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-Andia, Sef Saudí-Moro, Jesús M Esarte-Muniaín, Alejandro Serrablo-Requejo

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 wellbeing 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

ORIGINAL ARTICLE

**INTRODUCTION**

Colorectal cancer (CRC) is the 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[4]. In Spain, CRC is the second most frequently diagnosed malignant neoplasm and the second cause of death due to malignant neoplasms[2]. The role of colonoscopy in the screening of this pathology is crucial[4]. When CRC presents as a disease affecting the intestine, it has a high rate of cure (45-50%) with radical surgery[4,4]. The most frequent metastatic involvement in CRC, after ganglion invasion, is seen in the liver[4,4]. Since Woodington and Waugh[8] published the first favorable results concerning the surgical treatment of liver metastases originating in the colon/rectal region (colon/rectal-liver metasases: CLM) until now, survival at 5 years after surgery is 30-40% and 20-25% at 10 years[9].

Although much is known about the epidemiology, prognostic factors and treatment of CLM[8,10], 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[2] 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)[11], see annex, the Sickness Impact Profile (SIP)[12], the Psychological General Well-Being Index (PGWB)[13,14], the Psychological Adjustment to Illness Scale (PAISSR)[15] and the Nottingham Health Profile (NHP)[16,17]. Despite this, there are other questionnaires addressing QoL with items aimed at detecting specific situations of clinical pictures, such as the FDDQOL (Functional Digestive Disorders Quality of Life) proposed by Chassany et al[18], the GIQLI (Gastrointestinal Quality of Life Index) described and validated by Eypasch et al[19], the NIPE (Neoplastic Dyspepsia Index) designed by Talley et al[20], etc.

Nevertheless, the most widely used version of these indicators is the SF-36, which has a reduced version with only 12 items[21-23] and which has recently been validated for the Spanish population[24,25], 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[26,27], 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[41]. 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[20]) post-operative bleeding, biliary fistulas and intra-abdominal abscesses, while minor complications (grades 1 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[21].

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[19,22].

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].

253 © 2012 Thomson research. All rights reserved.
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).

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

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

<table>
<thead>
<tr>
<th>Total Score among dimensions of the SF-36 health questionnaire</th>
<th>Patients pre-treatment score</th>
<th>Patients post-treatment score</th>
<th>Comparison of patients and accompanying persons before treatment (p-value)</th>
<th>Accompanying persons pre-treatment score</th>
<th>Accompanying persons post-treatment score</th>
<th>Comparison of patients and accompanying persons after treatment (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=30</td>
<td>n=30</td>
<td></td>
<td>n=30</td>
<td>n=30</td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td>55.54±24.66</td>
<td>66.32±27.62</td>
<td>-10.78 (p&lt;0.01)</td>
<td>48.48±22.42</td>
<td>66.44±27.43</td>
<td>-17.99 (p&lt;0.01)</td>
</tr>
<tr>
<td>Role</td>
<td>0</td>
<td>75.55±41.28</td>
<td>-75.55 (p&lt;0.00)</td>
<td>0</td>
<td>67.22±39.99</td>
<td>-67.22 (p&lt;0.00)</td>
</tr>
<tr>
<td>Pain</td>
<td>47.92±18.59</td>
<td>56.67±27.41</td>
<td>-8.75 (p&lt;0.05)</td>
<td>22.61±15.18</td>
<td>56.67±27.41</td>
<td>-34.17 (p&lt;0.00)</td>
</tr>
<tr>
<td>Health</td>
<td>22.11±5.46</td>
<td>24.05±11.40</td>
<td>-19.94 (p&lt;0.00)</td>
<td>18.61±5.38</td>
<td>24.05±11.40</td>
<td>-17.99 (p&lt;0.00)</td>
</tr>
<tr>
<td>Vitality</td>
<td>41.05±5.65</td>
<td>44.11±15.44</td>
<td>-3.06 (p&lt;0.03)</td>
<td>38.77±25.21</td>
<td>45.10±12.94</td>
<td>-7.27 (p&lt;0.00)</td>
</tr>
<tr>
<td>Social</td>
<td>51.25±13.27</td>
<td>57.08±25.57</td>
<td>-5.83 (p&lt;0.01)</td>
<td>41.25±13.19</td>
<td>48.75±21.11</td>
<td>-7.50 (p&lt;0.00)</td>
</tr>
<tr>
<td>Emotional</td>
<td>63.89±41.07</td>
<td>19.44±29.06</td>
<td>44.44 (p&lt;0.00)</td>
<td>49.44±35.69</td>
<td>15.56±23.95</td>
<td>35.89 (p&lt;0.00)</td>
</tr>
<tr>
<td>Mental</td>
<td>45.50±3.41</td>
<td>40.63±11.95</td>
<td>4.86 (p&lt;0.01)</td>
<td>42.10±5.48</td>
<td>40.73±10.15</td>
<td>1.37 (p&lt;0.52)</td>
</tr>
</tbody>
</table>

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
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 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 and presumably it would have been possible to detect significant differences in some comparisons in which we 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 who have used very long follow-up periods. Other authors have 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 and presumably it would have been possible to detect significant differences in some comparisons in which we 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 who have used very long follow-up periods. Other authors have 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 and presumably it would have been possible to detect significant differences in some comparisons in which we 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 who have used very long follow-up periods. Other authors have 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 and presumably it would have been possible to detect significant differences in some comparisons in which we 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 who have used very long follow-up periods. Other authors have 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 and presumably it would have been possible to detect significant differences in some comparisons in which we 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 who have used very long follow-up periods. Other authors have 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 and presumably it would have been possible to detect significant differences in some comparisons in which we 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.
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. 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. 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. 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 in the latter location 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. 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. 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. Finally, we divided the colon from the rectum patients because according to some authors 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. 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 that 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 that 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 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-Martin J contributed equally to this work; Borrego-Estella VM participated in design of the study, data acquisition and helped to draft the manuscript; Montero-Martin J conceived and coordinated the study, helped to draft the manuscript and performed the statistical analysis; Molinos-Aruebo I and López-Marcos JF has been involved in drafting the manuscript; Pérez-Sánchez-Cua-drado 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-Villarón 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; Montero-Martin J conceived and coordinated the study, helped to draft the manuscript and performed the statistical analysis; Molinos-Aruebo 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. Serrablo-Requejo A participated in data acquisition and helped to draft the manuscript and the revisions.

REFERENCES

7 Wooding SF, Waugh JM. Results of resection of metastatic tumors of the liver. Ann Surg 1963; 150: 24-29
13 Stewart AL, Greenfield S, Hays RD, Wells K, Rogers WH, Berry SD, McGlynn EA, Ware JF. Functional status and well-being of patients with chronic conditions. Results from the Medical Outcomes Study. JAMA 1989; 262: 907-913
17 Derogatis LR. The psychosocial adjustment to illness scale (PAIS). J Persocial Res 1986; 30: 77-91
27 Cervera S, Aubé E. Calidad de vida y dinámica familiar tras el diagnóstico de cáncer de mama. Boletín de Psicología 2005, 85: 7-29
Borrego-Estella VM et al. Liver Metastases of Colorectal Cancer

Alonso J. Interpretation of SF-36 and SF-12 questionnaires in Spain: physical and mental components. Med Clin (Barc) 2008; 130: 726-735


37 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


© 2012 Thomson research. All rights reserved.


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


**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, Algecirias, Cadiz, Spain.