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Survival and quality of life after surgery for colorectal cancer in the elderly: a comparative study

Irene Jiménez¹, Miguel-Ángel Pachá², David Parés², María Esteve³, José Troya², Josep Roca³, Jaume Canet⁴, Joan-Francesc Julián² and Jaume Fernández-Llamazares²

¹Customer Care and Patient Experience. Hospital Germans Trias i Pujol. Badalona, Spain. Departments of ²General Surgery, ³Epidemiology and ⁴Anaesthesiology. Hospital Germans Trias i Pujol. Badalona, Spain

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Correspondence: David Parés. Department of General Surgery. Hospital Germans Trias i Pujol. Universitat Autònoma de Barcelona. C/ Canyet, s/n. 08916 Badalona, Barcelona. Spain
e-mail: dapares@gmail.com

ABSTRACT

Background: the aim of this study was to analyze the clinical results of the multidisciplinary management of elderly patients with colorectal cancer in a single center and to describe postoperative quality of life.

Methods: a comparative study was designed to compare the results and quality of life of patients treated in our center for colon cancer, aged from 80 to 84 years (study group) compared to a control group (aged from 75 to 79 years of age). Morbidity, mortality, oncological results and quality of life were analyzed.

Results: eighty-seven patients aged between 80 and 84 years of age (study group) were compared to a control group, which was formed by 91 patients aged from 75 to 79 years of age. There were no significant differences in technique and morbidity. Survival at 30 days, 90 days and at the end of follow-up (median 48 months) were similar in both groups. There were no differences in quality of life except for one item

with regard to physical function ($p = 0.0138$).

Conclusion: similar clinical results and quality of life were achieved after treating elderly patients with colon cancer with a multidisciplinary management approach.

Key words: Colorectal cancer. Elderly. Surgery. Results. Quality of life.

INTRODUCTION

Colorectal cancer is highly prevalent in the general population, especially in western countries (1,2). It is well known that surgical treatment is the mainstay of treatment (3,4). However, adjuvant chemotherapy has been proven to significantly increase overall and disease-free survival in specific selected populations. There is an overall increasing life expectancy in the western world (5). However, some age-related diseases are concomitantly more prevalent as the most significant factor for malignancy development is longevity (6). One of these diseases is colorectal cancer.

There are increasing data with regard to the surgical treatment of colorectal cancer in octogenarians (6,7). Except for age, general fitness is considered to be the most relevant factor for decision-making in this population (8). However, the management of specific concerns in frail or patients of advanced age requires some considerations (9). Thus, specific patient-based programs for elderly patients with colon cancer are warranted (10). There are case-series focused on a favorable outcome and survival after surgical treatment for colon cancer in the elderly population and thus, age itself is not a contraindication for surgery (3,11). However, it is difficult to define a control group, as very few studies have been designed to compare the management of these patients with other cohorts. We hypothesized that patients older than 80 years would have a similar postoperative outcome when applying a multidisciplinary approach in comparison to younger patients.

The aim of the present study was to analyze the results of the surgical treatment of colon cancer in the elderly population after the implementation of specific patient-based programs, in comparison to a control group of patients, also with an advanced age.

PATIENTS AND METHODS

A retrospective analysis of consecutive data obtained prospectively was used to compare two cohorts of patients with a diagnosis of colorectal cancer treated via a surgical resection in a single tertiary university hospital. Cases included from 2011 to 2014 were divided in two groups according to age at primary diagnosis: group 1 (control group) comprised patients diagnosed from age 75 to 79 years and group 2 (study group) included patients between 80 and 84 years old.

This study was presented and approved by our Institutional Review Board and Ethical Committee (reference number PI-15.096) and informed written consent was obtained in all patients.

Inclusion criteria and exclusion criteria

All patients aged 75 years old or over with a proven diagnosis of colorectal cancer were included in the study. Patients with no histological confirmation of colon cancer, metastatic disease, those unfit for surgery or who did not accept treatment were excluded from the long-term survival analysis.

Specific elderly patient-based program

A multidisciplinary team for the management of frail or patients with advanced age was set-up in our surgery department in 2011. The multidisciplinary team consisted of surgeons, an oncologist, internal medicine specialist, anesthesiologist, dietician and social care specialist. A pre-habilitation scheme was used to optimize patients, correct anemia (if hemoglobin less than 10 gr/dl), improve nutritional status and to perform a preoperative chest physiotherapy program.

Surgical technique and postoperative care

In general, a standard curative technique for colorectal cancer was used (3). However, a decision was made with regard to the use of primary anastomosis or stoma in the multidisciplinary patient-centered assessment. This decision took into account previous symptoms of fecal incontinence and patients at risk of an anastomotic leak (i.e., nutritional status, steroids, technical difficulties, etc.). The final decision was

made by the patient. Prophylactic antibiotics were used in all cases and a mechanical bowel preparation has not been performed since 2011. Patients received DVT prophylaxis with low weight heparin and mechanical measures during surgery.

Postoperative management included a patient adapted enhanced recovery program after surgery (12). This mainly included a prompt postoperative mobilization, no nasogastric (NG) tube, restricted fluid management, starting a diet six hours after surgery and a progressive diet if tolerated. Abdominal drains are not systematically used.

Study variables

Sociodemographic variables and details of the diagnosis and surgical treatment were obtained prospectively. The Charlson comorbidity index was used for the characterization of patient groups (13). An overall assessment of fragility was assessed using the Karnofsky (14) and Barthel indexes (15). Postoperative complications (using the Clavien-Dindo classification [16]), postoperative mortality and survival at 30 days and 90 days were assessed. The 9th version of TNM (17) was used for the pathological staging of colon cancer.

Disease free survival was defined as the length of time the patient survived after the primary treatment for cancer without any signs or symptoms of the disease. Overall survival was defined as the time from either the date of diagnosis or the start of treatment until death.

The Spanish validated SF-12 questionnaire was used for the analysis of quality of life (18,19). The SF-12 test is a generic quality of life measure. It provides a shorter, yet valid alternative to the longer SF-36 test. The SF-12 is weighted and summed to provide an easily interpretable scale for physical and mental health. The measure is computed using the scores of twelve questions and range from 0 to 100. The interpretation of the test ranges from zero, indicating the lowest level of health to 100, which indicates the highest level of health. Patients were encouraged to fill-in the quality of life questionnaire six months after surgery.

Follow-up

The primary endpoint of the study was the postoperative mortality at 90 days, overall survival and disease free survival. The secondary objective was the quality of life one year after surgery. Patients were followed up with the standard laboratory and imaging test at three, six and 12 months during the first year and every six months for the following five years, as recommended by the guidelines (4).

Sample size calculation and statistical analysis

A minimum sample size of 60 subjects per group was calculated, considering an alpha risk value of 0.05, a beta risk value of 0.2 (in a two-sided test) and an expected difference in postoperative mortality of 15% between the groups. Continuous variables are presented as the mean \pm standard deviation or median and ranges. Categorical variables are presented as absolute numbers or percentages. The Chi-square test was used to compare differences in categorical variables (the Fisher's exact test was used when necessary) and the Student's t test was used for continuous variables. The Kaplan-Meier test was used for survival curve analysis and a comparative log rank test was used to assess differences between the groups. All reported p values were two sided and a p value less than 0.05 was considered as statistically significant. Statistical analyses were performed using SAS™ version 9.3.

RESULTS

Characteristics of included patients

Two hundred and twenty eligible patients were identified from January 2011 to December 2014. Forty-two patients were excluded as they were aged older than 84 years. Therefore, 178 cases were finally included; 91 in the control group and 87 in the study group.

The general characteristics of the patients in both groups are presented in table 1. Age and ASA score differed between the two groups but gender and body mass index (BMI) were similar between the two groups. In addition, there were significant differences in indexes used for the overall assessment of patients such as the Charlson index ($p = 0.003$), Karnofsky index ($p = 0.030$) and Barthel index ($p < 0.001$).

The details of treatment and final histological analysis are presented in table 2. Laparoscopy was used in 28 patients; 14% in the control group and 1% in the study group ($p = 0.033$). Forty-one patients had a colostomy, 19 in the control group and 22 in the study group ($p = 0.480$). With regards to surgery, there were only significant differences in operative time, which was shorter in the study group. The percentage of patients who received adjuvant chemotherapy was significantly higher in the control group (Table 2).

Postoperative morbidity and mortality

Overall, 47 patients (26.4%) had some postoperative complication (25.3% in the control group and 27.6% in the study group, $p = 0.720$) and 11.8% of cases required a surgical re-intervention (9.9% vs 13.9%, $p = 0.420$). The type of complications are shown in table 3. There were no differences among groups ($p = 0.248$). The length of hospital stay was similar among the groups: nine days for the control group vs 12 days for the study group ($p = 0.830$). The 30-day postoperative mortality was 3.4%, which was similar between groups: 3.3% for the control group vs 4.6% for the study group ($p = 0.620$).

Survival

The overall survival 48 months after surgery was 65.3% vs 57.7% for control and study group, respectively. Figure 1 shows the Kaplan-Meier survival curves of the two groups (log rank test $p = 0.340$). There were significant differences in the overall series between 48-month survival according to the TNM distribution of colon cancer (log rank test $p < 0.001$) (Fig. 2).

Quality of life

One hundred and six patients completed the quality of life assessment during follow-up for colorectal cancer treatment, 56 from the control group and 50 from the study group. The results of this evaluation one year after surgical treatment are presented in table 4 and figure 3. There were no significant differences among groups.

DISCUSSION

The decision-making for the surgical management of colorectal cancer in elderly patients is still challenging. The clinical results of two homogeneous groups of patients with an advanced age after the implementation of a specific patient-centered surgery program was analyzed. In our experience, the clinical results were similar despite their age. In addition, and most importantly, quality of life was similar in both groups.

A large study in several cancer types considered the lower survival rate among older patients (20). However, there are several published series with the standard message that there is no contraindication with regard to age, if patients are fit for surgery for colorectal cancer treatment (21,22). There are several case series that communicate the results of postoperative and long-term survival after surgical colon cancer treatment. However, the key in our study is the design, which included a control group of patients older than 75 years of age. These are also considered by many investigators as elderly patients. In fact, the overall fragility assessment that used the most reliable tests were significantly different between the groups. However, neither postoperative survival nor long-term survival were different. Thus, accounting for the multidisciplinary management of these patients.

Surgery, in general, was not different among groups. There is an evident low rate of a laparoscopic approach in the overall series. This may explain the differences between operative time among the groups. Although we used the ERAS protocol for the management of these patients, the length of hospital stay was longer in our study than expected. This is probably due to the special nature of the elderly population that determines the need for a social discharge plan in most cases.

Although there were no differences with regard to TNM among the groups and the proportion of patients who received adjuvant chemotherapy was lower, there were no significant differences in long-term survival. These results require careful interpretation as the guidelines support the use of adjuvant treatment, even in elderly patients (23,24). Some special considerations must be taken into account when managing this population group (10). Surgical and medical complications can occur in patients with an advanced age and may also be followed by life-threatening situations. Thus, specific clinical pathways are warranted, especially in fragile patients. Failure-to-

rescue after surgery in the elderly population is of paramount importance (9).

The target of colon cancer treatment in these patients is to control symptoms, diminish morbidity and maintain the quality of life (6,10). In our experience, there were no differences in quality of life one year after surgery, except for some of subscales of physical function. It would be interesting to study the determinants of quality of life in a subgroup of patients, such as those with or without a stoma or patients with complications. However, this will form part of a future study. Interestingly, we did not find similar results using the same test in the literature and therefore, studies in other centers are warranted.

Long term survival is a controversial target in this aged population. This is due to the fact that very few studies have been focused on this goal. In our experience, the figures were acceptable, even in octogenarians (23). There is an overall increase in life expectancy in the western world. Thus, medical and surgical societies such as the American college of surgeons are promoting patient-centered initiatives to help clinicians in the management of surgical diseases in elderly patients (25). Quality in geriatric surgery is one of the main projects developed as part of quality programs initiatives and comprises several measures and guidelines to help clinicians and stakeholders (26).

The strength of our study is the fact that it compared a similar group of elderly patients who received surgical treatment for colorectal cancer. The main difference between the groups were age and variables related to this item. As far as we know, our study is unique in its design, including a quality of life assessment. However, our study also has some limitations. First, the retrospective nature of the study is a drawback. Even though data were collected prospectively, these were analyzed in a retrospective manner. In addition, there is a low rate of a laparoscopic approach and the proportion of adjuvant chemotherapy treatment were different among the groups. This could impact on the analysis of the results.

In summary, patients older than 80 years of age had a similar postoperative outcome in comparison to a control group of patients aged between 75 to 79 years. Quality of life was similar, except for significant differences in the physical component. The implementation of a patient-centered surgical program for elderly patients might be

justified in each surgery department.

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Table 1. Patient characteristics in each group

	<i>Control group</i> <i>n = 91</i>	<i>Study group</i> <i>n = 87</i>	<i>p-value</i>
Age (years)*	77 (75-79)	82 (80-84)	NC
Gender (%)			
Male	72.5%	65.6%	0.310 [†]
BMI (kg/m ²) [†]	26.77 (18.8-39.4)	27.07 (17.3-41.5)	0.800 [§]
ASA score (%)			
1-2	42.8	8.1	< 0.001 [†]
3	48.3	77	
4	8.8	14.9	
Charlson index [†]	3 (2-7)	3 (2-7)	0.003 [§]
Karnofsky index [†]	90 (60-100)	90 (50-100)	0.030 [§]
Barthel index [†]	100 (30-100)	70 (45-100)	< 0.001 [§]

NC: not compared. *Mean (range). [†]Median (range). [‡]Chi-square's test. [§]Mann-Whitney U t-test.

Table 2. Characteristics of the disease and details of treatment

	<i>Control group</i> <i>n = 91</i>	<i>Study group</i> <i>n = 87</i>	<i>p-value</i>
Surgical technique (%)			
Right colectomy	41.4	45.3	
Left colectomy	56.3	40.5	
Segmental resection	3.40	5.9	
APR	2.3	8.3	0.0983 [†]
Primary anastomosis (%)			
Yes	78.1%	73.6%	0.480 [†]
Operative time (minutes)*	130 (35-360)	120 (30-250)	0.010 ²
TNM classification (%)			
Stage I	9.2	5.9	
Stage II	20.7	16.7	
Stage III	44.8	47.6	
Stage IV	25.2	29.7	0.7187 [†]
Adjuvant chemotherapy (%)	45.5%	19.5%	0.0004 [†]

APR: abdominoperineal resection. *Median (range). [†]Chi-square's test. ²Mann-Whitney U test.

Table 3. Results of the quality of life assessment during the follow-up of patients treated for colorectal cancer using the SF-12 test

	<i>Control group</i> <i>n = 56</i>	<i>Study group</i> <i>n = 50</i>	<i>p-value*</i>
<i>Physical health</i>			
Physical function			
P1	68	72	0.643
P2	30	52	0.0138
P3	34	52	0.0602
Physical role			
P4	32	50	0.0616
P5	32	50	0.0616
P8	77	82	0.509
<i>Mental health</i>			
Emotional role			
P6	23	26	0.739
P7	23	22	0.882
Mental health			
P9	96	84	0.0540
P11	27	32	0.556
Vitality			
P10	77	62	0.0979
Social function			
P12	29	36	0.413

¹Mann-Whitney U test. Low score indicates the lowest level of health.

Table 4. Results of quality of life assessment in the follow-up of patients treated for colorectal cancer using SF-12 test

	<i>Control group</i> <i>n = 56</i>	<i>Study group</i> <i>n = 50</i>	<i>p-value*</i>
<i>Physical health</i>			
Physical function			
P1	68	72	0.643
P2	30	52	0.0138
P3	34	52	0.0602
Physical role			
P4	32	50	0.0616
P5	32	50	0.0616
P8	77	82	0.509
<i>Mental health</i>			
Emotional role			
P6	23	26	0.739
P7	23	22	0.882
Mental health			
P9	96	84	0.0540
P11	27	32	0.556
Vitality			
P10	77	62	0.0979
Social function			
P12	29	36	0.413

*U Mann Whitney test. Low score indicates the lowest level of health.

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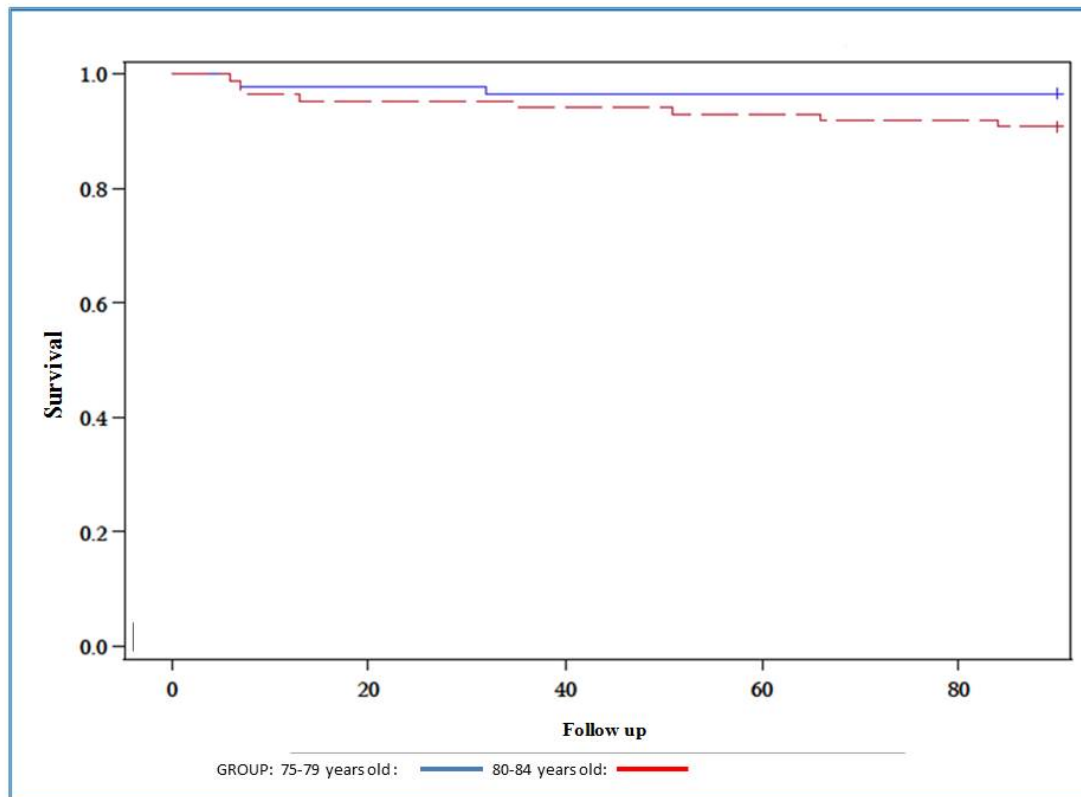


Fig. 1. Survival curves of the first 90 postoperative days in both groups ($p = 0.12$).

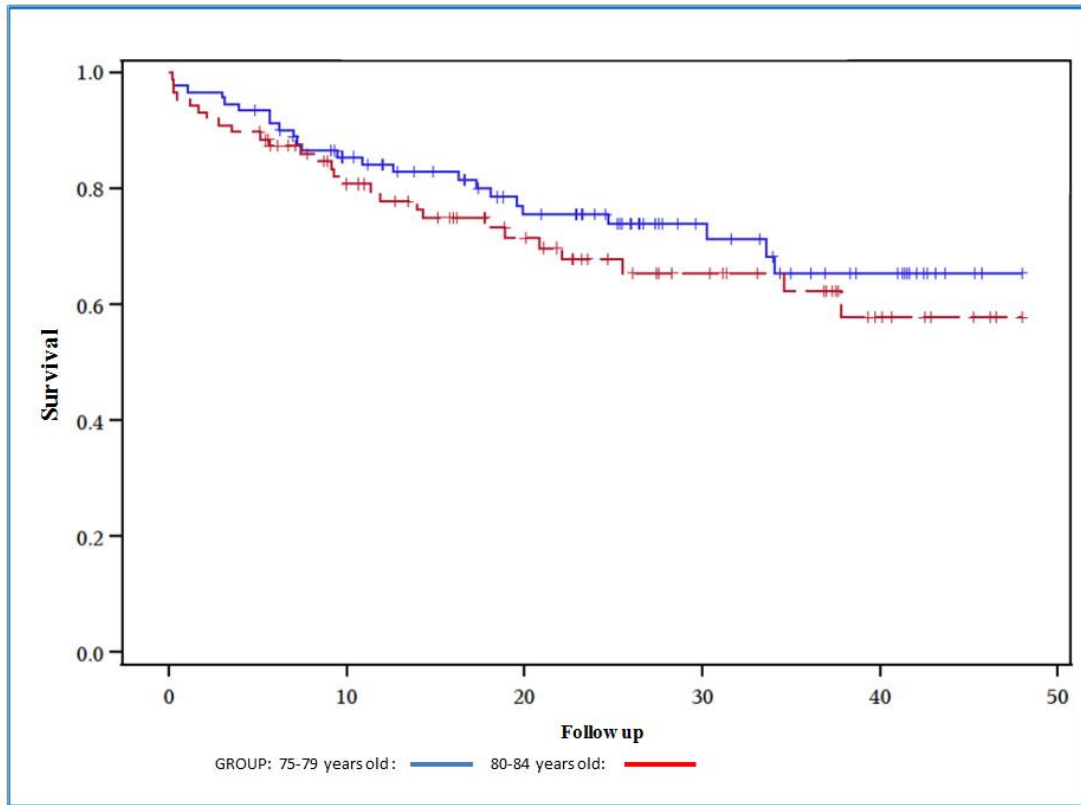


Fig. 2. Survival curves of overall survival in both groups with at follow-up of 48 months (p = 0.34).

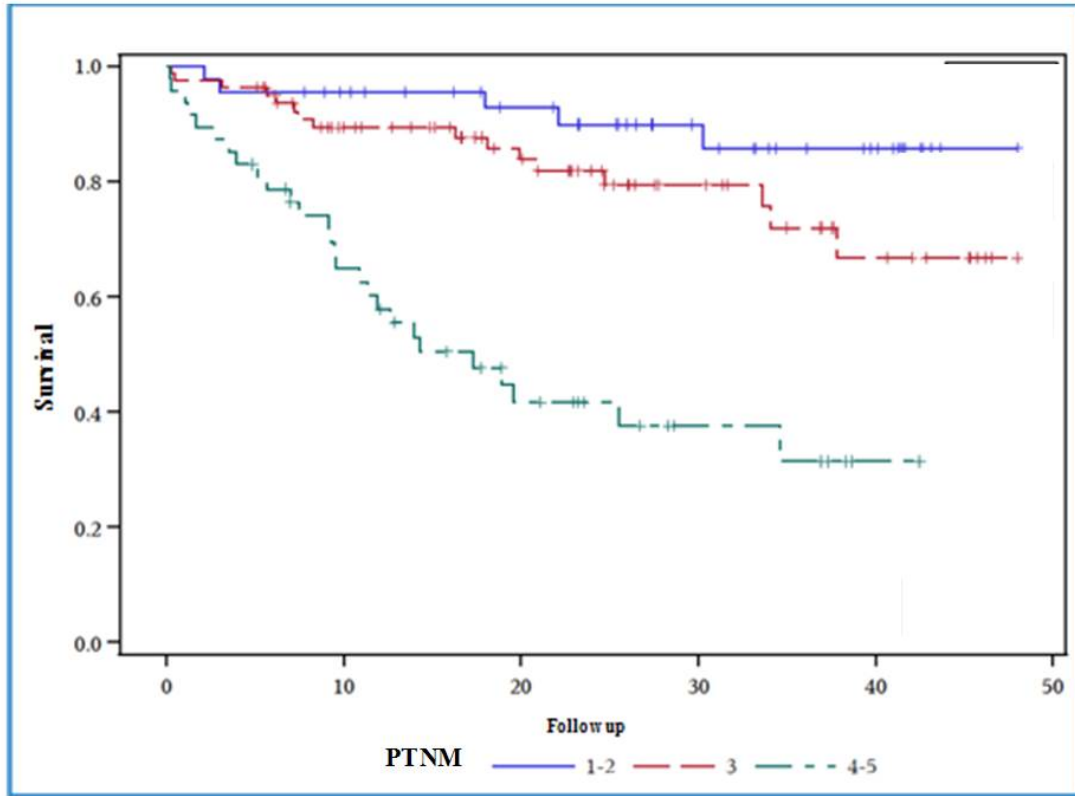


Fig. 3. Survival curves of overall survival according to PTNM ($p < 0.001$).

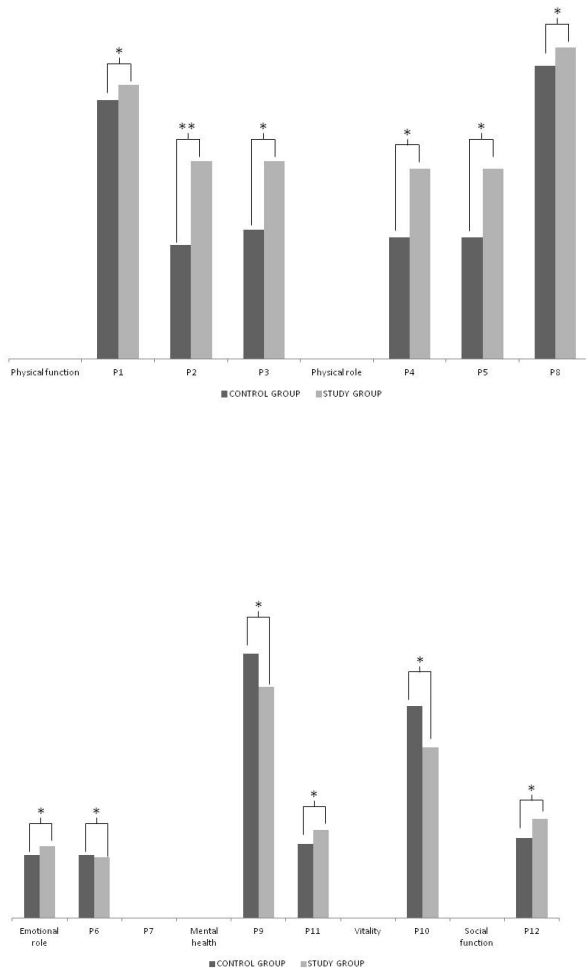


Fig. 4. A. Comparison of quality of life between groups using SF-12 test (physical health). *Not significant. ** $p = 0.0138$. B. Comparison of quality of life between groups using SF-12 test (mental health). *Not significant.