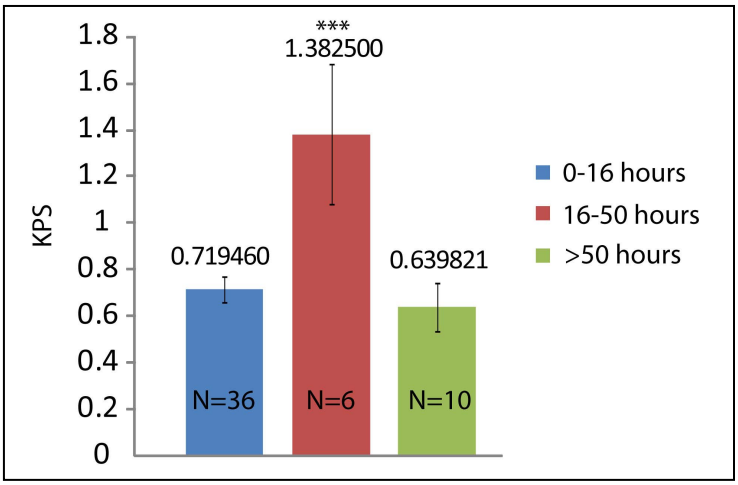
Progression of Blood Brain Barrier Permeability in patients with Acute Ischemic Stroke: from acute to early subacute phase

K. Huang[1], D. J. Mikulis[2], F. Silver[3], and A. Kassner[1]
[1]Medical Imaging, University of Toronto, Toronto, Ontario, Canada, [2]Medical Imaging, Toronto Western Hospital, Toronto, Ontario, Canada, [3]Neurology, Toronto Western Hospital, Toronto, Ontario, Canada

Introduction: Stroke is currently the third leading cause of death and disability in North America [1]. Blood–brain barrier (BBB) disruption following ischemia–reperfusion is associated with clinically important consequences including edema and hemorrhagic transformation (HT). Previous data on BBB permeability changes after acute ischemic stroke (AIS) is limited to the first several hours and virtually non-existent in the subacute phase (days to weeks) [2,3]. No longitudinal data exists. We therefore reviewed our existing data that included data points over one hour to several days. Precise knowledge of BBB dynamics after ischemic stroke is of importance in considering future treatment possibilities including BBB leakage-blocking agents, and neuroprotective and neurorestorative strategies [4,5]. The purpose of this study was to evaluate the time course of BBB disruption from acute to early subacute phase of AIS. We hypothesized that BBB permeability measured by DCE-MRI would continuously increase with time, a response caused initially by direct ischemic endothelial injury and subsequently by inflammatory reaction [6].

Materials and Methods: 39 patients (18 females, 21 males, 28-99 years) were included in the analysis. All patients received DCE-MRI as part of their acute stroke workup and were imaged on a 1.5 T GE MR system equipped with 8-channal head coil. 12/39 patients had follow-up DCE MRI. 1/39 developed a new lesion at follow-up scan, therefore was counted as 2 data points. Total data points were N=52. DCE-MRI parameters were as follows: dynamic 3D Gradient echo, FOV 240 mm, 128 x128 matrix, section thickness 5 mm, TR 5.9 ms, TE 1.5 ms, FA=35°, temporal resolution 9 sec, 31 volumes. The total imaging time was 4.48 min. Data were analyzed on an independent workstation using in-house software (MR analyst) developed in MATLAB. Areas of ischemia were identified as regions of reduced diffusion relative to normal cortex on apparent diffusion coefficient maps and were the basis for the region of interest (ROI) selection. Coefficients of BBB permeability estimates (KPS) were calculated using a unidirectional, 2-compartment kinetic model implemented as described previously [2,7]. Mean values (±SEM) for KPS were recorded for each lesion volume and each patient. All patients were divided into three groups according to time between scan and stroke onset. KPS between groups were compared using a one-way ANOVA.



Results: MRIs in the first 16 hours showed mean KPS values in the lesion of 0.72 ml/100g/min. Scans taken between 16-50 hours showed mean KPS values in the lesion of 1.4 ml/100g/min, which was statistically significant when compared to MRIs taken in the first 16 hours (1.38±0.30 vs. 0.72±0.06 mL/100g/min, P=0.0007). After 50 hours, mean KPS values of the lesion decreased significantly (1.38±0.30 vs. 0.64±0.10 mL/100g/min, P=0.01).

Discussion: Surprisingly, BBB permeability decreased after 50 hours. We believe that this represents transient stabilization of the initial ischemic endothelial BBB injury that stabilizes and reverses as a result of reperfusion [8]. The defect may again reappear due to the inflammatory phase in subsequent days to weeks after injury for which we currently do not yet have confirmatory data [8].

References:
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