

# Understanding Cardiac Cachexia among Patients with Heart Failure Using a Mixed–Methods Sequential Explanatory Design

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**Abstract:** In heart failure, cardiac cachexia often presents in people as weight loss accompanied by muscle wastage, loss of appetite and reduced quality of life. Such people often have a poor prognosis. However, the impact of these symptoms on Thai patients' quality of life is unknown. Therefore, this study aimed to explore cardiac cachexia, its symptoms, and its effect on quality of life using a mixed-method sequential explanatory design. Data for this study were collected from a specific cardiac failure clinic in a large hospital in Bangkok, Thailand, from August 2022 to January 2023. Forty-two patients with heart failure were screened for cardiac cachexia using cachexia consensus criteria and bioelectrical impedance vector analysis. They also completed the Simplified Nutritional Appetite Questionnaire, the Thirst Distress Scale for Heart Failure and the Kansas City Cardiomyopathy Questionnaire to assess appetite, thirst, and quality of life, respectively.

Thirty-eight participants were included for statistical analysis and divided into two groups: those with confirmed or suspected cardiac cachexia ( $n = 7$ ) and those without ( $n = 31$ ). The former group reported low appetite scores; however, no significant differences were observed between the two groups' appetite, thirst, or quality of life. After identifying patients with cardiac cachexia, six semi-structured interviews were conducted using an interview guide and analyzed through thematic analysis. The interviews revealed two common themes: Changes in diet and thirst and a Reduction in physical activity levels. Both themes complement the quantitative results. This study initiates a significant step in the understanding of cardiac cachexia in the Thai population with heart failure. Nurses can play a crucial role in identifying and managing patients with or at risk of cardiac cachexia.

**Keywords:** Cachexia, Heart failure, Mixed methods, Poor appetite, Quality of life, Sequential explanatory design, Thirst

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## Introduction

Heart failure (HF) results from abnormalities of heart structure and function, impairing pumping and resulting in inadequate cardiac output.<sup>1</sup> The global prevalence of HF was estimated to be between 1% and 3% in 2022 and is expected to rise due to increasing life expectancy and advances in HF therapies.<sup>2</sup> Cardiac cachexia (CC) develops in association with chronic HF. The prevalence of CC has been reported to be between 5% and 15% in people with HF and advanced HF, respectively.<sup>3</sup> CC is driven by chronic inflammatory activation and involves multiple systems, causing

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neurohormonal imbalances, significantly involving the circulatory and gastrointestinal systems.<sup>4</sup> Together, these result in a catabolic state and poor nutritional intake, leading to weight loss, reduced body mass, fatigue, abdominal discomfort, lack of appetite and reduced quality of life.<sup>4,5</sup>

Patients with HF commonly report thirst, and it is caused by the activation of the renin-angiotensin-aldosterone (RAAS) and sympathetic nervous systems, including HF treatments, such as diuretic treatments.<sup>6</sup> This increased thirst has been reported to lower patients' quality of life, with those with a higher New York Heart Association (NYHA) classification experiencing more severe thirst.<sup>7,8</sup> Thailand is a tropical country, and the Thai diet is high in salt, which can raise plasma osmolarity and increase thirst. These factors can lead to increased thirst but have not yet been explored in any detail among Thai patients with HF and those with CC.

There is also a lack of evidence assessing symptoms related to CC in Thai patients with HF. This might be due to the condition being infrequently found among patients with HF, as indicated in the Thai HF guideline.<sup>9</sup> This could lead to under-assessment for CC,

which has been previously identified among patients undergoing cardiac surgery.<sup>10</sup> However, the cachexia consensus by Evans et al.<sup>5</sup> has not been applied in these cases. Technologies like bioelectrical impedance vector analysis (BIVA) have been used to identify cachexia. Nonetheless, evidence of using these methods in the Thai population is lacking.

Given that CC is under-assessed and its symptoms among Thai patients with HF have not been examined, applying a quantitative approach to CC diagnosis helps this study to identify relevant participants that can then be further assessed qualitatively and to help provide a measurable and experiential understanding of HF patients in Thailand who have CC. A mixed methods approach overcomes the limitations of purely qualitative or quantitative studies alone, especially when exploring complex issues,<sup>11</sup> as may be found in chronic health conditions and rare disease populations.<sup>12</sup> Hence, a mixed-method design was deemed suitable for this study. A conceptual framework was developed to illustrate the research processes in this study, detailing the methods used for data collection, analysis, and interpretation (**Figure 1**).

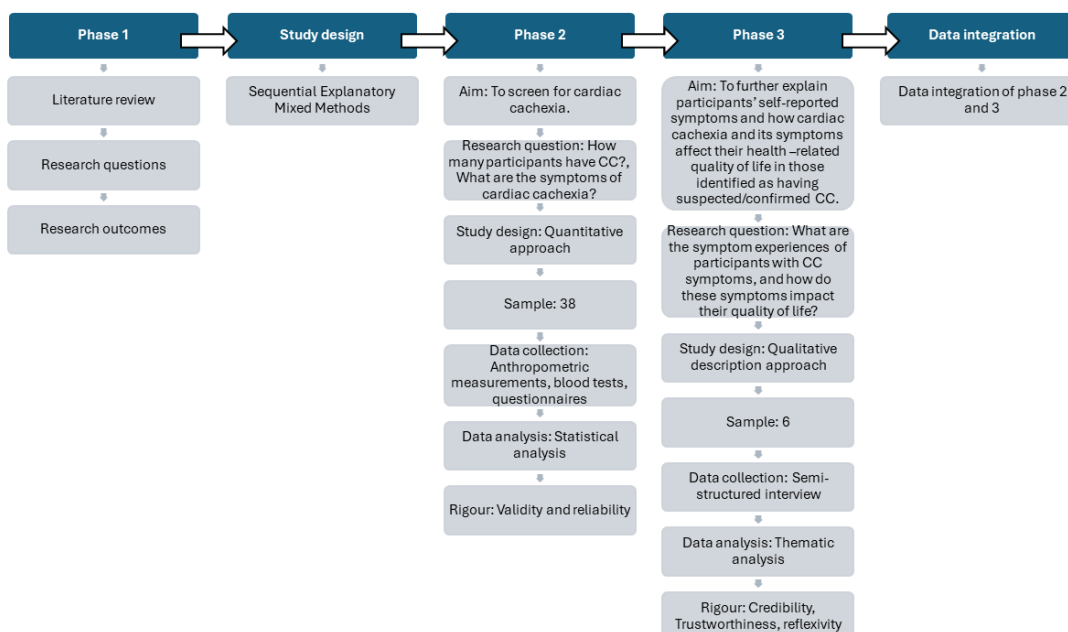


Figure 1. Conceptual framework of the use of sequential explanatory mixed methods

## Literature Review

CC involves several mechanisms, including hormonal imbalances, changes in the gut system, and the activation of inflammatory processes. Poor circulation further complicates the activation of the RAAS by elevating glucocorticoids and inflammatory mediators such as interleukins and cytokines. Together, these affect gut epithelium, making it susceptible to inflammation and infection and altering absorption.<sup>4</sup> Due to higher catabolic and lower anabolic rates, body weight loss and muscle depletion are observed among patients with CC.

As mentioned above, cachexia consensus by Evans et al.<sup>5</sup> has been used to identify CC. Recently, the Asian Cachexia Working Group released a cachexia consensus specifically for Asian populations.<sup>5,13</sup> Furthermore, bioelectrical impedance analysis (BIA) can generate parameters to plot a BIVA graph to diagnose CC. Two types of frequencies in BIA are used to evaluate body composition: single frequency and multiple frequency (MF-BIA). For individuals with HF, MF-BIA is recommended due to its ability to penetrate cells and assess fluid levels for accurate body composition calculations.<sup>14</sup> In fact, cardiac-cachectic symptoms have been previously identified in the literature following changes in its pathophysiology. Gastrointestinal symptoms such as poor appetite, bloating, nausea, vomiting, and fatigue have been reported among patients with CC. However, thirst has not yet been explored among patients with CC despite the shared similarities in RAAS activation. This is because angiotensin II levels are significantly higher in those with CC than those without CC ( $123.0 \pm 20.0$  pg/ml vs  $74.0 \pm 10.0$  pg/ml,  $p < .05$ ).<sup>15</sup> Thailand, where this study was undertaken, has a tropical climate with maximum temperatures frequently exceeding 40 degrees Celsius and humidity levels of 73–80%,<sup>16</sup> leading to insensible loss. Combined with HF treatments

and diet in Thailand, this results in decreased plasma volume and increased osmolarity, leading to intensified thirst. Interestingly, the brain's appetite and thirst regulation also involve similar pathways, which may interact.<sup>17</sup> The literature reports that heightened thirst can lower food intake, potentially worsening anabolic rates in patients with CC.

## Study Aim

This study aimed to quantitatively identify CC in Thai patients with HF and examine its impact on the quality of life, thirst and appetite in those with suspected or confirmed CC, then using qualitative interviewing to explore their experiences or insights regarding the condition.

## Method

**Study Design:** We used a mixed-method sequential explanatory design, beginning with a quantitative phase followed by a qualitative descriptive phase to help build on the quantitative findings. Quantitative and qualitative methods were given equal priority in this study (**Figure 1**). This study adhered to eight steps outlined for a mixed-method study by Johnson and Onwuegbuzie<sup>18</sup> The EQUATOR guidelines (COREQ and STROBE) were adhered to in the reporting of this study.

## Quantitative Phase

**Recruiting Process, Sampling and Setting:** A convenience sampling approach was employed to recruit participants from an outpatient HF clinic in Thailand in a single tertiary hospital. The prevalence of HF and/or CC in Thailand was not known at the time of this study, and participants were recruited during a defined period, the duration of which was dependent upon financial and human resources available to the study. A nurse screened clinic attendees for eligible potential participants each week. Inclusion criteria included adult patients attending an HF clinic

with a chronic HF diagnosis who could consent. Exclusion criteria were the presence of active cancer, hyperthyroidism, end-stage renal disease of non-cardiac origin, limb amputation, and liver dysfunction of non-cardiac origin.

All recruited participants underwent screening for CC using cachexia consensus as mandatory screening and BIVA as alternative screening due to

contraindications (for example, cardiac implantable electronic devices). Participants were categorized according to cachexia consensus criteria as ‘non-CC’ and those with ‘confirmed or suspected CC’ (Table 1). Body mass index (BMI) thresholds for CC required a population-related adjustment based on the World Health Organization guidelines<sup>19</sup> and previously used to define CC, including recommendations from Thai dieticians.

**Table 1.** Diagnostic criteria for cachexia

<b>Diagnostic criteria for cachexia using the international cachexia consensus<sup>5</sup></b> <b>(Two major criteria and three minor criteria need to be met to diagnose cachexia)</b> <b>(Mandatory diagnostic criteria)</b>	<b>Diagnostic criteria for cachexia using BIVA</b> <b>(Alternative diagnostic criteria)</b>
<b>Major criteria</b>	
1. Chronic diseases, such as chronic heart failure, chronic kidney disease, etc.	1. Using BIVA: the vector falls below 95% in the lower right quadrant <sup>20</sup>
2. Oedema-free body weight loss $\geq 5\%$ in the past 12 months or BMI $< 18.5 \text{ kg/m}^{2\ast,19}$	2. Normal oedema index (0.360–0.390).
<b>Minor criteria</b>	
1. Low fat-free mass index	
2. Fatigue	
3. Anorexia	
4. Reduced muscle strength	
5. Haemoglobin 12 g/dl	
6. Serum albumin 3.2 g/dl	
7. Elevated C-reactive protein $> 5.0 \text{ mg/l}$	

<sup>\ast</sup>BMI was adapted to be suitable for Asians, according to the World Health Organization.

dl = decilitre, etc = et cetera, g = Gram, kg = Kilogram, l = litre, m = metre

**Instruments:** The instruments used in this study are listed below, along with brief information on their usage, validity, and reliability.

*The Jamar dynamometer* for grip strength (model number 5030J1) was used to indicate muscle strength and prognostic predictor accurately.<sup>5</sup> The average of the three recorded values was then calculated and compared with the normal grip strength values for Thai populations.<sup>21</sup> The assessment was conducted following the protocol outlined by the American Society of Hand Therapists.<sup>22</sup>

*The Lange Skinfold Caliper* for skinfold thickness (model number 85300) by Beta Technology,<sup>TM</sup> Santa

Cruz, California, was utilized in this study to obtain a lean body mass index (LBMI). Also, an excellent intra-class correlation coefficient between DEXA and four skinfold thickness measurements of biceps, triceps, subscapular and supra iliac muscles in identifying percentage body fat ( $r^2 = 0.94$ ),<sup>23</sup> allowed for the accurate determination of LBMI. The instruction by the Sport Sciences Bureau, Thailand,<sup>24</sup> to assess skinfold thickness was followed.

*Bioelectrical impedance analysis (BIA) for BIVA graph:* The INBODY S10<sup>TM</sup> is a MF-BIA was used to assess body compositions and generate a BIVA

graph. In this graph, a vector outside the 95% ellipse in the right lower quadrant indicates cachexia.<sup>20</sup>

*The Simplified Nutritional Appetite Questionnaire (SNAQ)* is recommended for assessing anorexia in cachexia.<sup>5</sup> It consists of four questions, including those that ask about the level of appetite and meal frequency, and has a 5-point rating scale. The SNAQ has a reported Cronbach's alpha of 0.77.<sup>25</sup>

*The Thirst Distress Scale for Heart Failure (TDS-HF)* is specifically used to assess thirst in patients with HF. It contains eight items, including questions about thirst causing dry mouth and discomfort, with a rating scale where higher scores indicate greater thirst distress. The Cronbach's alpha of the original English version of the TDS-HF was reported to be 0.90.<sup>26</sup>

The SNAQ and TDS-HF were not available in Thai. Therefore, these two instruments were translated into Thai using a forward-backward translation process. The forward translation was conducted by native Thai speakers specializing in HF, academia, and linguistics, while native English speakers completed the backward translation. Expert panels reviewed and agreed upon the Thai versions of the TDS-HF and the SNAQ, which were subsequently piloted and examined for reliability and validity in patients with HF. Cronbach's alpha of 0.84 and 0.91 were reported for the SNAQ and TDS-HF, respectively.

*The Kansas City Cardiomyopathy Questionnaire (KCCQ)* was used to evaluate quality of life. It consists of 23 items, grouped into four quartiles, covering physical limitation, symptoms, self-efficacy, social limitation, and overall quality of life. The Thai version of the KCCQ is available and has been tested for reliability and validity.<sup>27</sup>

After the screening, each participant with suspected CC was discussed, and the diagnosis was confirmed in consultation with their cardiologist. Two participants were identified as confirmed CC and five with suspected CC. Of the seven participants identified, six were subsequently invited for interviews, as one participant died due to cardiac causes.

**Data Collection:** The data were collected solely by the primary investigator (PI) in the HF clinic, with each session taking approximately 30–45 minutes to complete, between August and November 2022. After obtaining written informed consent, demographic and clinical data, including body weight, grip strength, and questionnaire responses, were gathered.

**Data Analysis:** The normality of data distribution in the two groups was assessed using the Shapiro-Wilk test. The independent-sample t-test and Mann-Whitney U test were used to analyze data according to distribution. Fisher's exact test was used to analyze categorical variables. The p-value  $\leq 0.05$  indicates statistical significance. IBM SPSS Statistics 28 was used for statistical analysis.

## Qualitative Phase

**Design:** The approach used was qualitative description to further explore participants' experiences and perceptions of CC symptoms and their impact on quality of life. This approach offers a straight description of experiences and perceptions and is suitable for areas where the topic is less known and under investigation.<sup>28</sup> Hence, this approach was appropriate for this study.

**Recruiting Process, Sampling, and Setting:** Participants were purposively sampled based on their CC diagnosis. They were informed before participating in the quantitative phase that they would be contacted if cachexia was detected during the screening. Additionally, participants needed internet access at home for online interviews and could provide consent.

**Data Collection:** Semi-structured interviews were conducted by the female PI, a native Thai-speaking PhD researcher trained to conduct interviews. The interviews followed a qualitative semi-structured interview guide framework proposed by Kallio et al.<sup>29</sup> The interview questions were devised by PI and reviewed by the research team to investigate the symptoms of CC and their impact on quality of life. The questions were not piloted in the interviews before the main

interviews. The questions included: *What are your eating habits? How is your level of appetite? How is your thirst? and How do your symptoms (such as appetite, thirst, fatigue) affect your quality of life?* All interviews were conducted in Thai using LINE™ (a communication app that can be installed on mobile phones and other electronic devices) and lasted 30–45 minutes. Participants were given instructions before their interview. Both audio and video were recorded during the interviews to facilitate data analysis, allowing for a more in-depth understanding of the subject matter. Subsequently, interview data were anonymized and transcribed. The data were collected between December 2022 to January 2023. The interviews were not repeated.

**Data Analysis:** The datasets comprised 96 pages of transcripts. Six transcriptions from six participants were translated from Thai to English by the PI, and the accuracy of the translation was verified by a native Thai speaker who was part of the research team. The transcriptions were coded using NVIVO 12 Pro software. A thematic analysis approach was employed following Braun and Clarke's<sup>30</sup> framework to analyze the data.

**Trustworthiness:** Research rigor was ensured throughout the data collection and analysis, including credibility, transferability, reliability for thematic analysis and reflexivity. The translation of the transcriptions from Thai to English was done by the PI and rechecked by the research team to ensure the accuracy of the language. The coding processes and grouping themes were completed and subsequently cross-checked with two researchers in the team. Details of how data were collected and analysed were also provided in the previous sections. The qualitative findings are supported by participants' quotes describing their experiences. Reflexivity was maintained throughout the data collection or analysis stages.

**Data integration:** The findings from the two phases of the study were analyzed separately. 'Following a thread technique' was employed to identify the main

findings in the quantitative data, which were then used to create questions to further explain these findings. The results from each approach were integrated into a table to illustrate the process of combining the findings side-by-side. The quantitative and qualitative data results are reported using an analytical approach outlined by Östlund et al.<sup>31</sup> In this study, qualitative findings complemented the quantitative results, leading to a triangulated and complementary analytical approach.

**Ethical Considerations:** Before obtaining written consent, information sheets and consent forms were mailed to participants before their appointments, allowing them time to read and ask questions. At the clinic, the PI reiterated information about the research before patients signed the consent form. Only patients who provided written consent were included in the study. Ethical clearances were obtained from King's College London (HR/DP-21/22-2317) and the Siriraj Institutional Review Board, Faculty of Medicine Siriraj Hospital, Mahidol University (certificate of approval no. Si 105/2022). The research adhered to the ethical principles outlined in the 1964 Declaration of Helsinki and its subsequent revisions. Prior to their involvement in the study, all participants provided written informed consent. Information that could potentially reveal the identities of the individuals was removed from the data.

A portion of the results from the current study were presented at the Association of Cardiovascular Nursing and Allied Professions Congress in June 2023, Edinburgh, United Kingdom, and the abstract was published in the proceedings.<sup>32</sup>

## Results

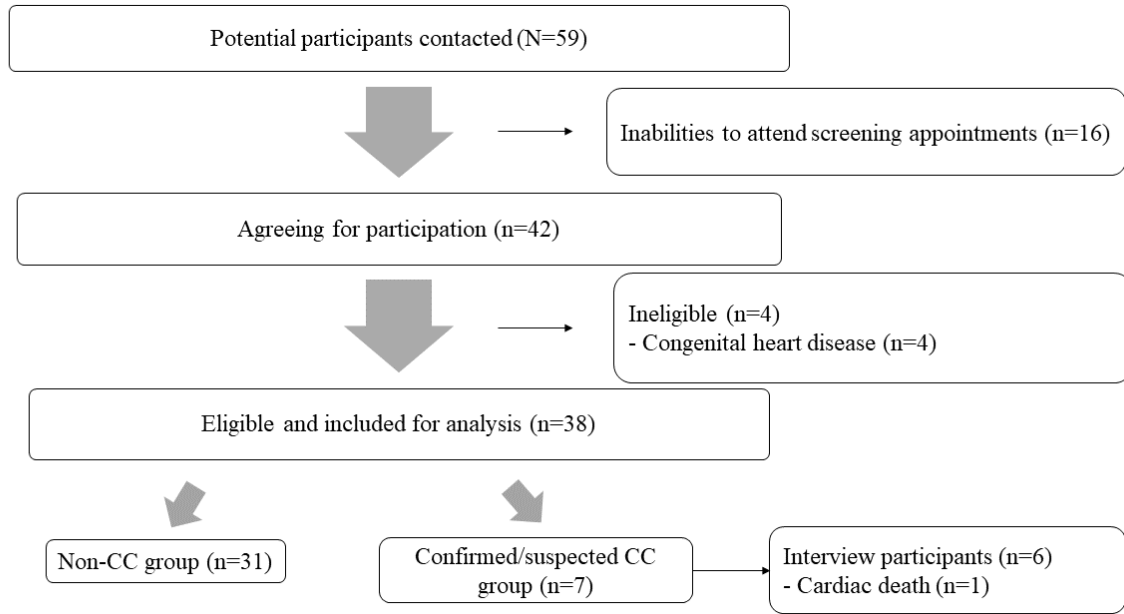
### Identifying cardiac cachexia

Fifty-nine participants were initially contacted, and 42 agreed to participate. Of these, four were excluded due to the presence of congenital heart disease (**Figure 2**). As a result, 38 participants were included

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in the analysis, non-CC (n = 31) and those with confirmed or suspected CC (n = 7) (Table 3). Four out of seven participants in the CC group and 15 out

of 31 participants in the non-CC group underwent BIA measurements.



**Figure 2.** Recruiting process

**Table 2.** Cut-off points used in this study

Types	Cut-off points
1. Fatigue	Yes/No
2. Anorexia	SNAQ $\leq 14$
3. Reduced muscle strength <sup>21</sup>	- Men (normal range: age below 60 years old > 39 kg; age over 60 years old > 30 kg) - Women (normal range: age below 60 years old > 24 kg; age over 60 years old > 18 kg)
4. Thirst scores	The higher scores demonstrate higher thirst.
5. Quality of life scores <sup>27</sup>	0 to 24: very poor to poor; 25 to 49: poor to fair; 50 to 74: fair to good; 75 to 100: good to excellent
6. Oedema index	> 0.039 indicates oedema

Most participants were prescribed HF medications, including beta-blockers, diuretics, angiotensin-converting enzyme Inhibitors (ACEIs), and angiotensin receptor/neprilysin inhibitors (ARNIs). No differences were noted in body compositions, lean body mass (LBM), percent body fat (PBF), body weight, height

and BMI, between CC and non-CC groups (Table 3). Similarly, haemoglobin, albumin and C-reactive protein (CRP), including N-terminal pro b-type natriuretic peptide (NT-proBNP) and serum osmolarity, were not significantly different between the groups (Table 3).

The BIA parameters measured were phase angle (PA), indicating fluid and/or nutritional status, and oedema index (OI), indicating fluid accumulation. There was no significant difference between non-CC group and CC groups in either of these parameters (PA: 4.59±1.04 vs 4.38±1.57, p-value = .748; OI:0.400±0.015 vs 0.405±0.018, p-value = .565) (Table 3).

Moreover, only four of 19 participants who underwent BIVA had a normal OI and were therefore eligible for using the alternative criteria for CC (Table 3). According to the standard cachexia consensus criteria, one of these four participants eligible for the alternative criteria was diagnosed with CC. However, BIVA did not identify CC in participants.

**Table 3.** Clinical characteristics

Characteristics	Frequency (percentage, %)		p-value
	Non-CC (n = 31)	CC (n = 7)	
Gender			
Men	23 (74.2)	7 (100)	0.307
Women	8 (25.8)	0 (0)	
NYHA Functional Classification			
I	0 (0)	0 (0)	0.276
II	25 (80.6)	4 (57.1)	
III	6 (19.4)	3 (43.9)	
IV	0 (0)	0 (0)	
Ejection fraction			
HFrEF	26 (83.9)	6 (85.7)	0.752
HFmrEF	3 (9.7)	1 (14.3)	
HFpEF	2 (6.4)		
Pitting oedema			
Yes	4 (12.9)	2 (28.6)	0.223
No	27 (87.1)	5 (71.4)	
Fatigue			
Yes	11 (35.5)	0	0.084
No	20 (64.5)	7 (100)	
Age, Mean (SD)	61.0(11.9)	59.6(11.3)	0.773
<b>Anthropometric measurements, Mean (SD)</b>			
Body weight, Mean (SD)			
Men	71.90(15.6)	74.8(15.6)	0.413
Women	62.2(15.1)	0	
Height			
Men	168.8(8.8) <sup>#</sup>	171.0(9.0)	0.162
Women	155.3(5.8)	0	
Body mass index, Mean (SD)			
Men	25.1(4.2)	25.5(4.7)	0.721
Women	25.9(6.4)	0	



**Table 3.** Clinical characteristics (Cont.)

Characteristics	Frequency (percentage, %)		p-value
	Non-CC (n = 31)	CC (n = 7)	
Waist circumferences, Mean (SD)			
Men	93.6(13.7)	99.9(12.3)	0.649
Women	98.9(11.4)	0	
Grip strength, Mean (SD)			
Men	28.6(9.7)	29.7(9.5)	0.641
Women	20.4(6.4)		
Skinfold thickness, Mean (SD)			
Men	70.9(25.1) <sup>#</sup>	67.0(20.0)	0.451
Women	88.9(24.3)		
Percent body fat, Mean (SD)			
Men	30.7(3.7) <sup>#</sup>	30.1(5.2)	0.204
Women	39.8(4.0)	0	
Lean body mass index, Mean (SD)			
Men	17.3(2.5)	17.7(2.3)	0.481
Women	15.5(3.4)		
<b>Biomarkers</b>			
Haemoglobin level (g/dl), Mean (SD)			
Men	13.3(1.9)	13.0(3.3)	0.969
Women	12.1(2.0)		
Albumin (g/dl), Mean (SD)	4.2(0.3)	4.3(0.5)	0.556
C-reactive protein (mg/dl), Median	1.3	4.4	0.209
NT-proBNP, Median (Range)	1,957(237-16,297)	3,889(36-12,566)	0.209
Serum osmolarity, Mean (SD)	293.6(7.9)	291(7.6)	0.438
<b>BIA and BIVA parameters</b>			
Oedema index, Mean (SD)	0.400(0.015)	0.405(0.018)	0.565
Phase angle, Mean (SD)	4.6(1.0)	4.4(1.6)	0.748

<sup>#</sup>Statistical differences between gender (p-values ≤ 0.05); CC = cardiac cachexia, HFrEF = heart failure with reduced ejection fraction, HFmrEF = heart failure with mildly reduced ejection fraction, HFpEF = heart failure with preserved ejection fraction, kg = kilogram, m = metre, NYHA = New York Heart Association, SD = standard deviation  
 BIA= Bioelectrical impedance analysis, BIVA = Bioelectrical impedance vector analysis, CC = cardiac cachexia, dl = decilitre, g = gram, kg = Kilogram, m = metre, NT-proBNP = N-terminal pro-brain natriuretic peptide, NYHA = New York Heart Association, SD = standard deviation

The SNAQ was not statistically significant in the CC group compared to the non-CC group (13.14±2.41 vs. 15.07±2.28, p-value = .054, 95% CI: -3.88, 0.03) (Table 4). The TDS-HF scores and quality of life scores were not statistically different

between those with suspected/confirmed and with no CC (TDS-HF scores: 20.57±7.28 vs. 19.74±9.54, p-value = .678, quality of life scores: 60.71±24.40 vs. 66.67±24.06, p-value = .556).

**Table 4.** Thirst, appetite and quality of life scores

	Non-CC (n = 31)	CC (n = 7)	p-value
<b>Symptoms measurements</b>			
SNAQ, Mean (SD)	15.1(2.3)	13.1(2.4)	0.054
TDS-HF score, Mean (SD)	19.7(9.5)	20.6(7.3)	0.678
Quality of life score, Mean (SD)	66.7(24.1)	60.7(24.4)	0.556

CC = cardiac cachexia, SD = standard deviation, SNAQ = Simplified Nutritional Appetite Questionnaire, TDS-HF = Thirst Distress Scale for Patients with Heart Failure

### Interview Findings

In this study, semi-structured interviews were conducted with six participants (Figure 2). Subsequently, the interviews revealed two themes: 1) changes in diet and thirst and 2) reduced physical activity.

#### Theme 1: Changes in diet and thirst

All the participants reported making changes to their diet; primarily, they intentionally reduced the amount of food they ate and also attempted to change their diet to lose weight (for example, to reduce blood glucose levels, especially in those with a diagnosis of diabetes and the need to improve physical fitness). The majority also reported their experience of thirst (4/6 participants) and how they alleviated it, such as sipping and drinking water.

*‘I have less food than before. I control my diet for a while, and then I get used to it. In the past, I like having sweet food, soft drinks, but now I cut it off roughly 70–80% ... Because I want to control my body weight, and I have high blood sugar.’* (male, 69 years old)

*‘I have food but I avoid having carbohydrate. I mostly have grass noodle soup or plain grass noodle soup or something like that. ... I had a lot of food in one meal before, but I change my eating habits now. ... I lose weight and it is good. I feel healthy .. previously, I got tired very easy and out of breath.’* (male, 48 years old)

*‘I get thirsty sometimes. Because in the restaurant, I can reach water easily. If I get thirsty, I drink water. But sometimes, when I do not drink water for a while, I am very thirsty. ... I almost finish one*

*bottle of water [500 millilitres] at once. I drink water around 300 or 400 millilitres because I usually drink a lot of water. I drink a lot of water.’* (male, 50 years old)

Although changes in thirst and diets resulted in long-term food reduction, most participants reported no impact on their quality of life.

*‘It is not like that. It is just normal like usual.’* (male, 52 years old)

*‘Ah no, no they do not [impact on daily activities/quality of life]. They do not [impact on daily activities/quality of life].’* (male, 69 years old)

#### Theme 2: Reduced physical activity level

A significant reduction in physical functioning and engagement in physical activities was reported (4/6 participants). The participants also reported diminished endurance levels during physical activities, disrupting their normal daily activities.

*‘But I feel that I have little energy, and I want to have more something like that ... I can also lift some stuff, but I know that I should have more energy and muscle power. I think I am not strong enough.’* (male, 50 years old)

*‘Yes, I have that [fatigue] sometimes. When I do just small activities, I get tired. I am tired like after I finish working out. ... When I have fatigue, I do not want to go out, I do not want to do anything, I cannot do much. ... When I do some activities, I am out of breath. I then lie down, and I feel like I get tired easily. After lying down for a little while, I get better.’* (male, 52 years old)

**Integration of quantitative and qualitative findings**

**Table 5** demonstrates the side-by-side data integration of quantitative and qualitative findings. The qualitative findings complemented the quantitative

results by confirming changes in diet and thirst, aligned with the alternations of appetite and thirst scores, but without impact on quality of life and the decrease in physical activity among participants with CC.

**Table 5.** Data integration

Quantitative	Qualitative	Integration of quantitative and qualitative data
Identifying potential participants with CC	Number of participants with suspected and confirmed CC for interview	Participants identified with CC in the quantitative approach were subsequently interviewed to explain the quantitative findings.
Reduced appetite and moderate thirst were reported among participants with confirmed and suspected CC	<p>Theme 1: Changes in thirst and appetite</p> <p>Example of patient’s experiences</p> <p><i>‘I have less food than before. I control my diet for a while then I get used to it. In the past, I like having sweet food, soft drinks, but now I cut it off roughly 70-80% ... Because I want to control my body weights, and I have high blood sugar.’</i> (male, 69 years old)</p> <p><i>‘I get thirsty sometimes. Because in the restaurant, I can reach water easily. If I get thirsty, I drink water. But sometimes that I do not drink water for a while, I am very thirsty. ... I almost finish one bottle of water [500 millilitres] at once almost. I drink water estimate 300 or 400 millilitres because I usually drink a lot of water. I drink a lot of water.’</i> (male, 50 years old)</p>	<p>The quantitative findings show reduced SNAQ and moderate thirst scores among participants with CC, indicating low appetite and thirst. The qualitative findings support these results, revealing that changes in thirst and diets among participants, highlighting changes in diets lead to a long-term decrease in food desire.</p>
Quality of life	<p>Theme2: Reduced physical activities</p> <p><i>‘But I feel that I have little energy and I want to have more something like that ... I can also lift some stuff, but I know that I should have more energy and muscle power. I think I am not strong enough.’</i> (male, 50 years old)</p>	<p>During the interviews, a decrease in physical activities was reported. This aligns with the quality of life scores ranging from fair to good.</p>

## Discussion

This study involved screening for CC within the Thai HF population. Of the participants with HF screened, seven were diagnosed with confirmed/suspected CC. No differences were observed in the SNAQ, thirst and quality of life scores between the two groups (**Table 3**). The study explored participants' experiences with symptoms perception, and they reported reduced physical activity and thirst and exerted control over their food intake, potentially leading to long-term diminished food desires and decreased food consumption.

While the appetite scores did not reveal a significant difference between groups, the 95% confidence interval leans towards a reduction in appetite with the minimal crossing of the zero line (**Table 3**). Confirming this trend would necessitate a larger sample size. It is noteworthy that five out of seven participants within CC reported low appetite, signified by an SNAQ score < 14. This aligns with existing literature, which associates the lack of appetite<sup>33</sup> with changes in gut physiology in CC. This lack of appetite contributes to body weight loss; thus, the findings highlight the utility of using the SNAQ as a screening tool for body weight loss. It can detect 5% body weight loss with 81.3% sensitivity and 76.4% specificity.<sup>34</sup> Therefore, the SNAQ could serve as a useful screening tool for CC. Additionally, all participants in the CC group were male. However, a previous study has reported a potential association between gender and appetite, indicating that females have less desire for food than males.<sup>35</sup> Therefore, this might affect the finding. Additionally, the higher incidence of CC in male patients may be linked to factors, such as heart failure with reduced ejection fraction (HFrEF), ischemic heart disease, mitochondrial dysfunction, and a lower prevalence of oestrogen protective factors.<sup>36-38</sup>

These factors have been reported more frequently in males compared to females. Indeed, including

females in this group might enhance our understanding of CC symptom characteristics. During interviews, participants in the CC group reported reduced food intake and dietary changes, without making beneficial adjustments, such as increasing protein intake. This reduction might decrease overall appetite and increase the risk of inadequate muscle-building nutrients. Hence, there is a need for an education program, particularly focusing on dietary adjustments, for participants with CC in Thailand.

Although thirst is reported among patients with HF in previous studies, it has not been examined in patients with CC.<sup>7</sup> This study reports on thirst in patients with CC from Thailand. Together with the thirst scores, serum osmolarity was utilised to further investigate thirst. Serum osmolarity can induce thirst when it reaches  $285.23 \pm 1.29$  mOsm/kg.<sup>39</sup> This study found serum osmolarity levels exceeded this threshold in both CC and non-CC, which aligns with the elevated thirst scores in both groups. However, there was no significant difference between the groups' elevated osmolarity or thirst scores (**Table 3**). These insignificant differences may be due to factors influencing heightened thirst in HF, such as stage of HF, sodium intake, diuretic usage, occupations, and local weather conditions, particularly in the tropical climate of Thailand.

During the interviews, participants' experiences of thirst were also reported. Consequently, this study affirms the presence of thirst in CC in the Thai population. This highlights the importance of assessing thirst and advising Thai patients with HF on thirst self-management, including adjusting fluid intake and techniques to alleviate thirst. It may also involve reviewing fluid restriction, limiting it to only patients with advanced HF and those with hyponatremia as outlined in the European Society of Cardiology heart failure guideline.<sup>1</sup>

This study reports the insignificance of quality-of-life scores in the participants with CC compared to participants with non-CC (**Table 4**). Similarly, participants with CC experienced decreased physical

activities, suggesting a reduced quality of life. Likewise, Krysztofiak et al. reported that CC impedes quality of life.<sup>40</sup> Furthermore, among participants with CC, a finding of fatigue, described as reduced physical activities, emerged during interviews despite being unreported in initial screenings. This suggests an intermittent perception of fatigue in HF and differences in describing fatigue among participants. This corresponds with the previous report of fatigue in patients with HF, regardless of the presence of CC.<sup>41</sup> Indeed, CC remains relatively unfamiliar in Thailand, and therefore, participants did not mention it. Similarly, participants in this study were queried regarding their familiarity with CC, and it was observed that 81.6% of participants had no prior knowledge of it. Likewise, in East Asian countries such as Japan, only 17.4% of healthcare professionals assessed patients for cachexia.<sup>42</sup> These data indicate that CC remains unrecognized by patients and healthcare professionals.

BIVA was employed as a diagnostic tool for identifying CC by using raw data, indicating fluid and nutritional status. However, the majority of participants had a high OI. According to the criteria outlined in **Table 1**, these participants were deemed ineligible to use this alternative criterion. Using BIVA in participants with fluid instability presents challenges despite its intended ability to address this concern. This is because, in the presence of fluid accumulation, the BIVA plots tend to deviate from the 95% ellipse, typically falling outside the 95% ellipse in the lower-left quadrant rather than the lower-right quadrant where CC is indicated. This excess fluid could be observed in patients with HF with high NT-proBNP levels, as the negative correlation between phase angle and NT-proBNP suggests possible fluid overload.<sup>32</sup> Similarly, we found a high median of NT-proBNP in both groups, potentially indicating fluid overload. Indeed, fluctuations in body weight among patients with HF throughout the year complicated weight reviews in this study, making CC diagnosis and screening challenging. Additionally, in Asian countries like Thailand, the absence of LBM

reference values for Thai populations can pose a challenge. However, due to the shared similarities of Vietnamese and Thai populations, supported by geographical and genetic proximity, the normal range of Vietnamese LBM index was employed.<sup>43,44</sup> Moreover, skinfold thickness and the percentage of body fat were higher in females than males, which is in line with the literature as females have a higher adipose tissue distribution than males.<sup>45</sup>

## **Limitations**

Several limitations need to be acknowledged; the sample sizes of suspected and confirmed cases of CC were low and data collection was from a single urban hospital and these are an important limitation. Future studies with larger sample sizes are necessary to investigate this further. Moreover, it is acknowledged that more biomarkers, such as interleukin-1 and angiotensin II, could enhance cachexia investigation. However, due to resource limitations, these tests were not feasible. Additionally, this study was conducted at a single centre. In the future, multicentred studies are encouraged to better understand CC among Thai patients with HF.

It is worth noting that the establishment of HF clinics in Thailand is still in its early stages, mainly within university hospitals. In the clinic where participants were recruited, criteria, such as ejection fraction below 40% and advanced HF, for patients with HF to register are employed, resulting in approximately 160 registered patients. This results in 15–20 patients visiting the clinic weekly for follow-up. Also, the clinic operates two mornings a week, constraining the time available for data collection, resulting in a small sample recruited, which could be considered as a key limitation of this study. Due to the small sample size, the number of participants for interviews was limited. Although data saturation was not reached, the main themes began to recur before data collection concluded.

## Conclusion

This study examined CC in Thailand. This study suggests a potential low appetite among CC. Reducing food intake in participants with CC can possibly have negative long-term consequences, such as reduced long-term appetite. Therefore, this suggests that the SNAQ could be applied in practice to assess changes in appetite and screen for CC in patients with HF. Nurses can play a role in using the SNAQ and providing suitable dietary recommendations for this group of participants, aiming to promote and maintain a healthy muscle mass. Thirst should be assessed in patients with HF, with nurses and multidisciplinary teams providing recommendations on how to manage it. A decreased physical activity in participants with CC was reported, which could hinder quality of life. BIVA could be useful for screening for CC. However, OI should be reasonably taken into consideration when interpreting results. Additionally, further research is required to establish reference values for LBM and explore CC in Thai patients with HF using a larger sample size.

## Implications for Nursing Practice

Our findings show the potential for integrating the utilisation of the SNAQ, the TDS-HF and BIVA into Thai clinical practice to identify symptoms, including changes in appetite, thirst, quality of life and nutritional status. This would enable tailoring recommendations for patients and screening for CC. Moreover, nurses can facilitate early detection of CC and prompt intervention by using these assessments in collaboration with a multidisciplinary team involving dietitians and cardiologists. This collaborative approach enhances healthcare providers' awareness and proficiency in identifying and managing CC, ultimately contributing to improved patient outcomes and quality of life. Further research should focus on co-creating educational programs for managing CC with patients and healthcare providers. These programs should be evaluated for

their impact on patient outcomes and their effectiveness in facilitating nursing management of this condition.

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# ความเข้าใจในโรคผอมแห้งหุ้มกระดูกในผู้ป่วยโรคหัวใจล้มเหลวโดยการ วิจัยแบบผสมผสานเชิงอธิบาย

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**บทคัดย่อ:** ภาวะผอมแห้งหุ้มกระดูกพบได้บ่อยในผู้ป่วยโรคหัวใจล้มเหลวนำมาซึ่งน้ำหนักที่ลดลงจากการสูญเสียกล้ามเนื้อและความอยากอาหารที่ลดลง ผลกระทบของอาการเหล่านี้ต่อคุณภาพชีวิตของผู้ป่วยยังไม่ทราบแน่ชัด งานวิจัยนี้มีวัตถุประสงค์เพื่อตรวจหาภาวะผอมแห้งหุ้มกระดูกในผู้ป่วยโรคหัวใจล้มเหลว รวมถึงอาการ และ ผลกระทบต่อคุณภาพชีวิต โดยใช้วิธีการวิจัยแบบผสมผสาน เก็บข้อมูลที่คลินิกโรคหัวใจล้มเหลว กรุงเทพมหานคร ประเทศไทย ระหว่างเดือนสิงหาคม พ.ศ. 2565 ถึง เดือนมกราคม พ.ศ. 2566 ผู้ป่วยได้รับการตรวจหาภาวะผอมแห้งหุ้มกระดูกโดยใช้เกณฑ์การวินิจฉัย และ เครื่องมือทำงานโดยใช้เทคนิคการวัดค่าความต้านทานของกระแสไฟฟ้าต่อเซลล์ในร่ายกายชนิดเวคเตอร์ ผู้เข้าร่วมวิจัยตอบแบบสอบถามความอยากอาหารฉบับง่าย แบบประเมินอาการกระหายน้ำและผลกระทบจากการกระหายน้ำในผู้ป่วยโรคหัวใจล้มเหลว และแบบประเมินคุณภาพชีวิต (Kansas City Cardiomyopathy Questionnaire) จากนั้นผู้ป่วยที่ได้รับการวินิจฉัยภาวะผอมแห้งหุ้มกระดูก หรือ สงสัยว่ามีภาวะผอมแห้งหุ้มกระดูกได้รับการสัมภาษณ์เพื่อหาผลกระทบของอาการจากภาวะผอมแห้งหุ้มกระดูกต่อคุณภาพชีวิต

ข้อมูลจากผู้ป่วยโรคหัวใจล้มเหลวจำนวน 38 ราย ได้รับการวิเคราะห์ โดยแบ่งผู้ป่วยเป็นสองกลุ่มคือ กลุ่มที่ได้รับการวินิจฉัยภาวะผอมแห้งหุ้มกระดูก หรือ สงสัยว่ามีภาวะผอมแห้งหุ้มกระดูก และ กลุ่มที่ไม่พบภาวะผอมแห้งหุ้มกระดูก ผู้ที่ได้รับการวินิจฉัยภาวะผอมแห้งหุ้มกระดูก หรือสงสัยว่ามีภาวะผอมแห้งหุ้มกระดูกมีคะแนนความอยากอาหารในระดับต่ำ อย่างไรก็ตาม ไม่มีความแตกต่างอย่างมีนัยสำคัญของคะแนนความอยากอาหาร การกระหายน้ำ หรือ คุณภาพชีวิต ระหว่างผู้ป่วยทั้งสองกลุ่ม ข้อมูลจากการสัมภาษณ์ผู้ที่ได้รับการวินิจฉัยภาวะผอมแห้งหุ้มกระดูก หรือ สงสัยว่ามีภาวะผอมแห้งหุ้มกระดูก สามารถระบุได้เป็น 2 แก่นหลัก คือ การเปลี่ยนแปลงของอาหารและการกระหายน้ำ และการทำกิจกรรมที่ลดลง ซึ่งผลลัพธ์จากขั้นตอนการวิจัยเชิงคุณภาพนี้สนับสนุนผลลัพธ์จากขั้นตอนการวิจัยเชิงปริมาณ

งานวิจัยนี้รายงานการตรวจหาภาวะผอมแห้งหุ้มกระดูก หนึ่งในความพยายามแรกในประเทศไทยซึ่งพยาบาลมีบทบาทสำคัญในการระบุ และ ในการจัดการดูแลผู้ที่มีภาวะหรือมีความเสี่ยงที่จะเป็นภาวะผอมแห้งหุ้มกระดูก

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