

Cognitive Effects of Androgen Deprivation Therapy for Prostate Cancer: A Systematic Review and Meta-Analysis

Maxine Sun, PhD¹ Alexander P. Cole MD¹, **Quoc-Dien Trinh, MD¹**

¹Division of Urological Surgery and Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

BACKGROUND:

Nearly 50% of men diagnosed with prostate cancer may receive treatment with some form of androgen deprivation therapy (ADT) with total expenditures of over 1 billion dollars annually. What's more, use of ADT may rise if recent recommendations against screening lead to increases in rates of metastatic disease at the time of presentation. While some side effects of ADT are well acknowledged, the specific impact of ADT on cognitive function is uncertain. We therefore designed a systematic review, whose purpose is to assess the impact of ADT on four neurocognitive domains using meta-analysis.

METHODS:

Relevant studies were identified through search of English language articles indexed in PubMed Medline, PsycINFO, Cochrane Library and Web of Knowledge/Science. Our meta-analysis included 10 unique studies of adult men receiving pharmaceutical ADT for prostate cancer, with objective, longitudinal assessment of neurocognitive status in one of three domains. Neurocognitive outcomes assessed included composite measure of cognitive performance (642 patients in 4 studies), verbal fluency (346 patients in 4 studies), and visual-spatial abilities (145 patients in 4 studies). Additionally, three large observational studies assessing rates of Alzheimer's or Parkinson dementia using diagnostic codes were included.

RESULTS:

Effect sizes were calculated using pairwise comparisons within each longitudinal study using either controls or patients' own baseline. With respect to overall cognitive status, patients receiving ADT had higher odds of overall cognitive impairment (OR 1.65 95% CI 1.03 to 2.66). Differences in scores of visuo-spatial reasoning and verbal skills were not significantly different between ADT and non-ADT groups. Mean difference for verbal skills was -1.59 in the ADT group (95% CI -4.78 to 1.60) and -0.20 for visual-spatial skills (95% CI -1.23 to 0.84). Men with a history of ADT for prostate cancer had higher rates odds of developing Alzheimer's and Parkinson dementia compared with men without ADT (OR 1.32 95% CI 1.27-1.37).

CONCLUSIONS:

Men receiving ADT for prostate cancer performed significantly worse on measures of overall cognitive function however statistically significant differences were not observed in pooled results for specific assessments of visual-spatial or verbal reasoning. Additionally, results from the three large observational trials included suggest men exposed to ADT for prostate cancer have higher rates of Parkinson/Alzheimer's compared to healthy controls. Though some heterogeneity was seen, these findings are consistent with generally acknowledged impact of ADT on cognitive function on men, and highlight the need for prospective standardized tools for measuring specific cognitive impact of ADT on men with prostate cancer.

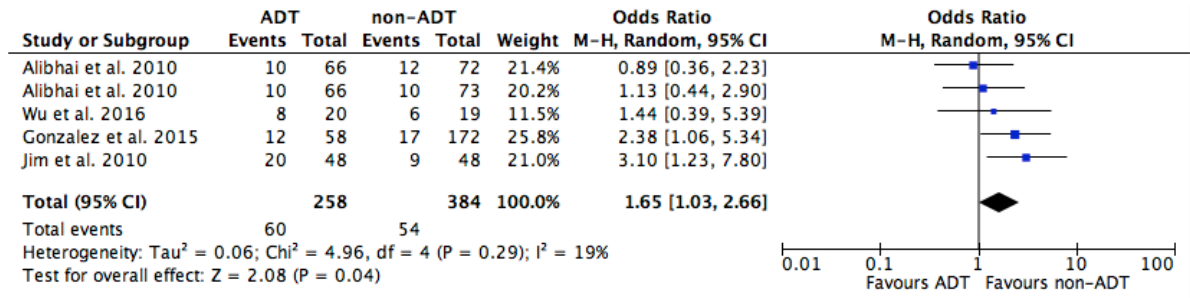


Figure 1: Forest plot of overall cognitive impairment among men 642 in 4 studies receiving ADT for prostate cancer.

CONFLICT OF INTEREST:

The authors declare no relevant conflicts of disclosures.

FUNDING ACKNOWLEDGMENTS:

Quoc-Dien Trinh is supported by an unrestricted educational grant from the Vattikuti Urology Institute, a Young Investigator Award from the Prostate Cancer Foundation and a Career Development Award from the Conquer Cancer Foundation of the American Society of Clinical Oncology. Alexander Cole is supported by a Brigham Research Institute micro-grant.