Diagnostic Utility of Unenhanced Computed Tomography for Acute Aortic Syndrome

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Background: The diagnostic value of unenhanced computed tomography (CT) for diagnosing acute aortic dissection (AAD) and ruptured thoracic aortic aneurysm (TAA) remains unclear.

Methods and Results: We examined 219 consecutive patients who visited the emergency room with suspected acute aortic syndrome (AAS) because of chest or back pain and who underwent both unenhanced and contrast-enhanced 64-row multi-detector CT. The unenhanced CT findings were evaluated by the cardiologist on duty who was blind to the findings of contrast-enhanced CT. Diagnosis of AAS was confirmed in 103 patients (47%, 95 AAD and 8 ruptured TAA patients) based on evaluation of both unenhanced and contrast-enhanced CT images, which was used as the reference standard for validating the diagnostic value of the unenhanced CT findings. Sensitivity and specificity of the findings of a high-attenuation crescent, which represents hematoma in the aortic wall, were 61.2% and 99.1%, respectively. Sensitivity and specificity of linear high density in the aorta, which represents an intimal flap, were 59.2% and 96.6%, respectively. If unenhanced CT showed none of high-attenuation crescent, linear high density, internal displacement of intimal calcification, or TAA, the negative predictive value was 93.3%.

Conclusions: Unenhanced CT is a good tool for ruling AAS in, but the false-negative rate of 6.7% is high for ruling AAS out because it has to be the minimum possible. (Circ J 2014; 78: 1928–1934)

Key Words: Acute aortic syndrome; Computed tomography; Diagnosis

Computed tomography (CT) is the most commonly used imaging modality for patients with suspected acute aortic syndrome (AAS), which includes acute aortic dissection (AAD), variant forms of AAD, and ruptured thoracic aortic aneurysm (TAA). Especially in patients with AAD, contrast-enhanced CT is known to have very high sensitivity and specificity. However, there are occasions when physicians hesitate to administer contrast medium, because of its allergenicity and nephrotoxicity. Unenhanced CT could be a valid alternative in such cases. For example, there are several signs of AAD on unenhanced CT, including high-attenuation crescent (Figure 1), which represents clotted blood in the false lumen, internal displacement of intimal calcification (Figure 1), thoracic aortic aneurismal change, and linear high density (Figure 2), which represents an intimal flap. Unenhanced CT may also identify ruptured TAA, with findings such as aortic aneurismal change and high-attenuation crescent of the aneurysmal aortic wall. However, there appear to be few studies that have quantified how well AAS can be diagnosed based solely on unenhanced CT images. Therefore, the aim of our study was to evaluate this question in patients presenting to the emergency room (ER) with chest or back pain.

Methods

Study Population
From January 2009 to December 2012, 392 patients visited the ER of the Yokohama City Minato Red Cross Hospital (1 of 8 tertiary medical centers in Yokohama) within 24 h of the onset of chest or back pain and were considered to have a low probability of acute coronary syndrome from electrocardiographic and laboratory data. Of these 392 patients, 227 were strongly suspected of having AAS by an experienced emergency physician or cardiologist, and underwent both unenhanced and contrast-enhanced CT; 8 of these patients were excluded from study because of a history of aortic surgery, aortic endovascular treatment, or aortic dissection. The remaining consecutive 219 patients were enrolled in this observational study in a prospective manner.
Unenhanced CT for Diagnosing AAS

that of the delayed phase was 120–180 s. Contrast-enhanced CT scans were reconstructed at 5-mm intervals in the transverse plane, and at 2-mm intervals in the transverse and oblique-sagittal planes parallel to the aortic arch in selected cases.

Definition of Unenhanced CT Findings
We wanted to evaluate the utility of 4 markers of AAS on unenhanced CT, namely, high-attenuation crescent, linear high density in the aorta, internal displacement of intimal calcification, and TAA. The first of these was defined as a crescent-shaped hyperattenuating region of thickening of the aortic wall (>7 mm).10,11 A cut-off value of 7 mm was chosen based on previous studies that had used this value for images ob-

Imaging Technique
Non-ECG-gated CT scanning was performed using a 64-row scanner (Aquilion 64, Toshiba Medical Systems) with the following parameters: 200 mA, 120 kV, pitch of 15 mm, and 1-mm collimation. Each scan began with unenhanced imaging from the apex of the lung to the pelvis. Unenhanced CT scans were reconstructed at 5-mm intervals in the transverse plane to match the intervals used for a screening inspection of the chest and the abdomen. Contrast-enhanced CT scans were subsequently performed over the same area. Contrast material (iopamidol, 300 mg/ml of iodine; total volume, 100 ml) was injected at a rate of 3–4 ml/s through a right arm vein using an automated injector. The scan delay of the early phase was 25–35 s, and that of the delayed phase was 120–180 s. Contrast-enhanced CT scans were reconstructed at 5-mm intervals in the transverse plane, and at 2-mm intervals in the transverse and oblique-sagittal planes parallel to the aortic arch in selected cases.

Figure 1. (A) Unenhanced axial computed tomography (CT) image shows internal displacement of intimal calcification (yellow arrow) and a high-attenuation crescent (yellow star). (B) Contrast-enhanced CT image shows a relatively unenhanced crescent area (black star), which is the high-attenuation area on the unenhanced CT image.

Figure 2. Identification of an intimal flap represented by linear high density. (A) Unenhanced axial computed tomography (CT) image shows linear high density traversing the aortic lumen (yellow arrowheads). (B) Contrast-enhanced CT image confirms that an intimal flap (black arrowheads) separates the true and false lumens of the aorta.
KURABAYASHI M et al. (K.O.) evaluated the findings of both unenhanced and contrast-enhanced CT, and made judgments regarding the presence or absence of AAS and its type. The rate of independent observer agreement for detection of AAS was 100%, and for distinction of the type of AAS (AAD or ruptured TAA) was 99% (102 of 103, \( \kappa > 0.80 \)). Conflicting results of the evaluation of unenhanced and contrast-enhanced CT for distinction of the type of AAS were resolved by a third blinded observer. The judgments based on unenhanced and contrast-enhanced CT were used as the reference standard for validating the diagnostic value of the unenhanced CT findings in each study patient. This study was approved by the institutional review board of the Yokohama City Minato Red Cross Hospital, and informed written consent was given by each patient before CT.

Statistical Analysis

The sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value and negative predictive value of unenhanced CT findings were calculated. Continuous variables were compared using Student’s t-test, or Welch’s t-test. Categorical data were compared using Fisher’s exact tests. A P value <0.05 was considered statistically significant. All data analysis was carried out using SPSS version 18.0 (SPSS, Inc, Chicago, IL, USA).

Results

Of 219 patients, 103 (47%) were diagnosed with AAS, of whom 95 patients had AAD and 8 patients had a ruptured TAA. The characteristics of patients with and without AAS are presented in Table 1. Baseline characteristics were comparable between both the patient groups, except that patients with AAS were

| Table 1. Characteristics of the Patients | Patients with AAS (n=103) | Patients without AAS (n=116) | P value |
|-----------------------------------------|--------------------------|-----------------------------|---------|
| Baseline characteristics                |                          |                             |         |
| Age (years)                             | 69.7±13.9                | 60.9±16.4                   | <0.001  |
| Male sex (%)                            | 64 (62)                  | 69 (59)                     | 0.782   |
| History of hypertension (%)             | 59 (57)                  | 56 (48)                     | 0.223   |
| Diabetes mellitus (%)                   | 14 (14)                  | 18 (16)                     | 0.707   |
| Dyslipidemia (%)                        | 26 (25)                  | 35 (30)                     | 0.453   |
| Current smoker (%)                      | 48 (47)                  | 47 (41)                     | 0.413   |
| Systolic blood pressure (mmHg)          | 168±53                   | 164±37                      | 0.491   |
| Heart rate (beats/min)                  | 76±18                    | 80±16                       | 0.076   |
| D-dimer >500 ng/ml (%)                  | 76/76 (100)              | 53/56 (95)                  | 0.074   |
| D-dimer (μg/ml)                         | 11.1±12.5                | 11.0±34.8                   | 0.970   |

Continuous variables are expressed as mean±standard deviation.

AAS, acute aortic syndrome; TAA, thoracic aortic aneurysm.
older than patients without AAS. There was no significant difference in the positive rate of D-dimer (>500 ng/ml) or the average value of D-dimer between both groups. Of the 95 AAD patients, 2 patients had a concomitant penetrating atherosclerotic ulcer. With regard to the Stanford classification of AAD, 34 patients (36%) were Stanford type A and 61 patients (64%) were Stanford type B. With respect to the status of the false lumen, 23 patients (24%) had the patent type, 18 patients (19%) had the partial thrombosis type, and 54 patients (57%) had complete thrombosis type false lumen. Of the 8 ruptured TAA patients, 3 were impending ruptures and 5 were acute ruptures.

The sensitivity, specificity, positive and negative likelihood ratios, positive and negative predictive values of the unenhanced CT findings for AAS patients vs. non-AAS patients are presented in Table 2. In general, a likelihood ratio >10 (<0.1) indicates that the test result has a large effect on increasing (decreasing) the probability of disease presence. A likelihood ratio of 5–10 (0.1–0.2) indicates that the test has a moderate effect on increasing (decreasing) the probability of disease presence. A likelihood ratio of 1–5 (0.2–0.5) indicates that the test result has a small effect on increasing (decreasing) the probability of disease presence. A likelihood ratio of 0.01–0.1 (10–50) indicates that the test has a considerable effect on increasing (decreasing) the probability of disease presence.

Presence of high-attenuation crescent was able to rule in AAS with a high specificity of 99.1%, a high positive predictive value of 98.4%, and a high positive likelihood ratio of 18.32. Because none of the 4 signs had low negative likelihood ratios, individually they were found not to have good properties for ruling out AAS.
Table 4. Diagnostic Value of the Unenhanced CT Findings for AAD

| Internal displacement of intimal calcification | Sensitivity | Specificity | PLR     | NLR     | PPV     | NPV     |
|----------------------------------------------|-------------|-------------|---------|---------|---------|---------|
| All AAD patients                             | 76.8%       | 89.7%       | 7.43    | 0.26    | 85.9%   | 82.5%   |
| (70.8–81.4)                                  | (84.7–93.4) | (4.64–12.25)| (0.20–0.34)| (79.2–90.9)| (78.0–85.9)|
| Stanford type                                |             |             |         |         |         |         |
| Type A                                       | 82.4%       | 7.96        | 0.20    | 70.0%   | 94.5%   |
| (69.8–90.8)                                  | (4.98–11.52)| (0.10–0.35)| (59.3–77.1)| (90.7–97.1)|
| Type B                                       | 73.8%       | 7.13        | 0.29    | 78.9%   | 86.7%   |
| (65.2–80.4)                                  | (4.39–11.67)| (0.21–0.41)| (69.8–86.0)| (82.3–90.0)|
| Status of false lumen                        |             |             |         |         |         |         |
| Patent                                       | 65.2%       | 6.30        | 0.39    | 55.6%   | 92.9%   |
| (48.1–79.0)                                  | (3.50–10.36)| (0.23–0.60)| (40.9–67.3)| (89.3–95.7)|
| Partial thrombosis                           | 88.9%       | 8.59        | 0.12    | 57.1%   | 98.1%   |
| (70.2–96.8)                                  | (5.31–10.62)| (0.04–0.34)| (45.2–62.2)| (94.9–99.5)|
| Complete thrombosis                          | 77.8%       | 7.52        | 0.25    | 77.8%   | 89.7%   |
| (88.6–84.7)                                  | (4.68–11.91)| (0.17–0.37)| (68.6–84.7)| (85.4–92.9)|
| High-attenuation crescent                    |             |             |         |         |         |         |
| All AAD patients                             | 60.0%       | 99.1%       | 69.60   | 0.40    | 98.3%   | 75.2%   |
| (55.9–60.9)                                  | (95.8–99.8) | (13.34–397.36)| (0.39–0.46)| (91.6–99.7)| (72.6–75.7)|
| Stanford type                                |             |             |         |         |         |         |
| Type A                                       | 52.9%       | 61.41       | 0.48    | 94.7%   | 87.8%   |
| (43.4–55.4)                                  | (11.85–358.05)| (0.44–0.59)| (77.6–99.1)| (85.3–88.4)|
| Type B                                       | 63.9%       | 74.16       | 0.36    | 97.5%   | 83.9%   |
| (58.0–65.3)                                  | (14.55–424.71)| (0.35–0.44)| (88.4–99.6)| (81.3–84.5)|
| Status of false lumen                        |             |             |         |         |         |         |
| Patent                                       | 0.0%        | 0.00        | 1.01    | 0.0%    | 83.3%   |
| (0.0–0.3)                                    | (0.00–19.21)| (0.97–1.01)| (0.0–79.2)| (83.3–83.9)|
| Partial thrombosis                           | 61.1%       | 70.89       | 0.39    | 91.7%   | 94.3%   |
| (45.7–65.7)                                  | (14.02–418.01)| (0.34–0.56)| (68.5–98.5)| (92.0–94.9)|
| Complete thrombosis                          | 85.2%       | 98.82       | 0.15    | 97.9%   | 93.5%   |
| (79.1–96.7)                                  | (21.36–557.94)| (0.13–0.22)| (90.9–99.6)| (90.8–94.2)|
| Linear high density in aortic lumen          |             |             |         |         |         |         |
| All AAD patients                             | 63.2%       | 96.6%       | 18.32   | 0.38    | 93.8%   | 76.2%   |
| (58.1–65.7)                                  | (92.4–98.6) | (7.65–47.19)| (0.35–0.45)| (86.2–97.5)| (72.9–77.8)|
| Stanford type                                |             |             |         |         |         |         |
| Type A                                       | 73.5%       | 21.32       | 0.27    | 86.2%   | 92.6%   |
| (62.3–80.1)                                  | (9.23–52.93)| (0.20–0.41)| (73.0–93.9)| (89.4–94.4)|
| Type B                                       | 57.4%       | 16.64       | 0.44    | 89.7%   | 81.2%   |
| (50.1–61.2)                                  | (6.86–43.38)| (0.39–0.54)| (78.3–95.8)| (77.9–82.9)|
| Status of false lumen                        |             |             |         |         |         |         |
| Patent                                       | 47.8%       | 13.87       | 0.54    | 73.3%   | 90.3%   |
| (33.2–57.6)                                  | (5.24–38.20)| (0.43–0.71)| (51.0–88.3)| (87.6–92.1)|
| Partial thrombosis                           | 72.2%       | 20.94       | 0.29    | 76.5%   | 95.7%   |
| (54.4–83.6)                                  | (8.74–49.45)| (0.17–0.49)| (57.6–88.5)| (93.0–97.5)|
| Complete thrombosis                          | 66.7%       | 19.33       | 0.35    | 90.0%   | 86.2%   |
| (58.7–71.0)                                  | (8.18–49.63)| (0.29–0.45)| (79.2–95.9)| (82.8–88.0)|
| Thoracic aortic aneurysm                      |             |             |         |         |         |         |
| All AAD patients                             | 40.0%       | 94.0%       | 6.63    | 0.64    | 84.4%   | 65.7%   |
| (34.4–43.6)                                  | (89.4–96.9) | (3.25–14.09)| (0.58–0.73)| (72.7–92.0)| (62.5–67.7)|
| Stanford type                                |             |             |         |         |         |         |
| Type A                                       | 73.5%       | 12.19       | 0.28    | 78.1%   | 92.4%   |
| (61.3–82.1)                                  | (6.38–23.29)| (0.19–0.43)| (65.2–87.2)| (88.9–94.8)|
| Type B                                       | 21.3%       | 3.53        | 0.84    | 65.0%   | 69.4%   |
| (14.6–26.7)                                  | (1.53–8.28)| (0.76–0.94)| (44.6–81.3)| (66.8–71.5)|
| Status of false lumen                        |             |             |         |         |         |         |
| Patent                                       | 34.8%       | 5.76        | 0.69    | 53.3%   | 87.9%   |
| (20.8–47.7)                                  | (2.36–13.78)| (0.54–0.87)| (31.9–73.2)| (85.3–90.3)|
| Partial thrombosis                           | 50.0%       | 8.29        | 0.53    | 56.3%   | 92.4%   |
| (31.9–65.5)                                  | (3.61–18.06)| (0.36–0.75)| (35.9–73.7)| (89.6–94.7)|
| Complete thrombosis                          | 38.9%       | 6.44        | 0.65    | 75.0%   | 76.8%   |
| (30.4–45.0)                                  | (3.04–14.09)| (0.57–0.77)| (58.7–86.8)| (73.5–79.1)|

Data in parentheses are 95% confidence interval. Abbreviations as in Tables 1,2.
crescent, linear high density, internal displacement of intimal calcification, and TAA, the negative likelihood ratio was 0.08 and the negative predictive value was 93.3%.

The diagnostic value of unenhanced CT for diagnosing AAD (ie, excluding ruptured TAA) is presented in Table 4. High-attenuation crescent had good rule-in properties for all types of AAD, with the exception of the patent false lumen type in which the false lumen did not contain thrombus. Linear high density had a good rule-in property regardless of the Stanford classification and the status of false lumen. Again, none of the unenhanced CT findings had good properties for ruling out AAD.

Discussion

The present study demonstrated that unenhanced CT could reliably rule in AAS based on diagnostic findings such as high-attenuation crescent and linear high density, which had high positive predictive values of >90%, and high positive likelihood ratios of >10. With regard to ruling out AAS, the individual unenhanced CT findings did not have good properties: they had negative likelihood ratios >0.10. However, if a patient had none of the 4 markers, the negative predictive value was 93.3% (equivalent to a false-negative rate of 6.7%) and the negative likelihood ratio was 0.08. In most diagnostic tests, a false-negative rate of 6.7% would be considered quite low, but the different consequences of AAS require a low threshold. This is especially true in light of the fact that the sensitivity and specificity of enhanced CT for diagnosing AAD are nearly 100%. Nevertheless, we believe it is of great benefit to know the predictive value of unenhanced CT because of the small number of patients in whom contrast injection should be avoided, and for whom the physician can make informed risk assessment regarding the type of AAS, the extent of AAD, the status of false lumen. The identification of an intimal flap and a true and a false aortic lumen are definitive signs of aortic dissection. In general, contrast medium injection is required to demonstrate the presence of the intimal flap by CT.5,6 Demos et al reported that unenhanced CT could be used to detect the intimal flap of aortic dissection.5 Because the density of the aortic wall of patients with AAD is frequently high because of atherosclerosis, the contrast between the density of the aortic wall and the aortic lumen could be large. If the density contrast is large, the intimal flap of aortic dissection is visible on unenhanced CT. In the present study, linear high density representing the flap had a high positive predictive value of 93.8%, and a high positive likelihood ratio of 18.32, which could reliably rule in AAD. Linear high density was not a good rule-in parameter for ruptured TAA, as expected, because TAA lacks an intimal flap.

High-attenuation crescent reflects clotted blood in the aortic wall and had favorable rule-in properties for AAS in the present study. Its diagnostic value depends on the status of the aortic wall, because it does not have any sensitivity in patients with the patent type of false lumen AAD in which the false lumen does not contain thrombus. On the other hand, high-attenuation crescent could be useful for distinguishing AAS in which the aortic wall contains fresh thrombus from stable aortic aneurysm containing chronic thrombus. On the unenhanced CT, fresh thrombus of thrombosed AAD or ruptured TAA showed high-attenuation crescent, whereas the chronic thrombus of stable aortic aneurysm did not show high attenuation. Furthermore, it has been found that high-attenuation crescent extending longitudinally on unenhanced CT images is evidence of hematoma in a false lumen and allows the diagnosis of AAD. Unenhanced CT is also useful for distinguishing between thrombosed false lumen of AAD and hematoma of ruptured aneurysmal wall.

In aortic dissection, a blood-filled false lumen divides the medial layer of the aorta and displaces the calcified intima inward. Similarly, in ruptured TAA, acute hematoma within the aneurysmal wall could displace the calcified intima inward. Internal displacement of intimal calcification may be simulated by the volume averaging effect at the aortic arch or bends in the aorta, non-vascular pathologic structures contiguous with the aortic wall, and calcification of the surface of a blood clot in an aortic aneurysm.5 In the present study, internal displacement of intimal calcification was occasionally false positive for non-AAS patients. This may be because the unenhanced CT scans were reconstructed at 5-mm intervals in transverse planes. If the scans had been reconstructed at smaller intervals, the internal displacement of intimal calcification might have had a higher specificity for AAS. However, the internal displacement of intimal calcification had a relatively high specificity and specificity regardless of the type of AAS.

A recent study reported that TAA might be associated with development of AAD because of the findings of a high frequency of AAD patients with ulcer-like projections or intimal tears contiguous with a TAA.18 In the present study, 40% (38 of 95 patients) with AAD were found to have TAA, a proportion found to be even higher at 73.5% (25 of 34 patients) when limited to patients with Stanford A type AAD. This suggests that thoracic aortic enlargement is associated with not only aortic rupture but also with aortic dissection.

As mentioned, diagnostic accuracy of CT for diagnosing AAD is very high. Some studies conducted before widespread use of ECG-gated CT demonstrated that motion artifact of the ascending aorta was not a major diagnostic problem.4,19 However, Reymond et al recently reported that there were 2 main reasons for false-positive diagnoses, namely, motion artifact of the ascending aorta arising from non-ECG-gated CT imaging, and the presence of complex anatomy following prior surgical or endovascular aortic repair.20 They also mentioned that the vast majority of hospitals did not have around-the-clock access to ECG-gated CT capabilities in the ER. This was true of the ER in the present study, so the ER patients did not undergo ECG-gated CT. Nevertheless, diagnoses of all the cases of Stanford type A aortic dissection were confirmed either at surgery or on follow-up CT, which was ECG-gated CT performed in the institution’s department of radiology. Because a major disadvantage of ECG-gated CT is increased radiation exposure, it is arguable whether ECG-gating should be used routinely for undifferentiated patients with chest or back pain. One strategy may be to perform ECG-gated enhanced CT with its increased diagnostic accuracy only when unenhanced CT shows several signs of AAS, and to perform non-ECG-gated enhanced CT, which leads to much less radiation exposure, when the unenhanced CT shows no sign of AAS.

Study Limitations

First, unenhanced CT was useful in confirming whether patients have AAS or not, but could not provide information regarding the type of AAS, the extent of AAD, the status of false lumen of AAD, or blood flow in aortic branches. This means that if a patient is found to have AAS based on unenhanced CT, he or she will have to undergo contrast-enhanced CT anyway to evaluate the therapeutic options, including emergency surgery.21 Second, the positive predictive value of the unenhanced CT findings was relatively high (eg, 83.5%) when...
all 4 markers were combined. This may have been partially related to a high prevalence of AAS in our study, because it is known that a positive predictive value is not independent of prevalence and high prevalence increases the positive predictive value. However, the most balanced assessment can be made by considering that combining the unenhanced CT signs showed a good positive likelihood ratio (ie, positive likelihood ratio >10), which is a parameter that does not depend on the prevalence of a disease. Third, 95 patients may not have been a large enough population to subtype the AAD and provide reliable sensitivity and specificity values. Fourth, the fact that evaluation of unenhanced CT was performed by only one observer, whoever happened to be on call, may be considered a limitation. However, we believe that this was realistic and similar to the ordinary situation in which a cardiologist or emergency physician in the ER must judge promptly whether a patient has AAS or not.

Conclusions

In patients with suspected AAS, including AAD and ruptured TAA, unenhanced CT is able to rule in AAS by findings such as high-attenuation crescent and linear high density. However, in patients whose unenhanced CTs show neither of these, nor internal displacement of intimal calcification, nor TAA change, the false-negative rate was 6.7%, which may be considered too high relative to the dire consequences of missing AAS, except in select patients in whom contrast agents need to be avoided.

Disclosures

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