Complications and long-term quality of life following liver transplantation and major gastrointestinal surgery

OBJECTIVE To record postoperative complications after liver transplantation and other major gastrointestinal surgical procedures and to compare the health-related quality of life (HRQoL) of the patients 7 years after surgery.

METHOD The study examined two groups of patients who had undergone either orthotopic liver transplantation (n=32) or major surgery for gastrointestinal disease, specifically tumors (n=32), all of whom were in the Intensive Care Unit after surgery for at least 3 days. The complications in the two groups during the immediate postoperative period were recorded, and in the survivors the HRQoL 7 years after surgery was examined using the SF-36 questionnaire, and compared with that of the general population.

RESULTS The most common complication in patients with liver transplantation was infection (78.1%). In patients with other abdominal surgery the most common complications were renal (46.9%), followed by cardiovascular problems (43.8%) and infection (34.4%). Concerning HRQoL, the SF-36 questionnaire was completed for 43.75% (14/32) of the patients in each group. Only in the domain of “mental health” were significant differences found between the two groups of patients, with the patients who had undergone liver transplantation recording a significantly higher score. The quality of life in other aspects of the survey was similar between the two groups of patients.

CONCLUSIONS Recognition of complications is essential for planning immediate treatment and thus decreasing morbidity and mortality in patients undergoing major abdominal surgery. Determination of the post-operative HRQoL is particularly important, since the choice of treatment should take into consideration how it may later affect the patient’s life.

Over the years, although great progress has been made in the technological, medical and surgical aspects of liver transplantation, it remains a complex process accompanied by significant morbidity. Since the liver is in constant interaction with all the other systems of the human body, a patient undergoing liver transplantation sustains a variety of changes. During the operation and in the immediate postoperative period, the liver is exposed to a variety of potentially harmful agents. In addition, results vary according to factors associated with the donor or the operation itself, or to a possible reaction of the immune system. The postoperative outcome of liver transplantation varies, depending on the pre-operative condition of the patient, the state of the graft and the complexity of the procedure. Immediate postoperative complications may be related to the functioning of the graft, the surgical technique, possible infection and the response of the body systems. The survival rates after liver transplantation show an annual increase, with most centers now recording survival rates of up to 90% at the end of the first year and up to 55–60% for the 9th year post-transplant.

Progress in surgical techniques and technological and medical advances made in the field of intensive care have led to a corresponding improvement in survival rates after major surgery for tumors of the gastrointestinal tract. Rapidly evolving diagnostic techniques have expanded the criteria for carrying out more extensive surgery, and for including older patients and those with severe disease requiring more complex treatment. The survival of these patients is related to various factors, including the size and the location of the tumor, the pre-operative condition of the patient, the time of diagnosis, postoperative complica-
lations and other features. The current 5-year survival rate for patients who have undergone major abdominal surgery is: for stomach cancer 10–30%, for pancreatic cancer 20–25% and for colorectal cancer with total tumor resection up to 82%. For esophageal adenocarcinoma a 5-year survival rate of 39% has been reported, and for hepatocellular carcinoma 50%.

Several studies have shown that determination of the health-related quality of life (HRQoL) of patients undergoing major surgery is an important component of the evaluation of its success. All the factors that affect the quality of life of patients must be examined when the consequences of a disease and its treatment are estimated. Most patients are more concerned about the quality of their life after surgery than about longevity. In this way, health professionals are now in a position to inform patients more fully about the surgery and its outcome, enabling them to decide whether to proceed with the surgical treatment of their disease, and can prepare them for the postoperative period, during which they may need to participate in intervention programs focusing on the areas of their life most affected.

MATERIAL AND METHOD

This was a retrospective study of two groups of postoperative patients, one of 32 patients who had undergone orthotopic liver transplantation and one of 32 patients who had undergone major surgery for gastrointestinal diseases (tumors). All the surgical interventions had been performed in an Athens General Hospital during the period July 2006 to July 2009 and all the patients had been nursed in the Intensive Care Unit (ICU) after surgery for at least three days. The complications during the immediate postoperative period were retrieved from the records. The HRQoL was examined 7 years postoperatively using the Greek version of the SF-36 questionnaire completed via telephone interview. Table 1 shows the demographic data and information regarding the treatment of the study patients. The average age of the patients with liver transplantation was 51.2 years (SD: 12.1 years), which was significantly lower than that of the patients operated on for a gastrointestinal tumor, which was 64 years (SD: 15.3 years). The majority in both groups were men (78.1% for liver transplant patients and 59.4% for patients with gastrointestinal tumors). Of the patients having surgery for gastrointestinal tumors, 37.5% had intestinal cancer (intestinal cancer or intestinal cancer and hepatectomy), 25% pancreatic cancer (pancreatic cancer or pancreatic cancer and hepatectomy), 15.6% liver cancer and stomach cancer and 3.1% liver hemangioma and liver tumors. Among the patients having a liver transplant, hepatitis B was the reason for transplantation in the majority of cases (34.4%) and alcoholic liver disease in 12.5%, as also infection with HCV and development of hepatocellular carcinoma, with smaller percentages having primary sclerosing cholangitis, primary biliary cirrhosis, etc.

Preoperatively, 75% of patients who underwent liver transplantation presented portal hypertension, 46.9% hyponatremia and 43.8% encephalopathy. The average MELD score was 20.1 points (SD: 10.2 points), while the average MELD-Na score was 21.1 units (SD: 10.7 units) while 40.6% of patients had a MELD score of less than 15 units.

The patients who had undergone liver transplantation remained intubated and were hospitalized for significantly more days than those with surgery for gastrointestinal tumors. The readmission rates into the ICU were similar (12.5%) for both groups of patients.

RESULTS

Complications

All the patients with liver transplantation (100%), but only 81.3% of the patients who underwent surgery for gastrointestinal tumor experienced at least one post-operative complication. The rates of infections, neurological complications and renal complications that required dialysis were all significantly higher in patients with liver transplantation. The post-operative mortality was 21.9% for patients with liver transplantation and 18.8% for patients with surgery for gastrointestinal tumor (no significant difference). The

| Table 1. Clinical data on patients undergoing liver transplantation or other major gastrointestinal surgery. |
|-------------------------------------------------|---------------------------------------------|------------------|
| Liver transplantation (n=32) | Gastrointestinal surgery (n=32) | p |
| Age in years: mean (SD) | 51.2 (12.1) | 64.0 (15.3) | <0.001* |
| Sex (n %) | | | 0.106* |
| Male | 25 | 78.1% | 19 | 59.4% |
| Female | 7 | 21.9% | 13 | 40.6% |
| ICU stay in days: mean (SD), median (range) | 15.9 (23.3) | 10 (8–14.5) | 15.8 (32.1) | 4.0 (3.0–11.5) | 0.002** |
| Re-admitted to ICU | No | 28 | 87.5% | 28 | 87.5% | 1.000** |
| Yes | 4 | 12.5% | 4 | 12.5% | |
| Intubation days: mean (SD), median (range) | 12.3 (21.2) | 6.5 (4.0–11.0) | 13.0 (29.7) | 2 (1–10.5) | 0.003** |

*Pearson’s x² test; **Fisher’s exact test; *Student’s t-test; **Mann-Whitney test; ICU: Intensive care unit; SD: Standard deviation
The most common complications in patients with liver transplantation were infection (78.1% of cases), followed by renal (65.6%) and respiratory complications (53.1%). Transplant rejection was recorded in 15.6% of cases. Correlation study of the MELD score and MELD-Na score with complications of patients with liver transplantation revealed a statistically significant association with renal complications requiring hemodialysis after liver transplantation (p=0.004 for MELD and p=0.008 for MELD-Na).

Encephalopathy, ascites, portal hypertension and hyponatremia in patients who received a liver transplant showed no significant correlation with post-operative complications, apart from hyponatremia which was associated with respiratory complications (p=0.041).

The most common complications in patients having surgery for gastrointestinal tumors were renal (46.9%), followed by cardiovascular complications (43.8%) and infection (34.4%).

Patients subjected to liver transplantation

Those undergoing hemodialysis remained intubated for longer than the patients who were not submitted to hemodialysis (p<0.001).

Patients subjected to surgery for gastrointestinal tumor

Those who experienced infections and neurological, renal, cardiovascular or respiratory complications, and who underwent hemodialysis, remained intubated for longer than the patients who did not present such complications (p<0.001, p=0.009, p=0.008, p=0.011, p=0.001, and p=0.003, respectively). The duration of intubation was significantly higher in patients who subsequently died (either in hospital or after discharge), compared with patients who survived (p=0.02, and p=0.003). Patients who had experienced at least one complication remained intubated for longer than patients who experienced no complications (p=0.009).

Patients subjected to liver transplantation

Those who experienced infection or respiratory complications and underwent hemodialysis had a significantly longer ICU stay than patients without such complications (p=0.006, p=0.001, and p<0.001).

Patients subjected to surgery for gastrointestinal tumor

Those who experienced infection or neurological, renal, cardiovascular or respiratory complications, and underwent dialysis, had a significantly longer ICU stay than patients who did not present such complications (p=0.001, p=0.011, p=0.009, p=0.049, p=0.002, and p=0.004, respectively). In cases where the patient died the length of stay in the ICU was significantly higher than that of patients who survived (p=0.006). Patients who had at least one complication had a significantly longer ICU stay compared with patients who had no complications (p=0.005).

Health-related quality of life

Table 2 shows the HRQoL of patients 7 years after surgery, according to the SF-36 questionnaire. The question-
naire was answered by 43.75% (14/32) of the patients in each group, the rest of them having died.

Only in the domain of “mental health” were there significant differences between the two groups. Specifically, the patients with liver transplantation reported a significantly higher score, i.e., better mental health, compared with the patients who had undergone gastrointestinal tumor surgery. The reported quality of life in the other aspects of the survey was similar in the two groups of patients.

Correlation between HRQoL and the demographic and clinical characteristics of patients with liver transplantation

This study showed no significant correlation between the HRQoL of patients after liver transplantation with their demographic and clinical characteristics.

Correlation between the HRQoL and the demographic and clinical characteristics of patients with gastrointestinal tumor surgery

On the SF-36, the men recorded significantly higher scores on the items “body function”, “general health”, “vitality”, “emotional involvement”, “mental health” and “brief mental health scale”, indicating better quality of life in these areas, in comparison with the women.

Significant inverse correlation was recorded between the items “physical function” and “general health” and the age of the patients, the older patients presenting worse physical function and overall health.

The study showed no correlation between the duration of hospitalization and intubation of patients with any item of HRQoL on the SF-36.

Comparison of the quality of life of patients with liver transplantation with that of the general population

In this study, patients 7 years after liver transplantation demonstrated a significant lower mean score in the item “physical role” than that recorded in the general population using the SF-36 questionnaire. In all other aspects of quality of life, this study demonstrated no significant difference (tab. 3).

Comparison of the quality of life of patients with gastrointestinal tumor, with that of the general population

This study showed that patients 7 years after surgery for gastrointestinal tumor had significantly lower scores in the items “body function”, “physical role”, “emotional involvement” and “mental health” than those recorded in the general population. In all other items on SF-36 this study demonstrated no significant difference (tab. 4).

DISCUSSION

With the development of improved surgical technique and technical equipment the survival rate after major surgery is constantly rising, although various factors continue to be associated with a poor prognosis. The better understanding of these factors may help to optimize the management of conditions requiring major abdominal surgery, thus contributing to further improvement in survival rates and in the quality of life of the patients post-operatively.27

In the present study the most frequent complication in patients undergoing liver transplantation was infection. Although currently several preventive measures are utilized,

Table 3. Comparison of the quality of life of patients after liver transplantation with that of the general population (based on the SF-36 questionnaire).

<table>
<thead>
<tr>
<th>Item</th>
<th>Liver transplantation</th>
<th>General population*</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>1. Body function</td>
<td>14</td>
<td>76.8</td>
<td>28.1</td>
</tr>
<tr>
<td>2. Physical role</td>
<td>14</td>
<td>57.1</td>
<td>43.2</td>
</tr>
<tr>
<td>3. Bodily pain</td>
<td>14</td>
<td>79.4</td>
<td>31.3</td>
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<td>4. General health</td>
<td>14</td>
<td>65.1</td>
<td>17.9</td>
</tr>
<tr>
<td>5. Vitality</td>
<td>14</td>
<td>63.6</td>
<td>17.6</td>
</tr>
<tr>
<td>6. Social role</td>
<td>14</td>
<td>76.8</td>
<td>25.4</td>
</tr>
<tr>
<td>7. Emotional involvement</td>
<td>14</td>
<td>69.0</td>
<td>44.3</td>
</tr>
<tr>
<td>8. Mental health</td>
<td>14</td>
<td>66.0</td>
<td>15.7</td>
</tr>
</tbody>
</table>

*Pappa et al40
SD: Standard deviation
such as antimicrobial prophylaxis, vaccination, etc., infection continues to be a major cause of morbidity and mortality after liver transplantation. Approximately 80% of liver transplant recipients are estimated to develop at least one infection during the first year after liver transplantation, some of which are fatal.

Approximately 25% of candidates for liver transplantation show some degree of renal insufficiency prior to transplantation, while approximately 2/3 of liver transplant recipients develop impaired renal function after liver transplantation. In this study the diagnostic criterion for renal dysfunction was a serum creatinine level of over 2 mg/dL, according to which 65.6% of the liver recipients demonstrated renal complications. Similar studies report renal complications in 64% of patients, using as a diagnostic criterion creatinine >1.5 mg/dL. Additionally, other studies indicate that 8–10% of liver recipients will need to undergo dialysis in the immediate postoperative period, and a percentage of 17% has been reported.

In the present series, 28.1% of liver recipients required hemodialysis, and the MELD score and MELD-Na scores were shown to be correlated with the need for dialysis, in agreement with Sanchez and colleagues who cited as one of the predictors for hemodialysis a MELD score of >21.

Respiratory complications were the third most common complication following liver transplantation, at a rate of 53.1%, in line with other authors who reported respiratory complications in 42.1–68.0% of patients.

Mortality after major surgery for tumors of the gastrointestinal tract may reach 17%, but usually ranges from 3% to 7%. The present study recorded a mortality of 18.8%. This figure is relatively high, probably due to the fact that the study included only patients admitted to the ICU after surgery and thus belonged to the group at highest risk. For the same reason, 81.3% of the patients in this study presented at least one complication, in contrast with 33.5% in another published series. In that study, delirium was the most frequent complication, in 12.8% of patients, which was the 8th most frequent complication in the present study (in 9.4% of the patients), consistent with other references. Finally, the average stay in the ICU after surgery for gastrointestinal tumor was reported to be 4.4 days, as in the present study (4 days).

Regarding the quality of life of patients after liver transplantation, their mean score on the item “physical role” on the SF-36 questionnaire was significantly lower than that of the general population, as in two other studies, which concluded that the main differences in the quality of life of liver transplant recipients from the general population concerned physical functions. Similar findings obtained from 5 other studies vividly indicated that although liver transplant recipients achieve a fairly satisfactory quality of life in general, and for physical activities, the level is lower than that of the general population.

The present study also demonstrated that the men who had undergone surgery for gastrointestinal tumor had better scores on the items “body function”, “general health”, “vitality”, “emotional involvement”, “mental health” and “brief mental health scale” than the women. As reported in the literature, women tend to report greater morbidity than men, possibly because of differences in their perception of the disease rather than substantial differences regarding the disease per se. Other studies, however, disagree with this hypothesis, claiming that the differences in morbidity between the two sexes are due to substantial variation in health-related issues which originate from social and psychological factors.

Table 4. Comparison of the quality of life of patients with gastrointestinal surgery, with the general population.

<table>
<thead>
<tr>
<th>Gastrointestinal surgery</th>
<th>General population*</th>
<th>p Student’s t-test</th>
</tr>
</thead>
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<tr>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>1. Body function</td>
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</tr>
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<td>14</td>
<td>58.4</td>
</tr>
<tr>
<td>5. Vitality</td>
<td>14</td>
<td>58.6</td>
</tr>
<tr>
<td>6. Social role</td>
<td>14</td>
<td>71.4</td>
</tr>
<tr>
<td>7. Emotional involvement</td>
<td>14</td>
<td>42.9</td>
</tr>
<tr>
<td>8. Mental health</td>
<td>14</td>
<td>53.7</td>
</tr>
</tbody>
</table>

*Pappa et al
SD: Standard deviation
Only a few studies have examined the long-term quality of life of patients undergoing major surgery for tumors of the gastrointestinal tract in comparison with the general population. In the present study the patients who underwent surgery for gastrointestinal tumors showed significantly lower scores than the general population on the SF-36 items “body function”, “physical role”, “emotional involvement” and “mental health”. Huang and colleagues reported that patients who had undergone Whipple resection for adenocarcinoma had significantly lower scores in physical and psychological health. In the study of Billings and colleagues patients after total pancreatectomy scored significantly lower in the items “physical role” and “general health” than the rating of the general population. A review article on HRQoL after gastrectomy for gastric cancer showed improvement between the 6th month and the first year after surgery, but after 5 years it is not maintained at the same level. Conversely, the quality of life of patients surviving colon cancer tends to improve as the survival is prolonged, although another study showed that 10–26% of patients are dissatisfied with their physical performance, their mental function, their financial situation and sexual function. A more recent study concluded that the negative impact of colorectal cancer was more significant during the first 3 years after diagnosis. In a study of females who survived colon cancer, while no significant differences were demonstrated in their quality of life from that of the general population, the HRQoL scores of women were observed to be generally lower than those of men. Finally, the present study showed a significant inverse correlation between the items “physical function” and “general health” and the age of patients, a finding consistent with other studies.

In conclusion, the immediate postoperative complications in patients undergoing liver transplantation are related to the function of the graft, the surgical technique, possible infection and the impact on the body systems. The survival of patients following other major gastrointestinal surgical procedures may be related to various factors including the size and the location of the tumor, the pre-operative condition of the patient, the time of diagnosis, postoperative complications, etc. Determination of the HRQoL of patients undergoing major surgery is also necessary, and most patients are concerned more about the quality of their life after surgery than about longevity. To summarize the main findings of this study, it can be observed that the most common complications in patients with liver transplantation were infections, followed by renal and respiratory complications, while graft rejection was recorded in only 15.6% of cases. The most common complications in patients who had undergone surgery for gastrointestinal tumors were renal, followed by cardiovascular complications and infections. In the HRQoL 7 years after surgery only the item “mental health” showed significant differences between the two patient groups with those who had undergone liver transplantation demonstrating a significantly higher score, i.e. better mental health, than the patients with gastrointestinal tumor surgery. The scores on the other items of HRQoL were similar in the two groups of patients.

The early recognition of complications after major abdominal surgery is absolutely essential in order to plan immediate intervention and thus decrease morbidity and mortality. The determination of HRQoL after such operations is particularly important, since knowledge of how it may affect the patient’s later life influences the choice of possible treatment. Consequently, the expected quality of life should be calculated in the design of the treatment of any disease, so that the patient receives better information on how to confront the disease.
υγεία ποιότητας ζωής χρησιμοποιήθηκε το ερωτηματολόγιο SF-36, το οποίο συμπληρώθηκε μέσω τηλεφωνικής συνέντευξης. ΑΠΟΤΕΛΕΣΜΑΤΑ Οι συμφόρτες επιπλοκές σε ασθενείς που υποβλήθηκαν σε μεταμόσχευση ήπατος ήταν οι λοιμώξεις (78,1%), ενώ στη δεύτερη ομάδα συμφόρτες ήταν οι νεφρολογικές επιπλοκές (46,9%), ακολουθούμενες από καρδιαγγειακές επιπλοκές (43,8%) και από λοιμώξεις (34,4%). Όσον αφορά στην ποιότητα ζωής, υπήρξαν σημαντικές διαφορές μόνο αναφορικά με τη διάσταση «ψυχική υγεία». Η ποιότητα ζωής στις διαστάσεις «σωματική λειτουργικότητα», «σωματικός ρόλος», «ρόλος συναισθηματικός ρόλος» ήταν σημαντικά χαμηλότερη σε σύγκριση με αυτή του γενικού πληθυσμού, ενώ για ασθενείς με όγκο γαστρεντερικού η βαθμολογία στις διαστάσεις «σωματικές διαφορές μόνο αναφορικά με τη διάσταση «ψυχική υγεία». Η ποιότητα ζωής στις διαστάσεις «σωματική λειτουργικότητα», «σωματικός ρόλος», «ρόλος συναισθηματικός ρόλος» ήταν σημαντικά χαμηλότερη σε σύγκριση με αυτή του γενικού πληθυσμού, ενώ για ασθενείς με μεταμόσχευση ήπατου η βαθμολογία στη διάσταση «σωματικές διαφορές μόνο αναφορικά με τη διάσταση «ψυχική υγεία». Η ποιότητα ζωής στη διάσταση «σωματική λειτουργικότητα», «σωματικός ρόλος», «ρόλος συναισθηματικός ρόλος» ήταν σημαντικά χαμηλότερη σε σύγκριση με αυτή του γενικού πληθυσμού, ενώ για ασθενείς με όγκο γαστρεντερικού η βαθμολογία στις διαστάσεις «σωματικές διαφορές μόνο αναφορικά με τη διάσταση «ψυχική υγεία». Ωστόσο, ο ασθενής να λαμβάνει πληρέστερη ενημέρωση για τους τρόπους αντιμετώπισης της ασθένειάς του.

ΑΠΟΤΕΛΕΣΜΑΤΑ Απαιτείται έγκαιρη αναγνώριση των επιπλοκών μετά από μείζονες χειρουργικές επεμβάσεις, ώστε να σχεδιάζεται έμεσα η στρατηγική αντιμετώπισής τους και να μειώνεται η νοσηρότητα και η θνητότητα των ασθενών. Εκτός από την επιβίωση, θα πρέπει να υπολογίζεται στον σχεδιασμό της θεραπείας κάθε ασθένειας και η αναμενόμενη ποιότητα ζωής, έτσι ώστε ο ασθενής να λαμβάνει πληρέστερη ενημέρωση για τους τρόπους αντιμετώπισης της ασθένειάς του.
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Corresponding author:
D. Mantas, 17 Agiou Thoma street, GR-115 27 Athens, Greece e-mail: dvmantas@med.uoa.gr