Noninvasive technique using fluorescence imaging to assess vascular permeability in sepsis

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Introduction:
Conventional assay technique to quantify vascular permeability in animal studies requires sacrifice animals; this becomes a barrier to evaluate of temporal changes or responses to therapeutic approaches in a single individual. In vivo fluorescence imaging potentially quantifies vascular permeability without sacrifice animals. However, the use of this noninvasive approach for the assessment of vascular permeability in remote organ injury caused by systemic inflammatory disease such as sepsis has not been reported.

Methods:
Cecal ligation and puncture (CLP)-induced septic mouse model was compared to sham and hydrocortisone pretreated (CLP + HC) mouse models. The lung was assumed as an injured remote organ and the footpad was assumed as a noninvasive observational site. The mixture of Evans blue (EB) and fluorescent dye of Genhance 750 were injected into mice, and the extraction of EB in harvested lung was assessed as a conventional indicator of vascular permeability. Fluorescent intensities in the harvested lung or footpad were assessed and their correlation was analyzed to investigate this novel, noninvasive approach to estimation of lung vascular permeability.

Results:
EB extraction in the harvested lung in the CLP group was significantly higher than in the other groups (CLP vs. sham, P=0.0012; CLP vs. CLP + HC, P=0.011). Fluorescent intensity in the footpad and harvested lung in the CLP group was also significantly higher than in the other groups (footpad, CLP vs. sham, P<0.0001; CLP vs. CLP + HC, P=0.0004; lung, CLP vs. sham, P<0.0001; CLP vs. CLP + HC, P<0.0001). The fluorescent intensity of the footpad was strongly correlated with that of the lung (r=0.95).

Conclusion:
The fluorescence imaging technique may be useful for assessment of vascular permeability based on EB quantification. The footpad fluorescent intensity was strongly correlated with that of the lung, and may be a suitable indicator in noninvasive estimation of lung vascular permeability.