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Postmortem water contents of major organs with regard to the cause of death

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Abstract

The water contents of individual organs are maintained in a narrow range, but altered in morbidity owing to a disturbance of water equilibrium. The present study investigated the tissue water contents of major organs with regard to the cause of death in serial autopsy cases within 3 days postmortem ($n = 329$; 223 males, 106 females; age range, 1–100 years). Individual tissue water contents differed markedly across organs, but no significant postmortem or survival-period dependence, gender-related difference, or age dependence was observed. However, the lung water contents were higher in drowning cases, especially in saltwater cases ($p < 0.05$), and in strangulation among the acute mechanical asphyxiation cases. The brain water contents were higher in hypothermia cases (cold exposure) and tended to be higher in hyperthermia cases (heatstroke). The kidney water contents were higher in drowning and acute cardiac cases than in fatal intoxication and fire fatality cases, but tended to be higher in fresh- and bathwater drowning cases than in saltwater cases ($p > 0.05$). The spleen water contents were higher in bathwater drowning than in saltwater and freshwater cases, but did not differ among other the causes of death. These findings suggest that the postmortem tissue water content of individual organs, especially the lungs and/or kidney, depends on the cause of death and particularly contributes to differentiation between saltwater and freshwater drowning, respectively. This work therefore provides insight into the investigation of varied tissue water imbalances during the death process. In conclusion, we recommend the measurement of tissue water content because it is easy to perform and appears to be useful for evaluating the pathophysiology of systemic circulatory failure.

Keywords: Pathophysiology, Tissue water content, Edema, Drowning, Hypoxia/ischemia, Circulatory failure

Graphical abstract

Water contents with regard to the cause of death in the upper lobes of the lung (a), lower lobes of lung (b), kidney (c), brain (d), spleen (e).
***Significantly higher †Significantly lower**

Highlights

- We investigated the tissue water contents of the lungs, brain, kidneys, and spleen.
- We evaluated the relationship between tissue water content and cause of death.
- Tissue water content is useful to distinguish saltwater and freshwater drowning.
- Tissue water content is useful for the pathophysiology of circulatory failure.

1. Introduction

The tissue water content (TWC) of individual human organs are generally stable and maintained as part of the whole-body water–electrolyte equilibrium that involves both water intake and renal excretion.¹ Fatal trauma or disease can cause organ-specific and/or systemic water imbalances, which present as visceral edemas in autopsy, often in the lungs and brain,^{2–4} which are reportedly caused by the activation of humoral regulation and/or more regulatory mechanisms. In addition, Starling forces govern the passive exchange of water between capillary microcirculation and interstitial fluid; therefore, abnormal Starling forces such as increased venous capillary pressure and decreased plasma oncotic pressure promote fluid extravasation and edema formation.⁵ Previous forensic studies have demonstrated that the postmortem lung weight depends strongly on the cause of death and survival time, which are associated with the development of pulmonary congestion and edema.^{6,7} Moreover, the severity of brain edema is typically related to the brain weight.⁸ Other organs, including the spleen and kidney, may also cause tissue edema owing to water imbalance.⁹ Recent studies have suggested that molecular pathology should be applied to investigate tissue edema,^{2–4} and quantitative analyses of water contents and their distribution by postmortem computed tomography are used to diagnose pulmonary congestion and edema.^{10,11} However, these studies remain rare, especially as they apply to the relationship between TWC and the cause of death.

Although the association between organ weight and TWC has been investigated,^{6–8} to our knowledge, no consensus has been reached on their relationship, and it remains unclear whether organ weight can be applied to the evaluation of edema in forensic autopsy cases. Furthermore, other than organ weight, no quantitative indicators are available to connect the effects of variation

in the TWC and the cause of death.¹² In the clinical medicine field, hematocrit is used to measure the ratio of erythrocyte flow to total blood flow. When the organs absorb water from the blood, hematocrit is expected to increase¹³; however, to our knowledge, no previous reports have evaluated this relationship using an autopsy sample.

In the present study, we investigated the relationship between TWC, organ weight, and hematocrit and evaluated the TWC of the lungs, brain, kidneys, and spleen among deceased individuals as a possible quantitative indicator of the pathophysiology of systemic water dynamics.

2. Material and methods

2.1. Samples

Serial autopsy cases examined within 3 days postmortem at our institution over the previous 8 years were analyzed. To minimize the possibility of bias, we examined all cases in which TWC could be measured, except for cases of natural death (excluding sudden cardiac death). Furthermore, in the present study, only clearly accountable cases were collected. In total, there were 329 cases (223 males and 106 females; median age, 63 years; age range 0–100 years). The causes of death were classified based on a complete autopsy and macromorphological, micropathological, and toxicological examinations as follows: injury (head blunt injury: n = 39; non-head blunt injury: n = 32; sharp instrument injury: n = 21), asphyxia (hanging: n = 17; strangulation: n = 16; others: n = 14), fatal intoxication (methamphetamines: n = 13; psychotropics: n = 9; others: n = 5), drowning (saltwater: n = 10; freshwater: n = 9; bathtub: n = 13), fire fatality (including cases with low [$<30\%$], intermediate [$30\text{--}60\%$], and high [$>60\%$] carboxyhemoglobin [CO-Hb] levels; n = 38, n = 24, and n = 15, respectively), hyperthermia (heat stroke: n = 16),

hypothermia (cold exposure: n = 9), and acute cardiac death (n = 29), which included acute myocardial ischemia without hemopericardium and other cardiac diseases. The hypothermia and hyperthermia cases involved cold and hot weather, respectively, at night or during the day, and the diagnosis was based on pathology and toxicology that considered circumstantial evidence, excluding other causes of death. The approximate survival time ranged from 0.5 h to 2 months (median, 0.5 h). The detailed case profiles are shown in Tables 1. The postmortem interval was defined as the time from the estimated time of death to the autopsy. The survival time was defined as the period from the onset of the fatal insult to death. All data, including organ weight, were collected from autopsy records. Tissue specimens were taken from consistent sites at autopsy as follows: The upper and lower lobes of the bilateral lungs, the left parietal lobe of the brain, the bilateral kidneys, and the spleen. These tissue specimens were stored at 4 °C in a refrigerator until use within 24 h.

2.2. *TWC measurements*

The TWC of the specimens was measured using a halogen moisture analyzer (model HB43, Halogen; Mettler Toledo International, Tokyo, Japan) and presented as the ratio (%) of the difference between the wet weight (WW) and the dry weight (DW) after the tissue samples were dried at 150 °C for 30 min ($TWC = (WW - DW) / WW \times 100$).⁴

2.3. *Blood analysis*

Bilateral heart blood hematocrit values were measured by flow cytometry using an automated hematology analyzer (SE-9000™; Sysmex Co., Ltd., Kobe, Japan) within 24 h after sampling.¹⁴

2.4. Statistical analysis

Statistical analyses were performed using SPSS (version 17.0; SPSS, Inc., Chicago, IL, USA). We used linear regression to examine the relationships between pairs of parameters. The Mann–Whitney *U* test was performed to assess differences between groups, and the Kruskal-Wallis test was conducted to determine differences among groups. In this report, graphs are presented as box and whisker plots, in which the central horizontal line in each box represents the median, the boxes span the interquartile range, and the whiskers represent 90% confidence intervals. Outliers are incidence rates more than 1.5 times the length of the box. In these analyses, *p*-values < 0.05 were considered statistically significant. The sensitivity and specificity of distinguishing between the two groups using cut-off drowning values was estimated using a receiver operating characteristic (ROC) analysis. The areas under the curve were calculated and analyzed using a one-tailed test. The optimal compromise between sensitivity and specificity was determined graphically.

3. Results

3.1. TWC measurements

The TWC in all organs ranged between 72.0–89.2% (median, 80.0%). The brain and spleen showed markedly lower TWC levels than the other organs, with the spleen and kidney showing markedly lower levels than the lung (Fig. 1). The differences in the TWC measurements between the bilateral sites of individual organs were 0.0–8.09% (median, 1.31%). These values ranged from 0.0–13.3% (mean, 1.06%) for the upper and lower lobes of the lung and 0.0–7.3% (median, 0.76%) for the kidneys. In all cases, the TWC was lower for the brain and spleen than for the other viscera ($p < 0.0001$), and was slightly lower for the kidney than for the lung (Table 3). The bilateral

correlations were $r = 0.687$ ($p < 0.0001$) and $r = 0.752$ ($p < 0.0001$) for the upper and lower lobes of the lungs, respectively, and $r = 0.746$ ($p < 0.0001$) for the kidneys.

Organ weights, the details of which are shown in Table 2, were then compared with TWC. Moderate correlations were found between the TWC and organ weights corrected by body height (the ratio of organ weight to body height) for the upper lobes of each lung (left: $r = 0.396$, $p < 0.0001$; right: $r = 0.375$, $p < 0.0001$). The correlations were weaker for the lower lobes (left: $r = 0.288$, $p < 0.0001$; right: $r = 0.289$, $p < 0.0001$) and kidneys (left: $r = 0.152$, $p < 0.01$; right: $r = 0.217$, $p < 0.001$), and no significant relationship was found in the brain and spleen. The TWC of all organs other than the brain showed a slight negative correlation with bilateral heart blood hematocrit values ($r = 0.202$ – 0.340 , $p < 0.01$ – 0.0001).

3.2. Influences of postmortem interval, survival period, age, and gender

No significant postmortem or survival-period dependencies were observed for the TWC of individual organs. The spleen TWC was greater for females (72.79–82.49; median, 78.38) than for males (76.25–82.46; median, 77.54; $p < 0.0001$), and the TWC of the brain and kidney showed slight to moderate negative correlations with age (brain: $r = 0.234$, $p < 0.0001$; left kidney: $r = 0.274$, $p < 0.0001$; right kidney: $r = 0.238$, $p < 0.0001$).

3.3. Relationship with the cause of death

3.3.1. Lung

The TWC of the bilateral lung upper lobes was significantly higher in the drowning than in the injury, asphyxia, fire fatality, fatal intoxication, hyperthermia, and acute cardiac death cases ($p < 0.0001$ – 0.05) (Fig. 2a). In both the right and left lower lobes, the TWC was higher for the drowning

than for the injury, asphyxia, fire fatality, fatal intoxication, hyperthermia, hypothermia, and acute cardiac death cases ($p < 0.0001-0.05$) (Fig. 2b). Among the drowning cases, the saltwater cases had markedly higher TWC levels than the bathtub cases in the lower lobe of the left lung ($p < 0.05$) (Fig. 3a,b). Among the asphyxia cases, the hanging cases had lower TWC levels than the strangulation cases in the upper lobe of the right lung ($p < 0.05$) (Fig. 4a,b). The cut-off values (sensitivity and specificity) from the ROC analysis were estimated for discriminating between groups with higher and lower TWC levels as follows: upper lobe of the left lung, 82.86% (0.719 and 0.795) for the drowning group and 83.81% (0.900 and 0.871) for the saltwater drowning cases; upper lobe of the right lung, 81.99% (0.750 and 0.704) for the drowning group and 83.50% (0.800 and 0.843) for the saltwater drowning cases; lower lobe of the left lung, 82.55% (0.813 and 0.791) for the drowning group and 84.01% (0.900 and 0.918) for the saltwater drowning cases; and lower lobe of the right lung, 82.40% (0.750 and 0.781) for the drowning group and 82.95% (0.900 and 0.803) for the saltwater drowning cases.

3.3.2. Brain

The brain TWC was higher in the hypothermia (cold exposure) than in the injury, asphyxia, fatal intoxication, and fire fatality cases ($p < 0.05$), and tended to be higher in the hyperthermia (heatstroke) cases (Fig. 5a). No significant differences were observed among the injury, asphyxia, fatal intoxication, or fire fatality subgroups ($p > 0.05$); however, the brain tended to show lower TWC levels in the saltwater compared with the freshwater and bathtub drowning cases (Fig. 5b).

3.3.3. Kidney

The kidney TWC was higher in the drowning and acute cardiac death groups than in the fatal

intoxication, asphyxia, fire fatality, and hyperthermia cases ($p < 0.0001$ – 0.05) (Fig. 6a). Among the subgroups, the saltwater had lower TWC levels than the freshwater and bathtub drowning cases in the left kidney ($p < 0.05$) (Fig. 6b). Among the fire fatality cases, those with intermediate CO-Hb levels (30–60%) had higher TWC in the left kidney than those with high CO-Hb levels ($p < 0.05$) (Fig. 6c). No significant differences were observed among the injury, mechanical asphyxia, and fatal intoxication subgroups ($p > 0.05$). However, in the asphyxia groups, the hanging cases tended to have lower TWC levels in the kidneys compared with the strangulation cases (Fig. 6d). Based on the ROC analysis, the cutoff values (sensitivity and specificity) for discriminating groups with higher and lower WTC levels were estimated as follows: left kidney, 80.69% (0.656 and 0.613) for drowning and 80.29% (0.828 and 0.513) for acute cardiac death; and right kidney, 80.49% (0.625 and 0.589) for drowning and 80.26% (0.862 and 0.573) for acute cardiac death.

3.3.4. Spleen

In the spleen, no significant differences in the TWC were observed among the different causes of death (Fig. 7a), or among the injury, asphyxia, fatal intoxication, and fire fatality subgroups ($p > 0.05$). However, among the drowning subgroups, the saltwater cases had lower spleen TWC levels than the bathtub cases ($p < 0.05$) (Fig. 7b).

4. Discussion

The aim of this study was to investigate the relationship between the TWC of the lungs, brain, kidneys, and spleen among deceased individuals as a possible quantitative indicator of the pathophysiology of systemic water dynamics.

The findings showed that the TWC levels of the lungs and kidneys in deceased patients were higher compared with those of the brain and spleen, consistent with circulatory failure. The correlation observed between TWC and organ weight in the lungs and kidneys showed that organ weights can be applied as TWC. The brain and spleen are considered to be uncorrelated because they are susceptible to conditions such as cerebral atrophy and splenomegaly. When the organs absorb water, the hematocrit value is expected to decrease. In the present study, decreases in hematocrit were observed against increases in TWC. Since the hematocrit value is influenced by the viscosity of the blood, organ edemas are more likely to occur when the viscosity of the blood is low.

The lungs showed significantly higher TWC levels in the drowning cases. Among the drowning subgroups, saltwater showed markedly higher TWC levels than bathtub cases. Among the asphyxia cases, strangulation had higher TWC levels in the lung than hanging cases. These results suggest that saltwater drowning is similar to hypoxia.¹⁵ Consistent with these findings, previous studies have suggested that the postmortem lung weight may depend on both the aspirated immersion medium involved in drowning cases^{16,17} and the acute respiratory distress and circulatory failure involved in fire fatalities.¹⁸

The kidneys showed a significantly higher TWC in the drowning and acute cardiac death groups. An increase in kidney TWC owing to cardiac disease is indicative of circulatory failure. Among the drowning subgroups, the saltwater cases tended to have lower TWC levels than the freshwater and bathtub cases. In the asphyxia groups, hanging tended to result in lower TWC levels in the kidney compared with strangulation. These results suggest that saltwater drowning is similar to ischemia in the kidney.¹⁹

In the brain and spleen, the TWC was lower compared with that of other organs, but no clear

differences were observed among the different causes of death. It is possible that the TWC of the brain and spleen manifest as the final condition of a case, but further evidence is needed before drawing conclusions.

5. Conclusion

In conclusion, TWC can indicate lung edema resulting from water aspiration and/or circulatory failure, which could be useful in pathophysiological analyses to distinguish between saltwater and freshwater drowning cases. In addition, kidney TWC may be an indicator of circulatory failure. We therefore recommend the measurement of TWC because it is easy to perform and appears to be useful for evaluating the pathophysiology of systemic circulatory failure.

Disclosures

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Competing interests

No authors have any conflicts of interest to declare.

Ethics statement

This study was approved by the ethics review board of the Osaka City University Medical School.

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Figure legends

Figure 1. Postmortem tissue water content (TWC) in all organs as a function of the cause of death.

Figure 2. TWC in the lung with regard to the cause of death. (a) *Significantly higher: in the upper lobes of the lung, the drowning cases had significantly higher TWC compared with the injury, asphyxia, fire fatalities, fatal intoxication, hyperthermia and acute cardiac death cases ($p < 0.0001-0.05$). (b) In the lower lobes of the lung, the drowning cases had higher TWC compared with the injury, asphyxia, fatal intoxication, fire fatality, hyperthermia, hypothermia, and acute cardiac death cases ($p < 0.0001-0.05$).

Figure 3. TWC in the upper (a) and lower (b) lobes of the lung in drowning cases. *Significantly higher: saltwater cases vs. bathwater cases in the lower lobe of the left lung ($p < 0.05$).

Figure 4. TWC in the upper (a) and lower (b) lobes of the lung in acute mechanical asphyxia cases.

†Significantly lower: the hanging cases vs. the strangulation, and other asphyxia cases in the upper lobe of the right lung ($p < 0.05$).

Figure 5. TWC in the brain with regard to the cause of death. (a) *Significantly higher: hypothermia vs. injury, asphyxia, fatal intoxication, and fire fatality cases ($p < 0.05$). (b) TWC in the brain in drowning cases: the saltwater cases tended to have lower TWC than the freshwater and bathtub drowning cases.

Figure 6. (a) TWC in the kidney with regard to the cause of death. Significantly higher: *drowning vs. fatal intoxication cases in both kidneys ($p < 0.01$) and **acute cardiac death vs. fatal intoxication, fire fatality, and hyperthermia cases in both kidneys ($p < 0.0001-0.05$). (b) TWC in the kidney in drowning cases. †Significantly lower: †Saltwater vs. freshwater and bathtub cases in the left kidney ($p < 0.05$). (c) TWC in the kidney in fire fatality cases. *Significantly higher: among the fire fatality cases, those with intermediate vs. high CO-Hb levels (left kidney: $p < 0.05$). (d) TWC in the kidney in asphyxia cases. The hanging cases tended to have lower levels than the strangulation cases.

Figure 7. (a) TWC in the spleen with regard to the cause of death. No significant differences were observed among the causes of death. (b) TWC in the spleen in drowning cases.

†Significantly lower: saltwater vs. bathtub cases ($p < 0.05$).

Table legends

Table 1

Case profiles (n = 329).

Cause of death	Male/female	Age (median)	Survival time (h) (median)	Postmortem time (h) (median)
Injury	68/24	1-100 (57)	0.1-240 (1.5)	8-69 (31)
Head blunt injury	28/11	1-93 (52)	0.1-240 (3.5)	15-63 (37)
Non-head blunt injury	25/7	23-100 (59)	0.1-6 (0.5)	8-69 (29)
Sharp instrument injury	15/6	40-91 (61)	0.1-5 (0.5)	10-60 (30)
Asphyxia	30/17	23-87 (61)	0.1-480 (0.5)	8-65 (31)
Hanging	13/4	26-77 (43)	0.1-480 (0.5)	10-65 (32)
Strangulation	7/9	23-87 (55)	0.5-3 (0.5)	9-61 (32)
Others	10/4	30-75 (66)	0.5-3 (0.5)	8-57 (25)
Fatal intoxication	12/15	20-75 (40)	0.5-6 (6)	16-62 (33)
Metamphetamine	7/6	25-60 (45)	0.5-6 (6)	25-61 (37)
Psychotropic drug	3/6	20-46 (27)	3.0-6 (6)	16-62 (33)
Others	2/3	29-75 (37)	0.5-6 (6)	18-39 (29)
Drowning	20/12	19-92 (64.5)	0.5-3 (0.5)	7-70 (30)
Salt water	6/4	19-79 (64)	0.5-3 (0.5)	7-70 (41)
Fresh water	7/2	34-87 (61)	0.5-3 (0.5)	20-62 (33)
Bathtub	7/6	49-92 (66)	0.5 (0.5)	17-61 (25)
Fire fatality	52/25	33-97 (71)	0.5-1440 (0.5)	7-41 (23)
CO-Hb <30 %	24/14	33-97 (76)	0.5-1440 (0.5)	11-38 (20)
CO-Hb >30 %, <60 %	20/4	41-95 (70)	0.5-3 (0.5)	7-41 (21)
CO-Hb >60 %	8/7	42-91 (67)	0.5-3 (0.5)	12-41 (25)
Hyperthermia	12/4	39-95 (72)	0.5-6 (6)	15-65 (31)
Hypothermia	6/3	50-91 (80)	6.0-12.0 (6)	17-62 (33)
Acute cardiac death	23/6	19-92 (62)	0.1-12 (0.5)	6-56 (23)
Total	223/106	1-100 (63)	0.1-1440 (0.5)	6-70 (29)

Table 2

Organ weights with regard to the cause of death (n = 329).

Cause of death	Left lung (g) (median)	Right lung (g) (median)	Left kidney (g) (median)	Right kidney (g) (median)	Brain (g) (median)	Spleen (g) (median)
Injury (n = 92)	65-1230 (400)	105-1330 (482.5)	36.8-310 (140)	20-255 (127.5)	955-1660 (1315)	16.8-210 (80)
Asphyxia (n = 47)	230-905 (470)	235-1230 (565)	22.5-250 (135)	75-230 (135)	855-1690 (1345)	25-370 (110)
Fatal intoxication (n = 27)	240-910 (485)	335-1060 (590)	95-215 (145)	85-205 (130)	1170-1635 (1335)	25-345 (105)
Drowning (n = 32)	280-840 (550)	315-890 (632.5)	60-255 (145)	80-205 (145)	910-1540 (1300)	20-165 (77.5)
Fire fatality (n = 77)	59.5-945 (400)	70.5-1115 (510)	40-285 (130)	45-260 (120)	915-1505 (1220)	16.8-280 (85)
Hyperthermia (n = 16)	275-925 (385)	295-1040 (520)	40-285 (130)	57.1-205 (117.5)	1035-1560 (1265)	26.6-420 (65)
Hypothermia (n = 9)	185-710 (345)	190-1150 (380)	75-190 (100)	80-215 (95)	1150-1430 (1305)	25-100 (65)
Acute cardiac death (n = 29)	220-1155 (560)	290-1350 (700)	80-310 (160)	65-325 (160)	1055-1580 (1340)	45-340 (125)
Total	59.5-1230 (450)	70.5-1350 (535)	22.5-310 (145)	20-325 (130)	855-1690 (1295)	16.8-420 (90)

Table 3

Ranges of water contents of the lung, brain, kidney, and spleen.

Organ			Minimum (%)	Maximum (%)	Median (%)	Mean (%)
Lung	Left	Upper lobe	72.23	89.29	80.98	81.16
		Lower lobe	71.00	89.15	80.60	80.76
	Right	Upper lobe	72.13	87.93	81.14	80.97
		Lower lobe	68.11	88.02	80.53	50.64
Kidney	Left		71.95	85.49	81.10	80.06
	Right		73.26	86.37	80.04	80.15
Brain			72.95	87.20	79.90	79.93
Spleen			71.98	82.49	77.82	77.83
Total			68.11	89.29	80.10	80.19

Significantly lower: †kidney vs. lung ($p < 0.0001$ – 0.05). ††Brain and spleen vs. other organs ($p < 0.0001$).