

MRI Visibility Stratifies Risk of Grade Group Progression and Treatment Initiation in Prostate Cancer Active Surveillance

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Introduction and overall goal: Active surveillance seeks to avoid overtreatment of lower-risk prostate cancer while preserving timely detection of clinically significant progression. MRI-invisible cancers may be biologically less aggressive than MRI-visible disease, but their longitudinal behavior during active surveillance remains incompletely defined. We evaluated whether MRI visibility across serial examinations stratifies the risks of pathologic progression and treatment initiation.

Specific aims: To (1) compare grade progression-free survival and adjusted progression risk among MRI-invisible, equivocal, and visible disease and (2) compare treatment initiation rates across these MRI visibility groups.

Rationale and background: Prior pathologic and radiogenomic studies link MRI visibility with molecular features of prostate cancer aggressiveness. Determining whether visibility corresponds to clinically meaningful progression during surveillance could support more individualized follow-up and biopsy strategies.

Methods and materials: This IRB-approved retrospective cohort study included 285 patients with Grade Group (GG) 1-2 prostate cancer managed with active surveillance from 2011 to 2023 who underwent baseline and follow-up MRI. MRI visibility was categorized by PI-RADS as invisible (1-2), equivocal (3), or visible (4-5). The primary outcome was pathologic progression, defined as biopsy upgrade from GG1 to $\geq$ GG2 or from GG2 to $\geq$ GG3; the secondary outcome was treatment initiation. For outcome analyses, visibility was categorized using the most recent MRI preceding the outcome of interest. Kaplan-Meier analysis and log-rank testing compared grade progression-free survival. Cox proportional hazards regression estimated progression risk after adjustment for age, PSA density, and baseline GG. Treatment rates were compared using the chi-square test.

Results: The cohort included 248 patients with baseline GG1 and 37 with baseline GG2 disease. Median follow-up was 4.5 years (IQR, 3.0-7.1), with a median of 3 MRIs per patient (IQR, 2-4). At baseline, 96 patients (33.7%) had MRI-invisible, 101 (35.4%) equivocal, and 88 (30.9%) visible disease. Of the 96 patients with initially MRI-invisible disease, 6 (6.3%) became equivocal and 17 (17.7%) became visible on follow-up MRI. Five-year grade progression-free survival was 83.0% for invisible, 69.0% for equivocal, and 41.3% for visible disease (log-rank $p < 0.001$). Relative to MRI-invisible disease, equivocal (adjusted HR, 1.95; 95% CI, 1.00-3.79; $p = 0.050$) and visible disease (adjusted HR, 5.52; 95% CI, 3.01-10.12; $p < 0.001$) were associated with higher progression risk. Treatment initiation increased across visibility groups: 13.7% for invisible, 28.0% for equivocal, and 61.3% for visible disease ($p < 0.001$).

Discussion and conclusion: Greater MRI visibility was associated with a stepwise increase in biopsy upgrading and treatment initiation during active surveillance. Longitudinal MRI visibility may help identify patients who could be considered for less intensive biopsy follow-up while prioritizing closer surveillance for MRI-visible disease. These findings could reduce unnecessary biopsy burden while directing resources toward patients at greater progression risk. Given the retrospective, single-center design and the potential influence of MRI on treatment decisions, external validation is needed before changing surveillance protocols.