Original Article

Cognitive Impairment in Caregivers of Cancer Patients:
A Cross-Sectional Study

Kanser Hastalarının Bakım Verenlerinde Bilişsel Bozukluk:
Kesitsel Bir Çalışma

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ABSTRACT

Introduction: The role of cancer caregivers (CCG) is crucial in well-being of cancer patients. They are responsible for making cognitively demanding decisions affecting the welfare of patients. In this study, we aimed to evaluate the cognitive impairment of CCG and compare with non-cancer caregivers (non-CCG).

Materials and Methods: This cross-sectional study targeted CCG and non-CCG in a university hospital. Caregiver reported outcomes were measured by mini-mental state examination (MMSE).

Results: 217 caregivers were included. 122 (56.3%) were in the CCG, and 95 (43.7%) were in the non-CCG group. The median age of the caregivers was 46.6 (20-76) years and 56.6% of them were female. The education level was significantly higher among CCG (64.7 vs 29.5%, p <0.001). Mean MMSE scores were 27.9 and 24.2 for the non-CCG and CCG, respectively corresponding to 0 and 40.1% of caregivers in non-CCG and CCG group with cognitive impairment. The mean difference in MMSE scores was statistically significant in all areas of cognitive function (p<0.001). In the CCG group with cognitive impairment, 15 patients had mild and 40 had moderate cognitive impairment. Cognitive impairment of CCG on MMSE was significantly associated with old age (p=0.006) and lower education level (p=0.001).

Conclusion: Our study revealed that cognitive impairment in CCGs is not an uncommon finding. Since the caregivers are the decision-makers during most of the disease process of cancer patients, any deterioration in their cognitive reserve should be checked to maintain optimal care for patients.

Keywords: Caregiver, cancer, cognitive impairment, mini-mental state examination

ÖZET

Amaç: Kanser hastalarının iyilik halinde kanser bakım verenlerinin (CCG) rolü çok önemlidir. Hastaların refahını etkileyen bilişsel açıdan zorlu kararlar vermekten sorumludurlar. Bu çalışmada CCG'nin bilişsel bozulmasını değerlendirmeyi ve kanser olmayan bakım verenlerle (CCG olmayan) karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Bu kesitsel çalışmaya bir üniversite hastanesinde CCG ve CCG olmayanlar dahil edildi. Bakım verenin durumu mini zihinsel durum muayenesi (MMSE) ile ölçüldü.

Bulgular: 217 bakım veren dahil edildi. 122'si (%56,3) CCG'de, 95'i (%43,7) CCG olmayan gruptaydı. Bakım verenlerin ortanca yaşı 46,6 (20-76) yıl olup %56,6'sı kadındı. Eğitim düzeyi CCG'de anlamlı derecede yüksekti (%64,7'ye karşı %29,5, p <0,001). Ortalama MMSE puanları, CCG olmayan ve CCG için 27,9 ve 24,2 idi; bu, bilişsel bozukluğu olan CCG olmayan ve CCG grubundaki bakım verenlerin sırasıyla %0 ve %40,1'ine karşılık geliyordu. MMSE puanlarındaki ortalama fark bilişsel işlevin tüm

alanlarında istatistiksel olarak anlamlıydı (p<0,001). Bilişsel bozukluğu olan CCG grubunda 15 hastada hafif, 40 hastada ise orta derecede bilişsel bozukluk mevcuttu. MMSE'de CCG'nin bilişsel bozulması ileri yaş (p=0,006) ve düşük eğitim düzeyi (p=0,001) ile anlamlı düzeyde ilişkiliydi.
Sonuç: Çalışmamız CCG'lerde bilişsel bozulmanın nadir bir bulgu olmadığını ortaya koydu. Kanser hastalarının çoğu hastalık sürecinde karar vericileri bakım verenleri olduğundan, hastaların optimal bakımının sürdürülebilmesi için bilişsel rezervlerindeki herhangi bir bozulmanın kontrol edilmesi gerekir.

Anahtar Kelimeler: Bakım veren, kanser, bilişsel bozukluk, mini-mental durum muayenesi

Introduction

The survival rates of cancer are increasing every day with new treatment modalities. Patients live longer with the psychological, social, and physical burden of the disease and treatment. Informal caregivers are non-professional, unpaid caregivers of patients who share this burden and more. They are usually a person from the family setting or a friend, who take on different roles secondary to physical or cognitive impairment of the patient [1]. According to a caregiving report in United States published in May 2020, cancer is the 2nd common illness for which a caregiver is needed [2].

Informal caregivers of patients with chronic diseases take on many responsibilities such as cooking, traveling, scheduling, hospital policies, economic difficulties, and most importantly deciding between treatment options. It has been found that cancer caregivers (CCG) are more likely to co-reside with the patient and provide care for approximately 33 hours weekly, help in different types of activities in daily living (getting in and out of a bed, chair, or toilet and feeding) [3,4]. Thus, it is important to evaluate informal caregivers' cognitive abilities to understand if they are capable enough to decide on behalf of the cancer patient [5]. Their health can be affected in longer run due to increasing stress causing changes in neurohormonal and inflammatory processes [6]. When the caregivers' quality of life deteriorates, especially their mental health, optimal support and long-term care for patients' may be compromised. This may even impact the patients' treatment. Since the course of the disease in cancer patients is different and clinical deterioration can progress more rapidly, caregiving may host some differences from other chronic diseases [7].

Mini-Mental State Examination (MMSE) is one of the most widely used screening tests to identify cognitive impairment. It was first developed by Folstein et al. [8] in 1975 and has been broadly used in research and clinical setting since then. Although it was designed for identifying cognitive impairment, in clinical practice, it is mostly used to identify dementia and Alzheimer's disease. To our knowledge, there are no studies evaluating cognitive status of caregivers using MMSE.

Herein, we aimed to evaluate the cognitive impairment of cancer caregivers and compare it with caregivers of patients with a chronic disease other than cancer (non-CCG) using MMSE.

Materials and Methods

Study design

This prospective cross-sectional study took place in a university hospital. The local ethics committee approved the study protocol on 17.09.2020 (approval number: 2020-20/5). The caregivers and patients were informed about the study. After receiving informed consent from the volunteering caregivers, questionnaires were conducted face-to-face by clinical nurses under supervision of a

doctor in the hospital's daily chemotherapy and endocrinology clinic.

Participants

The eligibility criteria for cancer caregivers were as follows; aged <18 years; caring for a cancer patient under treatment; not having any hearing abnormalities, any known psychological or central nervous system disorder, or any history of cancer; not undergoing active treatment that could influence cognitive abilities. For the control group, caregivers of patients receiving treatment for a chronic endocrinological disorder were included. Information about the caregivers was obtained from the caregivers themselves. The demographic and clinical characteristics of the patients and their treatment schedules were obtained from medical records.

In the cancer group, targeted treatments received by patients were defined as anti-vascular endothelial growth factor therapy, anti-endothelial growth factor therapy, anti-HER2 therapy. Hormone treatment was defined as anti-androgen and anti-estrogen treatment. The endocrinological group was composed of patients with hypothyroidism, diabetes mellitus, adrenal insufficiency, and Cushing's syndrome.

Assessments and Tools

Cognitive performance was assessed with Mini-Mental State Examination (MMSE). Validated Turkish version of MMSE was utilized [9]. MMSE is composed of 11 questions. It measures functions as registration, attention and calculation, recall, language and orientation. Administration of the test takes 5-10 minutes. Cognitive impairment was defined as a MMSE score below 24. Severe, moderate and mild cognitive impairment were defined as MSSE score under 9, 10-18 and 19-23, respectively.

Statistical analyses

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 25.0 (IBM, Armonk, New York, USA). Continuous variables were compared using independent samples t-test and Mann-Whitney U test. Binary logistic regression analysis was made to determine the odds ratio for predictive factors. Pearson's correlation test was used for the evaluation of correlations between continuous variables. p value of <0.05 was accepted as statistically significant.

Results

A total of 217 caregivers were included in the study. Of these, 122 (56.3%) were in the CCG, and 95 (43.7%) were in the non-CCG group. The median age of the caregivers was 46.6 (20-76) years and 56.6% of them were female. The detailed demographic and clinical characteristics of the caregivers are shown in Table 1. The education level was significantly higher among CCG (64.7 vs 29.5%, p <0.001). 64.7% of patients in the CCG and 29.5% of patients in the non-CCG group had a university degree or higher. Most of the relatives of cancer patients were spouses (35.2%) or children (29.5%) whereas for non-CCG group, the majority were spouses (45.3%) and parents (24.2%) (p <0.001). Patients were mainly diagnosed with breast cancer (n=39, 31.9%), gastrointestinal cancer (n=28, 22.9%) and lung cancer (n=23, 18.8%). The time since diagnosis was less than a year for most of the patients (n=59, 48.3%) and most of the patients had stage IV disease (n=78, 63.9%). The Eastern Cooperative Oncology Performance Status of patients were 0-1 for 76% of the patients. The demographic and clinical characteristics of cancer patients are shown in Table 2.

Mean MMSE scores were 27.9 and 24.2 for the non-CCG and CCG groups, respectively. Cognitive impairment was not seen in the non-CCG group, while 40% of the CCG group exhibited cognitive impairment. The mean difference in MMSE scores was statistically

Table 1. Demographic and clinical characteristics of caregivers

	Non-CCG (n = 95)	CCG (n = 122)	p
Age (min-max)	47.2 (20-76)	46.2 (20-72)	0.724
Sex			
Female	48 (50.5%)	75 (61.5%)	0.106
Male	47 (49.5%)	47 (38.5%)	
Social status			
Single/Divorced	18 (19%)	32 (26.2%)	0.448
Married	77 (81.1%)	90 (73.8%)	
Level of education			
Uneducated	1(1.1%)	3 (2.5%)	
Primary School	29 (30.5%)	7 (5.7%)	
Secondary School	8 (8.4%)	9 (7.4%)	*<0.001**
High School	29 (30.5%)	24 (19.7%).	
University	25 (26.3%)	63 (51.6%)	
Postgraduate	3 (3.2%)	16 (13.1%)	
Occupation			
Employed/Student	36 (37.9%)	50 (41%)	0.644
Unemployed/Retired	59 (62.1%)	72 (59%)	
Chronic Disease			
Present	26(27.4%)	22 (18%)	0.100
Absent	64 (72.6%)	100 (82%)	
Relationship with the patient			
Parents	23 (24.2%)	7 (5.7%)	
Siblings	5 (5.3%)	14 (11.5%)	
Children	14 (14.7%)	36 (29.5%)	*<0.001**
Partners	43 (45.3%)	43 (35.2%)	
Others	10 (10.5%)	22 (18.0%)	

* = p-value < 0.05

Table 2. Demographic and clinical characteristics of cancer patients

		n (%)
Age (years)	(min-max)	56 (28-80)
Sex	Female	75 (61.4)
	Male	47 (38.5)
Time since diagnosis	≤12 months	59 (48.3)
	12-24 months	21 (17.2)
	≥24 months	42 (34.4)
ECOG	0	46 (37.7)
	1	46 (37.7)
	2	27 (22.1)
	3	3 (2.4)
Stage	I	14 (11.4)
	II	16 (13.1)
	III	14 (11.4)
	IV	78 (63.9)
Treatment Type	Chemotherapy	72 (59)
	Chemotherapy+Targeted therapy	18 (14.7)
	Immunotherapy	6 (4.9)
	Hormone treatment	13 (10.6)
	Targeted Therapy	13 (10.6)

ECOG: Eastern Cooperative Oncology Group

Table 3 MMSE scores of caregivers

	Non-CCG (n = 95)	CCG (n = 122)	*p*
Orientation	9.99 ± 0.103	9.24 ± 1.068	<0.001*
Registration	3.04 ± 0.459	2.67 ± 0.787	<0.001*
Attention & Calculation	4.68 ± 0.593	3.20 ± 1.872	<0.001*
Recall	2.83 ± 0.519	2.22 ± 0.838	<0.001*
Language	8.96 ± 0.202	6.84 ± 1.410	<0.001*
Total	29.40 ± 1.086	24.17 ± 4.111	<0.001*
CI (total score < 24)	0 (0%)	49 (40.1%)	< 0.001*

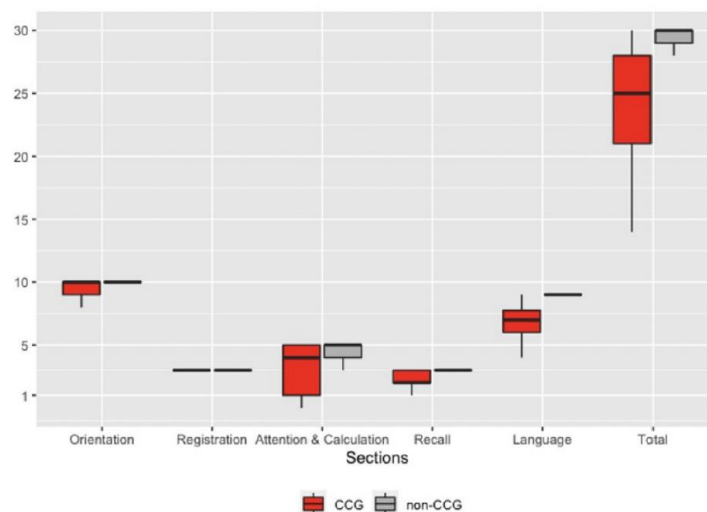CI; cognitive impairment, * = p-value < 0.05

Figure 1 Boxplots of MMSE scores for CCG and non-CCG groups

Table 4 Predictive factors of cognitive impairment in CCG group

	Score ≤24 (n=55)	Score >24 (n=67)	p
Age (Years)**	49.7±11.5	43.4±12.8	*0.006*
Sex (Male) **	18 (32.7%)	29 (43.3%)	0.233
Marital Status**	43 (78.2%)	47 (70.1%)	0.136
Education level of university**	27 (49.1%)	52 (77.6%)	*0.001*
Comorbidities **	14 (25.5%)	8 (11.9%)	0.053
Relatedness (First Degree) **	13 (23.6%)	30 (44.8%)	*0.015*
Sex (Male)***	21 (38.2%)	25 (37.3%)	0.922
Age (Years) ***	54 (23%)	57 (21%)	0.265
Stage 4 disease***	35 (66.1%)	43 (64.2%)	0.832
ECOG 0***	22 (40%)	24 (35%)	0.459
Mean Time After Diagnosis*** (Month)	14 (29%)	12 (34%)	0.451
Polypharmacy***	6 (10.9%)	14 (20.9%)	0.138

*p < 0.05. ECOG: Eastern Cooperative Oncology Group** Characteristics of the caregivers *** Characteristics of the patients

significant in all areas of cognitive function (p<0.001, Table 3). Figure 1 shows boxplots of the scores according to components of MMSE. Language subscale scores were significantly different between the two groups.

Regarding the CCG group with cognitive impairment, 40 patients had mild impairment (MCI) while 15 had moderate cognitive impairment. According to univariate analysis, cognitive impairment of CCG on MMSE was statistically associated with old age (p=0.006) and lower education level (p=0.001, Table 4). Multivariate analysis was performed to assess the independent predictors of cognitive impairment. Education level (p=0.009) was found to be the only predictor of cognitive impairment.

The variables were further analyzed with binomial logistic regression models to understand their predictive values for MCI in cancer caregivers. Patient relatives with a university degree or higher education were 59% less likely to have cognitive impairment. Caregivers who were children of the patient were 92% less likely to suffer from cognitive impairment. Treatment with chemotherapy was associated with a 71% decreased risk of MCI among different treatment modalities.

Discussion

In this study, we aimed to assess the cognitive impairment of cancer caregivers. The MMSE was used to evaluate the cognitive impairment, which, to our knowledge is the first study to use mini-mental test as a screening tool among caregivers. The MMSE scores of cancer caregivers were lower than those of non-cancer caregivers in all aspects, indicating higher cognitive impairment among CCGs. The majority of the CCG group suffered from mild cognitive impairment with a score between 19-24. Language was the mostly impaired area in the MMSE scores of CCGs. Education and age were found to be

predictors of cognitive impairment.

The MMSE is a commonly preferred test to screen cognitive mental status in the elderly population with an estimated sensitivity and specificity of 85% to 92% and 85% to 93%, respectively [10]. Though it cannot be used for making formal diagnoses, it is used as the first step in detecting cognitive impairment [11]. Cognitive impairment is described as having trouble concentrating, learning new things, and making everyday life decisions. While impairment has been proven in caregivers of patients with dementia or stroke, cognitive dysfunction in CCGs is a less frequently examined field [12,13]. In our study, MCI seen in 40% of CCGs is noteworthy. The statistically significant difference in MMSE scores between the two caregiver groups also proved the high disease burden on CCGs. Unlike non-CCGs, CCGs spend about 35 hours a week on the patient's daily activities [14]. This may cause them to withdraw from social life, have a negative impact on relationships, experience loss of communication and thus, weaken their cognitive functions. Therefore, the mild and moderate cognitive impairment seen among cancer caregivers may be the result of caregiver burden, leading to a decreased quality of life and interfering with the capacity of caregivers to provide optimal care [15]. High cortisol levels and stress, which are used to explain the cognitive dysfunction in patients with dementia, may also affect CCGs [16].

The effect of MMSE scoring on predicting dementia is well-known. However, cognitive dysfunction, apart from dementia, may be a primary indicator of functional impairment in major depressive disorder [17]. The global prevalence of depression among CCGs across studies was 42.08% and a subgroup analysis showed that the pooled prevalence of depression in the studies that used a cross-sectional study design (42%), like our study, was higher than those with a longitudinal

study design (34%) [18]. Sleep disturbances and fatigue may also affect cognitive impairment which may be seen in CCGs. However, when these secondary causes of cognitive dysfunction are excluded, cognitive dysfunction is a core component of depressive disorder. Thus, learning and memory, executive functioning, processing and attention/concentration may be significantly impaired [19]. Antidepressants and/or pharmacotherapy are found to improve the residual cognitive function [20]. Thus, the caregivers diagnosed with cognitive impairment may be referred for treatment.

Education level and age were found to be the predictors of cognitive impairment in our study. There are studies showing that mild cognitive impairment affects the quality of life [21]. In a study done by Decadt et al. [22], caregivers' age and education level were not associated with decreased quality of life or increased stress. However, the relationship to the patient and patient's diagnosis were significantly related to distress levels. In contrast, Kilic et al. [23] found gender, education level and relationship to the patient all significantly associated with quality of life. Education level, as well as employment status, is closely related to person's ability to communicate and cope with stress. Unemployed caregivers spend more time with the patient affecting their cognitive status and mood, increasing susceptibility to depression. Finding age as a predictor of cognitive impairment was an expected result since cognitive changes occur even with normal aging. This also explains the decreased risk of impairment seen if the caregiver is the child of the patient.

The study has several limitations. The MMSE scores were not interpreted taking into

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consideration age and education norms. The MMSE also has disadvantages, such as a lack of exploration of all cognitive domains. The possible reasons for low MMSE scores in the CCG group, such as depression, sleep problems, and dementia, were not examined. Owing to the cross-sectional design of our study, potential changes over time may be confounding factors of lower MMSE scores among CCGs. Longitudinal studies are needed to learn how caregiver outcomes evolve. Thirdly, the disease burden of control group may be too low compared to cancer patients, which may interfere with the reliability of the comparison. Lastly, the sample size is small, which may be the reason for the lack of influence of patient factors on cognitive impairment of caregivers.

Our results are worth attention by healthcare professionals to better address cancer caregivers who are in need of support during patient's active treatment. The MMSE, an easily applicable test, can be incorporated into screening methods of caregiver distress since cognitive impairment may be a sign of depression.

Conclusion

Most cancer patients seek physical or psychological support, generally provided by their informal caregivers. Thus, the cognitive functioning of CCGs is significant since they make many decisions on behalf of the patient. Our study, the first to use MMSE in caregivers, emphasized that cognitive assessment of caregivers is worth noting since cognitive impairment in CCGs is not an uncommon symptom and may interfere with the well-being of the patients. Interventions should develop to reduce the psychosocial and psychological burden of caregiving causing cognitive decline in the CCG group.

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