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Distinct attentional function profiles in older adults receiving cancer chemotherapy

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ABSTRACT

Purpose: While attentional function is an extremely important patient outcome for older adults, research on changes in function in this group is extremely limited. The purposes of this study were to: identify subgroups of older patients (i.e., latent growth classes) based on changes in their level of self-reported attentional function; determine which demographic and clinical characteristics were associated with subgroup membership; and determine if these subgroups differed on quality of life (QOL) outcomes.

Methods: Older oncology outpatients (n = 365) who were assessed for changes in attention and working memory using the Attentional Function Index a total of six times over two cycles of chemotherapy (CTX). QOL was assessed using the Medical Outcomes Study-Short Form 12 and the QOL-Patient Version Scale. Latent profile analysis (LPA) was used to identify subgroups of older adults with distinct attentional function profiles.

Results: Three distinct attentional functional profiles were identified (i.e., low, moderate, and high attentional function). Compared to the high class, older adults in the low and moderate attentional function classes had lower functional status scores, a worse comorbidity profile and were more likely to be diagnosed with depression. In addition, QOL scores followed an expected pattern (low class < moderate class < high attentional function class).

Conclusions: Three distinct attentional function profiles were identified among a relatively large sample of older adults undergoing CTX. The phenotypic characteristics associated with membership in the low and moderate latent classes can be used by clinicians to identify high risk patients.

1. Introduction

The number of older adults diagnosed with cancer is expected to increase by 67% between 2010 and 2030 (Smith et al., 2009). However, older adults are less likely to receive the most effective cancer treatments (Extermann et al., 2005), and to complete a standard course of chemotherapy (CTX) (Fairfield et al., 2011). Because age is a well-established risk factor for cognitive decline, researchers have speculated that older adults may be more vulnerable to the adverse cognitive effects of cancer treatments (Ahles et al., 2012; Hurria et al., 2006b; Lange et al., 2014). However, only limited information is available on the impact of CTX on older oncology patients' cognitive function (Joly et al., 2015).

In a longitudinal study of older women with breast cancer (Lange et al., 2016), 29% had a decline in working memory using the neuropsychological test Wechsler Adult Intelligence Scale-III (i.e., arithmetic, digit-span forward, digit-span backward, and letter-number sequencing) (Wechsler, 1997), from before to after the completion of CTX. In another study of older breast cancer patients (Hurria et al., 2006a), > 60% perceived pre-existing working memory problems and were more likely to perceive worsening memory after CTX. In addition, older adults with comorbidities (e.g., diabetes) have poorer cognitive performance prior to cancer treatment (Mandelblatt et al., 2014b). None of these studies evaluated patients at multiple time points over

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two cycles CTX to assess for more acute changes in cognitive function. In addition, these studies were limited because the sample sizes were relatively small and assessed only older women with breast cancer. As noted in three reviews (Joly et al., 2015; Loh et al., 2016; Mandelblatt et al., 2014a), longitudinal studies of changes in and factors associated with decrements in cognitive function in older adults receiving CTX are urgently needed to inform clinical decisions and follow-up care.

A number of instruments can be used to assess changes in cognitive function (Andreis et al., 2013; Collins et al., 2013; Minisini et al., 2008). However, shorter instruments, that are focused on an evaluation of changes in attention and working memory (i.e., executive function), may be easier for older adults to complete and more reflective of changes in their ability to manage daily activities. In addition, attention and working memory are the two most common domains of cognitive function that are affected by CTX (Vannorsdall, 2017; Vitali et al., 2017; Yao et al., 2017). One such self-reported instrument is the Attentional Function Index (AFI) (Cimprich et al., 2011). This instrument has been used in several studies of oncology patients and can detect changes attentional function over time (Askren et al., 2014; Jung et al., 2017; Moon et al., 2011; Myers et al., 2015; Visovatti et al., 2016; Von Ah et al., 2009).

In most studies of changes in cognitive function in older oncology patients (Hurria et al., 2006a; Lange et al., 2016), mean scores were used to evaluate for between groups differences or changes over time. This approach does not allow for the identification of subgroups of patients with distinct cognitive function profiles. The use of statistical approaches, like latent profile analysis (LPA), allows for the identification of these subgroups. Once these subgroups are identified, the demographic and clinical characteristics associated with subgroup membership can be evaluated.

While attentional function is an important patient outcome for older adults, research on changes in function in this vulnerable group is extremely limited. Therefore, the purposes of this study, in a sample of older oncology outpatients (n = 365) who were assessed for changes in attention and working memory using the AFI over two cycles of CTX were to: identify subgroups of older patients (i.e., latent growth classes) based on changes in their level of self-reported attentional function; determine which demographic and clinical characteristics were associated with subgroup membership; and determine if these subgroups differed on quality of life (QOL) outcomes.

2. Methods

2.1. Patients and settings

Details on the larger, longitudinal study are published elsewhere (Miaskowski et al., 2017, 2014). In brief, for the larger study, eligible patients were ≥18 years of age; had a diagnosis of breast, gastrointestinal (GI), gynecological (GYN), or lung cancer; had received CTX within the preceding four weeks; were scheduled to receive at least two additional cycles of CTX; were able to read, write, and understand English; and gave written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs. A total of 2234 patients were approached during their second or third cycle of CTX and 1343 consented to participate (60.1% response rate). The major reason for refusal was being overwhelmed with their cancer treatment. For this study, data from patients who were ≥65 years of age (n = 365) were used in the analysis of changes in attentional function.

2.2. Instruments

A demographic questionnaire obtained information on age, gender, ethnicity, marital status, living arrangements, education, employment status, and income. The Karnofsky Performance Status (KPS) scale was used to assess patients' overall performance status (Karnofsky et al., 1948). Patients rated their functional status using the KPS scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms) (Ando et al., 2001; Schnadig et al., 2008).

Self-Administered Comorbidity Questionnaire (SCQ) consists of thirteen common medical conditions simplified into language that can be understood without prior medical knowledge (Sangha et al., 2003). Patients indicated if they had the condition; if they received treatment for it (proxy for disease severity); and if it limited their activities (indication of functional limitations). Across the thirteen conditions, the total SCQ score can range from 0 to 39 with higher scores indicating a worse comorbidity profile. The SCQ has well established validity and reliability (Brunner et al., 2008; Cieza et al., 2006).

Alcohol Use Disorder Identification Test (AUDIT) is a 10-item questionnaire that assesses alcohol consumption, alcohol dependence, and consequences of alcohol abuse in the last 12 months. The AUDIT gives a total score that ranges between 0 and 40. Scores of ≥8 are defined as hazardous use and score of ≥16 are defined as use of alcohol that is likely to be harmful to health (Babor et al., 2001). The AUDIT has well-established validity and reliability (Berks and McCormick, 2008). The Cronbach's alpha for the AUDIT was 0.63.

Changes in attentional function over two cycles of CTX were assessed using the AFI score (Cimprich et al., 2011). AFI consists of 16 questions about attentional function. A higher total mean score on a 0 to 10 numeric scale (NRS) indicates greater capacity to direct attention (Cimprich et al., 2011). Total scores are grouped into categories of attentional function (i.e., < 5 low function, 5.0 to 7.5 moderate function, > 7.5 high function) (Cimprich et al., 2005). The AFI has well-established validity and reliability (Cimprich et al., 2011). The Cronbach's alpha for the AFI total score was 0.93.

Changes in QOL were assessed using the SF-12 (Ware et al., 1996). The SF-12 consists of 12 questions about physical and mental health as well as overall health status. The SF-12 was scored into two components that measure physical (i.e., PCS) and psychological (mental component summary (MCS)) function. These scores can range from 0 to 100. Higher PCS and MCS scores indicate better physical and psychological functioning, respectively. The PCS score includes the dimensions of physical functioning, role-physical, bodily pain, and general health perceptions. The MCS score includes the dimensions of mental functioning, emotional functioning, social functioning, and vitality. The SF-12 has well established validity and reliability (Ware et al., 1996).

Disease-specific QOL was evaluated using the Quality of Life Scale-Patient Version (QOL-PV) (Padilla et al., 1983, 1990). This 41-item instrument measures four domains of QOL (i.e., physical, psychological, social, and spiritual well-being) in oncology patients, as well as a total QOL score. Each item is rated on a 0 to 10 NRS with higher scores indicating a better QOL. The QOL-PV has well established validity and reliability (Ferrell, 1995; Ferrell et al., 1995; Padilla et al., 1983, 1990). The Cronbach's alpha for the QOL-PV total score was 0.92.

2.3. Study procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Board at each of the study sites. Eligible patients were approached by a research staff member in the infusion unit to discuss participation in the study. Written informed consent was obtained from all patients. Depending on the length of their CTX cycles, patients completed questionnaires in their homes, a total of six times over two cycles of CTX (i.e., prior to their next cycle of CTX (assessment symptoms during the period of recovery from the previous CTX cycle, Assessments 1 and 4), approximately 1 week after CTX administration (assessment of acute symptoms following the administration of CTX, Assessments 2 and 5), and approximately 2 weeks after CTX administration (assessment of symptoms during the potential nadir, Assessments 3 and 6)).