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ORIGINAL ARTICLE

# Psychopathological profile and health-related quality of life (HRQOL) in patients with hepatocellular carcinoma (HCC) and cirrhosis

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**Abstract** In some tumors, psychosocial interventions may enhance health-related quality of life (HRQOL) of patients. The effects of psychological variables on HRQOL in hepatocellular carcinoma (HCC) patients have been rarely assessed. The aim of this work is to evaluate the psychopathological profile of HCC and cirrhotic patients and its effect on HRQOL. Twenty-four HCC patients (median age 71, Child A 21, Child B 3), 22 cirrhotic patients (median age 68, Child A 20, Child B 2) and 20 control subjects were included in this study. Each subject completes four questionnaires: medical outcomes study short form-36 (SF-36, HRQOL evaluation); Hamilton-D (quantitative evaluation of depression; positive $\geq$8); symptom check list 90-revised (SCL 90-R, general psychopathological profile; nine domains, each positive >1); Toronto alexithymia scale (TAS 20) (positive $\geq$60). SCL 90-R: cirrhotic patients differ from HCC subjects for somatization (SOM) (M $\pm$ SD 1.09 $\pm$ 0.6 vs 0.65 $\pm$ 0.6; $p = 0.01$) and anxiety (M $\pm$ SD 0.85 $\pm$ 0.46 vs 0.58 $\pm$ 0.38; $p = 0.01$) items. TAS 20: positive in 50 % of HCC patients, in 54 % of cirrhotic patients ($p$ = n.s.) and in none of controls. Hamilton-D: higher scores in cirrhotic patients than in the HCC group (86 vs 46 %; $p = 0.005$). SF-36: each item, except bodily pain, is lower in both group of patients in comparison with controls. Pearson correlation analysis shows negative correlations on HRQOL of depression, SOM and anxiety both in cirrhotic and HCC subjects, also of obsessive–compulsive and hostility items in HCC. This is the first report on the psychopathological profile of HCC patients: the results open questions on the role of psychological interventions that may improve HRQOL of patients before treatment and in the follow-up.

**Keywords** Hepatocellular carcinoma · Liver cirrhosis · Health-related quality of life · Psychopathological profile

**Abbreviations**

| | |
|---|---|
| HRQOL | Health-related quality of life |
| HCC | Hepatocellular carcinoma |
| SF-36 | Medical outcomes study short form-36 |
| SCL 90-R | Symptom checklist 90-revised |
| TAS-20 | Toronto alexithymia scale |
| EASL | European association for the study of the liver |
| BCLC | Barcelona classification liver cancer |
| PCS | Physical component summary |
| MCS | Mental component summary |
| HCV | Hepatitis C virus |
| HBV | Hepatitis B virus |

## Background

The hepatocellular carcinoma (HCC) is the most common primary malignant tumor of the liver, and its diffusion is strongly affected on regional bases, varying from 5 to 15 cases/100,000/year in Western Europe and USA to 40 cases/100,000/year in Asia and Japan [1].

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Worldwide, HCC is the fifth most common of all malignancies and causes approximately one million deaths annually [2].

In the field of oncology, the effectiveness of diagnostic and therapeutic program was evaluated primarily in terms of survival, while in recent years, greater emphasis has been done on perceived health-related quality of life (HRQOL), whose evaluation constitutes an integral part of patient care [3].

Actually, it is well known that in some tumors (i.e., lung or breast), psychosocial interventions may reduce negative feelings and enhance HRQOL [4–7].

HCC is characterized by a poor prognosis even though in recent years different therapeutic options have been proposed and approved in relation to the staging of the disease: median 5-year survival ranges from 40 to 70 % in patients with early HCC undergoing to resection, liver transplantation or loco-regional treatment, to an overall survival <3 months in subjects with advanced disease [8].

Furthermore, most of patients receive the first diagnosis of HCC in an advanced stage of disease when treatment options are very limited [8].

For these reasons, the evaluation of the quality of life in patients with HCC may be considered a crucial point in the global strategy of treatment for this cancer [9].

A HRQOL compromised has been demonstrated in patients with liver disease including cirrhosis and viral hepatitis, in part as a consequence of severe symptoms, treatment and side effects, in part on the severity of the disease. An acceptable HRQOL has gradually been considered as an important aim to be achieved in clinical studies on the treatment for cancer, along with the traditional objectives, such as tumor response rate and time or frequency of survival. Studies on disease HRQOL in patients with HCC have included both general aspects as physical symptoms and psychological needs, and other specific and unique issues of the disease [10, 11].

Nevertheless, the effects of some psychopathological variables [anxiety, depression (DEP), psychoticism (PSY), alexithymia and somatization (SOM)] on the HRQOL of patients with HCC were rarely evaluated as well as the interaction between the physical and psychopathological variables in relation to the quality of life. Some reports underline the importance of evaluating these variables in the medical approach to these patients since health behavior changes following cancer diagnosis and treatment are associated with better psychological and physical well-being [12].

Actually, studies have focused on the positive effect of an integrated approach as a tool in aiding advanced colorectal cancer patients' ability to cope with their diagnosis and treatment [13].

Several psychopathological variables have been evaluated in patients affected by cancers including those explored by the symptom checklist 90-revised [14], the Hamilton-D scale for DEP [15] and the Toronto alexithymia scale (TAS) [16, 17] and related to the evaluation of quality of life, but none of these, to our knowledge, has never been applied to cirrhotic patients affected by HCC.

## Aim of the study

A possible relationship between the HRQOL of patients with HCC and psychopathological profile has never been evaluated. The aim of this work is to evaluate the behavioral and psychopathological profile of a group of patients with HCC in comparison with group of cirrhotic patients and to correlate it with the HRQOL and prognostic and clinical features.

## Patients and methods

The study was carried out on 24 consecutive outpatients affected by HCC in the Clinica Medica "A. Murri" in the Policlinico Hospital of Bari.

The diagnosis of HCC was confirmed in all patients by the execution of procedures for diagnostic imaging (CT or MRI) or/and by liver biopsy and subsequent histological or cytological examination [8].

Patients were classified according to the possible treatment for HCC on the basis of the criteria proposed by the Barcelona staging classification liver cancer (BCLC) [18].

On outpatient setting, the patients were evaluated for HRQOL by the medical outcomes study short form-36 (SF-36) questionnaires, Hamilton-D for the quantitative evaluation of DEP (positive for scores ≥8), symptom checklist 90-revised (SCL 90-R) for the evaluation of general psychopathological profile (90-items, each positive for score >1) and TAS 20 (positive if score ≥60).

Each questionnaire was further administered to a population represented by 22 consecutive cirrhotic outpatients without HCC, matched on the basis of Child-Pugh class (exclusion of Child-Pugh C subjects because of the interference on HRQOL of the hepatic encephalopathy). Furthermore, no patients with HCC or cirrhosis had ascites.

The clinical follow-up of HCC patients was carried out at 3 months interval while that of cirrhotic patients at 6 months interval. Both cirrhotic and HCC patients were made aware of the diagnosis and of the possible complications and clinical evolution of the disease as well as of the therapeutic changes.

As a control group, we enrolled 20 subjects considered as not affected by any disease on the basis of clinical and

laboratory evaluation among the health care personnel working in the Unit of Clinica Medica.

Both groups of patients and normal controls had no psychiatric positive history.

Both groups of patients and normal controls have been enrolled on voluntary basis after explanation of methods and finalities of the research. All patients and all normal subjects asked to participate to the study agreed and gave their written informed consensus.

### SF-36

HRQOL was assessed using the Italian version of the SF-36 [19]. The SF-36 is a valid, self-administered questionnaire used internationally to measure 8 domains of health: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH), during the last month. The raw scores of each subscale were transformed into scores that ranged from 0 to 100, with higher scores indicating higher levels of functioning or well-being. The level of HRQOL was assessed by comparing the mean value for the study sample with the mean value for a representative sample of the general population. Scores representing overall PF and mental functioning were calculated from the subscales and presented as two super groups: the physical component summary scale (PCS) and mental component summary scale (MCS). Four scales (PF, RP, BP and GH) correlated highly with the PCS and four (VT, SF, RE and MH) with the MCS [20].

### Hamilton-D

It is an observer-rated scale for quantitative assessment of DEP, which includes 21 items [21]. The most used modern version encloses four each item (except 2 two-part items) a rate on a 0–4 spectrum [22]. The total score ranges from 0 to 84. It has items on 17 symptoms of DEP on which the cut-off of severity is defined. Severity cut-off values are as follows: $\geq$25 severe DEP; 18–24 moderate DEP; 8–17 mild DEP; <7 absence of DEP. It has good validation and easy administration. The inter-rater reliability is 0.87–0.9 [15]. Hamilton-D questionnaire was administered by the researchers.

### Symptom checklist 90-revised (SCL 90-R)

The SCL 90-R is a 90-item self-report symptom inventory designed to reflect psychopathological symptom patterns of psychiatric and medical patients. Each item of the questionnaire is rated on a 5-point scale of distress from 0 (none) to 4 (extreme). The SCL 90-R consists of the following nine primary symptom dimensions: SOM (SOM, which reflects distress arising from bodily perceptions), obsessive–compulsive (OC, which reflects obsessive–compulsive symptoms), interpersonal sensitivity (IS, which reflects feelings of personal inadequacy and inferiority in comparison with others), DEP (DEP, which reflects depressive symptoms, as well as lack of motivation), anxiety (ANX, which reflects anxiety symptoms and tension), hostility (HOS, which reflects symptoms of negative effect, aggression and irritability), phobic anxiety (PHO, which reflects symptoms of persistent fears as responses to specific conditions), paranoid ideation (PAR, which reflects symptoms of projective thinking, HOS, suspiciousness, fear of loss of autonomy) and PSY (PSY, which reflects a broad of symptoms from mild interpersonal alienation to dramatic evidence of psychosis) [14, 23]. Each item is positive for score >1. The mean scores of the nine dimensions are expressed in terms of symptom profile. The SCL 90-R takes between 12 and 20 min to complete. With regard to its reliability, the internal consistency coefficient values for the nine symptom dimensions ranged from 0.77 for PSY to a high of 0.90 for DEP. SCL 90-R questionnaire was administered by the researchers.

#### *Toronto alexithymia scale (TAS-20)*

It is a 20-item self-report scale with a three-factor structure congruent with the alexithymia construct: difficulty in identifying feelings, difficulty in describing feelings and externally oriented thinking. Each item is rated on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), with five items negatively keyed. The TAS-20 score ranges from 20 to 100; subjects scoring 61 or more have been suggested to be alexithymic, whereas those scoring 51 or less are considered to be not alexithymic. The subjects that obtain a score between 52 and 60 have been suggested to be intermediate alexithymic [16, 24].

#### *Statistical analysis*

Descriptive statistics, including means and standard deviations for Gaussian distributed variables, median and quartile ranges for non-Gaussian distributed variables, count and percentages for qualitative variables, were used to characterize the study cases. Student's $t$ test was used to make comparison between independent samples. For variables, not Gaussian distributed nonparametric tests were performed: Kruskal–Wallis test for analysis of variance and Wilcoxon test for comparison between independent groups. Differences between proportions were tested by chi–square test. To address relationship between parameters, Pearson product moment correlation was performed. Results were considered significant when $p$ was $< 0.05$.

**Table 1** General characteristics of patients with liver cirrhosis, HCC and normal controls enclosed in the study[a]

| | Cirrhosis | HCC | Healthy controls |
|---|---|---|---|
| Number of patients | 22 | 24 | 20 |
| Median age (range) | 68 (51–75) | 71(56–82) | 36 (23–58) |
| Males/females | 10/12 | 18/6 | 5/15 |
| Etiology of hepatic disease | | | |
| HCV | 14 | 19 | 0 |
| HBV | 6 | 4 | 0 |
| Other | 2 | 1 | 0 |
| Child-Pugh Class | | | |
| A | 20 | 21 | 0 |
| B | 2 | 3 | 0 |
| C | 0 | 0 | 0 |

[a] Chi-square test and Wilcoxon test or Student's *t* test

**Table 2** Comparison of SCL 90-R, TAS 20 and Hamilton-D questionnaires results in HCC and cirrhotic patients in comparison with healthy controls (M ± SD)

| | Healthy controls ($n = 20$) | Cirrhosis ($n = 22$) | HCC ($n = 24$) |
|---|---|---|---|
| SCL 90-R | | | |
| Somatization (SOM) | 0.40 ± 0.41[a] | 1.09 ± 0.6[d] | 0.65 ± 0.6 |
| Obsessive–compulsive (O–C) | 0.26 ± 0.20[b] | 0.86 ± 0.5 | 0.67 ± 0.54 |
| Interpersonal sensitivity (IS) | 0.37 ± 0.27[c] | 0.51 ± 0.35 | 0.60 ± 0.54 |
| Depression (DEP) | 0.23 ± 0.22[b] | 0.88 ± 0.41 | 0.76 ± 0.59 |
| Anxiety (ANX) | 0.22 ± 0.18[b] | 0.85 ± 0.46[d] | 0.58 ± 0.38 |
| Hostility (HOS) | 0.38 ± 0.31[a] | 0.60 ± 0.47 | 0.60 ± 0.56 |
| Phobic anxiety (PHO) | 0.07 ± 0.12[a] | 0.32 ± 0.37 | 0.17 ± 0.36 |
| Paranoid ideation (PAR) | 0.45 ± 0.31 | 0.60 ± 0.40 | 0.66 ± 0.49 |
| Psychoticism (PSY) | 0.16 ± 0.17[b] | 0.51 ± 0.41 | 0.36 ± 0.30 |
| TAS-20 | 36.5 ± 8.9[b] | 59.6 ± 16.2 | 60.8 ± 15.1 |
| HAMILTON-D | 4.9 ± 2.9[b] | 11.3 ± 3.4[d] | 8.7 ± 4.4 |

Kruskal–Wallis test for analysis of variance and Wilcoxon test or Student's *t* test for comparison between independent groups

[a] Healthy controls versus cirrhosis: SOM = $p$ 0.0002; HOS = $p$ 0.05; PHO = $p$ 0.004

[b] Healthy controls versus cirrhosis and HCC: O–C = $p$ 0.00001 versus cirrhosis and $p$ 0.001 versus HCC; DEP = $p$ 0.0001; ANX = $p$ 0.00001 versus cirrhosis and $p$ 0.0001 versus HCC; PSY = $p$ 0.0005 versus cirrhosis and $p$ 0.004 versus HCC; TAS-20 = $p$ 0.000002; Hamilton-D = $p$ 0.000001 versus cirrhosis and $p$ 0.001 versus HCC

[c] Healthy controls versus HCC: IS = $p$ 0.04

[d] Cirrhosis versus HCC: SOM = $p$ 0.01; ANX = $p$ 0.01; Hamilton-D = $p$ 0.01

Calculations were performed with the NCSS 2009 statistical software (Kaysville, UT, USA).

## Results

The Table 1 shows the characteristics of patients affected by HCC, patients with cirrhosis and healthy controls. There is no difference between the population of patients in relation to age and Child-Pugh class.

In the group of HCC subjects, the number of females was significantly higher (chi square 4.207, $p = 0.04$) than that of males even if any results were affected by this difference.

The distribution of HCC patients on the basis of BCLC shows 17 patients in the class A (<3 nodules, each nodule <3 cm diameter), 4 patients in the class B (nodules more than 3 cm diameter or more than 3 nodules) and 3 patients in the class D (advanced disease). No patient was undergoing to specific therapy at the time of the administration of questionnaires.

The number of clinical visit in the last year was higher in the patients affected by HCC in comparison with that of subjects with cirrhosis (3.5 ± 0.5 vs 1.8 ± 0.4, $p < 0.00001$).

The results of the SCL 90-R test, TAS 20 and Hamilton-D questionnaires administered in both groups of patients and in normal subjects are highlighted in the Table 2.

The value of each item of the SCL 90-R in healthy controls is significantly lower in comparison with both groups of patients (obsessive–compulsive, DEP, anxiety and PSY), only to patients with cirrhosis (SOM, HOS and PHO anxiety) or only to patients with HCC (IS). TAS-20 and Hamilton-D results in healthy subjects are very lower than in cirrhotic and HCC patients (Table 2). Among the healthy controls, only one subject reports a positive result for the SOM item of the SCL 90-R questionnaire, no one is positive for alexithymia and three subjects have a value >7 for the Hamilton-D questionnaire.

As regards the SCL 90-R, patients affected only by cirrhosis differ from the HCC subjects for the values of the scores for SOM and anxiety.

Among patients with HCC, the alexithymia is present in the 50 % of cases, while it is positive in the 54 % of cirrhotic patients ($p$ = n.s.). Moreover, the proportion of intermediate alexithymic does not show any difference between the two groups of patients (12.5 % in HCC subjects vs 22 % in cirrhotic patients, $p$ = n.s.). No normal subject is positive for alexithymia.

The patients without HCC exhibit higher values and percentages of depressive positive scores in comparison with the HCC group.

The Table 3 shows the comparison of the results of the SF-36 questionnaire between HCC patients, cirrhotic patients and normal controls.

**Table 3** Results of the SF-36 questionnaire in patients with HCC or cirrhosis in comparison with normal controls[a]

| SF-36 | Healthy controls ($n = 20$) | Cirrhosis ($n = 22$) | HCC ($n = 24$) |
|---|---|---|---|
| PF | 95 ± 8.8[b] | 62.5 ± 27 | 65.8 ± 25.3 |
| RP | 92.8 ± 8.1[b] | 57.1 ± 40.3 | 56.2 ± 43 |
| BP | 69.6 ± 20.8 | 67.3 ± 23.7 | 71 ± 33.6 |
| GH | 84.3 ± 15.9[b] | 43.4 ± 24.1[d] | 57.1 ± 20.8 |
| VT | 71.5 ± 16.1[b] | 45.7 ± 23.6 | 57.5 ± 25.8 |
| SF | 87.5 ± 15.7[c] | 77.2 ± 27.4 | 70.7 ± 30.7 |
| RE | 94.1 ± 7.2[b] | 62.7 ± 34.1 | 49.8 ± 41.7 |
| MH | 77 ± 15.6[b] | 58.8 ± 18.3 | 60.8 ± 20.2 |

[a] Kruskal–Wallis test for analysis of variance and Wilcoxon test or Student's *t* test for comparison between independent groups

*PF* physical functioning, *RP* role limitations due to physical health problems, *BP* bodily pain, *GH* general health perceptions, *VT* vitality, energy/fatigue, *SF* social functioning, *RE* role limitations due to emotional health problems, *MH* general mental health, psychological distress and well-being

[b] Healthy controls versus cirrhosis and HCC: PF = $p$ 0.000008; RP = $p$ 0.0002; GH = $p$ 0.000001; RE = $p$ 0.0001; VT = $p$ 0.0001 versus cirrhosis and $p$ 0.02 versus HCC; MH = $p$ 0.001

[c] Healthy controls versus HCC: $p$ 0.01

[d] Cirrhosis versus HCC: GH $p$ 0.04

Except for BP, the value of most of items of the SF-36 in healthy controls is significantly higher in comparison with both groups of patients (PF, role limitations for physical problems, GH, VT, role limitations for emotional problems, MH), while for SF it is higher only in comparison with patients with HCC.

The presence of HCC does not modify the subjective perception of HRQOL in comparison with patients affected only by cirrhosis except for GH item that appears to be worse in subjects with cirrhosis.

The Tables 4 and 5 show the results of the analysis of the correlation between SCL 90-R, TAS 20, Hamilton-D and each item of SF-36 questionnaire in patients with cirrhosis and HCC, respectively.

In the first case, with regard to SCL 90-R, both PCS and MCS have a weak negative correlation with the SOM item (PCS) and with the anxiety item (MCS); further, PCS has a weak negative correlation also with the DEP assessed by Hamilton-D questionnaire, while MCS exhibits a strong negative correlation with the same parameter.

In the case of the HCC patients, the PCS result has a negative correlation with the SOM, obsessive–compulsive, DEP, anxiety and HOS items of the SCL 90-R questionnaire; the MCS result correlates negatively with each item of the SCL 90-R test except for PAR ideation. Finally, the MCS score has also a negative association with the Hamilton-D result.

## Discussion

To our knowledge, this is the first report on the psychopathological profile patients with HCC and on its relationship with HRQOL in comparison with cirrhotic and normal subjects. This issue is important because the psychological and social support may favor an adequate adherence to treatment for cancer [25].

In our study, patients affected by cirrhosis and those with HCC have higher scores in comparison with normal subjects for most of the items of the SCL 90-R test, among which the items for obsessive–compulsive, DEP, anxiety and PSY. The observation on the DEP is confirmed by the results of the Hamilton-D questionnaire, even though it seems that the use of methods that include somatic symptoms may increase the percentage of false positive results for DEP in cancer patients [26].

To our knowledge, this is the first report in which the results of SCL 90-R test of cirrhotic patients with or without HCC have been compared to those of normal subjects. Actually, in the recent work by Lopez et al. [27], the test is applied only to cirrhotic patients distinguished on the basis of the main etiology of the disease (alcoholic vs other etiologies). Among the items of the SCL 90-R, anxiety score in nonalcoholic cirrhotic patients studied by Lopez is much higher (46 %) than in our patients, both with (22 %) and without HCC (6 %). Actually in the work of Lopez, all patients are awaiting for liver transplantation (and therefore belonging to Child-Pugh class C), while in our patients Child-Pugh C class is not represented. On the other hand, our data on the distribution of anxiety are in agreement with those reported by Nardelli et al. [28].

These data therefore seem to endorse the importance of the use of the SCL 90-R questionnaire since it is strictly related to the functional hepatic reserve as evaluated by the Child-Pugh score and to the prognosis.

Further, in our study, HCC patients have lower scores than cirrhotic subjects for the items SOM, anxiety and DEP even though there is no difference in the distribution of Child Class between the two groups of patients. Moreover, the DEP as evaluated by the Hamilton-D test is higher in cirrhotic subjects than in those with HCC. In our opinion, this apparently paradoxical result may be explained by the fact that in our clinic, as we have shown, HCC patients are monitored more frequently than cirrhotic patients, and therefore, the interaction and communication between physician and patient are more appropriate and contribute to a better patient compliance and quality of life [29]. According to this hypothesis, the work by Wong et al. [30] demonstrated that the satisfaction of the patient relative to the quality of medical services is an independent major determinant of the quality of life of patients with liver cancer.

**Table 4** Pearson moment correlation between SCL 90-R, TAS 20, Hamilton-D and each item of SF-36 questionnaire in patients with cirrhosis ($n = 22$) (r,$p$)

| | PF | RP | BP | GH | VT | SF | RE | MH | PCS | MCS |
|---|---|---|---|---|---|---|---|---|---|---|
| SCL 90-R | | | | | | | | | | |
| SOM | −0.45 | −0.36 | −0.46 | −0.54 | −0.39 | −0.21 | −0.40 | −0.52 | −0.48 | −0.39 |
| | .04 | n.s. | .03 | .009 | n.s. | n.s. | n.s. | .01 | .02 | n.s. |
| O–C | −0.25 | −0.22 | −0.48 | −0.49 | −0.55 | −0.09 | −0.50 | −0.40 | −0.28 | −0.42 |
| | n.s. | n.s. | .02 | .02 | .008 | n.s. | .02 | n.s. | n.s. | n.s. |
| INS | −0.05 | 0.05 | −0.45 | −0.41 | −0.23 | −0.02 | −0.26 | −0.12 | −0.11 | −0.19 |
| | n.s. | n.s. | .03 | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| DEP | −0.23 | −0.10 | −0.28 | −0.42 | −0.43 | −0.23 | −0.45 | −0.41 | −0.17 | −0.41 |
| | n.s. | n.s. | n.s. | .04 | .04 | n.s. | .03 | n.s. | n.s. | n.s. |
| ANX | −0.22 | −0.10 | −0.25 | −0.33 | −0.35 | −0.28 | −0.44 | −0.51 | −0.18 | −0.44 |
| | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | .03 | .02 | n.s. | .04 |
| HOS | 0.02 | 0.17 | −0.25 | −0.28 | −0.17 | −0.26 | −0.15 | −0.13 | −0.02 | −0.25 |
| | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| PHO | −0.14 | 0.05 | −0.19 | −0.26 | −0.15 | −0.21 | −0.13 | −0.12 | −0.04 | −0.06 |
| | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| PAR | 0.17 | 0.33 | 0.11 | −0.03 | 0.11 | −0.02 | −0.25 | −0.07 | 0.17 | −0.16 |
| | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| PSY | −0.17 | −0.01 | −0.30 | −0.29 | −0.37 | −0.21 | −0.38 | −0.23 | −0.09 | −0.31 |
| | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| TAS-20 | 0.06 | 0.27 | −0.15 | 0.16 | −0.08 | −0.01 | −0.24 | 0.08 | 0.41 | 0.18 |
| | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| Hamilton-D | −0.21 | −0.30 | −0.27 | −0.62 | −0.38 | −0.33 | −0.31 | −0.50 | −0.47 | −0.64 |
| | n.s. | n.s. | n.s. | .02 | n.s. | n.s. | n.s. | .01 | .02 | .001 |

n.s. = $p \geq 0.05$

The data analysis of the quality of life assessed by SF-36 is consistent with that of the psychopathological profile: with the only exception of the BP item, each item in both cirrhotic and HCC patient is worse than in normal subjects. Our results confirm the conclusions of the only paper in which the quality of life of HCC patients has been compared with that of the cirrhotic subjects [31], even though in our study the score of GH item is lower in the cirrhotic patients in comparison with those with HCC. The possible role of the compliance of HCC subjects may be evoked to explain this difference but, due to absence of a specific study in this topic, our hypothesis needs to be confirmed. According to Kondo, the impairment of health-related quality of life is not associated with the presence of HCC but is dependent mainly on the level of liver function assessed by Child-Pugh. This observation is coherent with several papers [32–35] that underline that the deterioration of the quality of life in cirrhotic patients is related to the onset of complications of chronic liver disease, such as ascites and hepatic encephalopathy.

The patients with cirrhosis and HCC are more alexithymic than normal subjects, but there are no significant differences between cirrhotics and HCCs. The frequency of alexithymic symptoms in our population is very high (50 % in HCC and 54 % in cirrhosis) in comparison with that described in the cirrhotic population by Nardelli (25 %) [28] but comparable to that relieved in other chronic disease such as obstructive pulmonary disease (43 %) in Chinese patients [36].

The relevance of alexithymia symptoms in the evaluation of the quality of life in patients with cirrhosis or HCC is still debated. The work by Nardelli and other papers has found that such symptoms are one of the determinants of quality of life, while in our population we did not observe any correlation between the values of the TAS-20 and each items of the SF-36. This difference is probably related to the fact that our population is composed almost exclusively by patients in Child A class, while that of the above authors includes more than half of the patients in Child B and C classes. By the way, we think that our results seem consistent with the original meaning of the term alexithymia, since the alexithymic subjects in situations of stress or conflict such as the management of chronic or neoplastic disease do not sense the discomfort on a psychological level, implement inappropriate behavior (acting out) and do not have the capacity to suffer pain, but only to hear that [16, 24].

**Table 5** Pearson moment correlation between SCL 90-R, TAS-20, Hamilton-D and each item of SF-36 questionnaire in patients with HCC ($n = 24$) (r,$p$)

| | PF | RP | BP | GH | VT | SF | RE | MH | PCS | MCS |
|---|---|---|---|---|---|---|---|---|---|---|
| SCL 90-R | | | | | | | | | | |
| SOM | −0.62 | −0.51 | −0.56 | −0.57 | −0.77 | −0.54 | −0.32 | −0.78 | −0.67 | −0.66 |
| | .001 | .009 | .004 | .003 | .00001 | .006 | n.s. | .00001 | .0003 | .0004 |
| O–C | −0.42 | −0.36 | −0.54 | −0.32 | −0.69 | −0.59 | −0.33 | −0.62 | −0.47 | −0.64 |
| | .03 | n.s. | .006 | n.s. | .0001 | .002 | n.s. | .002 | .02 | .0007 |
| IS | −0.31 | 0.38 | −0.51 | −0.19 | −0.46 | −0.56 | −0.23 | −0.66 | −0.39 | −0.57 |
| | n.s. | n.s. | .01 | n.s. | .02 | .004 | n.s. | .0005 | n.s. | .003 |
| DEP | −0.54 | −0.58 | −0.43 | −0.45 | −0.70 | −0.63 | −0.41 | −0.75 | −0.54 | −0.74 |
| | .006 | .002 | .03 | .02 | .0001 | .0008 | .04 | .00001 | .006 | .00003 |
| ANX | −0.47 | −0.46 | −0.56 | −0.25 | −0.55 | −0.49 | −0.24 | −0.60 | −0.55 | −0.50 |
| | .02 | .02 | .004 | n.s. | .005 | .01 | n.s. | .002 | .005 | .01 |
| HOS | −0.49 | −0.32 | −0.76 | −0.29 | −0.38 | −0.55 | −0.29 | −0.58 | −0.59 | −0.48 |
| | .01 | n.s. | .00001 | n.s. | n.s. | .005 | n.s. | .003 | .002 | .02 |
| PHO | −0.11 | −0.16 | −0.24 | −0.35 | −0.44 | −0.34 | −0.37 | −0.45 | −0.12 | −0.57 |
| | n.s. | n.s. | n.s. | n.s. | .03 | n.s. | n.s. | .02 | n.s. | .003 |
| PAR | −0.28 | −0.43 | −0.26 | −0.17 | −0.20 | −0.52 | −0.006 | −0.43 | −0.38 | −0.29 |
| | n.s. | .03 | n.s. | n.s. | n.s. | .008 | n.s. | .03 | n.s. | n.s. |
| PSY | −0.18 | −0.48 | −0.23 | −0.25 | −0.51 | −0.47 | −0.29 | −0.51 | −0.27 | −0.57 |
| | n.s. | .02 | n.s. | n.s. | .01 | .02 | n.s. | .01 | n.s. | .003 |
| TAS-20 | −0.31 | −0.25 | −0.36 | 0.005 | −0.09 | −0.12 | −0.12 | −0.30 | −0.32 | −0.13 |
| | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. |
| Hamilton-D | 0.39 | −0.46 | −0.12 | −0.34 | −0.65 | −0.23 | −0.31 | −0.57 | −0.33 | −0.53 |
| | n.s. | .02 | n.s. | n.s. | .0005 | n.s. | n.s. | .003 | n.s. | .007 |

n.s. = $p \geq 0.05$

Our study shows that many traits of the psychopathological profile affect the quality of life of both cirrhotic and HCC patients, among which SOM, obsessive–compulsive, DEP and anxiety as it has been shown by the correlation analysis, even if this result should be confirmed in a larger population. The effect is evident on physical and mental components of the SF-36 questionnaire. These results are consistent with those reported by Nardelli [28] as well as some previous observation on the negative correlation between HRQOL and DEP [10].

Main limitation of our study is the relatively small sample size of patients in each group. However, the size of sample is not very different from that examined in the study by Nardelli et al. [28] represented by 60 patients of which 34 affected by HCC.

In conclusion, we have shown that the quality of life of cirrhotic and HCC patients is impaired at almost the same level and that some components of the psychopathological profile, such as SOM, anxiety, DEP, are main determinants of the HRQOL profile. In addition, the higher prevalence of DEP in cirrhotic subjects in comparison with HCC subjects underlines the importance of taking charge of the patients with a bio-psychosocial approach along the care pathway. The development of the HCC seems to imply the comparison of aspects of the personality profile (like HOS and PSY) already considered as psychological distress symptoms in other neoplastic disease such as the early colorectal cancer [37], but whose prognostic meaning needs to be clarified in longitudinal studies with a larger population than that considered in this study.

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**Conflict of interest** None.

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