Changes in MR signals associated with organizing processes of venous thrombi in rabbits.

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Introduction: Venous thrombus is subsequently organized and replaced by fibrous connective tissue. Sequential changes in venous thrombi cannot be reliably detected by current noninvasive diagnostic techniques. Although MR imaging has been advocated as a tool to detect venous thrombosis, MR images and changes related to thrombus age have not been adequately characterized. The present study investigates the potential of MR to detect venous thrombotic occlusion and to define thrombus age.

Materials and Methods: Venous thrombus was induced in the right jugular vein of rabbits (n = 24) by endothelial denudation and blood stasis. The left jugular vein served as a control vessel. MR images were obtained *in vivo* using 3D fast advanced spin echo T2-weighted (T2W) and 3D-gradient echo T1-weighted (T1W) sequences in a 1.5 T MR system at 4 hours, 1, 2 and 4 weeks later. The T2W or T1W images were acquired with a repetition time (TR) and echo time (TE) of 2,000 msec/120 msec, or with a TR, TE and flip angle (FA) of 38 msec/5msec/40°, respectively. Other MR imaging parameters comprised field of view, 120 × 120 mm; matrix, 256 × 256; 2-mm slice thickness and one-signal averages. Thrombus signal intensity (SI) was normalized to that of the adjacent muscle. Six rabbits were sacrificed for histological analysis at each time point. Fixed jugular veins with thrombi were stained with hematoxylin eosin, Berlin blue (Fe^{3+}) and Sirius red (collagen), or with anti-glycoprotein IIb/IIIa (platelets), anti-fibrin, anti-smooth muscle actin (smooth muscle cells) or anti-CD68 (macrophages). The cellular-, iron-, or matrix-areas in the thrombi were assessed with image analyzing software.

Results: All venous thrombi in the right jugular vein were detected by MRI. Fresh thrombi at 4 hours after endothelial denudation and blood stasis appeared as heterogeneous high or low signal intensity on T2W or T1W images, respectively (Figure 1A). These thrombi time-dependently decreased in size, and the axial area significantly correlated with corresponding thrombus areas in histological sections. The T2W signal intensity time-dependently decreased, while T1W signal intensity increased in the thrombi at 1 and 2 weeks after the procedure (Figure 1B, C). Histological analysis of venous thrombi showed time-dependent decrease of erythrocyte-, platelet-, and fibrin-areas, and time-dependent increase of collagen- and iron-areas, and peak smooth muscle cell-, macrophage-areas at 2 weeks (Figure 2).

Conclusion: MRI shows promise as a tool that can noninvasively detect venous thrombosis. Signal intensity measurements might support assessments of thrombus age which would provide valuable information for thrombolytic therapy.

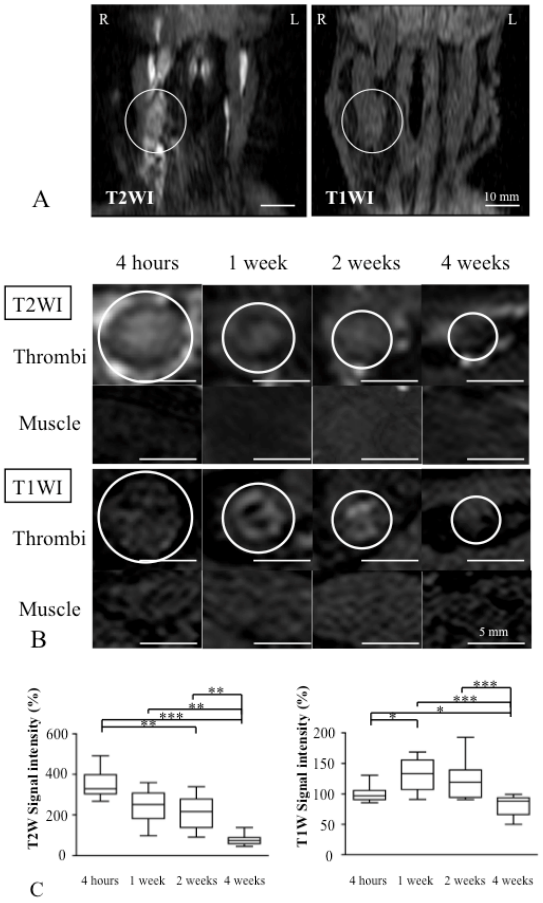

Figure 1. Representative T2W and T1W MR images and signal intensities of venous thrombi. Coronal MR images of fresh venous thrombi at 4 hours (A), Axial MR images of venous thrombi at 4 hours, 1 weeks, 2 weeks and 4 weeks (B), Thrombus signal intensity changes over the time of T2W and T1W images (C), *p<0.05, **p<0.01, ***p<0.001, n=18 in each.

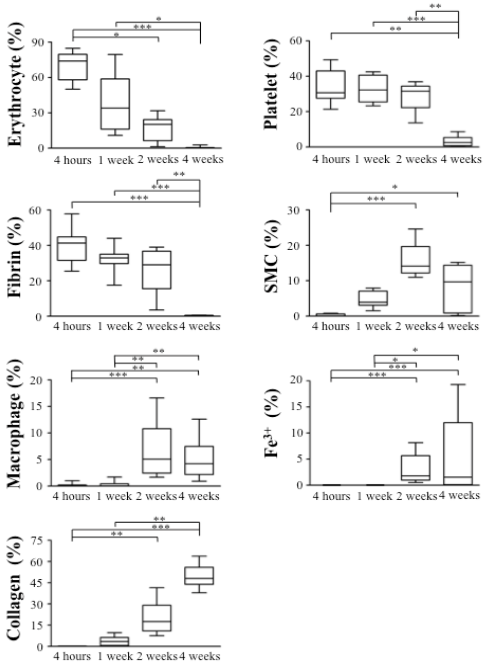

Figure 2. Changes in the ratio of erythrocyte, platelet, fibrin, smooth muscle cell (SMC), macrophage, Fe3+, and collagen areas in thrombi over the time. *p<0.05, **p<0.01, ***p<0.001, n=9 in each.