Cognitive function in patients on androgen suppression: A prospective, multicentric study


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Abstract
Objective: To assess the effect of androgen deprivation therapy (ADT) on cognitive performance (CP) in patients with prostate cancer (PCa) after 6 months of treatment with luteinizing hormone-releasing hormone (LHRH) analogs.

Material and methods: Prospective, observational, multicentre, open-label study of patients diagnosed with nonmetastatic or asymptomatic metastatic PCas scheduled to receive LHRH analogs for ≥6 months. We assessed four CP domains at baseline and after 6 months of ADT: (1) Working memory: Wechsler Adult Intelligence Scale III (WAIS III) Digit Span Subtest (WAIS III-Digit); (2) Visual memory: ad hoc visual memory test; (3) Visuospatial ability: Judgment of Line Orientation (JLO) and Mental Rotation of Three-Dimensional Objects (3D-Rotation); and (4) Nonverbal analytical reasoning: WAIS III Matrix Reasoning Test (WAIS III-MRT). Changes outside the baseline 95% confidence intervals were considered significant.


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Results: A total of 308 patients completed the study. Of these, 245 (79.6%) experienced no statistically significant changes on any test and 63 patients (20.4%) experienced significant changes in ≥1 test. Of these, most presented a change in only one test, distributed evenly between improvements (58 patients; 18.8%) and worsening (56 patients; 18.2%). For individual tests, most patients (87.8–91.8%) had no change from baseline; however, the significant changes (improvement vs. deterioration, respectively) were as follows: WAIS III-Digit (6.3% vs. 5.9%); visual memory (5.3% vs. 5.7%); JLO (5.3% vs. 4.5%); 3D-Rotation (4.1% vs. 4.1%); and WAIS III-MRT (4.8% vs. 5.8%).

Conclusions: CP in patients with PCa does not appear to be adversely affected by 6 months of LHRH analog administration.

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Introduction

More than one third of all men diagnosed with prostate cancer (PCa) receive androgen deprivation therapy (ADT), typically luteinizing hormone-releasing hormone (LHRH) analogs. ADT is indicated as primary systemic therapy in advanced disease and as neoadjuvant, adjuvant, or concomitant therapy in conjunction with radiation therapy in localized or locally-advanced PCa. The benefits of ADT are well-established, including a reduction in prostate-specific antigen (PSA) levels and, most importantly, an increase in overall survival.

Despite the clear benefits of LHRH analogs, these drugs are not without adverse effects, most of which are well understood. By contrast, the effect of castration on cognitive function in PCa patients has received relatively little attention. Consequently, the impact of ADT on cognitive performance (CP) remains unclear due to the inconclusive and often contradictory findings reported to date.

Nevertheless, interest in this topic has been increasing in recent years, as evidenced by the growing, but still limited, number of published studies. Unfortunately, all the studies published to date have consisted of small sample sizes (18–77 patients). The largest prospective study conducted to date found that ADT had no significant impact on cognitive function, although other studies have reported ambiguous findings, with deterioration in some cognitive functions but improvement in others. These highly heterogeneous and inconsistent results are attributable, at least partially, to the lack of large prospective studies.
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