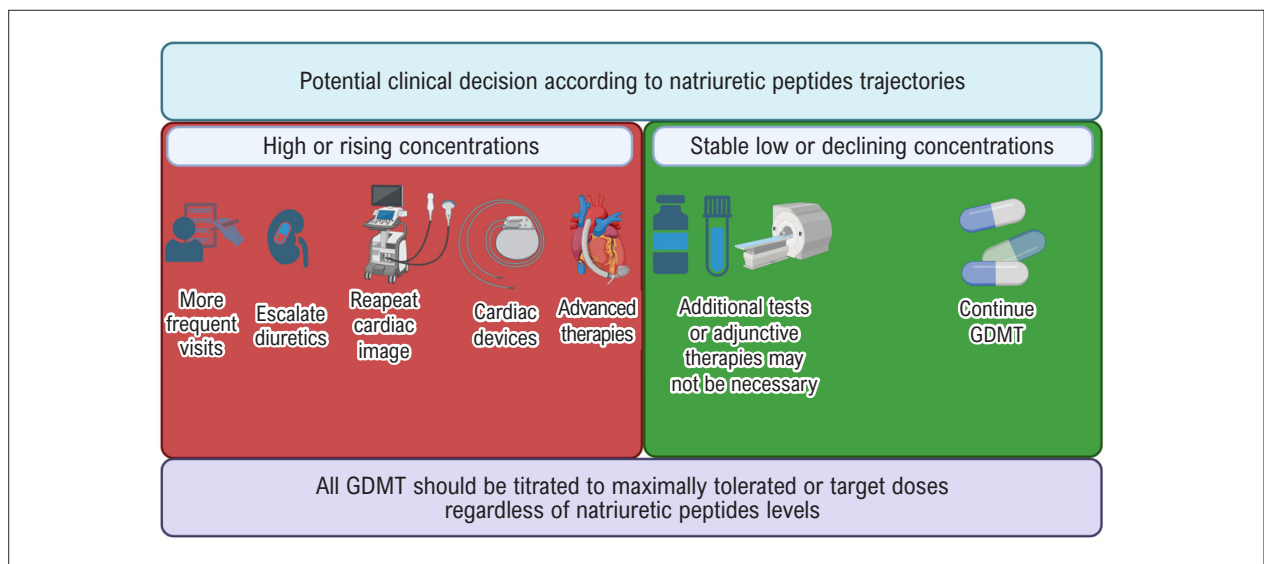


Figure 1 – Possible clinical decisions according to NP trajectories. If NP concentrations are high or rising, this indicates that the patient is not responding to current treatment, and something else should be done. These include more frequent medical visits, diuretic adjustments, cardiac image tests, adjunctive therapies, and referral to advanced therapies, such as left ventricular assist devices or cardiac transplantation. On the other hand, stable or declining concentrations indicate that no additional tests or therapies are necessary. GDMT: Guideline-directed medical therapy. Adapted from Khan et al.²⁴

References

1. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. *Card Fail Rev.* 2017;3(1):7-11. doi: 10.15420/cfr.2016:25:2.
2. Villacorta H, Villacorta AS, Villacorta LSC, Xavier AR, Kanaan S, Rohen FM, et al. Worsening Renal Function and Congestion in Patients with Acute Heart Failure: A Study with Bioelectrical Impedance Vector Analysis (BIVA) and Neutrophil Gelatinase-Associated Lipocalin (NGAL). *Arq Bras Cardiol.* 2021;116(4):715-24. doi: 10.36660/abc.20190465.
3. Latif A, Lateef N, Lundgren S, Kapoor V, Ahsan MJ, Aboeata A. Vulnerable Phase of Acute Heart Failure and its Association with Hospital Readmissions Reduction Program. *Curr Probl Cardiol.* 2022;47(5):100904. doi: 10.1016/j.cpcardiol.2021.100904.
4. Greene SJ, Fonarow GC, Vaduganathan M, Khan SS, Butler J, Cheorghiade M. The Vulnerable Phase after Hospitalization for Heart Failure. *Nat Rev Cardiol.* 2015;12(4):220-9. doi: 10.1038/nrcardio.2015.14.
5. Horiuchi Y, Villacorta H, Maisel AS. Natriuretic Peptide-Guided Therapy for Heart Failure. *Heart Int.* 2022;16(2):112-6. doi: 10.17925/HI.2022.16.2.112.
6. Volpe M, Carnovali M, Mastromarino V. The Natriuretic Peptides System in the Pathophysiology of Heart Failure: From Molecular Basis to Treatment. *Clin Sci.* 2016;130(2):57-77. doi: 10.1042/CS20150469.
7. Samad M, Malempati S, Restini CBA. Natriuretic Peptides as Biomarkers: Narrative Review and Considerations in Cardiovascular and Respiratory Dysfunctions. *Yale J Biol Med.* 2023;96(1):137-49. doi: 10.59249/NCST6937.
8. Parrinello G, Torres D, Paterna S, Di Pasquale P, Licata G. Wet BNP, Fluid and Hemodynamic Status at Discharge in Acute Heart Failure. *Int J Cardiol.* 2010;145(2):335-6. doi: 10.1016/j.ijcard.2009.11.059.
9. Aspromonte N, Valle R, Peacock WF, Vanderheyden M, Maisel A. Inpatient Monitoring and Prognostic Importance of B-Type Natriuretic Peptide. *Congest Heart Fail.* 2008;14(4 Suppl 1):30-4. doi: 10.1111/j.1751-7133.2008.tb00008.x.
10. Kazanegra R, Cheng V, Garcia A, Krishnaswamy P, Gardetto N, Clopton P, et al. A Rapid Test for B-Type Natriuretic Peptide Correlates with Falling Wedge Pressures in Patients Treated for Decompensated Heart Failure: A Pilot Study. *J Card Fail.* 2001;7(1):21-9. doi: 10.1054/jcaf.2001.23355.
11. Logeart D, Thabut G, Jourdain P, Chavelas C, Beyne P, Beauvais F, et al. PredischARGE B-Type Natriuretic Peptide Assay for Identifying Patients at High Risk of Re-Admission after Decompensated Heart Failure. *J Am Coll Cardiol.* 2004;43(4):635-41. doi: 10.1016/j.jacc.2003.09.044.
12. Bettencourt P, Azevedo A, Pimenta J, Friões F, Ferreira S, Ferreira A. N-Terminal-Pro-Brain Natriuretic Peptide Predicts Outcome after Hospital Discharge in Heart Failure Patients. *Circulation.* 2004;110(15):2168-74. doi: 10.1161/01.CIR.0000144310.04433.BE.
13. Kociol RD, Horton JR, Fonarow GC, Reyes EM, Shaw LK, O'Connor CM, et al. Admission, Discharge, or Change in B-Type Natriuretic Peptide and Long-Term Outcomes: Data from Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) Linked to Medicare Claims. *Circ Heart Fail.* 2011;4(5):628-36. doi: 10.1161/CIRCHEARTFAILURE.111.962290.
14. Mebazaa A, Davison B, Chioncel O, Cohen-Solal A, Diaz R, Filippatos G, et al. Safety, Tolerability and Efficacy of Up-Titration of Guideline-Directed Medical Therapies for Acute Heart Failure (STRONG-HF): A Multinational, Open-Label, Randomised, Trial. *Lancet.* 2022;400(10367):1938-52. doi: 10.1016/S0140-6736(22)02076-1.
15. Adamo M, Pagnesi M, Mebazaa A, Davison B, Edwards C, Tomasoni D, et al. NT-proBNP and High Intensity Care for Acute Heart Failure: The STRONG-HF Trial. *Eur Heart J.* 2023;44(31):2947-62. doi: 10.1093/eurheartj/ehad335.
16. Bayes-Genis A, Pascual-Figal D. Making STRONGer the Transition Phase: Personalized GDMT Through NT-proBNP Monitoring. *Eur Heart J.* 2023;44(31):2963-5. doi: 10.1093/eurheartj/ehad356.

Review Article

17. McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, et al. Angiotensin-Neprilysin Inhibition versus Enalapril in Heart Failure. *N Engl J Med*. 2014;371(11):993-1004. doi: 10.1056/NEJMoa1409077.
18. Zile MR, Claggett BL, Prescott MF, McMurray JJ, Packer M, Rouleau JL, et al. Prognostic Implications of Changes in N-Terminal Pro-B-Type Natriuretic Peptide in Patients with Heart Failure. *J Am Coll Cardiol*. 2016;68(22):2425-36. doi: 10.1016/j.jacc.2016.09.931.
19. Pocock SJ, Ariti CA, McMurray JJ, Maggioni A, Køber L, Squire IB, et al. Predicting Survival in Heart Failure: A Risk Score Based on 39 372 Patients from 30 Studies. *Eur Heart J*. 2013;34(19):1404-13. doi: 10.1093/eurheartj/ehs337.
20. Sartipy U, Dahlström U, Edner M, Lund LH. Predicting Survival in Heart Failure: Validation of the MAGGIC Heart Failure Risk Score in 51,043 Patients from the Swedish Heart Failure Registry. *Eur J Heart Fail*. 2014;16(2):173-9. doi: 10.1111/ehjhf.32.
21. Rohen FM, Ávila DX, Lemos CMC, Santos R, Ribeiro M, Villacorta H. The MAGGIC Risk Score in the Prediction of Death or Hospitalization in Patients with Heart Failure: Comparison with Natriuretic Peptides. *Rev Port Cardiol*. 2022;41(11):941-7. doi: 10.1016/j.repc.2021.07.015.
22. Masson S, Latini R, Anand IS, Barlera S, Angelici L, Vago T, et al. Prognostic Value of Changes in N-Terminal Pro-Brain Natriuretic Peptide in Val-HeFT (Valsartan Heart Failure Trial). *J Am Coll Cardiol*. 2008;52(12):997-1003. doi: 10.1016/j.jacc.2008.04.069.
23. Richards AM. Serial Measurements of Plasma B-Type Natriuretic Peptides: What do They Tell Us? *J Am Coll Cardiol*. 2008;52(12):1004-5. doi: 10.1016/j.jacc.2008.06.026.
24. Khan MS, Greene SJ, DeVore AD. Serial NT-proBNP Measurements and Implementation of Guideline-Directed Medical Therapy. *JACC Heart Fail*. 2024;12(3):488-91. doi: 10.1016/j.jchf.2024.01.003.
25. Fuery MA, Leifer ES, Samsky MD, Sen S, O'Connor CM, Fiuzat M, et al. Prognostic Impact of Repeated NT-proBNP Measurements in Patients with Heart Failure with Reduced Ejection Fraction. *JACC Heart Fail*. 2024;12(3):479-87. doi: 10.1016/j.jchf.2023.11.007.
26. Januzzi JL Jr, Rehman SU, Mohammed AA, Bhardwaj A, Barajas L, Barajas J, et al. Use of Amino-Terminal Pro-B-Type Natriuretic Peptide to Guide Outpatient Therapy of Patients With Chronic Left Ventricular Systolic Dysfunction. *J Am Coll Cardiol*. 2011;58(18):1881-9. doi: 10.1016/j.jacc.2011.03.072.
27. Felker GM, Anstrom KJ, Adams KF, Ezekowitz JA, Fiuzat M, Houston-Miller N, et al. Effect of Natriuretic Peptide-Guided Therapy on Hospitalization or Cardiovascular Mortality in High-Risk Patients with Heart Failure and Reduced Ejection Fraction: A Randomized Clinical Trial. *JAMA*. 2017;318(8):713-20. doi: 10.1001/jama.2017.10565.
28. Daubert MA, Adams K, Yow E, Barnhart HX, Douglas PS, Rimmer S, et al. NT-proBNP Goal Achievement is Associated with Significant Reverse Remodeling and Improved Clinical Outcomes in HFrEF. *JACC Heart Fail*. 2019;7(2):158-68. doi: 10.1016/j.jchf.2018.10.014.
29. Lee DJW, Aw TC. Natriuretic Peptides in Clinical Practice: A Current Review. *J Immunological Sci*. 2023;7(1):28-34.
30. Tsutsui H, Albert NM, Coats AJS, Anker SD, Bayes-Genis A, Butler J, et al. Natriuretic Peptides: Role in the Diagnosis and Management of Heart Failure: A Scientific Statement from the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society. *Eur J Heart Fail*. 2023;25(5):616-31. doi: 10.1002/ehjhf.2848.



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