

ORIGINAL ARTICLE

Relationship between sudden natural death and abdominal fat evaluated on postmortem CT scans

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Summary

Objective

This study examined the association between sudden natural death and abdominal fat using postmortem computed tomography (CT) scans.

Subjects and methods

Postmortem CT images at the umbilical level of 241 subjects were used to measure abdominal areas of subcutaneous- and visceral fat, the rate of visceral fat and the waist circumference. Of the study subjects, 174 died of sudden natural death (130 men and 44 women), and 67 died of different causes (46 men and 21 women). All were between 40 and 75 years of age. Logistic regression analysis was performed to identify independent abdominal parameters associated with sudden natural death.

Results

By univariate analysis, the areas of subcutaneous and visceral fat were significantly larger in sudden natural death than who died of different causes (subcutaneous fat, odds ratio [OR] = 1.004, 95% confidence interval [CI] = 1.000–1.007, $p = 0.03$; visceral fat, OR = 1.008, 95% CI = 1.003–1.013, $p < 0.01$). Multivariate analysis showed that the area of visceral fat was an independent factor associated with the risk of sudden natural death (OR = 1.008, 95% CI = 1.002–1.015, $p = 0.02$).

Conclusions

Postmortem CT revealed that sudden natural death was related to abdominal fat deposits.

Keywords: abdominal obesity, computed tomography, mortality.

Introduction

Sudden natural death is defined as death not attributable to a traumatic event or suicide within 24 hours of symptom onset in an apparently healthy individual or in a patient whose disease stage was not predictive of death (1–3). The frequency of sudden unexpected death due to cardiac or unidentifiable causes in employment age is 11 in 100,000 (4). In order, most sudden natural deaths are due to cardiovascular followed by infectious diseases (5,6). In individuals with acute chest pain, the cause of sudden natural death was pulmonary embolism, aortic dissection and obstructive coronary artery disease (7).

Obesity is a risk factor for cardiovascular, metabolic, neoplastic and musculoskeletal disorders, and abdominal obesity is associated with increased morbidity independent of age, race and gender (8–10). Abdominal adiposity is a significant predictor of mortality (11) independent of the body mass index. The association between the waist circumference and metabolic risk may be partly explicable by a strong association with visceral adiposity (12).

Computed tomography (CT) studies have shown that visceral fat was a significant predictor of mortality: in a model including three fat measures (subcutaneous, visceral and liver fat), age and length of follow-up, only visceral fat was a significant predictor of mortality (10). In women, standard deviation increment in visceral fat

was associated with a significantly increased all-cause mortality risk (13). CT also revealed visceral adiposity was associated with incident cardiovascular disease (14–17). In Japanese Americans, visceral fat was associated with obesity-related mortality (18). Although the association between abdominal adiposity and morbidity is known, there are no CT studies that used direct measurements of abdominal fat to elucidate the association between abdominal fat and sudden natural death.

In Japan, postmortem CT studies are performed to determine the cause of sudden death. Under the hypothesis that it is associated with abdominal fat, we investigated the relationship between sudden natural death and abdominal fat measured directly on postmortem CT scans.

Methods

Subjects and methods

This retrospective study was approved by our institutional review board. We used postmortem CT studies acquired between February 2008 and March 2016 of 241 subjects who were between 40 and 75 years of age at the time of their sudden death. Of these, 174 died of sudden natural death (group 1; 130 men and 44 women), and 67 died of different causes (group 2; 46 men and 21 women) (Table 1). There was no significant difference in the age of the two groups ($p = 0.09$, two-sample t -test) nor in their gender ($p = 0.34$, chi-square test).

The criteria for sudden natural death were death due to natural diseases and abrupt and unexpected death in individuals who appeared well. Individuals who died of non-natural causes such as trauma and suicide were

Table 1 Clinical data on 241 study subjects

	Natural death (group 1)	Different causes (group 2)	<i>P</i> - value
Subjects	174	67	
Median age [year] (range)	65 (40–75)	66 (40–75)	0.09
Gender [male/female]	130/44	46/21	0.34
Vascular risk factors			
Diabetes mellitus	19	1	N/A
Hypertension	39	0	N/A
Dyslipidemia	15	0	N/A
Smoking	13	0	N/A
Median interval between death and computed tomography scan [min] (range)	70 (10–720)	70 (20–660)	0.55
	65 (40–75)	66 (40–75)	0.09

N/A, not applicable.

Vascular risk factors were obtained from medical records.

excluded. Contrast-enhanced CT studies were performed in six group 1 subjects; two group 1 subjects and one group 2 subject were autopsied.

We perused their medical records to review the demographic data of our study subjects for vascular risk factors (diabetes mellitus, hypertension, dyslipidemia and smoking) and the interval between the time of death and imaging.

In individuals who died of sudden death, we routinely obtain whole-body postmortem CT scans on a 16-row CT scanner (Lightspeed16, GE Medical Systems, Milwaukee, WI, USA) or a 320-row CT scanner (Aquilion ONE, Toshiba Corp. Medical Systems, Otawara, Japan). Fat analysis was performed on a workstation (AZE Virtual Place Raijin; AZE Ltd., Tokyo, Japan). The areas of subcutaneous and visceral fat and the waist circumference were measured on 5-mm-thick CT images at the umbilical level. Adipose tissue areas were calculated using an attenuation range of -150 to -10 Hounsfield units. The abdominal subcutaneous fat area was defined as the area of adipose tissue between the skin and the outermost aspect of the abdominal muscle wall (Figure 1). We also calculated the rate of visceral fat using the equation:

$$\text{rate of visceral fat} = \frac{\text{area of visceral fat}}{\text{area of subcutaneous} + \text{visceral fat}}$$

Statistical analysis

We compared the interval between the time of death and imaging in groups 1 and 2 using the two-sample t -test. To compare abdominal parameters, we performed logistic regression analysis. Factors associated with sudden natural death (dependent variables) were identified by univariate analysis. Independent variables included the age, gender, interval between the time of death and imaging, area of subcutaneous fat, area of visceral fat, rate of

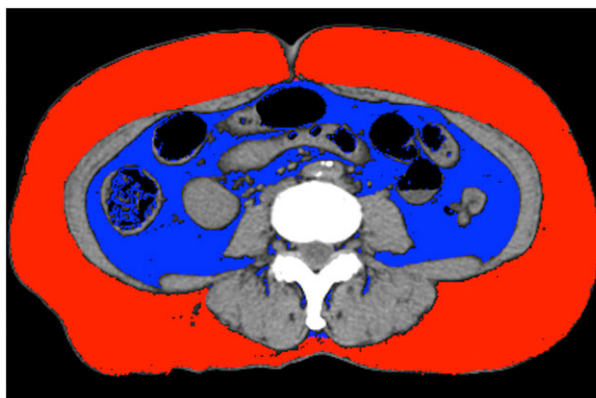


Figure 1 Screen capture from the fat analysis tool. The blue and red areas show visceral and subcutaneous fat, respectively, at the umbilical level.

visceral fat and waist circumference. All statistical tests were two-sided; probability values of <0.05 were considered statistically significant. Multivariate analysis adjusted for relevant factors was also performed using logistic regression analysis. All statistical analyses were with IBM SPSS Statistics 21.

Results

Postmortem CT scans revealed the cause of sudden natural death in 54 group 1 subjects (Table 2); in the other 120, it could not be ascertained. The causes of sudden death in group 2 are also shown in Table 2.

There was no significant difference in the interval between the time of death and imaging between group 1 (median 70 min and range 10–720 min) and group 2 (median 70 min and range 20–660 min) ($p = 0.55$ and two-sample *t*-test). In group 1, the mean area of subcutaneous and visceral fat was $152.5 \pm 96.4 \text{ cm}^2$ and $139.3 \pm 72.9 \text{ cm}^2$, respectively; the mean rate of visceral fat was 0.50 ± 0.12 , and the mean waist circumference was $94.7 \pm 26.7 \text{ cm}$. In group 2, the mean area of subcutaneous and visceral fat was $125.4 \pm 59.8 \text{ cm}^2$ and $108.0 \pm 47.3 \text{ cm}^2$, respectively; the mean rate of visceral

fat was 0.47 ± 0.11 , and the mean waist circumference was $97.9 \pm 28.0 \text{ cm}$.

By univariate analysis, the areas of subcutaneous and visceral fat were significantly larger in group 1 than in group 2 (subcutaneous fat, odds ratio [OR] = 1.004, 95% confidence interval [CI] = 1.000–1.007, $p = 0.03$; visceral fat, OR = 1.008, 95% CI = 1.003–1.013, $p < 0.01$) (Table 3). For multivariate analysis, we selected the area of visceral fat as an independent factor associated with sudden natural death (OR = 1.008, 95% CI = 1.002–1.015, $p = 0.02$) (Table 4). The difference between the two groups in the rate of visceral fat and the waist circumference was not statistically significant ($p = 0.13$ and $p = 0.42$, respectively).

Discussion

Our study showed that the areas of subcutaneous and visceral fat were significantly larger in group 1 than in group 2 and that the rate of visceral fat and the waist circumference were not significantly different. Multivariate analysis revealed that the area of visceral fat was an independent factor associated with the risk of sudden natural death. These findings support the hypothesis that sudden natural death is associated with abdominal fat deposits. Most identified causes of sudden natural death ($n = 54$)

Table 2 Cause of death in 241 subjects

Natural death (Group 1; $n = 174$)	
Pericardial tamponade due to proximal aortic dissection	20
Aortic aneurysm rupture	9
Pericardial tamponade of unknown etiology	8
Subarachnoid haemorrhage	5
Coronary artery obstruction	4
Putaminal haemorrhage with ventricular perforation	2
Pulmonary embolism	2
Dissection of the ascending aorta without pericardial tamponade	1
Pneumothorax	1
Hematoma of the diaphragm	1
Brainstem haemorrhage	1
Unknown	120
Different causes (Group 2; $n = 67$)	
Traffic accident	22
Falling	22
Suicide	7
Suffocation	5
Drowning	3
Crushing	2
Sports injury	1
Burns	1
Stabbing	1
Heatstroke	1
Anaphylactic shock	1
Drug overdose	1

Table 3 Univariate analysis to explore factors associated with sudden natural death

Variable	Odds ratio	95% CI	<i>P</i> -value
Age	1.025	0.996–1.054	0.09
Gender	1.349	0.726–2.505	0.34
Median interval between death and CT scan	0.999	0.996–1.002	0.55
Area of subcutaneous fat	1.004	1.000–1.007	0.03*
Area of visceral fat	1.008	1.003–1.013	$<0.01^{**}$
Rate of visceral fat	4.410	0.574–82.253	0.13
Waist circumference	0.996	0.986–1.006	0.42

CI, confidence intervals; CT, computed tomography.

* $p < 0.05$.

** $p < 0.01$.

Table 4 Multivariate analysis to explore factors associated with sudden natural death

Variable	Odds ratio	95% CI	<i>P</i> -value
Area of subcutaneous fat	0.999	0.995–1.005	0.93
Area of visceral fat	1.008	1.002–1.015	0.02*

CI, confidence intervals.

* $p < 0.05$.

were aortic diseases ($n = 30$). Others (5,6) suggested that in individuals without a definite radiologically identified cause of sudden natural death it was due to coronary artery disease and numerous studies found an association between abdominal adiposity and cardiovascular disease (14–20). The cellular lipid content determines the size of adipocytes; large, mature adipocytes were filled almost entirely by large lipid droplets (21,22). The adipocyte volume determines cell functionality and the larger the adipocytes, the higher the cardiometabolic risk (23,24).

Our multivariate analysis showed that the area of visceral fat is an independent factor associated with the risk of sudden natural death. This is consistent with earlier findings that cardiovascular disease was associated with visceral – rather than subcutaneous fat (14–17). Pickhardt *et al.* (25) documented that visceral fat in women was correlated with metabolic syndrome. While Fox *et al.* (26) showed that it was more strongly associated with risk factors for cardiovascular disease in women than in men; others (16,17) claimed that visceral fat areas were significantly related to cardiovascular disease in both genders. Sex differences are recognized in the distribution of adipose tissue. In men, adipose tissue is primarily found in the central or abdominal region; this raises their risk for metabolic disorders; women, on the other hand, harbour more subcutaneous than visceral fat (27). These gender-specific differences may explain the lack of significant differences in the rate of visceral fat between our two groups. Despite gender-specific differences in the distribution of abdominal fat distribution, we think that visceral fat is associated with obesity-related morbidity such as cardiovascular disease resulting in sudden natural death.

Earlier studies (10,28,29) reported an association between the waist circumference and mortality. In our series, the waist circumference was not associated with sudden natural death. The waist circumference reflects abdominal fat deposits, and the observation that it was not associated with sudden natural death is inconsistent with our finding that the areas of subcutaneous and visceral fat were significantly larger in group 1 than in group 2. We used postmortem CT scans in our analyses; these scans reflected postmortem-resuscitation and post-cardiopulmonary resuscitation changes including gastrointestinal distension (30) that increase the waist circumference. Consequently, our findings may not reflect the pre-mortem waist circumference.

Our study has some limitations. As only three subjects were autopsied, the true cause of death remains uncertain. We did not have full medical histories on all subjects, and the effect of premortem patient characteristics could not be considered in our analyses. For example, there is a strong association between depression and suicide, and

between obesity and depression (31,32); however, we did not study the history of depression in this investigation. Also, cardiovascular disease is the leading cause of death in postmenopausal women (33). Although the differences of subcutaneous and visceral fat between groups 1 and 2 were statistically significant and the area of visceral fat was an independent factor associated with sudden natural death, they were modest, and the clinical significance is questionable. Lastly, our study population was composed of a heterogeneous mixture of men and women because only 65 of the 241 subjects were women.

Conclusion

The areas of subcutaneous and visceral fat were significantly larger in individuals who died of sudden natural death than in those who died of other identified causes. Visceral fat was an independent factor associated with the risk of sudden natural death. This raises the possibility that abdominal fat deposits may be associated with sudden natural death due to obesity-related morbidity such as cardiovascular disease.

Conflict of interest statement

No conflict of interest statement.

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None.

Disclosure

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The other authors declare no conflict of interest.

Author contributions

YK conceptualized the study, performed statistical analyses and wrote the paper; HS, HH, YH, FT, YB and MI contributed to interpreting the CT images and critically reviewed the paper. KA contributed to interpreting the data and critically reviewed the paper. All authors approved the final version of the paper.

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