

# Assessment of Quality of Life Following Radiotherapy in Patients With Rectum Cancer

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## Research Article

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# Abstract

## Purpose

The aim of the present study is to investigate the effects of radiotherapy (RT) on quality of life (QoL) and influencing factors.

## Methods

Data of 106 patients who completely filled out the three questionnaires were evaluated in this prospective study. Quality of life was evaluated with cancer-specific QLQ-C30 and colorectal cancer module QLQ-CR29 created by European Organization for Research and Treatment of Cancer (EORTC). All statistical analyses were done with SPSS version 22 software. A p level of <0.05 was accepted as statistically significant.

## Results

Median age was 61 (27-86). Of the patients, 77 (72.6%) were male and 29 (27.4%) were female. When QLQ-C30 questionnaires were evaluated, it was observed that physical, role, cognitive and emotional function scores were impaired following RT however returned to pre-RT levels on control. According to the results of QLQ-CR29 questionnaire, after RT, impairment was observed in urination frequency, urinary incontinence, stool frequency, dysuria, fecal incontinence, embarrassment, sexual interest in males scales however they returned to pre-RT values on control. When evaluated with regard to age, financial difficulty, global health score, mucus in stool, dysuria, dyspareunia and abdominal pain were observed to be poorer in the young; urination frequency and urinary incontinence were observed to be poorer in the elderly.

## Conclusion

Although both functional and symptom scales were shown to impair, most of them were detected to be temporal and patients could well tolerate radiotherapy. Additional assessment is required for evaluating the late effects of treatments on QoL.

# Introduction

Colorectal cancer is the third leading cancer type worldwide in both genders [1]. Rectum cancer consists 25-30% of colorectal cancers [2, 3]. The main treatment approach is surgery in rectum cancer [4, 5]. In local advanced rectum cancer, the standard treatment is neoadjuvant chemo-radiotherapy (CRT), surgery and adjuvant chemotherapy (CT) [3]. Adjuvant radiotherapy (RT) is recommended in patients who do not receive neoadjuvant therapy and who carry high risk for local recurrence [5]. Local recurrence reduces and survival prolongs as the result of improvements in rectum cancer treatment [4, 6, 7]. As survival prolongs, quality of life (QoL) of the patients gains importance. QoL of the patients impairs as the result of the disease and the treatments [7, 8]. Patients may experience many problems including defecation problems, urinary and sexual dysfunction, stoma care problems [6].

The effect of treatment is evaluated with survival, local recurrence, treatment toxicity and functional outcomes. In recent years, the concept of quality of life has also gained importance [5]. QoL may be defined as psycho-physical, functional, emotional impairment or social impairment [8]. Some proper, validated questionnaires are used for estimation of QoL. Cancer-specific QLQ-C30 created by European Organization for research and Treatment of Cancer (EORTC) is among the most common resources (8). QLQ-CR38 has been used in many studies as colorectal cancer module and afterwards this questionnaire was revised to a shorter questionnaire, QLQ-CR29 [9].

Radiotherapy has also acute effects besides long-term effects. Diarrhea, dysuria, proctitis, dermatological problems and pain may be commonly observed during treatment [10]. These are usually temporal and relieve within several weeks following radiotherapy. In a few studies, the effects of adjuvant and neoadjuvant RT on QoL have been investigated. Being aware of the side effects of the treatment planned to be given is important for preparation of the next patients and for prevention [5]. In this prospective study, we aimed to investigate the effects of RT on QoL and influencing factors.

## **Material And Methods**

### **Patient selection**

One hundred and forty-one rectum cancer patients who were treated with curative purpose between 2018 and 2020 were included in the study. Data of 106 patients who completely filled out all three questionnaires were evaluated. The patients aged 18 years and above, whose diagnosis of rectum cancer was verified histologically, who did not have distant metastasis at the time of diagnosis and who completely filled the questionnaires were included in the study. The patients who were not volunteer for participation, who filled the questionnaires incompletely, who had distant metastasis, recurrent disease, a second primary tumor and who previously received pelvic surgery or RT were not included.

This prospective study was conducted in accordance with the ethical principles of Helsinki Declaration. Ethics committee approval was obtained prior to the study. Written informed consent was obtained from all patients participated in the study.

### **Study parameters**

Data about age, gender, education level, tumor characteristics (stage, location, grade, histologic type), treatment data (neoadjuvant CRT, adjuvant CRT, surgery), dose and type of RT were obtained from patient files and hospital data management system. Patient and treatment characteristics are summarized in Table 1.

Table 1  
Patient and treatment characteristics

<b>Patients and treatment characteristics</b>	<b>n (%)</b>
Gender	29 (27.4)
Female	77 (72.6)
Male	
Age (median)	61(27-86)
Treatment type	86 (81.1)
Neoadjuvant	20 (18.9)
Adjuvant	
Stoma	10 (9.4)
Present	96 (90.6)
Absent	
Radiotherapy type	70 (66)
IMRT	36 (34)
Conformal	65 (61.3)
Radiotherapy dose	32 (30.2)
50 Gy	4 (3.8)
50.4 Gy	5 (4.7)
45 Gy	
54 Gy	
IMRT: Intensity-modulated radiation therapy	

Quality of life was evaluated with EORTC QLQ-C30 and QLQ-CR29. The illiterate patients filled the questionnaire with the aid of a literate relative. They were asked to ask the physician the words or questions they could not understand. Both questionnaires were filled out three times. First before commencement of RT, second on the last day of RT and third 6 weeks after completion of treatment in neoadjuvant therapy-receiving group and at month 3 control in adjuvant therapy-receiving group.

## Treatment

Computed tomography was performed in all patients with 3-5 mm sections for planning purposes. The patients were treated in prone position with a full bladder. Intensity-modulated radiation therapy (IMRT) or conformal radiotherapy plans were made. In patients undergoing IMRT plan, 50 Gy was applied to the rectum and mesorectum in 25 fractions and 45 Gy to regional lymphatics using the stimulated integrated

boost technique. In patients with a conformal plan, 45 Gy +/- boost was applied to the pelvic region using the three-field technique. All patients were concurrently administered capecitabine 825 mg / m<sup>2</sup> twice a day, 5 days a week. In patients who received neo-adjuvant therapy, magnetic resonance imaging (MRI) was performed after 6 weeks to evaluate the response to the treatment and they were referred for surgery.

## Questionnaires

EORTC QLQ-C30 is composed of 5 functional scales (physical, role, cognitive, emotional, social function), global health score and 3 symptom scales (fatigue, pain, nausea-vomiting). In addition, dyspnea, loss of appetite, sleep disorder, diarrhea, constipation, financial difficulty are evaluated with one question. Questions are 4- point Likert type.

QLQ-CR29 is composed of 29 questions inquiring gastrointestinal symptoms, urination problems, pain and mental health. Some questions vary depending on the presence of stoma. Questions regarding sexual function are different for both genders.

Raw score is calculated for each scale. For standardization of raw score, the answers are linearly converted to 0-100 scores by using standard EORTC guidelines [11]. Higher scores of functional scales and global health status scale and lower scores of symptom scale indicate high QoL.

## Statistics

All statistical analyses were done by using SPSS version 22 software. Descriptive statistics were applied for determining patient and treatment characteristics. Descriptive statistics were given as mean and standard deviation for normally distributed variables, and median and quartiles for non-normally distributed variables. The patients were divided to two groups given that the median age is 61. While one group included the patients aged between 21 and 61, another included the patients between the age of 62 and 86.

Friedman test was used for evaluating whether there was a difference among three measurements for each question. When needed, paired comparisons were done by using Wilcoxon test and Bonferroni correction. Mann Whitney U test was used for paired group comparisons of numerical variables.

The effect of gender, age and treatment type on the change between time and measurements was evaluated with mixed ANOVA analysis. When sphericity assumption could not be provided, Greenhouse-Geisser correction was used. A p level of <0.05 was accepted as statistically significant.

## Results

The results of 106 patients who were applied curative chemoradiotherapy due to rectum cancer at our clinic between 2018 and 2020 were evaluated. Median age was 61 (27-86). While 77 patients (72.6%) were males, 29 (27.4%) were females. All patients concurrently received capecitabine. Only one patient was single. Patient and treatment characteristics are summarized in Table 1.

When QLQ-C30 questionnaire was evaluated, an impairment was observed in physical, role, cognitive, emotional and functional scales following RT, however the scores were observed to reach pre-RT values on control. In changes over time, no difference was observed in dyspnea, insomnia scales and financial difficulty. Fatigue, nausea-vomiting and loss of appetite were observed to impair with RT however, reduced on control. Pain scale was observed to be worse before and after RT and statistically significant improvement was observed on control. Constipation and diarrhea scales did not change before and after RT however better than all measurements on control. When evaluated with regard to global health, the best score was detected on control. Global health status was observed not to impair with RT as compared to previous level (Table 2).

Table 2  
Comparison of scores for all scales of EORTC QLQ-C30

	<b>BeforeRT</b>	<b>After RT</b>	<b>Three months afterRT</b>	<b>P value</b>
Functional scales	80.00(66.66-93.33)	73.33(58.33-86.66)	80.00(66.66-93.33)	<0.001
Physical functioning	100.00(66.66-100.00)	83.33(66.66-100.00)	100.00(66.66-100.00)	0.001
Role functioning	75.00(50.00-91.66)	75.00(50.00-91.66)	75.00(64.58-100.00)	<0.001
Emotional functioning	83.33(79.16-100.00)	83.33(66.66-100.00)	100.00(83.33-100.00)	0.019
Cognitive functioning	83.33(66.66-100.00)	83.33(66.66-100.00)	83.33(66.66-100.00)	<0.001
Social functioning	50.00(33.33-66.66)	83.33(66.66-100.00)	66.66(50.00-83.33)	<0.001
Global health status scale	33.33(19.44-58.33)	50.00(33.33-66.66)	33.33(22.22-47.22)	<0.001
Symptom scales	0.00(0.00-16.66)	44.44(33.33-66.66)	0.00(0.00-0.00)	0.051
Fatigue	33.33(0.00-50.00)	33.33(0.00-66.66)	16.66(0.00-33.33)	0.157
Nausea and vomiting	0.00(0.00-33.33)	16.66(0.00-33.33)	0.00(0.00-0.00)	<0.001
Pain	33.33(0.00-33.33)	33.33(16.66-66.66)	33.33(0.00-41.66)	<0.001
Dyspnea	0.00(0.00-33.33)	0.00(0.00-33.33)	0.00(0.00-33.33)	<0.001
Insomnia	33.33(0.00-66.66)	33.33(0.00-66.66)	0.00(0.00-33.33)	0.073
Appetite loss	33.33(0.00-66.66)	33.33(0.00-66.66)	33.33(0.00-33.33)	
Constipation	33.33(0.00-66.66)	33.33(0.00-66.66)	33.33(0.00-33.33)	
Diarrhea	33.33(0.00-66.66)	33.33(0.00-33.33)	0.00(0.00-33.33)	
Financial difficulties		33.33(0.00-66.66)	33.33(0.00-33.33)	

Values are given as median (quartiles). Scales were numbered between 0 and 100. While higher scores indicate better functioning in functioning scales and global health status, higher scores in symptom scales indicate poorer symptoms.

When QLQ-CR29 questionnaire was evaluated, body image, anxiety, impotence, dyspareunia, female sexual interest, stoma care and loss of hair did not differ in all three measurements. Urination frequency, urinary incontinence, defecation frequency, dysuria, fecal incontinence, male sexual interest scores were observed to impair after RT however, returned to pre-RT values on control. While mucus in stool was the worst before RT, improvement was observed after treatment. While abdominal pain, dry mouth, flatulence, bloated feeling did not differ before and after RT, they were found to be better on control. While loss of taste, embarrassment and skin wound were the best before RT, they impaired after RT (Table 3).

Table 3  
Comparison of scores for all scales of EORTC QLQ-CR29

	Before RT	After RT	Three months after RT	Pvalue
Functioning scales and items	88.88 (77.77-100.00)	88.88(75.00-100.00)	88.88(77.77-100.00)	0.059
Body images	66.66 (33.33-100.00)	66.66 (33.33-100.00)	66.66 (33.33-100.00)	0.154
Anxiety	66.66 (66.66-100.00)	100.00 (66.66-100.00)	100.00 (66.66-100.00)	0.007
Weight	66.66 (66.66-100.00)	100.00 (66.66-100.00)	100.00 (66.66-100.00)	<0.001
Sexual interest men **	100.00 (66.66-100.00)	66.66 (66.66-100.00)	100.00 (66.66-100.00)	0.076
Sexual interest women **	100.00 (100.00-100.00)	100.00 (100.00-100.00)	100.00 (100.00-100.00)	<0.001
Symptom scales and items	50.00 (16.66-66.66)	66.66 (45.83-83.33)	33.33 (33.33-66.66)	0.009
Urinary frequency	0.00 (0.00-33.33)	0.00 (0.00-33.33)	0.00 (0.00-33.33)	<0.001
Urinary incontinence	0.00 (0.00-33.33)	33.33 (33.33-100.00)	0.00 (0.00-33.33)	<0.001
Dysuria	33.33 (0.00-50.00)	33.33 (0.00-50.00)	0.00 (0.00-16.66)	<0.001
Blood and mucus in stool	16.66	50.00	16.66	0.003
Stool frequency***	0.00 (0.00-33.33)	50.00	0.00 (0.00-33.33)	<0.001
Abdominal pain	33.33 (0.00-66.66)	33.33 (0.00-33.33)	33.33 (0.00-33.33)	0.071
Buttock pain	33.33 (0.00-33.33)	66.66 (33.33-100.00)	0.00 (0.00-33.33)	<0.001
Bloated feeling	33.33 (0.00-33.33)	33.33 (0.00-33.33)	16.66 (0.00-33.33)	0.015
Dry mouth	33.33 (0.00-33.33)	33.33 (0.00-33.33)	33.33 (0.00-33.33)	0.012
Hairloss	0.00 (0.00-0.00)	33.33 (0.00-33.33)	0.00 (0.00-0.00)	<0.001
Trouble with taste	0.00 (0.00-0.00)	33.33 (0.00-33.33)	0.00 (0.00-33.33)	<0.001
Flatulence***	0.00 (0.00-0.00)	0.00 (0.00-0.00)	33.33 (0.00-33.33)	0.368
Fecal incontinence***	33.33 (0.00-33.33)	33.33 (0.00-33.33)	0.00 (0.00-33.33)	0.810
Sore skin***	0.00 (0.00-33.33)	33.33 (0.00-33.33)	0.00 (0.00-33.33)	0.444
Embarrassed by bowel movement***	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.00 (0.00-33.33)	

Values are given as median (quartiles). Scales were numbered between 0 and 100. While higher scores indicate better functioning in functioning scales and global health status, higher scores in symptom scales indicate poorer symptoms.\*\* Sexual function was evaluated with different questions for males and females \*\*\* There are sections which include different questions for the patients with or without stoma

	Before RT	After RT	Three months after RT	Pvalue
Stoma care problems	0.00 (0.00-33.33)	0.00 (0.00-33.33)	0.00 (0.00-41.66)	
Impotence	0.00 (0.00-41.66)	33.33 (33.33-66.66)	0.00 (0.00-33.33)	
Dyspareunia	0.00 (0.00-33.33)	33.33 (0.00-33.33)	0.00 (0.00-0.00)	
	0.00 (0.00-0.00)	0.00 (0.00-66.66)		
		0.00 (0.00-33.33)		
		0.00 (0.00-0.00)		

Values are given as median (quartiles). Scales were numbered between 0 and 100. While higher scores indicate better functioning in functioning scales and global health status, higher scores in symptom scales indicate poorer symptoms.\*\* Sexual function was evaluated with different questions for males and females \*\*\* There are sections which include different questions for the patients with or without stoma

When evaluated with regard to gender, on QLQ-C30, physical and emotional scale- scores and general health score, dyspnea, pain, fatigue, loss of appetite and nausea-vomiting scores; and on QLQ-CR29, anxiety, blood-mucus in feces, abdominal pain, loss of taste, skin wound and embarrassment were observed to be better among males.

When evaluated with regard to age, on QLQ-C30, financial difficulty and global health score were observed to be worse in the young. On QLQ-CR29, urination frequency and urinary incontinence were observed to be worse in the elderly, mucus in feces, dysuria, dyspareunia and abdominal pain were observed to be worse in the young.

When evaluated with regard to treatment type, on QLQ-C30, emotional scale and dyspnea were observed to be worse; on QLQ-CR29, mucus in stool, abdominal pain, loss of hair and bloated feeling were observed to be worse in neo-adjuvant therapy.

When evaluated with regard to type of RT, on QLQ-C30, emotional scale and insomnia; on QLQ-CR29, weight, mucus in stool, abdominal pain and buttock pain were observed to be worse in IMRT technique.

According to mixed ANOVA test results, the changes of cognitive function scale (p=0.049), social functioning scale (p=0.018), pain (p=0.020), nausea-vomiting (p=0.026), urinary incontinence (p=0.042) over time according to gender were found to be significant. When gender differences were evaluated, physical functioning scale (p<0.001), cognitive scale (p<0.001), emotional scale (p<0.001), dyspnea (p=0.013), pain (p=0.001), fatigue (p<0.001), loss of appetite (p=0.004), nausea-vomiting (p<0.001), anxiety scale (p=0.004), weight scale (p=0.007), abdominal pain (p<0.001), loss of taste (p=0.003), embarrassment (p=0.023) and global health score (p=0.003) were observed to be better among males (Figure 1).

In mixed ANOVA test results, the changes in general health score ( $p=0.006$ ), urination frequency ( $p=0.027$ ), blood and mucus in stool ( $p=0.007$ ), dysuria ( $p=0.029$ ) in time according to age were found to be significant. When age differences were evaluated, financial difficulty ( $p=0.043$ ), and dyspareunia ( $p=0.042$ ) were observed to be worse under the age of 61, urination frequency ( $P=0.002$ ), sexual interest in males ( $p=0.012$ ) and females ( $P=0.020$ ), and urinary incontinence scores ( $p=0.023$ ) were observed to be worse above the age of 61 (Figure 2).

In mixed ANOVA test results, diarrhea ( $p=0.031$ ), blood and mucus in stool ( $p=0.001$ ), embarrassment ( $p=0.042$ ) scores were found to significantly change over time. When the differences between treatments were evaluated, blood and mucus in stool ( $p<0.001$ ) and abdominal pain scores ( $p=0.034$ ) were found to be worse in neo-adjuvant therapy group (Figure 3).

## Discussion

The goal of the treatment of patients with locally advanced rectum cancer should be both to eliminate the disease and to prevent the impairment of and even to improve the quality of life. In this study, quality of life was evaluated during and after treatment in patients with rectum cancer who underwent chemoradiotherapy for curative purposes. In radiotherapy, the treatment area includes all pelvic structures [12]. So, a number of problems including radiation enteritis, increased bowel movements, some of which can affect daily life and quality of life may develop. In addition, there may be an increase in these acute side effects with the addition of chemotherapy [12]. QoL questionnaires provide valuable information for patients in clinical decision making and how patients will feel after treatment [9]. Detection of certain functional impairments during treatment enables the clinicians to take care for potential late side effects during patient follow up. Besides, being aware of the changes in QoL helps identification of the patients who require special care [12].

Couwenberg et al. found the global health score to be worse than the reference group until month 12. While some studies found no changes, others found better results [4]. This condition was shown to be temporal in those who have worsened during radiotherapy [13]. In our study, when the global health score was evaluated, it was observed that although there was no deterioration with radiotherapy, the best scores were detected on control. This may be due to the differences in patients' adaptation to their disease, and their expectations and priorities.

Physical, emotional, cognitive scale and some symptom scales including fatigue, nausea-vomiting, pain and loss of appetite were observed to be worse in females. Quality of life was shown to be worse in females with rectum cancer than in the normal population [12]. Similar to our study, it has been shown in the literature that females have a lower emotional, physical, and cognitive scale compared to males [7, 8, 14]. The addition of early menopause symptoms due to pelvic RT and pelvic surgery and more frequent occurrence of psychosomatic disease may lead to this situation. In addition, males are expected to better tolerate the disease due to their being more resistant to negative or positive circumstances with the effect of their being appreciated with the effect of the cultural structure of our community. Females' having

better inter-personal relationships, better expressing their disease and psychological status may also be related with this condition.

Different results are present in the literature with regard to the differences between age groups. In a study from Slovenia, poorer physical functioning, more urination frequency, urinary incontinence and buttockpain were shown in the elderly [8]. In the other population-based studies, lower functional and global health scores were found in young patients with colorectal cancer. Fatigue, loss of appetite, nausea-vomiting were reported to be more in young patients as compared to controls [15]. While stoma problems were observed in the elderly, sexual problems were found to be more in the young [12]. In our study, while urination frequency, urinary incontinence and both male and female sexual interest were poorer in the elderly, general health score, financial difficulty, abdominal pain and dyspareunia were observed to be poorer in young patients. Elderly patients' having more chronic diseases may contribute to this condition. Young patients may feel function losses more due to having a more active life, a family that should care and encountering a potentially fatal disease at young age. Dyspareunia may develop from vaginal dryness in females who receive pelvic RT.

Lim et al. evaluated QoL before and after treatment and before surgery in patients with local advanced stage rectum cancer who received neo-adjuvant therapy. While role function and cognitive function impaired during treatment, emotional function improved from baseline to pre-operative period [3]. In a similar study, while diarrhea, fatigue and loss of no functional difference could be shown [16]. Charlton et al. found that functional appetite increased after neo-adjuvant therapy and global QoL significantly reduced, no significant difference was found in nausea and pain scores [5]. A few studies are available in the literature comparing the effect of adjuvant and neo-adjuvant therapies on QoL. Less bowel movements were observed in the patients who receive pre-op RT as compared to the ones who receive post-op RT however status and QoL were significantly poorer in the patients who received adjuvant CRT as compared to the ones who received neo-adjuvant CRT or single therapies [17]. In our study, neo-adjuvant CRT was shown to be worse with regard to emotional scale, mucus in feces, abdominal pain. This may have resulted from the fact that in our clinic, most of the patients receive neo-adjuvant therapy, presence of symptoms before and during treatment and addition of side effects to these symptoms. Changes in these scores mostly improve when they come to control, along with getting used to the diagnosis of cancer, functional adaptation and disappearance of physical symptoms during treatment. Although there was deterioration in embarrassment and body image scores in patients with stoma in studies [18], we did not observe a difference due to the very low number of patients with stoma.

The present study has some limitations. We have relatively low number of patients. We could not evaluate risky organ dose in RT. Due to the small number of patients receiving adjuvant treatment, we did not evaluate whether there was a difference with regard to the effect of low anterior resection or abdomino-perineal resection on QoL which were evaluated in many studies. When evaluating sexuality-related questions, we did not consider whether the patients were sexually active or not. On the other hand, the strength of our study was its prospective design. All patients were treated with the same protocol. All

patients received the same chemotherapy. The patients who completely filled out all three questionnaires were included in the study.

In conclusion, although the present study indicates that both functional and symptom scales impair with RT, most of them were observed to be temporal and patients tolerated RT well. Additional assessments are required for detection of the late effects of therapies on QoL.

## Declarations

### Statements and Declarations

**Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Conflicts of interest:** All authors have declared no conflict of interest.

**Availability of data and materials:** Data can be requested through email to the corresponding author.

**Authors' contributions:** All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Berrin Benli Yavuz, Meryem Aktan, Gul Kanyilmaz and Lutfi Saltuk Demir. The first draft of the manuscript was written by Berrin Benli Yavuz, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Ethics approval:** All procedures were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethics committee approval was obtained prior to the study.

**Consent to participate:** Written informed consent was obtained from all patients participated in the study.

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## Figures

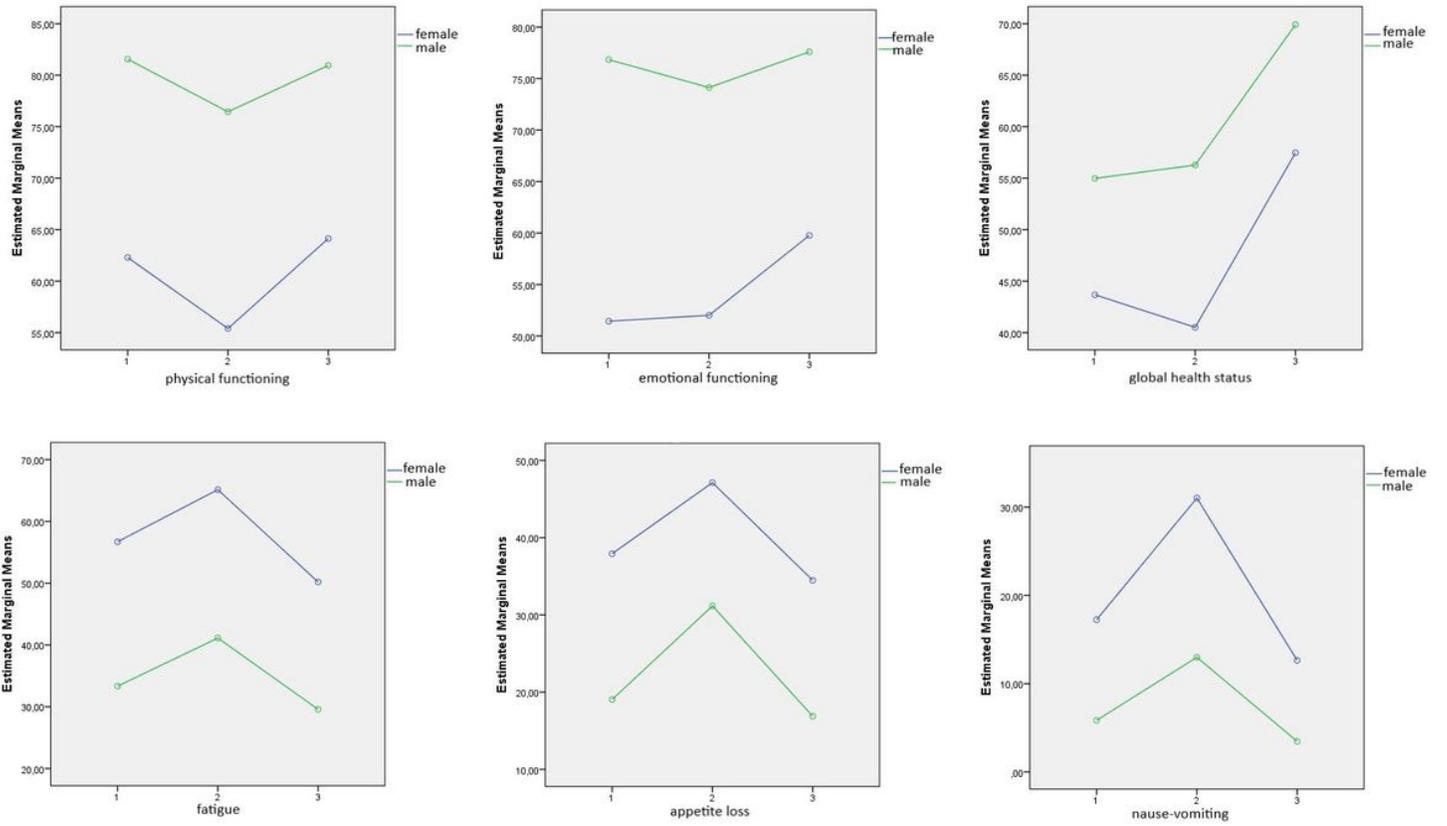
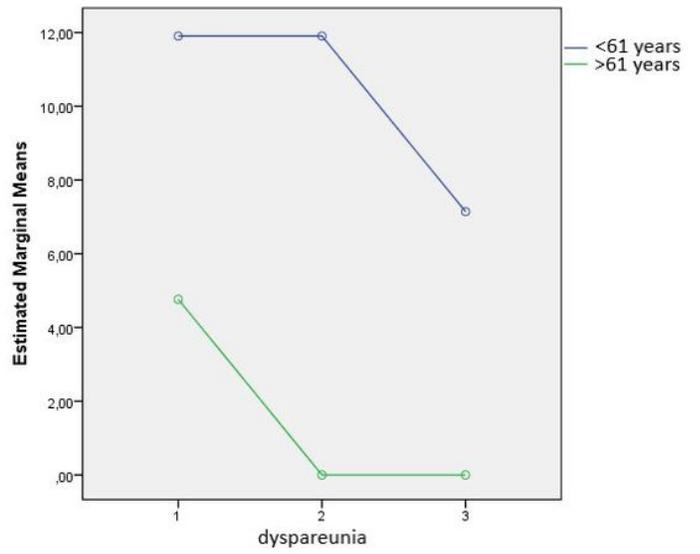
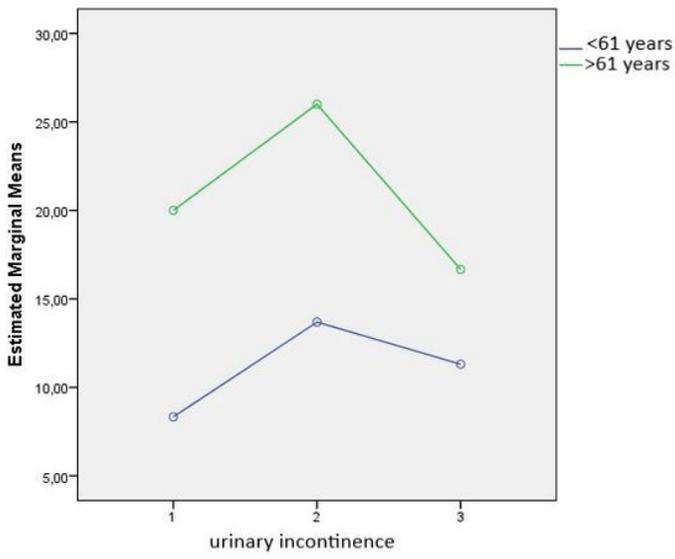
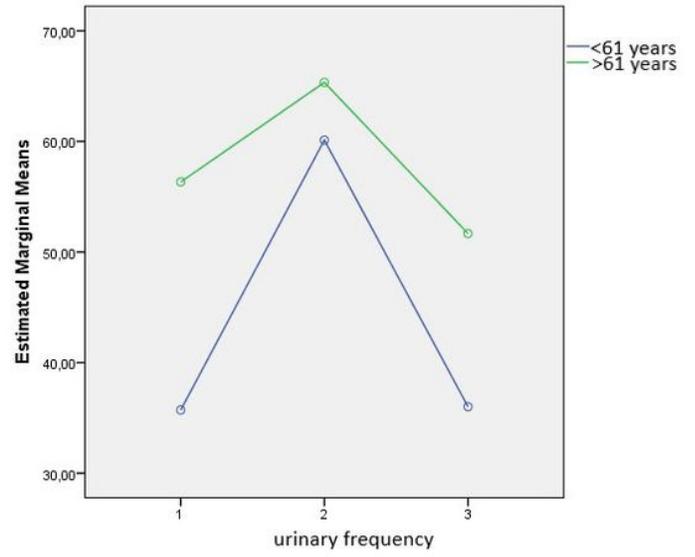
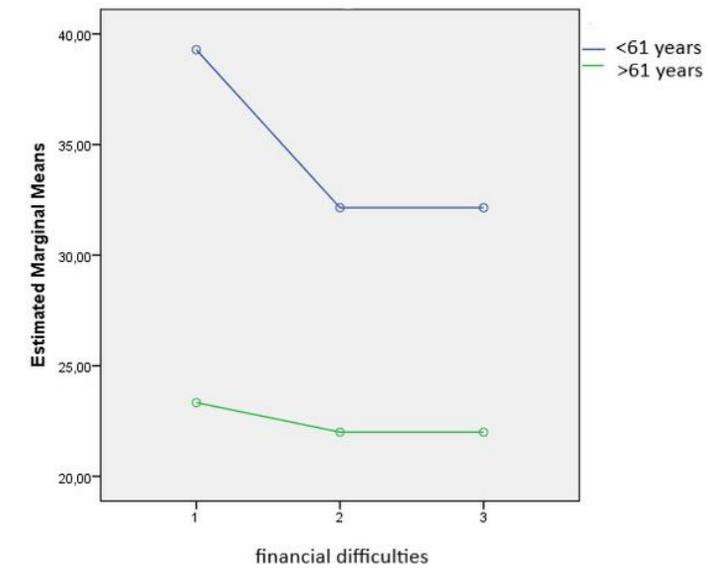


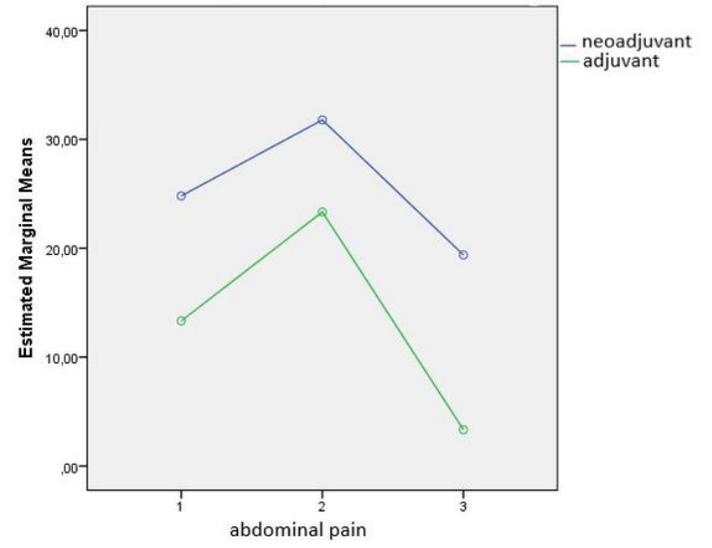
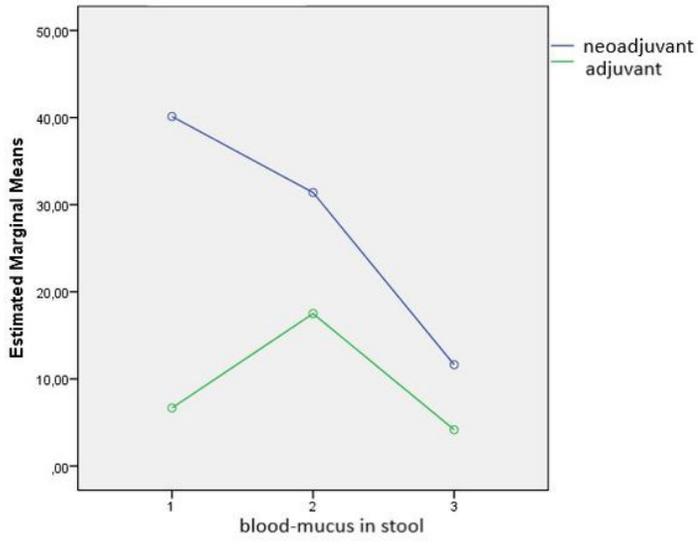
Figure 1

Change of the differences between values in all 3 measurements according to gender



**Figure 2**

Change of the differences between values in all 3 measurements according to age



**Figure 3**

Change of the differences between values in all 3 measurements according to treatment type