Social Science & Medicine 156 (2016) 80–89

Contents lists available at ScienceDirect

Social Science & Medicine

journal homepage: www.elsevier.com/locate/socscimed

Cognitive and neurobehavioral symptoms in patients with non-metastatic prostate cancer treated with androgen deprivation therapy or observation: A mixed methods study

Lisa M. Wu [a, *], Molly L. Tanenbaum [b], Marcel P.J.M. Dijkers [c], Ali Amidi [d], Simon J. Hall [e], Frank J. Penedo [a], Michael A. Diefenbach [e]

[a] Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, 633 North St. Clair, Suite 19-073, Chicago, IL 60611, USA
[b] Department of Pediatrics, Stanford University School of Medicine, Palo Alto, CA, USA
[c] Department of Rehabilitation Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[d] Unit for Psychooncology and Health Psychology, Department of Oncology and Department of Psychology and Behavioural Sciences, Aarhus University Hospital & Aarhus University, Aarhus C., Denmark
[e] Departments of Medicine and Urology, Northwell Health, Great Neck, NY, USA

ARTICLE INFO

Article history:
Received 9 November 2015
Received in revised form
26 February 2016
Accepted 11 March 2016
Available online 17 March 2016

Keywords:
Prostate cancer
Oncology
Cognitive functioning
Neurobehavioral functioning
Androgen deprivation therapy
Attributions
Quality of life

ABSTRACT

Background: Few studies have investigated prostate cancer patients' experiences of cognitive functioning or neurobehavioral symptoms (i.e., behavioral changes associated with neurological dysfunction) following androgen deprivation therapy (ADT).

Methods: Semi-structured interviews conducted from the US by phone and in-person were used to explore and characterize the: 1) experience of cognitive and neurobehavioral functioning in non-metastatic prostate cancer patients undergoing ADT ($n = 19$) compared with patients who had not undergone ADT ($n = 20$); 2) perceived causes of cognitive and neurobehavioral symptoms; 3) impact of these symptoms on quality of life; and 4) strategies used to cope with or compensate for these symptoms. Neuropsychological performance was assessed to characterize the sample.

Results: Overall, ADT patients experienced marginally more cognitive problems than non-ADT (nADT) patients even though there were no significant differences between groups in neuropsychological performance. ADT patients also experienced more declines in prospective memory and multi-tasking than nADT patients. Significant proportions of participants in *both* groups also experienced retrospective memory, attention and concentration, and information processing difficulties. With respect to neurobehavioral symptoms, more ADT patients experienced emotional lability and impulsivity (both aspects of disinhibition) than nADT patients. Among the causes to which participants attributed declines, both groups attributed them primarily to aging. A majority of ADT patients also attributed declines to ADT. For both groups, increased cognitive and neurobehavioral symptoms negatively impacted quality of life, and most participants developed strategies to ameliorate these problems.

Conclusion: ADT patients are more vulnerable to experiencing specific cognitive and neurobehavioral symptoms than nADT patients. This study highlights the importance of capturing: a) cognitive symptoms not easily detected using neuropsychological tests; b) neurobehavioral symptoms that can be confused with psychological symptoms, and c) causal beliefs that may affect how people cope with these symptoms. Effective interventions are needed to assist prostate cancer patients in managing these symptoms.

1. Introduction

Androgen deprivation therapy (ADT) is a mainstay treatment for prostate-specific antigen (PSA) recurrence following localized prostate cancer treatment (Han et al., 2001; Singh et al., 2010). However, ADT has been associated with side-effects, including

* Corresponding author.
E-mail addresses: lisa.wu1@northwestern.edu (L.M. Wu), mollyt@stanford.edu (M.L. Tanenbaum), Marcel.Dijkers@mountsinai.org (M.P.J.M. Dijkers), ali@psy.au.dk (A. Amidi), Shall12@Northwell.edu (S.J. Hall), fpenedo@northwestern.edu (F.J. Penedo), MDiefenbach@Northwell.edu (M.A. Diefenbach).

http://dx.doi.org/10.1016/j.socscimed.2016.03.016
0277-9536/

cognitive impairments. A recent systematic review and meta-analysis of research examining cognitive performance in ADT patients concluded that they performed significantly worse on visual motor tasks than non-cancer control groups, consistent with research highlighting the important role of testosterone on cognition (McGinty et al., 2014). A more recent controlled longitudinal study corroborated these findings (Gonzalez et al., 2015).

Although studies have examined neuropsychological performance in ADT patients, few have investigated ADT patients' experiences of changes in cognitive functioning. Self-reported cognitive functioning tends not to be highly correlated with neuropsychological performance (Joly et al., 2006) but there is evidence that self-reported symptoms: a) provide important complementary information about the lived experience of cognitive impairments (Wu et al., 2013); b) are an important harbinger of further cognitive decline that may not yet be detectable with neuropsychological tests (Reisberg et al., 2010), and c) are associated with reduced quality of life (Voerman et al., 2006).

The few studies that have examined self-reported cognitive functioning in ADT patients have resulted in mixed findings. One study compared 57 non-metastatic prostate cancer patients undergoing ADT with 51 healthy age-matched controls and found no differences in self-reported cognitive functioning (Joly et al., 2006). However, another study of 238 patients who had been on ADT for more than one year reported worse cognitive functioning than men who received ADT for less than a year (Voerman et al., 2006). In an earlier qualitative pilot study to examine 11 ADT patients' experiences of cognitive impairment since treatment (Wu et al., 2013), impairments affecting multiple cognitive domains were reported by patients from lower level functions (e.g., concentration) to higher level functions (e.g., executive functioning). Interestingly, neurobehavioral symptoms were also reported. *Neurobehavioral symptoms* are the behavioral signs and symptoms of neurological impairment and include apathy (e.g., loss of initiation, loss of spontaneity) and disinhibition (e.g., impulsivity, emotional lability) (Grace and Malloy, 2001; Larner, 2010). Neurobehavioral symptoms are closely related to cognitive functioning in that they are purported to underlie or are precursors to cognitive alterations in neurologic disorders (Andersson and Bergedalen, 2002; Cummings et al., 1994; Wu et al., 2013). Frontostriatal neuronal circuits of the brain are important for the mediation of both behavior and lower to higher level cognition (Tekin and Cummings, 2002) and are purported to be affected by testosterone loss (Batrinos, 2012).

There has been extensive focus on neuropsychological outcomes in ADT patients at the cost of comprehensive inquiry into patients' self-reported experiences of cognitive and neurobehavioral impairment, their understanding of the causes of impairments, and the impact of symptoms on quality of life. Furthermore, no studies have undertaken an in-depth examination of neurobehavioral symptoms in ADT patients.

To address this gap in the literature, this study was designed to explore and characterize: 1) the experience of cognitive and neurobehavioral functioning in non-metastatic prostate cancer patients undergoing ADT and compare them with those undergoing observation who had not undergone ADT; 2) the perceived causes of cognitive impairments and neurobehavioral symptoms; 3) the impact of cognitive and neurobehavioral changes upon quality of life; and 4) the strategies used to cope with or compensate for cognitive and neurobehavioral impairments. An additional objective was to assess neuropsychological performance in order to characterize the sample. Our inquiry was guided by a self-regulation framework that specifies individual cognitive attributes of a health threat and individual affective responses to a threat (Diefenbach et al., 2008). This framework identifies illness representations of identity, duration, cause, consequence and treatability of health threats and describes affective responses triggered by such representations that are associated with the formation and execution of health behaviors.

2. Methods

2.1. Recruitment and procedures

Approval was obtained by Mount Sinai's Program for the Protection of Human Subjects. Prostate cancer patients were recruited: a) from Mount Sinai Hospital in New York; and b) via listservs and advocacy groups housed online (that therefore had international reach) between August 2012 and February 2014. Informed consent was obtained from all participants.

A screening interview established that participants were men who: (1) had completed primary treatment (not ADT) for localized prostate cancer; (2) currently had prostate cancer with no nodal involvement; (3) were able to speak and read English; (4) had no active psychosis; (5) had no evidence of current substance abuse; (6) had no evidence of clinically significant depressed mood; and (7) were not suicidal. The *ADT group* had been treated with ADT for 3 months or longer. The *Non-ADT* (*nADT*) *group* had no history of ADT.

Eligible participants were invited to the medical center to participate in a semi-structured interview, and complete a computerized assessment of cognitive functioning and questionnaires. Those who were unable to come to the hospital were given the option to participate by phone and Internet, which facilitated community recruitment. Participants received a monetary incentive of $40.

2.2. Measures

2.2.1. Sociodemographic and medical information

This information was gathered directly from participants and through medical chart review and included age, race/ethnicity, level of education, cancer diagnosis, date of diagnosis, and cancer treatment.

2.2.2. Medical comorbidities

The self-administered comorbidity questionnaire assessed medical comorbidities (Sangha et al., 2003).

2.2.3. Objective cognitive functioning

CNS Vital Signs (Gualtieri et al., 2004), a computer-administered neuropsychological assessment battery, consisting of seven cognitive tests assessed verbal memory, visual memory, psychomotor speed, processing speed, executive functioning/cognitive flexibility, and sustained attention. Although brief (30 min), CNS Vital Signs is sensitive to mild cognitive dysfunction and has psychometric characteristics similar to conventional neuropsychological tests (Gualtieri et al., 2004).

2.2.4. Premorbid intellectual functioning

The Wechsler Test of Adult Reading was used to estimate premorbid intellectual ability (Wechsler, 2001).

2.3. Semi-structured interview

All interviews were undertaken by two of the authors (LW and MT) using an interview guide that mainly consisted of open-ended questions structured around cognitive and neurobehavioral changes since prostate cancer treatment (i.e., ADT for the ADT group and primary treatment for the nADT group). To limit the extent to which participants were primed to the study's aims, the