Journal of Community Hospital Internal Medicine Perspectives

Volume 13 | Issue 6 Article 26

2023

Natriuretic Peptides and need for reliable tool to assess pulmonary congestion for treatment monitoring in Heart Failure

Mandip Singh Bhatia
Department of Internal Medicine, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Ritu Attri
Department of General Medicine, Dr.BR. Ambedkar State Institute of Medical Sciences, Mohali, Punjab, India

Saurabh C Sharda
Department of Internal Medicine, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, saurabhcsharda@gmail.com

Pulkit Swarup
Medical & Clinical Affairs, Terumo India Pvt. Ltd., India

Amit Garg
Medical & Clinical Affairs, Terumo India Pvt. Ltd., India

Recommended Citation

Bhatia, Mandip Singh; Attri, Ritu; Sharda, Saurabh C; Swarup, Pulkit; and Garg, Amit (2023) "Natriuretic Peptides and need for reliable tool to assess pulmonary congestion for treatment monitoring in Heart Failure," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 13: Iss. 6, Article 26.
DOI: 10.55729/2000-9666.1260
Available at: https://scholarlycommons.gbmc.org/jchimp/vol13/iss6/26

Natriuretic Peptides and Need for Reliable Tool to Assess Pulmonary Congestion for Treatment Monitoring in Heart Failure

Mandip S. Bhatia [a], Ritu Attri [b], Saurabh C. Sharda [a,*], Pulkit Swarup [c], Amit Garg [c]

[a] Department of Internal Medicine, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India
[b] Department of General Medicine, Dr.BR. Ambedkar State Institute of Medical Sciences, Mohali, Punjab, India
[c] Medical & Clinical Affairs, Terumo India Pvt. Ltd., India

Abstract

Natriuretic peptides (NPs) play a significant role in the pathophysiology of heart failure (HF) and are considered reliable diagnostic and prognostic indicators of congestive HF. Pulmonary congestion in HF patients leads to clinical deterioration and hospitalizations. It remains an important aspect to address the management and treatment tailoring in HF patients. However, the role of NP-guided therapy remains debatable due to contrasting reports in the literature. Current guidelines do not recommend the use of NP-guided therapy in the treatment monitoring of HF. Therefore, there is an urgent need to identify reliable markers for treatment monitoring in congestive HF. For early detection of congestion, a technology-based approach to monitor pulmonary hemodynamics and absolute lung fluid measurement is found to be effective in guiding treatment. Remote dielectric sensing technology is one such non-invasive approach that measures pulmonary fluid levels in the lungs which results in reduced hospitalization and re-admission rate in HF patients. In this review, we summarized the role of natriuretic peptides and the need for a reliable tool to assess pulmonary congestion for treatment monitoring in HF.

Keywords: Natriuretic peptides, Heart failure, Pulmonary congestion, NP-guided therapy

1. Introduction

Heart failure (HF) is a highly progressive condition that is associated with substantial morbidity and mortality. The estimated prevalence of HF in India is about 10 million individuals. It is a major public health concern because of its high prevalence, poor prognosis, and high healthcare cost. HF is characterized by the inability of heart muscles to pump adequate blood. As a result, fluid builds up in the lungs that leads to pulmonary congestion. Pulmonary congestion is recognized as the primary reason for hospitalization in patients with HF therefore, HF in such cases, is referred to as "congestive HF" (CHF).[1] Congestion often remains unrecognized due to a lack of reliable biomarkers for therapy assessment and monitoring thus, resulting in adverse outcomes. Lately, the importance of early detection of congestion has been recognized and correlated with the assessment of circulating biomarkers in patients with HF. For this purpose, the natriuretic peptide (NP) system is frequently used in clinical practice for diagnosis, severity grading, and prediction of HF progression.[1]

NP system comprises of three family members: Atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), and C-type natriuretic peptide (CNP). Physiologically, both ANP and BNP circulate as hormones and induce vasodilation, diuresis, natriuresis, and inhibition of the renin–angiotensin–aldosterone system (RAAS) and sympathetic nervous system (SNS).[2] The activation of RAAS and SNS systems may lead to cardiac hypertrophy and fibrosis. In response, NPs are secreted that exhibit antagonistic effects against renin and angiotensin II. NPs display paracrine

Received 13 June 2023; revised 8 August 2023; accepted 10 August 2023.
Available online 4 November 2023

* Corresponding author at: Department of Internal Medicine, Level-4, F-Block, Nehru Hospital, Postgraduate Institute of Medical Education and Research (PGIMER) Chandigarh, 160012, India.
E-mail address: saurabhcsharda@gmail.com (S.C. Sharda).

https://doi.org/10.55729/2000-9666.1260

effects to prevent hypertrophy and fibrosis.[1,2] The molecular mechanism of NPs i.e., synthesis of NP as pre-prohormone to cleaving into mature and amino terminal (NT) proBNP is explained in Fig. 1.

NPs are the most widely used biomarkers in HF. Among the three NPs and their pre-hormones, BNP and NT-proBNP biomarkers are the most important clinical tools for the diagnosis, prognosis, and risk stratification in cardiac practice and are considered the reliable point of care testing for HF. A study done in a tertiary care center in India has shown that Pro-BNP values above 2000 pg/ml in patients with acute heart failure requiring emergency admission are associated with a poor prognosis.[3] Studies such as Breathing Not properly Multinational Study (2002)[4] and ProBNP Investigation of Dyspnea in the Emergency Department (PRIDE) study (2005)[5] suggested BNP and NT-proBNP as good diagnostic biomarkers to "rule out" HF.[4,5]

Clinical management of CHF is challenging. Diuretics have been used as the first line of treatment for congestion.[6] As congestion is also associated with cardiac, renal, and liver injury, the use of diuretics may not improve clinical outcomes. Rapid relief of congestion is highly recognized therapeutically to improve prognosis, and to reduce hospital stays and cost burden. For the same, recent clinical trials and research reported Angiotensin receptor-neprilysin inhibitor (ARNI) and sodium-glucose co-transporter-2 inhibitor (SGLT2i) as new class of drugs used for the management of diabetic patients with HF.[7,8] Notably, the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) provided the guidelines to demonstrate cardiovascular safety in patients with T2DM in order to prevent cardiovascular complications Based on these guidelines, the CardioVascular Outcome Trials (CVOTs) are designed to assess the safety of SGLT2 inhibitors concerning three-point Major Adverse Cardiovascular Agents (MACE) including, HF-related events, cardiovascular deaths, and non-fatal stroke.[9] Both the drugs i.e., ARNi and SGLT2i have shown potential benefits in treating HF by reducing the risk of cardiovascular events, hospitalization, and mortality. However, the underlying mechanisms remain conjectural.[7]

Further, NPs were considered for guided-therapies in patients with HF due to their strong diagnostic and prognostic values. However, several studies including Guiding Evidence Based Therapy Using Biomarker Intensified Treatment in Heart Failure (GUIDE-IT) trial have failed to establish that NPs can be used to improve outcomes with this approach.[10] In addition, the sensitivity and specificity of NPs also depend on several confounding factors such as age, gender, obesity, BMI, hepatic, pulmonary, and renal dysfunction.[11-15] Thus, the role of NPs and NP-guided therapy remains debatable in the treatment monitoring of HF.

2. NP and recommendations for the management of HF

The ESC guidelines recommend algorithms for the diagnosis and exclusion of HF sub-types based on clinical representation, elevated NP levels, and structural or functional alterations.[16] Levels of NPs are inversely proportional to ejection fraction (EF), suggesting a rise in BNP and NT-pro BNP levels are positively correlated with decreased and worsened

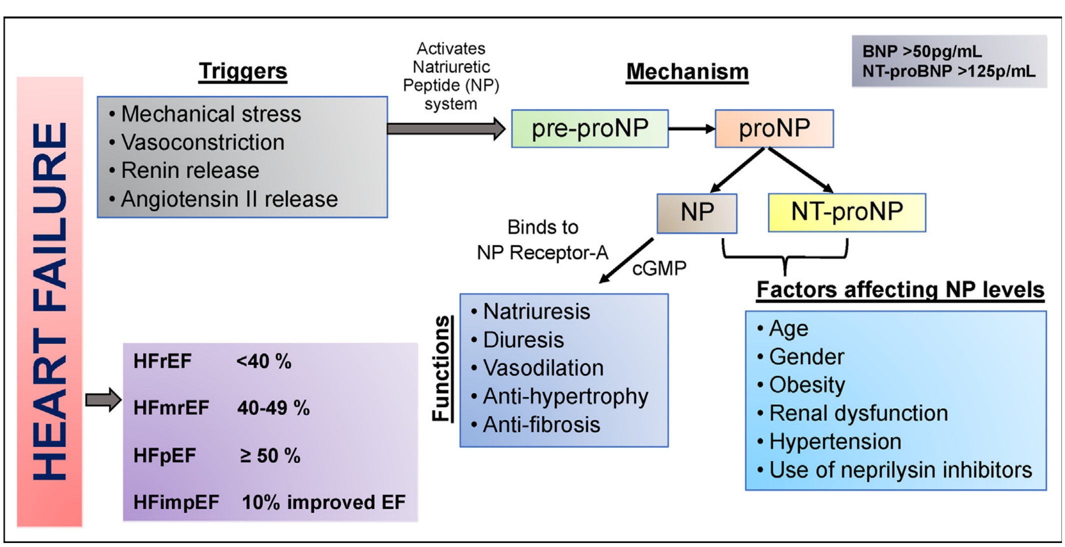

Fig. 1. Basic mechanism, functions, and factors affecting BNP levels in the management of heart failure.

EF. Studies highlight that BNP is an excellent marker for HFrEF diagnosis but less sensitive for HFpEF.[17,18]

Evidence-based guidelines such as the ESC (2021) and the American Heart Association (ACCF/AHA, 2022) recommended BNP and NT-proBNP levels assessment as (Class I) diagnostic markers of HF to determine prognosis or disease severity. Similarly, the ESC guideline recommends BNP and NT-proBNP for ruling out HF, establishing post-discharge prognosis, and risk stratification (Fig. 2). A single NP value provides prognostic details whereas serial measurement provides risk stratification including major cardiovascular events, all-cause mortality, and cardiovascular deaths.[16,19] The ACC/AHA guidelines (2022) do not recommend serial NP measurements in guiding therapy for the management of HF reduction.

3. Factors affecting NP levels in HF

The onset or development of HF may be delayed or prevented by modifying risk factors and using interventions. These factors affecting the levels of BNP and NT-proBNP in the management of HF include:

3.1. Obesity

High body mass index (BMI), a major risk factor for HF, suppresses NP synthesis resulting in lower levels of BNP and NT-proBNP.[20] Therefore, lower cut-offs are recommended in obese individuals so as to not miss patients with mild acute HF.

3.2. Neprilysin inhibitors

Neprilysin inhibitor drugs cause pharmacologic 'raising' of BNP levels. The utility of ARNIs is well-studied in the management of HF and it has received a Level I recommendation in ESC (2021) and ACC (2022) guidelines. ARNI therapy reduces NT-proBNP levels and increases BNP levels which may complicate NP value interpretation for the clinician.[21]

3.3. Other comorbidities

Several other factors such as age, gender, and comorbid conditions, including diabetes, renal dysfunction, and hypertension, are found to be associated with increased levels of NP. The BNP

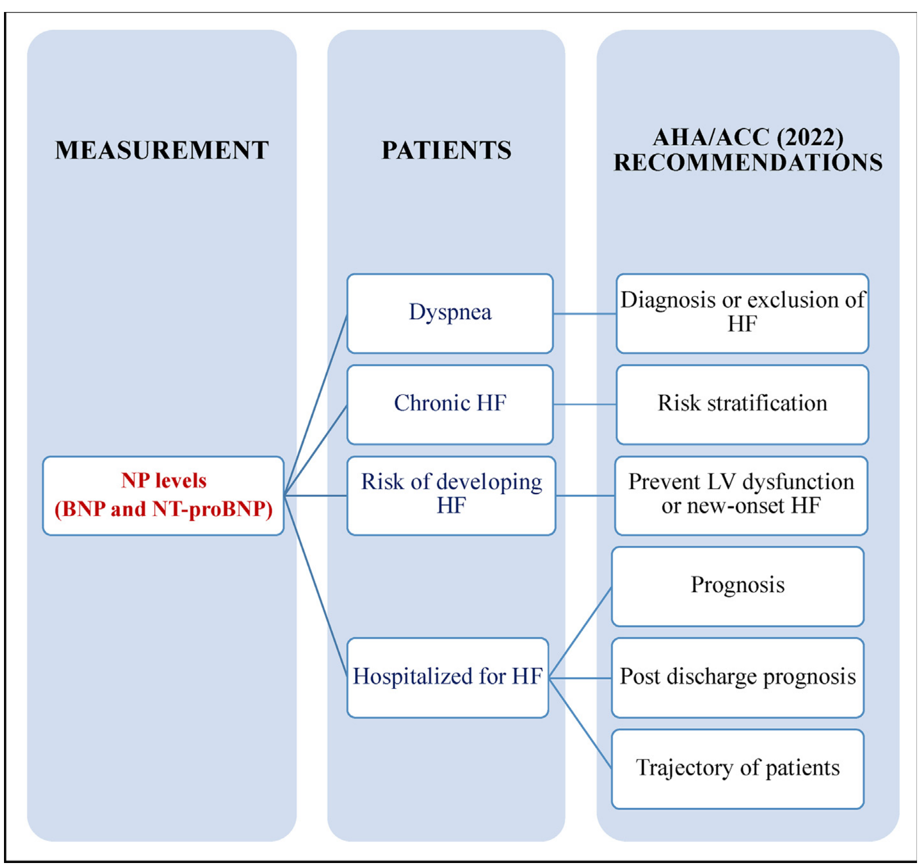

Fig. 2. AHA/ACC/HFSA recommendations for the Use of Biomarkers for Prevention, Initial Diagnosis, and Risk Stratification.

levels are altered by co-existing cardiovascular diseases (HF, acute coronary syndrome, atrial fibrillation, etc.) and non-cardiovascular diseases (pulmonary embolism, hypertension, sepsis, etc.).[20]

4. NP-guided therapy for HF management

At present, there is no common approach to medication adjustments for NP-guided therapy. BNP/NT-proBNP measurements or use of titration of therapy according to serial plasma concentrations of BNP/NT-proBNP for treatment monitoring in patients with HF is debatable. The multicentric STARBRITE study evaluated therapy titration basis clinical assessment and BNP measurement in patients presenting to HF clinic. This study failed to demonstrate significant benefits in mortality or hospitalization rates.[22] Several other studies and meta-analysis have been conducted to determine the role of NP in guiding treatment for HF patients however, these studies have yielded inconsistent results.[23-27]

GUIDE-IT is by far the largest multicentric trial which planned to recruit 1100 participant patients at 45 clinical sites in the United States and Canada with an aim to compare the efficacy of NT-proBNP–guided therapy with usual care for the management of patients with HF with reduced EF (HFrEF).[10] The trial failed to establish any significant difference in combined outcome of hospitalization or cardiovascular mortality. The strategy additionally increased the cost of therapy. Moreover, the trial was stopped early due to futility on composite outcome of HF admission and cardiovascular mortality. Moreover, this strategy had additional implications on the cost of the therapy. A meta-analysis of 18 randomized controlled trials (RCTs) conducted by Khan et al. (2018) reported no additional benefits of NP-guided therapy in terms of all-cause mortality and HF hospitalizations.[28] The usefulness of therapy for reduction in hospitalization or mortality is not well established.[24] Some patients are either non-responsive or less responsive to intensified NP-guided therapy as no significant improvement in NP levels are attained in these patients. Evidently, studies support that the concept of biomarker-guided therapy or serial measurement of NPs is not ideal for the management of HF in real-time.

5. Pulmonary congestion and role of NPs

A failing heart results in excessive accumulation of fluid in the alveolar walls and lung spaces causing pulmonary congestion. The acute decompensated heart failure (ADHF) National Registry report (2007) of >50,000 patients revealed that significant proportion of admitted patients are discharged with unresolved congestion. Congestion remains unrecognized until the condition of the patient worsens and requires hospitalization or re-admission. Some HF exacerbations may be prevented through early identification of congestive changes.[29] The ESC guidelines recommend measurement of NPs in patients with pulmonary edema. However, it is to be noted that there are other causes of elevated NPs, cardiac and non-cardiac, that might reduce their diagnostic accuracy.[18] In a study, Komarov & Kirov (2015) evaluated the relationship between plasma concentrations of NT-proBNP and pulmonary congestion.[30] The authors reported significantly higher levels of NT-proBNP at baseline with a trend of decreasing values during hospitalization, suggesting limited diagnostic value for pulmonary congestion. Current evidence does not support NP-guided titration of pharmacotherapy in HF patients especially in elderly patients.[18] For instance, The Trial of Intensified vs Standard Medical Therapy in Elderly Patients With Congestive Heart Failure (TIME-CHF) study reported that NP-guided HF therapy in elderly patients did not reduce all-cause hospitalizations.[31] Though advancements in medical therapy have reduced the rates of HF hospitalization by 30%, there has been no reduction in the rates of HF re-admissions. The HF re-admission rates range from 19 to 31% at 30 days and 50% at 6 months. Several studies have shown that 50–80% of hospitalizations can be avoided when physicians prescribe medicines in accordance with accepted guidelines and when patients adhere to prescribed medication regimens.[32] The effectiveness of implantable pulmonary artery hemodynamic monitoring system to assess impending volume overload was highlighted in the CHAMPION study.[33] The implantable device allowed regular hemodynamic monitoring of pulmonary artery and ensure treatment guidance. This lead to a significant decrease in HF related hospitalizations. However, the implantable nature and expertise required for the placement of device limits its used in the majority of patient population.[34,35]

Non-invasive measurement of lung fluid volume to guide the HF decongestion therapy was studied using a non-invasive electromagnetic energy-based technology (Remote Dielectric Sensing, ReDS™).[29] ReDS system is a miniature radar system that employs low-power electromagnetic energy that quantifies changes in the concentrations of pulmonary fluid in 90 s by wearing a noninvasive vest (Fig. 3). It also identifies the state of "euvolemia" during admission and early phase after discharge in

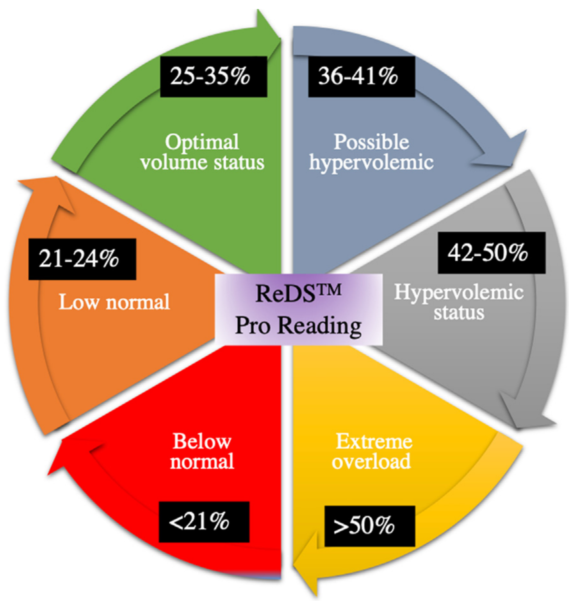

Fig. 3. ReDS™ monitoring device to assess volume status.

patients with HF, patients on diuretic or new treatment regimen *viz.* ARNI and SGLT2i, or patients recovering from other CVD events. Both these phases are considered vulnerable for congestion recurrence. The system is beneficial in early detection of congestion.

Substantial studies have determined the efficacy of the technology to monitor lung congestion and treatment decisions and reported significant reduction in hospitalisations and re-admissions in HF patients.[36,37] An absolute value of 37% of lung fluid determined by ReDS technology had sensitivity, specificity, positive predictive value, and negative predictive value of 89%, 83%, 74%, and 93%, respectively.[38,39] A meta-analysis of seven studies to determine effect of ReDS monitoring yielded a 60% reduction in 3 month rehospitalization rates.[29] This make non-invasive monitoring of lung fluid for treatment monitoring a potential tool in the management of HF patients to reduce rehospitalization.

6. Conclusions

BNP and NT-proBNP are the gold standard biomarkers for the diagnosis and prognosis of HF. However, the NP levels are found to vary according to age, comorbidities, and treatment strategies. The evidence and recommendations for use of NPs in treatment monitoring of HF are limited. This makes concept of NP-guided therapy inconclusive for treatment monitoring of HF patients. The hemodynamic monitoring and direct lung fluid measurement are promising technology with evidence for reduction in rehospitalization when used for treatment monitoring of HF patients. The invasive procedure and expertise required for invasive hemodynamic monitoring makes it less prevalent. Remote dielectric sensing technology is a non-invasive approach for measuring the fluid levels in the lungs. This technology may consider as a new paradigm for early detection of pulmonary congestion and treatment monitoring of HF patients.

Conflict of interest

Two of the co-authors, Dr Pulkit Swarup and Dr Amit Garg are associated with a Medical device company that markets Remote Dielectric sensing device. All other authors, Dr Mandip Singh Bhatia, Dr Ritu Attri, and Dr Saurabh C Sharda declare no conflict of interest.

Disclaimer

We declare that the work included in the manuscript has not been published previously or under review in any of the other journals.

Acknowledgement

We are grateful to Ms. Rajni Bala for writing assistance.

References

1. Koratala A, Kazory A. Extracorporeal ultrafiltration for acute heart failure: lost battle or lasting opportunity? *Blood Purif*. 2017;43:1–10.
2. Potter LR, Yoder AR, Flora DR, Antos LK, Dickey DM. Natriuretic peptides: their structures, receptors, physiologic functions and therapeutic applications. *Handb Exp Pharmacol*. 2009:341–366.
3. Bhatia MS, Sharda SC, Attri R, Pannu AK, Dahiya N. Correlation of mortality with Pro-BNP and precipitating factors of acute heart failure in patients presenting to a medical emergency of tertiary care hospital: an observational study from north India. *Eur Rev Med Pharmacol Sci*. 2022;26:6459–6468.
4. Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med*. 2002;347:161–167.
5. Januzzi Jr JL, Camargo CA, Anwaruddin S, et al. The N-terminal Pro-BNP investigation of dyspnea in the emergency department (PRIDE) study. *Am J Cardiol*. 2005;95:948–954.
6. Vazir A, Cowie MR. Decongestion: diuretics and other therapies for hospitalized heart failure. *Indian Heart J*. 2016;68:S61–S68.
7. Muscoli S, Barillà F, Tajmir R, et al. The new role of SGLT2 inhibitors in the management of heart failure: current evidence and future perspective. *Pharmaceutics*. 2022;14:1730.
8. Kim HM, Hwang IC, Choi W, Yoon YE, Cho GY. Combined effects of ARNI and SGLT2 inhibitors in diabetic patients with heart failure with reduced ejection fraction. *Sci Rep*. 2021 Nov 16;11(1):22342.
9. Tamargo J. Sodium-glucose cotransporter 2 inhibitors in heart failure: potential mechanisms of action, adverse effects and future developments. *Eur Cardiol*. 2019;14:23–32.

10. Felker GM, Anstrom KJ, Adams KF, 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):713–720.
11. Chioncel O, Lainscak M, Seferovic PM, et al. Epidemiology and one-year outcomes in patients with chronic heart failure and preserved, mid-range and reduced ejection fraction: an analysis of the ESC heart failure long-term registry. *Eur J Heart Fail*. 2017;19:1574–1585.
12. Keyzer JM, Hoffmann JJ, Ringoir L, Nabbe KC, Widdershoven JW, Pop VJ. Age- and gender-specific brain natriuretic peptide (BNP) reference ranges in primary care. *Clin Chem Lab Med*. 2014 Sep;52(9):1341–1346.
13. Madamanchi C, Alhosaini H, Sumida A, Runge MS. Obesity and natriuretic peptides, BNP and NT-proBNP: mechanisms and diagnostic implications for heart failure. *Int J Cardiol*. 2014;176(3):611–617.
14. Metwaly A, Khalik AA, Nasr FM, Sabry AI, Gouda MF, Hassan M. Brain natriuretic peptide in liver cirrhosis and fatty liver: correlation with cardiac performance. *Electron Physician*. 2016 Feb 25;8(2):1984–1993.
15. Takase H, Dohi Y. Kidney function crucially affects B-type natriuretic peptide (BNP), N-terminal proBNP and their relationship. *Eur J Clin Invest*. 2014;44(3):303–308.
16. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: executive summary: a report of the American college of cardiology/American heart association joint committee on clinical practice guidelines. *Circulation*. 2022;145:e876–e894.
17. Zordoky BN, Sung MM, Ezekowitz J, et al. Metabolomic fingerprint of heart failure with preserved ejection fraction. *PLoS One*. 2015;10:e0124844.
18. Moliner P, Lupón J, Barallat J, et al. Bio-profiling and bio-prognostication of chronic heart failure with mid-range ejection fraction. *Int J Cardiol*. 2018;257:188–192.
19. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure published correction appears. *Eur Heart J*. 2021; 42:3599–3726.
20. Yoo BS. Clinical significance of B-type natriuretic peptide in heart failure. *J Lifestyle Med*. 2014;4:34–38.
21. Vasquez N, Carter S, Grodin JL. Angiotensin receptor–neprilysin inhibitors and the natriuretic peptide Axis. *Curr Heart Fail Rep*. 2020;17:67–76.
22. Shah MR, Califf RM, Nohria A, et al. The STARBRITE trial: a randomized, pilot study of B-type natriuretic peptide-guided therapy in patients with advanced heart failure. *J Card Fail*. 2011;17:613–621.
23. Jourdain P, Jondeau G, Funck F, et al. Plasma brain natriuretic peptide-guided therapy to improve outcome in heart failure: the STARS-BNP Multicenter Study. *J Am Coll Cardiol*. 2007;49: 1733–1739.
24. Troughton R, Michael Felker G, Januzzi Jr JL. Natriuretic peptide-guided heart failure management. *Eur Heart J*. 2014; 35:16–24.
25. Bhardwaj A, Rehman SU, Mohammed A, Baggish AL, Moore SA, Januzzi Jr JL. Design and methods of the pro-B type natriuretic peptide outpatient tailored chronic heart failure therapy (PROTECT) study. *Am Heart J*. 2010;159: 532–538.e1.
26. Persson H, Erntell H, Eriksson B, Johansson G, Swedberg K, Dahlström U. Improved pharmacological therapy of chronic heart failure in primary care: a randomized study of NT-proBNP guided management of heart failure–SIGNAL-HF (Swedish intervention study–guidelines and NT-proBNP AnaLysis in heart failure). *Eur J Heart Fail*. 2010;12:1300–1308.
27. Castiglione V, Aimo A, Vergaro G, Saccaro L, Passino C, Emdin M. Biomarkers for the diagnosis and management of heart failure. *Heart Fail Rev*. 2022;27:625–643.
28. Khan MS, Siddiqi TJ, Usman MS, et al. Does natriuretic peptide monitoring improve outcomes in heart failure patients? A systematic review and meta-analysis. *Int J Cardiol*. 2018;263:80–87.
29. Sattar Y, Zghouzi M, Suleiman AM, et al. Efficacy of remote dielectric sensing (ReDS) in the prevention of heart failure rehospitalizations: a meta-analysis. *J Community Hosp Intern Med Perspect*. 2021;11:646–652.
30. Komarov SA, Kirov MY. Relationship between nt-probnp and extravascular lung water in ards. *Intensive Care Med Exp*. 2015; 3:A1006.
31. Sanders-van Wijk S, Maeder MT, Nietlispach F, et al. Long-term results of intensified, N-terminal-pro-B-type natriuretic peptide-guided versus symptom-guided treatment in elderly patients with heart failure: five-year follow-up from TIME-CHF. *Circ Heart Fail*. 2014;7:131–139.
32. Bennett SJ, Hustler GA, Baker SL, et al. Characterization of the precipitants of hospitalization for heart failure decompensation. *Am J Crit Care*. 1998;7:168–174.
33. Adamson PB, Abraham WT, Aaron M, et al. CHAMPION trial rationale and design: the long-term safety and clinical efficacy of a wireless pulmonary artery pressure monitoring system. *J Card Fail*. 2011;17(1):3–10.
34. Bourge RC, Abraham WT, Adamson PB, et al. Randomized controlled trial of an implantable continuous hemodynamic monitor in patients with advanced heart failure: the COMPASS-HF study. *J Am Coll Cardiol*. 2008;51:1073–1079.
35. Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. *Lancet*. 2011;377: 658–666.
36. Amir O, Ben-Gal T, Weinstein JM, et al. Evaluation of remote dielectric sensing (ReDS) technology-guided therapy for decreasing heart failure re-hospitalizations. *Int J Cardiol*. 2017; 240:279–284.
37. Lala A, Barghash MH, Giustino G, et al. Early use of remote dielectric sensing after hospitalization to reduce heart failure readmissions. *ESC Heart Fail*. 2021;8:1047–1054.
38. Olesen A, Sophie A, Miger K, et al. Diagnostic value of remote dielectric sensing (ReDS) technology to predict pulmonary congestion on computed tomography in consecutive patients with acute dyspnea. In: *EUROPEAN journal of heart failure*. NJ USA: WILEY 111 RIVER ST, HOBOKEN 07030-5774; 2019:110.
39. Amir O, Azzam ZS, Gaspar T, et al. Validation of remote dielectric sensing (ReDS™) technology for quantification of lung fluid status: comparison to high resolution chest computed tomography in patients with and without acute heart failure. *Int J Cardiol*. 2016;221:841–846.