Imaging the Clot: Does Clot Appearance Predict the Efficacy of Thrombolysis?

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See related article, pages 2379–2383.

Unlike in acute myocardial infarction, the underlying pathophysiological mechanism of vascular arterial occlusion in acute stroke is heterogeneous. Composition of cerebral embolic material may vary, depending on specific endothelial and flow conditions of the embolic source. Old, platelet-rich, and well-organized thrombi formed under flow conditions have been shown to be more resistant to thrombolysis than fresh, fibrin- and red cell–rich clots formed under conditions of stasis. More recently, clot structure may differ depending on whether the embolic source is a thrombus engrafted in a proximal atherosclerotic lesion or a clot formed in cardiac cavities. In this context, stroke subtypes may represent a surrogate of the composition of offending clot.

Efforts to image intravascular thrombus in acute ischemic stroke have been increasingly done in the last years. In acute ischemic stroke, the presence of hyperattenuated middle cerebral artery sign on computed tomography indicates intraluminal clot with a high specificity but low sensitivity (47%). On MRI, vessel signs of arterial occlusion have been described as hyperintense vessel sign on fluid-attenuated inversion recovery images and as susceptibility vessel sign on gradient-echo (GRE SVS) images. The basis for the detection of GRE SVS in patients with an acute intracranial artery occlusion is paramagnetic deoxyhemoglobin causing signal loss. In patients with acute ischemic stroke imaged at 24 hours of stroke onset, GRE SVS has been shown to have high sensitivity for detecting an acute intracranial occlusion compared with vessel status on magnetic resonance (MR) angiography. Sensitivity and specificity of GRE SVS increase over time because of an increase in deoxihemoglobin content and thrombus retraction as a result of clot aging.

In the accompanying article, Cho et al studied, retrospectively, 95 patients with acute ischemic stroke attributable to a major intracranial artery occlusion who underwent DWI, GRE, and MR angiography. Twenty patients received thrombolysis. Stroke subtypes were independently assessed using Trial of Org 10172 in Acute Stroke criteria. Recanalization on follow-up MR angiography was assessed in 66 patients. The authors found that GRE SVS was associated with cardioembolic (CE) stroke and independently predicted recanalization on MR angiography. Although exploring clot structure and embolic source based on the appearance of intravascular thrombus on GRE is an attractive approach with potential diagnostic and therapeutic implications, the observations of Cho et al. raise several considerations.

Does GRE-SVS Represent a Surrogate Marker of Clot Composition?

GRE-SVS detects deoxygenated hemoglobin components in trapped red cells. However, proportion and distribution of erythrocytes into the clot, as well as other cellular and biochemical components of the clot different than red cells, cannot be evaluated by GRE-SVS. Clot composition may be heterogeneous even among cardiac red clots, which may exhibit different degrees of aging and fibrin organization. On the other hand, in patients with unstable carotid artery disease or aortic atheroma, platelet-rich clots may be covered by fresh red cell-rich material, easily detectable on GRE images. Embolectomy material obtained by retrieval devices may provide pathological evidence of clot structure and the opportunity to be correlated with different MRI vessel signs.

In the article by Cho et al., GRE-SVS was found to be more frequently identified in patients with CE stroke compared with other stroke subtypes. The accuracy of the diagnosis of stroke subtypes in clinical practice is low, and systematic echocardiographic evaluation has been shown to increase dramatically the diagnosis of a cardiac source of emboli. The retrospective nature of the analysis and the fact that only 60% of patients underwent echocardiography in the study by Cho et al. limit the accuracy in the diagnosis of stroke subtypes. Should GRE-SVS be used to guide diagnostic work-up? GRE-SVS may indicate predominantly red and probably aged clots from different sources. Therefore, it is still premature to recommend GRE-SVS for the guidance of etiological diagnostic evaluation.

Does GRE-SVS Predict Response to Systemic Thrombolysis?

Although it is attractive, current data do not support this hypothesis. The article by Cho et al. showed that GRE-SVS was associated with recanalization on MR angiography during the first week after stroke. However, only 69% of patients underwent a follow-up MRI, and only 20% received thrombolytic therapy (IV, intraarterial, or combined). Moreover, the lack of clinical and imaging follow-up data precludes the assessment of the impact of recanalization on
outcome. In this context, recanalization mainly represents delayed spontaneous recanalization, which is a frequent phenomenon in the acute phase of CE stroke. Therefore, GRE-SVS seems to be associated with spontaneous but not tPA-induced recanalization. Schellinger et al. first explored the hypothesis that GRE-SVS reflects thrombus composition and may predict response to thrombolysis in 56 patients treated with tPA for <3 hours. In this study, neither recanalization nor clinical outcome was predicted by the presence GRE-SVS on pretreatment MRI. GRE-SVS is able to identify not only red but also mixed thrombi with different structures and response to thrombolysis. Moreover, susceptibility to clot lysis depends not only on clot composition but also on systemic factors, such as blood glucose and plasminogen activator inhibitor-1 levels. Therefore, although intravascular thrombus visualization on GRE may provide relevant information beyond the diagnosis of arterial occlusion, its capability to evaluate clot composition and response to reperfusion therapies remains to be elucidated.

References

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