Effect of The Body Water and The Body Composition, Calculated by Bioelectrical Impedance Analysis, On Contrast-Enhanced Dynamic Computed Tomography Images of The Liver.

Takanori Masuda (✉ takanorimasuda@yahoo.co.jp)

Kawasaki University of Medical Welfare

Takeshi Nakaura

Kumamoto University

Yoshinori Funama

Kumamoto University

Tomoyasu Sato

Tsuchiya General Hospital

Keiko Arataki

Tsuchiya General Hospital

Takayuki Oku

Tsuchiya General Hospital

Shouko Masuda

kawamura Clinic

Shinichi Arao

Kawasaki University of Medical Welfare

Jyunichi Hiratsuka

Kawasaki University of Medical Welfare

Kazuo Awai

Hiroshima University

Research Article

Keywords: body composition, CE-DCT, BIA, HAP

Posted Date: July 24th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-691821/v1>

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Abstract

To improve its diagnosis on contrast-enhanced dynamic CT (CE-DCT) scans, contrast injection protocol must yield stable arterial contrast enhancement. To investigate how the body-water distribution and the body composition, calculated by bioelectrical impedance analysis (BIA), affect aortic and hepatic enhancement on CE-DCT scans. 236 patients with liver cirrhosis underwent CE-DCT before BIA. The CT number (in Hounsfield units, HU) of the abdominal aorta at the celiac artery level on unenhanced scans and during the hepatic arterial phase (HAP) scans was recorded. And, the mean CT number of the hepatic parenchyma of both hepatic lobes at the celiac artery level on unenhanced and portal venous phase (PVP) scans was recorded. We calculated changes in the iodine dose per contrast enhancement (mgI/HU) (IDCE) to evaluate the effect of the patient age and of various constituents of the body composition by performing BIA. The IDCE of the abdominal aorta during HAP was 121.5 ± 32.1 mgI/HU; it was 698.7 ± 211.1 mgI/HU in the hepatic parenchyma during the PVP. Among the parameters used in our BIA, the total body weight (TBW) was the most important factor affecting the IDCE of the liver abdominal aorta on CE-DCT scans acquired during the HAP ($r = 0.83$). The TBW and the skeletal muscle index most strongly affected the IDCE of the hepatic parenchyma on CE-DCT scans obtained during the PVP ($r = 0.69$). The TBW had the strongest effect on contrast enhancement. The skeletal muscle index exhibited the strongest correlation with hepatic parenchymal contrast enhancement during the PVP.

Introduction

Contrast-enhanced dynamic CT (CE-DCT) facilitates the detection of hepatocellular carcinoma (HCC) ¹⁻⁴. To improve its diagnosis on CE-DCT scans, contrast enhancement must be at least 280 Hounsfield units (HU) with vessel and 50 HU with hepatic parenchyma ^{5,6} and the contrast injection protocol must yield stable arterial contrast enhancement ^{1,7,8}.

As the patient age, sex, total body weight (TBW), height, cardiac output, and the presence of other diseases affect contrast enhancement under identical contrast injection protocols ^{9,10}, body size index such as the TBW, body mass index (BMI), body surface area (BSA), and the lean body weight (LBW) must be taken into account in patients subjected to CE-DCT ^{5,6,11-14}.

The human body contains water, protein, fat, and minerals. Because bioelectrical impedance analysis (BIA) applies frequencies ranging from 1 kHz to 1 MHz ¹⁵, it yields accurate results irrespective of the body type, -composition, and water distribution. Under the hypothesis that BIA would reveal additional factors affecting aortic- and hepatic parenchymal contrast enhancement, we investigated the effects of the water distribution and the body composition on aortic- and hepatic parenchymal enhancement on CE-DCT scans.

Methods

This retrospective study was approved by our institutional review board (Tsuchiya General Hospital); informed patient consent was waived. We adhered to the tenets of the Declaration of Helsinki.

Patients

Between January 2019 and May 2020, 251 consecutive patients with suspected liver cirrhosis underwent CE-DCT. Excluded from subsequent BIA were 2 patients with a history of allergic reactions to iodinated contrast medium (CM) and 13 hemodialysis patients because contrast enhancement did not suffice for a precise evaluation ⁹. The final study population consisted of 236 patients (143 men and 93 women). Their age ranged from 30 to 89 years.

BIA

With the patient standing upright, BIA, performed with InBody770 (InBody Japan Inc., Tokyo, Japan), was carried out an average of one hour before CT scanning. The patients' age, height, and sex, obtained from our electronic medical record system, were entered for BIA. The PA was measured at 50 kHz; the estimated segmental body composition was obtained at multiple frequencies. The direct segmental multi-frequency bioimpedance analysis method was applied using a tetra-, polar 8-point tactile electrode system; 30 impedance measurements were obtained using 6 frequencies.

For body composition determination, BIA considers the age, height, TBW, and the 16 constituents listed in Table 1 ¹⁶.

Table 1
Patient characteristics and parameters included in BIA

Age (years)	66.8 ± 11.8
Height (cm)	161.7 ± 9.1
Total body weight (kg)	64.5 ± 11.6
Total body water (l)	33.2 ± 6.6
Protein (kg)	8.8 ± 1.8
Minerals (kg)	3.1 ± 0.6
Body fat mass (kg)	19.4 ± 6.8
Soft lean mass (kg)	42.5 ± 8.5
Lean body mass (kg)	45.1 ± 8.9
Body mass index (kg/m ²)	24.6 ± 3.4
Trunk of the lean body mass (kg)	20.3 ± 4.3
Ratio of extracellular- to total body water	0.4 ± 0.1
Intracellular water (l)	20.3 ± 4.3
Extracellular water (l)	12.9 ± 2.4
Skeletal muscle mass (kg)	24.5 ± 5.4
Basal metabolic mass (cal)	1343.1 ± 192.1
Osseous mineral mass (kg)	2.5 ± 0.5
Body cell mass (kg)	29.1 ± 5.9
Skeletal muscle index (kg/m ²)	7.0 ± 1.1

CT and injection protocol

Using a 40 mm volume CT scanner (Lightspeed VCT; GE Healthcare, Milwaukee, WI), CE-DCT was performed with the patient in the supine position during a breath-hold. We scanned craniocaudally from the top of the liver to the lower end of the kidney. The scanning parameters were 0.5-sec rotation scan, 5.0-mm detector row width, 0.516 helical pitch (beam pitch), 41.2-mm table movement, 50-cm scan field of view, 120 kVp, and 100–770 mA with the automatic tube current modulation (noise index, 12). Depending on the geometry, the scanning time varied from 5 to 10 sec¹⁰.

For 30-sec CM delivery with a power injector (Dual Shot; Nemoto-Kyorindo, Tokyo, Japan) we inserted a 20-gauge catheter into an antecubital vein (600 mgI/kg, Omnipaque-300; Daiichi-Sankyo, Tokyo, Japan). Unenhanced CT images and scans obtained during the hepatic arterial- and the portal venous phase

(HAP, PVP) were inspected; to scan during the equilibrium phase (EP) we applied a 180-sec delay. For HAP scanning we used a computer-assisted bolus tracking technique to synchronize the arrival of the CM at the abdominal aorta at the level of the celiac artery with the start of scanning. To monitor the arrival of the CM, we performed axial scans of the abdominal aorta at the celiac artery level 20 sec after the start of contrast injection. Scanning started automatically 15 sec after contrast enhancement reached 100 HU in a region of interest within the abdominal aorta. For PVP scanning we started the scan 20 seconds after the HAP ¹⁰.

Contrast enhancement in the abdominal aorta and hepatic parenchyma

In all patients we measured the CT number in the abdominal aorta at the celiac artery level on unenhanced scans and during HAP. We also measured the mean CT number in the hepatic parenchyma of the right- and left hepatic lobe at the celiac artery level on unenhanced and PVP scans ¹⁰. The CT number was recorded as the pixel value within an approximately 10 mm² circular region of interest. Contrast enhancement was expressed as the change in the CT number calculated by subtracting the HU on unenhanced images from the HU recorded during the HAP and PVP. We also calculated the change in iodine dose per contrast enhancement (IDCE) (mgI/HU) to evaluate the effect of the patient age, TBW, height, and the 16 constituents comprising the body composition on the measured values obtained by BIA.

Statistical analysis

We performed univariate linear regression analysis to determine the effect of the body composition on BIA results and on IDCE of the abdominal aorta during the HAP and on enhancement of the hepatic parenchyma during the PVP. We used the Pearson product moment correlation coefficient (r) to assess the strength of associations involving normal data distributions as absolute values of r, where 0–0.19 was recorded as a very weak-, 0.2–0.39 as a weak-, 0.40–0.59 as a moderate-, 0.6–0.79 as a strong-, and 0.8–1.0 as a very strong correlation. Variables with a p value less than 0.05 were considered statistically significant. We used “R” (R, version 3.2.2; The R Project for Statistical Computing; <http://www.r-project.org/>).

Results

Table 1 shows the characteristics and the mean values returned by BIA of our 236 patients.

Contrast enhancement and IDCE on CE-DCT

Contrast enhancement of the abdominal aorta during the HAP was 327.3 ± 47.6 HU; IDCE was 121.5 ± 32.1 mgI/HU. For the hepatic parenchyma these values were 58.1 ± 11.7 HU (PVP) and 698.7 ± 211.1 mgI/HU (PVP).

Effect of body data on IDCE of the abdominal aorta on CE-DCT scans acquired during the HAP

As shown in Table 2, univariate linear regression analysis revealed a significant correlation between IDCE of the abdominal aorta and the items included in BIA (all: $p < 0.01$). The TBW had the strongest effect on IDCE on CE-DCT scans acquired in the HAP.

Table 2. Bioelectrical impedance analysis of body factors that the affect aortic and hepatic enhancement on contrast-enhanced dynamic CT scans

	Iodine dose per contrast enhancement on abdominal aorta	Iodine dose per contrast enhancement on hepatic parenchyma
Age (years)	0.01	0.23
Height (cm)	0.57	0.46
Total body weight (kg)	0.83	0.69
Total body water (l)	0.73	0.63
Protein (kg)	0.72	0.63
Minerals (kg)	0.71	0.62
Body fat mass (kg)	0.50	0.36
Soft lean mass (kg)	0.73	0.63
Lean body mass (kg)	0.73	0.63
Body mass index (kg/cm ²)	0.59	0.53
Trunk of the lean body mass (kg)	0.72	0.64
Ratio of extracellular-to total body water	0.20	0.26
Intracellular water (l)	0.72	0.63
Extracellular water (l)	0.74	0.62
Skeletal muscle mass (kg)	0.72	0.63
Basal metabolic mass (cal)	0.73	0.63
Osseous mineral mass (kg)	0.70	0.56
Body cell mass (kg)	0.72	0.63
Skeletal muscle index (kg/cm ²)	0.75	0.69

Effect of body data on IDCE of the hepatic parenchyma on CE-DCT scans acquired during the PVP

Table 2 also shows the results of univariate linear regression analysis of the correlation between IDCE of the hepatic parenchyma and the items included in BIA (all: $p < 0.01$). The TBW and the skeletal muscle index (SMI) had the strongest effect on IDCE on CE-DCT scans acquired in the PVP.

Representative images

Representative unenhanced CT-, HAP-, PVP-, and EP images are presented in Figs. 1 and 2.

Discussion

The human body is comprised of body water, protein, minerals, and body fat. The weight of human tissues such as muscles and somatic cells can be calculated from their relationship to the different components.

To our knowledge, this is the first clinical study to assess the effect of items included in BIA on IDCE on CE-CT scans of the aorta and hepatic parenchyma. In BIA, the body water- and the body components comprising the weight of the human body are further subdivided into their constituents and calculated.

The TBW exhibited the greatest effect on IDCE of the abdominal aorta scanned during the HAP, it also had the greatest effect on hepatic parenchymal enhancement observed during the PVP. The SMI most strongly affected enhancement of the hepatic parenchyma during the PVP. The other components addressed in BIA showed a moderate to high correlation with the TBW and SMI.

Earlier studies suggested that among assessed body parameters, the LBW and the BSA exhibited the strongest correlation with aortic and hepatic enhancement^{14,17}. The most commonly used parameter for determining the iodine dose has been the TBW. However, in obese patients, the iodine dose may be excessive because a large proportion of their TBW is comprised of poorly perfused adipose tissue in which iodine distributes poorly¹⁸⁻²¹. In small patients, it may also be excessive.

Ours diverge from earlier findings possibly because the difference between the LBW or the BSA and the TBW was relatively small with respect to IDCE reported earlier¹⁴. Also, while the LBW and the BSA are factors that influence IDCE more strongly than the TBW in overweight and underweight patients, the weight distribution in our subjects was very narrow and there were only a few high-weight patients.

We found that during the PVP, the SMI exhibited the greatest effect on IDCE of the hepatic parenchyma. The SMI was calculated by dividing the limb skeletal muscle mass (kg) by the square of the height (m²). The SMI is an index for the skeletal muscle mass and it is used as a criterion for the diagnosis of sarcopenia, defined as an age-related loss in the skeletal muscle mass that results in a reduction in muscular strength and physical function²². The blood vessels in muscles contain a larger blood volume than does fat; this is thought to exert a strong effect on contrast enhancement²³⁻²⁵. The SMI is highly correlated with liver fibrosis and a correlation between liver fibrosis and contrast enhancement of the hepatic parenchyma has been reported²⁶. Consequently, IDCE on CE-DCT scans may be strongly affected by the SMI.

We found that many body parameters included in BIA affect IDCE on CE-DCT images. Most exhibited a more than moderate correlation with IDCE of vessels and the hepatic parenchyma.

The performance of machine-learning algorithms applied to medical data is high and machine learning is useful for predicting clinical outcomes^{27,28}. Therefore, we think that the integration of parameters included in BIA into machine learning may yield more accurate predictions.

Our study has some limitations. Ours was a retrospective, single-center study and the study population was small. As the median and the range of the TBW of Japanese is lower than of Western populations, our findings cannot be extrapolated to non-Japanese individuals. In this study we did not compare contrast enhancement with the BSA index, we did not confirm the relationship between contrast enhancement and the image quality, and we did not address the detectability of liver tumors. These issues are currently under investigation.

In conclusion, BIA showed that among the components comprising the weight of the human body, the TBW had the strongest effect on aortic and hepatic enhancement on CE-DCT scans. With respect to hepatic parenchymal contrast enhancement during the PVP; the SMI exhibited the greatest effect.

Declarations

Author contributions

TM. (Conceived and designed the analysis, Collected the data,

Contributed data or analysis tools, Performed the analysis, Wrote the paper)

TN. (Conceived and designed the analysis, Performed the analysis, Collected the data)

YF. (Conceived and designed the analysis, Collected the data)

TS. (Conceived and designed the analysis, Collected the data)

KA. (Conceived and designed the analysis, Collected the data)

TO. (Conceived and designed the analysis, Collected the data)

SM. (Conceived and designed the analysis, Collected the data)

SA. (Conceived and designed the analysis, Collected the data)

JH. (Conceived and designed the analysis, Collected the data)

KA. (Conceived and designed the analysis, Collected the data, Contributed data or analysis tools, Wrote the paper)”

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Figures

Figure 1

CE-CT images obtained in a 49-year-old woman with liver cirrhosis. Her height was 157cm and her total body weight was 115 kg. a) Unenhanced axial image b) Hepatic arterial phase c) Portal venous phase d) Equilibrium phase Her skeletal muscle index was high (9.4 kg/m²) and contrast enhancement during the portal venous phase was low (63 HU).

Figure 2

CE-CT images obtained in an 80-year-old woman with liver cirrhosis. Her height was 155cm and her total body weight was 46 kg. a) Unenhanced axial image b) Hepatic arterial phase c) Portal venous phase d) Equilibrium phase Her skeletal muscle index was low (4.8 kg/m²) and contrast enhancement during the portal venous phase was high (140 HU).