Fujimoto et al., Int J Radiol Med Imag 2021, 7: 131
https://doi.org/10.15344/2456-446X/2021/131

International Journal of
Radiology & Medical Imaging

Original Article Open Access

Early Postmortem Changes in Liver Volume and CT Value: An Antemortem and Postmortem Computed Tomography Study

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Abstract

Background: The aim of this study was to compare antemortem and postmortem volumes and computed tomography (CT) values of the liver.

Method: The sample included 24 subjects that were treated and died in our hospital and underwent antemortem CT, postmortem CT and conventional autopsy between January 2013 and December 2016. All included subjects were diagnosed to have normal liver by conventional autopsy. The time since death at performing CT imaging, as well as the volume and CT value of the liver on both antemortem and postmortem CT were recorded.

Results: There were no statistically significant changes between antemortem and postmortem imaging CT values (antemortem median value = 51.9 HU [interquartile range (IQR), 50.0-53.9 HU], postmortem median value = 49.1 HU [IQR, 44.8-54.9 HU], P = 0.07) or volumes (antemortem mean volume= 1094 cm^3 [IQR, 783-1281 cm^3], post-mortem mean volume = 1049 cm^3 [IQR, 821-1339 cm^3], P = 0.73). However, there could be an underlying tendency for CT values to increase with time since death (Spearman's rank correlation coefficient; r= 0.70; P < 0.001).

Conclusion: In conclusion, these results suggest the possibility of estimating liver condition before death on the basis of postmortem images early after death.

Publication History:

Received: October 24, 2021
Accepted: December 02, 2021
Published: December 04, 2021

Keywords:

Autopsy, Corpse, Case-control study, CT Attenuation, Forensic radiology, Postmortem imaging

Introduction

Postmortem computed tomography (CT) plays an important role in complementing conventional autopsy [1,2]. Postmortem imaging shows many specific changes that are not recognized on antemortem imaging [3]. To accurately interpret postmortem imaging, it is essential to distinguish pathological findings from non-pathological findings, which requires special training.

Many previous studies have reported differences in CT values and organic volume between antemortem and postmortem imaging [4-11]. A previous study suggested that postmortem liver CT values <30 HU were likely to indicate fatty liver [12], while another study reported a positive correlation between CT values and liver density [13]. According to a case report, the CT values of the liver may show a markedly diffuse decrease after death in some patients [14]. It has been noted that gas in the portal vein of the liver can be seen on postmortem imaging with or without cardiopulmonary resuscitation [15]. A previous study found that postmortem liver weight can be estimated from postmortem imaging and that postmortem liver density was constant regardless of time after death [13], while several studies examined changes in the liver CT value over time after death [12,14,15]. Contrastingly, few studies have compared antemortem and postmortem images of the liver within the same subject. To address this research gap, the present study aimed to assess the CT values and volume of the liver on both antemortem and postmortem imaging.

Materials and Methods

The Research Ethics Committee of our university hospital approved this study, which was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the families of the deceased subjects to use radiographic and clinical data for this study. This study was approved by the Institutional Review Board (2076-(15)).

Subjects

The inclusion criteria for this study were as follows: (1) died in our hospital after treatment between January 2013 and December 2016; (2) underwent antemortem CT within one month before death, postmortem CT, and conventional autopsy; (3) had a healthy liver as confirmed by autopsy. The exclusion criteria were as follows: (1) an autopsy-proven diffuse or localised lesion in the liver; (2) a history of liver resection or treatment; (3) insufficient CT image quality; (4) underwent CPR; (5) high bilirubin level before death; (6) abnormally high CT value of antemortem liver. Further details of the inclusion and exclusion criteria are shown in Figure 1. Ultimately, 24 subjects were included in the present study. Postmortem CT was performed once in each case, and the median time since death at postmortem CT was 5.9 hours (interquartile range [IQR], 3.7-12.1 hours). The cause of death of each subject is listed in Table 1. All cadavers were placed in the supine position at room temperature (approximately 20°C in the summer using air conditioning; approximately 10°C-15°Cin winter, depending on the temperature outside) from the time of death until postmortem CT imaging within one day after death. A conventional autopsy was performed within one hour after the postmortem CT examination.

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Citation: Fujimoto K, Gonoi W, Ishida M, Okimoto N, Nyunoya K, et al. (2021) Early Postmortem Changes in Liver Volume and CT Value: An Antemortem and Postmortem Computed Tomography Study. Int J Radiol Med Imag 7: 131. doi: https://doi.org/10.15344/2456-446X/2021/131

Computed tomography protocol and imaging analysis

All antemortem CT scans were performed without contrast agent on multi-detector CT scanners (Aquilion 64 and Aquilion ONE, Canon Medical Systems Corporation, Ohtawara, Japan; Discovery CT750 HD and LightSpeed VCT, GE Healthcare, Buckinghamshire, UK) in the craniocaudal direction. The subjects were in the supine position with arms raised on antemortem CT. The following scan parameters were used: slice thickness 5 mm; slice interval 5 mm; tube voltage 120 kVp. The tube current was automatically controlled by using Volume EC (Toshiba) and Autom A (GE). From the raw data, contiguous 5 mm CT axial sections were reconstructed.

All postmortem CT scans were performed without contrast agentson a four-detector-row CT scanner (Robusto, Hitachi Medical Corporation) using the helical mode in the craniocaudal direction. All cadavers were laid in the supine position with arms down beside the body. The scan parameters were as follows: slice thickness 2.5 mm; slice interval 1.25 mm; tube voltage 120 kVp; tube current 250 mA. Images were reconstructed at 1.25 mm intervals.

All images were interpreted by a radiologist (with 3 years of experience) under the supervision of two board-certified diagnostic radiologists with a decade of experience in postmortem imaging. We used the latest antemortem CT acquired at 5 mm intervals, and postmortem CT images acquired at 2.5 mm intervals and contoured them manually as the region of interest (ROI) using Digital Imaging and Communications in Medicine image-processing software (Horos, Horos project). The liver volume and average whole liver value (average value) were automatically calculated using a function of the imaging-processing software. When drawing the outline of the liver, we excluded the arteries, portal veins, and bile ducts at the porta hepatis (Figure 2). To investigate the difference in CT values between ventral and dorsal sides of the liver, we set two circular ROIs with 10 mm diameter on the ventral side of the liver parenchyma (S2 section) and on the dorsal side (S7 section) on the same slice level as the umbilical portion, avoiding veins, on the same positions in the antemortem images and postmortem images (Figure 3).

Cause of death	Cases
Respiratory failure	10
Heart failure	5
Infectious disease	2
Tumour death	2
Multiple organ failure	2
Stroke	1
Pulmonary embolism	1
Arterial dissection	1
Total	24

Table 1: The causes of death of 24 cases.

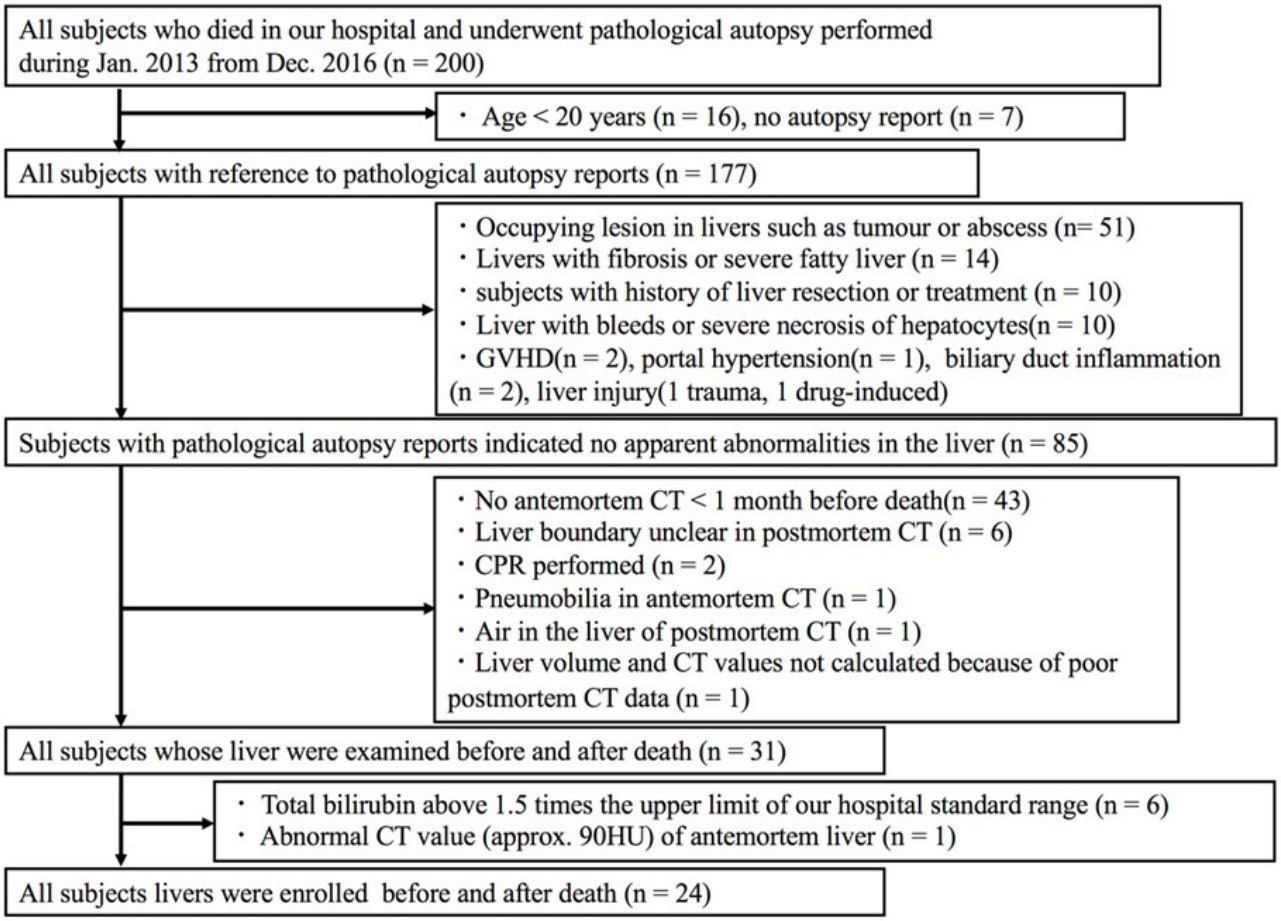

Figure 1: Subject selection tree based on the inclusion and exclusion criteria.
We selected 24 cases with normal livers based on the pathological autopsies performed at our institution.

Laboratory data

We obtained the following blood test data within one week before death: serum haemoglobin, lactate dehydrogenase, aspartate transaminase, alanine transaminase, alkaline phosphatase (ALP), gamma-glutamyl transpeptidase, total bilirubin. Within one week before death, we recorded the minimum values of haemoglobin and the maximum values of the other parameters (i.e. the clinically worst values).

Statistical analysis

Statistical analyses were performed using EZR software [17] (Saitama Medical Center, Jichi Medical University), a graphical user interface for R software (The R Foundation for Statistical Computing, Vienna, Austria).The level of statistical significance was set at $P< 0.05$. The normality of the tested variables was evaluated by performing the Shapiro-Wilk test. As the value and volume of the liver could differ between subjects due to their body constitution and underlying

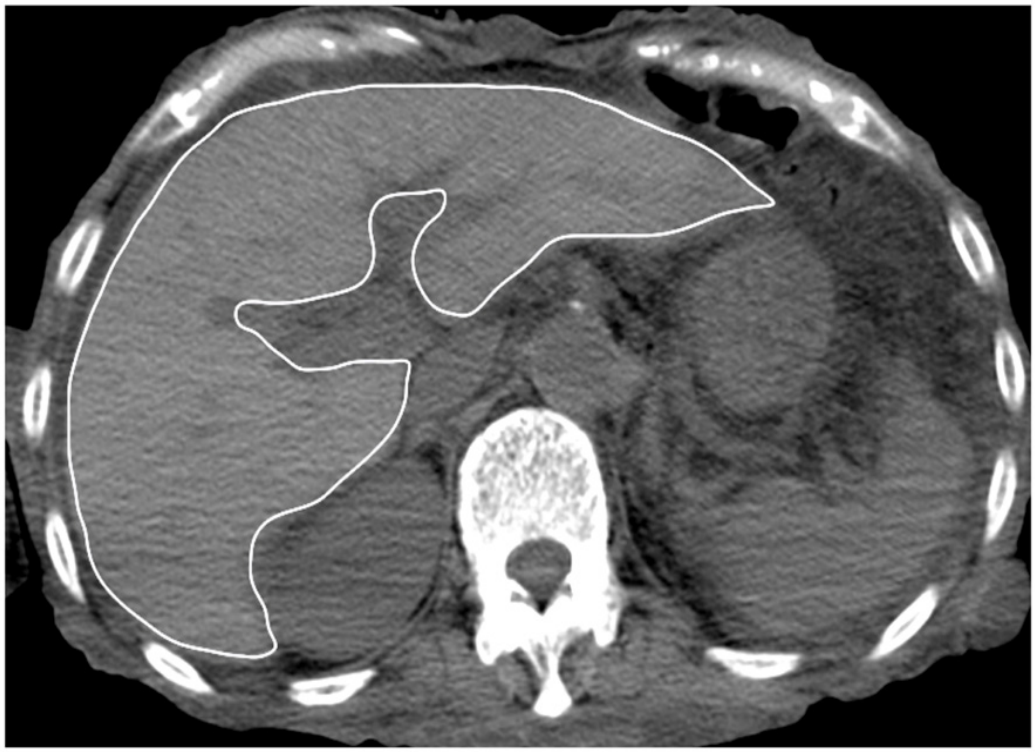

Figure 2: Boundaries of the liver were generated except for the vein, artery, and bile duct of theporta hepatis.

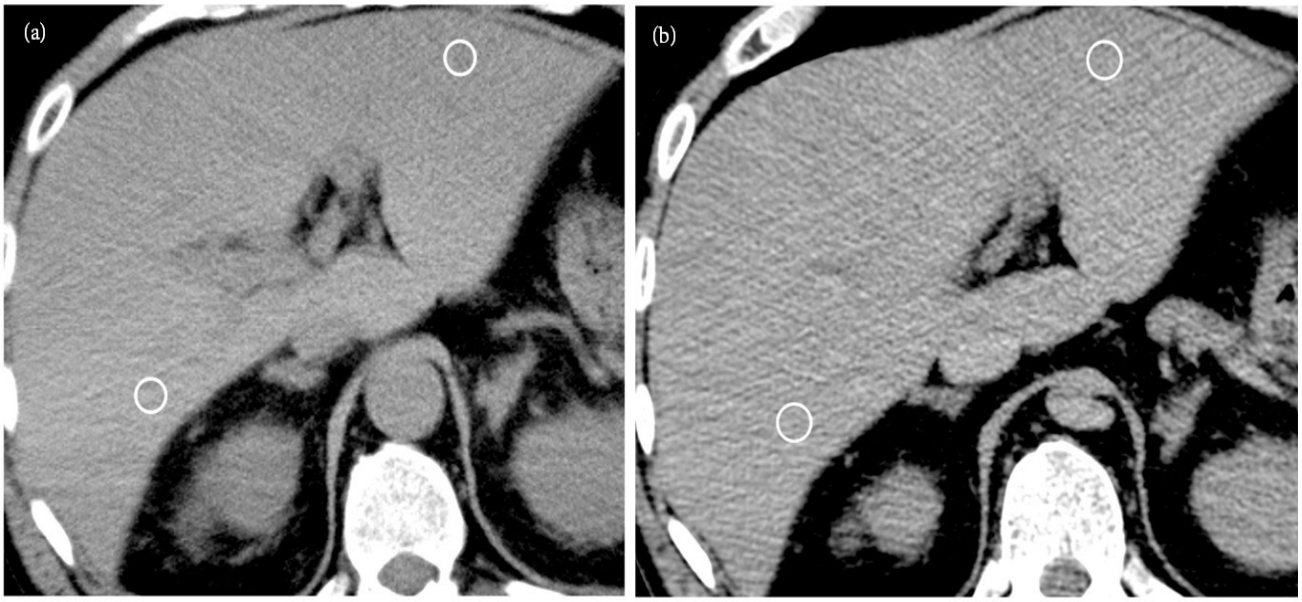

Figure 3: We set the regions of interest (ROIs; 10-mm diameter circles) at the ventral and dorsal sides of the liver. These ROIs were set on the same level as the umbilical portion and avoiding cysts, tumours, or veins, on the same positions in the antemortem images (a) and postmortem images (b).

conditions [18,19], changes between antemortem and postmortem CT were standardised using the following formulas: $value_{PM/AM}$ = (postmortem liver average CT value / antemortem liver average CT value); and (2) $volume_{PM/AM}$ = (postmortem liver volume / antemortem liver volume). The paired t-test was used to compare antemortem to postmortem CT value changes between the dorsal and ventral sides. To test the difference between cases with $value_{PM/AM}$ <1 and $value_{PM/AM}$ >1, Wilcoxon's signed-rank test was used for time since death and Welch's t-test was used for $volume_{PM/AM}$. Spearman's rank correlation test was used to assess the correlation between the following pairs of variables: the time since death and $volume_{PM/AM}$; time since death and $value_{PM/AM}$; $value_{PM/AM}$ and $volume_{PM/AM}$.

Results and Discussion

Subject data

Subject characteristics were as follows: sex, 16 males and 8 females; median age, 74 years (IQR, 64-81 years); median body mass index (BMI), 21.8 kg/m^2 (IQR, 20.2-24.0 kg/m^2).

The laboratory data before death are presented in Table 2. The subjects were generally anaemic, as shown by low haemoglobin levels. Five of 24 subjects had high ALP values that were more than twice the upper limit of the standard range, resulting in a high average ALP level for the overall sample. The high ALP values were due to myelodysplastic syndrome, lymphoma, and biliary infiltration of pancreatic cancer for one subject each, and unknown causes for two subjects. Close investigation of the liver at autopsy revealed no pathological abnormality; therefore, the elevated ALP level in those subjects was deemed not attributed to liver diseases.

Comparison of antemortem and postmortemliver CT values and volumes

No statistically significant differences in average CT values or volumes for the whole liver were detected between antemortem and postmortem CT scans (Table 3). The valuePM/AM was 0.96 (95% confidence interval [CI]: 0.92-1.002) and volumePM/AM was 1.02 (95% CI: 0.96-1.08). No significant differences in the local CT value change after death were detected between the ventral side (mean decrease of 3.7 HU; 95% CI: 1.5-5.9 HU) and dorsal side (mean decrease of 4.8 HU; 95% CI: 1.4-8.2 HU; P = 0.50). The results of the comparison between cases with $value_{PM/AM}$ < 1 and $value_{PM/AM}$ > 1 are summarised in Table 4. The time since death was significantly shorter in the $value_{PM/AM}$ < 1 group than in the $value_{PM/AM}$ > 1 group. $Value_{PM/AM}$ tended to increase with time since death (Spearman's rank correlation coefficient: 0.70, P < 0.001; Figure 4A), whereas $volume_{PM/AM}$ was not significantly correlated with time since death (P = 0.36). $Value_{PM/AM}$ was inversely correlated with $volume_{PM/AM}$ (Spearman's rank correlation coefficient: -0.44, P = 0.03; Figure 4B).

Discussion

The present study is the first case-control study to longitudinally compare CT values and volumes of pathologically-proven normal livers on both antemortem CT and postmortem CT in the same subjects. We detected no changes in the liver CT values or liver volumes between antemortem CT and postmortem CT, which suggests that the CT values and volumes of the liver on antemortem CT could be extrapolated from those on postmortem CT.

Although CT values and volumes on postmortem CT remained the same as those on antemortem CT in the present study, two possible mechanisms have been proposed to explain changes in CT values after

	Standard range	Subject data
Aspartate transaminase (U/L; IQR)	13–30	45 [24, 70]
Alanine transaminase (U/L; IQR)	10–42	39 [21, 69]
Lactate dehydrogenase (U/L; IQR)	124–222	484 [305, 1206]
Alkaline phosphatase (U/L; IQR)	106–322	344 [265, 430]
Gamma-glutamyl transpeptidase (U/L; IQR)	13–64	62 [45, 120]
Total bilirubin (mg/dl; IQR) *	0.4–1.5	0.9 [0.6, 1.6]
Haemoglobin (g/dl; IQR)	13.7–16.8 (male)	8.1 [7.0, 9.0]
	11.6–14.8 (female)	

Table 2: Blood test data before death.
IQR, interquartile range
*Total bilirubin was measured by enzyme method using bilirubin oxidase.

	Antemortem	Postmortem	P-value
Average value (HU; IQR)	51.9 [50.0, 53.9]	49.1 [44.8, 54.9]	0.07
Liver volume (cm3; IQR)	1094 [783, 1281]	1049 [821, 1339]	0.73

Table 3. Comparisons of liver CT values and volume between antemortem and postmortem.
HU: Hounsfield unit; IQR: interquartile range.

	Whole subjects (n = 24)	$Value_{PM/AM}$ < 1 (n = 15)	$Value_{PM/AM}$ > 1 (n = 9)	*P* value
Time since death (hours; IQR)	5.9 [3.7, 12.1]	2.9 [1.8, 3.8]	7.1 [2.8, 16.1]	<0.01
$Volume_{PM/AM}$ (95% CI)	1.02 (0.96–1.08)	1.05 (0.98–1.13)	0.97 (0.85–1.08)	0.16

Table 4: Comparison of cases with $value_{PM/AM}$ < 1 and $value_{PM/AM}$ > 1.

death. First, the temperature decrease of the bodies would lead to an increase in CT values. After death, the body temperature decreases by approximately 1°C per hour [20], and the CT value is known to increase by 0.5 HU when the temperature decreases by 1°C [21]. Thus, in the present study, the body temperature at the time of postmortem CT is expected to have increased by 3 HU due to the decreased body temperature after death (-6°C); however, a change of 3 HU is clinically insignificant. The trend observed in the present study where valuePM/AM increased with time since death is consistent with the phenomenon described above.

Second, congestion in the liver after death is expected to lead to a decrease in the liver CT value on postmortem CT. Specifically, the cessation of the circulatory system causes dilatation of the right heart system [22] followed by blood reflux into the hepatic veins [23], resulting in liver congestion. Given that our cohort included a large number of anaemic subjects and that the CT value of anaemic blood [24 -26] is lower than that of liver [18,27], congestive livers might have become more hypodense in the present study. Regarding liver weight, a previous study reported that congestion increased liver weight after death [23]. The finding of aninverse correlation between valuePM/AM and volumePM/AM in the present study is consistent with changes due to liver congestion after death and the speculation described above. The combination of an increase in the CT value due to temperature decrease and a decrease in the CT value due to liver congestion might have balanced our results. However, as shown in Table 4 and Figure 4, the CT value of the postmortem liver may increase as the time since death passes longer. While the body temperature gradually decreases after death, postmortem hepatic congestion occurs immediately only after death. Therefore, at sometime point after death, the increase in CT value due to the temperature loss after death exceeds the decrease in CT value due to postmortem hepatic congestion.

Livor mortis, putrefaction and gravity play important roles in forming the characteristic ventral to dorsal CT value difference on postmortem CT within anorgan, such as horizontal plane formation in the circulatory system or lungs and intra-vessel and intra-organic gas collection [28,29]. Therefore, we hypothesised that the CT values after death would change differently between the ventral and dorsal sides; however, we observed only minimal and clinically insignificant changes. It is possible that postmortem ventral to dorsal CT value differences due to livor mortis or putrefaction might be better facilitated in the vascular system and lungs compared to parenchymal organs, such as the liver. A longer observation time after death might enable detection of a ventral to dorsal CT value difference in the liver.

There were several limitations of our study. First, postmortem CTs were performed with the hands placed down and are therefore slightly more likely to show artefacts in the images. Multiple CT vendors were also used for antemortem CT. Second, we included antemortem CT performed up to one month before death. As livers were confirmed to have no pathological abnormalities at autopsy, it is unlikely that significant changes occurred from antemortem CT imaging to death, including during the agonal stage.

In conclusion, although there is an implicit possibility that CT values could increase with time after death, the normal liver CT values and volumes early in the postmortem period remained the same as those before death. Based on these findings, postmortem imaging may enable estimation of the state of a non-pathological liver before death.

Competing Interests

The authors declare that they have no competing interests.

Author's Contributions

K. Fujimoto as the first author and W. Gonoi as the corresponding author made substantial contributions to the conception and design, acquisition of data, analysis and interpretation of data. M. Ishida, N. Okimoto, K. Nyunoya, H Abe, T Ushiku and O. Abe made substantial contributions to data acquisition and involved in drafting and revising the manuscript.

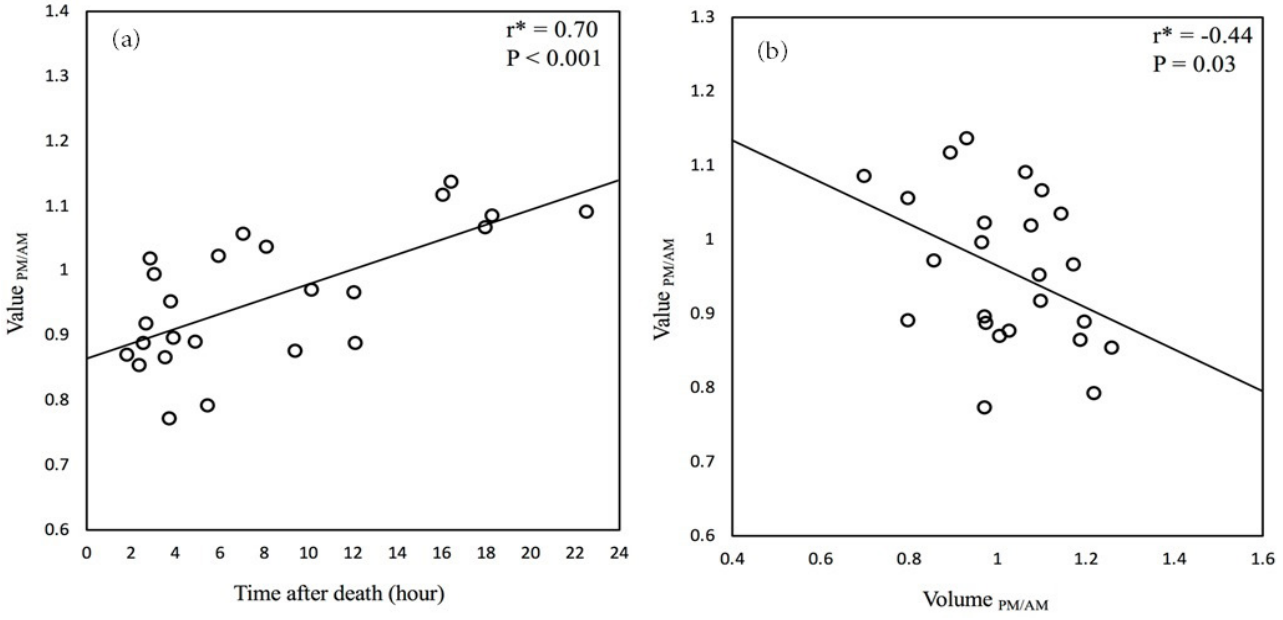

Figure 4: Scatter plot of (a) value$_{PM/AM}$ vs. time after death and (b) value$_{PM/AM}$ vs. volume$_{PM/AM}$ with correlation analysis.
* Spearman's rank correlation.

Funding

This work was supported by (1) JSPS KAKENHI Grant Number 17K17644 entitled 'Establishment of the basis of postmortem imaging as a clue to cause of death investigation' (2017–2020); (2) JSPS KAKENHI Grant Number 20K07989 entitled 'Establishment of Academic Basis of Postmortem Imaging and Its Application for Determining Cause of Death' (2020-2024); and (3) JSPSKAKENHI Grant Number 19K19482 entitled 'Establishment of proper interpretation and imaging method of postmortem CT in medical-related death'.

Acknowledgements

We thank Drs. M. Fukayama, Y. Shintani-Domoto, T. Wada, T. Tajima, and Mr. K. Ino for supporting this study.

References

1. Thali MJ, Yen K, Schweitzer W, Vock P, Boesch C, et al. (2003) Virtopsy, a new imaging horizon in forensic pathology: virtual autopsy by postmortem multislice computed tomography (MSCT) and magnetic resonance imaging (MRI)--a feasibility study. J Forensic Sci 48: 386-403.
2. O'Donnell C, Rotman A, Collett S, Woodford N (2007) Current status of routine post-mortem CT in Melbourne, Australia. Forensic Sci Med Pathol 3: 226-232.
3. Ishida M, Gonoi W, Okuma H, Shirota G, Shintani Y, et al. (2015) Common postmortem computed tomography findings following atraumatic death: Differentiation between normal postmortem changes and pathologic lesions. Korean J Radiol 16: 798-809.
4. Shirota G, Gonoi W, Ishida M, Okuma H, Shintani Y, et al. (2015) Brain Swelling and Loss of Gray and White Matter Differentiation in Human Postmortem Cases by Computed Tomography. PloS one 10: e0143848.
5. Ishida M, Gonoi W, Hagiwara K, Takazawa Y, Akahane M, et al. (2011) Postmortem changes of the thyroid on computed tomography. Leg Med 13: 318-322.
6. Okuma H, Gonoi W, Ishida M, Shirota G, Shintani Y, et al. (2014) Comparison of attenuation of striated muscle between postmortem and antemortem computed tomography: Results of a longitudinal study. PLoS One 9: e111457.
7. Hasegawa I, Shimizu A, Saito A, Suzuki H, Vogel H, et al. (2016) Evaluation of post-mortem lateral cerebral ventricle changes using sequential scans during post-mortem computed tomography. Int J Legal Med 130: 1323-1328.
8. Ishida M, Gonoi W, Hagiwara K, Takazawa Y, Akahane M, et al. (2011) Hypostasis in the heart and great vessels of non-traumatic in-hospital death cases on postmortem computed tomography: Relationship to antemortem blood tests. Leg Med 13: 280-285.
9. Okuma H, Gonoi W, Ishida M, Shirota G, Kanno S, et al. (2016) Comparison of volume and attenuation of the spleen between postmortem and antemortem computed tomography. Int J Legal Med 130: 1081-1087.
10. Takahashi N, Yajima K, Otaki M, Yoshikawa Y, Ishihara A, et al. (2019) Postmortem volume change of the spleen and kidney on early postmortem computed tomography: comparison with antemortem computed tomography. Jpn J Radiol 37: 534-542.
11. Takahashi N, Satou C, Higuchi T, Shiotani M, Maeda H, et al. (2010) Quantitative analysis of brain edema and swelling on early postmortem computed tomography: Comparison with antemortem computed tomography. Jpn J Radiol 28: 349-354.
12. Tisch C, Brencicova E, Schwendener N, Lombardo P, Jackowski C, et al. (2019) Hounsfield unit values of liver pathologies in unenhanced post-mortem computed tomography. Int J Legal Med 133: 1861-1867.
13. Inai K, Noriki S, Kinoshita K, Nishijima A, Sakai T, et al. (2014) Feasibility of liver weight estimation by postmortem computed tomography images: An autopsy study. Pathol Int 64: 315-324.
14. Ishida M, Gonoi W, Shirota G, Okuma H, Yamazawa S, et al. (2019) Diffusely decreased liver attenuation on post-mortem computed tomography: Comparison with ante-mortem computed tomography and autopsy findings. J Forensic Radiol Imaging 16: 1-4.
15. Ishida M, Gonoi W, Hagiwara K, Takazawa Y, Akahane M, et al. (2011) Intravascular gas distribution in the upper abdomen of non-traumatic in-hospital death cases on postmortem computed tomography. Leg Med 13: 174-179.
16. Shiotani S, Kobayashi T, Hayakawa H, Homma K, Sakahara H, et al. (2016) Hepatic Relaxation Times from Postmortem MR Imaging of Adult Humans. Magn Reson Med Sci 15: 281-287.
17. Kanda Y (2013) Investigation of the freely available easy-to-use software "EZR" for medical statistics. Bone Marrow Transplantation 48: 452-458.
18. Pickhardt PJ, Park SH, Hahn L, Lee SG, Bae KT, et al. (2012) Specificity of unenhanced CT for non-invasive diagnosis of hepatic steatosis: Implications for the investigation of the natural history of incidental steatosis. Eur Radiol 22: 1075-1082.
19. Um EH, Hwang S, Song GW, Jung DH, Ahn CS, et al. (2015) Calculation of standard liver volume in Korean adults with analysis of confounding variables. Korean J Hepato-Biliary-Pancreatic Surg 19: 133.
20. Brooks JW (2016) Postmortem Changes in Animal Carcasses and Estimation of the Postmortem Interval. Veterinary Pathology 53: 929-940.
21. Pandeya GD, Greuter MJW, Schmidt B, Flohr T, Oudkerk M, et al. (2012) Assessment of thermal sensitivity of CT during heating of liver: An ex vivo study. Br J Radiol 85: e661-665.
22. Shiotani S, Kohno M, Ohashi N, Yamazaki K, Nakayama H, et al. (2003) Dilatation of the heart on postmortem computed tomography (PMCT): Comparison with live CT. Radiat Med-Med Imaging Radiat Oncol 21: 29-35.
23. Li X, Elwell MR, Ryan AM, Ochoa R (2003) Morphogenesis of Postmortem Hepatocyte Vacuolation and Liver Weight Increases in Sprague-Dawley Rats. Toxicol Pathol 31: 682-688.
24. New PFJ, Aronow S (1976) Attenuation measurements of whole blood and blood fractions in computed tomography. Radiology 121: 635-640.
25. Qanadli SD, Jouannic AM, Dehmeshki J, Lu TL (2015) CT attenuation values of blood and myocardium: Rationale for accurate coronary artery calcifications detection with multi-detector CT. PLoS One 10: e0124175.
26. Lan H, Nishihara S, Nishitani H (2010) Accuracy of computed tomography attenuation measurements for diagnosing anemia. Jpn J Radiol 28: 53-57.
27. Kodama Y, Ng CS, Wu TT, Ayers GD, Curley SA, et al. (2007) Comparison of CT methods for determining the fat content of the liver. AJR Am J Roentgenol 188: 1307-1312.
28. Wagensveld IM, Blokker BM, Wielopolski PA, Renken NS, Krestin GP, et al. (2017) Total-body CT and MR features of postmortem change in in-hospital deaths. PLoS One 12: e0185115.
29. Jackowski C, Thali M, Aghayev E, Yen K, Sonnenschein M, et al. (2006) Postmortem imaging of blood and its characteristics using MSCT and MRI. Int J Legal Med 120: 233-240.