J. Phys. Ther. Sci. 31: 462–465, 2019

The Journal of Physical Therapy Science

Case Study

Association between changes in subcutaneous fat mass and heart failure-induced cachexia: a case report

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Abstract. [Purpose] We investigated whether an increase or decrease in subcutaneous fat mass secondary to cardiac cachexia can be evaluated using diagnostic ultrasonography in patients with heart failure. [Participant and Methods] We report a case of cardiac cachexia in a patient in whom cachexia was confirmed by weight loss, decreased dietary intake, and biochemical indicators measured by blood tests. We measured the subcutaneous fat mass in the patient's thigh using ultrasonic diagnostic equipment during the cachectic state, as well as 1 and 2 months later. [Results] An increase in weight and ultrasonographically documented femoral subcutaneous fat mass was confirmed by improvement in heart failure-induced cachexia. [Conclusion] Clinically convenient ultrasonic diagnostic equipment is useful to assess subcutaneous fat mass, which serves as an indicator of the degree of cachexia.
Key words: Cachexia, Femoral subcutaneous fat mass, Heart failure

(This article was submitted Dec. 15, 2018, and was accepted Feb. 19, 2019)

INTRODUCTION

Cachexia has been reported to be complicated by cancer as well as by respiratory and cardiovascular diseases, and it has been documented as causing numerous physical problems[1–3)], such as weakness due to low activity, skeletal muscle atrophy due to malnutrition and skeletal muscle catabolism autophagy[1–4)]. In contrast, heart failure cachexia has been reported to be associated with 8–48% of patients with heart failure[5, 6)], although the severity of heart failure (using the NYHA cardiac function classification) and cachexia are not correlated, and are considered independent risk factors[7)]. Moreover, in addition to usual cachexia pathology, heart failure cachexia has been reported to specifically increase metabolism and decrease fat mass[8, 9)]. In recent years, it has been documented that body weight and body mass index (BMI) are closely related to the survival prognosis of patients with heart failure and that these are extremely important factors[10–12)]. Several aspects regarding the development of cardiac insufficiency cachexia, and in particular, its important pathological mechanism still remain unclear. However, to date, no clear specification regarding the assessment of the fat mass of cachexia in heart failure is available as well as no clear understanding of the pathological condition involved. In the present report, we describe our experience with a patient who showed prominent weight loss, decreased meal intake, and decreased subcutaneous fat mass due to cachexia in heart failure. We aimed to confirm both the increase and decrease of the subcutaneous fat mass in the cachectic condition using ultrasonic diagnostic imaging and to capture the improvement course.

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PARTICIPANT AND METHODS

Here, we report a case of a patient who had developed cachexia in heart failure. After hospitalization due to heart failure, lower limb muscule strength and daily living behavior were preserved, but on the other hand appetite decline and weight loss appeared and accompanied cachexia (Table1). The observation period was 120 days from the onset of heart failure, and the progress of cachexia was confirmed during 5–20 days after onset. As a treatment for cachexia in the patient during the observation period, using the insights provided by Flynn et al., a standard physical therapy and a low intensity exercise regime, combined with nutritional status reports, were provided at the pace of 5 days/week[13–15]. Moreover, based on the study by Aquilani et al., the patient received appropriate guidance regarding meals and nutritional intake by administrative nutritionists[16, 17]. The determination criterion for cachexia in the present study was assessed based on weight loss rate, appetite loss, nutritional status, and hemoglobin values, as described by Evans et al[18]. Each of these metrics was measured every month to follow improvement in the patient's condition. In particular, dietary intake (1,450 Kcal/day), weight (kg), and BMI were measured as cachexia-related parameters. The values for the brain natriuretic peptide (BNP), Albumen (Alb), and hemoglobin (Hb) were obtained from the blood data. The lower limb thigh was used as the site for the evaluation of the subcutaneous fat mass[9], which was measured using the ARIETTA Prologue, an ultrasonic diagnostic imaging machine (Hitachi, Tokyo, Japan). For this measurement, the patient was placed in a supine position, and LOGIQLEAN Hard Type Gel (GE Healthcare Japan, Tokyo, Japan) was painted completely on the front of the femoral skin, the femoral subcutaneous fat, and the rectus femoris muscle. For generating its recordings, the machine exerts considerable pressure on these areas of the body (Figs. 1A and 1B). The area of the subcutaneous fat layer and the area of the rectus femoris muscle were calculated using the image analysis software IMAGE J[20] from cross section of the ultrasonic image, and the average and standard deviation of the values of from three measurements were adopted. Thereafter, these data were visually examined. This study was conducted in accordance with the Declaration of Helsinki and sufficient informed consent was obtained in writing and verbally from the patient, paying attention to the protection of personal information.

RESULTS

Dietary intake and body weight decreased at the onset of cachexia, and same two metrics subsequently increased as the cachexia improved, shown in Fig. 2 and Table 3. Numerous assessments of the patient's nutritional status showed unfavorable values during the occurrence of cachexia (Table 2). The subcutaneous fat area at the time of weight loss showed low value, but this increased with the subsequent weight gain (Figs. 2 and 3).

DISCUSSION

The results of the present study confirmed a decrease in dietary intake, a decrease in body weight, and a decrease in the amount of subcutaneous fat at the onset of cachexia. Several findings of decreased appetite have been reported at the onset of cachexia, and it is widely believed that this is caused by the decrease in blood flow in the gastrointestinal tract resulting

Table 1. Patient characteristics

Gender	Female
Age (years)	91
Body weight (kg)	33.8
Height (cm)	154
Quadriceps (MMT)	4
FIM Motor (points)	62
FIM Cognitive (points)	29

MMT: Manual Muscle Testing; FIM: Functional Independence Measure.

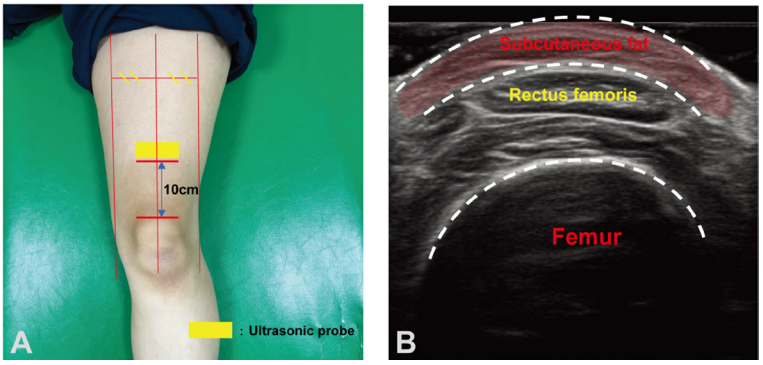

Fig. 1. A: Measurement position of ultrasonic imaging method.
Measurements were taken at the knee extension in a supine position. The ultrasonic probe was on the straight line in the center of the thigh and the height was 10 cm from the patella.
B: Analysis of ultrasonic image.
Measurements were taken at the knee extension position in a supine position. The ultrasonic probe was on the straight line in the center of the thigh and the height was 10 cm from the patella.

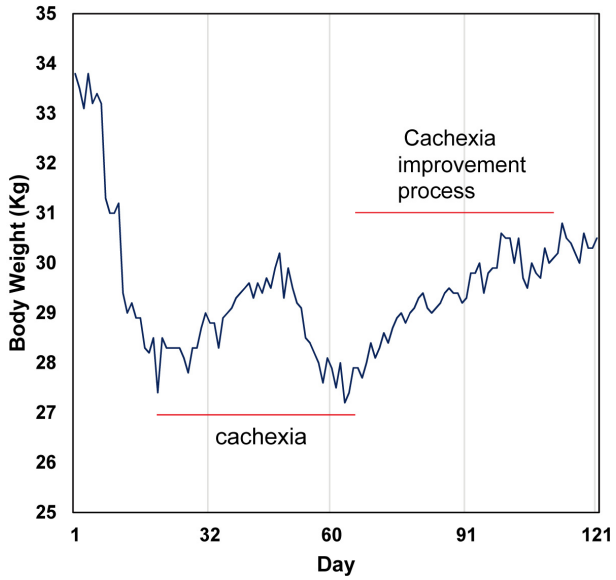

Fig. 2. Change in body weight.
Body weight was measured daily from onset and was observed for 120 days. Weight loss due to cachexia was confirmed at about 20 days.

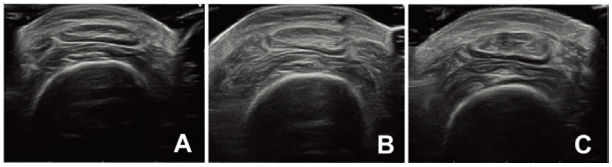

Fig. 3. Femur subcutaneous fat mass ultrasonic image by heart cachexia.
A: Cachexia (60-day stage). B: 1 month after onset of cachexia (100-day stage). C: 2 months after onset of cachexia (120-day stage). Reduction of subcutaneous fat mass and atrophy of rectus femoris muscle were confirmed.

Table 2. Body weight and blood test data in a cachexia patient with heart failure

Stage	HF	Cachexia	Cachexia 1M	Cachexia 2M
Body weight (kg)	33.8	27.4	29	30.3
BMI (kg/m^2)	14.2	11.5	12.2	12.7
BNP (pg/mL)	477.2	616.1	445.8	326.1
ALB (g/dL)	3.8	2.4	3.4	3.5
Hb (g/dL)	10.7	7.1	10.4	11.8
CRP (mg/dL)	0.36	6.16	0.14	0.13

BNP: brain natriuretic peptide; ALB: albumen; Hb: hemoglobin; CRP: C-reactive protein; HF: Immediately after heart failure; Cachexia: Immediately after onset of cachexia (60-day stage); Cachexia 1M: 1 month after cachexia onset (100-day stage); Cachexia 2M: 2 months after cachexia onset (120-day stage).

Table 3. Food intake and femur subcutaneous fat mass in a cachexia patient with heart failure

Stage	HF	Cachexia	Cachexia 1M	Cachexia 2M
Food intake (%)	60.5 (13.4)	68.2 (11.7)	68.6 (16)	74.3 (10.6)
Femur subcutaneous fat mass	-	66.4 (0.3)	99 (0.3)	99.5 (0.5)

The data values represent the mean (± standard deviation). Food intake is the average value up to that period, femoral subcutaneous fat mass is the average value of three measurements on the same measurement day.
HF: Immediately after heart failure; Cachexia: Immediately after onset of cachexia (60-day stage); Cachexia 1M: 1 month after cachexia onset (100-day stage); Cachexia 2M: 2 months after cachexia onset (120-day stage).

from a decrease in cardiac output, thereby causing the inflammatory cytokines to act directly on the brain and producing the decreased appetite[16]. Regarding body weight loss, certain studies have reported that the development of heart failure is often accompanied or partly caused by a long-term increase in calorie consumption and the metabolism of the resulting excess weight is closely related to the severity of heart failure[8, 12]. Following the event, it often happens that the caloric ingestion and expenditure balance become negative because of a decrease in calories consumed that results from a decrease in appetite, thereby producing a decrease in body weight[9, 19]. Regarding the decrease in subcutaneous fat mass due to heart failure, it is well established that systemic lipid metabolism increases substantially with energy metabolism of acute heart failure patients with a BNP of ≥200 and an ejection fraction of ≤55%[21]. It is considered that the enhancement of lipid metabolism is supposed to be promoted also in cachexia and heart failure the influence of both sides. The course of improvement in cachexia in the present case was accompanied by a gain in body weight caused by an increase in meal intake, and an increase in the fat

mass was confirmed. In heart failure, the amount of fat mass is closely related to life prognosis[10–12], because it is recognized as a marker for nutritional status, which makes it an extremely important indicator.

In the present study, it was possible to evaluate subcutaneous fat using ultrasonic diagnostic equipment and to use this approach to closely follow the profile of improvement in the patient's health. These results suggest that it is useful to measure the degree of nutritional disorder and assess the weight gain as an index for evaluating cachexia in the future. As a limitation of the present study we demonstrated the use of an evaluation index by following the improvement course of one patient; however, it would be valuable to study this topic further including a larger cohort. Although we focused here on the amount of subcutaneous fat, it could be useful to reconsider the location of subcutaneous fat to be monitored because it may be characterized in adipose tissues at various sites.

Funding and Conflict of interest

There was no involvement with companies or any conflicts of interest in the preparation of this research.

ACKNOWLEDGEMENT

The author of course extends his deep appreciation to the participant analyzed in this study and to everyone who help support this research effort.

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