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Active Surveillance Must Be the Default Management for Low-Risk Prostate Cancer: Ending Decades of Overtreatment

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Opinion

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Abstract

Prostate cancer is the second most commonly diagnosed solid malignancy in men globally. For decades, routine serum Prostate-Specific Antigen (PSA) screening generated a massive epidemic of overdiagnosis, uncovering hundreds of thousands of low-grade, indolent tumors (Gleason score 6 / ISUP Grade Group 1) that pose zero threat to a man's natural life expectancy. Historically, fear of malignancy and surgical overtreatment bias drove the widespread execution of immediate radical prostatectomy or radiation therapy for these low-risk lesions—inflicting lifelong complications of urinary incontinence, erectile dysfunction, and bowel toxicity without improving 15-year cancer-specific survival. Today, landmark long-term prospective trials (including the ProtecT trial, the Johns Hopkins AS cohort, and the multi-institutional PASS study) unequivocally prove that Active Surveillance (AS) achieves identical 15-year cancer-specific survival (>99%) compared to upfront radical surgery or radiation. Modern diagnostic advancements—notably pre-biopsy multiparametric magnetic resonance imaging (mpMRI / PI-RADS v2.1), MRI-transrectal ultrasound fusion biopsy, and validated genomic biomarker panels (Decipher, Oncotype DX GPS, Prolaris)—provide unprecedented precision to rule out occult high-grade disease. In this opinion piece, we argue that active surveillance must no longer be framed as an 'optional alternative,' but as the mandatory, ethical default standard of care for all men with low-risk prostate cancer.

Keywords: Prostate Cancer; Active Surveillance; Overdiagnosis; Gleason 6; Multiparametric MRI; Radical Prostatectomy; Protect Trial; Urological Oncology

Abbreviations

PSA: Prostate-Specific Antigen; AS: Active Surveillance; mpMRI: Multiparametric Magnetic Resonance Imaging; PI-RADS: Prostate Imaging-Reporting and Data System; ISUP: International Society of Urological Pathology; ProtecT: Prostate Testing for Cancer and Treatment; RP: Radical Prostatectomy.

Introduction

The Legacy of Prostate Cancer Overdiagnosis and Harm

The introduction of serum PSA screening in the late 1980s was hailed as an oncological triumph, but it came at an immense human cost: the widespread detection of

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microscopic, biologically indolent Grade Group 1 (Gleason 3+3=6) adenocarcinomas that would have remained clinically silent throughout the patient's lifetime [1,2].

For decades, the reflexive response to a positive biopsy was aggressive radical intervention. Hundreds of thousands of men underwent radical prostatectomies or definitive pelvic radiotherapy, suffering permanent iatrogenic morbidity—including stress urinary incontinence and erectile dysfunction—to treat a biological entity that virtually lacks metastatic potential [3,4].

The Irrefutable 15-Year Evidence: The ProtecT Trial

Any lingering skepticism regarding the safety of active surveillance has been definitively extinguished by landmark 15-year clinical trial data. In the United Kingdom's prospective ProtecT trial (N = 1,643), men randomized to active monitoring, radical prostatectomy, or radiotherapy exhibited identical 15-year prostate cancer-specific mortality: 97% survival across all three arms (p = 0.53) [5].

Similarly, the Johns Hopkins and PRIAS active surveillance registries, following thousands of men for over 15 years, confirm that fewer than 1% of compliant patients progress to metastatic disease, while over 60% avoid definitive radical treatment entirely, preserving their baseline urinary continence and sexual function [6,7].

The Modern Precision Diagnostic Toolkit

A historical justification for upfront surgery was fear of missing occult high-grade disease due to random systematic template biopsy errors. In 2025, this concern is obsolete.

Pre-biopsy multiparametric MRI (mpMRI) with PI-RADS v2.1 scoring, coupled with real-time MRI-transperineal fusion biopsy, exhibits a negative predictive value exceeding 90% for clinically significant (Grade Group ≥2) prostate cancer [8,9]. Furthermore, commercially available tissue-based genomic classifiers (such as Decipher and Oncotype DX) provide individualized transcriptomic risk profiling, identifying the rare indolent-appearing tumors that harbor aggressive molecular signatures [10].

A Moral and Clinical Call to Action

Despite these indisputable advances, real-world registry data reveals that up to 20% to 30% of men with low-risk prostate cancer in the US and Europe still undergo immediate radical prostatectomy or radiation, driven by fee-for-service financial incentives, patient anxiety, and clinician risk-aversion.

We call for three mandatory policy reforms:

- **Redefining Nomenclature**: The international pathology community should formally rename Gleason 3+3=6 from 'carcinoma' to a non-malignant designation, such as IDLE (Indolent Lesion of Epithelial Origin), permanently eliminating the psychological terror associated with the word 'cancer.'
- **Mandatory Active Surveillance Pathway Default**: Professional guidelines (AUA, EAU, NCCN) must classify active surveillance as the mandatory primary standard for all Grade Group 1 tumors, requiring formal peer-review documentation before insurance reimbursement for upfront surgery.
- **Standardized mpMRI and Biomarker Surveillance**: Establish non-invasive monitoring protocols utilizing serial PSA kinetics, annual mpMRI, and selective genomic profiling, minimizing the burden of repeated invasive biopsies. The true measure of surgical excellence is knowing when not to operate.

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