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The Quality of Life in Heart Failure Reduced Ejection Fraction (HFrEF) Patients: A Phenomenon of Obesity Paradox

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ABSTRACT

Background: Obesity place patients at risk of cardiovascular disease (CVD). There may be an inverse relationship between obesity and CVD prognosis-a phenomenon known as the "obesity paradox". Obese HF patients might have a better prognosis, especially in terms of quality of life (QoL).
Aims: The purpose of this study was to examine the QoL of HF patients based on obesity classification.
Methods: This cross-sectional study was conducted at the HF clinic of Hasna Medika Cardiovascular Hospital, Cirebon, Indonesia. Samples were HFrEF patients who had received medication at the HF clinic for at least 6 months and the patient must have received optimal *guidelines directed medical* therapy (GDMT) with at least 3 pillar drugs according to Indonesian heart failure guidelines. Inclusion criteria were HF patients with ejection fraction <40% on echocardiographic examination. Exclusion criteria were HF patients with motor impairments, such as post-stroke, severe osteoarthritis, paralysis, and patients who did not receive optimal GDMT.
Results: A total of 40.3% sample were obese, 9.7% were underweight and 67.5% had central obesity. Coronary artery disease (89.6%), smoking (67.5%) and hypertension (49.4%) were the most common comorbidities and risk factors found. About 12.3% of sample experienced rehospitalization 3 times a year. Based on Kansas City Cardiomyopathy Questionnaire (KCCQ)-12, about 3.2% of the sample had poor QoL, 55.8% had good QoL and 9.7% had excellent QoL. HFrEF patients with excellent QoL had a proportion of 66.7% obese and 20% overweight. While there were no obese patients in HFrEF patients with poor QoL. The proportion of HFrEF patients with excellent QoL who had central obesity was 80%. Meanwhile, 65.1% of HFrEF patients with good QoL were obese.
Conclusion: Obese HF patients have better QoL outcomes. This phenomenon is called obesity paradox. A good quality of life in HF patients is an important goal of HF management in addition to reducing mortality.

Keywords: *Heart failure; HFrEF; Obesity; Obesity paradox; Quality of life*.
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1. Introduction

Heart failure is a clinical syndrome with symptoms and/or signs caused by structural and or functional disorders of the heart with elevated natriuretic peptide levels and/or evidence of pulmonary or systemic congestion. The ineffectiveness of the heart in receiving or pumping blood leads to impaired perfusion of organs. As a result, the patient feels several symptoms and signs, such as shortness of breath, limb oedema, rales, increased jugular venous pressure, etc. (Golla et al., 2024; Schwinger, 2021). The condition of reduced left ventricular ejection <40% accompanied by progressive left ventricular dilatation and cardiac remodeling is called heart failure reduced ejection fraction (HFrEF) (Aizawa, 2020). Good quality of life (QoL) is an important target in the treatment of HFrEF patients in addition to reducing mortality. The QoL of HFrEF patients shows how much impact is caused by HF symptoms, both limitations in carrying out daily activities and social activities (Albakri, 2018; Murphy et al., 2020).

Atherosclerosis Risk in Communities (ARIC) study showed several comorbidities in HFrEF patients that affect mortality and QoL (Pandey et al., 2020). One of the comorbidities thought to be associated with mortality and QoL is obesity. Obesity causes morphological and functional changes of the cardiovascular system. The pathogenic mechanisms of obesity are associated with left ventricular remodelling, epicardial fat accumulation, endothelial dysfunction and microvascular coronary dysfunction (Horwich et al., 2018; Lembo et al., 2024). Although increased BMI and obesity place patients at risk of CVD, research suggests that there may be an inverse relationship between obesity and CVD prognosis-a phenomenon known as the “obesity paradox”. Studies show that obese HF patients have a better prognosis than lean HF patients, especially in terms of QoL (Hamzeh et al., 2017). So this study aims to examine the QoL of HF patients based on obesity classification.

2. Methods

Study design and sample

A cross-sectional study was conducted at the HF clinic of Hasna Medika Heart Hospital, Cirebon, Indonesia, which is one of the HF clinics in Indonesia. The samples in this study were HFrEF patients who treated at the HF clinic and had received heart failure therapy for 6 months. All patients included in this study were HF patients who had received optimal guidelines directed medical therapy (GDMT) or at least 3 pillars of therapy according to the Indonesian HF guidelines. The sample technique used was consecutive sampling with the inclusion criteria being HF patients with ejection fraction <40% on echocardiographic examination results. Heart failure patients with motor impairment, such as post-stroke, severe osteoarthritis, paralysis, and patients who did not receive optimal GDMT were excluded.

Data collection and definition of variables

The data for this study were collected through secondary data from medical records and primary data, by physical examination and questionnaires. Data collected through medical records, including gender, age, risk factors for HF, comorbidities and rehospitalization. Physical examination was conducted to measure weight, height and waist circumference. Body mass index (BMI) was then calculated and categorized based on the BMI classification for Indonesia population into [1] underweight: BMI <18.5 kg/m2; [2] normal: BMI 18.5-25 kg/m^2; [3] overweight: BMI >25-27 kg/m^2; and [4] obese: BMI >27 kg/m^2 (Kementerian Kesehatan Republik Indonesia, 2018). Waist circumference was categorized as central obesity if ≥90 cm in male and ≥80 cm in female (Kementerian Kesehatan Republik Indonesia, 2021).

Quality of life

Quality of life was assessed using Kansas City Cardiomyopathy Questionnaire (KCCQ-12) that was translated into Indonesia language and tested for validity and reliability. The KCCQ-12 consists of 12 questions regarding: [1] physical limitation (showering, walking, jogging); [2] symptom frequency (swelling, fatigue, shortness of breath, paroxysmal nocturnal dyspnoea); [3] quality of life (enjoyment of life, life satisfaction); and [4] social limitation (hobbies/recreation, working, social life)(Spertus et al., 2020). We modified the question on the questionnaire

from walking 1 block on level ground to walking ±80 meters because Indonesian people are more familiar with meters as distance measurement. The questionnaire has been tested for validity (r >0,312) and reliability (Cronbach's α>0,6). The total score of KCCQ-12 ranged from 12-70 and QoL was categorized as: poor (score 12-26), fair (score 27-41), good (score 42-56) and excellent (score 57-70).

Statistical analysis

Continuous data is described through mean and standard deviation. Categorical data were described by frequency and percentage. In this study, sub analysis of the distribution of gender, age, BMI, central obesity and rehospitalization based on QoL was carried out in the form of percentages and displayed using bar charts.

Ethical approval

Eligible patients were given informed consent before data were collected. All data were confidential and only used for research purposes. This study has received ethical exemption from health research ethics committee of Gunung Jati General Hospital Indonesia, No. 042 / LAIKETIK / KEPKRSGJ / XII / 2019.

3. Results

There were 154 sample participating in this study, comprising 68.8% males and 31.2% females. The majority of samples were aged 45-64 years (64.9%) and 5.2% were younger (<45 years). A total of 40.3% samples were obese, 9.7% were underweight and 65.6% had central obesity. In this study, 12.3% of HFrEF patients underwent rehospitalization more than 3 times a year. Based on the KCCQ-12, there were 3.2% of samples who had poor QoL and 31.2% had good QoL. The characteristics of this research sample are summarized in Table 1 below.

Table 1. Characteristics and QoL of HFrEF patients (N=154)

Characteristics		n (%) or Mean ± SD
Gender	Male	106 (68.8)
	Female	48 (31.2)
Age (years)	<45	8 (5.2)
	45-64	100 (64.9)
	≥65	46 (29.9)
	Age in year; Mean±SD	58.95 ± 8.84
BMI	Underweight	15 (9.7)
	Normal	47 (30.5)
	Overweight	30 (19.5)
	Obese	62 (40.3)
	BMI in kg/m2; Mean±SD	24.57 ± 4.89
Central obesity	No	50 (32.5)
	Yes	104 (67.5)
	Waist circumference in cm, Mean±SD	92.9 ± 14.07
Rehospitalization (per year)	0	41 (26.6)
	1	38 (24.7)
	2	56 (36.4)
	≥3	19 (12.3)
Quality of life	Poor	5 (3.2)
	Fair	48 (31.2)
	Good	86 (55.8)
	Excellent	15 (9.7)

Abbreviations: BMI, body mass index; SD, standard deviation

Figure 1 shows the proportion of comorbidities and risk factors of HFrEF patients in this study. The Figure illustrates that coronary artery disease (CAD) is the most common risk factor for HFrEF patients, followed by smoking and hypertension, with the percentages of 89.6%, 67.5% and 50% respectively.

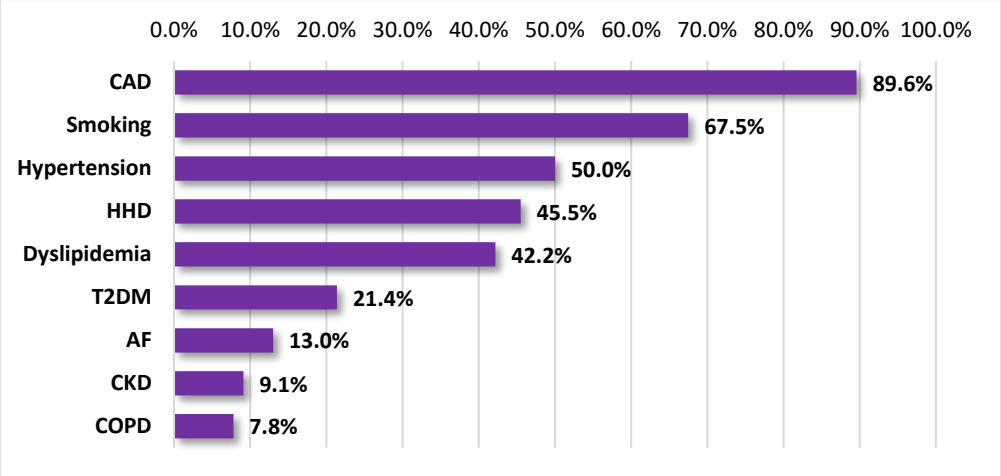

Figure 1. Comorbidities and risk factors of HFrEF patients

Abbreviations: T2DM, type 2 diabetes mellitus; AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; HHD, hypertensive heart disease; CKD, chronic kidney disease;

The proportion of responses from the KCCQ-12 that indicate quality of life is described in Figure 2. Darker colours on the bar chart indicate more severe complaints. It can be seen that he most severe symptoms are shortness of breath, fatigue and physical limitation while jogging.

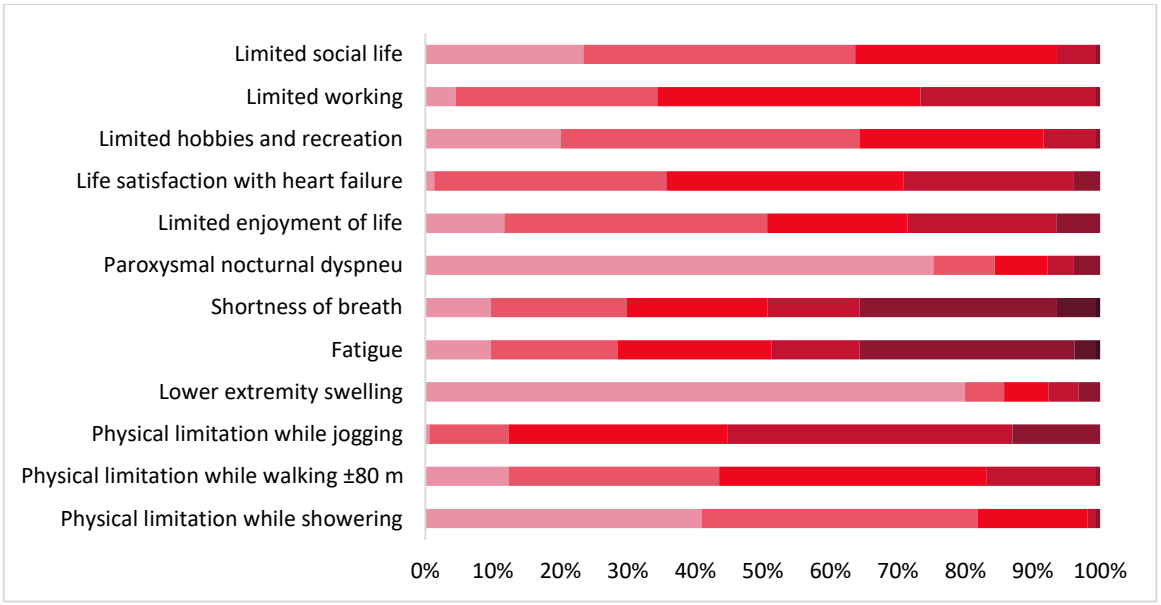

Figure 2. The proportion of answers on KCCQ-12. Darker colors indicate more severe symptoms.

The distribution of gender, age, BMI, central obesity and rehospitalization based on QoL in HFrEF patients is presented in Figure 3. In HFrEF patients who had poor QoL, 60% were female and 40% male, while in good and excellent QoL, there was a smaller proportion of females (good QoL 29.1% and excellent QoL 26.7%). Among them with poor QoL, all were ≥45 years old with the majority being ≥65 years old (60%). Whereas in good and excellent QoL, the proportion of younger age (<45 years old) was 5.8% and 13.3% respectively. In addition, the proportion of those aged ≥65 years who had good QoL was also lower (32.6%), and none had excellent QoL.

The proportion of BMI in poor QoL showed that 20% were underweight, 20% were overweight and none were obese. Conversely, in good QoL, the proportion of underweight was 11.6%, overweight 20.9% and obese 38.4%. Likewise, in excellent QoL, no underweight was found but 20% were overweight and 66.7% were obese. Central obesity in poor QoL was 60%, good QoL was 65.1% and excellent QoL was 80%. In poor QoL, 60% of HFrEF patients were hospitalized ≥3 times a year. Whereas in good and excellent QoL, the rehospitalization rate was found to be less frequent.

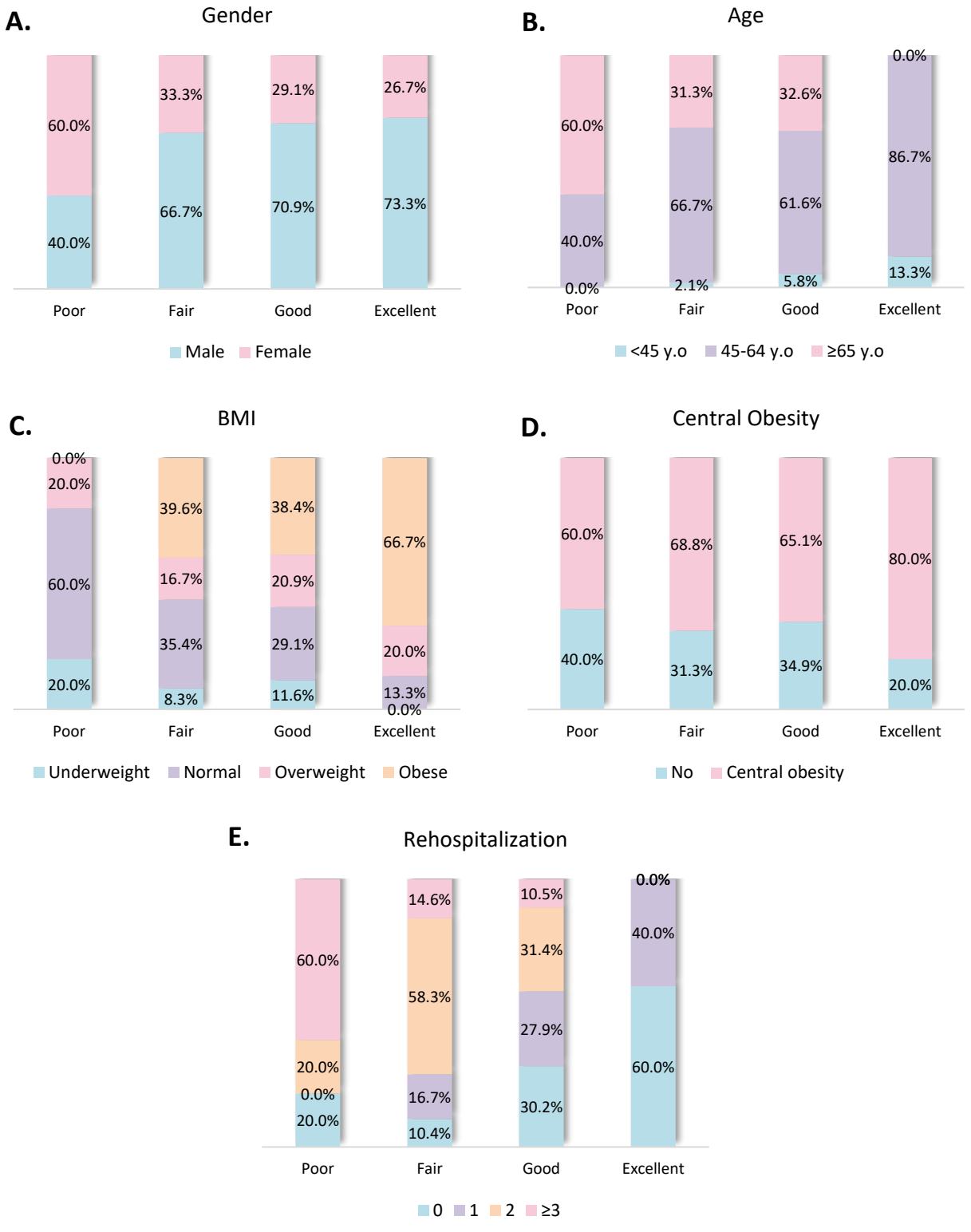

Figure 3. Distribution of gender, age, BMI, central obesity and rehospitalization by QoL

Figure 4 displays the distribution of QoL in obese HFrEF patients. The results showed that obese II patients had more excellent QoL than obese I patients (44% and 29.7% respectively).

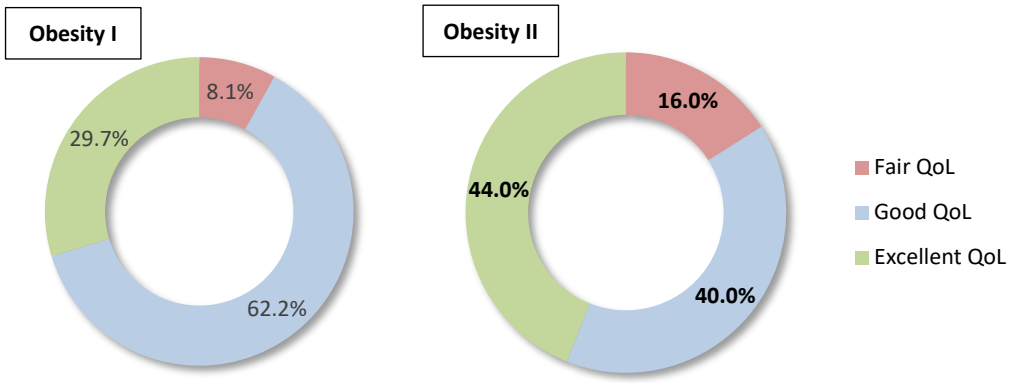

Figure 4. QoL in obese HFrEF patients

4. Discussion

Obesity is often associated with cardiovascular (CV) risk factors, such as hypertension, diabetes, and dyslipidemia, which have a harmful impact on cardiac function (Sattar et al., 2024). Obesity increases the risk of developing HF. In fact, obesity can be considered a perfect storm for CV disease which is the main cause of HF (Lembo et al., 2024). However, there are also many study reports that show that obesity may play a better role in HF patients regarding their quality of life (Donini et al., 2020).

Based on the data of this study, the prevalence of HF patients is mostly at a relatively young age (45-64 years), most of them are obese (40.3%) and central obesity (67.5%). But interestingly, HF patients who have received HF therapy for 6 months, although obese, have a good quality of life (55.8%) based on the KCCQ-12 questionnaire. In more detail, the quality of life of obese HF patients is better. Obese patients showed an excellent quality of life of 66.7% and a good quality of life of 38.4%. Likewise, in HF patients with central obesity, 80% of patients have excellent quality of life and 65.1% with good quality of life. Obesity and central obesity are two different conditions. Including these two categories in this study is expected to show that both conditions have better quality of life outcomes than lean HF patients. This shows the "obesity paradox" in HF patients. There are several things that might cause this, obese HF patients will have more metabolic reserves, more protective cytokines or adipokines, higher response to the renin-angiotensin-aldosterone system and higher blood pressure. These will increase muscle mass and strength which will maintain cardiorespiratory fitness. And the relatively higher blood pressure will make it easier to optimize the HF treatment dose (Chen et al., 2019; Rafaqat, 2023).

The exact mechanism to explain the obesity paradox is still unclear. There are several hypotheses that attempt to explain this. First, it relates to malnutrition/inflammatory syndrome complex (MICS) and endotoxin/lipopolysaccharide hypothesis. Endotoxin/lipopolysaccharide hypothesis that explains obesity and its inverse relationship. Based on the MICS concept, it is believed that cardiac cachexia is an independent risk factor of mortality. Hypoalbuminemia and increased tumor necrosis factor will occur in cardiac cachexia. These conditions will cause inflammation which is considered to be the link between cachexia and HF mortality. Second, the endotoxin/lipid hypothesis which suggests that lipids in the circulating blood will bind to endotoxins and prevent their unwanted effects. Hyperlipidemia provide more molecules to bind the endotoxins and prevent the inflammatory response. This theory might explain the role of lipids in neutralizing the harmful effects of obese HF patients. Another theory also explains that HF is a catabolic condition, obese HF patients have more metabolic reserves and, thus have a better prognosis, and muscle shrinkage in lean HF patients leads to worse outcomes (Hamzeh et al., 2017; Khan et al., 2021).

The quality of life of HF patients is certainly related to the rate of rehospitalization. This study also shows a similar thing where HF patients who have good and excellent quality of life rarely experience rehospitalization (figure 3E). This explanation may also be related to a higher risk of rehospitalization for cardiac cachexia. Studies show that HF patients with cardiac cachexia have a worse prognosis associated with worse decline in LV function (Fröhlich et al., 2022; Hweidi et al., 2021).

The term obesity paradox is not without debate. Most of the debate is about the measurement of obese classification based on BMI. The limitation of using the BMI measure is that the index does not take into account the body composition consisting of muscle, fat, and bone. It also does not reflect the distribution of fat in the body, such as visceral, subcutaneous or ectopic fat. Indeed, BMI conflates pathologies that may be completely unrelated. This knowledge highlights the importance of assessing body composition using indices other than BMI especially in patients with HF. Another study on the obesity paradox in HF included natriuretic peptide levels in its assessment, which is the most important prognostic biomarker in HF. As a result, the terminology of obesity paradox is widely opposed, while others suggest using the 'obesity paradigm', as its existence seems very obvious (Hobbach et al., 2024; Sato & Von Haehling, 2023).

Limitations and Future Research

This study only used BMI as a classification of obesity. Alternative anthropometric measurement than BMI, such as waist circumference to height ratio (WHtR) can be used for next research. WHtR can be a strong predictor in CVD patients, with a more accurate estimation of central adiposity. The advantage of WHtR also does not consider ethnic and gender differences.

5. Conclusion

Obese HF patients have better QoL outcomes. This phenomenon is called obesity paradox. A good quality of life in HF patients is an important goal of HF management in addition to reducing mortality.

Conflict of Interest

There is no conflict of interest to declare.

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