

THE ACUTE IMPACT OF CHEMOTHERAPY ON THE COGNITIVE AND EMOTIONAL DOMAINS AND ON QUALITY OF LIFE OF OLDER CANCER PATIENTS

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There are data suggesting that chemotherapy may have a negative impact on cognitive function; on the other hand, aging itself causes changes in the cognitive domain. This area is commonly evaluated in the context of a comprehensive geriatric assessment (GCA) by the Mini-mental state examination (MMSe). (Chen H. et al., 2002)

Aim of the study:

The first aim of the observational study "ONCOGER" would be to evaluate elderly patients receiving chemotherapy

- 1.the acute impact (maximum of 30 days after the end of the first cycle of therapy) of the treatment on the cognitive functions and on the quality of life
2. the possible correlation between emotional status and change on the cognitive functions after treatment

By documenting the changes in these aspects, we would be better able to understand how chemotherapy may affect life and tolerance level of older patients, who are sometimes under-treated.

This information can help us to provide optimal cancer therapy and adequate supportive care to older people who undergo chemotherapy.

Study Design:

This is an observational study.

Patients aged 70 years or older with solid tumor who are candidates to chemotherapy will be proposed to enter in the study, that is based on the collaboration of geriatricians and medical oncologists, in order to have a comprehensive approach to the treatment of the tumor and of the older patients. Before and after 12 weeks of treatment the patients will be followed in order to perform geriatric assessments which will allow to better define the cognitive functions of the patient and to detect the acute effect of chemotherapy on this domain.

Measurements:

Physical function was measured by the Eastern Cooperative Oncology Group performance status (ECOG PS). Scores on the ECOG PS range from 0 (fully independent) to 4 (totally bedridden).

The cognitive functions will be investigated by the Mini-Mental State Examination (MMSE) and the Clock Test. The first investigates the mental health using a 30 items questionnaire that evaluates some specific areas of the cognitive domain. In particular it detects space-temporal orientation, short time memory, attention, apraxia, comprehension and verbal fluidity.

The MMSE score ranges from 0 to 30, the higher the score on the MMSE is, the better is the cognition, scores >24 are considered abnormal.

The only analysis of the Mini-Mental total score does not allow to detect if there are specific sub-areas of the cognitive domain particularly affected by the treatment. For this reason, it was performed a comprehensive evaluation of the cognitive domain through specific tests.

The sub-area test, with threshold of normality are reported in the table below

SUB-AREA OF COGNITIVE DOMAIN	NAME OF TEST	THRESHOLD*
Short-time memory	Babcock	>4.75
	15 word of Ray – immediate	>25.3
	15 word of Ray - delay	>4.69
Attention	Matrix care	>31
Apraxia	Copy design	>8
Comprehension	Token Test	>26.5
	Category verbal fluency	>7.25
Verbal fluidity	Letter verbal fluency	>17.35

* Value of test under the threshold indicate a loss in the specific cognitive area

The Clock test values the space-visual ability and the problem-solving capability. The score ranges from 0 to 9 and score >6 are considered abnormal. Patient's **Quality of life (QOL)** was measured with 27-items questionnaire (FACT-G) divided in 4 subscales: physical well-being, social family well-being, emotional well-being and functional well-being. The sum of subscale score gives the total score of the test (range 0-108), the higher the score is, the better is the QOL. **The Geriatric Depression Scale (GDS)** questionnaire was performed to measure the emotional domain. The score ranging from 0 to 15 and values between 6 and 10 indicate presence of a light depression, score <10 indicates heavy depression.

Statistical methods:

Descriptive data on patients' demographic characteristics were assessed at the beginning of the study.

All test score was summarized by means and standard deviation at baseline (T1) and after the first 12 weeks of treatment (T2). Changes after therapy in MMSE, Clock Test and the other evaluations on cognitive function are graphically evaluated.

For the possible correlation between emotional status and the score in same cognitive test, like verbal fluency test, matrix care test and clock test, changes in this test are evaluated among patients with light or heavy depression (GDS>6) at T2.

Results:

Of 87 patients entered in the study only 30 are resulted valuable in this first phase, 19 females and 11 males.

The average age was 75.7 years (range 70-82). 24 patients were affected by an advanced tumor.

At T1 16 (59%) patients had an ECOG-PS of 0 and 7 (26%) scored 1 point.

We find that the means score are lower after the treatment for all test except for the clock test.

We report the distribution of changes in the geriatric assessment scores after the chemotherapy

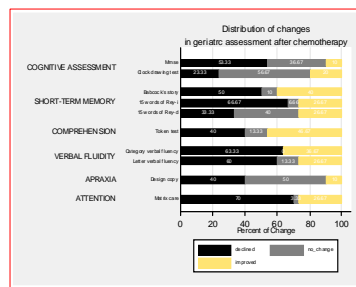


Table 1: Changes in Test scores before and after receiving chemotherapy (Mean and SD)

TEST	Baseline (T1)	After treatment (T2)	Changes
COGNITIVE DOMAIN			
MMSE	27.5 (2.15)	26.9 (2.5)	-0.7 (1.49)
Clock test	8.5 (2.86)	8.7 (2.41)	+0.2 (2.55)
Sub-area of cognitive domain			
Short-term memory	5.45 (1.7)	5.12 (1.7)	-0.3 (1.1)
15 word of Ray - immediate recall	11.98 (11.21)	10.31 (9.77)	-1.67 (2.42)
15 word of Ray - delay recall	5.25 (2.29)	5.15 (1.67)	-0.1 (2.62)
Attention	45.52 (8.13)	43.95 (8.94)	-1.57 (4.20)
Matrix care	30.2 (5.4)	29.94 (3.24)	-0.27 (2.12)
Apraxia	12.18 (1.83)	11.53 (2.35)	-0.65 (1.32)
Copy design	30.2 (5.4)	29.94 (3.24)	-0.27 (2.12)
Comprehension	11.7 (4.33)	11.4 (4.17)	-0.3 (1.16)
Verbal fluency	20.26 (8.62)	18.58 (8.77)	-1.68 (3.75)
Category verbal fluency	11.7 (4.33)	11.4 (4.17)	-0.3 (1.16)
Letter verbal fluency	20.26 (8.62)	18.58 (8.77)	-1.68 (3.75)
EMOTIONAL DOMAIN			
GDS	5.13 (2.56)	6.07 (3.40)	+0.93 (2.84)
QUALITY OF LIFE (FACT-G)			
Total score	75.90 (13.29)	72.96 (10.91)	-2.94 (13.73)
Physical well-being	24.46 (3.26)	23.27 (4.16)	-1.19 (3.27)
Social family well-being	18.42 (4.42)	18.83 (3.24)	+0.41 (4.43)
Emotional well-being	17.05 (3.46)	17.69 (3.48)	+0.64 (3.75)
Functional well-being	16.92 (4.11)	15.89 (4.24)	-1.03 (5.89)

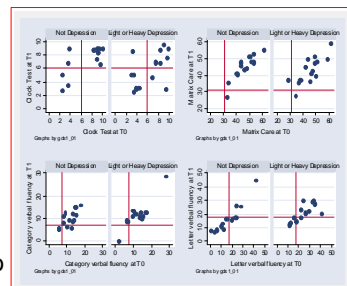
*P-values are at T1 and T2 are available on request.

NOTE: in this report table the sign in the scores, the value in the table. The higher is the difference (T1 - T2), the higher is the worst after therapy.

We observed that one-half of patients, after receiving chemotherapy had lower scores in: MMSe, 15 words of Ray-immediate recall, verbal fluency and Matrix care tests. **Most patients (57%) had no score changes on Clock test and Copy design (50%).**

In the graph we report the relationship between the GDS score and the correlate cognitive test
The GDS test gives 12 patients with depression at T0 and 15 at T1.

The GDS means that the score at T0 is 5.13, at T1 6.07. 8 of 15 patients with depression after therapy had a pathologic score also at the clock test, 5 of these had just at T0 a pathologic score. For the other tests there is no evidence of improvement due to the presence of depression.



Discussions:

This study was limited by the small sample size and the short follow-up period due to its pilot nature. The results of the current study revealed that cancer patients aged 70 years and older who were treated experienced limited deteriorations in functional and emotional measurements after receiving chemotherapy. This results will be the basis to design a more complete and adequately sized study.