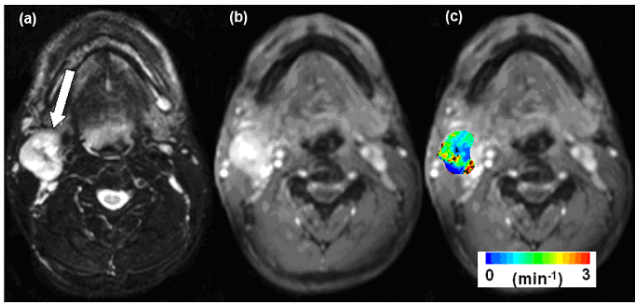
Prediction of Disease Specific Survival in Patients with Head and Neck Cancer using Dynamic MRI

S. Chawla[1], S. Kim[2], L. A. Loevner[1], H. Quon[3], W. T. Hwang[4], G. Weinstein[5], A. Chalian[1], and H. Poptani[1]
[1]Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]Radiology, New York University, New York, NY, United States, [3]Radiation Oncology, University of Pennsylvania, Philadelphia, PA, United States, [4]Biostatistics, University of Pennsylvania, Philadelphia, PA, United States, [5]Otorhinolaryngology, University of Pennsylvania, Philadelphia, PA, United States

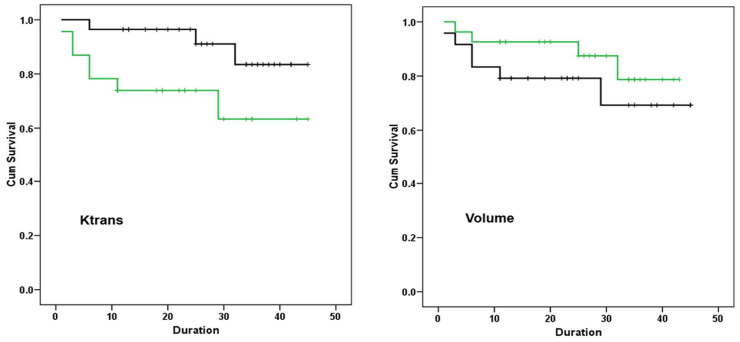
Introduction: Metastatic lymphadenopathy in patients with squamous cell carcinoma of head and neck (HNSCC) is generally associated with development of distant metastases, poor prognosis and survival[1]. Dynamic CT and MRI perfusion studies have shown that HNSCC patients with high pretreatment blood flow/volume respond more positively to chemo-radiation therapy than patients with low blood flow/volume[2, 3]. We have recently reported that pretreatment volume transfer constant (K^{trans}) value from DCE-MRI can predict for local response to chemo-radiation therapy[4]. It is highly desirable to stratify high-risk patients who are likely to have poor prognosis and shorter survival outcome, prior to initiation of treatment so that these patients can be subjected to alternative treatment strategy for improved survival and better quality of life. Therefore, the purpose of the present study was to evaluate the potential of pretreatment K^{trans} in predicting disease specific survival in patients with HNSCC.

Materials and Methods: Sixty-six patients with newly diagnosed HNSCC and planned for chemo-radiation therapy followed by neck dissection surgery were recruited and were followed up clinically. All patients underwent DCE-MRI prior to surgery, radiation, or chemotherapy. The median follow up time for the surviving patients (n=41) was 24.0 months. Data from 12 patients was censored because of death unrelated to HNSCC or incomplete MRI/clinical information. Three patients underwent neck dissection surgery and were also excluded from analysis. Data from remaining 51 patients was analyzed for this study. Prior to analysis, all MR images were co-registered using a two-step non-rigid image registration technique. Volume of the nodal mass was measured by drawing free hand regions of interest (ROI) around the nodal mass on all the slices encompassing the node. Pharmacokinetic analysis of the DCE-MRI data was performed for each voxel in the selected ROI using the shutter speed model (SSM)[5]. The median pretreatment K^{trans} and volume from the node were considered as threshold values to separate patients into two groups (above and below the threshold value). Using K^{trans} and nodal volume as analytical parameters, disease specific survival analyses were performed by means of Kaplan-Meier method. Cumulative survival between the two groups was compared using a log rank test.

Results: Representative pretreatment structural MRI images and color coded K^{trans} map from a patient who received concurrent chemotherapy are shown in figure 1. The median pretreatment K^{trans} from the nodal mass of 51 patients was 0.41min^{-1} and was used as the threshold K^{trans} value. Of 51 patients, 28 (54.90%) had K^{trans} higher than the threshold value while 23 patients (45.09%) had K^{trans} lower than the threshold value. Of the 28 patients with higher K^{trans} value, three died during follow up, while 7/23 patients died in the lower K^{trans} group. The median survival for the patients with higher K^{trans} was significantly prolonged compared to patients with lower K^{trans} value ($p<0.05$, Figure 2a). The median pretreatment nodal volume was 10.16cm^3 and when this value was used for assessing disease specific survival, we observed that 24/51 (47.05%) patients exhibited nodal volumes higher than the threshold volume, while 27/51 (52.94%) patients exhibited nodal volumes lower than the threshold value. The median survival for the patients with lower nodal volume was not significantly different from the patients with higher pretreatment nodal volume ($p>0.05$, Figure 2b).



Axial T2 weighted image (a) demonstrating a heterogeneous hyperintense metastatic lymph node at level IIa of the right neck (arrow). This nodal mass exhibited heterogeneous enhancement on contrast enhanced T1 weighted image (b). DCE-MRI derived pixel-wise K^{trans} map is shown as color image overlaid on post contrast T1 weighted image (c).



Kaplan-Meier plots using pretreatment K^{trans} values and nodal volume. X-axis shows follow-up duration in months. Patients with higher pretreatment K^{trans} (black lines) demonstrated significantly prolonged disease specific survival compared to patients with lower K^{trans} values (green lines; $p<0.05$). Patients with lower pretreatment nodal volume demonstrated marginally improved survival (green lines) compared to patients with higher nodal volume (black lines), ($p>0.05$).

Discussion: These results indicate that pretreatment K^{trans} of the metastatic node is a significant and independent prognostic factor for prediction of disease specific survival in patients with HNSCC. Tumor vasculature and oxygenation are critical factors that markedly influence the efficacy of chemoradiation therapies[6]. We believe that patients with higher pretreatment blood flow/permeability respond well to chemo-radiotherapy leading to better disease free survival and hypothesize that pretreatment K^{trans} can be a useful prognostic parameter that may help in identifying patients requiring intensive treatment protocols.

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