Predicting Active Surveillance Failure in the Magnetic Resonance Imaging Era: A Multicentre Transatlantic Cohort Study

Nikita Sushentsev [a †], Irene G. Li [b †], George Xu [b †], Anne Y. Warren [c], Celeste Y. Hsu [b], Madison Baxter [b], Dev Panchal [b], Christof Kastner [d], Sean Fernando [e], Ekaterina Pazukhina [f], Oleg Blyuss [f g], Alexey Zaikin [h i j], Ahmed Shabaik [k], Anders M. Dale [l], Michael Liss [m], Tristan Barrett [a ‡], Tyler M. Seibert [b l m n ‡]

[†] These authors contributed equally to this work.

[‡] These authors jointly supervised this work.

Affiliations:

[a] Department of Radiology, Addenbrooke's Hospital and University of Cambridge, Cambridge, UK

[b] Department of Radiation Medicine, University of California-San Diego, San Diego, CA, USA

[c] Department of Pathology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

[d] Department of Urology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

[e] School of Clinical Medicine, University of Cambridge, Cambridge, UK

[f] Wolfson Institute of Population Health, Queen Mary University of London, London, UK

[g] Department of Paediatrics and Paediatric Infectious Diseases, Institute of Child's Health, Sechenov First Moscow State Medical University, Moscow, Russia

[h] Department of Women's Cancer, Institute for Women's Health, University College London, London, UK

[i] Department of Mathematics, University College London, London, UK

[j] Institute for Cognitive Neuroscience, University Higher School of Economics, Moscow, Russia

[k] Department of Pathology, University of California-San Diego, La Jolla, CA, USA

[l] Department of Radiology, University of California-San Diego, La Jolla, CA, USA

[m] Department of Urology, University of California-San Diego, La Jolla, CA, USA

[n] Department of Bioengineering, Jacobs School of Engineering, University of California-San Diego La Jolla, CA, USA

Background:

Active surveillance (AS) is increasingly used for the management of prostate cancer (PCa), helping patients avoid or delay treatment-related side-effects while keeping the window of opportunity open for curative treatment. While some guidelines limit AS to patients with low-risk PCa, some also allow patients with favorable intermediate-risk and magnetic resonance imaging (MRI)-visible grade group (GG) 2 disease. Our study investigated the oncological safety of contemporary MRI-driven AS and evaluated whether there are patient subgroups at increased risk of AS failure.

Methods:

This retrospective cohort study included AS patients with MRI-localized PCa from Cambridge University Hospitals, The University of California San Diego, and The University of Texas San Antonio. The primary outcome, AS failure, was defined as a composite of PCa-specific mortality, radiological progression to metastatic disease, histological progression to GG 4 disease, or post-treatment biochemical recurrence. The secondary outcome, disease progression, was defined as histological progression to GG 3 or histological/definitive radiological progression to locally advanced disease. Multivariable Cox proportional-hazards models were used to estimate hazard ratios (HRs). Multiplicity-adjusted log-rank tests were used to compare event-free survival across subgroups.

Results:

Of the 799 patients enrolled in this study, 80 patients were excluded for having less than 12 months of follow-up, entering a therapeutic clinical trial while on AS, or missing any baseline data. Of the 719 patients that remained for analysis (median follow-up 5.2 years), 629 (87%) had stable disease; 36 (5%) experienced AS failure, including eight (1%) cases of metastasis and no PCa-related deaths; and 54 (8%) had disease progression. Cribriform GG 2 histology was the strongest predictor of AS failure (HR 12.7, 95% confidence interval (CI) 4.8–33.6; $p<0.001$). Other significant predictors included tumor MRI visibility (HR 5.0, 95% CI 1.5–16.5; $p=0.009$) and non-cribriform GG 2 histology (HR 3.4, 95% CI 1.6–7.0; $p=0.001$). MRI-invisible non-cribriform GG 2 and all GG 1 tumors had comparable event-free survival (adjusted $p>0.05$ for both).

Conclusions:

This study provides evidence that contemporary MRI-based AS for PCa may be safe for suitable patients, including those with non-cribriform GG 2 tumors and MRI-invisible tumors. In addition, this study shows that patients with cribriform GG 2 disease are at higher risk of AS failure and may benefit from upfront treatment.

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Conflicts of Interest Disclosure Statement:

None