

# Apparent diffusion coefficient (ADC) predicts risk of disease upgrading in men on active surveillance (AS)

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## Background

- No consensus on how to best monitor patients on active surveillance (AS)
- Prior studies have shown an association between apparent diffusion coefficient (ADC), a measurement of water molecule movement on diffusion-weighted mpMRI, and clinically significant prostate cancer (PCa)

• **OBJECTIVE:** To determine if ADC on baseline MRI is associated with increased risk of upgrading to Grade Group  $\geq 2$  (Gleason Grade  $\geq 3+4$ ) while on AS.

## Methods

### COHORT

- Retrospectively identified 244 men from the Johns Hopkins AS registry with baseline prostate mpMRI (2010 – 2015) showing lesions assessed with ADC. Median time in AS prior to mpMRI was 16.5 months (IQR 7 – 51.5)

### MRI REVIEW

- Due to inconsistencies in acquiring and reporting of ADC values in the original radiology reports, 2 expert radiologists reviewed all 244 cases and re-scored the original index lesions, using the mean ADC from maps generated with b-values 50 and 800, or 0 and 800

### STATISTICAL ANALYSIS

- Study group characteristics at time of mpMRI were assessed and compared between upgraders (GG=1) and non-upgraders (GG  $\geq 2$ )
- Association between baseline ADC and upgrading to GG  $\geq 2$  was evaluated using survival analysis and an optimal cut-off for ADC was determined using an outcome oriented method (Contal and O'Quigley)
- Association between ADC and upgrading was adjusted for age, PSA density (PSAD), and risk status (low-risk [LR] vs. very low-risk [VLR]).

## Results

- Of the 244 men included in our study, 71 (27%) upgraded to GG  $\geq 2$  with a median post-MRI follow-up of 16 months (IQR 5 – 28).
- Compared to non-upgraders, upgraders had higher PSAD (median: 0.10 vs. 0.08,  $p = 0.002$ ), higher proportion of low-risk cancer (51% LR vs. 38% VLR,  $p = 0.005$ ), and lower ADC values on baseline mpMRI (median: 1043 vs. 1147,  $p = 0.01$ ). There was no significant decrease in originally-reported ADC values (median: 861 vs. 880,  $p = 0.38$ )
- Significantly higher proportion of men with baseline ADC  $< 1128$  upgraded compared to ADC  $\geq 1128$  (39% vs. 18%, respectively,  $p < 0.001$ ) [Fig 1]
- Men with ADC  $< 1128$  had significantly higher risk of upgrading compared to ADC  $\geq 1128$  ( $p < 0.001$ ) [Fig 2]
- On univariate analysis ADC was significantly associated with upgrading to GG  $\geq 2$  (as categorical variable,  $< 1128$  vs.  $\geq 1128$ : **HR = 2.49, 95% CI = 1.5 – 4.15**,  $p = < 0.001$ ; as continuous variable (per 100-unit decrease: **HR = 1.13, 95% CI = 1.03 – 1.23**,  $p = 0.009$ )
- Adjusting for age PSAD and risk-status (LR vs. VLR), baseline ADC remained significantly associated with upgrading to GG  $\geq 2$  (as categorical variable,  $< 1128$  vs.  $\geq 1128$ : **HR = 2.86, 95% CI = 1.66 – 4.90**,  $p = < 0.001$ ; as continuous variable (per 100-unit decrease: **HR = 1.13, 95% CI = 1.03 – 1.24**,  $p = 0.008$ )

Figure 1. Distribution of individual patients' ADC values around ADC cut-off ( $1128 \times 10^{-6} \text{ mm}^2/\text{s}$ )

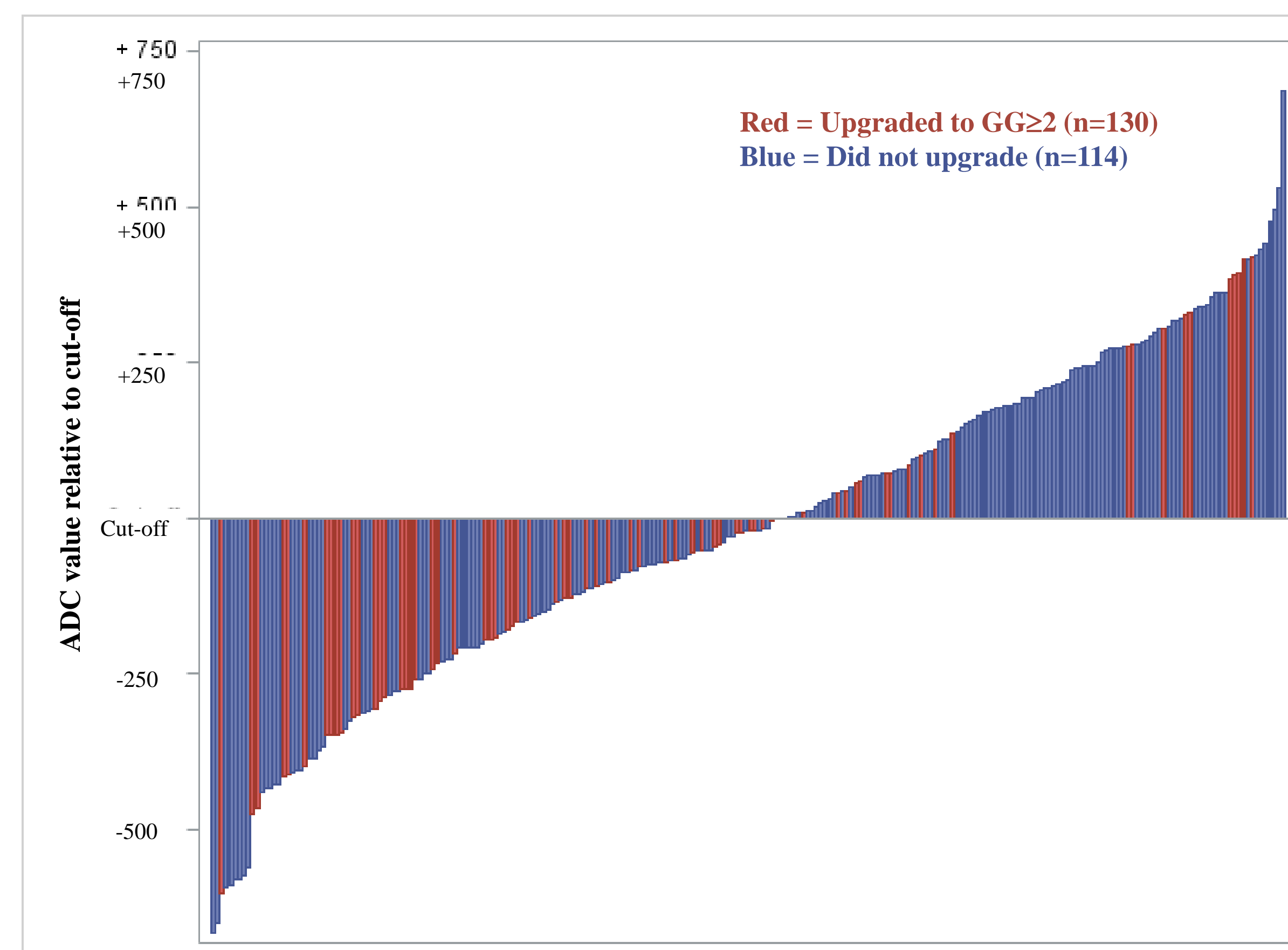
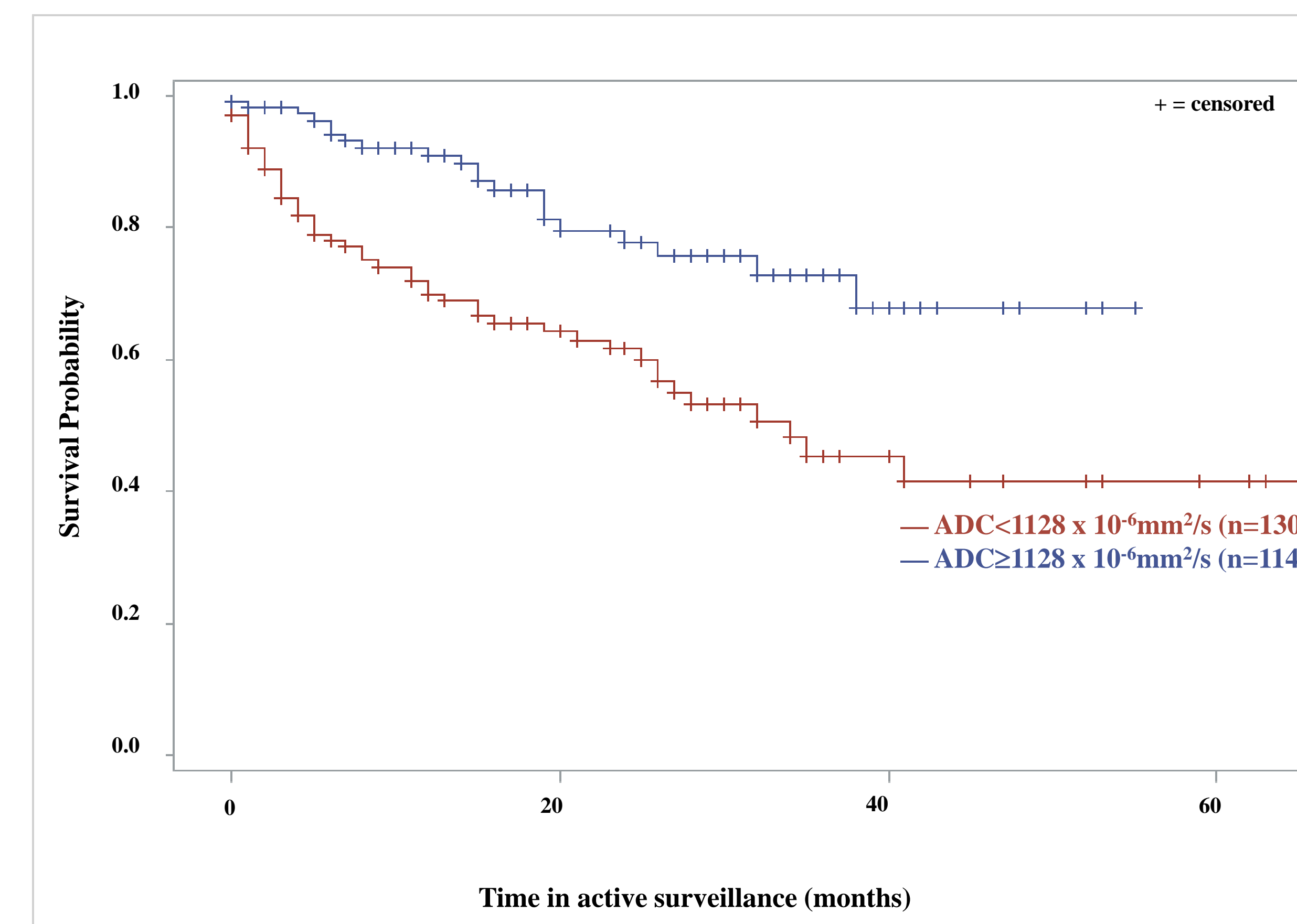


Figure 2. K-M analysis: Freedom from upgrading to Grade Group  $\geq 2$



## Limitations

- Retrospective study
- Excluded men who underwent MRI, but did not have an ADC value reported
- Single institution study, with more selective criteria for participation in active surveillance

## Conclusions

- For men in AS, lower ADC value on baseline MRI is associated with increased risk of upgrading to GG  $\geq 2$  and thus could be a useful component of multivariable risk prediction tools
- These data suggest that a clinically relevant ADC cut-off for men who are in AS (low volume GG1) is likely to be higher than previously reported ADC cut-offs for identifying high grade cancer ( $750 \times 10^{-6} \text{ mm}^2/\text{s}$ ).