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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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PROGNOSTIC SIGNIFICANCE OF SST2 IN HEART FAILURE WITH REDUCED EJECTION FRACTION, A BIOMARKER OF CARDIOVASCULAR MORTALITY AND REHOSPITALIZATION

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Abstract.

Introduction: Heart failure (HF) poses a substantial burden on healthcare systems and society, necessitating effective diagnostic tools for enhanced patient management. The soluble suppression of tumorigenesis 2 protein (Soluble Suppression of Tumorigenesis 2 (sST2)) has emerged as a promising biomarker linked to cardiac remodeling and fibrosis. This study investigates Soluble Suppression of Tumorigenesis 2 (sST2)'s potential as a diagnostic and prognostic marker for chronic heart failure (CHF) and explores its clinical utility in predicting outcomes.

Aims and objectives: To evaluate the utility of Soluble Suppression of Tumorigenesis 2 (sST2) as a predictive and diagnostic marker in patients with heart failure with reduced ejection fraction (HFrEF). The study aims to explore the connection between Soluble Suppression of Tumorigenesis 2 (sST2) levels and cardiovascular (CV) mortality in patients suffering from chronic heart failure (CHF), providing insights into how Soluble Suppression of Tumorigenesis 2 (sST2) levels correlate with patient outcomes. Additionally, it seeks to assess the ability of Soluble Suppression of Tumorigenesis 2 (sST2) to predict critical clinical events such as hospital readmissions and adverse 02composite outcomes, offering a deeper understanding of its potential role in disease management. Furthermore, the research compares the prognostic accuracy of Soluble Suppression of Tumorigenesis 2 (sST2) with NT-proBNP, a well-established biomarker, to determine which marker is more reliable and informative for predicting the progression and severity of CHF.

Methods: This prospective cohort study included 111 CHF patients enrolled from May 2020 to January 2022. Participants were classified into two groups based on their Soluble Suppression of Tumorigenesis 2 (sST2) concentrations (<35 ng/mL and >35 ng/mL) and monitored over a year. Comprehensive demographic, clinical, and echocardiographic data were collected, alongside blood samples for Soluble Suppression of Tumorigenesis 2 (sST2) and NT-proBNP analysis. Kaplan-Meier survival analysis, Cox regression modeling, and chi-square tests were employed, with statistical significance defined as $P < 0.05$.

Results: Patients with Soluble Suppression of Tumorigenesis 2 (sST2) levels above 35 ng/mL experienced a markedly higher one-year cardiovascular (CV) mortality rate of 27.3%, compared to just 2.2% in those with lower levels. Similarly, elevated Soluble Suppression of Tumorigenesis 2 (sST2) levels were strongly associated with an increased risk of hospital readmissions, as 27.3% of high-Soluble Suppression of Tumorigenesis 2 (sST2) patients required multiple hospitalizations within a year, compared to only 2.3% in the low-Soluble Suppression of Tumorigenesis 2 (sST2) group. In contrast to NT-proBNP, Soluble Suppression of Tumorigenesis 2 (sST2) levels were not affected by factors like age or kidney function, making it a more reliable and consistent marker of cardiac remodeling. Additionally, patients who did not show a reduction in Soluble Suppression of Tumorigenesis 2 (sST2) levels were significantly more likely to face adverse composite outcomes, with 45.5% affected, compared to 12.4% among those whose levels decreased.

Conclusion: Soluble Suppression of Tumorigenesis 2 (sST2) has emerged as a valuable prognostic biomarker for CHF, offering advantages over NT-proBNP due to its independence from confounding factors such as renal function and atrial rhythm. Elevated Soluble Suppression of Tumorigenesis 2 (sST2) levels are strongly correlated with increased mortality, hospitalizations, and adverse outcomes. While baseline Soluble Suppression of Tumorigenesis 2 (sST2) levels provide meaningful insights into disease severity, short-term changes are less indicative of prognosis. Integrating Soluble Suppression of Tumorigenesis 2 (sST2) into routine clinical practice could improve CHF management by enabling early identification of high-risk patients and guiding personalized treatment strategies.

Key words. Soluble Suppression of Tumorigenesis 2 (sST2) (Soluble Suppression of Tumorigenesis 2 Protein), NT-proBNP (N-terminal pro-B-type Natriuretic Peptide), Heart Failure with Reduced Ejection Fraction (HFrEF), prognostic indicators, and CV mortality risk stratification.

Introduction.

Due to the impact of heart failure on medical systems and society there is a big need to establish an efficient diagnostic tool that can be used as predictive clinical tool. Therefore, it's crucial to find and apply biological markers to assess the actual results of medication, as well as finding a freshly trustworthy biological markers to research its important significance for the improvement of heart failure care systems and the development of medical care procedures.

Soluble suppression of tumorigenesis 2 protein (Soluble Suppression of Tumorigenesis 2 (sST2)) is circulating as the cell-surface receptor and is expressed by cardiomyocytes and vascular endothelial cells, so when it's attached with its ligand, interleukin 33, during cardiovascular damage, This binding of Interleukin-33 to Soluble Suppression of Tumorigenesis 2

(sST2) is anticipated to decrease unwanted cardiac remodeling and plays an important role in preventing myocardial hypertrophy and fibrosis [1,2].

So, whenever the Soluble Suppression of Tumorigenesis 2 (sST2) and ST2L compete with one another for binding with interleukin-33, the cardiovascular preventive benefits of the interleukin_33/ST2L interaction are probably lightened [1,2].

Therefore, there is an increasing interest in Soluble Suppression of Tumorigenesis 2 (sST2) which is a possible tool to help manage treatment and the approach for chronic heart failure (CHF) and predict prognosis [3,4]. The interleukin-33/ST2L axis in CHF is still unresolved yet at this time, nevertheless Soluble Suppression of Tumorigenesis 2 (sST2) levels in plasma have been found to be typically higher in CHF patients compared with total healthy individuals [4,5].

In this manuscript, the role and significance of Soluble Suppression of Tumorigenesis 2 (sST2) as an HF biomarker will be explored with the particular emphasis on the analytical issues covering Soluble Suppression of Tumorigenesis 2 (sST2) measurement as well as the clinical applications of Soluble Suppression of Tumorigenesis 2 (sST2) measurement for the prognosis, diagnosis, and monitoring of chronic HF.

The primary results of this study have been published in "quality in primary care'' which is a peer review journal [6].

Aims and objectives.

Soluble suppression of tumorigenesis 2 protein (Soluble Suppression of Tumorigenesis 2 (sST2)) is a part of interleukin-1 receptor family, and it has been found that it's elevated in different cardiovascular conditions. Nevertheless, its usefulness in predicting the severity of a disease or CV mortality rates is still questionable, therefore we have conducted this study to assess the prognostic and diagnostic value of this biological marker (Soluble Suppression of Tumorigenesis 2 (sST2)) in patients with a heart failure with reduced ejection fraction.

Study population.

A prospective cohort study was conducted on 111 CHF patients who were enrolled between May 2020 and January 2022 of this research. They were divided into two subgroups based on their Soluble Suppression of Tumorigenesis 2 (sST2) concentration. N=65 for T1 (<35 ng/mL) and N=46 or T2 (>35 ng/mL). These patients were monitored for the emergence of the primary endpoints 1 month and 1 year later. By making use of the Cox proportional hazards model the prognostic significance of Soluble Suppression of Tumorigenesis 2 (sST2) for the clinical outcome was determined. The main purpose of this cohort study was to analyze and establish the biomarkers of heart failure in comprehensive detail. Patients with ejection fraction less than 40% (EF<40%), diagnosed with heart failure within the last year during either stationary (inpatient) or ambulatory (outpatient) visits, Heart failure treatments were managed 4 weeks prior to enrollment. Those with heart failure who were referred to Vivamedi Clinic were chosen randomly and placed into groups with suitable sampling techniques. Our samples included patients over the age of eighteen diagnosed with CHF. The current study has received approval from Vivamedi's local ethics committee. After enrollment, each patient was managed with Optimal Medication Therapy (OMT) with prescribed drugs and doses for at least the one month prior to the screening, and adequate treatment of coexisting diseases. The criteria for exclusion were: Age<18 years, pregnancy, a systolic blood pressure of less than 100 mmHg, glomerular filtration rate<30 mL/min/1.73 m2, acute hospitalization owing to ADHF in prior 4 weeks, congenital valve defects, severe valvular stenosis any significant cardiovascular events within the previous four weeks, such as resuscitation, acute myocardial infarction, stroke, peripartum cardiomyopathies, Takotsubo cardiomyopathy, end-stage and active cancer.

Demographic and clinical information, including age, gender, and body mass index, were gathered. Vital signs (BP, HR, RR, SPO2, t), anomalies on the 12-lead electrocardiogram, echocardiography, and the following parameters were measured. EF, LA dimension, IVS, LV end-diastolic dimensions, comorbidities (CKD, CAD, Arterial Hypertension, Diabetes Mellitus, atrial fibrillation, metabolic syndrome), medication (ACEi/ARB, ARNI, MRA, Beta-blockers, SGLT2 inhibitors, Diuretics, Ivabradine, Digoxin), device therapy, and KCCQ-12 questions were assessed. The study included 111 patients who provided blood samples for ST2 and NT-probing. The key outcomes included cardiovascular mortality, rehospitalizations for Acute Decompensated Heart Failure (ADHF), and the composite rate of death from cardiovascular illness and ADHF diagnoses. Blood samples were taken within an hour of admission. Serum Soluble Suppression of Tumorigenesis 2 (sST2) levels were consistently measured using an enzyme-linked immunosorbent assay (ELISA).

Collection of clinical and echocardiographic parameters:

Clinical and echocardiographic data were collected by reviewing hospital records. Patients received follow-ups through telephone calls or in-person visits. Follow-up lasted for 1 year from the time of enrollment.

Statistical analyses.

Continuous variables were reported as mean ± SD or median with IQR.

The chi-square test was used to compare categorical variables (representation by percentage). Correlations were examined using Pearson or Spearman rank coefficients. Survival curves were estimated using the Kaplan-Meier technique, and group comparisons were made using the log-rank test. Survival curves were estimated and shown, with the log-rank test used for group comparisons. The Hazard Ratio (HR) and 95% Confidence Interval (CI) were used to show how the variables related to the primary endpoint.

Analyzing Cox regression, Soluble Suppression of Tumorigenesis 2 (sST2) and NT-probing data were log-transformed because of their skewed distributions. The data was analyzed using a significance level of $P < 0.05$.

Results.

Sst2 variations based on cardiac rhythm:

In the final analysis of sst2 levels in a fib and sinus rhythm patients, while comparing to NT- pro BNP, sst2 is independent of rhythm and sst2 can help in conditions where there are

limitations to NT-pro BNP, given the fact that NT-pro BNP is higher in AF patients.

NT- pro BNP is mainly secreted from atrium and remodelling in atrium in atrial fibrillation is much higher than in sinus rhythm. The most important stimulus for release of NT-pro BNP is increase in end diastolic wall stress due to volume overload and it is less affected by cardiac homeostasis, and it can be used for understanding if there is a response to medications. Atrial dilation is main feature of left atrial remodelling which is due to cardiac hemodynamic overload [11].

Soluble Suppression of Tumorigenesis 2 (sST2) act as a decoy receptor in ST2L/IL-33 pathway promoting cardiac hyperplasia and cardiac remodelling. Therefore, Soluble Suppression of Tumorigenesis 2 (sST2) helps in risk stratification and disease activity prediction of AF (Figure 1) [10].

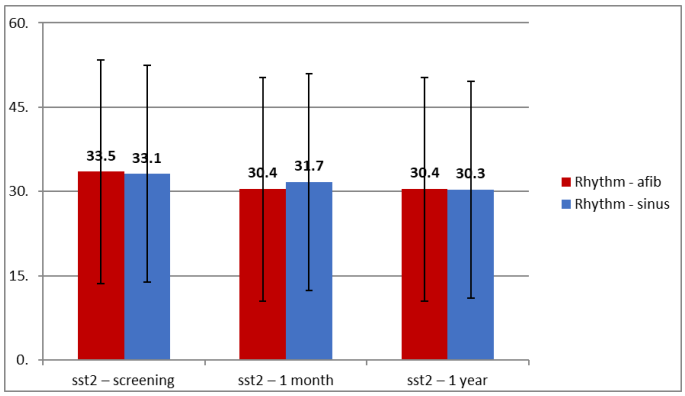

Figure 1. *Analysis of sst2 levels in a fib and sinus rhythm patients.*

Soluble Suppression of Tumorigenesis 2 (sST2) act as a decoy receptor in ST2L/IL-33 pathway promoting cardiac hyperplasia and cardiac remodelling. Therefore, Soluble Suppression of Tumorigenesis 2 (sST2) helps in risk stratification and disease activity prediction of AF [10].

Upon analysing the data of mean sst2 levels in patients with a fib and sinus rhythm over period of screening, 1 month and 1 year. No significant difference was observed in SST2 levels between sinus rhythm and AFB rhythm patients during both the screening and follow-up phases. This implies that there is no difference between sst2 values of a fib patients and sinus rhythm patients till 1 year of follow up. Thus, concluding that the combination of sst2 and NT-pro BNP can help us understand the level of cardiac modelling thus helping us predict the prognosis. Unlike NT- pro BNP, SST2 can be considered rhythm-independent ($P < 0.01$).

Relationship between Soluble Suppression of Tumorigenesis 2 (sST2) levels and primary outcomes in the main groups.

This study aimed to evaluate the CV mortality rate by analysing two distinct groups. The study revealed a significant change in the mortality rate within 1 year between the groups, in group 1(<35 ng/mL), the mortality rate is 2.2% and survival rate is 97.8% and in group 2(>35 ng/mL), the CV mortality rate was increased significantly to 27.3% (Figures 2 and 3).

The result of the study indicates that the concentration of SST2 can be used as a marker for predicting the mortality rate

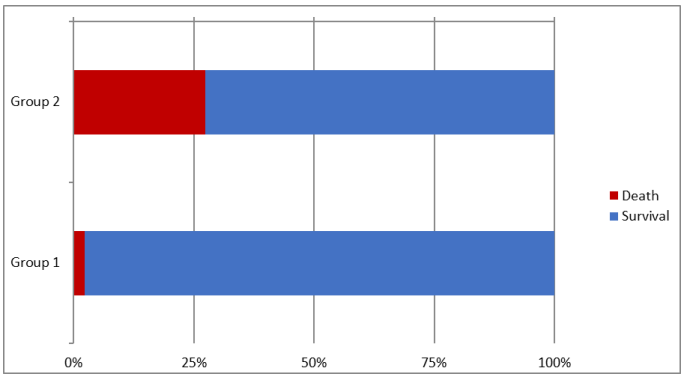

Figure 2. *1 year CV mortality in main groups.*

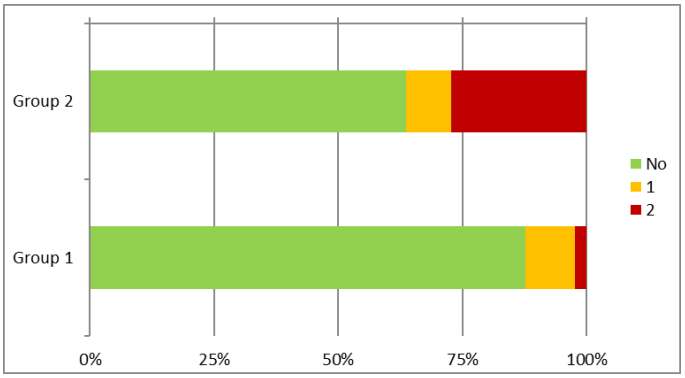

Figure 3. *1-year rehospitalizations in main groups.*

and the no. of times patients need to get re-hospitalized. The patients with more SST2 concentration were found to have a more mortality rate and a rehospitalization necessity compared to patients with less SST2 concentration. Therefore, it can be concluded that SST2 concentration in heart failure patients is a prognostic indicator ($P<0.001$).

Biomarkers variations in survivors and deceased patients.

We analyzed subgroup's and assessed the Delta NT- pro BNP at 1-month follow-up in two subgroups of Patients—Group 1 (Survived Patients) and Group 2 (Deceased Patients)—we examined NT- pro BNP reductions in these groups. Typically, elevated NT- pro BNP levels are associated with worse outcomes and higher mortality. However, NT- pro BNP levels might decrease significantly in deceased patients compared to survivors: These are several factors that can influence NT- pro BNP concentration. Typically, NT- pro BNP levels are lower among acute decompensated heart failure (ADHF) patients with obesity or preserved Left Ventricular Ejection Fraction (LVEF) and it affects the outcomes [7]. Certain treatments or medications like diuretics and other heart failure medications can significantly lower NT- pro BNP levels even If a patient dies shortly after the treatment [8]. If NT- pro BNP levels are measured at the initial treatment, the recorded values might be lower even in patients with a poor outcome/ End-Stage heart failure: Brain natriuretic peptide NT- pro BNP is a hormone secreted by cardiomyocytes in the heart ventricles in response to stretching caused by increased ventricular blood volume. In heart failure, the heart chambers are stressed causing them to produce and release extra NT- pro BNP, which pours into the bloodstream. Advanced heart failure may lead to a significant

myocardial damage and dysfunction, which can impair the heart's ability to produce and secrete NT- pro BNP. As the heart fails, its ability to respond to stress by producing NT- pro BNP may be diminished and NT- pro BNP levels might not rise as expected. This could lead to lower NT- pro BNP levels at the time of death [9].

Study revealed a significant difference between these two groups. In Group 1 (N=103), the mean NT-PROBN reduction was -464.38. In contrast, Group 2 (N=8) exhibited a mean NT- proBNP reduction of -2115.56. This indicates that the NT- proBNP reduction was substantially greater in group 2 (Deceased Patients), and this result is statistically Significant. While these factors can be considered for reducing NT- proBNP levels, we propose that in the end-stage heart failure patients, a reduction in NT- proBNP levels may not serve as a predictive value for Heart failure (HF) prognosis (Figure 4).

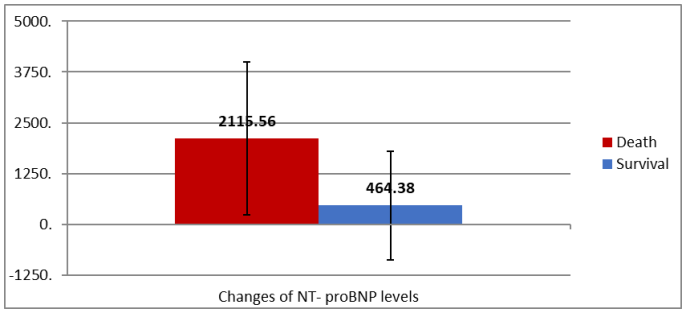

Figure 4. *Delta NT- pro BNP at 1-month follow-up in within Survived and Deceased Patients.*

Means of Changes of NT-probing levels.

In the analysis of data focusing on delta s ST2 levels at 1 month follow up in two groups of patients group 1 (n = 103) survivors and group 2 (n=8) non survivors, results do not reveal a significant difference for the change in s ST2. In group 1, the mean reduction was – 1.99 and group 2 it was -4.84. That test = 0.92 and p = 0.362 which implies that the rate of decrease of sst2 in survivors does not differ significantly from rate of decrease of sst2 in deceased.

In conclusion of data regarding delta sst2 levels in survivors and non survivors, it can be seen that during 1 month follow up there is no significant difference that in turn implies that there is no requirement of serial measurements of sst2 at 1 month follow up and one initial measurement of sst2 can be of prognostic value. Since sst2 is an indicator of myocardial fibrosis and remodelling, no notable change in sst2 indicate might take more time to reduce sst2, thus decreasing effect of deltas sst2 as a prognostic indicator (Figure 5).

Biomarkers Reduction at one month follow up in main groups.

The assessment of mean biomarkers at the one-month follow-up reveals notable differences between the main groups. As depicted in Graph N6, Group 1(sst2<35ng/mL) had an average screening NT-pro BNP level of 844.17 ng/mL, whereas Group 2(sst2> 35ng/mL) exhibited a significantly higher level of 2396.03 ng/mL. Similarly, Graph N7 highlights that the mean screening Soluble Suppression of Tumorigenesis 2 (sST2) level was 20.46 ng/mL in Group 1, compared to 51.75 ng/mL in Group 2 (Figures 6 and 7).

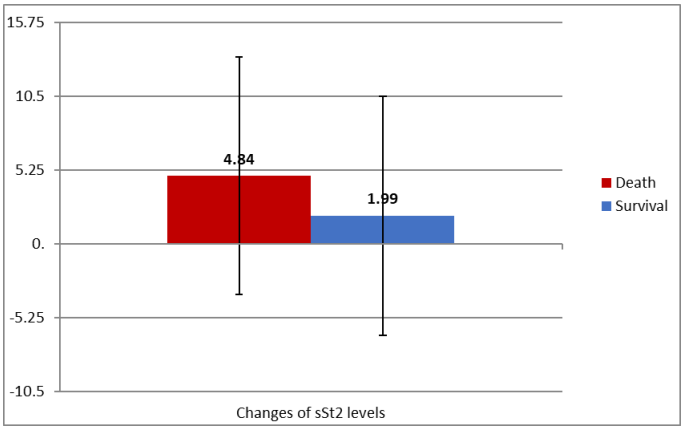

Figure 5. *Means of Changes of sSt2 levels.*

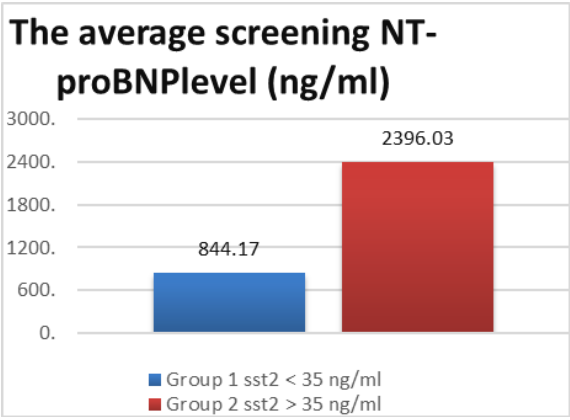

Figure 6. *An average screening NT-pro BNP levels in main groups.*

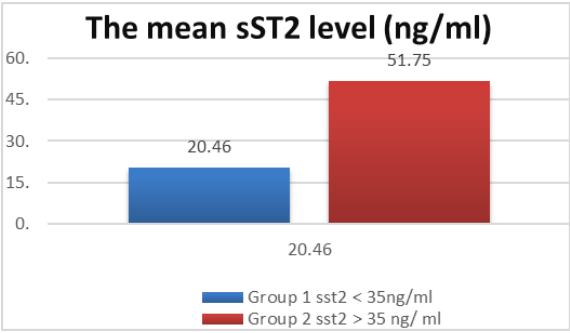

Figure 7. *An average screening SSt2 in main groups.*

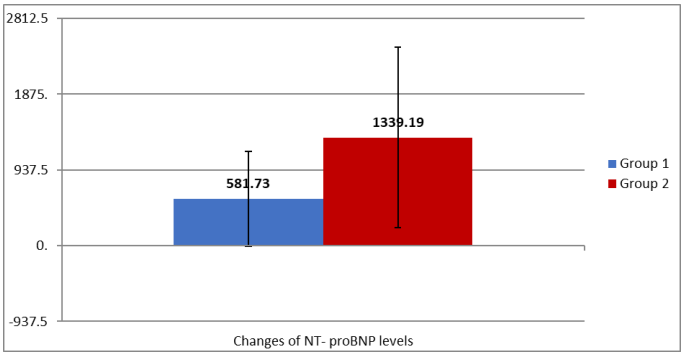

Figure 8. *Mean NT-pro BNP levels - 1 month follow-up in main groups.*

The mean NT-pro BNP levels at the 1-month follow-up are significantly higher in Group 2 (SST2 < 35 ng/mL, n=46n = 46, mean = 1339.19) compared to Group 1 (SST2 > 35 ng/mL, n=65n = 65, mean = 581.73; t=4.61, p<0.001t = 4.61, p < 0.001) (Figure 8).

The second chart depicts the mean Soluble Suppression of Tumorigenesis 2 (sST2) levels after a one-month follow-up. It clearly shows that in Group 1 (n=65, Soluble Suppression of Tumorigenesis 2 (sST2) concentration > 35 ng/mL), the mean is 20.35 ng/mL, whereas in Group 2 (n=46, Soluble Suppression of Tumorigenesis 2 (sST2) concentration < 35 ng/mL), there is reduction, but it is still high -46.88 ng/mL. Therefore, the mean Soluble Suppression of Tumorigenesis 2 (sST2) levels after the one-month follow-up are higher in Group 2 (Figure 9).

Limitations of Soluble Suppression of Tumorigenesis 2 (sST2) as a short-term prognostic marker.

In a separate analysis focusing on the Delta sSt2 levels at 1-month follow-up in two groups of patients: Group 1 (<35 ng/mL) and Group 2 (>35 ng/mL). The objective was to evaluate the reductions in sSt2 levels within these groups. Results revealed a notable sSt2 levels reduction in group 2. In Group 1 (N=65), the mean sSt2 reduction was -0.30. In contrast, Group 2 (N=46) exhibited a mean sSt2 reduction of -4.87 (Figure 10).

Soluble Suppression of Tumorigenesis 2 (sST2) is a new biomarker associated with heart failure and other cardiovascular conditions, and it is typically high in the patients with those diseases. Patients with Soluble Suppression of Tumorigenesis 2 (sST2) concentrations >35 ng/mL might experience more significant reductions in Soluble Suppression of Tumorigenesis 2 (sST2) levels compared to those with Soluble Suppression of Tumorigenesis 2 (sST2) concentrations <35 ng/mL and that is because of the treatment response to an intensive intervention. Patients with higher Soluble Suppression of Tumorigenesis 2 (sST2) levels (>35 ng/mL) typically have more severe heart failure and they undergo more intensive treatment strategies. Therefore, the reduction in Soluble Suppression of Tumorigenesis 2 (sST2) levels in these patients might be more significant than patients with lower Soluble Suppression of Tumorigenesis 2 (sST2) levels (<35 ng/mL), whose levels are already closer to normal or less impacted by the intervention.

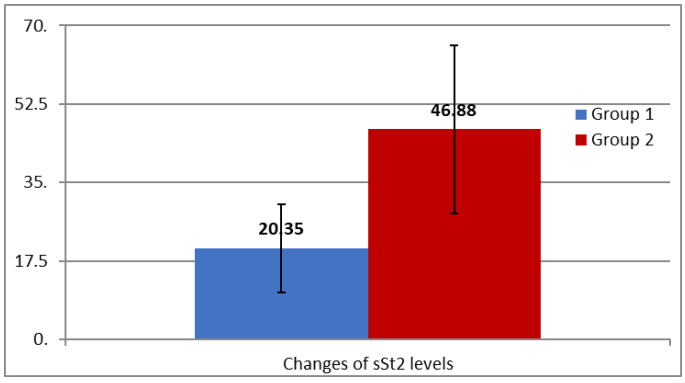

Figure 9. *Mean sSt2 levels - 1 month follow-up in main groups (t-test=9.68, p<0.001).*

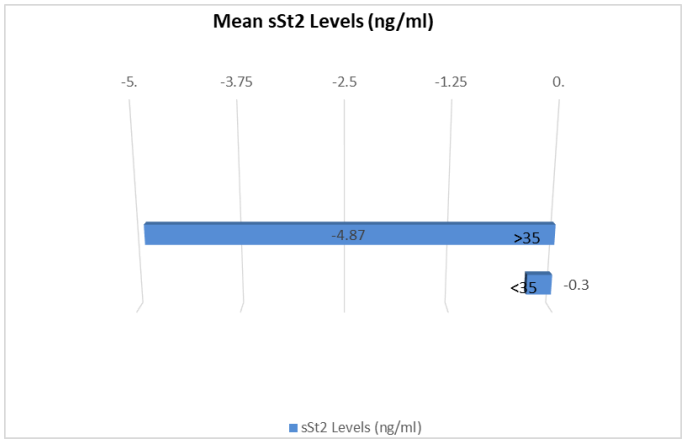

Figure 10. *Delta sSt2 levels at 1-month follow-up in main groups.*

In our study, patients had been managing heart failure for at least one month prior to screening, which demonstrated a strong correlation between treatment intervention and reduction in sSt2 levels. Our observations indicated that, patients with blood pressure <130 mmHg experienced less reduction in sSt2 levels compared to patients with blood pressure >130 mmHg who were receiving intensified medication (P<0.001).

Primary outcome analysis in the subgroups of the deceased or surviving patients.

We also assessed cardiovascular (CV) mortality, rehospitalization rates, and their composite outcomes between the two subgroups, Group 1 with whom SST2 and NT- proBNP decreased (89 patients) and group 2 with whom SST2 and NT-proBNP did not decrease (22 patients). In the table 1 we analyzed the rehospitalization within 1 year for these 2 groups. In group 1(total 89 patients), 78 patients needed no rehospitalization, 9 patients needed a 1-time rehospitalization and 2 patients needed a 2 times rehospitalization.

In group 2 (total -22 patients), 14 patients needed no rehospitalization, 2 patients needed a 1-time rehospitalization and 6 patients needed a 2-time rehospitalization.

Patients with no reduction in SST2 had a significantly higher frequency of hospitalization. (chi2=16.57, p<0.001) (Tables 2 and 3).

Correlation between NYHA classification and Soluble Suppression of Tumorigenesis 2 (sST2) levels.

We also discovered a correlation between the reduction in Soluble Suppression of Tumorigenesis 2 (sST2) levels and a decrease in the NYHA (New York Heart Association) functional classification score. This suggests that as Soluble Suppression of Tumorigenesis 2 (sST2) levels decrease, patients experience an improvement in their heart failure symptoms and functional status, as indicated by a lower NYHA classification (P< 0.01) (Figure 11).

Higher Soluble Suppression of Tumorigenesis 2 (sST2) levels are associated with increased hospitalizations rates.

The scatter plot reveals a positive correlation between Soluble Suppression of Tumorigenesis 2 (sST2) levels after one year and rehospitalization cases, suggesting that patients with elevated Soluble Suppression of Tumorigenesis 2 (sST2) levels are more likely to experience rehospitalization within the follow-up period. This indicates Soluble Suppression of Tumorigenesis 2 (sST2) levels may serve as a potential predictor for rehospitalization risk (Figure 12).

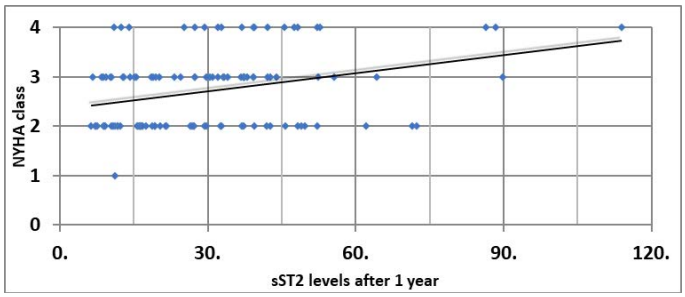

Figure 11. *Relationship between NYHA and SST2.*

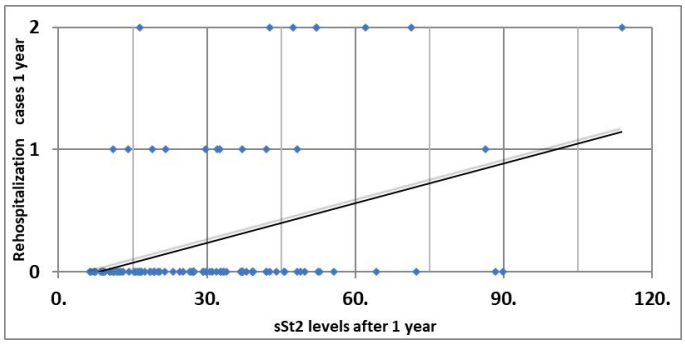

Figure 12. *Correlation between Rehospitalization cases and Ssst2 levels at 1 year follow up.*

Table 1. *Patients with no reduction in SST2 had a significantly higher frequency of hospitalization. (chi2=16.57, p<0.001).*

Rehospitalization 1 year	Group 1	Group 2	Total
0	78 (87.6%)	14 (63.6%)	92 (82.9%)
1	9 (10.1%)	2 (9.1%)	11 (9.9%)
2	2 (2.3%)	6 (27.3%)	8 (7.2%)
Total	89 (100.0%)	22 (100.0%)	111 (100.0%)

Table 2. *Patients with no reduction in SST2 had a significantly higher rate of CV mortality . (chi2=16.57, p<0.001) (chi2=12.18, p=0.001).*

MORS 1 year	Group 1	Group 2	Total
Yes	0 (0.0%)	8 (36%)	8 (7.2%)
No	89(100.0%)	14 (63,6%)	103 (92.8%)
Total	89 (100.0%)	22 (100.0%)	111 (100.0%)

Table 3. *Patients with no reduction in SST2 had a significantly higher rate of composite outcomes (chi2=12.60, p=0.002).*

Composite 1 year	Group 1	Group 2	Total
Yes	11 (12.4%)	10 (45.5%)	21 (18.9%)
No	78 (87.6%)	12 (54.5%)	90 (81.1%)
Total	89 (100.0%)	22 (100.0%)	111 (100.0%)

Discussion.

Biomarkers are essential tools in the management of chronic heart failure (CHF), providing valuable insights into the underlying pathophysiological processes, disease severity, and patient prognosis. Clinicians use biomarkers in making decisions about diagnosis, risk stratification, therapeutic interventions, and monitoring disease progression. Among the array of biomarkers used in CHF, sST2 has garnered significant attention due to its ability to reflect cardiac remodelling and fibrosis, processes that are central to the prognosis of heart failure.

Elevated levels of sST2 signify heightened cardiac stress and fibrosis, distinguishing it as a direct marker of myocardial injury and structural remodelling. Unlike traditional biomarkers such as NT-proBNP, which primarily reflect hemodynamic stress and neurohormonal activation, sST2 offers complementary information by capturing the progressive fibrotic changes that underlie chronic heart failure.

One of the most compelling advantages of sST2 is its relative stability across a range of clinical conditions. Factors like age, obesity, atrial fibrillation, and renal dysfunction, which can significantly influence NT-proBNP levels and introduce variability, do not affect sST2 to the same extent. This makes sST2 a more reliable marker in patients with complex comorbidities. For instance, in patients with chronic kidney disease, where NT-proBNP levels may be elevated due to reduced clearance rather than cardiac dysfunction, sST2 provides a clearer picture of the cardiac-specific pathological processes.

Moreover, sST2 has demonstrated strong prognostic capabilities. Elevated baseline sST2 levels have been consistently associated with increased risks of cardiovascular mortality, heart failure hospitalization, and composite outcomes. These findings emphasize its utility not only in identifying high-risk patients but also in tailoring management strategies. Monitoring changes in sST2 levels over time can provide additional insights, as persistently high levels may indicate ongoing myocardial stress and a higher likelihood of poor outcomes. This dynamic assessment sets sST2 apart from static measurements of traditional biomarkers.

Integrating sST2 into clinical practice could revolutionize the management of CHF by enabling earlier identification of high-risk patients, guiding therapeutic adjustments, and potentially improving long-term outcomes. Its complementary role alongside NT-proBNP and other biomarkers enhances the ability to provide a multidimensional evaluation of heart failure, addressing both hemodynamic and structural aspects of the disease. As evidence supporting its clinical utility continues to grow, sST2 is poised to become a cornerstone biomarker in the personalized management of CHF.

The findings of this study reinforce the growing recognition of sST2 as a valuable biomarker in the management of heart failure with reduced ejection fraction (HFrEF).

However, it is worth noting that while baseline sST2 levels were strongly predictive of outcomes, short-term changes in sST2 were less indicative of prognosis. This finding aligns with the understanding that sST2 reflects chronic processes like fibrosis rather than acute hemodynamic changes. Future research could explore optimal thresholds and intervals for measuring sST2 to maximize its clinical utility. Furthermore, the combination of Soluble Suppression of Tumorigenesis 2 (sST2) and NT-pro BNP was shown to enhance predictive accuracy, as NT-pro BNP is influenced by factors such as atrial fibrillation and renal function, while Soluble Suppression of Tumorigenesis 2(sST2) remains largely independent of these variables. When compared to NT-proBNP, sST2 showed superior prognostic accuracy in certain contexts. While NT-proBNP remains a cornerstone in heart failure management, our findings suggest that integrating sST2 into routine clinical practice could complement existing biomarkers, providing a more comprehensive risk assessment framework.

In conclusion, sST2 is a robust biomarker that enhances the ability to predict adverse outcomes in CHF, particularly in HFrEF patients. Its independence from confounding factors and strong correlation with CV mortality and Heart failure hospitalization risks make it a valuable addition to the biomarker arsenal. Incorporating sST2 into clinical workflows may enable more personalized and effective management strategies for heart failure patients, ultimately improving outcomes and reducing the healthcare burden.

Limitations and Future Directions.

Limitations of the study include the relatively small sample size and the potential impact of inter-individual variability in treatment regimens. Future studies should aim to validate these findings in larger, more diverse cohorts.

Conclusion.

This study highlights the importance of Soluble Suppression of Tumorigenesis 2 (sST2) as a powerful biomarker for evaluating heart failure patients, especially those with reduced ejection fraction. Higher Soluble Suppression of Tumorigenesis 2 (sST2) levels are closely linked to an increased risk of death and rehospitalization, making it an essential tool for identifying patients who need closer monitoring and more aggressive treatment. While changes in Soluble Suppression of Tumorigenesis 2 (sST2) levels over short periods may not carry as much significance, baseline levels provide valuable insight into how severe a patient's condition is and their long-term outlook. By using Soluble Suppression of Tumorigenesis 2 (sST2) to identify patients at higher risk, healthcare providers can make more informed decisions about treatment and prioritize care for those who need it most. Incorporating Soluble Suppression of Tumorigenesis 2 (sST2) monitoring into everyday clinical practice could greatly improve how heart failure is managed. It can help doctors spot early warning signs of worsening health, adjust treatments as needed, and track how well patients respond to therapy. When combined with other markers like NT-pro BNP, Soluble Suppression of Tumorigenesis 2 (sST2) adds another layer of precision to care, offering a more tailored approach to managing heart failure. Ultimately, this biomarker has the potential to make a real difference in the lives of patients by improving outcomes and providing more personalized care.

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