Radiology

Attenuation of Acute and Chronic Clots

From
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Editor:

We read with interest the article by Dr Wittram and colleagues, in the June 2005 issue of *Radiology*, about the possibility to distinguish between acute and chronic pulmonary embolism through the evaluation of the attenuation of the clots with contrast material–enhanced computed tomography (CT) (1).

In our opinion, some points of this work are not completely clear. In particular, the authors report the mean attenuation of acute clots to be 33 HU; this value is hardly correct, because the blood itself has an attenuation of 20–30 HU (2,3). The intravascular clots are mainly composed of red blood cells and fibrin, so their hematocrit level is higher than is that of the circulating blood and consequently, their attenuation is higher (3). If the reported mean attenuation of the acute clots is correct, this implies that probably all of the patients were anemic.

The chronic clots are reported to have very high attenuation (87 HU ± 30 [standard deviation]); the authors are not able to explain this, since they did not perform unenhanced CT. In our opinion, the high attenuation of the clots is caused by the vascularization or by the calcification (the authors do not describe the presence of calcification in the zone of the clots in which they place the region of interest) of the clots themselves. It is not probable for the high attenuation to be due to the hemoglobin concentration of the chronic clots; in fact, in the first period after the embolus constitution, the clot has a high concentration of the protein fraction of hemoglobin and, therefore, an elevated attenuation level. But, in a second period, the attenuation decreases because of the progressive breakdown of red blood cells and the removal of cell elements, predominantly proteins, by means of phagocytes action. Because the chronic clots mentioned in the article are probably old and in an advanced phase of reorganization in which they appear vascularized, it is improbable that the finding of elevated attenuation is justified by the presence of a high concentration of hemoglobin.

In the January-February issue of the *Journal of Computer Assisted Tomography*, our team reported (2) the results of a study in which we evaluated the percentage of cases in which emboli can be detected on unenhanced CT scans. The main difference between our study and that of Dr Wittram and colleagues refers to the attenuation evaluation of the clots, which we performed exclusively on the unenhanced CT scans. In

our results, the mean attenuation of the clots that appeared hyperattenuating on the unenhanced scans and were, also in accordance with their morphologic features, classified as strongly probably acute, was reported to be 74.25 HU ± 10.07 (95% confidence interval [mean ± confidence interval]: 74.25 ± 4.93). These results, which are very different from the findings reported by Dr Wittram and colleagues, confirm the data reported in other articles in which the attenuation of acute clots was evaluated. The emboli that appeared to be hypoattenuating and were characterized by means of a morphologic appearance that was strongly evocative of chronic pulmonary embolism had a value of 27.7 HU ± 11.69 (mean ± 95% confidence interval: 27.7 ± 11.45), with a range of 21–46 HU. We considered this value to be evocative for chronic thrombosis, a condition in which the clot is in an advanced reorganizing phase and the hemoglobin content is low.

In conclusion, we think the article by Dr Wittram and colleagues is very interesting but contains some limitations; the authors evaluated the attenuation of clots only at contrast-enhanced CT. In our opinion, this fact may cause pitfalls in the densitometric analysis of acute clots and prevent a correct evaluation of the attenuation of chronic clots. We therefore suggest, in every CT examination performed in patients suspected of having chronic pulmonary embolism, obtaining an unenhanced CT scan, with the aim of differentiating chronic from acute clots.

References

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3. New PF, Aronow S. Attenuation measurements of whole blood and blood fractions in computed tomography. Radiology 1976;121: 635–640.

Response

From

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To address the first issue, in response to the letter by Dr Cobelli and colleagues, a review of the histologic background of venous thromboembolism is appropriate: An acute thrombus is formed from fibrin, platelets, neutrophils, and red blood cells, and as the cells necrose, swelling often occurs. Activation of the fibrinolytic pathways can lead to rapid total lysis of acute emboli. When this is incomplete, endothelial cells become activated, and sprouts with irregular clefts lined by endothelial cells develop within a few days. A general rule of thumb is that cellular penetration can advance at the rate of approximately 1 mm per day, depending on conditions. Fibroblastic proliferation occurs with and adjacent to capillary formation. Reticulin may be detected after about 4 days and collagen in 5–10 days and thereafter hemosiderin may appear at about 1 week, which is later than the 2 days it takes to appear after bleeding into skin or meninges. Fibrocytic proliferation reaches a maximum at about 4 weeks, and at this time elastin may be present. Remodeling gradually transforms the clot into compartments; this process can continue for longer than a year (1). An acute thrombus has a CT attenuation value that is dependant largely on the proportions of red blood cells, with its hemoglobin and iron moiety, and fibrin. It is therefore of no surprise that the Hounsfield unit value of acute pulmonary embolism in our study (2) is similar to previously published attenuation measurements of whole blood (3). Clot contraction, and a possible increase in thrombus attenuation owing to an increase in hemoglobin and iron moiety concentration, can only occur after capillary formation and fibroblastic proliferation.

The second issue is that our institution does not perform unenhanced CT prior to CT pulmonary angiography, because this is considered unnecessary and an insensitive test for this indication. In the population we studied, calcium deposition in chronic thrombus was not obvious on CT scans (2). Within our discussion we clearly state, "The reasons for the higher attenuation in patients with chronic PE [pulmonary embolism] compared with those with acute PE are likely related to enhancement of organizing thrombus, retraction of thrombus with concentration of hemoglobin and its iron moiety, and possibly, calcium deposition" (2).

The third issue relates to a variance of results between the article by Dr Cobelli and colleagues (4) and our work (2). In our study, corroborative evidence of acute and chronic pulmonary embolism from the clinical history or imaging was a selection criterion, 1.25-mm section thickness was used in all cases, there were two readers, and contrast material was used to define the clot margins (2); the article by Dr Cobelli and colleagues did not address these four important methodologic points (4). Dr Cobelli and colleagues measured thrombus attenuation values on unenhanced CT scans; of 51 cases, they found 10 clots that demonstrated hyperattenuation, five with hypoattenuation, six with mixed attenuation, and 30 with isoattenuation with respect to blood. One obvious question is, in the 30 cases that demonstrated a thrombus that was isoattenuating with respect to blood, how can one accurately measure something one cannot see? The article by Dr Cobelli and colleagues is entitled "Clinical Usefulness of Computed Tomography Study without Contrast Injection in the Evaluation of Acute Pulmonary Embolism," and in the materials and methods of this article they describe imaging patients with "the clinical suspicion of pulmonary embolism." There is no stratification into acute or chronic embolism or corroborative evidence of acute or chronic emboli. They

interpret their results by stating that thrombi that demonstrate hyperattenuation are acute and that thrombi that demonstrate hypoattenuation with respect to blood are chronic. These conclusions cannot be made from their results, as clinical, imaging, or histologic corroborative evidence of thrombus age was not present within their study (4). In the conclusion of their letter to us, Dr Cobelli and colleagues state, "We therefore suggest, in every CT examination performed in patients suspected of having chronic pulmonary embolism, obtaining an unenhanced CT scan, with the aim of differentiating chronic from acute clots." However, their study did not evaluate chronic pulmonary emboli (4). In conclusion, the article by Dr Cobelli and colleagues is interesting in the fact that pulmonary emboli can be identified on 41% of unenhanced CT scans in a retrospective study. However, one is uncertain of the age of the thromboemboli that the authors investigated, and therefore the Hounsfield unit values found in the article by Dr Cobelli and colleagues are called into question. The purpose of our work was to compare the attenuation values of acute and chronic emboli corroborated with clinical and imaging evidence; the results are derived from in situ acute and chronic thromboemboli on contrast-enhanced CT scans and are therefore of substantial practical value.

References

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