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Investigation of Postmortem Hounsfield Unit Value of Hyperthermia

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ABSTRACT

The antemortem stage and postmortem changes influence postmortem computed tomography (CT). The Hounsfield unit (HU) values of several organs are higher after death than before death. In addition, hyperthermia-specific findings of postmortem CT have not yet been reported. In the present study, we hypothesized that HU values of fused striated muscles, myoglobin-filtering organs of the kidney, and myoglobinuria might vary in patients with severe hyperthermia that contributes to death. Therefore, we investigated the methods of diagnosing hyperthermia with postmortem HU values. The HU values of urine, the iliopsoas, and kidney did not differ significantly between patients with hyperthermia and control patients. No correlation was found between the urinary myoglobin level and the HU values of each measurement target. The HU value specific to hyperthermia could not be obtained with postmortem CT examinations. Because few studies have examined the HU values of postmortem CT, the present study provides valuable data on postmortem CT images, which are affected by postmortem changes. (Jikeikai Med J 2023；70：79-87)

Key words：Hounsfield unit value, postmortem computed tomography, hyperthermia, myoglobin, rhabdomyolysis

INTRODUCTION

Computed tomography (CT) is an imaging technique in which X-rays transmitted through an internal organ are converted into data and processed with a computer to obtain a cross-sectional image. The Hounsfield unit (HU) value indicates the absorption coefficient of X-rays and is 0 HU for water and −1,000 HU for air[1]. In general, HU values are high for calcification and acute hematomas are are low for steatosis and air lesions. Measuring the HU value is useful for diagnosis in clinical practice；fatty liver is characterized by a low HU value, whereas hepatic hemochromatosis, hematuria, and pyuria have high HU values[2]. Autopsy imaging, which involves postmortem CT imaging, has recently begun to gain popularity and plays a complementary role in autopsies[3]. However, CT images are reported to be affected by the agonia and postmortem changes[4,5], and applying the antemortem diagnostic criteria to diagnose the cause of death is difficult. In particular, compared with antemortem HU values, postmortem HU values of the aortic wall, myocardium, spleen, and thyroid increase[6-9]. Additional information is needed regarding postmortem HU values for various structures and individual diseases.

In Japan, the incidence of hyperthermia-related deaths has been increasing owing to extreme heat caused by abnormal weather[10]. Owing to this increase, postmortem methods of diagnosing hyperthermia are needed. In the field of forensic medicine, hyperthermia is comprehensively

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diagnosed from a high rectal temperature that does not correspond with the postmortem time (PMT), dehydration findings, color change in striated muscle, or myoglobinuria at autopsy. Within postmortem CT, the vessel flattening index can be calculated as follows : the ratio of the minor axis to the major axis of the aorta and inferior vena cava divided by the area of a circle that is the same as the circumference of aorta and inferior vena cava[11]. Additionally, the weight and capacity of the heart and lungs can be estimated in previous studies[11-13]. However, none of these studies reported specific findings regarding hyperthermia.

Postmortem methods of diagnosing hyperthermia is needed but not reported in postmortem CT. We focused on the fact that myoglobin in muscles is released into the blood by rhabdomyolysis, filtered by the kidneys, and excreted through urine during hyperthermia. In the present study, we investigated the potential variability of the HU values of fused striated muscles, myoglobin-filtering units of the kidney, and myoglobinuria. This variability can be significant if severe hyperthermia leads to death. Therefore, we used the HU values from postmortem CT scans to examine a diagnostic method for hyperthermia-related death.

MATERIALS AND METHODS

The deceased persons included in this study were patients with a PMT < 120 hours who underwent postmortem CT before forensic autopsy at our institution from October 2019 through August 2022. The diagnosis of hyperthermia was made comprehensively on the basis of the autopsy findings of dehydration, muscle color changes, brown urine, myoglobinuria, environment at the time of death, and high body temperature. This study was approved by the Ethics Committee of The Jikei University School of Medicine for Biochemical Research 32-457(10549).

Postmortem CT imaging

A 64-row multidetector CT scanner (SOMATOM go.ToP, Siemens Healthineers, Erlangen, Germany) was used for CT imaging at the following settings : tube voltage, 120 kV ; slice pitch, 64 × 0.5 mm ; tube current, adjusted according to body size ; and whole-body imaging. Multiplanar reconstruction images were obtained with a slice thickness of 1.0 mm. During imaging the patient was placed in the supine position.

To measure HU values, circular regions of interest (ROIs) of ~1 cm^2 were placed as follows : for urine, in the centers of the horizontal and sagittal sections at each non-overlapping location ; for the iliopsoas, in the horizontal section at each location on either side at the level of the fifth lumbar vertebra ; and for the kidney, at each location at the upper left pole, lower left pole, upper right pole, and lower right pole in the coronal section (Fig. 1). The deceased persons were excluded if the measurement targets for an appropriate ROI could not be obtained (organ gas due to postmortem changes or life-saving procedures, organ atrophy or missing and lack of bladder contents, and few normal parts due to cysts) or for artificial factors that affect the HU value : contrast agents before death and the presence of artifacts because of internal metals.

Measurement of urinary myoglobin level

Urine was collected during autopsy after postmortem CT examinations, and the myoglobin levels were measured by SRL, Inc., (Tokyo, Japan) via a chemiluminescent enzyme immunoassay.

Statistical analysis

The HU values of urine and the iliopsoas were the average of 2 locations, whereas those of kidneys were the average of 4 locations. Statistical analyses (simple regression analysis and the Mann-Whitney U and Kruskal-Wallis tests) were performed with the software programs Microsoft Excel (Microsoft Corp., Redmond, WA, USA) and GraphPad Prism, version 9 (GraphPad Software, Inc., San Diego, CA, USA), and $P < 0.05$ was considered statistically significant.

RESULTS

Participants included in this study were 223 patients (of whom 26 had hyperthermia) and 197 controls patients (40 with intracranial hemorrhage, 68 with ischemic heart failure, 29 with pneumonia, 35 with toxicosis, and 25 with hypothermia). The mean age was 60.99 ± 15.57 years, and the mean PMT was 39.48 ± 18.54 hours ; of the participants 156 were men and 67 were women. Although age did not differ significantly between the sexes ($p = 0.90$), PMT was significantly longer in women (Table 1).

A weak positive correlation was observed between age

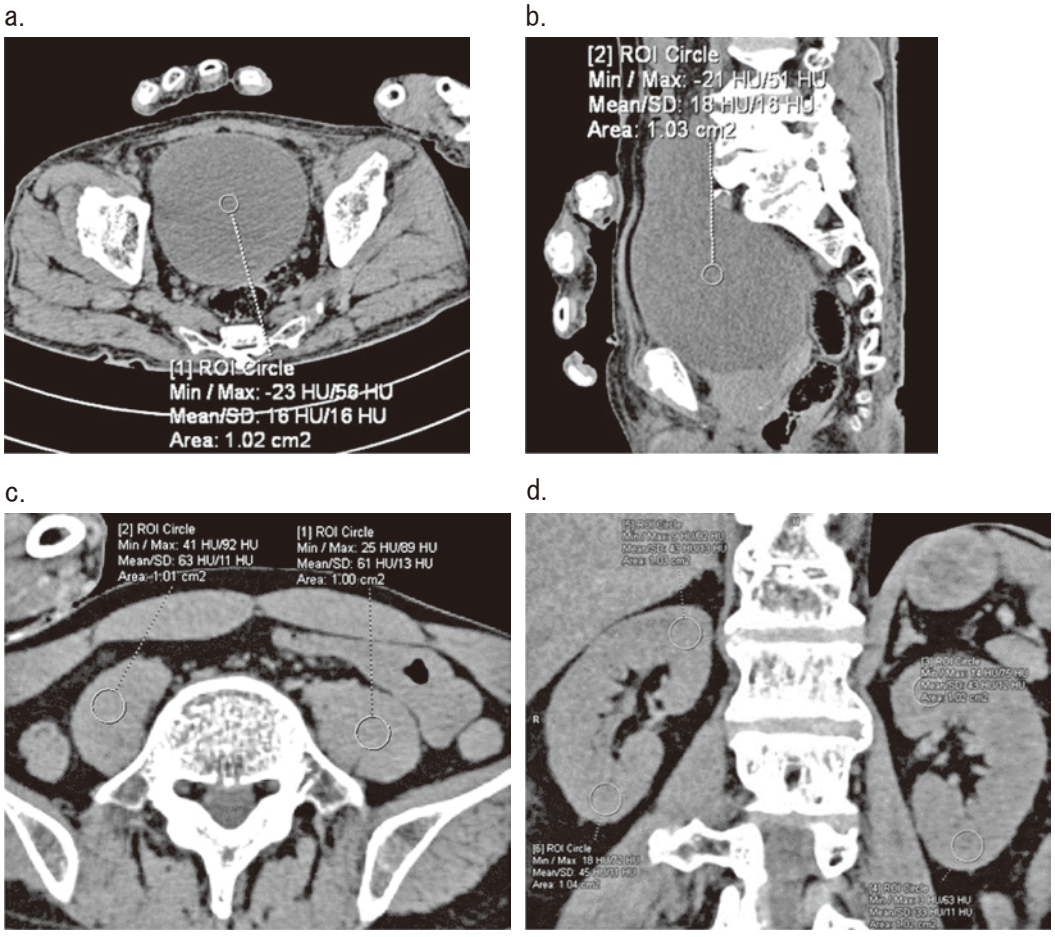

Fig. 1. Hounsfield unit value measurements in postmortem computed tomographic images of horizontal section urine (a), sagittal section urine (b), the iliopsoas (c), and the kidney (d).

and urinary HU values ($y = 1.96 \times +51.44$, $p = 0.011$, $R^2 = 0.045$), and negative correlation was observed between age and iliopsoas HU values ($y = -1.06 \times +115.8$, $p < 0.0001$, $R^2 = 0.12$). However, age and kidney HU values were weakly correlated ($y = -0.045 \times +50.12$, $p = 0.048$, $R^2 = 0.020$) (Fig. 2), and PMT, urinary HU values, and iliopsoas HU values were not correlated ($y = 0.032 \times +15.11$, $p = 0.34$, $R^2 = 0.0062$) ($y = 0.064 \times +55.31$, $p = 0.013$, $R^2 = 0.029$). A weak correlation was observed between PMT and kidney HU values ($y = 0.099 \times +43.29$, $p < 0.0001$, $R^2 = 0.088$) (Fig. 3). Urinary HU values were higher in men than in women ($p = 0.038$), whereas kidney HU values were higher in women than in men ($p = 0.0006$). The iliopsoas HU values did not differ regarding sex (Table 1).

A comparison between patients with hyperthermia and control patients (Table 2) showed that patients with hyperthermia were significantly younger than patients with toxicosis ($p = 0.0062$). Regarding the other causes of death, no significant differences were found in age, PMT, or sex. Urinary, iliopsoas, and kidney HU values did not differ significantly between patients with hyperthermia and control patients (Table 3). Among control patients, those with toxicosis had significantly lower urinary HU values ($p = 0.0054$), and those with ischemic heart failure had significantly higher kidney HU values ($p = 0.029$).

Urinary myoglobin levels measured in 19 patients were not correlated with HU values of urine ($y = 156.6 \times -109.5$, $p = 0.51$, $R^2 = 0.025$), the iliopsoas ($y = 359.8 \times -17299$, $p = 0.19$, $R^2 = 0.11$), or the kidney ($y = 22.74 \times +2446$, $p = 0.95$, $R^2 = 0.00025$) (Fig. 4).

Urinary HU values were not correlated with urine volume ($y = -0.0019 \times +16.73$, $p = 0.56$, $R^2 = 0.0023$), and urinary HU values did not differ significantly between the presence or absence of macroscopic urinary turbidity ($p =$

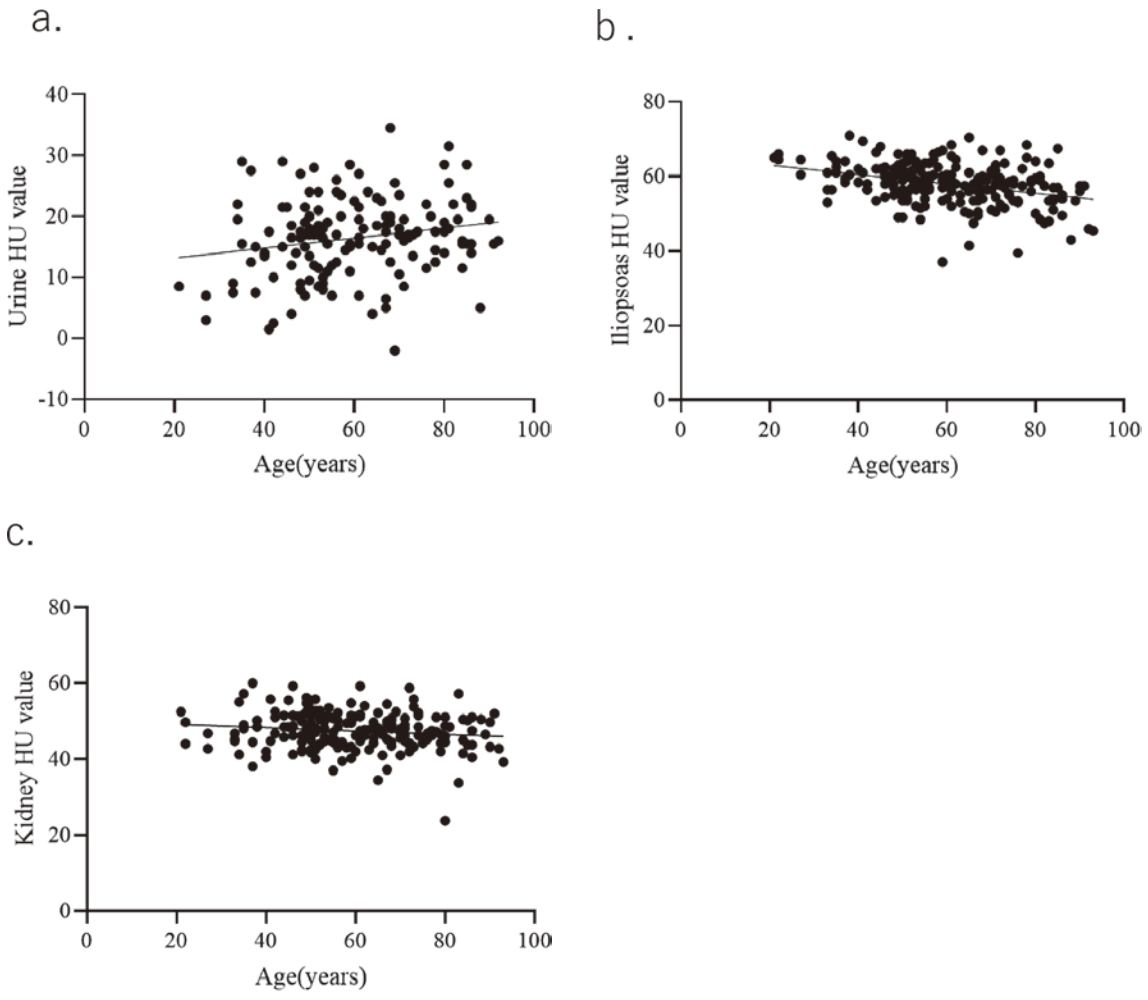

Fig. 2. Association between age and Hounsfield unit (HU) values in urine (a), the iliopsoas (b), and the kidney (c). The sloped line represents the fitted regression curve.

0.14) (Fig. 5).

DISCUSSION

To the best of our knowledge, the present study is the first to attempt to diagnose hyperthermia with HU values of postmortem CT scans. Because hyperthermia causes brown urine owing to rhabdomyolysis, we hypothesized that fatal hyperthermia causes changes in HU values. However, in the present study, HU values of urine, the iliopsoas, and kidney did not differ significantly between patiets with hyperthermia and control patients. Because the urinary myoglobin level, which is the cause of brown urine, was not correlated with urinary HU values, brown urine was difficult to detect with HU values of postmortem CT scans. Myoglobin is a pigment protein with a molecular weight of 17,800 daltons. In the present study, the average myoglobin concentration measured in patients with hyperthermia was 3,647.86 ng/mL. Consequently, such patients should have a urine protein level higher than that of a healthy individual. Levels of N-terminal pro-brain natriuretic peptide are elevated in the urine of patients with acute myocardial infarction, hyperthermia, and sepsis[14]. Additionally, the concentration of acetylcarnitine in urine is elevated in patients with acute stroke[15]. Postmortem urine contains leaked substances indicative of different diseases ; therefore, myoglobinuria in patients with hyperthermia could not be identified with urinary HU values alone in the present study. In addition, an increase in serum HU values with increasing cellular impurities has been attributed to an increase in radiation density due to particulate cellular components[1,16]. Because the myoglobin protein has a molecular weight of

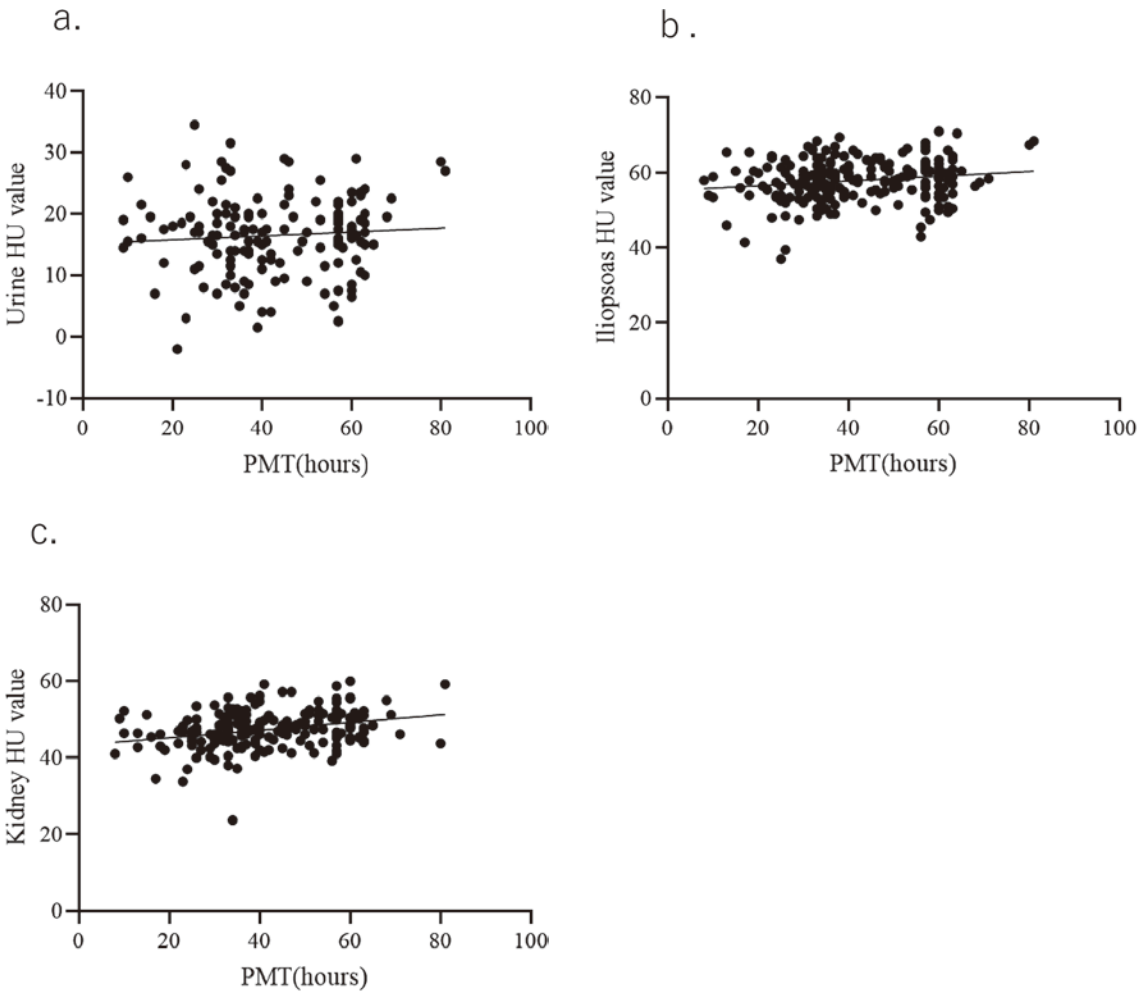

Fig. 3. Association between postmorterm time and Hounsfield unit (HU) values in urine (a), the iliopsoas, (b) and the kidney (c). The sloped line represents the fitted regression curve.

Table 1. Characteristics of 223 patients in which postmortem computed tomography was performed and Hounsfield unit values of each site were measured

	Men (n = 156)	Women (n = 67)	p value
Age (years)	61.26	60.99	0.90
Postmortem time (hours)	38.29 ± 19.05	45.41 ± 22.44	0.019
Mean Hounsfield unit value			
Urine	17.12 ± 6.53 (n = 109)	14.65 ± 6.15 (n = 39)	0.038
Iliopsoas	51.71 ± 5.76 (n = 151)	58.62 ± 5.02 (n = 62)	0.33
Kidney	46.65 ± 5.02 (n = 136)	49.26 ± 4.23 (n = 60)	0.0006

17,800 and is extremely small compared with the cellular components, X-ray permeability might not be affected as much as the HU value.

To investigate the relationship between urinary cell impurities and urinary HU values, in the present study we compared the urinary HU values with and without macroscopic urinary turbidity. The HU values in pleural fluid increase owing to an increase in the content of blood cells and shed cell components due to putrefaction[17]. The HU values did not differ signficantly on the basis of the presence or absence of turbidity[17]. Because the patients in the present study did not have fatal urinary tract infections during

Table 2. Age, postmortem time, and sex for causes of death

	Hyperthermia (n = 26)	Control patients (n = 197)					
		Total	Intracranial hemorrhage (n = 40)	Ischemic heart failure (n = 68)	Pneumonia (n = 29)	Drug intoxication (n = 35)	Hypothermia (n = 25)
Age (years)	65.23 ± 14.66	61 ± 15.64	56.36 ± 12.67	61.55 ± 13.40	69.68 ± 14.39	49.73 ± 15.94	72.69 ± 13.16
p value vs hyperthermia		0.34	0.39	> 0.99	> 0.99	0.0062	0.79
Postmortem time (hours)	46.29 ± 19.15	41.65 ± 14.27	43.57 ± 13.85	38.94 ± 14.17	43.29 ± 13.70	40.11 ± 13.23	46.19 ± 16.37
p value vs hyperthermia		> 0.99	> 0.99	0.85	> 0.99	>0 .99	> 0.99
Sex (male/female)	16/10	140/57	27/13	57/11	24/5	16/19	16/9
p value vs hyperthermia		0.63	>0.99	0.99	>0.99	>0.99	>0.99

Table 3. Hounsfield unit values for causes of death

	Hyperthermia patients	Control patients					
		Total	Intracranial hemorrhage	Ischemic heart failure	Pneumonia	Drug intoxication	Hypothermia
Urine	18.63 ± 5.79 (n = 20)	16.15 ± 6.50 (n = 128)	15.99 ± 5.08 (n = 35)	18.26 ± 6.91 (n = 33)	17.35 ± 4.28 (n = 17)	11.72 ± 8.00 (n = 25)	17.67 ± 3.83 (n = 18)
p value vs hyperthermia		0.79	0.88	> 0.99	> 0.99	0.0054	> 0.99
Ilipsoas	57.53 ± 5.17 (n = 19)	58.04 ± 5.55 (n = 191)	59.81 ± 4.47 (n = 40)	58.33 ± 4.54 (n = 65)	55.58 ± 7.63 (n = 26)	58.76 ± 5.08 (n = 36)	55.90 ± 5.93 (n = 24)
p value vs hyperthermia		> 0.99	0.36	> 0.99	> 0.99	> 0.99	> 0.99
Kidney	49.38 ± 5.01 (n = 19)	47.24 ± 4.89 (n = 174)	49.62 ± 4.06 (n = 39)	45.42 ± 3.83 (n = 56)	46.38 ± 6.14 (n = 26)	47.93 ± 5.11 (n = 34)	47.67 ± 4.37 (n = 19)
p value vs hyperthermia		> 0.99	> 0.99	0.029	> 0.99	> 0.99	> 0.99

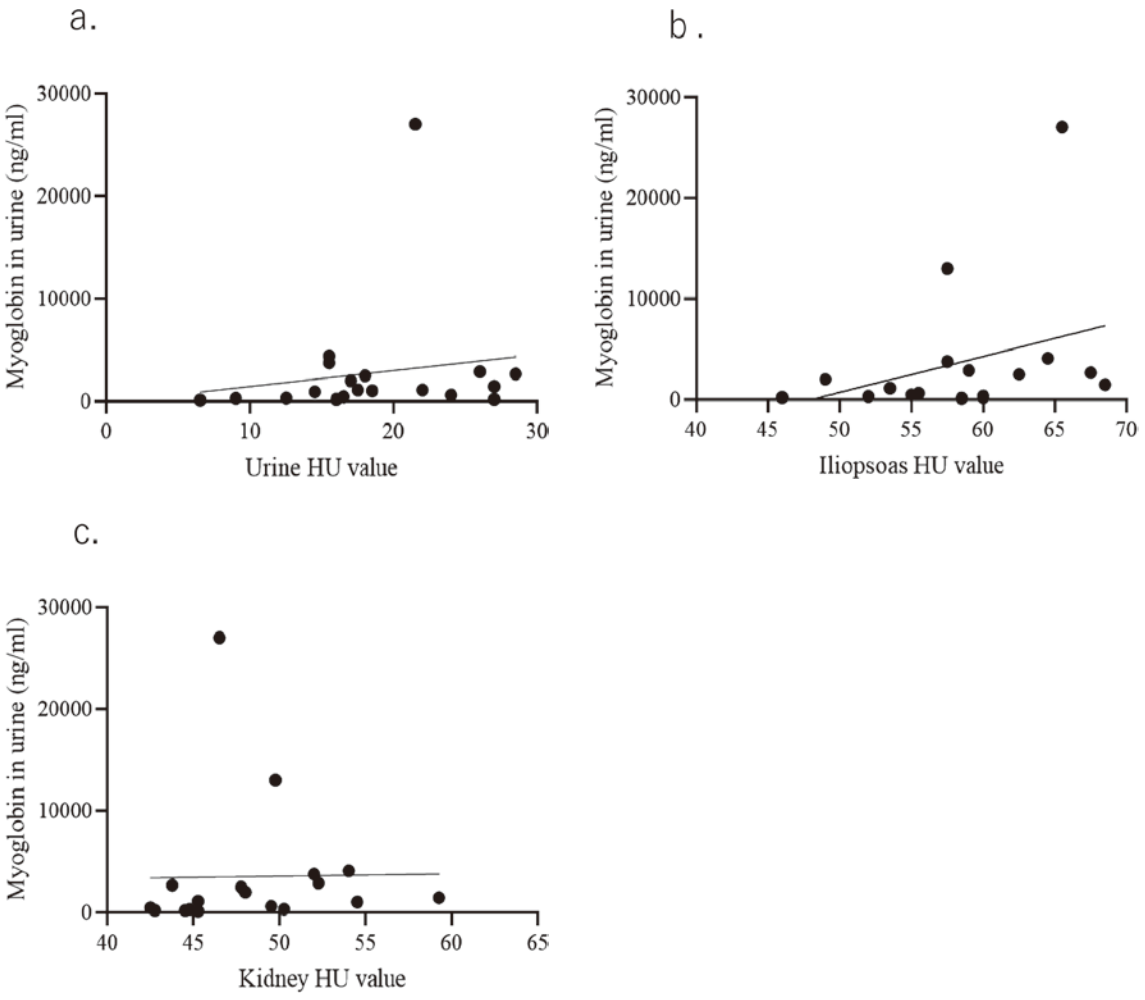

Fig. 4. Association between myoglobin value in urine and Hounsfield unit (HU) values in urine (a), the iliopsoas, (b) and the kidney (c). The sloped line represents the fitted regression curve.

which substantial amounts of cellular components were released to the urine, we presume that no significant difference in the amount of cellular impurities affected HU values. However, the HU values tended to be higher in urine with turbidity. Therefore, to examine the factors that affect the HU value of urine, it is necessary to increase the number of patients, including those with urinary tract infections, and to examine urinary epithelial cell count, urinary blood cell count, urinary protein levels, and specific gravity.

A weak positive correlation was observed between the age and urinary HU values in the present study. A previous studies has found that the incidence of urinary tract infections increases with age[18] and others have found that glomerular filtration rate, an indicator of renal function, decreases with aging[19-21]. In the present study, the increase in urinary HU values with age was attributed to an increase in impure urinary cellular components caused by an age-related decline in renal function and an increase in urinary tract infections. In contrast, the iliopsoas HU value was negatively correlated with age. In skeletal muscles, the ability of fibers to process triglycerides decreases with age, leading to an increase in lipid stores in the form of droplets along the cell membranes[22]. The HU value of the femoral muscle decreases owing to fat infiltration with aging[22]. Similar to the HU values of thigh muscles, those of the iliopsoas skeletal muscles were measured in the present study : age-related fat infiltration occurred before death ; the iliopsoas HU values were lower for postmortem CT images.

No correlation was observed between urine PMT and HU values in the present study. A study that found that the HU value in pleural fluid increases owing to putrefaction included patients with a PMT of 1 to 60 days or longer[17]. In

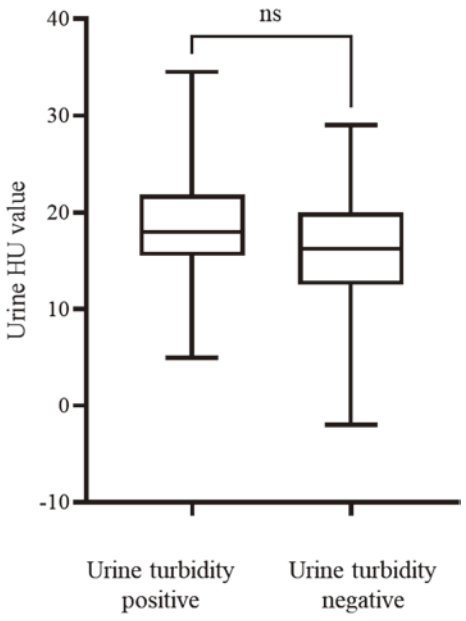

Fig. 5. The comparison of the urinary Hounsfield unit (HU) value and macroscopic urine turbidity positive to negative.
The horizontal line in the box plot shows the median HU value in each group, bounded between the upper and lower quartiles, and the whiskers indicate the range between the minimum and maximum values. The *P* value was 0.14 (Mann-Whitney *U* test). *ns, not significant, $p > 0.05$.

the present study, the PMT of patients was less than 120 hours and was weakly correlated with iliopsoas HU values. This finding supports a previous study that found no difference between antemortem and postmortem skeletal muscle HU values[7]. In contrast, kidney HU values were positively correlated with PMT in the present study. A previous study of the spleen found that postmortem CT scans showed splenic attenuation and high HU values[8] ; the study inferred that the spleen had become more compact owing to blood components being reduced by postmortem changes and that the HU value had increased owing to the higher density of splenic components. The kidney also had a significantly smaller volume postmortem then antemortem[23] and, as a blood-rich organ, might have increased HU values in correlation with PMT by a mechanism similar to that of the spleen. Additionally, the vascular wall of the aorta thickens after death[6]. If the walls of blood vessels other than the aorta also thicken after death, the HU value might increase because the kidney is rich in blood vessels. We speculate that the increase in the density of these components and thickening of the vascular wall are involved in the increase in HU values.

In the present study urinary HU values were significantly higher in men than in women. This difference might be due to increased urinary HU values, which have been reported to result in urine being more concentrated in men than in women[24]. The kidney HU values were significantly higher in women, but the PMT was significantly longer in women than in men, suggesting that the PMT-induced elevation of HU was affected.

Urinary HU values in patients with toxicosis were significantly lower than those in patients with hyperthermia and tended to be lower than those in patients with other diseases in the present study. The urinary HU values were expected to be affected by age, and age was significantly lower in patients with toxicosis than patients with hyperthermia. In addition, the kidney HU values in patients with ischemic heart failure were significantly lower than those in patients with hyperthermia and tended to be lower than those in patients with other diseases. Because ischemic heart failure is a vascular disease affected by hyperlipidemia, hypertension, and diabetes, it might have thinned the renal cortex and made the fat mass of the renal pelvis greater than in other disease groups. The kidney HU values in patients with ischemic heart failure might have decreased owing to increased fat content affecting radiolucency changes ; therefore, serum markers and renal macroscopic and microscopic images, which are indicators of renal damage, should also be examined.

By focusing on urinary myoglobin excretion due to rhabdomyolysis during hyperthermia, we investigated whether the HU value of postmortem CT images is useful for diagnosing hyperthermia ; however, we were unable to obtain a specific HU value for hyperthermia. However, few studies have examined the HU value of postmortem CT images. Therefore, this study provides valuable data on postmortem CT, which is affected by postmortem changes.

Authors have no conflict of interest.

REFERENCE

1. Huda W, Slone RM. Review of radiologic physics, 2nd ed. Philadelphia : Lippincott Williams & Wilkins ; 2003.
2. Jinzaki M editor. CT of the Abdomen 3rd ed (in Japanese). Tokyo : Medical Science International, Ltd. ; 2017.
3. Cafarelli FP, Grilli G, Zizzo G, Bertozzi G, Giuliani N, Mahak-

kanukrauh P, et al. Postmortem imaging : An update. Semin Ultrasound CT MR. 2019 ; 40 : 86-93.
4. Christe A, Flach P, Ross S, Spendlove D, Bolliger S, Vock P, et al. Clinical radiology and postmortem imaging (Virtopsy) are not the same : specific and unspecific postmortem signs. Leg Med (Tokyo). 2010 ; 12 : 215-22.
5. Ishida M, Gonoi W, Okuma H, Shirota G, Shintani Y, Abe H, et al. Common postmortem computed tomography findings following atraumatic death : differentiation between normal postmortem changes and pathologic lesions. Korean J Radiol. 2015 ; 16 : 798-809.
6. Okuma H, Gonoi W, Ishida M, Shintani Y, Takazawa Y, Fukayama M, et al. Greater thickness of the aortic wall on postmortem computed tomography compared with antemortem computed tomography : the first longitudinal study. Int J Legal Med. 2014 ; 128 : 987-93.
7. Okuma H, Gonoi W, Ishida M, Shirota G, Shintani Y, Abe H, et al. Comparison of attenuation of striated muscle between postmortem and antemortem computed tomography : results of a longitudinal study. PLoS One. 2014 ; 9 : e111457.
8. Okuma H, Gonoi W, Ishida M, Shirota G, Kanno S, Shintani Y, et al. Comparison of volume and attenuation of the spleen between postmortem and antemortem computed tomography. Int J Legal Med. 2016 ; 130 : 1081-7.
9. Ishida M, Gonoi W, Hagiwara K, Takazawa Y, Akahane M, Fukayama M, et al. Postmortem changes of the thyroid on computed tomography. Leg Med (Tokyo). 2011 ; 13 : 318-22.
10. Vital Statistics Japan. Tokyo ; Ministry of Health, Labour and Welfare, 2023. https://www.mhlw.go.jp/english/database/db-hw/index.html. [accessed 2023-09-01]
11. Sogawa N, Michiue T, Ishikawa T, Inamori-Kawamoto O, Oritani S, Maeda H. Postmortem CT morphometry of great vessels with regard to the cause of death for investigating terminal circulatory status in forensic autopsy. Int J Legal Med. 2015 ; 129 : 551-8.
12. Michiue T, Sogawa N, Ishikawa T, Maeda H. Cardiac dilatation index as an indicator of terminal central congestion evaluated using postmortem CT and forensic autopsy data. Forensic Sci Int. 2016 ; 263 : 152-7.
13. Michiue T, Sakurai T, Ishikawa T, Oritani S, Maeda H. Quantitative analysis of pulmonary pathophysiology using postmortem computed tomography with regard to the cause of death. Forensic Sci Int. 2012 ; 220 : 232-8.
14. Takasu S, Matsumoto S, Kanto Y, Kodama S, Iwadate K. Postmortem urine concentration of N-terminal pro-brain natriuretic peptide in relation to the cause of death. Forensic Sci Int. 2020 Jan ; 306 : 110079.
15. Sidorov E, Bejar C, Xu C, Ray B, Reddivari L, Chainakul J, et al. Potential metabolite biomarkers for acute versus chronic stage of ischemic stroke : a pilot study. J Stroke Cerebrovasc Dis. 2020 ; 29 : 104618.
16. Jackowski C, Thali M, Aghayev E, Yen K, Sonnenschein M, Zwygart K, et al. Postmortem imaging of blood and its characteristics using MSCT and MRI. Int J Legal Med. 2006 ; 120 : 233-40.
17. Zech WD, Jackowski C, Buetikofer Y, Kara L. Characterization and differentiation of body fluids, putrefaction fluid, and blood using Hounsfield unit in postmortem CT. Int J Legal Med. 2014 ; 128 : 795-802.
18. Yang X, Chen H, Zhend Y, Qu S, Wang H, Yi F. Disease burden and long-term trends of urinary tract infections : a worldwide report. Front Public Health. 2022 ; 10 : 888205.
19. Imai E, Horio M, Yamagata K, Iseki K, Hara S, Ura N, et al. Slower decline of glomerular filtration rate in the Japanese general population : a longitudinal 10-year follow-up study. Hypertens Res. 2008 ; 31 : 433-41.
20. Imai E, Horio M, Watanabe T, Iseki K, Yamagata K, Hara S, et al. Prevalence of chronic kidney disease in the Japanese general population. Clin Exp Nephrol. 2009 ; 13 : 621-30.
21. Berg UB. Differences in decline in GFR with age between males and females. Reference data on clearances of inulin and PAH in potential kidney donors. Nephrol Dial Transplant. 2006 ; 21 : 2577-82.
22. Lang T, Cauley JA, Tylavsky F, Bauer D, Cummings S, Harris TB, et al. Computed tomographic measurements of thigh muscle cross-sectional area and attenuation coefficient predict hip fracture : the health, aging, and body composition study. J Bone Miner Res. 2010 ; 25 : 513-9.
23. Takahashi N, Yajima K, Otaki M, Yoshikawa Y, Ishihara A, Sato Y, et al. Postmortem volume change of the spleen and kidney on early postmortem computed tomography : comparison with antemortem computed tomography. Jpn J Radiol. 2019 ; 37 : 534-42.
24. Hancock ML 2nd, Bichet DG, Eckert GJ, Bankir L, Wagner MA, Pratt JH. Race, sex, and the regulation of urine osmolality : observations made during water deprivation. Am J Physiol Regul Integr Comp Physiol. 2010 ; 299 : R977-80.