

# Prevalence and Risk Factors Associated with Frailty Syndrome in Chronic Heart Failure Patients at Heart Failure Clinic at Vajira Hospital

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## ABSTRACT

**OBJECTIVE:** The prevalence of frailty syndrome in patients with chronic heart failure (HF) at Vajira Hospital was investigated, and risk factors associated with frailty syndrome and chronic HF were identified for optimizing management and improving outcomes in this vulnerable population.

**METHODS:** A prospective cross-sectional study was conducted at chronic HF clinic of Vajira Hospital by history taking, collecting data with questionnaires, and performing specific tests (Fried Frailty Phenotype). Echocardiogram and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were obtained from chronic HF patients from January 2022 to December 2023. A physician collected clinical data and baseline characteristics. All patients were tested for the Fried Frailty Phenotype by a physical therapist. Determinants were evaluated using univariate and multivariate logistic regression models.

**RESULTS:** A total of 94 patients were enrolled. The prevalence of frailty syndrome in patients with HF was 27.70% (95% CI: 18.90–37.80). Univariate analysis showed that factors associated with increased likelihood of frailty syndrome in patients with chronic HF included chronic kidney disease (CKD stages IV–V, unadjusted OR = 4.00, 95% CI: 1.11–14.43, p-value = 0.03), New York Heart Association (NYHA; III–IV, unadjusted OR = 39.00, 95% CI: 8.30–183.29, p-value < 0.001), left ventricular ejection fraction ( $\leq 40\%$ , unadjusted OR = 3.84, 95% CI: 1.13–13.02, p-value = 0.031), NT-proBNP ( $> 1000$  pg/mL, unadjusted OR = 5.50, 95% CI: 1.71–17.66, p-value = 0.004) and diuretics (unadjusted OR = 8.33, 95% CI: 1.05–66.22, p-value = 0.045) but multivariate analysis showed only NYHA (III–IV), adjusted OR = 30.51, 95% CI: 6.01–154.94, p-value < 0.001) increase risk of frailty syndrome.

**CONCLUSION:** The prevalence of frailty syndrome in patients with chronic HF was found, and the main associated factor affecting frailty is NYHA(III–IV). NYHA classification and frailty in HF patients are crucial for comprehensive management. Regular assessment of NYHA class, frailty status, and associated factors (physical, cognitive, nutritional, and psychosocial) is essential for personalized care planning.

## KEYWORDS:

chronic heart failure, frailty syndrome, Fried Frailty Phenotype

## INTRODUCTION

Heart failure (HF) is a significant health issue in Thailand, as it is in many parts of the world. The prevalence of HF in Thailand has been increasing over the years, primarily due to several factors including an aging population, lifestyle changes, and an increasing burden of cardiovascular risk factors. The study highlighted that the prevalence increased significantly with age, reaching 7.70% among those aged 75 years and older<sup>1-2</sup>. The death rate of HF has increased over the past decade. A five-year European study of death rates from the Framingham Heart Study and the Cardiovascular Health Study reported a death rate of 67% within five years since diagnosis<sup>3</sup>. The death rate or mortality rate is associated with HF in Thailand, like in many other countries, but the key factor associated is aging<sup>4</sup>.

HF and frailty often coexist and can have significant implications for patients. Frailty is a condition characterized by decreased physiologic reserve and increased vulnerability to stressors, which can include chronic diseases like HF. The relationship between HF and frailty is related to increasing age, congenital diseases, mechanisms of disease, inflammatory processes, and increased free radicals. A combination of at least two of these conditions results in poor prognosis<sup>5-6</sup>. The presence of frailty in individuals with HF is associated with worse outcomes. Frailty increases mortality, rehospitalization rate, and medical costs, especially for patients with chronic HF. It also affects the quality of life of both patients and caregivers<sup>7</sup>. Now frailty is not routinely assessed in clinical practice as part of HF management, but its recognition is crucial. Tools such as the Fried Frailty Phenotype or the Clinical Frailty Scale can help in identifying frail patients<sup>8</sup>. Therefore, the assessment of frailty status in patients with chronic HF is essential to their prognosis and treatment<sup>9-10</sup>.

Methods for measuring frailty in patients with chronic HF have been established, such as the Fried Frailty Phenotype<sup>11</sup>, deficit index<sup>12</sup>, Edmonton Frailty Scale<sup>13</sup>, and Clinical Frailty

Scale<sup>14</sup>, which mainly consist of questionnaires and physical tests. The Fried Frailty Phenotype is one of the accepted methods and widely used, providing concrete results<sup>15</sup> based on the symptoms of diseases and including three of the following criteria: unintentional weight loss (information is obtained through questionnaire responses); fatigue status measured by the Center for Epidemiological Studies-Depression Scale; muscle weakness measured by handgrip strength; slowness, which is indicated by a decrease in walking time after walking for 15 feet or approximately 4.5 meters relative to normal values based on gender and body mass index (BMI); and low physical activity assessed according to normal values based on gender and height. A questionnaire measurement tool based on the Minnesota Leisure Time Activity questionnaire was used. The level of physical activity was calculated as energy per week (kcal/week). In the evaluation, a total score of 3 indicated frailty; 1-2, onset of frailty; and 0, no frailty. Most studies on frailty in patient groups have used the Fried Frailty Phenotype, including comparative studies that measured the degree of frailty in patients with chronic HF patients with various tools. It was found that the Fried Frailty Phenotype has a higher sensitivity and specificity of 93.00% and 76.00%, respectively<sup>15</sup>. In endurance of patients with respiratory diseases is typically evaluated with a six-minute walking test (6 MWT). It is a simple test, and its results are easy to interpret. It is also applied to groups of patients with cardiovascular diseases, such as chronic HF. A study in a group of patients with chronic HF found that the 6 MWT test results are associated with mortality and disability rates, especially in those with poor left ventricular contraction<sup>16-17</sup>.

In previous study showed that the prevalence of frailty in 26 evidence-based studies (systemic review and meta-analysis) related to frailty in patients with chronic HF was 44.50%<sup>18</sup>. A total of 14 ongoing studies is exploring mortality and hospital admission rates of 5186 patients with chronic HF; frailty increased the mortality rate 1.54-fold, the hospital admission rate

increased 1.56-fold, and the change was statistically significant<sup>19</sup>. A recent study in Asian found the prevalence of 69% of HF patients and had a Higher frailty index in older age, Southeast Asian residency, and Malay ethnicity. In frailty, group found more comorbidities than the non-frailty group<sup>20</sup>. In another study of a specific group in HF with reduced ejection fraction group using a 42-item frailty index to identify frailty status found that the frailest patients were female, older, and had more clinical symptoms than non-frailty. High rates of all-cause death or all-cause hospitalization in frailty group<sup>21</sup>.

Elderly people with HF are vulnerable. In the past studies were limited generalizability some studies may focus on specific demographics, settings, or conditions, limiting the applicability of findings to other populations or contexts and no study has evaluated frailty in patients with brittle HF in Thailand. Thus, the objective of this study was to determine the prevalence of frailty and to identify the factors involved and tailoring treatment for HF in frail individuals with a multidisciplinary approach involve optimizing medications, focusing on symptom management, encouraging physical activity within the individual's capabilities, and addressing nutritional status.

## METHODS

A prospective cross-sectional study was conducted at HF clinic of Vajira Hospital. Patient histories were obtained, and questionnaires and specific tests (Fried Frailty Phenotype) were used. Echocardiogram, and NT-proBNP data from chronic HF patients from January 2022 to December 2023. All patients were tested by a physical therapist using the Fried Frailty Phenotype.

The inclusion criteria included patients aged  $\geq 65$  years and those with a diagnosis with chronic HF. Chronic HF patients are stage C HF refers to a specific classification of HF according to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines<sup>22-23</sup>. The exclusion criteria were acute heart attack defined as acute HF, acute myocardial infarction, pulmonary embolism

or cardiogenic shock, hospitalization 3 months, severe heart valve abnormalities defined as severe aortic regurgitation/stenosis or severe mitral regurgitation/stenosis or severe tricuspid regurgitation/stenosis, absence of echocardiogram results, cancer diagnosis, psychiatric disease, myasthenia gravis, major stroke and incapability to communicate or perform tests. This study uses the Fried Frailty Index to evaluate frailty. It consists of five components: unintentional weight loss; has the individual experienced significant weight loss ( $\geq 10$  pounds in the past year) without trying to lose weight, exhaustion, low physical activity, weakness measured using a dynamometer, slow walking speed. Each component is scored 0 or 1, with 1 indicating the presence of that component. A higher score (0-5) indicates greater frailty (0 points = not frail, 1-2 points = pre-frail, 3 or more points = frail). This study was approved by the Institutional Review Board of the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University (COA 113/65).

Sample size estimation using sample size calculation formula for proportion estimation:

$$n = \frac{Z_{\alpha/2}^2 p(1-p)}{d^2}$$

when  $Z_{\alpha/2}$  defined as 1.96 (standard statistical value under the normal curve that corresponds to the significant level and  $\alpha = 0.05$ ),  $d$  defined as 0.1 (desired margin of error by determining the percentage deviation of 10%),  $p = 0.474$  (population proportion reference from study of the prevalence of frailty in HF<sup>16</sup> when using the formula the sample size calculated is 96 people for each group).

Statistical analyses were performed using SPSS Statistics for Windows, version 26 (IBM Corp., Amok, NY, USA). Baseline characteristics and categorical variables were presented as percentages and numbers. Continuous variables were presented as means and standard deviations. Categorical variables using Chi-Square or Fisher's Exact Tests, and continuous variables were compared using the Independent Samples T-Test,

Mann-Whitney U Test. Two groups (frailty and non-frailty) were compared using one-way ANOVA and Kruskal-Wallis Test for the comparison of more than two groups (non-frailty, pre-frailty, and frailty). Univariable and multivariable analyses of factors associated with frailty syndrome in patients with chronic HF were analyzed using binary logistic regression. Statistical significance was set at  $p < 0.05$ .

## RESULTS

A total of 94 patients with chronic HF were included in this study. The baseline characteristics of patients with chronic HF were as follows: average age,  $68.55 \pm 7.04$  years; male, 77.70%;

average BMI,  $23.32 \pm 4.52$  kg/m<sup>2</sup>; and comorbidities (diabetes mellitus, 56.40%; hypertension, 90.40%; dyslipidemia, 96.80%); atrial fibrillation, 36.20%; and ischemia heart disease, 57.40%. The patients had New York Heart Association (NYHA) II about 50.00%, the average left ventricular ejection fraction (LVEF) value was  $41.09\% \pm 13.89\%$ , average 6MWT was  $298.54 \pm 113.03$  meters, the median NT-proBNP value was 1459.00 pg/mL (IQR: 420–2863). The patients mostly use angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers/ or angiotensin receptor-neprilysin inhibition, beta blocker and mineralocorticoid receptor antagonist; all data is shown in Table 1.

**Table 1** Demographic and baseline characteristics of chronic heart failure patients

Variables	Total (n = 94)	Non-frailty (n = 31)	Pre-frailty (n = 37)	Frailty (n = 26)	P-value
Age (years)	$68.55 \pm 7.04$	$68.45 \pm 6.62$	$67.76 \pm 7.63$	$69.81 \pm 6.74$	0.526
Sex					0.254
Male	73 (77.70)	27 (87.10)	28 (75.70)	18 (69.20)	
BMI (kg/m <sup>2</sup> )	$23.32 \pm 4.52$	$24.59 \pm 4.83$	$22.72 \pm 4.24$	$22.66 \pm 4.37$	0.160
Comorbidity					
Diabetes mellitus	53 (56.40)	17 (54.80)	23 (62.20)	13 (50.00)	0.618
Hypertension	85 (90.40)	29 (93.50)	34 (91.90)	22 (84.60)	0.510
Dyslipidemia	91 (96.80)	31 (100.00)	36 (97.30)	24 (92.30)	0.276
Chronic kidney disease					0.311
No	36 (38.30)	12 (38.70)	16 (43.20)	8 (30.80)	
Stage III	43 (45.70)	16 (51.60)	17 (45.90)	10 (38.50)	
Stage IV	13 (13.80)	3 (9.70)	4 (10.80)	6 (23.10)	
Stage V	2 (2.10)	0 (0.00)	0 (0.00)	2 (7.70)	
Atrial fibrillation	34 (36.20)	12 (38.70)	14 (37.80)	8 (30.80)	0.795
Ischemia heart disease	54 (57.40)	16 (51.60)	19 (51.40)	19 (73.10)	0.166
NYHA					< 0.001
I	7 (7.40)	5 (16.10)	2 (5.40)	0 (0.00)	
II	47 (50.00)	19 (61.30)	26 (70.30)	2 (7.70)	
III	37 (39.40)	7 (22.60)	9 (24.30)	21 (80.80)	
IV	3 (3.20)	0 (0.00)	0 (0.00)	3 (11.50)	
LVEF (%)	$41.09 \pm 13.89$	$46.54 \pm 13.21$	$40.54 \pm 14.29$	$35.38 \pm 11.97$	0.009
LVEF group					0.025
≤ 40	45 (47.90)	9 (29.00)	17 (46.00)	19 (73.10)	
40-49	24 (25.50)	11 (35.50)	10 (27.00)	3 (11.50)	
≥ 50	25 (26.60)	11 (35.50)	10 (27.00)	4 (15.40)	
6MWT (m)	$298.54 \pm 113.03$	$366.32 \pm 64.12$	$317.22 \pm 85.40$	$191.15 \pm 117.83$	< 0.001
NT-proBNP (pg/ml)	1459 (420-2863)	767 (354-1796)	1621 (353-2980)	2392 (1453-4447)	0.002
NT-proBNP group ≥ 1000	56 (59.60)	12 (38.70)	22 (59.50)	22 (84.60)	0.002

**Table 1** Demographic and baseline characteristics of chronic heart failure patients (continued)

Variables	Total (n = 94)	Non-frailty (n = 31)	Pre-frailty (n = 37)	Frailty (n = 26)	P-value
Medication					
ACEI, ARB, ARNI	77 (81.90)	29 (93.50)	30 (81.10)	18 (69.20)	0.059
Beta Blocker	94 (100.00)	31 (100.00)	37 (100.00)	26 (100.00)	NA
MRA	67 (71.30)	25 (80.60)	25 (67.60)	17 (65.40)	0.364
SGLT2i	36 (38.30)	14 (45.20)	16 (43.20)	6 (23.10)	0.169
Diuretic	76 (80.90)	25 (80.60)	26 (70.30)	25 (96.20)	0.037
CRT	6 (6.40)	1 (3.20)	3 (8.10)	2 (7.70)	0.761
ICD	4 (4.30)	1 (3.20)	2 (5.40)	1 (3.80)	1.000

Abbreviations: 6MWT, six mins walk test; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor-neprilysin inhibition; BMI, body mass index; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; kg/m<sup>2</sup>, kilogram per square meter; LVEF, left ventricular ejection fraction; m, minute; MRA, mineralocorticoid receptor antagonist; n, number; NA, data not applicable; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association classification; pg/ml, picograms per milliliter; SGLT2i, sodium-glucose transport protein 2 inhibitors

Data are presented as number (%), mean ± standard deviation or median (interquartile range).

P-value corresponds to One-way ANOVA, Kruskal-Wallis Test, Chi-Square Test or Fisher's Exact Test.

Approximately 27.70% (95% CI: 18.90–37.80) of patients with chronic HF were frail, 33.00% (95% CI: 23.60–43.40) were not frail, and 39.30% (95% CI: 29.40–50.0) showed signs of frailty (table 2).

Factors related to frailty in patients with chronic HF patients were assessed with univariate analysis. Simple logistic regression analysis found that the factors related to frailty in these patients were statistically significant (p-value < 0.05), including CKD stages IV–V (unadjusted OR = 4.00, 95% CI: 1.11–14.43, p-value = 0.034), NYHA (III–IV, unadjusted OR = 39, 95% CI: 8.30–183.29, p-value < 0.001), LVEF (≤ 40%, unadjusted OR = 3.84, 95% CI: 1.13–13.02, p-value = 0.031), NT-proBNP ≥ 1000 pg/mL, unadjusted OR = 5.5, 95% CI: 1.71–17.66,

p-value = 0.004) and diuretics use (unadjusted OR = 8.33, 95% CI: 1.05–66.22, p-value = 0.045). All results are shown in Table 3. When multiple logistic regression analysis (multivariate analysis) was used, which considers only variables, the factors related to frailty in patients with chronic HF were significantly different (p-value < 0.05) from the factors determined through univariate analysis using simple logistic regression analysis, including CKD, NYHA, LVEF, NT-proBNP, and diuretics use. Factors associated with frailty in patients with chronic HF patients showed statistically significant (p-value < 0.05) when controlling for the influence of co-factors in the analysis, only NYHA factors (III–IV, adjusted OR = 30.51, 95% CI: 6.01–154.94, p-value < 0.001). All results are shown in Table 3.

**Table 2** Prevalence of frailty syndrome in chronic HF patients

Variables	Total (n = 94)	Non-frailty (n = 31)	Pre-frailty (n = 37)	Frailty (n = 26)	P-value
All patients	94 (100.00)	31 (33.00)	37 (39.30)	26 (27.70)	
Test 1 (BW)	14 (14.90)	0 (0.00)	7 (18.90)	7 (26.90)	0.003
Test 2 (exhaust)	22 (23.40)	0 (0.00)	2 (5.40)	20 (76.90)	< 0.001
Test 3 (MET/min/wk)	26 (27.70)	0 (0.00)	5 (13.50)	21 (80.80)	< 0.001
Test 4 (WT)	27 (28.70)	0 (0.00)	6 (16.20)	21 (80.80)	< 0.001
Test 5 (HGS)	57 (60.60)	0 (0.00)	31 (83.80)	26 (100.00)	< 0.001
Fried frailty score	1.55 ± 1.50	0.00 ± 0.00	1.38 ± 0.49	3.65 ± 0.63	< 0.001
Min – Max	(0-5)	(0)	(1-2)	(3-5)	

Abbreviations: BW, body weight; HGS, hand grips strength; max, maximum; MET, metabolic equivalents; min, minimum; n, number; wk, week; WT, walking times

Data are presented as number (%), mean ± standard deviation or median (interquartile range).

P-value corresponds to One-way ANOVA, Chi-Square Test or Fisher's Exact Test.

**Table 3** Univariate and multivariate analysis of factors associated with frailty syndrome in chronic HF patients

Factors	Univariate analysis		Multivariate analysis	
	OR* (95%CI)	P-value	Adjusted OR** (95%CI)	P-value
Age (years)	1.04 (0.97-1.11)	0.286		
Sex				
Male	1.00		Reference	
Female	1.88 (0.67-5.26)	0.229		
BMI (kg/m <sup>2</sup> )	0.96 (0.86-1.06)	0.381		
Comorbidity				
Diabetes mellitus	0.70 (0.28-1.74)	0.441		
Hypertension	0.44 (0.11-1.77)	0.246		
Dyslipidemia	0.18 (0.02-2.07)	0.168		
Chronic kidney disease				
No-CKD	1.00		Reference	1.00
CKD stage III	1.06 (0.37-3.05)	0.913	0.78 (0.17-3.59)	0.753
CKD stage IV-V	4.00 (1.11-14.43)	0.034	1.09 (0.20-6.12)	0.920
Atrial fibrillation	0.72 (0.27-1.89)	0.501		
Ischemia heart disease	2.56 (0.95-6.88)	0.062		
NYHA				
I-II	1.00		Reference	1.00
III-IV	39.00 (8.30-183.29)	< 0.001	30.51 (6.01-154.94)	< 0.001
LVEF (%)				
≤ 40	3.84 (1.13-13.02)	0.031	1.23 (0.20-7.52)	0.821
40-49	0.75 (0.15-3.77)	0.727	0.36 (0.04-2.92)	0.339
≥ 50	1.00		Reference	1.00
NT-proBNP (pg/ml)				
< 1000	1.00		Reference	1.00
≥ 1000	5.50 (1.71-17.66)	0.004	2.02 (0.40-10.35)	0.398
Medication				
ACEI, ARB, ARNI	0.34 (0.12-1.02)	0.054		
B-Blocker		NA		
MRA	0.68 (0.26-1.80)	0.436		
SGLT2i	0.38 (0.14-1.07)	0.066		
Diuretic	8.33 (1.05-66.22)	0.045	3.40 (0.31-37.69)	0.318
CRT	1.33 (0.23-7.76)	0.749		
ICD	0.87 (0.09-8.73)	0.903		

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor-neprilysin inhibition; BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; kg/m<sup>2</sup>, kilogram per square meter; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NA, data not applicable; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association classification; OR, odds ratio; pg/ml, picograms per milliliter; SGLT2i, sodium-glucose transport protein 2 inhibitors

\*Unadjusted odds ratio estimated by Logistic regression model.

\*\*Adjusted odds ratio estimated by Logistic regression model adjusting for chronic kidney disease, NYHA, LVEF, NT-proBNP and diuretic drug.

## DISCUSSION

Frailty is a strong predictor of adverse outcomes in HF, including increased mortality, hospitalizations, and decreased quality of life. Identifying frailty can help stratify patients into different risk categories and guide appropriate management strategies but now frailty assessment in HF patients remains underutilized despite its potential benefits. In the past, there have been no studies done on urban medicine patients. Thus, in

this study, we explored the prevalence and factors associated with fragility in chronic HF patients for the early identification of status and factors of frailty, aiming to for optimizing management and improving outcomes in this vulnerable population.

In this study was showed that the prevalence of frailty in HF patients about 27.70% which is not a small number. Factors of increasing age, LV systolic dysfunction, or high NT-proBNP may be associated factors of frailty syndrome but do not

show statistical significance because confounding factors include unequal medication treatment due to difficult access to services and socioeconomic problems. The key factor associated between HF and frailty is NYHA III-IV, the results show were 39 times more likely to develop frailty compared with the group with NYHA I-II. Thus for frailty patients with NYHA class III-IV HF, there must be early intervention because some patients may be underestimated and incorporate frailty assessment tools (such as the Fried Frailty Phenotype, Clinical Frailty Scale, or others validated in your setting) into routine clinical evaluations consider more specific treatment strategies, comprehensive geriatric assessments, and targeted rehabilitation programs to optimize functional status.

To promote routine frailty assessment in HF care, efforts should focus on raising awareness, providing training, developing standardized assessment tools, and integrating frailty evaluation into existing clinical workflows. Collaborative efforts between cardiologists, geriatricians, nurses, and other healthcare professionals can facilitate the implementation of frailty assessment as part of comprehensive HF management particularly in patients with NYHA class III-IV HF, enhances risk assessment, supports personalized care planning, and improves overall management strategies. This approach not only optimizes patient outcomes but also fosters a more patient-centered and evidence-based approach to healthcare delivery. This study can be adapted to urban medicine patients because the population we studied was the patients we actually encountered and the demographic characteristics were similar, which has not been studied in this way before.

This study has some limitations. The first limitation is only patients with HF at a specific time were included. The second limitation is only includes outpatient HF clinics and is conducted in a single hospital. The third limitation is the number of sample sizes is a small group. Expanding the study to different patient groups and hospitals will facilitate the identification of more factors.

## CONCLUSION

The prevalence of frailty syndrome in chronic HF patients was found, and the main associated factor affecting frailty is NYHA(III-IV). NYHA classification and frailty in HF patients are crucial for comprehensive management. Regular assessment of NYHA class, frailty status, and associated factors (physical, cognitive, nutritional, and psychosocial) is essential for personalized care planning. Recognizing frailty in HF patients is essential for optimizing management and improving outcomes in this vulnerable population.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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## DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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