ORIGINAL RESEARCH ARTICLE　　　　　　　　　　　　　　　　　　　　　　　**OPEN ACCESS**

CORRELATION BETWEEN DUAL-ENERGY X-RAY ABSORPTIOMETRY (DXA) METHOD AND COMPUTED TOMOGRAPHY (CT) MEASUREMENT METHOD FOR DIAGNOSIS OF SARCOPENIA IN CHRONIC LIVER DISEASE

*,[1]Toru Ishikawa, [2]AsamiHoshii, [2]Tamaki Hokari, [1]Michitaka Imai, [1]Takashi Owaki, [1]Hiroki Sato, [1]Yujiro Nozawa, [1]Tomoe Sano, [1]Akito Iwanaga, [1]Keiichi Seki, [1]Terasu Honma and [1]Toshiaki Yoshida

[1]Department of Gastroenterology and Hepatology, Saiseikai Niigata Daini Hospital, Niigata, Japan
[2]Department of Medical Radiology, Medical Radiographer, Saiseikai Niigata Daini Hospital, Niigata, Japan

ARTICLE INFO

ABSTRACT

Background/Aims: Sarcopenia has recently been drawing attention as a factor related to the prognosis of life and quality of life of chronic liver disease. Diagnosis through muscle mass evaluation is typically performed using reference values for dual-energy X-ray absorptiometry (DXA) from the Asia Working Group for Sarcopenia (AWGS). On the other hand, consensus has not been obtained for the cut-off value of normal value in the computed tomography (CT) measurement method to be obtained from the area of the skeletal muscle or the psoas muscle. We investigated the correlation between CT method and DXA.
Materials and Methods: Chronic liver disease patients (n=150) who underwent both DXA and CT for muscle mass measurement at our hospital between October 2015 and January 2016 were investigated. Participants comprised 90 males and 60 females, with a mean age of 66.6 years. Underlying liver diseases were: hepatitis B virus (n=30), hepatitis C virus (n=60), non-alcoholic fatty liver disease (NAFLD) (n=22), and others (n=38). Hepatocellular carcinoma was present in 41 patients. We examined the correlation between DXA and CT findings.
Results: A most significant positive correlation was found between DXA and skeletal muscle index (SMI; skeletal muscle area by height squared (cm2/m2)) at the level of the third vertebra (L3) with CT attenuation (-29 to 150 HU) (r=0.90, p<0.01).
Conclusion: In order to diagnose sarcopenia, image diagnosis with objectivity is also necessary. The most accurate measurement by CT method is available for extracting the region of skeletal muscle (-29 to 150 HU) and using SMI at L3. However, considering complementarity with DXA, consideration in a large number of cases is necessary in the future.

INTRODUCTION

The liver is the most important metabolic organ (Lockwood *et al*., 1979). It is easy to induce secondary sarcopenia due to malnutrition in chronic liver disease (Silva *et al*., 2015). The rate of merger of sarcopenia in chronic liver disease is greatly influenced by diagnostic criteria (Kalafateli *et al*., 2015). Computed tomography (CT) is often taken in daily clinic but there are few reports on criteria from dual energy X-ray absorptiometry (DXA) for chronic liver diseases. Therefore, in this study, considering its versatility, we examined the correlation of optimal CT measurement method of sarcopenia with DXA based on the criteria from the Asia Working Group for Sarcopenia (AWGS) (Chen *et al*., 2016) in chronic liver disease patients.

MATERIALS AND METHODS

One hundred fifty patients with chronic liver disease who underwent DXA method and CT imaging from October 2015

Corresponding author: **Toru Ishikawa,**
Department of Gastroenterology and Hepatology, Saiseikai Niigata Daini Hospital, Niigata, Japan.

to January 2016 and measured muscle mass at our hospital. DXA was measured with Discovery QDR SERIES Wi (HOLOGIC), CT was taken at Aquilion ONE (TOSHIBA) on the same day, the iliopsoas and skeletal muscles were surrounded by region of intensity (ROI) at the level of third vertebra (L3) level and the CT value was set. Images were analyzed using SYNAPSE VINCENT V3.3 software (Fuji Film Medical Co., Ltd.) that enables specific tissue demarcation using previously reported Hounsfield unit (HU) thresholds. Skeletal muscle tissue was separated according to different density thresholds: a density value of +35HU was used to separate fat from muscle tissue and +150HU to separate muscle form bone tissue (Lauretani *et al.*, 2033). Furtherore, the skeletal muscles were identified and quantified within a HU range of -29 to 150HU (water and air defined as 0 and 1000 HU, respectively) (Mitsiopoulos *et al.*, 1998). We used CT to measure the cross-sectional area of the skeletal muscles at the levels of L3, which accurately represents the whole-body muscle mass (Shen *et al.*, 2004). The method of extracting the area the method of extracting the CT value (-29 to 150 HU) and the range of (+35 to 150 HU) were carried out. In addition, the L3 psoas muscle index (PMI) and skeletal muscle index (SMI) was expressed as cross-sectional muscle area/height squared (cm^2/m^2).

Statistical Analysis

Patient characteristics were summarized with means and standard deviations. Continuous variables were compared by Student's t-test or Mann-Whitney U test. Categorical variables were compared by Fisher's exact test. The Friedman test was used for comparison of repeated measures over time, and Bonferroni's multiple comparison correction was used for post-hoc analysis. Values of $P<0.05$ were considered statistically significant. All statistical analyses and the receiver operating characteristic (ROC) curve analysis were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics (Kanda, 2013).

Ethics Statement

The study was approved by the Institutional Review Board of Saiseikai Niigata Daini Hospital and was conducted inaccordance with the principles of the Declaration of Helsinki. All patients provided written informed consent.

RESULTS

Patient characteristics are shown in Table 1. There are correlation between DXA and L3 iliopsoas muscle area (r=0.74, p<0.01), L3 iliopsoas muscle area with CT attenuation of 35 to 150 HU (r=0.72, p<0.01), L3 PMI (r=0.72, p<0.01), L3 PMI with CT attenuation 35 to 150 HU (r=0.70, p<0.01), L3 skeletal muscle area (r=0.88, p<0.01), L3 skeletal muscle area with CT attenuation 35 to 150 HU (r=0.79, p<0.01), L3 skeletal muscle area with CT attenuation -29 to 150 HU (r=0.88, p<0.01), L3 SMI (r=0.88, p<0.01), and L3 SMI with CT attenuation 35 to 150 HU (r=0.79, p<0.01). A most significant positive correlation was found between DXA and L3 SMI with CT attenuation (-29 to 150 HU) (r=0.90, p<0.01).

Table 1. Patient characteristics

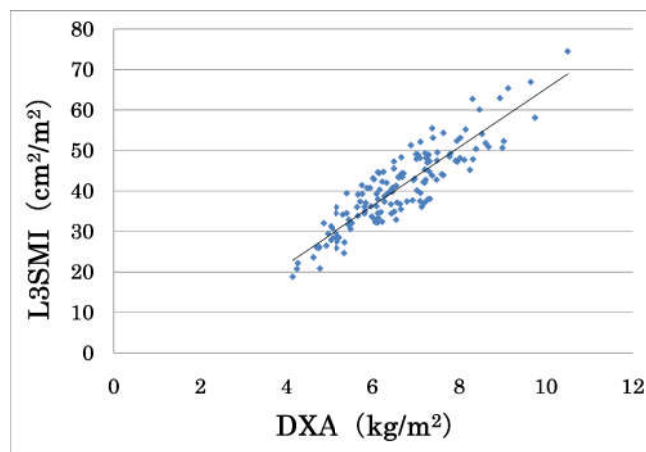| Categories	male	female
n	90	60
Age (years)	66.55±11.97	66.62±11.98
HCC/no HCC	26/64	15/45
HCC back ground	HBV/HCV/NASH/alc/other 9/11/2/3/1	HBV/HCV/NASH/other 1/12/1/1
no HCC back ground	HBV/HCV/NASH/alc/other 16/22/8/10/8	HBV/HCV/NASH/alc/other 4/15/11/2/13

r=0.90, p<0.001

Figure 1. The correlation between measure muscle mass from dual-energy X-ray absorptiometry (DXA) and skeletal muscle index (SMI) from computed tomography (CT) at the third vertebra level (L3) in patients with chronic liver disease.
* SMI: Skeletal muscle index (cm^2/m^2)

DISCUSSION

Since the liver is the central organ of carbohydrate, fat, protein and energy metabolism, the frequency of falling into protein-energy-malnutrition (PEM) especially in cirrhotic patients is high (Moctezuma-Velázquez *et al.*, 2013). PEM causes muscle atrophy and muscle weakness (Nishikawa and Osaki, 2015). "Sarcopenia" was originally a concept, and there were no definite definitions and diagnostic criteria, but standards focusing on muscle "quantity" only were first proposed by Baumgartner *et al.* in 1998. They suggested to diagnose sarcopenia if SMI is 7.26 kg/m^2 for men and less than 5.45 kg/m^2 for women by dual energy X-ray absorptiometry method (Baumgartner *et al.*, 1998). Meanwhile, SMI criteria proposed by the Asian Working Group for Sarcopenia (AWGS) mainly in Asia differs depending on the muscle mass measurement method, and in the case of using the DEXA method, the male is less than 7.0 kg / m^2, the femaleis less than 5.4 kg/m^2 (Chen *et al.*, 2014). As described above, the reference value in the case of using SMI is also various, and slight confusion occurs. The dual energy X-ray absorptiometry (DXA) method uses X-ray transmittance, which is the difference in energy attenuation that occurs when X-rays pass through a substance, by using two types of energy. It is a method of measuring bone mineral content, body fat mass, and fat free mass by irradiating with X rays.

Recently, sarcopenia has received attention as a factor related to the prognosis of life and quality of life (QOL) of chronic liver disease (Dasarathy, 2012). In the diagnosis of sarcopenia muscle mass in Japan, AWGS and Sanada *et al.* (14)proposed

by the Dual-Energy X-ray Absorptiometry (DXA) method values are used. On the other hand, there is no consensus on the normal value cut-off value in the CT measurement method to be obtained from the area of the iliopsoas or skeletal muscle. In this study we used the DXA method and CT measurement method for diagnosis of sarcopenia for chronic liver disease. The relation of correlation was investigated. CT is often taken in everyday clinical practice in liver disease. Therefore, this study aimed to determine DXA criteria from Sarcopenia criteria obtained from CT criterion and considering its versatility. SMI at L3 SMI CT value -29 to 150 HU was most correlated with male <7.0 kg/m^2 female <5.4 kg/m^2 DXA, which is the sarcopenia cutoff value (based on Sanada) at AWGS advocated DXA. In the future, further analysis and validation of each liver disease are necessary, but the Sarcopenia criteria for liver diseases when implementing DEXA at the same time as CT may be useful for treatment guidelines. In conclusion, objective diagnostic imaging is necessary for diagnosis of sarcopenia. The most accurate measurement method by CT method is the method to obtain the SMI by extracting the skeletal muscle region (-29 to 150 HU) of L 3 level, but considering the complementarity with DXA, In the future, analysis by disease and examination of validity are necessary.

Author contributions

Ishikawa T, Hoshii A and Hokari T contributed equally to this work

REFERENCES

Baumgartner RN1, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ. and Lindeman RD. 1998. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol*., 147(8):755-63.

Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, Chou MY, Chen LY, Hsu PS, Krairit O, Lee JS, Lee WJ, Lee Y, Liang CK, Limpawattana P, Lin CS, Peng LN, Satake S, Suzuki T, Won CW, Wu CH, Wu SN, Zhang T, Zeng P, Akishita M. and Arai H. Sarcopenia, 2014. in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc*., (2):95-101. doi: 10.1016/j.jamda.2013.11.025.

Dasarathy S. 2012. Consilience in sarcopenia of cirrhosis. *J Cachexia Sarcopenia Muscle*, 3(4):225-37. doi: 10.1007/s13539-012-0069-3. Epub 2012.

Kalafateli M, Konstantakis C, Thomopoulos K. and Triantos C. 2015. World J Gastroenterol. Impact of muscle wasting on survival in patients with liver cirrhosis. 21(24):7357-61.

Kanda Y. 2013. Investigation of the freely available easy-to-use software "EZR" for medical statistics. Bone Marrow Transplant, 48; 452–59.

Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, Corsi AM, Rantanen T, Guralnik JM. and Ferrucci L. 2003. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol*., 95(5):1851-60.

Lockwood AH, McDonald JM, Reiman RE, Gelbard AS, Laughlin JS, Duffy TE. and Plum F. 1979. The dynamics of ammonia metabolism in man. Effects of liver disease and hyperammonemia. *J Clin Invest*., 63(3):449-60.

Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D. and Ross R. 1998. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. *J Appl Physiol*., 85(1):115-22.

Moctezuma-Velázquez C, García-Juárez I, Soto-Solís R, Hernández-Cortés J. and Torre A. 2013. Nutritional assessment and treatment of patients with liver cirrhosis. *Nutrition*, 29(11-12):1279-85.

Nishikawa H, Osaki Y. Liver Cirrhosis: Evaluation, Nutritional Status, and Prognosis. Mediators Inflamm. 2015;2015:872152. doi: 10.1155/2015/872152.

Recent Advances in Sarcopenia Research in Asia: 2016 Update From the Asian Working Group for Sarcopenia. Chen LK, Lee WJ, Peng LN, Liu LK, Arai H, Akishita M; Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2016 Aug 1;17(8):767.e1-7.

Sanada K, Miyachi M, Tanimoto M, Yamamoto K, Murakami H, Okumura S, Gando Y, Suzuki K, Tabata I. and Higuchi M. 2010. A cross-sectional study of sarcopenia in Japanese men and women: reference values and association with cardiovascular risk factors. *Eur J Appl Physiol*., 110(1):57-65.

Shen W, Punyanitya M, Wang Z, Gallagher D, St-Onge MP, Albu J, Heymsfield SB. and Heshka S. 2004. Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. *J Appl Physiol*., 97(6):2333-8.

Silva M, Gomes S, Peixoto A, Torres-Ramalho P, Cardoso H, Azevedo R, Cunha C. and Macedo G. 2015. Nutrition in Chronic Liver Disease. *GE Port J Gastroenterol*., 22(6):268-276.

****