Pretreatment diffusion-weighted imaging at 3T for overall survival prediction in chemoradiotherapy treated advanced cervical cancer patients.

Martine I Dujardin[1], Martin D Pickles[1], Abdullah Aldosary[2], Peter Gibbs[1], and Lindsay W Turnbull[1]

[1]Centre for MR Investigations, University of Hull in association with Hull York Medical School, Hull, United Kingdom, [2]King Fahad Medical City, Riyadh, Saudi Arabia

Purpose

Cervical cancer is the second most common cancer in women and a significant cause of mortality worldwide [1]. Moreover, as many women fail to respond to recommended therapy, the management of advanced cervical cancer remains challenging in terms of patient outcome, therapeutic toxicity and cost. Hence, a biomarker that can predict therapy outcome [2] or overall survival would clearly be beneficial. The use of 1.5T-based diffusion weighted imaging (DWI) and apparent diffusion coefficients (ADCs) to predict tumour response to combined chemoradiation in cervical cancer has already shown some potential [3, 4]. The purpose of this pilot study was to investigate the ability of pretreatment ADCs acquired at 3T to predict which patients are likely to have shorter overall survival (OS) in a group of advanced cervical cancer patients treated with chemoradiotherapy.

Methods

Prior to chemoradiotherapy, 26 women (median and range for age 48 years (24-77 years) with histopathologically proven advanced squamous cell carcinoma of the cervix (FIGO stage IIa to IVa) underwent conventional pelvic MRI including DWI on a 3T MRI system (HDXt or Discovery 750, GE Healthcare) using a dedicated pelvic phased array coil. DWI imaging parameters were: b-value of either 0 and 1200 or 0 and 600 mm^2/s, TR= 3500 ms, TE= 67.5 ms, slice thickness= 6 mm, gap= 0.6 mm, matrix= 160*160. ADC maps were calculated pixel-by-pixel using built-in software (AW 4.5 Functool; GE Healthcare). Multislice whole tumour regions of interest were manually drawn on the ADC maps by a radiologist blinded to patient OS with the aid of the corresponding T2-weighted series. Patients were either categorised as having a critical event (cancer related death) or censored (well at last follow up or if lost to follow up). The OS time interval was defined from the diagnostic scan at 3T (which was used to determine pretherapy ADC values) until the critical or censored event. Average follow up was 575 days. For univariate Kaplan-Meier analysis of survival pretherapy whole tumour ADC values were split into two groups: first, $\leq$ median or > median; second, $\leq$ 75th percentile or > 75th percentile and third $\leq$ 25th percentile or > 25th percentile.

Results

11/26 patients had a critical event (cancer related death), whereas the remaining 15 patients were censored. Follow up time for critical and censored data was 429 and 682 days, respectively. Average pretreatment whole tumour ADC value was $(0.94 \pm 0.14) \times 10^{-3}$ mm^2/s. Kaplan-Meier survival plots using the group median $(0.94 \times 10^{-3}$ mm^2/s) (Figure 1, top) and 25th percentile of group ADC values $(0.85 \times 10^{-3}$ mm^2/s) (Figure 1, bottom) to dichotomize the patients are presented. The use of group median (p= 0.16) or 75th percentile of group ADC values (p=0.86) as dichotomizing values did not result in a significant difference for survival between a high and low ADC group. Kaplan-Meier analysis showed that the survival rate in the low-ADC group was significantly worse than that in the high-ADC value group (p= 0.042); when groups where dichotomized on the basis of the 25th percentile $(0.85 \times 10^{-3}$ mm^2/s) of group pretreatment ADC values.

Figure 1: Kaplan-Meier survival plot using the median (top, 0.94 10-3 mm2/s) and 25th percentile (bottom, 0.85 10-3 mm2/s) of group pretreatment whole tumour ADC values obtained at 3T as a dichotomising factor to split the advanced cervical cancer patient group into a group with high and low ADC values.

Conclusion

ADC values in whole tumour were in the range of literature values for cervical carcinoma [3, 4]. Within our small cohort of advanced cervical squamous cell carcinoma patients treated with chemoradiotherapy, the patient group with pretherapy whole tumour ADC values equal to or below 0.85×10^{-3} mm^2/s had a significantly poorer overall survival compared to those with higher pretreatment ADC values. Our findings are discordant to the results of Liu et al. [4], who found a negative correlation between pretreatment ADCs and percentage size reduction after 2 months of chemoradiation in cervical cancer patients, although this study was concerned with the shorter term treatment response as opposed to longer term survival as in this work. However, the results of our study are in line with the results of Aoyagi et al [5], who found a significant better survival rate in the higher ADC group (above 1.1×10^{-3} mm^2/s) in a cohort of esophageal squamous cell carcinoma. We conclude that this result supports further study in a larger cohort to assess whether pretherapy ADC values may be a useful marker to predict overall survival in cervical squamous cell carcinoma patients treated with chemoradiotherapy.

References

[1] Monk et al (2009) J Clin Oncol 27: 1069-1074
[2] Harry et al (2009) Obst Gynecol Surv 64(8): 548-60
[3] McVeigh et al (2008) Eur Radiol 18: 1058-1064
[4] Liu et al (2009) Clin Radiol 64: 1067-1074
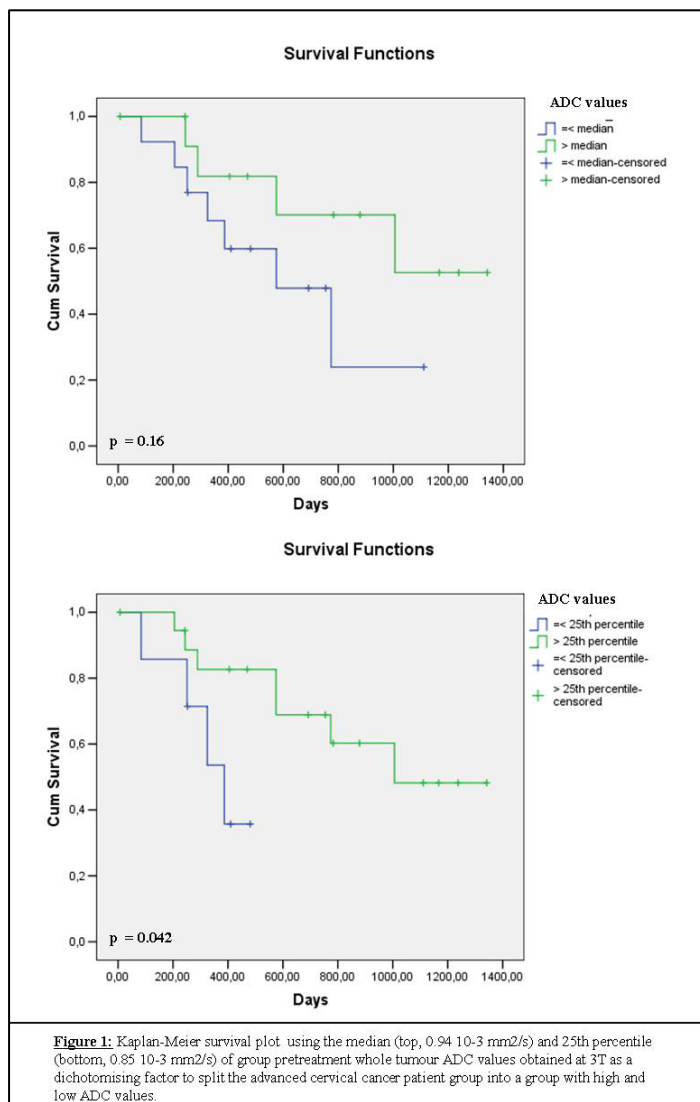[5] Aoyagi et al (2011) Dis Surg 28(4): 252-257