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Clock Drawing Test Common Errors in Older People with Cancer

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Abstract

Introduction: The Clock drawing test (CDT) is a time-efficient cognitive screening instrument validated in older patients with cancer. Our aim was to describe the CDT patterns of errors in a sample of older patients with different cancer diagnosis.

Methods: We retrospectively analyzed baseline CDT of older cancer patients that received care at Moffitt Cancer Center. The CDT were scored using the Rouleaux method as described by Parsey and Schmitter.

Results: Data from 364 subjects was analyzed. Median age 77(70-97), 61.3% female, mean score for CDT baseline was 12.27 (SD 1.54); 165 had breast cancer, 82 gastrointestinal, 22 head and neck, 69 genitourinary, and 26 others. Pearson correlation was found to be statistically significant for age and the score in CDT (p=0.001). In this study, across different types of cancers, the most common error in the CDT was in the conceptual deficits category, with misinterpretation of time being the most frequent subtype of error. No correlation was found between comorbidities, previous exposure to chemotherapy or history of previous cancer and the CDT score. At 3 months follow up, there were no associations between the type of treatment received and the CDT score.

Discussion/conclusion: While the CDT worsened with age in cancer patients, no association was found with cancer or treatment types. Misinterpretation of time was the most frequent subtype of error. Breast cancer patients had significantly different CDT scores compared to the other groups.

Keywords: Cancer related cognitive impairment; Cognitive decline; Clock drawing test; Chemobrain; Cognitive impairment.

Abbreviations: CDT: Clock Drawing Test; SD: Standard Deviation; SAOP: Senior Adult Oncology Program; GI: Gastrointestinal; H&N: Head and Neck; GU: Genitourinary; CT: Computed Tomography.

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Introduction

While we typically think of cancer-related cognitive impairments as being associated with chemotherapy, research has suggested that cancer by itself may impact cognitive function. Studies have demonstrated that 20-30% of patients with breast cancer have impaired cognition prior to receipt of adjuvant chemotherapy or endocrine therapy [1]. Edwards et al, reported an elevated prevalence of neurocognitive deficits –mild cognitive impairment and dementia- in older adults with solid tumors and hematologic malignancies when compared to population-based studies [2].

Some studies have shown evidence that cancer related cognitive impairment may be present before the initiation of treatment and that the cognitive profile found in assessment may vary by type and localization of the cancer [3]. Different cognitive domains have been reported to be affected between breast, colorectal, testicular, head and neck and hematological cancers [4-8]. These changes may be due to, on one hand, to inconsistency in how neuropsychological tests are selected, performed, and scored, but on the other hand, due to the different biology of different cancers [9].

General consensus-based guidelines recommend that providers use cognitive assessment tools when evaluating older patients with cancer [10]. Outside of the clinical trial setting, incorporating a full neuropsychological evaluation into routine oncology practice is not practically feasible. However, if a brief evaluation with a short screening tool suggests possible cognitive impairment, referral for a more comprehensive cognitive assessment may be warranted [11].

The "Clock Drawing Test (CDT)" has been proposed as an acceptable and time-efficient cognitive screening instrument, its reliability and validity has been extensively reported [12-14], and it is validated in older cancer patients [15]. The person is instructed to draw a clock with all the numbers and the hands pointing to a specific time. Cognitive skills necessary for completion of the CDT include: comprehension, planning, visual memory and reconstruction in a graphic image, visuospatial abilities, motor programming and execution, numerical knowledge, abstract thinking, auditory comprehension, verbal working memory, inhibition of the tendency to be pulled by perceptual features of the stimulus and concentration and frustration tolerance [16]. Both quantitative (reports of the number of errors in the drawing) and qualitative (reports of the type of errors in the drawing) scoring approaches have been described and both have been associated with neuroanatomical correlates [17,18]. The fact that clock drawing requires a wide range of cognitive skills suggests that detailed qualitative analyses of clock drawings could reveal the changes or disturbances of those cognitive skills, and neuropsychological profiles can be developed [19]. This has been done for patients with breast cancer in a descriptive way, but no particular follow up or outcomes were assessed [20].

The aims of this study were to analyze qualitatively and quantitatively the CDT of older adults with different types of tumors, as well as to analyze whether the CDT score or the types of errors are associated with the type of tumor, history of previous chemotherapy, treatment modification and unplanned hospitalization.

Materials and methods

As part of usual care in the Senior Adult Oncology Program at Moffitt Cancer Center (Florida, U.S.A.) a CDT is performed by the nursing personnel at the first visit, as part of a geriatric assessment questionnaire called SAOP-3. We conducted a retrospective analysis of those tests. Electronic medical records were reviewed for first visits from January 2012 to December 2018. Patients over 65 years were eligible. Patients with brain metastasis, dementia or mild cognitive impairment were excluded. The analyses of the CDT were done as described by Parsey and Schmitter [21] by one of the authors and a subset of CDT was rated by a second author for interrater validity, with a moderate intraclass correlation for continuous CDT score (r=0.697, CI 0.504-0.824) and a moderate agreement for normal vs abnormal CDT (k=0.469) [22]. This method of scoring gives a score from 1 to 3 to the errors made by the subject. Errors are divided in six categories: size of the clock, graphic difficulties, stimulus-bound response, conceptual deficits, spatial and/or planning deficits, and perseveration. Each category is subdivided in a particular type of error (see appendix). This method of scoring has been used widely in the literature [18,21,23-30]. The CDT is scored as 16 – number of errors. Since the evaluation at SAOP gives a pre drawn circle, we eliminated that category and used 14 – number of errors, then the scores can be classified as normal (14 or more points), mild impairment (12-13 points) and cognitive impairment (11 or less points). The electronic medical records were also reviewed to gather data about tumor characteristics, history of chemotherapy, treatment received, comorbidities, polypharmacy, alcohol and tobacco consumption, unplanned hospitalizations and demographic variables reported to be associated with cognitive impairment (marital status, education level, environmental exposure to toxics). Other data from the SAOP-3 was collected such as medications used by the patient and functionality on instrumental and basic activities of daily living.

Also, as part of an ongoing prospective practice improvement study, patients are reevaluated with a SAOP-3 screen every 3 months, which includes a CDT, so a follow up analysis of the scores was performed in a subset of 48 patients who received this 3-months assessment to get insight in the evolution of the CDT during treatment.

Correlations were tested for CDT score and comorbidities and sample characteristics; Kruskal-Wallis tests were used to compare the types of cancer and types of treatment with the CDT score. One-way chi square tests were used to determine if a type of error was statistically more frequent in each type of cancer category. Fort the follow up group, a Wilcoxon test was performed to compare the before and after treatment scores in the CDT. The protocol was approved by the Advarra Institutional Review Board.

Results

Data from 364 individuals was used for analysis. Median age was 77(70-97), 61.3% were female, mean score for CDT baseline was 12.27 (SD 1.54); 177 participants (48.6%) were completely independent in their basic activities of daily living (bathing, dressing, transferences, continence, feeding), 272 participants (74.7%) were completely independent in their instrumental activities of daily living (driving, preparing meals, shopping, managing finances, using a phone, taking medications). Types of cancer were grouped as follows: breast (n=165), gastrointestinal (GI;

n=82), head and neck (H&N; n=22), genitourinary (GU; n=69), and others (n=26). Table 1 presents the complete characteristics of the sample. No correlation was found between comorbidities (neither to individual nor to the number of comorbidities a single patient had) and the CDT score. The individual comorbidities we analyzed were depression, hypothyroidism, heart failure, chronic kidney disease, type 2 diabetes mellitus, hypertension, chronic obstructive pulmonary disease, ischemic heart disease, history of stroke or transient ischemic attack, and hypoacusis. No correlation was found between de CDT score and the number of drugs taken. A Pearson correlation was found to be statistically significant between age and the CDT score (p=<0.001). We found in the electronic health records that before CDT, 16.8% and 23.4% of the participants reported using benzodiazepines and opioids respectively, and since those drugs have been classically reported to cause cognitive alterations, Mann-Whitney U Tests were performed to compare the CDT score and the use of these drugs without statistically significant results. Table 2 has the CDT scores of the sample by type of cancer, while Table 3 has the scores of the CDT by exposure to chemotherapy and metastasis.

To compare the effect of the type of cancer on the CDT score, Kruskal-Wallis test was conducted. The result was significant [X^2 (4)=19.397, p=0.001]. Post hoc comparisons were made to find where the differences between groups were located. Statistically significantly differences were found between

Breast and GI (p=0.030, effect size 0.019); Breast and H&N (p<0.001, effect size 0.074); Breast and GU (p=0.007, effect size 0.031); GI and H&N (p=0.013, effect size 0.060); H&N and others (p=0.016, effect size 0.12).

In the group of patients that had a 3 month follow up CDT (N=48), Kruskal-Wallis was performed to see if the type of treatment received had any effect on the CDT score. No statistically significantly differences were found. No patient in the "other tumor" category had a follow-up CDT. A signed ranks Wilcoxon test was performed to compare before and after treatment scores in the CDT. No statistically significantly difference was found (Negative ranks=14, positive ranks=19, ties=15; p=0723).

One-way chi square tests were performed to determine whether a pattern exists in the type or errors the subjects made in the CDT. In the breast cancer group, errors in the conceptual deficit category (58) were statistically more frequent than the other error categories, X^2 (4, N=170) = 36.706, p=<0.001. While errors in misinterpretation of time (54) were the most frequent subtype of error. (X^2 (11, N=179) = 171.413, p=<0.001). In the GI cancer group, errors in the conceptual deficit category (48) were statistically more frequent than the other error categories, X^2 (4, N=110) = 48.273, p=<0.001. Errors in misinterpretation of time (44) were the most frequent subtype of error (X^2 (11, N=118) = 191.89, p=<0.001). In the GU cancer group, errors in the conceptual deficit category (33) were more frequent than the other error categories (X^2 (4, N=88) = 25.523, p=<0.001). Errors in misinterpretation of time (28) were the most frequent subtype of error (X^2 (11, N=113) = 63.602, p=<0.001).

In the head and neck cancer group, errors in the conceptual deficit category (13) were the most common, but not statistically significantly difference was found (X^2 (4, N=43) = 5.256, p=0.262); errors in misinterpretation of time (10) were the most frequent subtype of error (X^2 (12, N=53) = 23.283, p=0.025)

In the other cancer group (N=23), errors in the graphic difficulties category (10) were more frequent than the other error categories (X^2 (4, N=27) = 11.333, p=0.023). No subtype of error was statistically more frequent (X^2 (10, N=32) = 18, p=0.055)

The most common category of error in the CDT for breast, GI, GU and H&N was conceptual deficits. While perseveration was the most common in the "others" group. Misinterpretation of time was the subtype of error the most common in all the population.

It is interesting that 3 subjects had neglect of the left hemispace, all were female, had gastrointestinal tumors, were taking more than 4 drugs at the time of evaluation, had 12 or more years of education; two of the 3 needed reductions in the chemotherapy dosage, and all of them had impairment in at least one of the activities of daily living interrogated in the SAOP-3 questionnaire. There were no common comorbidities between these 3 participants. Also, 2 subjects had numbers written counterclockwise, but no common variables were found among them. These 2 types of error have not been described as common in non-cognitively impaired populations. Figure 1 has the subtype of errors according to cancer type.

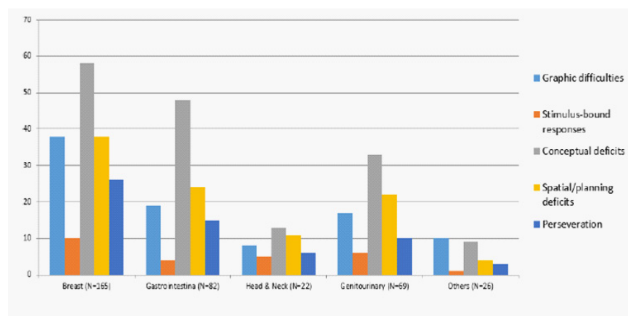

Figure 1: Subtype of errors according to cancer type.

Mann-Whitney U tests were performed to compare the baseline CDT of patients that had chemotherapy 3 years or more before baseline (n=69), patients that had chemotherapy in the 3 years before baseline (n=179), and patients that had metastatic disease at baseline (n=197), with patients that did not have any of these conditions. None of the tests were statistically significant. (p=0.751, p=0.179, p=0.417, respectively). In the three groups, conceptual deficits and misinterpretation of time were the most common errors. No correlation was found between baseline CDT score and treatment modifications or non-planned hospitalizations.

Discussion/conclusion

The aim of this study was to describe the CDT of older cancer patients both quantitatively (the total numeric score of the drawing) and qualitatively (the type of errors found in the drawing) and to identify possible associations between the score and types of errors with the type of tumor, and exposition to cancer treatment. The sample was composed of adults 65 years and older that all had a CDT as usual care in their first visit to the SAOP at Moffitt Cancer Center. The CDT was scored as described by Parsey and Schmitter [21].

Table 1: Characteristics of the sample.

N=364		Others	26(7.1)
Age in years, median (range)	77(70-97)	ECOG*, n (%)	
Female (%)	223(61.3)	0	156(42.9)
Has a partner (%)	236(64.8)	1	155(42.6)
Currently employed (%)	25(6.9)	2	45(12.4)
12 years or more of formal education (%)	285(78.3)	3	5(1.4)
Number of drugs taken, median (range)	8(0-27)	Metastasis at baseline evaluation, n (%)	197(54.1)
Subjects taking 4 or more drugs, n (%)	349(87.6)	Treatment intention, n (%)	
Independent in BADL, n (%)	177(48.6)	No treatment	21(5.8)
Dependent in one BADL, n (%)	137(37.6)	Neoadjuvant	13(3.6)
Dependent in two BADL, n (%)	43(11.8)	Adjuvant	104(28.6)
Dependent in three or more BADL, n (%)	7(1.9)	Palliative	203(55.8)
Independent in IADL, n (%)	272(74.7)	Curative	23(6.3)
Dependent in one IADL, n (%)	49(13.5)	Had previous cancer, n (%)	105(28.8)
Dependent in two IADL, n (%)	11(3)	Had chemotherapy in the 3 previous years, n (%)	179(49.2)
Dependent in three or more IADL, n (%)	32(8.8)	CDT normal (%)	126(34.6)
Type of cancer, n (%)		CDT mean score (SD)	12.59(1.46)
Breast	165(45.3)		
Gastrointestinal	82(22.5)		
Head and Neck	22(6)		
Genitourinary	69(19)		

*Information was missing for 3 subjects.
BADL: Basic activities of daily living (bathing, dressing, transferences, continence, feeding), IADL: Instrumental activities of daily living (driving, preparing meals, shopping, managing finances, using a phone, taking medications); ECOG: Eastern Cooperative Oncology Group performance status; CDT: Clock drawing test, SD: Standard deviation

Table 2: CDT scores according to type of cancer.

	Breast(n=165)	GI(n=82)	H&N(n=22)	GU(n=69)	Others(n=26)
Mean	12.88	12.52	11.5	12.26	12.65
Normal (14 points)	64(38.8%)	25(30.5%)	3(13.6%)	21(30.4%)	11(42.3%)
Mild impairment (12-13)	78(47.3%)	42(51.2%)	8(36.3%)	25(36.2%)	10(38.5%)
Cognitive impairment (≤11)	23(13.9%)	15(18.3%)	11(50%)	23(33.3%)	5(19.2%)

GI: Gastrointestinal; H&N: Head and neck; GU: Genitourinary

Table 3: Clock drawing test scores according to previous treatment and metastasis.

	Chemotherapy older than 3 years (n=69)	Chemotherapy in previous 3 years (n=179)	No history of chemo (n=197)	Metastasis at baseline (n=151)
Mean	12.58	12.73	12.54	12.42
Normal (14 points)	20(29%)	64(35.8%)	62(31.5%)	47(31.1%)
Mild impairment (12-13)	37(53.6%)	85(47.5%)	91(46.2%)	64(42.4%)
Cognitive impairment (≤11)	12(17.4%)	30(16.8%)	44(22.3%)	40(26.5%)

Across all types of cancers, the most common error was in the conceptual deficits category. This finding was also reported by Spenciere et al. [30]. That study was performed with a sample of 49 community dwelling older adults over 60 years from Brazil. Interestingly, in that healthy older population, all drawings had spatial and/or planning deficits and the mean score was 11.4 which is lower than in our sample. This can be explained by the higher education level reported for developed countries or by the fact that there was a high prevalence of depression in the Spenciere study, which in our sample was only present in 15.7% of the subjects. In this healthy older adult population, no patients had severe graphic difficulties nor neglect of the left hemispace. These errors were found in our sample, and they could signify that the subject that presents them does have cognitive impairment, whether this is caused by the cancer itself, the treatment, or other patient characteristics can´t be known with our data, a prospective study could clarify this. In total, 34 subjects of our sample had one of these types of errors (29 had numbers written outside the clock, 3 had neglect of left hemispace and 2 had the numbers written counter clockwise). The small number of patients with these errors in our sample makes it impossible to extrapolate or doing a deeper analysis but nevertheless these should be considered for further studies, especially because several patients needed a modification of treatment or had unplanned hospitalizations, and it highlights the importance of sending these patients for further cognitive examination.

Making this more interesting, a study by Teixeira et al. [31], also found that severe graphic difficulties, neglect of the left hemispace, numbers written outside of the clock face or numbers written counterclockwise were not found in healthy older patients. They found that in cognitively impaired individuals the most common error were conceptual deficits, followed by planning mistakes, size of the clock, perseveration and stimulus bound response. In this study they classified the patients by years of formal education (1-4 years, 5-8 years, and >8 years) and found that the misrepresentation of the clock and counterclockwise number display occurred only in the least educated group, mild graphic difficulties occurred in all groups, and that neglect of the left hemi-space of the clock was not observed in any level of schooling. In our study the most common conceptual deficit was the hands being the same length. In the aforementioned studies, this was found as commonly in the healthy population. Also, this error was associated with reduced cerebral blood flow in the posterior and middle temporal lobes in studies with single photon emission CT [29,32,33]. Since atrophy in these regions has been described as normal in aging, this kind of conceptual deficit could be just a marker of aging. Further research is needed to confirm this.

Another interesting finding in our study is that the mean score in the CDT was not significantly changed at baseline and follow up, even after receiving some type of cancer treatment (chemotherapy, hormonal or targeted). In a study by Hurria and colleagues, 39% of patients had a decline in cognitive function from baseline, 50% had no change, and 11% had improvement in cognitive testing [34]. They performed a complete cognitive evaluation, while we only used a screening test, which reinforces the importance of complete cognitive examination in those that have positive screening. This can be reflective of the insensitivity of the CDT to detect subtle changes over a short period of time between examinations. We must acknowledge that our follow-up sample of 48 patients has a low power of detecting subtle changes, so a prospective study should be performed.

We had a high heterogeneity of cancer subtypes and treatment regimens, and a small sample, which makes it hard to extrapolate our findings. Even while the SAOP-3 does a pretty good baseline evaluation of our patients, the retrospective nature of our study could have missed some important clinical data, as it might have been lost or unrecorded. On the other hand, we added to the evidence that some types of errors in the CDT (neglect of left hemi-space, numbers written counterclockwise) that suggest the need for a deeper cognitive evaluation even if the overall (quantitative) score classifies the patient as normal, are present among older cancer patients even before starting treatment. Adequate working memory has been associated with decision-making ability [35], which is of paramount importance when dealing with a cancer diagnosis and treatment possibilities, as well as when navigating medical services. Thus, the detection of those individuals with cognitive problems and their timely referral for a complete evaluation could be carried out with the CDT, both to find modifiable causes (polypharmacy, vitamin deficiencies, lack of control of comorbidities) and to appoint substitutes and representatives in decision-making.

This study was made with a retrospective convenience sample, and our sample size of participants with a follow up CDT provided a low power in assessing the effect of treatment. A prospective study with a higher number of subjects in each cancer group and a healthy group for comparison, could help clarify if the errors in the CDT are related to specific pathophysiological effects of the type of cancer, effects of a particular treatment, or characteristics of aging.

In this study, across different types of cancers, the most common error in the CDT was in the conceptual deficits category, with misinterpretation of time being the most frequent subtype of error. No correlation was found between comorbidities, previous exposure to chemotherapy or history of a previous cancer and the CDT score. Breast cancer patients had significantly different CDT scores compared to the other groups. At 3 months follow up, there were no associations between the type of treatment received and the CDT score.

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