

Impact on Quality of Life of Patients with Surgical Treatment for Liver Metastases of Colorectal Cancer

Vicente M Borrego-Estella, Javier Montero-Martín, Irene Molinos-Arruebo, Joaquín F López-Marcos, María P Vicente-Galindo, Antonio López-Valverde, María P Galindo-Vicente, José M Ramia-Angel, María Pérez Sánchez-Cuadrado, Gabriel Inaraja-Pérez, José L Moyá-Andía, Sef Saudí-Moro, Jesús M Esarte-Muníaín, Alejandro Serrablo-Requejo

Vicente M Borrego-Estella, MD, PhD and Surgeon at the Hepatopancreatic biliary Surgical Unit, Department of General Surgery, Miguel Servet General University Hospital, Zaragoza, Spain

Javier Montero-Martín, PhD in Dentistry, Graduate in Odontology, Tenured Lecturer of Prosthodontics, Faculty of Medicine, University of Salamanca, Campus Miguel de Unamuno, Salamanca, Spain

Irene Molinos-Arruebo, Department of Anesthesia, Miguel Servet General University Hospital, Zaragoza, Spain

Joaquín F López-Marcos, MD, Assistant Professor, Department of Dentistry, School of Medicine, University of Salamanca, Salamanca, Spain

María P Vicente-Galindo, MD, Assistant Professor, Department of Biostatistics, School of Medicine, University of Salamanca, Salamanca, Spain

Antonio López-Valverde, MD, Assistant Professor, Department of Dentistry, School of Medicine, University of Salamanca, Salamanca, Spain

María P Galindo-Villardón, MD, PhD, Department of Biostatistics, School of Medicine, University of Salamanca, Salamanca, Spain

José M. Ramia-Angel, MD, PhD and Chief Surgeon Hepatobiliary and Pancreatic Surgical Unit, Department of General Surgery, Guadalajara General University Hospital, Guadalajara, Spain

Guillermo Pérez-Navarro, Department of Anesthesia, Miguel Servet General University Hospital, Zaragoza, Spain

María Pérez Sánchez-Cuadrado, MD, General Practitioner, Valladolid-Este, Valladolid, Spain

Gabriel Inaraja-Pérez, MD, PhD, Department of Vascular Surgery, Miguel Servet, General University Hospital, Zaragoza, Spain

José L Moyá-Andía, Surgeon at the Hepatopancreatic biliary Surgical Unit, Department of General Surgery, Miguel Servet General University Hospital, Zaragoza, Spain

Sef Saudí-Moro, Surgeon at the Hepatopancreatic biliary Surgical Unit, Department of General Surgery, Miguel Servet General University Hospital, Zaragoza, Spain

Jesús M Esarte-Muníaín, MD, PhD, Surgeon and Chief of Department of General Surgery, Miguel Servet General University Hospital, Zaragoza, Spain

Alejandro Serrablo-Requejo, MD, PhD and Surgeon at the Hepatopancreatic biliary Surgical Unit, Department of General Surgery, Miguel Servet General University Hospital, Zaragoza Spain

Correspondence: Vicente M Borrego-Estella, Hepatopancreatic biliary Surgical Unit, Department of General Surgery, Miguel

Servet General University Hospital, C/ Isabel la Católica 1-3, CP: 50009, Zaragoza, Spain. vicen1001@gmail.es

Telephone: +976765500 Ext. 1366

Received: June 9, 2012

Revised: July 23, 2012

Accepted: July 24, 2012

Published online: November 21, 2012

ABSTRACT

AIM: To assess the quality of life of patients with liver metastases from colorectal cancer, before and four weeks after surgery.

METHODS: From September 2008 to March 2009 we performed a study of prospective cohorts by means of a consecutive sampling of patients undergoing liver resection for colorectal metastases ($n=30$) and a positive control group ($n=30$) formed by accompanying persons (relatives of the patients). Both groups filled in SF-36 questionnaires before the intervention and at 4 weeks after surgery. The groups were compared before and after treatment, using Student's t test and a comparison of means in paired samples (paired t tests). We also calculated the effect of the intervention (effect size). ANOVA and Chi-squared tests were used to determine the modulating factors of the impact on quality of life.

RESULTS: Before treatment the patients had a better quality of life in all dimensions than after treatment and never attained that of the accompanying persons, either before or after treatment. The perception of pain was greater in the men but these showed a better mental wellbeing with respect to the women. The main effect of the intervention on the quality of life was perceived in the pain, mental and social dimensions.

CONCLUSION: Patients with liver metastases colorectal cancer the diagnosis and surgical treatment causes a decrease in their quality of life, above all in pain, mental and social SF-36 dimensions.

© 2012 Thomson research. All rights reserved.

Key words: Quality of life; Health-related quality of life; SF-36; Colorectal cancer; Liver metastases

Borrego-Estella VM, Montero-Martín J, Molinos-Arruebo I, López-Marcos JF, Vicente-Galindo MP, López-Valverde A, Galindo-Vicente MP, Ramia-Angel JM, Pérez Sánchez-Cuadrado M, Pérez-Navarro G, Moyá-Andía JL, Saudí-Moro S, Esarte-Muníaín JM,

Serrablo-Requejo A. Impact on Quality of Life of Patients with Surgical Treatment for Liver Metastases of Colorectal Cancer. *Journal of Gastroenterology and Hepatology Research* 2012; 1(10): 252-259 Available from: URL: <http://www.ghrmet.org/index./joghr/>

INTRODUCTION

Colorectal cancer (CRC) is third most frequent in men in developed countries (after lung and prostate tumors) and second among women (after breast cancer), with approximately one million new cases per year throughout the world (550 000 men and 470 000 women), representing 14.6% and 15.2% respectively, of all malignant tumors diagnosed^[1]. In Spain, CRC is the second most frequently diagnosed malignant neoplasm and the second cause of death due to malignant neoplasm^[1,2]. The role of colonoscopy in the screening of this pathology is crucial^[3]. When CRC presents as a disease affecting the intestine, it has a high rate of cure (45-50%) with radical surgery^[4-6]. The most frequent metastatic involvement in CRC, after ganglion invasion, is seen in the liver^[5,6]. Since Woodington and Waugh^[7] published the first favorable results concerning the surgical treatment of liver metastases originating in the colon/rectal region (colon/rectal-liver metastases: CLM) until now, survival at 5 years after surgery is 30-40% and 20-25% at 10 years^[1].

Although much is known about the epidemiology, prognostic factors and treatment of CLM^[5,8-11], nothing is known about the impact that surgery of liver metastases from colorectal cancer has on the QoL of these patients. Although there is no exact definition of QoL, according to WHO definition^[12] it is known that it is an abstract, subject-dependent perception about the degree of wellbeing that each subject feels in the different dimensions in which health is involved (emotional, social, pain, etc).

The most widely used generic questionnaires about the QoL are the Medical Outcomes Study (SF-36)^[13], see annex, the Sickness Impact Profile (SIP)^[14], the Psychological General Well-Being Index (PGWB)^[15,16], the Psychological Adjustment to Illness Scale (PAIS-SR)^[17] and the Nottingham Health Profile (NHP)^[18,19]. Despite this, there are other questionnaires addressing QoL with items aimed at detecting specific situations of clinical pictures, such as the FDDQL (Functional Digestive Disorders Quality of Life) proposed by Chassany *et al*^[20], the GIQLI (Gastrointestinal Quality of Life Index) described and validated by Eypasch *et al*^[21], the NDI (Nepean Dyspepsia Index) designed by Talley *et al*^[22], etc.

Nevertheless, the most widely used version of these indicators is the SF-36, which has a reduced version with only 12 items^[23-26] and which has recently been validated for the Spanish population^[27], but we used the SF-36 because is still the most widespread instrument.

Despite the clinical benefits of surgery, it is necessary to monitor patients as regards their wellbeing and satisfaction during both the pre-operative and peri-operative period and in the follow-up (immediate and late post-operative period). However, although there are studies that have used the SF-36 to study the QoL of patients with CRC^[28-30], as far as we are aware no studies have addressed the surgical treatment of liver metastases originating from CRC in terms of patient QoL.

METHODS

Design

This was a prospective observational study involving a consecutive sampling of 30 patients who since September 2008 to March 2009 had undergone liver resection as a result of CLM, with or without other concomitant treatments such as chemotherapy and/or radiotherapy. This test group was compared in terms of QoL with a positive control

group that was comparable in sociodemographic terms formed by people accompanying the patients who did not need either surgical or medical treatment and were similar in age (wife/husband, brother/sister, etc). These positive controls were hypothesized to suffer closely from the social or psychologic effect of the disease or treatment of the patient companion, but they are healthy.

To provide a national context for interpreting changes in health status following this surgery, patients' SF-36 scores were compared with the published norms for SF-36 for the Spanish population of the same age and sex^[31]. As the standard errors for the published norm scores were very small, the mean values of the normative scores were used to represent the "real" values for the population of each age and sex group.

The study was performed at the Miguel Servet General Hospital in Zaragoza, Spain, which is a third-level reference facility responsible for the health of 800 000 people.

The necessary sample size was estimated a priori at 30 subjects in order to have 90% power to detect differences of 10% between groups, with a level of significance of 5%.

The Test group ($n=30$) and the Control Group ($n=30$) were given a questionnaire addressing their QoL on two occasions: before patient surgery and at 4 weeks after the intervention.

The project was favorably assessed by the Bioethics Commission of the hospital and all participants received information as to the nature and aims of the project before providing consent.

Data acquisition

Data were collected from patients in whom surgery has been performed, with or without other treatments such as chemotherapy and radiotherapy. From the test group we collected sociodemographic data (age, sex), data concerning their neoplastic process [TNM classification (see annex), location of the colorectal tumor (colon, rectum)]; therapeutic data, such as the use or not of neoadjuvant chemo (initial resectability), reintervention, mean stay in hospital, survival and post-operative complications [we considered as "major" complications (grades III and IV of the classification of Clavien and Dindo^[32]) post-operative bleeding, biliary fistulas and intra-abdominal abscesses, while minor complications (grades I and II of the classification of Clavien and Dindo) were febrile syndrome, surgical wound infection, nosocomial pneumonia and post-operative ileus. Regarding the control group, we only collected sociodemographic data (age and sex) before the participants completed the questionnaires.

Impact on quality of life according to the SF-36 questionnaire.

To assess the impact on QoL we used a self-completed indicator previously validated in the Spanish population; namely, the Medical Outcomes Study, or SF-36^[27].

The advantage of the SF-36 is its demonstrated psychometric capacity, its applicability and its multinational validity. Thus, it is considered as the gold standard in the estimation of the general QoL^[29, 33].

The SF-36 has 32 items with replies in a Likert format grouped conceptually in 8 dimensions: 4 physical (physical function, occupational role activity, pain and perception of health) and 4 mental (vitality, social function, emotional activity and mental wellbeing).

The scoring system used transforms the Likert replies into a value between 0 and 100, 0 representing the least favorable reply and 100 the reply indicating the greatest wellbeing. In the multiresponse items, the values between 0 and 100 must be equidistant (for example, 0, 25, 50, 75, 100). This transformation allows a more intuitive value of overall or dimensional health to be obtained and has been used successfully in previous studies^[34,37].

Table 1 Sociodemographic and clinical description of the Test Group (n=30).

VARIABLES	n (x±sd)	n (%)
Sociodemographic factors		
Age	30 (66.57±10.08)	
Sex	Man	19 (63.3%)
	Woman	11 (36.7%)
Surgery-dependent factors		
Mortality	No	30 (100%)
	yes	0 (0%)
Morbidity	No	16 (53.3%)
	Minor complications	11 (36.7%)
	Major complications	3 (10%)
Reintervention	No	29 (96.7%)
	Yes	1 (3.3%)
Mean stay (days)	30 (12.87±7.14)	
Initial resectability	No	11 (36.7%)
	Yes	19 (63.3%)
Factors dependent upon the primary CRC tumour		
Location	Colon	23 (76.7%)
	Rectum	7 (23.3%)
Initial size of CCR (according to TNM classification)	T3	18 (60%)
	T4	12 (40%)
Ganglion affectation of CCR (according to TNM classification)	N0	4 (13.3%)
	N1	20 (66.7%)
	N2	6 (20%)
Metastatic affectation of CRC (according to TNM classification)	Synchronous liver metastases or M0	14 (46.7%)
	Metachronic liver metastases or M1	16 (53.3%)

v15. Chigago, IL), considering a *p* value of <0.05 as statistically significant.

RESULTS

The mean age of our patients (Table 1) was 66.57±10.85 years. The proportion of men with respect to women was almost double, (63.3 vs. 36.7). Regarding the location of the primary CRC, the primary location in the colon was 76.7% vs. 23.3% with a rectal location. At the start, 36.7% of patients were not resectable. The mean stay of the patients was 12.87±7.14 d. 46.7% of the patients had some kind of complication after surgery (minor complications 36.7% and major ones 10%).

A comparison of the mean scores of the SF-36 in the patients and accompanying persons before and after surgery is shown in table 2. Strikingly, before treatment the patients were more affected in the physical-occupational role and health dimensions with respect to the accompanying persons, but had better mental and emotional wellbeing than them. The emotional dimension was the only one in which after treatment the patients continued to enjoy better comparative wellbeing. The main dimensions affected after treatment were the occupational role and pain dimensions (Table 2). The dimensions worst valued by both the patients and accompanying persons were general health, mental health and vitality, on average scoring below the wellbeing mean (a value of 50). The effect of surgery was strong on the pain, mental and social dimensions of the patients and was weak on the social dimension of the accompanying person (Table 3). Both the patient and the control group scored significantly lower among all SF-36 subscales than the reference population-based scores (Figure 1).

Table 2 Comparison of the QoL of patients and accompanying persons before and after surgery.

Total Score among dimensions of the SF-36 health questionnaire	Patients pre-treatment score n= 30	Accompanyng persons pre-treatment score n= 30	Comparison of patients and accompanying persons before treatment (p-value)	Patients post-treatment score n= 30	Accompanyng persons post-treatment score n= 30	Comparison of patients and accompanying persons after treatment (p-value)
Physical	55.54±24.66	66.32±27.62	-10.78 (p=0.12)	48.48±22.42	66.44±27.43	-17.99 (p<0.01)
Role	0	75.55±41.28	-75.55 (p<0.00)	0	67.22±39.99	-67.22 (p<0.00)
Pain	47.92±18.59	56.67±27.41	-8.75 (p=0.15)	22.50±15.18	56.67±27.41	-34.17 (p<0.00)
Health	22.11±5.46	42.05±11.40	-19.94 (p<0.00)	18.61±5.38	41.22±11.74	-22.61 (p<0.00)
Vitality	41.05±5.65	44.11±15.44	-3.06 (p=0.32)	38.77±5.25	41.50±12.94	-2.72 (p=0.29)
Social	51.25±13.27	57.08±25.57	-5.83 (p=0.27)	41.25±13.19	48.75±21.11	-7.50 (p=0.10)
Emotional	63.89±41.07	19.44±29.06	44.44 (p<0.00)	49.44±35.69	15.56±23.95	33.89 (p<0.00)
Mental	45.50±3.41	40.63±11.95	4.86 (p=0.04)	42.10±5.48	40.73±10.15	1.37 (p=0.52)

Statistical analyses

To compare the mean QoL score between the test and control groups, we used Student’s *t* test. To assess the effect of the intervention (ES = effect size), on the QoL score we used the procedure recommended by Kazis^[38], in which the total score of the post-treatment groups is subtracted from that of the pre-treatment group and is divided by the standard deviation of the pre-treatment scores, using Student’s *t* test for paired samples. The ES provides a coefficient that reflects the effect size as small (<0.5), moderate (0.5-0.8) and high (>0.8).

We used an ANOVA test to compare the mean of the items of the dimensions of the patients as regards the value of the TNM classification of CRC and a Chi-squared test to compare the proportion of subjects who scored >50 according to the coding of the Likert scale as a function of having received neoadjuvant chemo or not.

All analyses were performed using the SPSS™ statistical package version 15.0 (Statistical Package for the Social Sciences

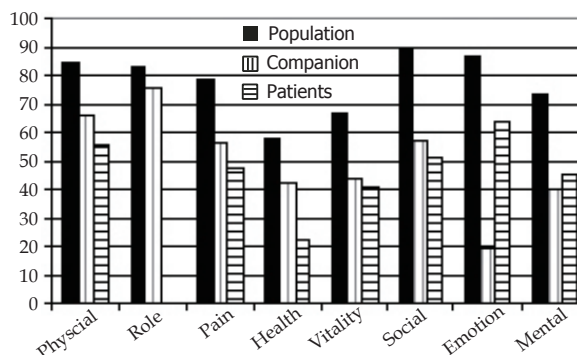


Figure 1 Comparison of the SF-36 subscales of the patient and companion groups (pretreatment scores) with population norms.

Some modulating factors have been found. Regarding sex (Table 4), the men perceived more pain than the women (p<0.05), although they perceived greater mental wellbeing (p<0.05) according to the initial assessment of their QoL. Regarding age (≤65 years vs. <65 year) no

Table 3 Effect of surgery on the QoL of the patients (n=30) and accompanying persons (n=30).

Groups	Dimensions	Pre-operative Mean Value (sd)	Post-operative Mean Value (sd)	Mean differences# (sd)	p-value	Effect Size
Patients	Physical Role	55.5 (24.7)	48.5 (22.4)	7.1 (10.0)	0.001	0.29
	Pain	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	1.0	0.0
	Health	47.9 (18.6)	22.5 (15.2)	25.4 (22.4)	0.000	1.37
	Vitality	22.1 (5.5)	18.6 (5.4)	3.5 (5.1)	0.001	0.64
	Social	41.1 (5.7)	38.8 (5.3)	2.3 (4.3)	0.008	0.40
	Emotion	51.3 (13.3)	41.3 (13.2)	10.0 (12.9)	0.000	0.75
	Mental	63.9 (41.1)	49.4 (35.7)	14.4 (24.7)	0.003	0.35
		45.5 (3.4)	42.1 (5.5)	3.4 (5.7)	0.003	1.00
Accompanying persons	Physical Role	66.3 (27.6)	66.4 (27.4)	-0.1 (1.4)	0.64	0.00
	Pain	75.6 (41.3)	67.2 (40.0)	8.3 (17.8)	0.02	0.20
	Health	56.7 (27.4)	56.7 (27.4)	0.0 (0.0)	1.0	0.00
	Vitality	42.1 (11.4)	41.2 (11.7)	0.8 (2.0)	0.03	0.07
	Social	44.1 (15.4)	41.5 (12.9)	2.6 (5.7)	0.02	0.17
	Emotion	57.1 (25.6)	48.8 (21.1)	8.3 (14.4)	0.004	0.32
	Mental	19.4 (29.1)	15.6 (24.0)	3.9 (15.0)	0.17	0.13
		40.6 (12.0)	40.7 (10.2)	-0.1 (4.8)	0.91	0.00

Mean differences come from preoperative values-postoperative values; p-values obtained from paired t-tests.

Table 4 Odulating factors of QoL in patients pre-treatment scores.

Total Score among dimensions of the SF-36 health questionnaire	Patient Comparison By Sex:			Patient Comparison By Age:			Patient Comparison By Crc Location :		
	Women n=11	Men n=19	p	≥65 Years n=18	<65 Years n=12	p	Colon n=23	Rectum n=7	p
Physical Role	59.20±27.39	53.42±23.45	NS	50.49±23.51	63.12±25.87	NS	55.27±24.86	56.43±25.93	NS
Pain	0	0	NS	0	0	NS	0	0	NS
Health	55.68±6.53	43.42±21.80	p<0.05	45.14±21.06	52.08±13.93	NS	46.19±18.24	53.57±20.04	NS
Vitality	23.94±5.66	21.05±5.19	NS	22.36±6.24	21.74±4.24	NS	23.26±5.08	18.33±5.24	p<0.05
Social	42.42±7.28	40.26±4.49	NS	40.65±5.43	41.67±6.15	NS	41.08±5.97	40.95±4.80	NS
Emotional	54.54±12.84	49.34±13.48	NS	53.47±14.10	47.92±11.72	NS	50.00±13.05	55.35±14.17	NS
Mental	54.54±45.39	69.30±38.59	NS	62.04±41.15	66.67±42.64	NS	63.77±43.71	64.29±33.92	NS
	43.91±4.21	46.42±2.54	p<0.05	45.72±3.59	45.17±3.24	NS	45.82±2.76	44.42±5.16	NS

significant differences were found in any dimension. In the location of the primary colorectal tumor the differences in pretreatment scores between colon and rectum only reflected significant differences as regards the general health perceived (Table 5). With respect to the TNM classification, there were no significant differences as regards the effect of tumor size, ganglion involvement or synchronous/metachronic liver metastases.

Regarding the comparison of the dimensions of the patients in the scores of the possibility of initial resectability (without neoadjuvant chemo) according to the Chi-squared statistical test, it was observed that the percentage of patients suffering from social impact was significantly greater (81.8%) in those who had received neoadjuvant chemo than in those undergoing surgery directly (42.1%).

DISCUSSION

This study aimed to assess the quality of life of patients needing surgical treatment for liver metastases deriving from colorectal cancer, before and 4 weeks after surgery. For that purpose, we used the Spanish version of a widely used and nationally^[39-41] and internationally^[42-44] accepted questionnaire. However, some limitations of the study should be acknowledged. Although the size of the sample seemed to be sufficient to satisfy the exploratory aims of the study, it is smaller than in other series such as those performed on breast cancer^[25,45,46] and presumably it would have been possible to detect significant differences in some comparisons in which we

Table 5 Comparison of pre-treatment scores according to the location of the CRC tumor in patients.

Total Score Among dimensions of The SF-36 health questionnaire	Patient comparison by crc Location:		
	Colon n=23	Rectum n=7	p
Physical Function Dimension (Items 3-12)	55.27±24.86	56.43±25.93	NS
Physical Role-Occupational Dimension (Items 13-16)	0	0	NS
Pain Dimension	46.19±18.24	53.57±20.04	NS
Health Dimension (Items 1-2, 33-36)	23.26±5.08	18.33±5.24	p<0.05
Vitality Dimension (Items 23, 27, 29 And 31)	41.08±5.97	40.95±4.80	NS
Social Dimension (Items 20 And 32)	50.00±13.05	55.35±14.17	NS
Emotional Dimension (Items 17-19)	63.77±43.71	64.29±33.92	NS
Mental Wellbeing Dimension (Items 24-26, 28, 30)	45.82±2.76	44.42±5.16	NS

only observed a certain trend. Future efforts of the research team should be directed towards collecting more patients treated according to distinct protocols. However, the longitudinal design of this project legitimizes the assessment of the intra-subject changes in terms of QoL, increasing the level of evidence of the findings detected after the intervention.

The follow-up period (4 weeks), although short, seemed to be sufficient to detect immediate variations in QoL during the immediate post-operative period, in agreement with other authors in the use of colonoscopy as a screening method in CRC^[3,47]. We hypothesized that the shorter recall period the more sensitive to recent changes in wellbeing. Nevertheless, this monitoring period was insufficient to observe a normalization of QoL patients. Table 3 showed that all patient scores decrease after surgery, which indicate that they are in fact still recovering from their surgery at the time of assessment. Therefore authors acknowledged that assessments were made too soon after surgery and for this reason, we earnestly recommend to monitor changes in QoL after surgery using a greater follow-up periods. Other authors^[44] have used very long follow-up times in patients with different types of cancer or pathological conditions^[29,30,48-53], or have simply handed out the questionnaire only once^[54-61].

Another debating issue is related to the control group used. Incorporating adequate controls is an essential part of the design of scientific investigations. For this study we have used a positive control instead of a negative control group. A negative control group

negative control (baseline value of the HQoL) should be comprised by healthy persons matched to the patients by age and socioeconomic status and municipality, but with no direct relationships to the patient (in our case we used the reference values of the Spanish adult population, figure 1). However we have focussed our comparisons on a positive control group to isolate the effect of the physical consequences of the disease and the surgical treatment (i.e. physical functioning, role physical, Bodily Pain and General Health dimensions of the SF-36). Because it was checked that the mental health dimensions (Vitality, Social, Emotional and Mental Health) could also be as disturbed in Test than in the positive controls. Table 2 and figure 1 captured this finding. Other quality of life research have used healthy accompanying persons as positive controls^[62]. Otherwise, the differences between patients and negative controls are much higher in all domains than that reported for the positive controls (Figure 1).

The mean age and distribution by sexes of our series are consistent with all current literature reporting fairly similar epidemiological data^[1,2]. Although the influence of age and sex would require a larger sample size for a statistically significant effect to be detected, this study supports the tendency to observe a better physical function in subjects younger than 65 than in older patients (Table 4). Likewise, sex seems to affect the pain and mental health dimension, although in view of the small sample size and the exploratory aims of this study no linear and logistic regression analysis controlling potential factors was conducted.

Regarding the location of the primary CRC (colon or rectum) the pattern observed in our series is in agreement with the current literature^[1,2,63,64]. We made this subdivision for three reasons; first, because the surgical approach to some of these patients made it necessary to take into account that in the case of the distal-most tumors (rectal) in certain types of surgery if the anastomosis or colorectal union is very close to the anus it is necessary to perform an ostomy (ileostomy or colostomy) for protective purposes, which—later— must be closed as soon as possible in a second intervention owing to patient dissatisfaction^[64,65]. This ostomy may sometimes affect the QoL of many patients negatively, but its clinical usefulness is good owing to the risk of dehiscence or anastomotic leakage in these patients^[29,53]. Second, we made the subdivision because in the case of very low rectal tumors affecting sphincters it is necessary to perform an abdominoperineal amputation or a Miles intervention; that is, a highly mutilating intervention for the patient, who then becomes the bearer of a colostomy with no possibility of future closure^[49,51,60]. Finally, we divided the colon from the rectum patients because according to some authors^[11,28] tumors in the latter location seem to have a poorer prognosis, affecting the QoL of the patients. In our patients reflected significant differences as regards the general health perceived better in the group of colon location (Table 5).

The 46.7% of the patients in our series had some kind of complication after surgery. However, these did not excessively affect the time spent in hospital by the patients who underwent liver resection, since they were mainly minor complications.

Regarding the patients and accompanying persons pretreatment, the results indicate that at mental or emotional level an accompanying person may suffer even more than the patient (Table 3 and Figure 1). Moreover looking at the results for the healthy controls (Table 3) it is shown that levels of role functioning and social functioning significantly decrease, whereas the other domains don't. It seems that this may be due to the fact that they are looking after their partner who has just had surgery, and they have been restricted in their normal functioning roles. In this sense, it would be interesting

to incorporate programs offering home assistance for patients in the immediate post-operative period so as to minimize the load on the family environment.

Between the patients before and after the treatment we observed significant differences that suggest that before the intervention the patients had a better QoL in the mental and emotional dimensions than after the liver resection. As expected, in the post-operative period the accompanying persons had a much better QoL than the patients. Thus, in the immediate post-operative period this intervention generates an overall deterioration of the QoL, especially in terms of perceived pain (Table 3), although also at mental level and in the perception of general health. Such effects are probably even attenuated, since the perception of the internal standards of the quality of life may be affected to an appreciable extent in patients who have undergone liver resection because of the occurrence of the so-called beta changes after surgery^[66]. In fact, controls also underwent some type of change in the internal standards of QoL when living in close contact with a family patient (beta change), and scored significantly lower than the reference healthy Spanish population (Figure 1).

With the limitations of this study we only could ensure that QoL of patients treated surgically of liver metastasis from CLM are significantly worse than the positive controls (family companions) during the immediate postoperative period (4 weeks). However, the detrimental effect on quality of life among patients along this short term follow-up period could be due to the disease itself, or to the concomitant medical treatment or the postsurgery recovery; but the heterogeneous nature of the Test group of this study does not allow to clarify this issue.

Regarding the TNM classification, no significant differences were observed between the QoL of either group (results not shown). However, bearing in mind the sample size, our results could perhaps be considered limited.

Thus, according to the present results it is possible that not so much importance should be given to factors such as the TNM classification, the location of the primary colorectal tumor, etc; instead, we should worry more about the factors involved in the restoration of a QoL comparable to that of the general population. In this sense, it should be noted that the patients who received neoadjuvant chemotherapy to facilitate the later liver surgery suffered a greater impact on their QoL than the rest, especially at social level. It is possible that the effects of chemo on patients (such as immunosuppression, alopecia, etc) and the increase in the number of visits to the hospital required by intravenous medication negatively affect the QoL. In this regard, some authors^[50,67] recommend a more widespread use of oral courses over intravenous administration for CRC with a view to alleviating the therapeutic impact on these patients.

Further multicentre studies following different therapeutic approaches, but using the same QoL indicators, are necessary to check the cost-benefit of the different clinical protocols on the different pathologies as regards the QoL. Assessments with longer follow-up times should be carried out with a view to configuring the curves of the impact on wellbeing of the surgical interventions.

CONCLUSIONS

The diagnosis of CLM and their surgical treatment are stressful events leading to deterioration in patient QoL. After liver resection, patients perceive a poorer QoL and the strongest effect is seen in the pain and mental dimensions. At four week's follow-up, the QoL of the patients does not reach the values seen in the positive control group.

The sex of the patients and neoadjuvant chemo are modulating factors per se of perceived wellbeing. However, age and the location and TNM classification of the initial CRC do not seem to be factors modulating the QoL of our patients.

ACKNOWLEDGMENTS

Authors acknowledge to the reviewers of this manuscript for the insights shared during the revision process. This study was funded in part by the Department of Surgery of the University of Salamanca where the first author worked as a postgraduate student developing research under the guidance and supervision of the second author. Authors are so grateful with the General Surgery Department of the Miguel Servet General University Hospital (Zaragoza, Spain) because of the effective involvement on the practical issues of this project. Nevertheless this Hospital did not influence the design, analysis or interpretation of the data.

Authors' contributions: Borrego-Estella VM and Montero-Martín J contributed equally to this work; Borrego-Estella VM participated in design of the study, data acquisition and helped to draft the manuscript; Montero-Martín J conceived and coordinated the study, helped to draft the manuscript and performed the statistical analysis; Molinos-Arruebo I and López-Marcos JF has been involved in drafting the manuscript; Pérez Sánchez-Cuadrado M, Inaraja-Pérez G and the revisions; López-Valverde A has made substantial contributions to the manuscript and participated in data acquisition and helped to draft the manuscript. Vicente-Galindo MP and Galindo-Villardón MP have made substantial contributions to the interpretation of data and data analysis; Ramia-Angel JM participated in data acquisition and helped to draft the manuscript has been involved in drafting the manuscript; Pérez-Navarro G and Moyá-Andía JL, participated in data acquisition and helped to draft the manuscript; Saudí-Moro S and Esarte-Munía JM has made substantial contributions to the manuscript and participated in data acquisition and helped to draft the manuscript and the revisions.

REFERENCES

- Borrás JM, Borrás J, Viladiu P, Bosch FX. Epidemiología y prevención del cáncer en España 1975-2002. Barcelona: Servei Català de la Salut, Departament de Sanitat i Seguretat Social, Generalitat de Catalunya 2004; 1-22
- Ardanaz E, Moreno-Iribas C, Pérez de Rada ME, Ezponda C, Floristán Y, Navaridas N, Martínez-Peñuela JM, Puras A, Santamaría M, Ezpeleta I, Valerdi JJ, Pardo FJ, Monzón FJ, Lizarraga J, Ortigosa C, Resano J, Barricarte A. Incidence and mortality due to cancer in Navarre, 1998-2002. Trends in the last 30 years. *An Sist Sanit Navar* 2001; **30**: 245-270
- Corbett M, Chambers SL, Shadbolt B, Hillman LC, Taupin D. Colonoscopy screening for colorectal cancer: the outcomes of two recruitment methods. *Med J Aust* 2004; **181**: 423-427
- Winawer SJ, Zauber AG, Ho MN, O'Brien MJ, Gottlieb LS, Sternberg SS, Wayne JD, Schapiro M, Bond JH, Panish JF. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med* 1993; **329**: 1977-1981
- Adam R, Avisar E, Ariche A, Giachetti S, Azoulay D, Castaing D, Kunstlinger F, Levi F, Bismuth F. Five-year survival following hepatic resection after neoadjuvant therapy for nonresectable colorectal. *Ann Surg Oncol* 2001; **8**: 347-353
- Giachetti S, Itzhaki M, Gruia G, Adam R, Zidani R, Kunstlinger F, Brienza S, Alafaci E, Bertheault-Cvitkovic F, Jasmin C, Reynes M, Bismuth H, Misset JL, Lévi F. Long-term survival of patients with unresectable colorectal cancer liver metastases following infusional chemotherapy with 5-fluorouracil, leucovorin, oxaliplatin and surgery. *Ann Oncol* 1999; **10**: 663-669
- Woodington GF, Waugh JM. Results of resection of metastatic tumors of the liver. *Am J Surg* 1963; **105**: 24-29
- Tanaka K, Shimada H, Ueda M, Matsuo K, Endo I, Togo S. Role of hepatectomy in treating multiple bilobar colorectal cancer metastases. *Surgery* 2008; **143**: 259-270
- Bennett JJ, Schmidt CR, Klimstra DS, Grobmyer SR, Ishill NM, D'Angelica M, DeMatteo RP, Fong Y, Blumgart LH, Jarnagin WR. Perihepatic lymph node micrometastases impact outcome after partial hepatectomy for colorectal metastases. *Ann Surg Oncol* 2008; **15**: 1130-1136
- Marín C, Robles R, Pérez D, López A, Parrilla P. Prognostic factors after resection of colorectal cancer liver metastases. *Cir Esp* 2009; **85**: 32-39.
- Figueras J, Torras J, Valls C, Llado L, Ramos E, Marti-Ragué J, Serrano T, Fabregat J. Surgical resection of colorectal liver metastases in patients with expanded indications: a single-center experience with 501 patients. *Dis Colon Rectum* 2007; **50**: 478-488
- WHO. Study protocol for the World Health Organization project to develop a Quality of Life assessment instrument (WHOQOL). *Qual Life Res* 1993; **2**: 153-159.
- Stewart AL, Greenfield S, Hays RD, Wells K, Rogers WH, Berry SD, McGlynn EA, Ware JE. Functional status and well-being of patients with chronic conditions. Results from the Medical Outcomes Study. *JAMA* 1989; **262**: 907-913
- Bergner M, Bobbitt RA, Pollard WE, Martin DP, Gilson BS. The sickness impact profile: validation of a health status measure. *Med Care* 1976; **14**: 57-67
- Dupuy HJ. The Psychological General Well-Being (PGWB) Index. In: Wenger NK, Mattson ME, Furberg CF, Elinson J, editors. Assessment of quality of life in clinical trials of cardiovascular therapies. *Atlanta: Le Jacp* 1984: 170-183.
- Wiklund I, Glise H, Jerndal P, Carlsson J, Talley NJ. Does endoscopy have a positive impact on quality of life in dyspepsia? *Gastrointest Endosc* 1998; **47**: 449-454
- Derogatis LR. The psychosocial adjustment to illness scale (PAIS). *J Psychosom Res* 1986; **30**: 77-91
- Hunt SM, McKenna SP, McEwen J, Williams J, Papp E. The Nottingham Health Profile: subjective health status and medical consultations. *Soc Sci Med A* 1981; **15**: 221-229
- Alonso J, Prieto L, Antó JM. The Spanish version of the Nottingham Health Profile: a review of adaptation and instrument characteristics. *Qual Life Res* 1994; **3**: 385-393
- Chassany O, Marquis P, Scherrer B, Read NW, Finger T, Bergmann JF, Fraitag B, Geneve J, Caulin C. Validation of a specific quality of life questionnaire for functional digestive disorders. *Gut* 1999; **44**: 527-533
- Eypasch E, Williams JI, Wood-Dauphinee S, Ure BM, Schmülling C, Neugebauer E, Troidl H. Gastrointestinal Quality of Life Index: development, validation and application of a new instrument. *Br J Surg* 1995; **82**: 216-222
- Talley NJ, Verlinden M, Jones M. Validity of a new quality of life scale for functional dyspepsia: a United States multicenter trial of the Nepean Dyspepsia Index. *Am J Gastroenterol* 1999; **94**: 2390-2397
- Wu CL, Naqibuddin M, Rowlingson AJ, Lietman SA, Jermyn RM, Fleisher LA. The effect of pain on health-related quality of life in the immediate postoperative period. *Anesth Analg* 2003; **97**: 1078-1085
- Chiaffarino F, Parazzini F, Lavezzari M, Giambanco V. Impact of urinary incontinence and overactive bladder on quality of life. *Eur Urol* 2003; **43**: 535-538
- Cervera S, Aubá E. Calidad de vida y dinámica familiar tras el diagnóstico de cáncer de mama. *Boletín de Psicología* 2005; **85**: 7-29
- Vilagut G, Valderas JM, Ferrer M, Garin O, López-García E,

- Alonso J. Interpretation of SF-36 and SF-12 questionnaires in Spain: physical and mental components. *Med Clin (Barc)* 2008; **130**: 726-735
- 27 Alonso J, Prieto L, Antó JM. The Spanish version of the SF-36 Health Survey (the SF-36 health questionnaire): an instrument for measuring clinical results. *Med Clin (Barc)* 1995; **104**: 771-776
- 28 Anthony T, Hynan LS, Rosen D, Kim L, Nwariaku F, Jones C, Sarosi G. The association of pretreatment health-related quality of life with surgical complications for patients undergoing open surgical resection for colorectal cancer. *Ann Surg* 2003; **238**: 690-696
- 29 Camilleri-Brennan J, Ruta DA, Steele RJ. Patient generated index: new instrument for measuring quality of life in patients with rectal cancer. *World J Surg* 2002; **26**: 1354-1359
- 30 Mosconi P, Apolone G, Barni S, Secondino S, Sbanotto A, Filiberti A. Quality of life in breast and colon cancer long-term survivors: an assessment with the EORTC QLQ-C30 and SF-36 questionnaires. *Tumori* 2002; **88**: 110-116
- 31 Alonso J, Regidor E, Barrio G, Prieto L, Rodríguez C, de la Fuente L. Population reference values of the Spanish version of the Health Questionnaire SF-36. *Med Clin (Barc)* 1998; **111**: 410-416
- 32 Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009; **250**: 187-196
- 33 Apolone G, Filiberti A, Cifani S, Ruggiata R, Mosconi P. Evaluation of the EORTC QLQ-C30 questionnaire: a comparison with SF-36 Health Survey in a cohort of Italian long-survival cancer patients. *Ann Oncol* 1998; **9**: 549-557
- 34 Camfield CS, Camfield PR. Juvenile myoclonic epilepsy 25 years after seizure onset: a population-based study. *Neurology* 2009; **73**: 1041-1045
- 35 Coroneos CJ, Mastracci TM, Barlas S, Cinà CS. The effect of thoracoabdominal aneurysm repair on quality of life. *J Vasc Surg* 2009; **50**: 251-255
- 36 Blomstrand A, Björkelund C, Ariai N, Lissner L, Bengtsson C. Effects of leisure-time physical activity on well-being among women: a 32-year perspective. *Scand J Public Health* 2009; **37**: 706-712
- 37 Coyne KS, Sexton CC, Thompson CL, Milsom I, Irwin D, Kopp ZS, Chapple CR, Kaplan S, Tubaro A, Aiyer LP, Wein AJ. The prevalence of lower urinary tract symptoms (LUTS) in the USA, the UK and Sweden: results from the Epidemiology of LUTS (EpiLUTS) study. *BJU Int* 2009; **104**: 352-360
- 38 Kazis LE, Anderson JJ, Meenan RF. Effect sizes for interpreting changes in health status. *Med Care* 1989; **27**: S178-S189
- 39 Sierra-Montenegro E, Fernández-Rivero JM, Villanueva-Sáenz E, Peña-Ruiz Esparza JP, Martínez-Hernández Magro P, Solo-Quirino R. Quality of life after restorative proctocolectomy with ileo-anal J pouch in patients with ulcerative colitis. *Cir Cir* 2007; **75**: 449-452
- 40 Luis DA, Izaola O, Prieto R, Mateos M, Aller R, Cabezas G, Rojo S, Terroba C, Martín T, Cuéllar L. Effects of a diet with products in texture modified diets in elderly ambulatory patients. *Nutr Hosp* 2009; **24**: 87-92
- 41 Zaragoza J, Lugli-Rivero Z. Development and validation of a quality of life questionnaire for patients with chronic respiratory disease (CV-PERC): preliminary results. *Arch Bronconeumol* 2009; **45**: 81-86
- 42 Hopman WM, Coo H, Pavlov A, Day AG, Edgar CM, McBride EV, Brunet DG. Multiple sclerosis: change in health-related quality of life over two years. *Can J Neurol Sci* 2009; **36**: 554-561
- 43 Sonn GA, Sadetsky N, Presti JC, Litwin MS. Differing perceptions of quality of life in patients with prostate cancer and their doctors. *J Urol* 2009; **182**: 2296-2302
- 44 Lazovich D, Robien K, Cutler G, Virnig B, Sweeney C. Quality of life in a prospective cohort of elderly women with and without cancer. *Cancer* 2009; **115**: 4283-4297
- 45 Psychological response to mastectomy. A prospective comparison study. Psychological aspects of Breast Cancer Study Group. *Cancer* 1987; **59**: 189-196
- 46 Vinokur AD, Threatt BA, Vinokur-Kaplan D, Satariano WA. The process of recovery from breast cancer for younger and older patients. Changes during the first year. *Cancer* 1990; **65**: 1242-1254
- 47 Kröz M, Büssing A, von Laue HB, Reif M, Feder G, Schad F, Girke M, Matthes H. Reliability and validity of a new scale on internal coherence (ICS) of cancer patients. *Health Qual Life Outcomes* 2009; **7**: 59
- 48 Wuthrich P, Gervaz P, Ambrosetti P, Soravia C, Morel P. Functional outcome and quality of life after restorative proctocolectomy and ileo-anal pouch anastomosis. *Swiss Med Wkly* 2009; **139**: 193-197
- 49 Fazio VW, Zutshi M, Remzi FH, Parc Y, Ruppert R, Fürst A, Celebrezze J, Galanduk S, Orangio G, Hyman N, Bokey L, Tietz E, Kirchdorfer B, Medich D, Tietze M, Hull T, Hammel J. A randomized multicenter trial to compare long-term functional outcome, quality of life, and complications of surgical procedures for low rectal cancers. *Ann Surg* 2007; **246**: 481-48
- 50 Kopec JA, Yothers G, Ganz PA, Land SR, Cecchini RS, Wieand HS, Lembersky BC, Wolmark N. Quality of life in operable colon cancer patients receiving oral compared with intravenous chemotherapy: results from National Surgical Adjuvant Breast and Bowel Project Trial C-06. *J Clin Oncol* 2007; **25**: 424-430
- 51 Bretagnol F, Rullier E, Laurent C, Zerbib F, Gontier R, Saric J. Comparison of functional results and quality of life between intersphincteric resection and conventional coloanal anastomosis for low rectal cancer. *Dis Colon Rectum* 2004; **47**: 832-838
- 52 Camilleri-Brennan J, Steele RJ. Prospective analysis of quality of life and survival following mesorectal excision for rectal cancer. *Br J Surg* 2001; **88**: 1617-1622
- 53 O'Leary DP, Fide CJ, Foy C, Lucarotti ME. Quality of life after low anterior resection with total mesorectal excision and temporary loop ileostomy for rectal carcinoma. *Br J Surg* 2001; **88**: 1216-1220
- 54 Krouse RS, Herrinton LJ, Grant M, Wendel CS, Green SB, Mohler MJ, Baldwin CM, McMullen CK, Rawl SM, Matayoshi E, Coons SJ, Hornbrook MC. Health-related quality of life among long-term rectal cancer survivors with an ostomy: manifestations by sex. *J Clin Oncol* 2009; **27**: 4664-4670
- 55 Conklin A, Hassan I, Chua HK, Wietfeldt ED, Larson DR, Thomsen KA, Nivatvongs S. Long-term functional and quality of life outcomes of patients after repair of large perianal skin defects for Paget's and Bowen's disease. *J Gastrointest Surg* 2009; **13**: 951-955
- 56 Ko CY, Rusin LC, Schoetz DJ, Moreau L, Collier JC, Murray JJ, Roberts PL, Marcello PW. Long-term outcomes of the ileal pouch anal anastomosis: the association of bowel function and quality of life 5 years after surgery. *J Surg Res* 2001; **98**: 102-107
- 57 Barton JG, Paden MA, Lane M, Postier RG. Comparison of postoperative outcomes in ulcerative colitis and familial polyposis patients after ileoanal pouch operations. *Am J Surg* 2001; **182**: 616-620
- 58 Burgdorf SK, Fischer A, Myschetzky PS, Munksgaard SB, Zocca MB, Claesson MH, Rosenberg J. Clinical responses in patients with advanced colorectal cancer to a dendritic cell based vaccine. *Oncol Rep* 2008; **20**: 1305-1311
- 59 Ripetti V, Ausania F, Bruni R, Campoli G, Coppola R. Quality of life following colorectal cancer surgery: the role of alexithymia. *Eur Surg Res* 2008; **41**: 324-330
- 60 Jess P, Christiansen J, Bech P. Quality of life after anterior resection versus abdominoperineal extirpation for rectal

- cancer. *Scand J Gastroenterol* 2002; **37**: 1201-1204
- 61 Frosch D, Porzsolt F, Heicappell R, Kleinschmidt K, Schatz M, Weinknecht S, Kaplan RM. Comparison of German language versions of the QWB-SA and SF-36 evaluating outcomes for patients with prostate disease. *Qual Life Res* 2001; **10**: 165-173
- 62 Vermeulen RC. Translation and validation of the Dutch language version of the CDC Symptom Inventory for assessment of Chronic Fatigue Syndrome (CFS). *Popul Health Metr* 2006; **4**: 12
- 63 Fielding LP, Arsenault PA, Chapuis PH, Dent O, Gathright B, Hardcastle JD, Hermanek P, Jass JR, Newland RC. Clinicopathological staging for colorectal cancer: an International Documentation System (IDS) and an International Comprehensive Anatomical Terminology (ICAT). *J Gastroenterol Hepatol* 1991; **6**: 325-344
- 64 Bisset IP, Chau KY, Hill GL. Extrafascial excision of the rectum: surgical anatomy of the fascia propria. *Dis Colon Rectum* 2000; **43**: 903-910
- 65 Siassi M, Hohenberger W, Lösel F, Weiss M. Quality of life and patient's expectations after closure of a temporary stoma. *Int J Colorectal Dis* 2008; **23**: 1207-1212
- 66 Golembiewski RT, Billingsley K and Yeager S. Measuring Change and Persistence in Human Affairs: Types of Change Generated by OD Designs. *Journal of Applied Behavioral Science* 1976; **12**: 133-157.
- 67 Scalapogna R, Brugnattelli S, Tinelli C, Sagrada P, Gattoni E, Tronconi MC, Riccardi A, Luchena G, Corazza GR. UFT as maintenance therapy in patients with advanced colorectal cancer responsive to the FOLFOX4 regimen. *Oncology* 2007; **72**: 267-273

Peer reviewer: Luis Tejedor, MD, European Board of Surgery Qualification in Surgical Oncology, General Surgery Department, Hospital Punta de Europa, Ctra Getares s/n 11207, Algeciras, Cadiz, Spain.