

## REVIEW ARTICLE

# Age-related differences in self-report and objective measures of cognitive function in older patients prior to chemotherapy

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## Abstract

**Aim:** Evaluate for differences in demographic and clinical characteristics and subjective and objective measures of cognitive function (CF) between younger older adults (YOA, 60–69 years) and older adults (OA, ≥70 years).

**Design:** Cross-sectional.

**Methods:** Older oncology patients ( $n = 139$ ) completed subjective (Attentional Function Index, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC) CF scale) and objective (Montreal Cognitive Assessment, Trail Making Test (TMT) A & B) measures of CF prior to chemotherapy. Data were analyzed using parametric and nonparametric tests.

**Results:** No differences were found between the two groups for any of the subjective or objective CF measures, except that OA patients had higher TMT B scores. Compared with the general population, OAs had significantly higher EORTC CF scores and YOAs had significantly worse scores for all of the objective tests. Clinically meaningful difference between group differences was found for the TMT B test.

## KEYWORDS

cancer, cognitive function, older adult, patient-reported outcomes, performance-based outcomes

## 1 | INTRODUCTION

Cancer-related cognitive impairment (CRCI) is one of the most feared adverse effects of cancer treatment (Ahles & Root, 2018). While occurrence rates vary based on the cognitive measures and impairment

criteria used, CRCI occurs in 12%–75% of patients receiving chemotherapy (CTX) (Loh et al., 2016). Older adults may be more vulnerable to CRCI (Ahles & Root, 2018; Lange, Rigal, et al., 2014) because the cancer itself and associated treatments may accelerate the neurodegenerative changes seen with aging (Freedman et al., 2013; Lange,

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Rigal, et al., 2014). While findings regarding differences between younger and older oncology patients receiving CTX are inconclusive (Bompaire et al., 2017; Wefel et al., 2015), recent evidence suggests that compared with age-matched controls, older oncology patients undergoing CTX experience a decline in cognitive function (Ahles & Root, 2018; Lange, Rigal, et al., 2014). Of particular importance to older adults is how a cancer diagnosis and its treatments will influence their level of cognitive function, as well as how to evaluate cognitive function in older adults. This information can be used to identify older patients who may be at increased risk for cognitive deficits.

## 2 | BACKGROUND

While findings regarding the correlations between subjective and objective measures of CRCI are inconsistent (Wefel et al., 2015) and most of these studies have not included older adults (Hutchinson et al., 2012), most investigators suggest that to obtain a complete picture of cognitive function, both types of measures are needed (Hutchinson et al., 2012). Two common self-report measures of CRCI are the Attentional Function Index (AFI) (Cimprich et al., 2011) and the cognitive function scale of the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) (Aaronson et al., 1993). While the AFI assesses attention and executive function, the EORTC cognitive function scale assesses memory and concentration.

In terms of objective measures, the Mini-Mental State Examination (MMSE) is one of the most common cognitive screening measures that is recommended as part of a Comprehensive Geriatric Assessment (CGA) (Hernandez Torres & Hsu, 2017). However, the MMSE does not have the sensitivity to detect mild cognitive impairment in older oncology patients (Kurita et al., 2018). Findings from several studies suggest that the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) is a more sensitive measure to detect these subtle changes (Olson et al., 2011; Pendlebury et al., 2010; Zadikoff et al., 2008). In fact, the Canadian Consortium on Neurodegeneration in Aging recommended that the MoCA and Trail Making Test (TMT) A & B (Tombaugh, 2004) be used as a minimum set of measures to evaluate cognitive function in older adults (Montero-Odasso et al., 2019).

In terms of studies that used both subjective and objective measures to evaluate CRCI in older patients (Lange, Giffard, et al., 2014; Lange et al., 2016, 2019; Mandelblatt et al., 2014), all of them evaluated patients with breast cancer. In the first study, which compared older patients to age-matched healthy controls, prior to the administration of CTX (Lange, Giffard, et al., 2014), 41% of the patients had cognitive deficits based on a battery of neuropsychological tests (i.e. episodic memory, working memory, processing speed and executive function). Of note, while the patients reported better scores on the Functional Assessment of Cancer Therapy-cognitive scale (FACT-Cog) than healthy controls, the

majority of the objective measures did not correlate with the subjective measures. In a follow-up study from this research team, that evaluated for changes in cognitive function from before to after the completion of adjuvant therapy (Lange et al., 2016), compared with the healthy controls, 49% of the older patients with breast cancer had a decline in cognitive function based on the objective measures. Of these women, 12% had cognitive impairment before adjuvant treatment that increased after treatment and 64% of them developed impairment after treatment. In addition, patients who were  $\geq 75$  years of age were at the highest risk for cognitive decline at the end of treatment. Again, no significant correlations were found between the majority of the subjective and objective measures. In a third report from this research group that included a post hoc secondary analysis of previously published data (Lange et al., 2019), inter-individual variability in the change trajectories of the objective measures of cognitive function was evaluated. Five change patterns were identified and named no decline, normal aging, nonpathologic decline, accelerated cognitive decline and no pretreatment cognitive impairment followed by the development of cognitive impairment.

In another study of 164 patients with breast cancer who were  $\geq 60$  years of age (Mandelblatt et al., 2014), cognitive function was evaluated using the FACT-Cog and a battery of neuropsychological tests, prior to the initiation of CTX. Compared with healthy controls ( $n = 182$ ), no differences were found in any of the subjective or objective measures. However, while not related to being a patient or a healthy control, older age increased the odds of having cognitive impairment.

While the reports from these two samples of older women with breast cancer provide interesting results (Lange, Giffard, et al., 2014; Lange et al., 2016, 2019; Mandelblatt et al., 2014), they suggest significant inter-individual variability in older adults responses to CTX. In addition, only patients with breast cancer were evaluated and potential changes in CRCI with increasing age were not reported. Given that the population of older adults is expected to reach 2.1 billion by 2050 (Jacobsen et al., 1999); that nearly two-thirds of all cancers will be diagnosed in individuals over 60 years of age (Siegel et al., 2019); and the paucity of research on CRCI in older adults, the purposes of this study, in a sample of older patients with gynecological and colorectal cancer ( $n = 139$ ) whose cognitive function was measured prior to the initiation of CTX, using both subjective and objective measures, were to: evaluate for differences in demographic and clinical characteristics between younger older adults (YOA, 60–69 years of age) and older adults (OA,  $\geq 70$  years of age); identify differences in subjective and objective measures of cognitive function between YOA and OA; compare the scores for both cognitive function measures from our sample of YOA and OA with age-matched samples without cancer drawn from the general population (Fossa et al., 2007; Thomann et al., 2018; Tombaugh, 2004). In addition, associations between the subjective and objective measures of cognitive function were evaluated.

### 3 | DESIGN

This study has a cross-sectional design.

### 4 | METHODS

#### 4.1 | Patients and settings

Patients were recruited from one community and two university hospitals in Norway. The inclusion criteria were as follows: aged  $\geq 60$  years; diagnosis of gynecological or colorectal cancer; scheduled to receive primary or adjuvant CTX; had a MoCA score of  $\geq 23$  (Nasreddine et al., 2005) and had a Karnofsky Performance Status (KPS) score of  $\geq 60$  (Schag et al., 1984). A total of 208 patients were approached and 149 consented to participate (71.6% response rate). Of these 149 patients, one withdrew and nine were excluded because they had a MoCA score of  $< 23$ . For this analysis, 139 patients were included as shown in Figure 1.

#### 4.2 | Instruments

##### 4.2.1 | Demographic and clinical characteristics

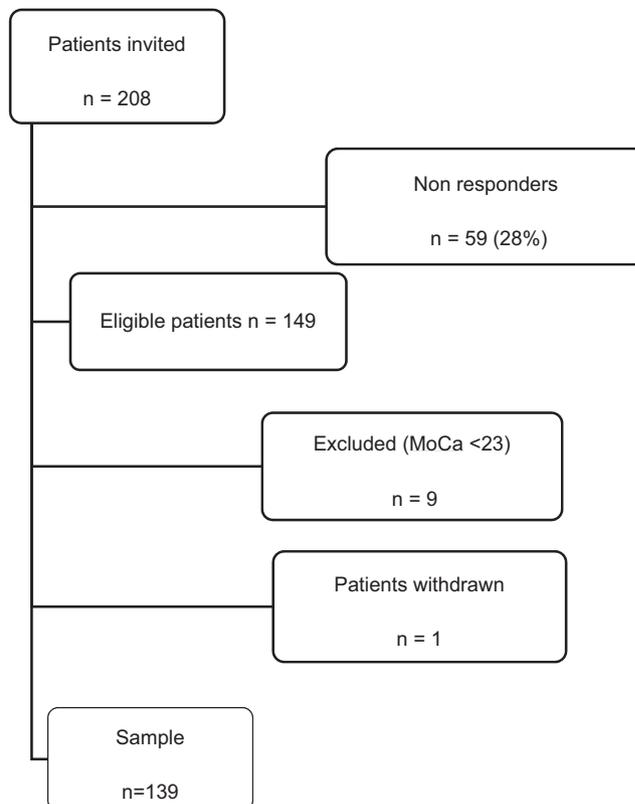
At enrollment, patients completed a demographic questionnaire that obtained information on gender, living arrangements, marital status, education, weight and height and employment status. In addition, they completed the KPS scale that ranged from 40 (disabled; requires special care and assistance) to 100 (normal no complaints; no evidence of disease) (Schag et al., 1984) and the Self-Administered Comorbidity Questionnaire (SCQ-16) (Sangha et al., 2003). The SCQ-16 includes 16 common medical conditions. Patients evaluated the occurrence, treatment and functional impact of each of the comorbid conditions. Total SCQ scores can range from 0–48. The SCQ-16 has well-established validity and reliability (Sangha et al., 2003).

Patients reported visual and hearing impairments and the occurrence of tinnitus. The occurrence and severity of visual and hearing impairments were assessed by two questions adapted from the 15D questionnaire (Sintonen, 2001): (i) Do you have problems with vision/hearing? and (ii) Do you use any aids to read/hear? To assess the occurrence of tinnitus, patients were asked whether they were bothered by tinnitus (yes/no).

##### 4.2.2 | Subjective measures of cognitive function

The AFI (Cimprich et al., 2011) and the cognitive function scale from the EORTC QLQ-C30 (Aaronson et al., 1993) were the subjective measures of cognitive function used in the study.

The 16-item AFI assesses an individual's perceived effectiveness in performing daily activities that are supported by attention and working memory (Cimprich et al., 2011). The first 12 items assess



**FIGURE 1** Flow chart of patient enrollment. Abbreviation: MoCA, Montreal Cognitive Assessment

four components of executive functioning (i.e. goal formulation, planning, carrying out activities and monitoring effective performance). The last four items assess behavioral and affective responses associated with a lowered capacity to direct attention (i.e. making mistakes, forgetting, irritability and impatience). Each item is rated on a 0–10 scale. Total and subscales scores (i.e. effective action, attentional lapses and interpersonal effectiveness) are calculated as the means of the items. A higher total AFI score indicates greater capacity to direct attention (Cimprich et al., 2011). Total scores are grouped into three categories of attentional function (i.e.  $< 5.0$  low function, 5.0–7.5 moderate function and  $> 7.5$  high function). The AFI has well-established validity and reliability (Cimprich et al., 2011). In the current study, its Cronbach's  $\alpha$  was 0.93.

The EORTC QLQ-C30 consists of five function scales (i.e. physical, role, cognitive, emotional and social), seven symptom scales (i.e. fatigue, pain, nausea and vomiting, dyspnea, insomnia, appetite loss and constipation), a financial difficulties scale and an overall health and QOL scale (Aaronson et al., 1993). The questionnaire has a 1-week time frame and uses a four-point response format ("not at all," "a little," "quite a bit" and "very much"), with the exception of the global health status scale, that is scored on a 1 (very poor) to 7 (excellent) scale. The raw scores were linearly transformed to a 0–100 scale, using the algorithm in the EORTC QLQ-C30 scoring manual. Higher scores indicate a better level of function and QOL. For the symptom scales, higher scores indicate more severe symptoms. The cognitive function scale was used in these analyses.

### 4.2.3 | Objective measures of cognitive function

The MoCA and the TMT were the objective measures of cognitive function used in this study.

The MoCA is a brief screening tool designed to detect mild forms of cognitive impairment (Nasreddine et al., 2005). It evaluates six cognitive domains: memory, visuospatial abilities, executive functioning, attention and concentration, language and orientation (Nasreddine et al., 2005). The short-term memory recall task involves recalling five words after 5 min. Visuospatial abilities are assessed by having the patient draw a clock and copy a three-dimensional cube. Multiple aspects of executive function are assessed using a portion of the TMT, a phonemic fluency task and a two-item verbal abstraction task. Attention, concentration and working memory are evaluated using a sustained attention task, a serial subtraction task and a digit's forward and backward task. Language is assessed using a three-item confrontation naming task with low-familiarity animals (i.e. lion, camel and rhinoceros), the repetition of two syntactically complex sentences and the aforementioned fluency task. Finally, orientation to time and place is evaluated. If an individual's education is  $\leq 12$  years, 1 point is added to the total score to achieve a maximum score of 30 (Nasreddine et al., 2005). Scores of  $\leq 25$  indicate the presence of cognitive impairment (Nasreddine et al., 2005). The MoCA has good psychometric properties, is sensitive to change over time (Freitas et al., 2012) and was used in several studies of older oncology patients (Carlson et al., 2018; Edwards et al., 2018; Loh et al., 2017).

The TMT consists of two timed tasks. TMT A provides information on difficulties with visual search, visually focused attention and psychomotor speed (Luck et al., 2018). TMT B provides information on difficulties with executive function (i.e. mental flexibility, including task switching, shared attention, working memory, simultaneous capacity and planning) (Luck et al., 2018; Tombaugh, 2004). TMT A requires an individual to draw lines sequentially connecting 25 encircled numbers in order as quickly as possible. Task requirements are similar for TMT B except that the person must alternate between 13 numbers and 13 letters (e.g. 1, A, 2, B, 3, C, ...13, L). The score for each part is the amount of time required to complete each task (Tombaugh, 2004). The TMTs A & B do not have established cut-off scores (Luck et al., 2018; Tombaugh, 2004). The TMT is a valid measure to assess cognitive function in older patients (Reitan, 1958; Tombaugh, 2004) and was used in several studies of older oncology patients (Hlubocky et al., 2018; Khan et al., 2019; Weerink et al., 2018).

### 4.3 | Study procedures

Oncologists or nurses approached patients prior to the initiation of CTX to assess their interest in study participation. Then, patients were introduced to the research staff who explained the study, obtained written informed consent and scheduled an appointment to perform the measures. The study questionnaires, MoCA and TMT A & B were administered in the clinic or in the patient's home before,

the same day or immediately after the first infusion of CTX. The administration of the MoCA and TMT A & B took approximately 15 min. Reliability testing for all of the study measures was done on an annual basis with all of the research staff. An inter-rater reliability of  $>90$  was achieved for all of the study measures. Research staff reviewed patients' medical records for disease and treatment information.

### 4.4 | Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences version 26 (SPSS, IBM Corporation). While no clear age cut-off or definition of an older cancer patient exists, consistent with the guidelines from the International Society of Geriatric Oncology (Extermann et al., 2005), in this study, older was defined as a person of  $\geq 70$  years of age. Differences between the two older age groups in demographic and clinical characteristics and cognitive function were evaluated using independent sample *t* tests and Chi-square analyses.

For each of the older age groups, one-sample *t* tests were used to compare the oncology patients' scores on the EORTC QLQ-C30 cognitive scale with scores for women from the general Norwegian population (YOA =  $\geq 60$  years to 70 years and OA =  $\geq 70$  years to 80 years) (Fossa et al., 2007). For the MoCA, patients' scores were compared with the general German population (YOA =  $\geq 65$  years to 70 years and OA =  $\geq 75$  years to 80 years) (Thomann et al., 2018). TMT A & B scores were compared with normative data from community-dwelling individuals in Canada (YOA =  $\geq 65$  years to 70 years and OA =  $\geq 75$  years to 80 years) (Tombaugh, 2004). The female scores for the EORTC QLQ-C30 were used as the reference values because the majority of older adults in our sample were female (Fossa et al., 2007). No general population scores are available for the AFI.

To evaluate for clinically meaningful differences in subjective and objective measures of cognitive function between the patients and individuals drawn from the general population, effect size calculations were done (i.e. Cohen's *d*) and were evaluated with cut-offs for small (from 0.2–0.5), medium (from 0.5–0.8) and large ( $>0.8$ ) effects (Cohen, 2013). Associations between the subjective and objective measures of cognitive function for the total sample were done using Pearson product-moment correlation coefficients. A *p*-value of  $<.05$  was considered statistically significant. The STROBE Statement – Checklist for cross-sectional studies was used.

## 5 | RESULTS

### 5.1 | Differences in demographic and clinical characteristics

Of the 139 patients, 49.6% were YOA with a mean age of 65.6 ( $SD = 3.0$ ) years and 50.4% were OA with a mean age 75.3 ( $SD = 4.9$ ) years (Table 1). Overall, the sample was predominately female

(93.5%), married or partnered (62.9%), and 37% had a college degree. Except for age, employment status and the occurrence of high blood pressure, no differences were found in any of the demographic and clinical characteristics between the two age groups. Compared with the YOA, OA were less likely to be employed (i.e. 32.8% versus 1.5%,  $p < .001$ ).

In terms of clinical characteristics, the total sample had a body mass index (BMI) of 25.8 ( $SD = 6.0$ ), had a KPS score of 86.7 ( $SD = 10.9$ ) and were 1.3 ( $SD = 3.6$ ) years from their cancer diagnosis. Of the total sample, 87.1% had a diagnosis of gynecological cancer, 54.0% had had surgery just prior to CTX, and 33.1% were being treated for recurrent disease. In addition, these patients had 1.9 ( $SD = 1.8$ ) comorbidities and had an SCQ score of 3.7 ( $SD = 4.0$ ). In terms of high blood pressure, compared with the YOA group (24.1%), patients in the OA group (45.5%,  $p = .015$ ) had a higher occurrence rate.

## 5.2 | Differences in subjective and objective measures of cognitive function

No differences were found between the two age groups, for any of the subjective measures of cognitive function (Table 2). However, when each of the age groups' EORTC cognitive function scores were compared with normative data from the Norwegian general population, the OA group had a significantly higher score (i.e. better cognitive function) than the general population (Figure 2a).

In terms of the objective measures of cognitive function (Table 2), no differences were found between the two age groups on the MoCA (Figure 2b) and TMT A (Figure 2c) scores. However, the OA patients had worse TMT B scores than the YOA patients (Figure 2d). Compared with the general population (Thomann et al., 2018; Tombaugh, 2004), YOA patients had significantly worse scores for all of the objective tests of cognitive function (Figure 2b–d).

## 5.3 | Clinically meaningful differences in subjective and objective measure of cognitive function

As shown in Table 3, when effect size calculations were done to evaluate for clinically meaningful differences in the subjective and objective measures of cognitive function, between the YOA group and the general population, effect sizes ranged from  $-0.15$  for the EORTC cognitive function scale to  $1.27$  (i.e. large effect size) for the TMT B score. When similar calculations were done between the OA group and the general population, effect sizes ranged from  $-0.06$  for the TMT A score to  $0.61$  (i.e. medium effect size) for the EORTC cognitive function scale.

## 5.4 | Associations between subjective and objective measures of cognitive function

As shown in Table 4, significant correlations between the subjective and objective measures ranged from  $r = .21$  for the MoCA total score versus the EORTC cognitive function score ( $p = .018$ ) to  $r = .28$  for the MoCA total score versus the AFI total score ( $p < .002$ ). No significant correlations were found between either the EORTC cognitive function score or the AFI total score and TMT A.

## 6 | DISCUSSION

This study is the first to evaluate for age-related differences in both subjective and objective measures of cognitive function in two groups of older oncology patients prior to the initiation of CTX. Using valid and reliable subjective (i.e. EORTC cognitive function, AFI) and objective (i.e. MoCA, TMT A & B) measures of cognitive function, except for the TMT B, no differences were found between the two age groups, for any of these measures.

In terms of the TMT B, our mean score for the total sample (115.9) is consistent with a previous study of older women with breast cancer prior to therapy (111.4) (Lange, Giffard, et al., 2014). Of note, compared with the YOA, worse scores on the TMT B for the OA group represent not only a statistically significant but a clinically meaningful difference ( $d = 0.44$ ). While no established cut-off scores exist for the TMT (Luck et al., 2018; Tombaugh, 2004), the same pattern was found between younger ( $\geq 65$ –70 years of age) and older ( $\geq 75$ –80 years of age) women ( $d = 0.57$ ) in a German population-based study. (Luck et al., 2018). These findings suggest that independent of a cancer diagnosis, TMT B scores can detect age-related changes in executive function (Luck et al., 2018; Tombaugh, 2004).

In terms of comparisons with the general population, while no differences were found between our sample of OA and the general population, our YOA had worse scores on all of the objective measures. Of note, for the TMT B, this difference was quite large ( $d = 1.27$ ). Given that executive function requires the integration of many domains of cognitive function (i.e. mental flexibility, including task switching, shared attention, working memory, simultaneous capacity and planning) and is critical for adaptive responses to the changing demands of the environment (Scherling & Smith, 2013; Utne et al., 2018), several explanations for the worse TMT B scores in our YOA are plausible. First, given that our YOA were more likely to be employed, they may have been experiencing higher levels of stress associated with work demands and changes in roles and responsibilities at work as a result of cancer treatment (Greidanus et al., 2018). In addition, several studies of oncology patients found that younger patients reported higher levels of general and cancer-specific stress (Langford et al., 2020; Thomas et al., 2010) and that higher levels of stress were associated with decrements in cognitive function (Atallah et al., 2020). As noted in one review (Ahles &

TABLE 1 Differences in demographic and clinical characteristics between Younger Older Adults (YOA) and Older Adults (OA)

Characteristics	Total (n = 139)	YOA (<70) 49.6% (n = 69)	OA (≥70) 50.4% (n = 70)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	70.5 (6.4)	65.6 (3.0)	75.3 (4.9)	$t = -14.13; p < .001$
Karnofsky Performance Status score	86.7 (10.9)	86.0 (10.4)	87.2 (11.4)	$t = -0.61; p = .546$
Body mass index (kg/m <sup>2</sup> )	25.8 (6.0)	25.1 (4.9)	26.6 (6.8)	$t = -1.53; p = .129$
Number of comorbidities	1.9 (1.8)	1.7 (1.6)	2.1 (1.9)	$t = -1.30; p = .195$
Self-administered Comorbidity Questionnaire score	3.7 (4.0)	3.2 (3.4)	4.1 (4.4)	$t = -1.27; p = .208$
Time since cancer diagnosis (years)	1.3 (3.6)	1.7 (4.3)	1.0 (2.7)	$t = 1.22; p = .225$
Hemoglobin (g/dl)	12.6 (1.7)	12.4 (1.7)	12.7 (1.6)	$t = -1.15; p = .253$
	% (n)	% (n)	% (n)	
Gender				
Females	93.5 (130)	91.3 (63)	95.7 (67)	FE; $p = .326$
Males	6.5 (9)	8.7 (6)	4.3 (3)	
Married or partnered (% yes)	62.9 (83)	59.4 (38)	66.2 (45)	FE; $p = .473$
Lives alone (% yes)	34.4 (45)	35.9 (23)	32.8 (22)	$\chi^2 = 1.25; p = .536$
Currently employed (% yes)	16.5 (21)	32.8 (20)	1.5 (1)	FE; $p < .001$
Education				
Primary school	16.0 (19)	12.5 (7)	19.0 (12)	$\chi^2 = 0.09; p = .607$
High school	47.1 (56)	50.0 (28)	44.4 (28)	
College	37.0 (44)	37.5 (21)	36.5 (23)	
Vision deficit (% yes)	10.4 (12)	9.8 (5)	10.9 (7)	FE; $p = 1.000$
Aids for reading (% yes) (n = 85)	76.5 (65)	82.1 (32)	71.7 (33)	FE; $p = .312$
Hearing deficit (% yes)	14.8 (18)	10.7 (6)	18.2 (12)	FE; $p = .310$
Aids for hearing (% yes) (n = 75)	12.0 (9)	5.9 (2)	17.1(7)	FE; $p = .171$
Tinnitus (% yes)	18.4 (23)	19.0 (11)	17.9 (12)	FE; $p = 1.000$
Specific comorbidities (% yes)				
Heart disease	13.2 (16)	10.3 (6)	15.9 (10)	FE; $p = .429$
High blood pressure	35.5 (44)	24.1 (14)	45.5 (30)	FE; $p = .015$
Lung disease	10.7 (13)	6.9 (4)	14.3 (9)	FE; $p = .245$
Diabetes	7.4 (9)	5.2 (3)	9.4 (6)	FE; $p = .496$
Ulcer or stomach disease	7.4 (9)	3.4 (2)	10.9 (7)	FE; $p = .168$
Bowel disease	9.9 (12)	10.5 (6)	9.4 (6)	FE; $p = 1.000$
Kidney disease	1.7 (2)	1.8 (1)	1.6 (1)	FE; $p = 1.000$
Liver disease	1.7 (2)	0.0 (0)	3.1 (2)	FE; $p = .498$
Anemia/ blood disease	3.4 (4)	0.0 (0)	6.6 (4)	FE; $p = .120$
Headache	8.5 (10)	3.6 (2)	12.9 (8)	FE; $p = .099$
Depression	10.1 (12)	12.3 (7)	8.1 (5)	FE; $p = .548$
Osteoarthritis	41.0 (50)	38.6 (22)	43.1 (28)	FE; $p = .713$
Back pain	32.5 (38)	35.7 (20)	29.5 (18)	FE; $p = .555$
Rheumatoid arthritis	3.4 (4)	1.8 (1)	4.8 (3)	FE; $p = .621$
Disease in connective-tissue	6.8 (8)	10.7 (6)	3.3 (2)	FE; $p = .150$
Skin disease	6.7 (8)	9.1 (5)	4.7 (3)	FE; $p = .469$
Cancer diagnosis				
Gynecological	87.8 (122)	84.1 (58)	91.4 (64)	FE; $p = .206$
Colorectal	12.2 (17)	15.9 (11)	8.6 (6)	

TABLE 1 (Continued)

Characteristics	Total (n = 139)	YOA (<70) 49.6% (n = 69)	OA (≥70) 50.4% (n = 70)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Surgery prior to chemotherapy (% yes)	54.0 (75)	53.6 (37)	54.3 (38)	FE; <i>p</i> = 1.000
Metastasis (% yes)	77.6 (104)	74.6 (50)	80.6 (54)	FE; <i>p</i> = .535
Treated for recurrent disease (% yes)	33.1 (46)	39.1 (27)	27.1 (19)	FE; <i>p</i> = .152
Type of prior cancer treatment (out of 46 patients)				
Surgery (% yes)	90.4 (40)	92.0 (23)	89.5 (17)	FE; <i>p</i> = 1.000
Radiation therapy (% yes)	15.9 (7)	7.7 (2)	27.8 (5)	FE; <i>p</i> = .103
Chemotherapy (% yes)	90.9 (40)	96.2 (25)	83.3 (15)	FE; <i>p</i> = .289
Other cancer treatment (% yes)	31.6 (12)	37.5 (9)	21.4 (3)	FE; <i>p</i> = .472

Abbreviations: dl, deciliters; FE, Fisher's Exact; g, grams; kg, kilograms; m<sup>2</sup>, meters squared; SD, standard deviation.

TABLE 2 Differences in subjective and objective measures of cognitive function between Younger Older Adults (YOA) and Older Adults (OA)

Characteristics	Total (n = 139)	YOA (<70) 49.6% (n = 69)	OA (≥70) 50.4% (n = 70)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Subjective measures of cognitive function				
EORTC QLQ-C30 Cognitive Function scale	87.1 (16.4)	84.5 (19.2)	89.4 (13.3)	<i>t</i> = -1.672, <i>p</i> = .097
AFI effective action subscale	7.4 (1.8)	7.2 (1.7)	7.6 (1.9)	<i>t</i> = -1.048, <i>p</i> = .297
AFI attentional lapses subscale	7.4 (2.0)	7.4 (2.0)	7.5 (2.1)	<i>t</i> = -0.258, <i>p</i> = .797
AFI interpersonal effectiveness subscale	7.6 (1.6)	7.4 (1.5)	7.8 (1.6)	<i>t</i> = -1.626, <i>p</i> = .107
AFI total score	7.4 (1.5)	7.3 (1.4)	7.6 (1.6)	<i>t</i> = -1.176, <i>p</i> = .242
Objective measures of cognitive function				
MoCA visuospatial/executive	4.3 (0.8)	4.2 (0.8)	4.3 (0.8)	<i>t</i> = -0.812, <i>p</i> = .418
MoCA naming	2.9 (0.3)	2.9 (0.2)	2.9 (0.3)	<i>t</i> = 0.629, <i>p</i> = .530
MoCA attention	5.4 (0.8)	5.4 (0.9)	5.5 (0.8)	<i>t</i> = -1.073, <i>p</i> = .285
MoCA language	2.6 (0.6)	2.7 (0.5)	2.5 (0.7)	<i>t</i> = 1.865, <i>p</i> = .064
MoCA abstraction	1.5 (0.6)	1.6 (0.6)	1.4 (0.6)	<i>t</i> = 1.663, <i>p</i> = .099
MoCA delayed recall	3.1 (1.3)	3.1 (1.3)	3.1 (1.3)	<i>t</i> = -0.056, <i>p</i> = .955
MoCA orientation	6.0 (0.2)	6.0 (0.1)	6.0 (0.2)	<i>t</i> = 1.000, <i>p</i> = .319
MoCA total score	26.2 (2.1)	26.2 (2.2)	26.1 (2.0)	<i>t</i> = 0.046, <i>p</i> = .963
Trail making test A	50.1 (19.7)	48.2 (21.1)	51.9 (18.3)	<i>t</i> = -1.085, <i>p</i> = .280
Trail making test B	115.9 (51.8)	104.7 (49.4)	126.6 (52.1)	<i>t</i> = -2.52, <i>p</i> = .013

Abbreviations: AFI, Attentional Function Index; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; MoCA, Montreal Cognitive Assessment; OA, older adults; SD, standard deviation; YOA, younger older adults.

Root, 2018), age and stress likely interact to contribute to changes in cognitive function in oncology patients. Future studies need to include an assessment of general and cancer-specific stress to examine these inter-relationships.

While no differences were found in EORTC cognitive function scores between GP (81.3) and YOA, OA in our study had significantly higher scores (89.4; *d* = 0.61). Our finding is consistent with a study of older patients with breast cancer that found that compared with healthy controls the patients reported fewer cognitive complaints prior to adjuvant treatment (Lange, Giffard, et al., 2014).

One possible explanation is that YOAs are more aware of or are more likely to report cognitive problems (Magnuson et al., 2019). However, it is possible that the two-item EORTC cognitive function scale (i.e. concentration and memory) is not sensitive enough to detect subtle changes.

In older adults, impairments in both cognition and mobility are associated with central nervous system pathology, even in the absence of overt neurological disease (Montero-Odasso et al., 2012). Brain areas and networks that are involved in gait control and navigation, including prefrontal cortex and hippocampus, are essential

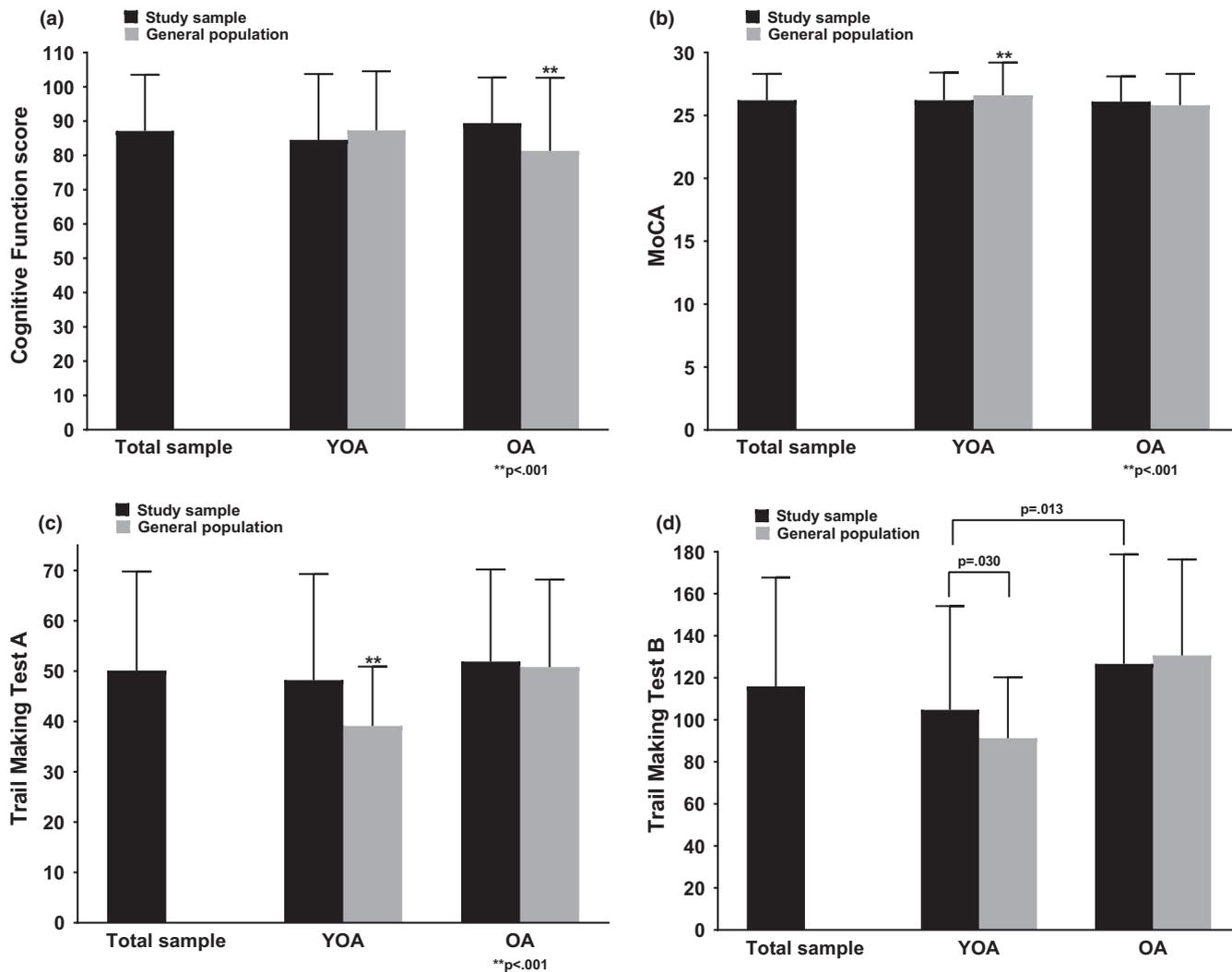


FIGURE 2 Scores for the total sample and differences in scores for the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire cognitive function scale (a), Montreal Cognitive Assessment (MoCA) scale (b), Trail Making Test A (c) and Trail Making Test B between the younger older adults (YOA) and the older adults (OA), as well as between each of the older adult age groups and the general population. All values are plotted as mean ± standard deviations

Measure	Comparison between YOA and GP	Comparison between OA and GP
Subjective measures of cognitive function		
EORTC cognitive function scale	-0.15	0.61 <sup>§</sup>
Attentional function index	n/a	n/a
Objective measures of cognitive function		
Montreal cognitive assessment	-0.18	0.15
Trail making test A (sec)	0.43 <sup>‡</sup>	0.06
Trail making test B (sec)	1.27 <sup>§</sup>	-0.08

TABLE 3 Evaluation of clinically meaningful differences in subjective and objective measures of cognitive function between the general population and each of the two age groups<sup>†</sup>

Abbreviations: EORTC, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire; GP, general population; n/a, not available; OA, older adults (≥70 years); sec, seconds; YOA, younger older adults (60–69 years).

<sup>†</sup>Evaluation done using Cohen's d (see Cohen, 2013).

<sup>‡</sup>Small effect size.

<sup>§</sup>Medium effect size.

<sup>¶</sup>Large effect size.

**TABLE 4** Correlations between subjective and objective measures of cognitive function

Measures		MoCA Total Score <sup>†</sup>	TMT A <sup>†</sup>	TMT B <sup>†</sup>	AFI Total Score <sup>‡</sup>
TMT A <sup>†</sup>	<i>r</i>	-.11			
	<i>p</i>	.199			
TMT B <sup>†</sup>	<i>r</i>	-.23	.43		
	<i>p</i>	.006	<.001		
AFI Total Score <sup>‡</sup>	<i>r</i>	.28	-.08	-.22	
	<i>p</i>	.002	.418	.013	
EORTC QLQ-C30 Cognitive Function <sup>‡</sup>	<i>r</i>	.21	-.02	-.25	.57
	<i>p</i>	.018	.837	.006	<.001

Abbreviations: AFI, Attentional Function Index; EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire; MoCA, Montreal Cognitive Assessment; TMT A and B, Trail Making Test A and B.

<sup>†</sup>Objective measures of cognitive function.

<sup>‡</sup>Subjective measures of cognitive function.

for higher-level cognitive function. Therefore, Montero-Odasso and colleagues (Montero-Odasso et al., 2019) recommended that tests that capture both cognitive and motor function and cognitive-motor interactions be used with older adults. They suggest that these tests may be able to detect subtle decline and/or predict adverse outcomes. They recommended that the TMT A & B be used because it: has well-established validity and reliability; is sensitive to changes in both cognitive performance and mobility; can be used in both research and practice; is free; and requires no special training to administer (Montero-Odasso et al., 2019). Our findings would support this recommendation for the assessment of both younger and older oncology patients.

The use of self-report measures to assess cognitive function is as important as an objective evaluation because subjective measures assess the impact of cognitive impairment on individuals' daily lives and ability to function (Hutchinson et al., 2012). While several subjective measures are available, in this study we used the AFI and the EORTC cognitive function scale. Based on the correlation coefficient between the two measures ( $r = .57, p < .001$ ), they are evaluating different aspects of cognitive function. While no population data are available for the AFI, it should be noted that for both groups of older adults, the AFI total score would be categorized as a high level of cognitive function. Similarly, the EORTC cognitive function scores were relatively high. Future studies need to examine the sensitivity and specificity of various subjective measures to be able to detect subtle changes in cognitive function in older oncology patients.

Consistent with the previous reports (Ahles & Root, 2018; Hutchinson et al., 2012), the correlations between the subjective and objective measures of CRCI in this study were low (Table 4). While a debate exists on the specific subjective and objective measures to use to assess CRCI in oncology patients, based on the findings from this study and the comments offered by Savard and Ganz (Savard & Ganz, 2016), both types of measures are needed to obtain a more complete picture of CRCI. Additional research is warranted

that examines associations between each of these measures and the results of functional imaging studies. This type of examination may reveal common and distinct brain regions that are associated with subjective and objective measures of CRCI (Sousa et al., 2020).

A number of study limitations need to be acknowledged. First, the majority of the sample were women with gynecological cancer. Therefore, our findings may not generalize to all oncology patients. Second, given that older patients are less likely to enroll in clinical studies (Abbasi, 2019), it is possible that our participants represent a sample of older oncology patients with higher levels of function. This hypothesis is supported by the low level of comorbidities in this sample. Unfortunately, information on the patients who declined participation is not available because of the restrictions on data collection imposed by the Regional Committee for Medical and Research Ethics. While the overall sample size was relatively large, the two age groups were relatively small. Therefore, findings from this study should be replicated in a larger sample. Longitudinal studies are needed to evaluate for inter-individual differences in cognitive function in older oncology patients and determine which demographic, clinical and symptom characteristics are associated with changes in cognitive function over time.

## 7 | CONCLUSIONS

Subjective and objective measures of cognitive function evaluate different aspects of cognitive function in older oncology patients. Trail Making Test B may be a useful screening measure of cognitive function in older patients.

## 8 | RELEVANCE TO CLINICAL PRACTICE

Nurses can use these findings to evaluate older oncology patients' cognitive function prior to treatment. Clinicians need to use both

subjective and objective measures of cognitive function with older oncology patients because they evaluate different aspects of cognitive function. This approach would allow clinicians to obtain a more complete picture of CRCI. The self-reported measures can be used to assess the impact of CRCI on individual patient's daily lives and ability to function. Nurses can use this information to identify older patients who may be at increased risk for CRCI and warrant ongoing monitoring.

## ACKNOWLEDGEMENT

This work was supported by grant from Faculty of Health Sciences, OsloMet - Oslo Metropolitan University, Oslo, Norway.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

## AUTHOR CONTRIBUTIONS

Inger Utne: Conceptualization and design, Funding acquisition, Data curation, Investigation, Formal analysis and interpretation of data, Writing original draft, review and editing, Final approval. Borghild Løyland: Conceptualization and design, Data curation, Investigation, Review and editing draft, Final approval. Ellen K. Grov: Conceptualization and design, Data curation, Investigation, Review and editing draft, Final approval. Hege L. Rasmussen: Acquisition of data, Investigation, Formal analysis, Review and editing draft, Final approval. Ann Helen Torstveit: Acquisition of data, Investigation, Formal analysis, Review and editing draft, Final approval. Steven M. Paul: Formal analysis, Review and editing draft, Final approval. Christine Ritchie: Conceptualization and design, Review and editing draft, Final approval. Kristina Lindeman: Acquisition of data, Review and editing draft, Final approval. Ingvild Vistad: Acquisition of data, Review and editing draft, Final approval. Claudia Rodriguez-Aranda: Conceptualization and design, Review and editing draft, Final approval. Christine Miaskowski: Conceptualization and design, Investigation, Formal analysis and interpretation of data, Writing original draft, review and editing, Final approval.

## ETHICAL APPROVAL

The Regional Committee for Medical and Research Ethics, Norway, and the Institutional Review Board at each of the study sites approved the study (Reference No. 2015/1277/REK South East). These approvals ensured that the participation in the study was voluntary. Once a physician or nurse confirmed that a patient was interested in the study, s/he informed the research staff. The staff met with the patient in the clinic or phoned the patient and explained the purpose of the study and the various study procedures. Informed and written consent, that included an explanation of confidentiality and anonymity, was obtained from all of the patients. All of the patients received oral and written information about the study including the right to refuse participation or to withdraw at any point. If the patient chose to withdraw from the study, their present or future medical treatment was not affected.

## DATA AVAILABILITY STATEMENT

Due to restrictions from the Regional Committee for Medical and Research Ethics, data for this study is not available.

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**How to cite this article:** Utne, I., Løyland, B., Grov, E. K., Rasmussen, H. L., Torstveit, A. H., Paul, S. M., Ritchie, C., Lindemann, K., Vistad, I., Rodríguez-Aranda, C., & Miaskowski, C. (2021). Age-related differences in self-report and objective measures of cognitive function in older patients prior to chemotherapy. *Nursing Open*, 00, 1–12. <https://doi.org/10.1002/nop2.1141>