ORIGINAL

Postmortem temporal chest CT and its pathological correlation in piglets

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Abstract : Post-mortem computed tomography (PMCT) is a useful tool to investigate the cause of death. To appropriately use PMCT for cause-of-death analysis, it is necessary to know natural courses after death such as hypostasis in the lungs. We aimed to investigate the natural time-course change of postmortem chest CT findings and its pathological correlation in piglets. Serial chest PMCT scans of four piglets were performed each hour for 24 h and the chronological changes of the lung were evaluated. Immediately after the final CT scan, the autopsy was conducted and bilateral lungs were taken for pathological examination. Two additional piglets were sacrificed and pathological specimens were prepared immediately after death for reference. On pulmonary PMCT, ground glass attenuation (GGA) appeared after the first several hours and increased gradually. Histologically, GGA corresponded to pulmonary edema. The time-related increase in CT attenuation was more prominent in the dorsal lung. Consolidation, endotracheal air defects, and pleural effusion were not observed on PMCT. GGA appeared after the first several hours and increased gradually, and it corresponded to pulmonary edema. GGA in the lung as one of the natural postmortem processes needs to be distinguished from pathogenic findings depending on the time elapsed since death. J. Med. Invest. 71 : 232-236, August, 2024

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INTRODUCTION

Post-mortem computed tomography (PMCT) is becoming a good alternative approach to investigate the cause of death, especially in nations with a low autopsy rate (1, 2). PMCT can show fatal injuries in victims with traumatic death (3, 4) and detect hemorrhagic lesions, such as cerebral hemorrhage, aortic dissection, and aortic aneurysm rupture (1). PMCT has been reported to detect the cause of death in about 30% of subjects (5, 6). In order to determine the cause of death using PMCT appropriately, knowledge of natural postmortem changes is required, such as hypostasis in the lungs (7), a hyperattenuating aortic wall (8), and dilatation of the right heart (9).

Focusing on chest imaging, Shiotani *et al*. reported that various imaging findings were seen on PMCT, such as dependent density, ground glass attenuation (GGA), consolidation, pleural effusion, and endotracheal air defects, and they were useful when combined with clinical information to prepare a death certificate (7). However, it might be challenging to interpret the pulmonary findings on PMCT, because some of them were reported to show time-related progression after death (10, 11). Compared with immediate PMCT, delayed PMCT showed progression in dependent opacity, consolidation (10), and pleural effusion volume (11). Without detailed knowledge of time-related postmortem changes, it is difficult to discern whether the imaging finding is a natural postmortem process or is reflective of antemortem pathology related to the cause of death.

The purpose of this study was to investigate the serial changes in piglet lungs on PMCT for 24 hours after death and to clarify the time-related natural postmortem processes.

MATERIALS AND METHODS

This study was conducted according to the guidelines of the Declaration of Helsinki, and approved by our hospital Institutional Ethics Committee.

Four piglets (age range 2-4 months) were sacrificed by intravenous KCL injection, and subsequently scanned in the supine position each hour for 24 hours using a whole-body multi-detector-row CT (Eclos 8-detector, Hitachi, Ibaragi, Japan). The scan parameters were as follows : 120 kV, 175 mA, 1.0 s/rotation, beam pitch 0.875, collimation 2.5×8, and slice thickness 5.0 mm. The room temperature was maintained at almost 20°C.

All sequential PMCT examinations were reviewed by two board-certified radiologists with more than 20 years of experience, and consensus was achieved after discussion focusing on chest findings such as dependent density, GGA, consolidation, pleural effusion, and endotracheal air defects. Dependent density was defined as an increased attenuation representing a band in the dependent lung showing a clear border with normal lung. GGA or consolidation was defined as some degree of increased lung attenuation other than dependent density as described above. The presence of an endotracheal (or endobronchial) air defect was diagnosed when something such as water or hemorrhage that excluded air was present in the trachea or main bronchi. To evaluate chronological changes of lung attenuation, several circular regions of interest (ROIs) with a diameter of 5 mm were set at ventral and dorsal lung fields and the mean

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attenuation (HU) was measured (Figure 1). The difference in increased attenuation between initial examination and each further examination was calculated with position correction. Differences in increased attenuation between three time points of 0, 8, and 24 hours were assessed using a one-way repeated measures analysis of variance (ANOVA). Differences in increased attenuation at 24 hours were compared between ventral and dorsal lung fields using a paired t test. All statistical analyses were performed using SPSS statistics version 22 (IBM, Armonk, NY, USA). $p < 0.05$ was considered to be significant. The effect sizes, partial eta squared ($\eta^2 p$) in a one-way ANOVA and Cohen's d in a paired t test, were calculated as standardized indices independent of sample size (12).

Immediately after the final CT at 24 hours after death, an autopsy was performed, and bilateral lungs were taken for examination. Pathological specimens were prepared and investigated microscopically after hematoxylin and eosin staining by a board-certified pathologist. Two additional piglets were sacrificed and pathological specimens were prepared immediately after death for reference.

RESULTS

In all four piglets, sequential PMCT was successfully performed each hour for 24 hours after death.

Figure 2 shows the chest PMCT images scanned each hour for 24 hours after death. Increased lung attenuation with ground glass density was observed after the first several hours in all 4 piglets, whereas it was not observed on the initial examination. The increased attenuation appeared more prominent in the dorsal area, including the dependent area. This finding was diagnosed as GGA, not dependent density, because there was no clear border with normal lung.

Table 1 summarizes the frequency of PMCT findings in the chest at 0 and 24 hours after death. Increased lung attenuation was observed in all 4 piglets at 24 hours, whereas it was not observed on the initial examination. It was diagnosed as GGA, not as dependent density or consolidation as described above. A

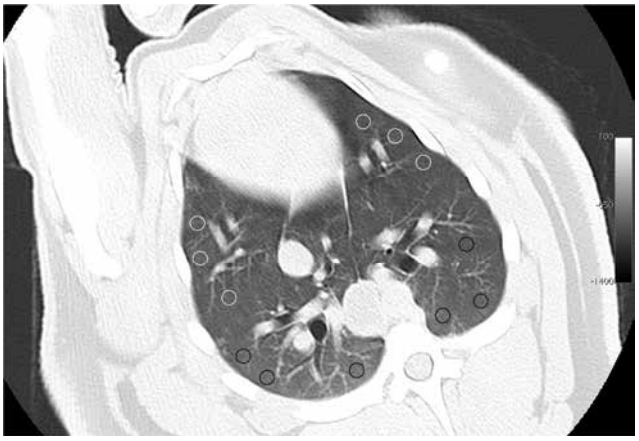

Figure 1. Placement of ROIs in the dorsal and ventral lung fields
Circular regions of interest (ROIs) with a diameter of 5 mm were set at ventral and dorsal lung fields. White circles in the ventral lung field ; Black circles in the dorsal lung field.

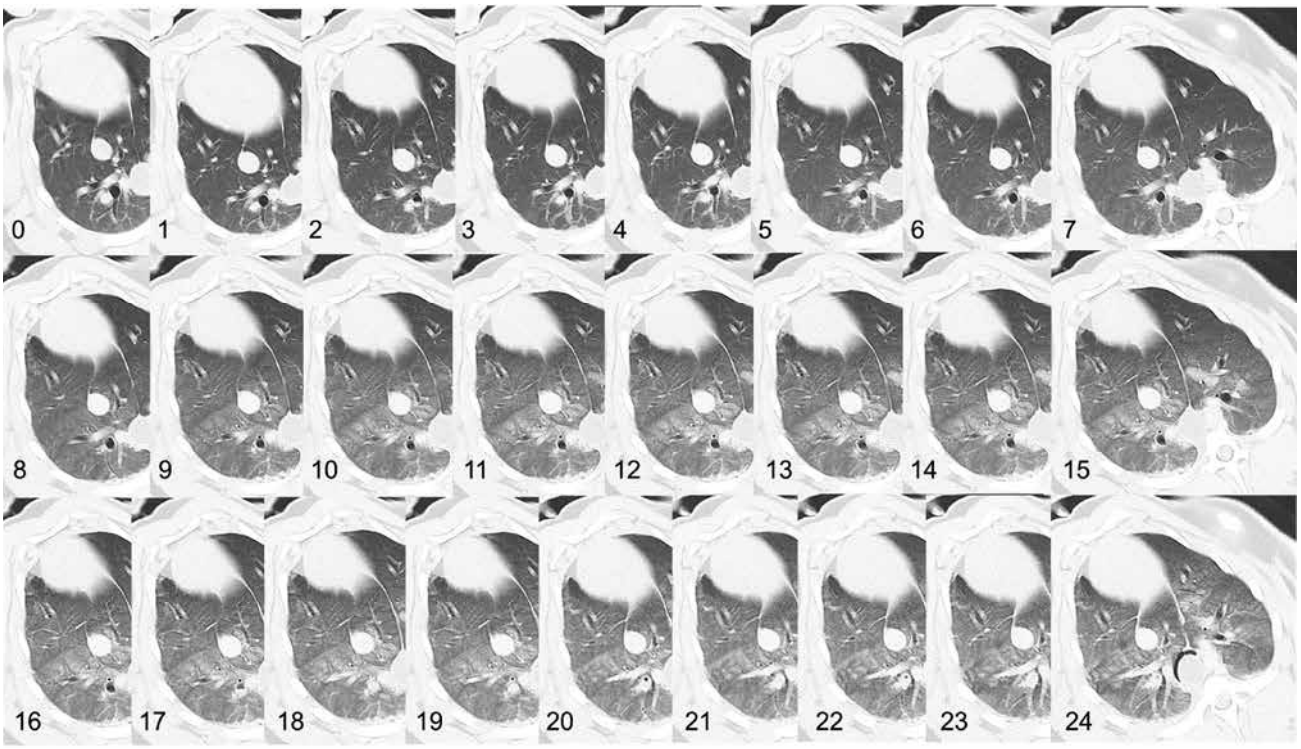

Figure 2. Chest PMCT Images taken every hour up to 24 hours after death
Increased lung attenuation with ground glass density appeared after the first several hours, but it was not observed at the initial examination. The increased attenuation became more prominent in the dorsal area, including the dependent area.

pleural effusion or an endotracheal air defect was not observed at both 0 and 24 hours after death. A small amount of fluid was seen in the peripheral bronchi, but not in the trachea or main bronchi. Thus, it was not diagnosed as an endotracheal air defect. Dependent density, consolidation, pleural effusion, and an endotracheal air defect did not appear on the other sequential PMCT examinations from 1 to 23 hours after death.

GGA typically began to appear at several hours and become clear at 8 hours after death (Figure 2). Figure 3 shows the increase in CT attenuation in dorsal and ventral ROIs each time compared to the initial examination in order to evaluate the time-related changes of GGA. In the dorsal ROI, the difference in CT attenuation increased rapidly in the early 8 hours and increased continuously until 24 hours. The difference between initial and 8-hour examinations was significant ($p = 0.026$) and that between initial and 24-hour examinations was significant ($p = 0.027$), whereas the difference between 8- and 24-hour examinations was not significant. In the ventral ROI, the difference in the CT attenuation value gradually increased over 24 hours and the difference between initial and 24-hour examinations was marginally significant ($p = 0.051$), whereas the differences between the initial and 8-hour examinations, and between the 8- and 24-hour examinations were not significant. At 24 hours after death, the difference in the CT attenuation value was significantly higher in the dorsal ROI than in the ventral ROI ($p = 0.046$). The effect sizes were as follows : $\eta^2 p = 0.834$ and 0.597 for the increased CT attenuation in dorsal and ventral ROIs, respectively compared to the initial examination, and Cohen's $d = 0.787$ for the difference in CT attenuation value between dorsal and ventral ROIs at 24 hours.

On pathological examination of a lung specimen taken from the lungs of a piglet 24 hours after death, the alveolar space was filled with homogeneous pink-staining material showing pulmonary edema, without hemorrhage or inflammatory cell infiltration (Figure 4A). On the other hand, there was no pulmonary edema in the control specimen taken from a piglet immediately after death (Figure 4B).

Table 1. Frequency of PMCT findings in the chest

Postmortem CT finding	0 hours	24 hours
Dependent density	N	N
Ground-glass attenuation	N	4/4
Consolidation	N	N
Pleural effusion	N	N
Endotracheal air defect	N	N

N : Not observed in any piglets

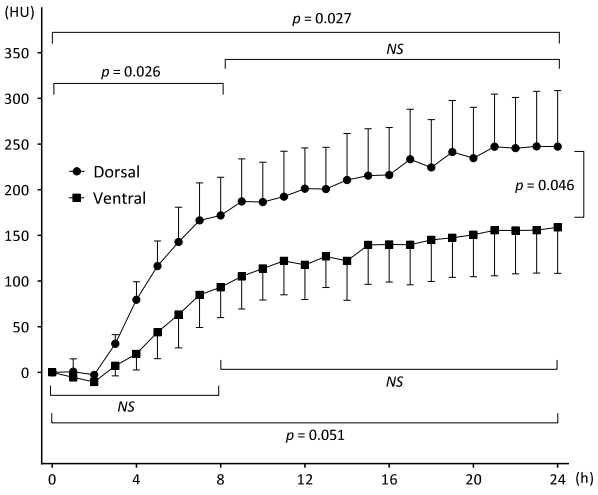

Figure 3. Increased CT attenuation in the dorsal and ventral ROIs compared to the initial examination
In the dorsal ROI, the difference in CT attenuation increased rapidly in the early 8 hours and increased continuously until 24 hours. The difference between initial and 8-hour examinations was significant ($p = 0.026$) and that between initial and 24-hour examinations was significant ($p = 0.027$), whereas the difference between 8- and 24-hour examinations was not significant. In the ventral ROI, the difference in the CT attenuation value gradually increased over 24 hours and the difference between initial and 24-hour examinations was marginally significant ($p = 0.051$). At 24 hours after death, the difference in the CT attenuation value was significantly higher in the dorsal ROI than in the ventral ROI ($p = 0.046$).

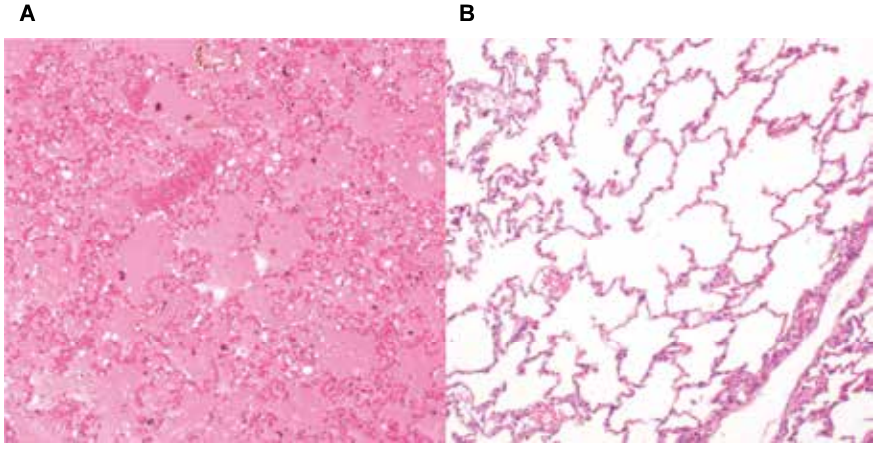

Figure 4. Histological findings of lungs taken from piglets at 24 hours (A) and immediately (B) after death
A) Histological specimen taken from a piglet 24 hours after death. GGA on PMCT corresponds to pulmonary edema microscopically. There is no hemorrhage or inflammatory cells.
B) Histological specimen taken from a piglet immediately after death as a control. There is no pulmonary edema microscopically.

DISCUSSION

In the present study, GGA was observed on PMCT at several hours after death, but it was not observed initially. The measured CT attenuation value in the ROI increased gradually over time. Histopathologically, GGA corresponded to pulmonary edema. The time-related increase in CT attenuation was more prominent in the dorsal lung. In forensic medicine, hypostasis is a well-known postmortem time-dependent change. Hypostasis of the lung shows differences in fluid content from front to back, with congestion and edema being more marked posteriorly (13). Two factors responsible for formation of pulmonary edema in the postmortem period are a pressure gradient between the pulmonary vasculature and the alveolar spaces, and a change in capillary permeability (14).

GGA was not clearly demonstrated in the first several hours in the present study. On the other hand, previous reports using immediate PMCT of human cadavers demonstrated increased pulmonary density more frequently (7, 10, 15). Shiotani reported that GGA was observed in 57% of cadavers on PMCT images performed within 2 hours after certification of death (7). This discrepancy might be caused by antemortem conditions. While the animal is healthy until sacrifice in the experiments, in human cadavers there is pre-existing pathology in the body immediately before death, such as cardiac dysfunction, pulmonary inflammation, or overhydration due to transfusion. They may alter the intravascular pressure or capillary permeability and cause accelerated time-related changes in pulmonary density on PMCT compared to animal experiments. When GGA is observed on PMCT within several hours after death, the presence of antemortem pathology should be considered.

GGA was observed after several hours and became more prominent as time passed in the present study. This suggests that GGA on PMCT after several hours may indicate natural postmortem processes corresponding to pulmonary edema. GGA was also observed in several pathological conditions, such as viral pneumonia, interstitial pneumonia, pulmonary hemorrhage, and pathological edema (16, 17). When GGA is seen on PMCT after several hours, natural postmortem processes should be included in the differential diagnosis, and it is necessary to obtain clinical information before death.

Dependent density on PMCT is also reported to appear frequently immediately (less than 2 hours) after death in humans, and it corresponded to pulmonary congestion that might be related to antemortem pathology (7). On the other hand, it was not observed over the 24-hour period of the present study. Therefore, if dependent density is observed on PMCT, it might reflect pre-existing pathology. However, GGA corresponding to natural postmortem processes became more prominent in dependent areas and might be similar to dependent density. Dependent density on PMCT may usually suggest pre-existing pathology, but it might be a part of natural postmortem processes when dependent density shows GGA.

Consolidation and endotracheal air defects were not observed on the serial PMCT examinations. Therefore, these PMCT findings observed within 24 hours may suggest antemortem pathology. However, clinical information before death should also be taken into consideration. For example, preexisting overhydration due to copious fluid infusion may rapidly advance GGA and result in consolidation within 24 hours without any other pathology.

No pleural effusion was seen on the serial PMCT examinations within 24 hours. A clinical report of cadavers also found no pleural fluid collection on PMCT within 30 hours (11). If there is a pleural effusion on PMCT within 24 hours, it may reflect pre-existing antemortem pathology.

The limitation of this study is the small sample size (4 piglets). However, the effect sizes for the increased CT attenuation in dorsal and ventral ROIs compared to the initial examination were considerably large ($\eta^2p = 0.834$ and 0.597, respectively), and the effect size for the difference in CT attenuation value between dorsal and ventral ROIs were moderate to large (Cohen's $d = 0.787$). The large effect sizes indicate that a considerable degree of significance can be attributed to the data. In any case, further studies with larger sample size are warranted to validate our findings.

CONCLUSIONS

Chest PMCT findings of piglets within 24 hours after sacrifice were evaluated. GGA appeared after the first several hours and increased gradually, and it corresponded to pulmonary edema. Dependent density, consolidation, pleural effusion, and endotracheal air defects were not observed. Knowledge of the natural postmortem processes in the lung is important to interpret pulmonary findings of PMCT correctly. The postmortem time and antemortem clinical information are also helpful to diagnose pulmonary pathology using PMCT.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest concerning the publication of this manuscript.

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AUTHOR CONTRIBUTIONS

K.K., T.S., K.I., and H.K. conceptualized the work ; K.K. and T.S. performed post-mortem CT scans of 4 piglets ; K.I., S.N., H.N. performed pathological examinations ; K.K., T.S., and T.T. performed statistical analyses and data visualization ; K.K. prepared the manuscript ; Y.H. and S.K. supervised data analysis ; H.K. and T.T. supervised the manuscript preparation. All authors have read and agreed to the published version of the manuscript.

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