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Biochemistry

DIAGNOSTIC VALUES OF SERUM GAL-3 ALONG WITH NATRIURETIC PEPTIDES (BNP AND NT-PROBNP) IN HEART FAILURE

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ABSTRACT **Background:** The prevalence of heart failure is rising progressively. Its diagnosis, which is still challenging and debatable, mostly relies on echocardiographic detection of raised filling pressures and left ventricular diastolic dysfunction. **Aim and objectives:** Our study currently aims to identify quick, easy, and noninvasive approaches to detect it rather than using complicated methods. Given that the biochemical pattern changes significantly in this condition, the current study assessed the relevance of certain biomarkers in disease detection among the northwest Punjabi population. **Material and Method:** This study was undertaken in the Department of Biochemistry, Sri Guru Ram Das Medical Institute of Science and Research, Amritsar in collaboration with the Department of Medicine, Sri Guru Ram Das Hospital, Amritsar. The study comprised 50 individuals with confirmed heart failure from OPD and IPD of the Medicine department, Sri Guru Ram Das Hospital, Amritsar, and 50 healthy individuals of comparable age. Serum Galectin-3 levels and natriuretic peptides (BNP and NT-pro BNP) were investigated and compared. **Result:** Serum Galectin 3 levels > 12.12±1.64 ng/ml and < 24.90±16.59 ng/ml and Serum BNP > 100 pg/ml <270.44±134.92 pg/ml and NT pro-BNP >125 pg/ml <1337±86.8 pg/ml could be helpful in the diagnosis of the disease. When compared to healthy control participants, heart failure patients' serum levels of Galectin-3 ($p<0.001$) and natriuretic peptides ($p<0.001$) were significantly higher. With the severity of the condition, the levels of these biomarkers were significantly increased as well. **Conclusion:** The levels of serum Galectin-3 along with natriuretic peptide are positively correlated, indicating that serum natriuretic peptide estimation can be performed in conjunction with serum Galectin-3 estimation for the diagnosis of heart failure.

KEYWORDS : Heart Failure, Galectin-3, Brain natriuretic peptide, amino-terminal proB-type natriuretic peptide

INTRODUCTION

Heart Failure (HF) is a complex, fatal health condition with high expenses, major mortality, and morbidity, significantly impacting performance and quality of life. Globally, over 64.3 million individuals suffer from heart failure, more than double the 1990 figures of 33.5 million (Bragazzi NL et al., 2021). Approximately 500,000 new cases are diagnosed annually (Sanjay G. et al., 2018).

Symptoms arise from insufficient cardiac output and, unable to meet the body's metabolic needs (Ponikowski P et al., 2016). The left ventricle ejection fraction (EF) categorizes heart failure into three primary categories based on the percentage of blood pumped with each beat, as recommended by the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. (American Heart Association et al., 2023) The categories are as follows:

a) Heart failure with reduced ejection fraction (HFrEF): EF less than or equal to 40%
b) Heart failure with preserved EF (HFpEF): EF is greater than or equal to 50%
c) Heart failure with mid-range EF (HFmrEF) 40 to 49%. (Ponikowski P et al., 2016).

It is now practically widely recognized that biomarkers serve as the key endpoints in clinical trials because of their widespread usage in scientific and clinical research, as well as in clinical practice. (Slikker, W. 2017) The World Health Organization (WHO) in collaboration with the United Nations and the International Labor Organization, has described a biomarker as "any substance, structure, or process that can be measured in the body or its products and influence or predict the incidence of outcome or disease" (WHO 2001; Califf RM et al 2018). The determination of patients with heart failure also significantly depends on biomarkers. (Nadar & Shaikh, 2019) In present-day medical settings, the heart releases B-type natriuretic peptide (BNP) and amino-terminal proB-type natriuretic peptide (NTproBNP) as vital biomarkers for the diagnosis and monitoring of heart conditions. (Goetze JP et al., 2020) However, our study introduces an additional biomarker Galectin-3 by utilizing the pre-existing natriuretic peptides to strengthen the assurance of the diagnosis. This contributes to a more comprehensive and reliable diagnostic approach in our research.

Galectin-3 (Gal-3), recognized as a galactoside-binding protein, emerges as an innovative clinical biomarker with implications in individuals with heart failure (HF). In the context of heart failure, it acts as a biomarker, a signal that helps us understand changes in the heart. In heart failure, Galectin-3 (Gal-3) levels increase due to the heart's response to stress and injury. Gal-3 is involved in a variety of processes that contribute to heart failure, including inflammation, fibrosis, and ventricular remodeling (structural changes in the heart). The heart releases Gal-3 as a defense mechanism, attempting to repair damaged tissue. Studying Gal-3 provides insights into these heart issues and can be useful for understanding and managing heart failure. (Soares LC et al., 2021)

Elevated plasma GAL-3 is associated with higher risks of adverse events, including death and recurrent heart failure. (Blanda V et al., 2020) Therefore, Gal-3 stands out as a promising biomarker in the context of heart failure, offering insights into the fundamental processes of cardiac dysfunction, remodeling, and adverse outcomes. These correlations highlight its potential as a clinically significant marker for assessing risk in individuals with heart failure. The present study aimed to determine the affordable, reliable, and non-invasive parameters to diagnose the condition. We assessed the serum levels of Galectin-3, along with the established biomarkers natriuretic peptides (BNP and NT-pro BNP), in individuals already diagnosed with cardiac failure, comparing them to a control group of healthy individuals.

One of the established biomarkers is B-type natriuretic peptide (BNP). It is a natriuretic hormone initially identified in the brain but released primarily from the heart, particularly the ventricles. (Colucci WS et al2023) In healthy people, circulating BNP/NT-proBNP levels usually remain quite low. BNP has a variety of physiological effects, including natriuresis and diuresis, peripheral vasodilatation, and suppression of the sympathetic nervous system (SNS) and the renin-angiotensin-aldosterone system (RAAS). (Okamoto R et al 2019) The BNP gene becomes activated in cardiomyocytes in response to increased cardiac wall stress caused by volume- or pressure-overload conditions (such as in HF). An intracellular precursor propeptide (proBNP108) is produced as a consequence of the aforementioned, and when this propeptide is processed further, the physiologically inert amino-terminal fragment (NT-proBNP) and the biologically active BNP are

released. (Don-Wauchope & McKelvie, 2015) Despite being released in a 1:1 ratio, NT-proBNP is passively removed from the circulation which is much slower (half-life of 120 versus 20 minutes), which contributes to the observed NT-proBNP level being more than that of BNP. Both the biologically active BNP and NT-proBNP could be found in plasma (Sasaki T et al., 2021; Yu J et al., 2023)

A study showcased that among patients at risk of heart failure, BNP-based screening and collaborative care significantly reduce the combined rates of LV systolic dysfunction, diastolic dysfunction, and heart failure. (Lyngbakken et al., 2020) In another research, it was observed that the ratio of NT-proBNP to BNP in heart failure and reduced ejection fraction appears to be significantly greater. (Rørth R et al. 2020) Another research connected that NT-proBNP testing was valuable for diagnostic evaluation and short-term prognosis estimation in dyspnoeic subjects with suspected or confirmed acute HF. (Lee et al., 2022)

By our present study, another investigation revealed a notable increase in Galectin-3 levels heart failure patients. (Besler C et al 2017) A similar type of study revealed the role of galectin-3 in the development of heart failure, its value in screening and clinical decision-making and its possible predictive application in follow-up as a "routine" test in addition to established biomarkers, such as B-type natriuretic peptide and N-terminal prohormone of B-type natriuretic peptide. (Dong R et al2017)

The current analytical methods for diagnosing heart failure are expensive, invasive, and only available at specialized facilities with the latest technology. This makes them unapproachable for the general population. Therefore, there is a need for simpler and more affordable biomarker investigations that can be easily assayed to detect this fatal condition. Our study improves the accuracy of diagnosis by adding Galectin-3 as a supplementary biomarker to the existing natriuretic peptides, enhancing the overall reliability of the diagnostic approach.

MATERIALS AND METHODS

A total number of 50 participants were in the present study which included 17,19 and 14 patients in HFrEF, HFmrEF, and HFpEF respectively of cardiac failure. 50 age-matched normal healthy individuals were taken as controls from the general population. Informed consent was taken from all the participants for drawing their blood samples. This study was undertaken in the Department of Biochemistry, Sri Guru Ram Das Medical Institute of Science and Research, Amritsar in collaboration with the Department of Medicine, Sri Guru Ram Das Hospital, Amritsar. The participants were selected from OPD and IPD of Sri Guru Ram Das Hospital, Amritsar attached to Sri Guru Ram Das Medical Institute of Science and Research, Amritsar. The study was done after approval by the Institutional Research and Ethical Committee. The patients with hypertension/CAD/DM/LV dysfunction or patients presenting to OPD/IPD with a history of breathlessness were included. Patients were labeled as suffering from HF based on the American Heart Association classification. The patients suffering from Chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), Chronic liver disease (CLD), or Previous history of inflammatory disorder. were excluded as these conditions interfered with the analysis. History of patients was collected and thorough clinical examination was conducted in all the cases according to the performa. Blood samples were collected from healthy controls and heart failure patients and analyzed and compared for serum Galectin-3, BNP, and NT-proBNP.

METHODS

1. The estimation of Serum Galectin-3(Gal-3), Serum BNP and Serum NT pro-BNP by ELISA method (Kit Method) in heart failure patients and compared with healthy controls.
2. The comparison between different classes of Heart Failure and healthy controls
3. The correlation between different classes of Heart Failure and healthy controls

Statistical analysis:

Statistical analyses were carried out using the student's t-test. Unpaired t-test was used to find significant differences between the two different groups. In cardiac failure patients, changes in the serum levels of biochemical parameters were analyzed by the coefficient of correlation for all classes.

RESULT

In our present study, the age distribution was matched in both the groups i.e. cases(50) and control(50). Fig1. shows the age distribution in the control group ranged from 43-77 years with a mean±SD of 55±8 years while in the Case group, it ranged from 45-85 years with a mean±SD of 63±9 years.

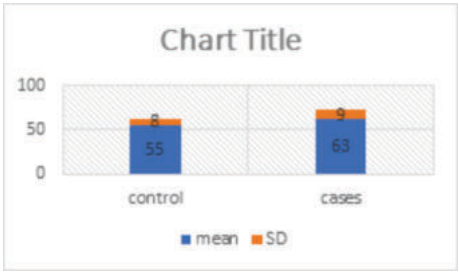

Figure 1: Distribution of age among cases and controls.

Fig 2. Distribution of Heart failure patients in different classes in percent

The graphical representation in Figure 2 provides insights into the distribution of heart failure patients across different classes. The data reveals that the largest proportion (38%) of patients were observed in the HFmrEF class, characterized by a mid-range ejection fraction, followed by 34% in the HFrEF class, which is associated with a reduced ejection fraction. Conversely, the HFpEF class, which is indicative of a preserved ejection fraction, accounted for 28% of the total patients.

Table 1: Variation in serum Galectin 3 among cases and controls

Parameter ↓	Case(50) ng/ml	Control (50) ng/ml	t-value	P value
Mean	24.90	12.122	51.044	0.042*
Std. Deviation	16.59	1.6436		

According to Table 1, there was a statistically significant ($p < 0.05$) rise in serum Gal-3 levels in heart failure patients compared to age-matched, normally healthy controls. Serum Gal-3 levels were higher in heart failure (24.90±16.59 ng/ml vs. 12.12±1.64 ng/ml of mean±SD) than in healthy people (normal values).

Table 2: Variation in serum BNP among cases and controls

Parameter ↓	Case(50) ng/ml	Control (50) ng/ml	t-value	P value
Mean	270.44	55.18	51.287	0.000*
Std. Deviation	134.92	14.948		

Table 2 demonstrates that serum BNP levels were statistically significantly ($p < 0.001$) higher in heart failure patients than in age-matched, otherwise healthy controls. Serum Gal-3 levels in heart failure were higher than those in normal people, who had mean and SD values of 270.44 and 55.18 pg/ml, respectively, of 134.92 and 14.94 pg/ml.

Table 3: Variation in NT pro-BNP among cases and controls

Parameter ↓	Case(50) ng/ml	Control (50) ng/ml	t-value	P value
Mean	1337.20	175.02	84.914	0.000*
Std. Deviation	86.835	42.730		

As per Table 3, the elevated levels of serum NT proBNP were highly significant ($p < 0.001$) in heart failure patients in comparison with normal healthy controls. The levels of serum NT pro-BNP in cardiac failure cases were 1337.20±86.83 pg/ml while it was within normal limits with 175.02±42.73 pg/ml observed.

Table 4: Serum Galectin-3 in different classes of cardiac failure in comparison with normal healthy controls

Individual	Range (ng/ml)	mean±SD (ng/ml)
Healthy individuals (Control) (50)	9.1-15.7	12.12 ±1.64
HFrEF (17)	29.3-40.7	35.3±3.98
HFmrEF(19)	12.7-27.4	18.74±4.36
HFpEF (14)	9.9-18.2	12.30±2.07

(HFrEF= Heart failure with reduced ejection fraction, HFrEF= Heart failure with mid-range ejection fraction, HFrEF= Heart failure with preserved ejection fraction)

Table 4 represents the levels of serum Gal-3 were highest in the HFrEF at 35.3±3.98 ng/ml followed by HFmrEF with 18.74±4.36ng/ml and 12.30±2.07 ng/ml in HFpEF. The levels estimated in normal healthy control were 12.12 ±1.64 ng/ml.

Table 5: Serum BNP in different classes of cardiac failure in comparison with normal healthy controls

Individual	Range (pg/ml)	mean±SD (pg/ml)
Healthy individuals (Control) (50)	28-85	55.18± 14.9
HFrEF (17)	320-460	373.85±45.70
HFmrEF(19)	308-435	359.82±33.52
HFpEF (14)	33-96	56.40±16.77

In Table 5, With 373.85±45.70 pg/ml, HFrEF had the highest serum BNP levels, followed by HFmrEF (359.82±33.52 pg/ml) and HFpEF (56.40±16.77 pg/ml). 55.18± 14.9 pg/ml was estimated in normal, healthy control participants.

Table 6 Serum NT pro-BNP in different classes of cardiac failure in comparison with normal healthy controls

Individual	Range (pg/ml)	mean±SD (pg/ml)
Healthy individuals (Control) (50)	129-375	175.02±42.72
HFrEF (17)	1123-1458	1503.95 ± 74.2
HFmrEF(19)	1120-1458	1325.06± 91.52
HFpEF (14)	147-399	179.13± 52.51

Table 6 shows that the highest serum NT pro-BNP concentrations (1353.95 ± 74.2 pg/ml) were found in the HFrEF, preceded by those in the HFmrEF (1325.06± 91.52 pg/ml) and the HFpEF (179.13± 52.51 pg/ml). The values in the normally healthy control group were assessed to be 175.02±42.72 pg/ml

Table 7 Coefficient of correlation (r) between Galectin-3, BNP, and NT pro-BNP in various classes of Cardiac Failure

Classes of heart failure	Galectin-3/BNP		Galectin-3/NTproBNP		BNP/NT pro-BNP	
	r	p	r	p	r	p
HFrEF (17)	+0.35	<0.01*	+0.30	<0.01*	+0.76	<0.001**
HFmrEF(19)	+0.61	<0.01*	+0.38	<0.01*	+0.80	<0.001**
HFpEF (14)	+0.98	<0.001**	+0.35	<0.01*	+0.39	<0.01*

*- significant , ** = highly significant

The results in Table 7 shows that there is a positive correlation between serum Gal-3 and BNP levels in HFrEF (heart failure with reduced ejection fraction), HFmrEF (heart failure with mid-range ejection fraction), and HFpEF (heart failure with preserved ejection fraction). However, the correlation was found to be highly significant in HFpEF.

Furthermore, the study also examined the relationship between Galectin-3/NTproBNP levels in all classes of heart failure. The results showed a positive correlation in all classes of heart failure. In HFrEF and HFmrEF, a highly positive correlation was noted, while in HFpEF, the correlation was significant.

These findings provide important insights into the pathophysiology of heart failure and may help to improve the diagnosis and treatment of this condition.

Figure 3 depicts the distribution of the condition across different classes. The highest levels of the condition are observed in the HFrEF class (38%), which is characterized by significant impairment of the heart. Following this, the HFmrEF class (34%) shows the second-highest levels of the condition. The HFpEF class (28%) also shows significantly elevated levels of the condition compared to normal healthy individuals.

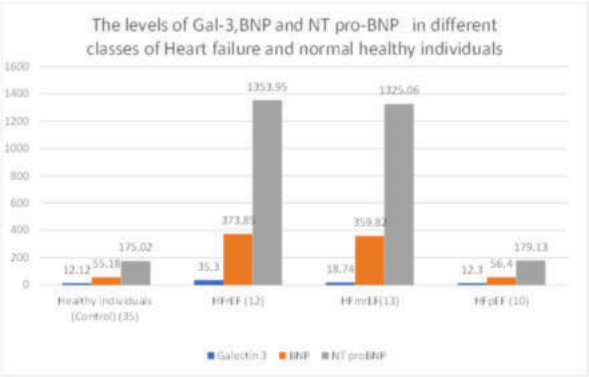

Fig 3 The levels of Gal-3, BNP, and NT pro-BNP in different classes of Heart failure and normal healthy individuals.

DISCUSSION

The objective of this study was to evaluate the levels of Gal-3, BNP, and NT pro-BNP among individuals with heart failure against healthy individuals. As the population ages, the prevalence of heart failure and cardiac dysfunction increases, making it crucial to detect and diagnose these conditions as early as possible. The consequences of these ailments can be severe, which further emphasizes the significance of timely detection and diagnosis. Heart failure can be a costly and invasive medical condition. In light of this, our study aimed to detect this condition early, in a cost-effective and non-invasive marker. Thus, we present Galectin-3 as a new biomarker, utilizing known natriuretic peptides to strengthen diagnostic confidence and advance a more thorough and dependable diagnostic process.

The observed elevation in galectin-3 (Gal-3) levels in the heart failure condition in the present study indicates a potentially useful approach for comprehending and identifying cardiac dysfunction. Gal-3 is linked to heart failure through processes such as inflammation, fibrosis, and ventricular remodeling (structural heart alterations). The heart releases Gal-3 as a defense mechanism to repair injured tissue. Thus, the results of this study suggest that higher Gal-3 levels may serve as a valuable biomarker of heart failure.

The findings of our study closely align with the research conducted by Gehlken C et al. in 2018 and Zaborska B et al. in 2023, emphasizing the critical role of galectin-3 in heart remodeling processes. Galectin-3's expression in activated macrophages and damaged cardiomyocytes signifies involvement in myocardial fibrogenesis underscoring its association with structural changes contributing to heart failure. The consistent correlation between our study and these two works strengthens the significance of galectin-3 as a biomarker for cardiac dysfunction. This shared understanding provides valuable insights into levels of galectin-3 in heart failure.

Similar to our findings, a study demonstrated an association between higher NT-proBNP levels and cardiovascular. These associations signify traditional risk, indicating that NT-proBNP is valuable for identifying individuals at high risk for cardiac events (Rudolf H et al., 2020). With ongoing advancements in precise BNP and NT-proBNP measurement, these biomarkers can play a crucial role in evaluating cardiac function in both clinical and forensic settings (Cao Z et al., 2019). Recent research has uncovered that the NT-proBNP to BNP ratio in individuals with heart failure and reduced ejection fraction is elevated. These findings carry significant implications for the analysis of natriuretic peptide levels in individuals dealing with heart failure and reduced ejection fraction (Rørth R et al., 2020).

Our study's results find support in another investigation, suggesting that the diagnostic and prognostic value of acute heart failure can be significantly improved by incorporating both plasma galectin-3 and B-type natriuretic peptide (BNP) concentrations in the evaluation process (p = 0.05) (Sani MU et al., 2021). Similarly, a different study observed elevated galectin-3 concentrations in chronic heart failure patients, irrespective of the underlying etiology and typology, including cases with preserved or reduced ejection fraction. The researchers concluded that galectin-3 has the potential to serve as a biomarker for the diagnosis and management of heart failure (Dong R et al., 2017). These consistent findings across studies further emphasize the significance of galectin-3 as a valuable diagnostic and prognostic tool in the realm of heart failure.

These findings suggest that the severity of the condition is closely related to the degree of impairment of the heart. Given the significance of early detection, our study was designed to ensure that the process is affordable and non-intrusive. By utilizing cutting-edge technology and innovative methods, we hope to provide accurate and reliable results that can inform early intervention and ultimately improve patient outcomes. By adding Galectin-3 as a new biomarker to the list of recognized natriuretic peptides, our work improves diagnostic accuracy and strengthens the diagnostic approach's overall dependability.

CONCLUSION

The present research revealed that the elevated Gal-3, BNP, and NTpro BNP levels in heart failure patients, implying a direct correlation with condition severity and heart impairment, while the incorporation of Galectin-3 alongside established natriuretic peptides enhances diagnostic accuracy and overall reliability in heart failure assessment.

Conflicts of interest: There aren't any conflicts of interest.

Limitation of the study: The study was conducted with a limited number of participants. A small sample size can impact the statistical power of the study. Therefore, further research is recommended with a larger and more diverse cohort of participants.

REFERENCES:

1. American Heart Association (AHA). 2023. Ejection Fraction and Heart Failure. https://www.heart.org/en/health-topics/heart-failure/diagnosing-heart-failure/ejection-fraction-heart-failure-measurement
2. Besler, C., Lang, D., Urban, D., Rommel, K. P., von Roeder, M., Fengler, K., Blazek, S., Kandolf, R., Klingel, K., Thiele, H., Linke, A., Schuler, G., Adams, V., & Lurz, P. (2017). Plasma and Cardiac Galectin-3 in Patients With Heart Failure Reflects Both Inflammation and Fibrosis. Circulation: Heart Failure,10(3). https://doi.org/10. 1161/circheartfailure.116.003804
3. Blanda, V., Bracale, U. M., Di Taranto, M. D., & Fortunato, G. (2020, December 3). Galectin-3 in Cardiovascular Diseases. International Journal of Molecular Sciences, 21(23), 9232. https://doi.org/10.3390/ijms21239232
4. Brunner-La Rocca, H. P., & Sanders-van Wijk, S. (2019). Natriuretic Peptides in Chronic Heart Failure. Cardiac Failure Review, 5(1), 44–49. https://doi.org/10. 15420/cfr.2018.26.1
5. Califf, R. M. (2018). Biomarker definitions and their applications. Experimental Biology and Medicine,243(3),213–221. https://doi.org/10.1177/1535370217750088
6. Cao, Jia, & Zhu. (2019). BNP and NT-proBNP as Diagnostic Biomarkers for Cardiac Dysfunction in Both Clinical and Forensic Medicine. International Journal of Molecular Sciences, 20(8), 1820. https://doi.org/10.3390/
7. Colucci WS, Chen HH. Natriuretic peptide measurement in heart failure. (2023) https://www.uptodate.com/contents/natriuretic-peptide-measurement-in-heart-failure
8. Dong, R., Zhang, M., Hu, Q., Zheng, S., Soh, A., Zheng, Y., & Yuan, H. (2017). Galectin-3 as a novel biomarker for disease diagnosis and a target for therapy (Review). International Journal of Molecular Medicine. https://doi.org/10.3892/ijmm.2017.3311
9. Don-Wauchope, A. C., & McKelvie, R. S. (2015). Evidence-based application of BNP/NT-proBNP testing in heart failure. Clinical Biochemistry, 48(4–5), 236–246. https://doi.org/10.1016/j.clinbiochem.2014.11.002
10. Gehlken, C., Suthahar, N., Meijers, W. C., & de Boer, R. A. (2018). Galectin-3 in Heart Failure. Heart Failure Clinics, 14(1), 75–92. https://doi.org/10.1016/j.hfc.2017.08.009
11. Goetze, J. P., Bruneau, B. G., Ramos, H. R., Ogawa, T., de Bold, M. K., & de Bold, A. J. (2020, May 22). Cardiac natriuretic peptides. Nature Reviews Cardiology, 17(11), 698–717. https://doi.org/10.1038/s41569-020-0381-0
12. Hara, A., Niwa, M., Kanayama, T., Noguchi, K., Niwa, A., Matsuo, M. (2020, September 4). Galectin-3: A Potential Prognostic and Diagnostic Marker for Heart Disease and Detection of Early Stage Pathology. Biomolecules, 10(9), 1277. https://doi.org/10.3390/biom10091277
13. Lee, K. K., Doudesis, D., Anwar, M., Astengo, F., Chenevier-Gobeaux, C., Claessens, Y. E. (2022, June 13). Development and validation of a decision support tool for the diagnosis of acute heart failure: systematic review, meta-analysis, and modelling study. BMJ, e068424. https://doi.org/10.1136/bmj-2021-068424
14. Lyngbakken, M. N., Kvisvik, B., Aagaard, E. N., Berge, T., Pervez, M. O., Brynildsen, J., Tveit, A. (2020, December 5). B-Type Natriuretic Peptide Is Associated with Indices of Left Ventricular Dysfunction in Healthy Subjects from the General Population: The Akershus Cardiac Examination 1950 Study. Clinical Chemistry, 67(1), 204–215. https://doi.org/10.1093/clinchem/hvaa257
15. Nadar, S. K., & Shaikh, M. M. (2019, February 11). Biomarkers in Routine Heart Failure Clinical Care. Cardiac Failure Review, 5(1), 50–56. https://doi.org/10.15420/cfr.2018.27.2
16. Okamoto, R., Ali, Y., Hashizume, R., Suzuki, N., & Ito, M. (2019, July 22). BNP as a Major Player in the Heart-Kidney Connection. International Journal of Molecular Sciences, 20(14), 3581. https://doi.org/10.3390/ijms20143581
17. Okamoto, R., Ali, Y., Hashizume, R., Suzuki, N., & Ito, M. (2019, July 22). BNP as a Major Player in the Heart-Kidney Connection. International Journal of Molecular Sciences, 20(14), 3581. https://doi.org/10.3390/ijms20143581
18. Rørth, R., Jhund, P. S., Yilmaz, M. B., Kristensen, S. L., Welsh, P., Desai, A. S., Køber, L., Prescott, M. F., Rouleau, J. L., Solomon, S. D., Swedberg, K., Zile, M. R., Packer, M., & McMurray, J. J. (2020, February). Comparison of BNP and NT-proBNP in Patients With Heart Failure and Reduced Ejection Fraction. Circulation: Heart Failure,13(2). https://doi.org/10.1161/circheartfailure.119.006541
19. Rudolf, H., Mügge, A., Trampisch, H. J., Scharnagl, H., März, W., & Kara, K. (2020, August). NT-proBNP for risk prediction of cardiovascular events and all-cause mortality: The getABI-study. IJC Heart & Vasculature, 29, 100553. https://doi.org/10.1016/j.ijcha.2020.100553
20. Sani, M. U., Damasceno, A., Davison, B. A., Cotter, G., Mayosi, B. M., Edwards, C., Azibani, F., Adam, T., Arif, G., Jessen, N., & Sliwa, K. (2020, November 28). N.terminal pro BNP and galectin.3 are prognostic biomarkers of acute heart failure in sub.Saharan Africa: lessons from the BAHEF trial. ESC Heart Failure, 8(1), 74–84. https://doi.org/10.1002/ehf2.13032
21. Sanjay, G., Jeemon, P., Agarwal, A., Viswanathan, S., Sreedharan, M., Vijayaraghavan, G. (2018). In-Hospital and Three-Year Outcomes of Heart Failure Patients in South India: The Trivandrum Heart Failure Registry. Journal of Cardiac Failure, 24(12), 842–848. https://doi.org/10.1016/j.cardfail.2018.05.007
22. Sasaki, T., Oishi, E., Nagata, T., Sakata, S., Chen, S., Furuta, Y., Honda, T., Yoshida, D., Hata, J., Tsuboi, N., Kitazono, T., Yokoo, T., & Ninomiya, T. (2021). N-Terminal Pro–B-Type Natriuretic Peptide and Incident CKD. Kidney International Reports, 6(4), 976–985. https://doi.org/10.1016/j.ekir.2021.01.006
23. Slikker, W. (2017). Biomarkers and their impact on precision medicine. Experimental Biology and Medicine, 243(3), 211–212. https://doi.org/10.1177/1535370217733426
24. Soares, L. C., Al-Dalahmah, O., Hillis, J., Young, C. C., Asbed, I., Sakaguchi, M., O'Neill, E., & Szele, F. G. (2021, November 5). Novel Galectin-3 Roles in Neurogenesis, Inflammation and Neurological Diseases. Cells, 10(11), 3047. https://doi.org/10.3390/cells10113047
25. WHO International Programme on Chemical Safety Biomarkers in Risk Assessment: Validity and Validation. 2001. Retrieved from http://www.inchem.org/documents/ehc/ehc/ehc222.html.
26. Yu, J., & Wang, W. (2023, October 10). N-terminal pro-B-type natriuretic peptide is associated with clinical outcomes after transcatheter aortic valve replacement. Journal of Cardiothoracic Surgery, 18(1). https://doi.org/10.1186/s13019-023-02391-2
27. Zaborska, B., Sikora-Frąc, M., Smarż, K., Pilichowska-Paszkiet, E., Budaj, A., Sitkiewicz, D., & Sygitowicz, G. (2023). The Role of Galectin-3 in Heart Failure—The Diagnostic, Prognostic and Therapeutic Potential—Where Do We Stand? International Journal of Molecular Sciences, 24(17), 13111. https://doi.org/10.3390/ijms241713111