BMC Research Notes

RESEARCH NOTE Open Access

Prevalence of high N-terminal prohormone of brain natriuretic peptide levels and associated factors among community-dwelling older adults aged over 75 years (The SONIC study): a cross-sectional study

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Abstract

Objectives Considering the heart failure (HF) pandemic, numerous older adults in the community may exhibit potential cardiac overload or asymptomatic HF without apparent HF diagnosis. This study aimed to examine the distribution of serum N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels in community-dwelling old age adults aged ≥ 75 years, and to investigate the associated factors for each NT-proBNP classification.

Results A cross-sectional analysis revealed that 52.0% of 611 participants had NT-proBNP ≥ 125 pg/mL. Multinomial logistic regression analysis showed that female sex, older age (80s and 90s), and uncontrolled high blood pressure were significantly associated with 125 ≤ NT-proBNP < 300 pg/mL, while older age (80s and 90s), coronary artery disease, atrial fibrillation, and renal dysfunction were significantly associated with NT-proBNP ≥ 300 pg/mL. Independent association between higher salt intake and NT-proBNP ≥ 300 pg/mL was also observed. Appropriate management of common HF risk factors, such as uncontrolled high blood pressure and high salt intake, is crucial to prevent the progression of overt HF.

Keywords NT-proBNP, Older adults, Aging population, Community, Heart failure, Cardiac overload, Asymptomatic heart failure, Salt intake, Screening, Risk factors

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Introduction

With global population aging [1], the proportion of old age adults aged ≥ 75 years is expected to reach approximately 18% in Japan by 2025 [2]. Consequently, heart failure (HF) pandemic has emerged, characterized by a rapid increase in the number of HF patients [3, 4]. Given that this occurs with aging [4], a growing number of old age adults may experience potential cardiac overload or asymptomatic HF [5]. The serum N-terminal prohormone of brain natriuretic peptide (NT-proBNP) is mainly used as a screening biomarker for HF [6, 7], as it is elevated with ventricular overload [8–10]. Given its diagnostic and prognostic value of HF [11–13], its measurement is recommended in clinical guidelines [14, 15]. Additionally, since HF is known for its high mortality and rehospitalization rates [16, 17], its diagnostic thresholds have been revised to enable earlier detection [14, 18]. Moreover, focusing on individuals with below the threshold value may also contribute to primary prevention [19]. However, identifying individuals at risk of HF without any symptoms remains challenging [5, 11]. Although understanding the distribution of NT-proBNP levels and their associated factors among older adults may contribute to the early HF detection, few studies have specifically examined this issue in community-dwelling old age adults (≥ 75 years).

This study aimed to examine the distribution of serum NT-proBNP levels in this population, and to investigate the associated factors for each NT-proBNP classification divided by HF diagnostic thresholds [14, 18], providing data to support more appropriate screening and preventive strategies of HF.

Main text

Methods

Study design and participants

A cross-sectional analysis was conducted using data from the longitudinal cohort study (Septuagenarian, Octogenarian, Nonagenarian, Investigating the Centenarian: SONIC study), which investigates the factors associated with healthy longevity among community-dwelling older adults aged ≥ 70 years. This study includes participants from the western and eastern parts of Japan [20]. Old age adults aged 75 years and above who participated in the SONIC study between July 2016 and December 2018 were included. The eligibility criteria were as follows: subjects who participated in the western part of Japan survey, underwent laboratory tests, and were absence of HF (Supplementary file 1).

Data collection

Demographic and clinical information, including medical history, smoking behavior (never, past, and current), and alcohol consumption (never, moderate, and excessive) were collected using questionnaires through face-to-face interviews. Medication use was obtained from prescription records. Blood pressure (BP) was measured twice in each arm using mercury sphygmomanometers by clinicians or nurses, and mean values were used. Mean artery pressure (MAP) was calculated as *diastolic BP(DBP) +(systolic BP (SBP)-DBP) / 3*, and pulse pressure as *SBP-DBP*. Laboratory tests were performed by clinicians or nurses using vacuum tubes, followed by centrifugation at 3000 × *g* for 10 min at 4 degrees. Serum NT-proBNP levels were estimated using an electrochemical luminescence immunoassay (ECLIA) (Cobas 8000 Analyzer; Roche Diagnostics., Ltd.). (Nihon Rinsho, Inc.) The amount of salt intake was obtained from a Brief-type self-administered Diet History Questionnaire (BDHQ) [21, 22]. Energy-adjusted values of salt intake were calculated by both density (g/1000 kcal) and residual methods (g/day) [23]. Mild cognitive function (MCI) was evaluated using a Montreal Cognitive Assessment-Japanese (MoCA-J) [24].

Definition

- Hypertension: Antihypertensive use, SBP ≥ 140 mmHg or DBP ≥ 90 mmHg [25].
- Uncontrolled high BP: SBP ≥ 150 mmHg or DBP ≥ 90mmHg, regardless of taking antihypertensives [25].
- Diabetes: Hypoglycemic agent use, casual blood glucose ≥ 200 mg/dL or HbA1c ≥ 6.5% [26].
- Dyslipidemia: Antihyperlipidemic drug use, low-density lipoprotein cholesterol (LDL-C) ≥ 140 mg/dL, high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL or triglycerides (TG) ≥ 150 mg/dL [27].
- Anemia: Hemoglobin < 13 g/dL (males), < 12 g/dL (females) [28].
- Renal dysfunction: Estimated glomerular filtration rate based on cystatin C (eGFRcys) calculated as: $eGFRcys\ (mL/min/1.73m^2) = [104 \times cystatin\ C(mg/L)^{-1.019} \times 0.996^{age} (\times 0.929, if\ female)] - 8$ [29]. Defined as eGFRcys < 60 mL/min/1.73m^2, further categorized as 30 ≤ eGFRcys < 60 mL/min/1.73m^2 and eGFRcys < 30 mL/min/1.73m^2.
- High levels of inflammation: High sensitive C-reactive protein (hs-CRP) > 1.0 mg/dL [30].
- MCI: MOCA-J score ≤ 25 [24].
- Smokers: Past and/or current smokers.
- Alcohol consumption: Moderate or excessive current alcohol consumers.

Statistical analysis

Participants were divided into three groups based on HF diagnostic thresholds as follows: NT-proBNP < 125 pg/mL, 125 ≤ NT-proBNP < 300 pg/mL

and NT-proBNP ≥ 300 pg/mL [14, 18]. Categorical variables were analyzed using the Pearson's chi-square test and Fisher-Freeman-Halton test, while continuous variables were compared using the Kruskal-Wallis test. The Dann-Bonferroni test was performed to compare the serum NT-proBNP levels by age group. Multinomial logistic regression analysis was used to investigate the associations between traditional risk factors for HF and NT-proBNP groups, as well as between salt intake and NT-proBNP groups. Independent variables were determined based on both traditional risk factors for HF and factors which commonly influence serum NT-proBNP levels, showed by previous studies [11, 15, 31–38]: sex, age groups, smokers, alcohol consumption, uncontrolled high BP, coronary artery disease (CAD), atrial fibrillation (AF), renal dysfunction, diabetes, obesity, anemia, and high levels of inflammation. Uncontrolled high BP was included instead of hypertension due to its clinical relevance [39–41]. AF, not arrythmia, used as an independent variable since it influences serum NT-proBNP levels [33]. Three models were used to analyze the relationship between salt intake and NT-proBNP groups:

- Model 1: Univariate analysis.
- Model 2: Adjusted for sex and age groups.
- Model 3: Further adjusted for traditional risk factors for HF.

Statistical significance was set at a two-tailed $p < 0.05$. SPSS 28 (IBM Japan, Tokyo, Japan) was used to perform all statistical analysis.

Results

The total number of participants was 611 (females: 47.1%, $p = 0.007$; 70s: $n = 317$; 80s: $n = 205$; 90s: $n = 89$) (Table 1). 52.0% of those exhibited NT-proBNP ≥ 125 pg/mL. Individuals with NT-proBNP ≥ 300 pg/mL tended to be older ($p < 0.001$), have heart diseases ($p < 0.001$) including AF ($p < 0.001$), renal dysfunction ($p < 0.001$), and anemia ($p = 0.001$). Serum NT-proBNP levels increased significantly with age (Supplementary file 2).

The association between traditional risk factors and NT-proBNP groups using multinomial logistic regression analysis is shown in Table 2. Compared to NT-proBNP < 125 pg/mL group (reference group), female sex (odds ratio [OR] 1.63; 95% confidence interval [CI] 1.04–2.56; $p = 0.034$), older age (80s and 90s, compared to 70s) (OR 2.59; 95% CI 1.64–4.09; $p < 0.001$, OR 3.33; 95% CI 1.68–6.61; $p < 0.001$, respectively), and uncontrolled high BP (OR 1.88; 95% CI 1.25–2.82; $p = 0.002$) were significantly associated with 125 ≤ NT-proBNP < 300 pg/mL group, while older age (80s and 90s, compared to 70s) (OR 1.95; 95% CI 1.09–3.47; $p = 0.024$, OR 6.60; 95% CI 3.21–13.59; $p < 0.001$, respectively), CAD (OR 2.89; 95% CI 1.28–6.55; $p = 0.011$), AF (OR 19.01; 95% CI 5.04–71.75; $p < 0.001$) and renal dysfunction (30 ≤ eGFRcys < 60 mL/min/1.73 m^2: OR 2.45; 95% CI 1.42–4.23; $p = 0.001$, eGFRcys < 30 mL/min/1.73 m^2: OR 9.35; 95% CI 2.98–29.33; $p < 0.001$) were significantly associated with NT-proBNP ≥ 300 pg/mL group.

Table 3 shows the results of multinomial logistic regression analysis examining the association between salt intake (g/1000 kcal and g/day) and NT-proBNP groups. Salt intake (g/1000 kcal) was independently associated with NT-proBNP ≥ 300 pg/mL, compared to NT-proBNP < 125 pg/mL (OR 1.20; 95% CI 1.02–1.41; $p = 0.025$) (Model 1), even after adjusting for sex, age groups and traditional risk factors for HF (OR 1.30; 95% CI 1.07–1.58; $p = 0.009$) (Model 3). A similar relationship was observed using the residual method for salt intake (g/day) (OR 1.14; 95% CI 1.04–1.25; $p = 0.008$) (Model 3). Conversely, no association was found between salt intake and 125 ≤ NT-proBNP < 300 pg/mL.

Discussion

By categorizing participants using HF diagnostic thresholds [14], about half of community-dwelling old age adults (≥ 75 years) had serum NT-proBNP levels ≥ 125 pg/mL, indicating potential cardiac overload. In multinomial logistic regression analysis, the associated factors for each serum NT-proBNP group, and significant association of salt intake and NT-proBNP ≥ 300 pg/mL were identified.

The prevalence of individuals with 125 ≤ NT-proBNP < 300 pg/mL and NT-proBNP ≥ 300 pg/mL group was slightly higher than in previous studies, likely due to age differences. While previous studies included participants aged ≥ 40 or ≥ 60 years [42, 43], our study focused on those ≥ 75 years. Given the limited studies describing the serum NT-proBNP distribution of community-dwelling old age adults with HF diagnostic thresholds (serum NT-proBNP: 125 and 300 pg/mL) [14], our findings are relevant to understand the actual conditions in aging societies.

The associated factors with each NT-proBNP group were identified. In 125 ≤ NT-proBNP < 300 pg/mL group, demographic and lifestyle-related factors were predominant, whereas in NT-proBNP ≥ 300 pg/mL group, cardiorenal diseases were more significant. The association with older age (80s and 90s) in both groups was likely due to increased preload and afterload [15, 44]. Regarding 125 ≤ NT-proBNP < 300 pg/mL group, females are often show higher serum NT-proBNP levels than males, possibly due to longer life expectancy [45, 46] and its association with obesity [47, 48] and diabetes [49, 50]. Uncontrolled high BP increases afterload, leading to diastolic failure [51, 52]. Thus, biologically and afterload-related factors might be important in this group.

Table 1 The basic characteristics of study participants classified by serum NT-proBNP levels (< 125, 125–299, and ≥ 300 pg/mL)

	All	NT-proBNP < 125pg/mL	125 ≤ NT-proBNP < 300pg/mL	NT-proBNP ≥ 300pg/mL	*p* value
	(*n* = 611)	(*n* = 293)	(*n* = 187)	(*n* = 131)	
Female	288 (47.1)	137 (46.8)	102 (54.5)	49 (37.4)	0.007
Age (years)	78 (76–86)	77 (76–85)	85 (76–87)	86 (77–89)	< 0.001
Smokers, n (%)	34 (5.6)	15 (5.2)	10 (5.4)	9 (7.0)	0.747
Alcohol consumption, n (%)	253 (42.3)	121 (41.9)	71 (39.2)	61 (47.7)	0.328
History of fall during one year, n (%)	137 (22.4)	58 (19.8)	39 (20.9)	40 (30.5)	0.041
BMI (kg/m^2)	22.4 (20.4–24.3)	22.5 (20.7–24.4)	21.9 (20.1–23.9)	22.7 (20.3–24.7)	0.025
Clinical characteristics					
SBP (mmHg)	135 (126–147)	134 (125–143)	139 (128–151)	134 (125–147)	0.004
DBP (mmHg)	74 (68–81)	74 (68–82)	75 (69–82)	72 (66–79)	0.028
Pulse pressure (mmHg)	61 (52–70)	60 (51–69)	63 (53–73)	60 (52–71)	0.014
Mean arterial pressure (mmHg)	95 (88–101)	94 (87–101)	97 (89–103)	94 (87–100)	0.008
Uncontrolled high BP, n (%)	246 (40.5)	101 (34.6)	93 (50.0)	52 (40.0)	0.004
High levels of inflammation, n (%)	161 (26.4)	70 (23.9)	46 (24.6)	45 (34.4)	0.063
Comorbidities, n (%)					
Heart diseases	151 (24.8)	51 (17.5)	44 (23.5)	56 (42.7)	< 0.001
Coronary artery diseases	46 (7.5)	18 (6.1)	13 (7.0)	15 (11.5)	0.150
Arrythmia (without AF)	44 (7.2)	13 (4.4)	17 (9.1)	14 (10.7)	0.035
AF	24 (3.9)	3 (1.0)	4 (2.1)	17 (13.0)	< 0.001
Cardiomyopathy	2 (0.3)	0 (0.0)	1 (0.5)	1 (0.8)	0.270
Valvular heart disease	8 (1.3)	2 (0.7)	4 (2.1)	2 (1.5)	0.337
Others	21 (3.4)	7 (2.4)	7 (3.7)	7 (5.3)	0.293
Hyperthyroidism	2 (0.3)	2 (0.7)	0 (0.0)	0 (0.0)	0.706
Hypothyroidism	4 (0.7)	4 (1.4)	0 (0.0)	0 (0.0)	0.144
Hypertension	448 (73.3)	210 (71.7)	134 (71.7)	104 (79.4)	0.208
Diabetes	115 (18.8)	68 (23.2)	26 (13.9)	21 (16.0)	0.026
Dyslipidemia	418 (68.4)	227 (77.5)	116 (62.0)	75 (57.3)	< 0.001
Stroke	61 (10.0)	27 (9.2)	19 (10.2)	15 (11.6)	0.746
Renal dysfunction	317 (52.9)	119 (41.3)	107 (57.8)	91 (72.2)	< 0.001
Obesity	110 (18.0)	57 (19.5)	27 (14.4)	26 (19.8)	0.307
Anemia	157 (25.7)	55 (18.8)	57 (30.5)	45 (34.4)	< 0.001
Lung diseases	144 (23.6)	71 (24.2)	41 (22.0)	32 (24.6)	0.824
COPD	3 (1.0)	0 (0.0)	0 (0.0)	3 (0.5)	0.316
Liver diseases	19 (3.1)	9 (3.1)	7 (3.8)	3 (2.3)	0.754
Cancer	136 (22.4)	58 (19.9)	46 (24.6)	32 (24.8)	0.362
Mild cognitive impairment	468 (77.2)	209 (71.8)	150 (80.6)	109 (84.5)	0.007
Blood sampling data					
NT-proBNP (pg/ml)	128 (72–252)	71 (51–94)	177 (145–221)	572 (383–902)	< 0.001
eGFRcre (ml/min/1.73m^2)	60 (51–69)	64 (56–72)	59 (48–66)	54 (45–63)	< 0.001
eGFRcys (ml/min/1.73m^2)	58 (46–70)	64 (52–75)	55 (44–67)	50 (37–61)	< 0.001
AST (U/L)	24 (20–27)	24 (20–26)	23 (21–27)	24 (21–30)	0.031
ALT (U/L)	16 (13–21)	17 (14–22)	15 (12–19)	16 (13–22)	< 0.001
Hb (g/dL)	13.3 (12.4–14.1)	13.6 (12.8–14.4)	13.1 (12.2–13.8)	13.2 (12.1–14.1)	< 0.001
WBC (/μg)	5500 (4700–6400)	5500 (4600–6400)	5500 (4750–6500)	5500 (4600–6300)	0.868
hs-CRP (mg/L)	0.489 (0.238–1.035)	0.481 (0.238–0.974)	0.438 (0.217–0.999)	0.566 (0.268–1.390)	0.085
TCHO (mg/dL)	197 (174–219)	201 (183–224)	198 (171–219)	183 (166–207)	< 0.001

Table 1 (continued)

	All	NT-proBNP < 125pg/mL	125 ≤ NT-proBNP < 300pg/mL	NT-proBNP ≥ 300pg/mL	*p* value
	(*n* = 611)	(*n* = 293)	(*n* = 187)	(*n* = 131)	
TG (mg/dL)	121 (86–165)	129 (94–177)	114 (85–159)	105 (78–152)	0.003
HDL-C (mg/dL)	59 (49–71)	59 (50–72)	58 (48–71)	56 (48–67)	0.355
LDL-C (mg/dL)	109 (91–127)	112 (93–129)	110 (95–128)	100 (86–123)	0.005
Non-HDL (mg/dL)	137 (116–157)	141 (124–159)	135 (116–158)	128 (106–148)	< 0.001
TP (g/dL)	7.0 (7.0–8.0)	7.0 (7.0–8.0)	7.0 (7.0–8.0)	7.0 (7.0-7.8)	0.899
Albumin (g/dL)	4.3 (4.1–4.5)	4.4 (4.1–4.6)	4.3 (4.0-4.5)	4.1 (4.0-4.4)	< 0.001
Medication use, n (%)					
ACE inhibitor	25 (4.1)	10 (3.4)	10 (5.3)	5 (3.8)	0.571
ARB	140 (22.9)	69 (23.5)	37 (19.8)	34 (26.0)	0.409
MRA	12 (2.0)	4 (1.4)	2 (1.1)	6 (4.6)	0.077
βblocker	28 (4.6)	10 (3.4)	6 (3.2)	12 (9.2)	0.018
αβblocker	17 (2.8)	6 (2.0)	5 (2.7)	6 (4.6)	0.340
Diuretic	43 (7.0)	6 (2.0)	13 (7.0)	24 (18.3)	< 0.001
Vasodilator	152 (24.9)	64 (21.8)	49 (26.2)	39 (29.8)	0.192
Cardiotonic	12 (2.0)	5 (1.7)	5 (2.7)	2 (1.5)	0.743
Calcium channel blocker	215 (35.2)	92 (31.4)	69 (36.9)	54 (41.2)	0.124
User of medication for HF	242 (39.6)	92 (31.4)	77 (41.2)	73 (55.7)	< 0.001

Categorical variables are expressed as numbers (%), and continuous variables are expressed as medians (interquartile ranges).

Pearson's chi-square test, Fisher-Freeman-Halton test, and Kruskal-Wallis test were used.

BMI indicates Body Mass Index; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; BP, Blood Pressure; CAD, Coronary artery disease; AF, Atrial Fibrillation; COPD, Chronic Obstructive Pulmonary Disease; NT-proBNP, N-terminal prohormone of Brain Natriuretic Peptide; eGFRcre, estimated Glomerular Filtration Rate based on creatinine; eGFRcys, estimated Glomerular Filtration Rate based on cystatin C; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; Hb, Hemoglobin; WBC, White Blood Cell: hs-CRP, high sensitive C-reactive protein; TCHO, Total cholesterol; TG, Total glycerin; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; TP, Total Protein; ACE inhibitor, Angiotensin converting enzyme inhibitor; ARB, Angiotensin Receptor Blocker; MRA, Mineralocorticoid receptor antagonist.

In NT-proBNP ≥ 300 pg/mL group, the associated factors were likely due to cardio-renal interaction. Ischemic damage from CAD [53], reduced cardiac output due to AF leading to elevated heart rate and irregular ventricular response [54], and higher BP triggered by renin-angiotensin-aldosterone system (RAAS) activation from renal dysfunction [55] increases afterload. Myocardial stiffening and diastolic dysfunction from CAD [53, 56] along with diastolic dysfunction due to AF further impact preload [57]. Renal dysfunction increases blood volume through water and sodium retention, affecting preload [58]. Moreover, renal dysfunction raises serum NT-proBNP levels due to impaired metabolism [31, 34, 59], and AF frequently coexists with HF and renal dysfunction [60, 61].

The salt intake was more likely to be independently associated with NT-proBNP ≥ 300 pg/mL, compared to NT-proBNP < 125 pg/mL, even after adjusting for sex, age groups and traditional HF risk factors. This appears to be due to fluid retention, increasing in cardiac load, and impaired sodium excretion. High salt intake contributes to an elevated circulating volume to maintain osmotic balance, which in turn increases preload [62–64]. Especially in individuals with renal dysfunction, activation of RAAS promotes sodium and fluid reabsorption, and impaired sodium excretion occurs due to reduced clearance [62, 65, 66].

The key strengths of this study are its focus on community-dwelling old age adults (≥ 75 years) including super-old adults (≥ 90 years), a rarely analyzed group in previous studies, and showing their distribution of serum NT-proBNP levels. Additionally, we identified the associated factors for each serum NT-proBNP group. Since HF risk factors vary across populations [67] and high serum NT-proBNP concentration is not HF-specific [15, 31, 33, 35, 36, 68], standardized HF screening using serum NT-proBNP remains difficult [67, 69]. Nevertheless, serum NT-proBNP is a useful, stable and easily measurable biomarker in HF diagnostic and prognostic value [11–13, 70] in community healthcare settings where cardiac echocardiography is unavailable [69]. Considering about half of our study participants had NT-proBNP ≥ 125 pg/mL, indicating potential cardiac overload, proactive measurement of serum NT-proBNP levels in these populations may help evaluate early HF, even in asymptomatic cases. Furthermore, our findings would identify individuals who need comprehensive check-up and follow-up, and underscore management of risk factors to prevent overt HF progression in aging societies.

Table 2 The association of traditional risk factors with NT-proBNP groups using multinomial logistic regression analysis

	125 ≤ NT-proBNP < 300 pg/mL *		NT-proBNP ≥ 300 pg/mL *	
	OR (95%CI)	p value	OR (95%CI)	p value
Female (ref: Male)	1.63 (1.04–2.56)	0.034	1.00 (0.59–1.72)	0.990
Age group: 90s (ref: 70s)	3.33 (1.68–6.61)	< 0.001	6.60 (3.21–13.59)	< 0.001
Age group: 80s (ref: 70s)	2.59 (1.64–4.09)	< 0.001	1.95 (1.09–3.47)	0.024
Smokers	1.85 (0.74–4.63)	0.186	1.21 (0.41–3.61)	0.734
Alcohol consumption	1.23 (0.78–1.92)	0.373	1.47 (0.87–2.51)	0.154
Uncontrolled high BP	1.88 (1.25–2.82)	0.002	1.24 (0.76–2.05)	0.393
CAD	1.48 (0.66–3.30)	0.339	2.89 (1.28–6.55)	0.011
AF	2.87 (0.61–13.52)	0.183	19.01 (5.04–71.75)	< 0.001
eGFRcys < 30 mL/min/1.73 m^2 (ref: eGFRcys ≥ 60 mL/min/1.73 m^2)	1.35 (0.39–4.66)	0.638	9.35 (2.98–29.33)	< 0.001
30 ≤ eGFRcys < 60 mL/min/1.73 m^2 (ref: eGFRcys ≥ 60 mL/min/1.73 m^2)	1.37 (0.90–2.11)	0.146	2.45 (1.42–4.23)	0.001
Diabetes	0.59 (0.34-1.00)	0.050	0.61 (0.33–1.13)	0.115
Obesity	0.71 (0.41–1.22)	0.213	1.07 (0.59–1.94)	0.822
Anemia	1.49 (0.91–2.44)	0.117	1.21 (0.67–2.18)	0.532
High levels of inflammation	1.08 (0.68–1.71)	0.751	1.46 (0.86–2.48)	0.162

*, Reference category: NT-proBNP < 125 pg/mL.

Multinomial logistic regression analysis model was used.

NT-proBNP indicates N-terminal prohormone of Brain Natriuretic Peptide; BP, Blood Pressure; CAD, coronary artery disease; AF, Atrial Fibrillation; eGFRcys, estimated Glomerular Filtration Rate based on cystatin C.

Conclusion

About half of community-dwelling old age adults (≥ 75 years) had NT-proBNP ≥ 125 pg/mL, indicating potential cardiac overload or asymptomatic HF. Additionally, the associated factors for each NT-proBNP distribution group, classified based on HF diagnostic thresholds, were identified. To reduce apparent HF prevalence, proactive measurement of serum NT-proBNP levels would lead to early HF detection in this population. Furthermore, effective management of HF risk factors, such as uncontrolled high BP and excessive salt intake, is essential to prevent overt HF progression.

Table 3 The association of salt intake (g/1000 kcal and g/day) and NT-proBNP groups and using multinomial logistic regression analysis

Salt intake (g/1000 kcal) adjusted by the density method				
	125 ≤ NT-proBNP < 300 pg/mL *		NT-proBNP ≥ 300 pg/mL *	
	OR (95%CI)	p value	OR (95%CI)	p value
Model 1	0.99 (0.85–1.15)	0.888	1.20 (1.02–1.41)	0.025
Model 2	0.98 (0.84–1.14)	0.784	1.22 (1.03–1.46)	0.019
Model 3	1.00 (0.63–1.64)	0.990	1.30 (1.07–1.58)	0.009
Salt intake (g/1000kcal) adjusted by the density method				
	125 ≤ NT-proBNP < 300 pg/mL *		NT-proBNP ≥ 300 pg/mL *	
	OR (95%CI)	p value	OR (95%CI)	p value
Model 1	0.98 (0.91–1.05)	0.530	1.10 (1.01–1.19)	0.021
Model 2	0.98 (0.91–1.05)	0.504	1.10 (1.01–1.20)	0.024
Model 3	0.98 (0.91–1.06)	0.657	1.14 (1.04–1.25)	0.008

*, Reference group: NT-proBNP < 125 pg/mL.

Multinomial logistic regression analysis model was used.

Model 1: Association with salt intake

Model 2: Association with salt intake adjusted for sex and age groups

Model 3: Association with salt intake adjusted for sex, age groups, smokers, alcohol consumption, uncontrolled high BP, CAD, AF, renal dysfunction, diabetes, obesity, anemia, and high levels of inflammation.

NT-proBNP indicates N-Terminal prohormone of Brain Natriuretic Peptide; BP, Blood Pressure, CAD; Coronary artery disease, AF; Atrial Fibrillation.

Limitations

- Since this was a cross-sectional study, causal relationships between serum NT-proBNP levels and risk factors for HF, and salt intake remain unclear.
- Medication use was not considered, though its impact on serum NT-proBNP levels during data collection was not fully detectable.
- Participants maintained high activities of daily living (ADL) levels or lived independently enough to visit the survey venue, though randomly selected from the residence registration system.
- Due to the limited sample size and collected data, we could not sufficiently adjust for HF risks and factors influencing serum NT-proBNP levels in multinomial logistic regression analysis.
- Salt intake was estimated rather than directly measured, though its correlation with 24-h urine collection has been validated [71].
- Data on HFrEF and HFpEF through cardiac echocardiography were unavailable. Medical history was collected via face-to-face interviews by medical workers rather than measurement tools like electrocardiography, limiting participants characterization.

Abbreviations

ADL Activities of daily living
AF Atrial fibrillation
ALT Alanine aminotransferase

AST	Aspartate aminotransferase
BDHQ	Brief-type self-administered Diet History Questionnaire
BP	Blood pressure
CAD	Coronary artery disease
CI	Confidence interval
COPD	Chronic Obstructive Pulmonary Disease
DBP	Diastolic blood pressure
ECLIA	Electrochemical luminescence immunoassay
eGFRcre	Estimated glomerular filtration rate based on creatinine
eGFRcys	Estimated glomerular filtration rate based on cystatin C
HDL-C	High-density lipoprotein cholesterol
HF	Heart failure
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
hs-CRP	High sensitive C-reactive protein
IQRs	Interquartile ranges
LDL-C	Low-density lipoprotein cholesterol
MAP	Mean artery pressure
MCI	Mild cognitive function
MoCA-J	Montreal Cognitive Assessment-Japanese
NT-proBNP	N-terminal prohormone of brain natriuretic peptide
OR	Odds ratio
RAAS	Renin-angiotensin-aldosterone system
SBP	Systolic blood pressure
TG	Triglycerides

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13104-025-07280-6.

Supplementary Material 1

Supplementary Material 2

Acknowledgements
We are grateful to all the staff members involved in the SONIC study. We sincerely appreciate all SONIC participants for their kind cooperation.

Author contributions
ST: Writing - original draft, Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Validation, Visualization, KG: Conceptualization, Investigation; Methodology; Software, Project administration, Writing - review & editing, MKabayama: Funding acquisition, Investigation, Project administration, Writing - review & editing, MKido: Investigation, Writing - review & editing, YA: Methodology, Software, Investigation, Project administration, Writing - review & editing, HA: Methodology, Investigation, Writing - review & editing, YT: Investigation, Writing - review & editing, TN: Investigation, SY: Investigation, YG: Funding acquisition, Investigation, Resources, Writing - review & editing, KI: Investigation, YA: Investigation, Writing - review & editing, YM: Investigation, TH; Investigation, KY: Writing - review & editing, KK: Conceptualization, Funding acquisition, Methodology, Investigation, Writing - review & editing. All authors reviewed the manuscript.

Funding
This work was supported by JSPS KAKENHI [grant numbers 22H00089, 20H03576, 23K24672]; the Ministry of Health Labour and Welfare [grant numbers K24FA1005, 23AA2006]; by AMED [grant number 24dk0110049h0002]; the Nippon Foundation [grant number JM00000160]; Osaka University's International Joint Research Promotion Program Support Type A [grant number J219713005]; and JST SPRING [grant number JPMJSP2138].

Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study has been performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Osaka University Graduate School of Medicine, Dentistry, and Human Science and the Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology (Tokyo, Japan; approval numbers 266, H22-9, 22 018 and 38, respectively). Written informed consent was obtained from all participants prior to the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Conflict of interest
The authors declare no conflict of interest.

Clinical trial number
not applicable.

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Received: 9 March 2025 / Accepted: 2 May 2025
Published online: 20 May 2025

References

1. United Nations. World Population Prospects - Population Division– 2024. https://population.un.org/wpp/ (accessed June 1, 2024).
2. Statistics Bureau of Japan. Population Estimates. 2023 2024. https://www.stat.go.jp/data/jinsui/new.html (accessed June 1, 2024).
3. Díez-Villanueva P, Jiménez-Méndez C, Alfonso F. Heart failure in the elderly. J Geriatr Cardiol. 2021;18:219–32. https://doi.org/10.11909/j.issn.1671-5411.2021.03.009.
4. Shimokawa H, Miura M, Nochioka K, Sakata Y. Heart failure as a general pandemic in Asia. Eur J Heart Fail. 2015;17:884–92. https://doi.org/10.1002/ejhf.319.
5. Bergamasco A, Luyet-Déruaz A, Gollop ND, Moride Y, Qiao Q. Epidemiology of asymptomatic Pre-heart failure: a systematic review. Curr Heart Fail Rep. 2022;19:146–56. https://doi.org/10.1007/s11897-022-00542-5.
6. Taylor CJ, Roalfe AK, Iles R, Hobbs FDR. The potential role of NT-proBNP in screening for and predicting prognosis in heart failure: a survival analysis. BMJ Open. 2014;4:e004675. https://doi.org/10.1136/bmjopen-2013-004675.
7. Tsutsui H, Isobe M, Ito H, Ito H, Okumura K, Ono M, et al. JCS 2017/JHFS 2017 guideline on diagnosis and treatment of acute and chronic heart

failure —— digest version ——. Circ J. 2019;83:2084–184. https://doi.org/10.1253/circj.CJ-19-0342.
8. Mukoyama M, Nakao K, Hosoda K, Suga S, Saito Y, Ogawa Y, et al. Brain natriuretic peptide as a novel cardiac hormone in humans. Evidence for an exquisite dual natriuretic peptide system, atrial natriuretic peptide and brain natriuretic peptide. J Clin Invest. 1991;87:1402–12. https://doi.org/10.1172/JCI115146.
9. Nakao K, Ogawa Y, Suga S, Imura H. Molecular biology and biochemistry of the natriuretic peptide system. I: natriuretic peptides. J Hypertens. 1992;10:907–12.
10. Yoshimura M, Yasue H, Okumura K, Ogawa H, Jougasaki M, Mukoyama M, et al. Different secretion patterns of atrial natriuretic peptide and brain natriuretic peptide in patients with congestive heart failure. Circulation. 1993;87:464–9. https://doi.org/10.1161/01.CIR.87.2.464.
11. Bozkurt B, Coats AJ, Tsutsui H, Abdelhamid M, Adamopoulos S, Albert N, et al. Universal definition and classification of heart failure. J Card Fail. 2021;27:387–413. https://doi.org/10.1016/j.cardfail.2021.01.022.
12. Escande M. Expérience de La Valeur Pronostique du BNP à l'admission En cardiogériatrie. Ann Cardiol Angeiol (Paris). 2009;58:284–8. https://doi.org/10.1016/J.ANCARD.2009.09.002.
13. Wang TJ, Larson MG, Levy D, Benjamin EJ, Leip EP, Omland T, et al. Plasma natriuretic peptide levels and the risk of cardiovascular events and death. N Engl J Med. 2004;350:655–63. https://doi.org/10.1056/NEJMoa031994.
14. The Japanese Heart Failure Society. Statements regarding management for heart failure using blood BNP and NT-proBNP levels revised 2023. 2023. (accessed May 10, 2024).
15. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European society of cardiology (ESC) with the special contribution of the heart failure association (HFA) of the ESC. Eur Heart J. 2021;42:3599–726. https://doi.org/10.1093/eurheartj/ehab368.
16. Ide T, Kaku H, Matsushima S, Tohyama T, Enzan N, Funakoshi K, et al. Clinical characteristics and outcomes of hospitalized patients with heart failure from the Large-Scale Japanese registry of acute decompensated heart failure (JROADHF). Circ J. 2021;85:CJ–20. https://doi.org/10.1253/circj.CJ-20-0947.
17. Tomasoni D, Adamo M, Lombardi CM, Metra M. Highlights in heart failure. ESC Heart Fail. 2019;6:1105–27. https://doi.org/10.1002/ehf2.12555.
18. Bayes-Genis A, Docherty KF, Petrie MC, Januzzi JL, Mueller C, Anderson L, et al. Practical algorithms for early diagnosis of heart failure and heart stress using NT-proBNP: A clinical consensus statement from the heart failure association of the ESC. Eur J Heart Fail. 2023;25:1891–8. https://doi.org/10.1002/ejhf.3036.
19. Kara K, Mahabadi AA, Geisel MH, Lehmann N, Kälsch H, Bauer M, et al. B-type natriuretic peptide: distribution in the general population and the association with major cardiovascular and coronary events - The heinz Nixdorf recall study. Clin Res Cardiol. 2014;103:125–32. https://doi.org/10.1007/s00392-013-0628-4.
20. Kamide K, Ikebe K, Masui Y, Nakagawa T, Kabayama M, Akasaka H, et al. Multidimensional insights about healthy aging from the cohort study for community-dwelling older adults: the SONIC study. Geriatr Gerontol Int. 2025. https://doi.org/10.1111/GGI.70003.
21. Kobayashi S, Murakami K, Sasaki S, Okubo H, Hirota N, Notsu A, et al. Comparison of relative validity of food group intakes estimated by comprehensive and brief-type self-administered diet history questionnaires against 16 d dietary records in Japanese adults. Public Health Nutr. 2011;14:1200–11. https://doi.org/10.1017/S1368980011000504.
22. Kobayashi S, Honda S, Murakami K, Sasaki S, Okubo H, Hirota N, et al. Both comprehensive and brief Self-Administered diet history questionnaires satisfactorily rank nutrient intakes in Japanese adults. J Epidemiol. 2012;22:151–9. https://doi.org/10.2188/jea.JE20110075.
23. Willett W, Howe G, Kushi L. Adjustment for total energy intake in epidemiologic studies. Am J Clin Nutr. 1997;65. https://doi.org/10.1093/ajcn/65.4.1220S.:1220S-1228S.
24. Fujiwara Y, Suzuki H, Yasunaga M, Sugiyama M, Ijuin M, Sakuma N, et al. Brief screening tool for mild cognitive impairment in older Japanese: validation of the Japanese version of the Montreal cognitive assessment. Geriatr Gerontol Int. 2010;10:225–32. https://doi.org/10.1111/J.1447-0594.2010.00585.X.
25. Shimamoto K, Ando K, Fujita T, Hasebe N, Higaki J, Horiuchi M, et al. The Japanese society of hypertension guidelines for the management of hypertension (JSH 2014). Hypertens Res. 2014;37:253–390. https://doi.org/10.1038/hr.2014.20.
26. Haneda M, Noda M, Origasa H, Noto H, Yabe D, Fujita Y, et al. Japanese clinical practice guideline for diabetes 2016. Diabetol Int. 2018;9:1–45. https://doi.org/10.1007/s13340-018-0345-3.
27. Kinoshita M, Yokote K, Arai H, Iida M, Ishigaki Y, Ishibashi S et al. Japan Atherosclerosis Society (JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017. J Atheroscler Thromb. 2018;25:846–984. https://doi.org/10.5551/jat.GL2017.
28. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity 2011. https://www.who.int/publications/i/item/WHO-NMH-NHD-MNM-11.1 (accessed June 1, 2024).
29. Horio M, Imai E, Yasuda Y, Watanabe T, Matsuo S. GFR Estimation using standardized serum Cystatin C in Japan. Am J Kidney Dis. 2013;61:197–203. https://doi.org/10.1053/j.ajkd.2012.07.007.
30. Arima H, Kubo M, Yonemoto K, Doi Y, Ninomiya T, Tanizaki Y, et al. High-Sensitivity C-Reactive protein and coronary heart disease in a general population of Japanese. Arterioscler Thromb Vasc Biol. 2008;28:1385–91. https://doi.org/10.1161/ATVBAHA.107.157164.
31. Forfia PR, Watkins SP, Rame JE, Stewart KJ, Shapiro EP. Relationship between B-Type natriuretic peptides and pulmonary capillary wedge pressure in the intensive care unit. J Am Coll Cardiol. 2005;45:1667–71. https://doi.org/10.1016/j.jacc.2005.01.046.
32. Horwich TB, Hamilton MA, Fonarow GC. B-Type natriuretic peptide levels in obese patients with advanced heart failure. J Am Coll Cardiol. 2006;47:85–90. https://doi.org/10.1016/j.jacc.2005.08.050.
33. Knudsen CW, Omland T, Clopton P, Westheim A, Wu AHB, Duc P, et al. Impact of atrial fibrillation on the diagnostic performance of B-Type natriuretic peptide concentration in dyspneic patients. J Am Coll Cardiol. 2005;46:838–44. https://doi.org/10.1016/j.jacc.2005.05.057.
34. McCullough PA, Sandberg KR. B-Type natriuretic peptide and renal disease. Heart Fail Rev. 2003;8:355–8. https://doi.org/10.1023/A:1026195332025.
35. Zaphiriou A, Robb S, Murray-Thomas T, Mendez G, Fox K, McDonagh T, et al. The diagnostic accuracy of plasma BNP and NTproBNP in patients referred from primary care with suspected heart failure: results of the UK natriuretic peptide study. Eur J Heart Fail. 2005;7:537–41. https://doi.org/10.1016/j.ejheart.2005.01.022.
36. Daniels LB, Clopton P, Bhalla V, Krishnaswamy P, Nowak RM, McCord J, et al. How obesity affects the cut-points for B-type natriuretic peptide in the diagnosis of acute heart failure. Am Heart J. 2006;151:999–1005. https://doi.org/10.1016/j.ahj.2005.10.011.
37. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. Eur J Heart Fail. 2020;22:1342–56. https://doi.org/10.1002/ejhf.1858.
38. Escande M, Mordarska M, Marsoubian L. Influence de La Fonction Rénale Sur La pertinence diagnostique du BNP Chez L'insuffisant cardiaque âgé. Ann Cardiol Angeiol (Paris). 2010;59:260–2. https://doi.org/10.1016/J.ANCARD.2010.08.007.
39. Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, et al. Treatment of hypertension in patients 80 years of age or older. N Engl J Med. 2008;358:1887–98. https://doi.org/10.1056/NEJMoa0801369.
40. Kostis JB, Davis BR, Cutler J, Grimm RH, Berge KG, Cohen JD, et al. Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension. JAMA. 1997;278:212–6. https://doi.org/10.1001/jama.1997.03550030052033.
41. Sciarretta S, Palano F, Tocci G, Baldini R, Volpe M. Antihypertensive treatment and development of heart failure in hypertension. Arch Intern Med. 2011;171. https://doi.org/10.1001/archinternmed.2010.427.
42. Doi Y, Ninomiya T, Hata J, Hirakawa Y, Mukai N, Ikeda F, et al. N-Terminal Pro-Brain natriuretic peptide and risk of cardiovascular events in a Japanese community: the Hisayama study. Arterioscler Thromb Vasc Biol. 2011;31:2997–3003. https://doi.org/10.1161/ATVBAHA.111.223669.
43. Nagata T, Ohara T, Hata J, Sakata S, Furuta Y, Yoshida D, et al. NT-proBNP and risk of dementia in a general Japanese elderly population: the Hisayama study. J Am Heart Assoc. 2019;8:e011652. https://doi.org/10.1161/JAHA.118.011652.
44. Cheitlin MD. Cardiovascular Physiology—Changes with aging. Am J Geriatr Cardiol. 2003;12:9–13. https://doi.org/10.1111/j.1076-7460.2003.01751.x.
45. Dunlay SM, Roger VL, Redfield MM. Epidemiology of heart failure with preserved ejection fraction. Nat Rev Cardiol. 2017;14:591–602. https://doi.org/10.1038/nrcardio.2017.65.
46. Ho JE, Enserro D, Brouwers FP, Kizer JR, Shah SJ, Psaty BM, et al. Predicting heart failure with preserved and reduced ejection fraction. Circ Heart Fail. 2016;9: e003116. https://doi.org/10.1161/CIRCHEARTFAILURE.115.003116

47. Eaton CB, Pettinger M, Rossouw J, Martin LW, Foraker R, Quddus A, et al. Risk factors for incident hospitalized heart failure with preserved versus reduced ejection fraction in a multiracial cohort of postmenopausal women. Circ Heart Fail. 2016;9. https://doi.org/10.1161/CIRCHEARTFAILURE.115.002883.
48. Savji N, Meijers WC, Bartz TM, Bhambhani V, Cushman M, Nayor M, et al. The association of obesity and cardiometabolic traits with incident HFpEF and HFrEF. JACC Heart Fail. 2018;6:701–9. https://doi.org/10.1016/j.jchf.2018.05.018.
49. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. JAMA. 1979;241:2035–8. https://doi.org/10.1001/jama.241.19.2035.
50. Ohkuma T, Komorita Y, Peters SAE, Woodward M. Diabetes as a risk factor for heart failure in women and men: a systematic review and meta-analysis of 47 cohorts including 12 million individuals. Diabetologia. 2019;62:1550–60. https://doi.org/10.1007/s00125-019-4926-x.
51. Carabello BA. The pathophysiology of afterload mismatch and ventricular hypertrophy. Struct Heart. 2021;5:446–56. https://doi.org/10.1080/24748706.2021.1944708.
52. Kuznetsova T, Cauwenberghs N. Hemodynamic mechanisms. Hypertens Heart Fail. 2019;59–70. https://doi.org/10.1007/978-3-319-93320-7_4.
53. Ogawa A, Seino Y, Yamashita T, Ogata K, Takano T. Difference in elevation of N-Terminal Pro-BNP and conventional cardiac markers between patients with ST elevation vs Non-ST elevation acute coronary syndrome. Circ J. 2006;70:1372–8. https://doi.org/10.1253/circj.70.1372.
54. Verma A, Kalman JM, Callans DJ. Treatment of patients with atrial fibrillation and heart failure with reduced ejection fraction. Circulation. 2017;135:1547–63. https://doi.org/10.1161/CIRCULATIONAHA.116.026054.
55. Hartupee J, Mann DL. Neurohormonal activation in heart failure with reduced ejection fraction. Nat Rev Cardiol. 2017;14:30–8. https://doi.org/10.1038/nrcardio.2016.163.
56. John JE, Claggett B, Skali H, Solomon SD, Cunningham JW, Matsushita K, et al. Coronary artery disease and heart failure with preserved ejection fraction: the ARIC study. J Am Heart Assoc. 2022;11:e021660. https://doi.org/10.1161/JAHA.121.021660.
57. Manea M, Marcu D, Stoian AP, Gaman MA, Gaman AM, Socea B, et al. Heart failure with preserved ejection fraction and atrial fibrillation A review. Rev Chim. 2018;69:3280–4. https://doi.org/10.37358/RC.18.11.6730.
58. Patterson JH, Adams KF. Pathophysiology of heart failure: changing perceptions. Pharmacotherapy: J Hum Pharmacol Drug Therapy. 1996;16. https://doi.org/10.1002/j.1875-9114.1996.tb02956.x.
59. Srisawasdi P, Vanavanan S, Charoenpanichkit C, Kroll MH. The effect of renal dysfunction on BNP, NT-proBNP, and their ratio. Am J Clin Pathol. 2010;133:14–23. https://doi.org/10.1309/AJCP60HTPGIGFCNK.
60. Prabhu S, Voskoboinik A, Kaye DM, Kistler PM. Atrial fibrillation and heart Failure — Cause or effect?? Heart Lung Circ. 2017;26:967–74. https://doi.org/10.1016/J.HLC.2017.05.117.
61. Wang Y, Yang Y, He F. Insights into concomitant atrial fibrillation and chronic kidney disease. Rev Cardiovasc Med. 2022;23:0105. https://doi.org/10.31083/j.rcm2303105.
62. Brooks VL, Scrogin KE, McKeogh DF. The interaction of angiotensin II and osmolality in the generation of sympathetic tone during changes in dietary salt intake. Ann N Y Acad Sci. 2001;940:380–94. https://doi.org/10.1111/j.1749-6632.2001.tb03692.x.
63. Hall JE. Renal dysfunction, rather than nonrenal vascular dysfunction, mediates Salt-Induced hypertension. Circulation. 2016;133:894–906. https://doi.org/10.1161/CIRCULATIONAHA.115.018526.
64. Meneton P, Jeunemaitre X, de Wardener HE, Macgregor GA. Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. Physiol Rev. 2005;85:679–715. https://doi.org/10.1152/physrev.00056.2003.
65. Chaney E, Shaw A. Pathophysiology of fluid retention in heart failure. Contrib Nephrol. 2010;164:46–53. https://doi.org/10.1159/000313720.
66. Kataoka H. The chloride theory, a unifying hypothesis for renal handling and body fluid distribution in heart failure pathophysiology. Med Hypotheses. 2017;104:170–3. https://doi.org/10.1016/j.mehy.2017.06.005.
67. Tsutsui H, Albert NM, Coats AJS, Anker SD, Bayes-Genis A, Butler J, et al. Natriuretic peptides: role in the diagnosis and management of heart failure: A scientific statement from the heart failure association of the European society of cardiology, heart failure society of America and Japanese heart failure society. J Card Fail. 2023;29:787–804. https://doi.org/10.1016/j.cardfail.2023.02.009.
68. Plichart M, Orvoën G, Jourdain P, Quinquis L, Coste J, Escande M, et al. Brain natriuretic peptide usefulness in very elderly dyspnoeic patients: the BED study. Eur J Heart Fail. 2017;19:540–8. https://doi.org/10.1002/EJHF.699.
69. Braisch U, Koenig W, Rothenbacher D, Denkinger M, Friedrich N, Felix SB, et al. N-terminal pro brain natriuretic peptide reference values in community-dwelling older adults. ESC Heart Fail. 2022;9:1703–12. https://doi.org/10.1002/ehf2.13834.
70. Goryacheva OA, Ponomaryova TD, Drozd DD, Kokorina AA, Rusanova TY, Mishra PK, et al. Heart failure biomarkers BNP and NT-proBNP detection using optical labels. TRAC Trends Anal Chem. 2022;146:116477. https://doi.org/10.1016/J.TRAC.2021.116477.
71. Sakata S, Tsuchihashi T, Oniki H, Tominaga M, Arakawa K, Sakaki M, et al. Relationship between salt intake as estimated by a brief self-administered diet-history questionnaire (BDHQ) and 24-h urinary salt excretion in hypertensive patients. Hypertens Res. 2015;38:560–3. https://doi.org/10.1038/hr.2015.35.

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