



CO-RELATION BETWEEN COGNITIVE IMPAIRMENT, FUNCTIONAL CAPACITY AND QUALITY OF LIFE IN PATIENTS UNDERGOING CHEMOTHERAPY

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ABSTRACT

Background and Objectives: Multiple impairments, participation restrictions, activity limitations are caused due to cancer and its treatment. Cognitive dysfunction is one of the commonest impairments reported in people with cancer. Due to cytostatics that are often accompanied by side-effects having major impact on the quality of life (QoL) of patients, the 6-minute walk distance (6MWD) is one of the most commonly used measure to find functional capacity of an individual. However, there is paucity in literature to show correlation between cognitive impairment, functional capacity and QoL in cancer patients undergoing chemotherapy. Hence, the present study was taken up to study the same. **Methods:** Sixty (60) patients undergoing chemotherapy, were assessed for cognitive impairment, functional capacity and quality of life using outcome measures like MMSE scale, 6 MWT and FACT-G scale. **Results:** Correlation between 6-MWD and chemotherapy cycles, 6-MWD in meters and MMSE, 6-MWD and Fact-G was done using Spearman's rank which showed a positive correlation between 6-MWD and MMSE with $r=0.2584$. **Conclusion:** The present study showed that the patients were cognitively fit and had better quality of life even though there is negligible correlation between 6-MWD and chemotherapy cycles thus stating that the functional capacity is not affected in patients undergoing chemotherapy.

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INTRODUCTION

Cancer starts when cells grow out of control and gathers out normal cells. Since cancer can start at any place in the body, it makes it hard for the body to work the way it should.¹ According to GLOBOCAN, about 14 million new cancer cases were diagnosed all over the world in 2012 and more than 8 million cancer deaths occurred. In India, this is home to about 17% of the global population discovered 1 million of these new cases and nearly 700000 of the deaths occurred.² Surgery, chemotherapy and radiation have been the most common treatment option for cancer. Alone or in combination with other drugs or treatments, more than 100 chemotherapy or chemo drugs are used to treat cancer which differ in their chemical composition, administration, uses and their side effects.⁴ Side-effects of chemotherapy includes nausea, vomiting, anorexia, malabsorption, weight loss, anemia, fatigue, increased risk of sepsis, constipation, diarrhea, etc. A review of clinical studies on biological markers associated with cognitive impairments in cancer patients during and after chemotherapy have shown that there are a number of circulating factors and cerebrospinal fluid constituents which

were associated with chemotherapy induced persistent cognitive dysfunctions. These factors along with genetic polymorphisms might be used as predictive markers to identify patients predisposed to cognitive deficits caused by chemotherapy.⁵

In patients with cancer, neurocognitive and neuropsychiatric symptoms are highly prevalent and cause significant impairments in their ability to function and to tolerate their treatment.⁶ Cognitive problems are commonly received as a probable effect of brain irradiation or of intrathecal or intraventricular chemotherapy for CNS disease.⁷ A significant percentage of patients with various types of cancer had multiple symptoms, including impairments of memory, significant fatigue, and depression, before treatment is initiated was found in previous studies. Aggressive treatment for cancer not only worsens these distressing symptoms but also causes development of additional symptoms.⁶ Cytotoxic drugs given systemically for non-CNS tumours might also have cognitive side-effects has been shown in neuropsychological studies.⁷ The ability to perform activities of daily living is reflected by the assessment of functional capacity which require sustained aerobic metabolism. In a wide variety of clinical and research settings, the assessment of functional capacity provides important diagnostic and prognostic information according to various investigations.⁸

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Quality of life(QOL) is multifaceted concept encompassing the cognitive, physical, and spiritual domains of an individual's life along with emotional and social domains.⁹ There is reduction in QOL during and after cancer treatment especially during the intense period of cancer treatment. Patients may experience pain, sleep disturbance, fatigue, nausea, distress, mood disturbance, spiritual uncertainty, mental status difficulties, or relationship challenges.¹⁰ In cancer patients functional impairment is a significant contributor in physical fitness leading to decreased quality of life.¹¹

The aim of the present study was to find the co-relation between cognitive impairment, functional capacity and quality of life in patients undergoing chemotherapy using the mini mental state examination scale (MMSE), 6 minute walk test (6MWT) and the functional assessment in cancer therapy-general (FACT-G) scale.

MATERIALS AND METHODS

Study Design and Setting

This observational study was conducted in a tertiary care hospital in North Karnataka, India in patients undergoing chemotherapy. Ethical clearance for the study was obtained by the Institutional Ethical Review Committee prior to commencement of the study. A written informed consent was obtained from the patients willing to participate. Both males and females undergoing chemotherapy above eighteen(18) years and able to ambulate independently were included in the study. Patients who were bed ridden, lower limb trauma and not willing to participate were excluded from the study. A total of sixty(60) cancer patients undergoing chemotherapy were included in this study to find the correlation between cognitive impairment, functional capacity and quality of life. All patients were evaluated for cognitive impairment using Mini Mental State Examination Scale (MMSE) and quality of life was evaluated using Functional Assessment Of Cancer Therapy-General (Fact-G) Scale. The collected data was then given for data analysis.

Outcome Measures

Mini Mental State Examination Scale

Mini Mental state examination was assessed using MINI Mental State Examination scale which is divided into two parts, the first of which requires vocal responses only and covers orientation, memory, and attention; the maximum score is 21 while the second part tests ability to name, follow verbal and written commands, write a sentence spontaneously, and copy a complex polygon similar to a Bender-Gestalt Figure; the minimum score is 9. Maximum total score is 30. The test is not timed. The Mini-Mental Status is found to be a valid and reliable scale with reliability 0.887.¹²

Functional Assessment of Cancer Therapy-General (FACT-G) Scale: The Functional Assessment of Cancer Therapy- (FACT-G) scale consists of a questionnaire which comprises of 4 subscales that include physical well-being, social/family well-being, emotional wellbeing, functional well-being. Lower scores on the FACT-H&N are reflective of poorer quality of life outcomes. The FACT-G questionnaire used has been found to be the most common, valid, and reliable tool to assess QOL in cancer survivors in clinical research.¹³

6 Minute Walk Distance (in meters): It is a simple, safe, and inexpensive measure of functional status. To assess the functional capacity of the patient 6minute walk distance test is reliable tool with intraclass correlation coefficients = 0.917.¹⁴ **PROCEDURE:** Functional capacity was assessed using 6 min walk test. The distance of 30m is marked and the patient is asked to walk for 6 minutes over the marked distance. Before and after vitals (ie. PR,RR and BP) were measured. Time was measured using a stop watch. In between patients were allowed to rest if they felt tired but the time was not stopped. At the end of the 6 minutes the distance covered in 6 minutes was measured.

Statistical Analysis

Data was analyzed using SPSS software version 21.0. Various statistical measures such as mean, standard deviation and test of significance were used. Test for normality of variables like Chemotherapy cycles, MMSE, FACT-G AND 6-MWD were done using Kolmogorov Smirnov test scores since they did not follow a normal distribution. The non-parametric Spearman's rank correlation method was used. Correlation between 6-MWD with Chemotherapy cycles, 6-MWD with MMSE, 6-MWD with Fact-G and its components scores of all the patients in the study was done using Spearman rank test.

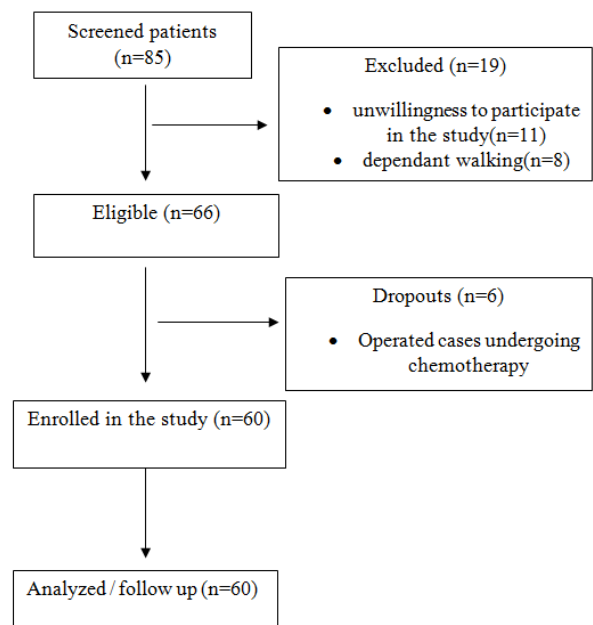


Figure 1 Flow Chart

Table 1 Distribution of gender with mean age and BMI of all patients in the study

Variables	Summary	Male	Female	Total
	N	21	39	60
Age	Mean±SD	51.81±12.56	49.77±9.05	50.48±10.35
BMI	Mean ±SD	22.75±3.46	22.78±3.77	22.77±3.63

RESULTS

Correlation between chemotherapy cycles and MMSE showed statistical significance with p=0.140 and p=0.0020 respectively. Among the domains of FACT-G emotional component p=0.0001, social/family component p=0.0001 and functional component p=0.0001 demonstrated significant correlation.[Refer table 2]

Table 2 Normality of outcome measures in the study

Outcome Measures	Z-value	p-value
Chemotherapy cycles	1.5710	0.0140*
- MMSE	1.8460	0.0020*
+ Fact –G	1.2150	0.1050
Physical	1.2560	0.0850
Social	2.1010	0.0001*
Emotional	2.9980	0.0001*
Functional	2.8110	0.0001*
^ 6-MWD in meters	0.6470	0.7970

*p<0.05, level of significance
 - MMSE: Mini Mental State Examination
 +Fact-G: Functional Assessment Of Cancer Therapy-General
 ^ 6-MWD: 6 Minute Walk Distance

Correlation between 6-MWD with MMSE demonstrated statistical significance with p=0.0500. [Refer table 3] Correlation between 6-MWD with chemotherapy cycles showed no statistical significance. [Refer figure 2]

Table 3 Correlation between 6-MWD with MMSE of all patients in the study

Outcome Measure	Correlation between 6-MWD in meters			
	N	Spearman R	t-value	p-level
MMSE	60	0.2584	1.9633	0.0500*

*p<0.05, level of significance

Table 4 Correlation between 6-MWD with FACT-G and its components scores of all patients in the study

Outcome Measure	Correlation between 6-MWD in meters			
	N	Spearman R	t-value	p-level
Fact –G	60	-0.3129	-2.5092	0.0149*
Physical	60	-0.3837	-3.1647	0.0025*
Social	60	0.0136	0.1039	0.9176
Emotional	60	0.1508	1.1620	0.2500
Functional	60	-0.0019	-0.0142	0.9888

*p<0.05, level of significance

Table 5 Correlation between Chemotherapy cycles with other outcome measures of all subjects in the study

Outcome measures	Correlation between Chemotherapy cycles with			
	N	Spearman R	t-value	p-level
-MMSE	60	-0.0441	-0.3359	0.7382
+ Fact –G	60	0.2805	2.2253	0.0300*
Physical	60	0.1091	0.8357	0.4068
Social	60	0.1591	1.2273	0.2247
Emotional	60	-0.0361	-0.2750	0.7843
Functional	60	0.2990	2.3859	0.0203*
^ 6-MWD in meters	60	0.0960	0.7343	0.4657

*p<0.05
 - MMSE: Mini Mental State Examination
 +Fact-G: Functional Assessment Of Cancer Therapy-General
 ^ 6-MWD: 6 Minute Walk Distance

Table 6 Correlation between MMSE with all components of FACT-G of all patients in the study

Outcome Measure	Correlation between MMSE			
	N	Spearman R	t-value	p-level
Fact –G	60	-0.1653	-1.2768	0.2068
Physical	60	-0.2699	-2.1343	0.0371*
Social	60	-0.1400	-1.0766	0.2861
Emotional	60	0.2864	2.2769	0.0265*
Functional	60	-0.0330	-0.2515	0.8023

*p<0.05, level of significance

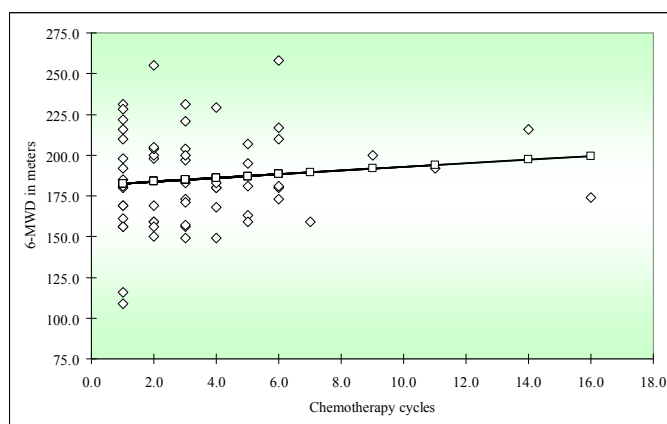


Figure 2 Correlation between 6-MWD with chemotherapy cycles in all patients in the study

DISCUSSION

The present study was done to find the correlation between cognitive impairment, functional capacity and quality of life in patients undergoing chemotherapy. The findings of the present study stated that there was statistically significant positive correlation found between functional capacity and cognition in all patients.

The longitudinal effects of cognitive impairment on quality of life in a large group of patients with newly diagnosed Parkinson disease. They have demonstrated that cognitive impairment contributes to longitudinal quality of life change in people with Parkinson Disease due to decline in attention in the subjects.¹⁵ A systemic review suggests that in patients with solid tumours, where there is a relationship between chemotherapy treatment and cognitive impairment, the type and level of cognitive decline does not consistently appear to have an impact on patients health related quality of life.¹⁶ Statistically significant correlation between the 6-MWD with MMSE scores was noted in the present study. It can be possible due to lack of cognition impairment in the patients undergoing chemotherapy which assisted the patients to follow the commands given to them by the therapist by being attentive along with normal functional capacity and good quality of life. Also, the present study did not include patients who had CNS tumors. This may be one of the reasons for patients to have good cognition level which helped them to undergo the 6 minute walk test efficiently.

Quality of life(QOL) as influenced by the treatment of cancer is an important factor in cancer survivorship. The quality of life in women recently diagnosed with breast cancer suggested that the younger women with breast cancer have lower QOL than older women with breast cancer.¹⁷ A longitudinal cohort study of patients with end-stage cancer suggested QOL in the last week of life was significantly and meaningfully lower than in those not receiving chemotherapy.¹⁸ It was observed that the diagnosis of lung cancer in the advanced stage of illness and with the poor prognosis associated with the disease and the side effects of chemotherapy all have an impact on various domains of quality of life along with a greater decline in physical functioning and increased mortality.¹⁹ The quality of life (QOL) and symptom burden among breast cancer patients have demonstrated that patients ≤50 years old, 2–10 years post-treatment, treated with chemotherapy have increased symptom burden and decreased QOL. Younger patients may have more exposure to the emotional burden and psychological

impact of breast cancer. In contrast, the authors suggested that older patients may be more vulnerable to a reduced quality of life which is partially due to their reduced physical functioning after surgery and adjuvant therapy, leading loss of independence. The impact of aging may influence symptom burden and also decrease physical functioning.²⁰ Statistically significant correlation was observed between 6-MWD (in meters) and Fact -G in the present study. In both males and females, it could have been due to their physical ability to perform the 6MWD at their own pace and functionally independent, thereby there was no functional limitations for mobility in them. The QOL domains in the present study were not influenced by the chemotherapy treatment and the patients were able to do their daily activities of living on their own and not depending on family member for help.

Physical activity was observed to decrease at six(06) months after treatment in patients with colorectal cancer receiving chemotherapy or radiotherapy after surgery due to longer stay in hospital leading to muscular deconditioning and decreased pulmonary capacity and functional capacity. Pain is an important reason for the decrease seen in functional status of these patients particularly in the elderly. As for QoL, only the physical and functional aspects were seen to decline up to six months of the treatment.²¹ Previous study has shown that there was statistically significant decline in 6minute walk test after two cycles of chemotherapy. The authors suggested that the deterioration of patient's functional status was due to decreased BMI along with the decline in 6 MWD which may have been due to more advanced stage of cancer.²² 6MWT distance and fatigue have shown to play a vital role in predicting health related quality of life which changes with chemotherapy treatment as well physical performance.²³ In the present study, statistically there was negligible correlation seen between 6MWD and chemotherapy cycles which may be because both are independent variables and does not depend on each other. The patients included in the present study, had undergone more than 2 chemotherapy cycles and still it showed no decline in their functional capacity and were able to walk for 6 minutes without any complaints contraindicating the previous studies done. It can be also possible due to good functional capacity and less of fatigue which helped them to walk without complaining. This can also be explained by the fact that different types of cancer populations with different stages react differently to the chemotherapy treatment.

The study would have given better results if it was carried out in a larger number of patients. However, the present study helped to find the correlation between the cognition, functional capacity and quality of life. Assessment of functional capacity in patients undergoing chemotherapy should be given importance, so as to maintain their quality of life. Functional capacity can be maintained or increased by indulging patients into early physical therapy training programs and interventions which may prevent them from restraining themselves from physical activity, aiding in faster recovery and improved quality of life.

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