Initial management of prostate-specific antigen-detected, low-risk prostate cancer and the risk of death from prostate cancer.

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Abstract

WHAT'S KNOWN ON THE SUBJECT? AND WHAT DOES THE STUDY ADD?: The recently published Prostate Cancer Intervention versus Observation Trial (PIVOT) did not identify differences in prostate cancer-specific mortality or all-cause mortality among patients with low-risk disease managed conservatively vs those managed definitively; however, recently published data suggest that older men may harbour more aggressive disease than is identified at biopsy owing to sampling error and undergrading. Whether older men with apparent low-risk disease are placed at risk of prostate cancer-specific mortality when managed conservatively remains unknown. The study used population-level data to show that non-curative approaches for older men with low-risk prostate cancer do result in an increased risk of prostate cancer-specific mortality. Differences between our study and the PIVOT trial include the fact that we included a larger sample size, analysed the data using an 'as-treated' approach, and included a healthier cohort of men as evinced by lower 4-year all-cause mortality estimates in our study than in the PIVOT. Our results suggest that older men with apparent low-risk prostate cancer are at risk of undergrading, which probably explains the differences in prostate cancer-specific mortality observed between men managed conservatively vs those managed definitively. Our study suggests that alternative approaches to excluding occult, high grade prostate cancer are needed in such men.

OBJECTIVE: To evaluate whether older age in men with low-risk prostate cancer increases the risk of prostate cancer-specific mortality (PCSM) when non-curative approaches are selected as initial management.

PATIENTS AND METHODS: The study cohort consisted of 27 969 men, with a median age of 67 years, with prostate-specific antigen (PSA)-detected, low-risk prostate cancer (clinical category T1c, Gleason score ≤6, and PSA ≤10) identified by the Surveillance, Epidemiology and End Results programme between 2004 and 2007. Fine and Gray's competing risk regression analysis was used to evaluate whether management with non-curative vs curative intent was associated with an increased risk of PCSM after adjusting for PSA level, age at diagnosis and year of diagnosis.

RESULTS: After a median follow-up of 2.75 years, 1121 men died, 60 (5.4%) from prostate cancer. Both older age (adjusted hazard ratio [AHR] 1.05; 95% confidence interval (CI) 1.02-1.08; P < 0.001) and non-curative treatment (AHR 3.34; 95% CI 1.97-5.67; P < 0.001) were significantly associated with an increased risk of PCSM. Men > the median age experienced increased estimates of PCSM when treated with non-curative as opposed to curative intent (P < 0.001); this finding was not seen in men ≤ the median age (P = 0.17).

CONCLUSION: Pending prospective validation, our study suggests that non-curative approaches for older men with 'low-risk' prostate cancer result in an increased risk of PCSM, suggesting the need for...
alternative approaches to exclude occult, high grade prostate cancer in these men.

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**KEYWORDS:** active surveillance, non-curative, prostate cancer, prostatectomy, radiation, undergrading

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