

Psychological impact of chronic hepatitis C: Comparison with other stressful life events and chronic diseases

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psychological and emotional burden that a diagnosis of CHC represents, even in the absence of significant liver disease. They should be taken into account when announcing a diagnosis of CHC in order to reduce its negative effects.

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Key words: Hepatitis C; Stressful life event; Perceived severity; Visual analogue scale

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Abstract

AIM: To examine the psychological impact of chronic hepatitis C (CHC) diagnosis in a large cohort of CHC patients as compared with other stressful life events and chronic diseases carrying a risk of life-threatening complications.

METHODS: One hundred and eighty-five outpatients with compensated CHC were asked to self-grade, using a 100-mm visual analogue scale (VAS), the degree of stress caused by the learning of CHC diagnosis and the perceived severity of their disease. Diagnosis-related stress was compared to four other stressful life events and perceived CHC severity was compared to four other common chronic diseases.

RESULTS: Learning of CHC diagnosis was considered a major stressful event (mean \pm SD scores: 72 ± 25), significantly less than death of a loved-one (89 ± 13 , $P < 0.0001$) and divorce (78 ± 23 , $P < 0.007$), but more than job dismissal (68 ± 30 , $P < 0.04$) and home removal (26 ± 24 , $P < 0.0001$). CHC was considered a severe disease (74 ± 19), after AIDS (94 ± 08 , $P < 0.001$) and cancer (91 ± 11 , $P < 0.001$), but before diabetes (66 ± 23 , $P < 0.001$) and hypertension (62 ± 20 , $P < 0.001$). Perceived CHC severity was not related to the actual severity of liver disease, assessed according to Metavir fibrosis score. In multivariate analysis, diagnosis-related stress was related to perceived disease severity ($P < 0.001$), trait anxiety ($P < 0.001$) and infection through blood transfusion ($P < 0.001$).

CONCLUSION: Our results show the considerable

INTRODUCTION

Despite the fact that chronic hepatitis C (CHC) may lead to life-threatening complications such as cirrhosis, liver failure and hepatocellular carcinoma, most patients with CHC are asymptomatic and unaware of their liver disease prior to diagnosis. Nonetheless, these patients consistently report a significant reduction in health-related quality of life (HRQOL) as compared with population controls^[1-6]. This impairment of HRQOL has been documented even in the absence of significant liver disease^[3] and is usually improved after sustained viral clearance^[4,5]. In addition, clinically significant emotional distress and depressive disorders have been reported in untreated CHC patients with a prevalence ranging from 11 to 53%^[2,7-13], questioning the role of HCV itself in their occurrence^[16]. Whether these disorders are due to the uncertainty of living with a chronic disease with potential life-threatening complications or to other psychosocial factors remains unclear. However, it has been recently shown that CHC patients aware of their diagnosis had worse HRQOL scores as compared with unaware seropositive patients^[6,17], suggesting that the psychological impact of diagnosis knowledge may play an important role.

The aim of this prospective study was to examine the psychological impact of CHC diagnosis in a large cohort of CHC patients as compared with other stressful life events and chronic diseases carrying a risk of life-threatening complications.

MATERIALS AND METHODS

Study population

A total of 185 patients with a confirmed diagnosis of HCV infection (defined as detectable hepatitis C antibodies and HCV RNA in serum) attending the Hepatology Clinics at the University of Bordeaux were studied. Exclusion criteria were: age below 18 years, decompensated cirrhosis, co-infection by hepatitis B virus or human deficiency virus (HIV), current psychotic or manic disorders, obvious intellectual impairment, and inability to communicate in French.

Measures

Immediately prior to or following an outpatient clinic appointment, and after their written informed consent had been obtained, participants were asked to self-grade, using a 100-mm visual analogue scale (VAS), the degree of stress caused by the learning of CHC diagnosis. On that scale, the left endpoint 0 was defined as not stressful at all, the right endpoint 100 as extremely stressful. There were no further marks on the line. Instructions were as follows: "Put a mark on the line at the point that best describes how stressful you consider the learning of hepatitis C diagnosis". The degree of stress experienced was indicated by the distance in millimeters from the left endpoint. Perceived disease severity was assessed using the same method. VAS has been shown to be a reliable tool to assess subjective variables, such as stress^[18], pain^[19] and fatigue^[20].

In addition to validate the reproducibility of measurements over time, a second assessment was performed 3 mo later in a subgroup of randomly selected patients.

Trait anxiety was assessed using the Spielberger State Trait Anxiety Inventory^[21], a 20-item standardized self-report scale ranging from 20 (low tendency to be anxious) to 80 (high tendency to be anxious).

The influence on diagnosis-related stress of age, gender, marital status, educational level, route of HCV transmission, time since diagnosis, antiviral therapy, perceived severity of illness, actual severity of liver disease (assessed according to the fibrosis score of the METAVIR scoring system^[22] in patients in whom a liver biopsy specimen was available), and trait anxiety was also studied.

Comparison with other stressful life events and chronic diseases

Using VAS mean scores, diagnosis-related stress was compared to four other stressful life events (i.e., home removal, job dismissal, divorce, or death of a loved-one) selected from the Paykel life-event scale^[23]. Perceived CHC severity was compared to four other common chronic diseases carrying a risk of life-threatening complications (i.e., hypertension, diabetes mellitus, cancer and AIDS).

Statistical analysis

VAS scores for diagnosis-related stress and perceived disease severity were expressed as mean \pm SD. Chi-square test was used for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. A *P* value < 0.05 was considered statistically significant. Using paired Student's *t*-test, test-retest reliability was

Table 1 Characteristics of the 185 patients studied

	<i>n</i> = 185 (%)
Age (yr)	45 \pm 11
Gender (male/female)	111/74
Educational level	
No diploma	24 (13)
High school	83 (45)
College undergraduate	35 (19)
College graduate	43 (23)
Marital status	
Single/divorced	57 (31)
Married	92 (50)
Non-married couple	36 (19)
Routes of transmission for HCV	
Blood transfusion	74 (40)
Intravenous drug use	48 (26)
Others*	63 (34)
Histological severity (Metavir fibrosis score)	<i>n</i> = 169
F0-1	39 (23)
F2	83 (49)
F3	19 (11)
F4	28 (17)
Trait anxiety (STAI)	45 \pm 11 (20-80)

assessed for VAS mean scores in a randomly selected sample of patients. For the study of factors associated with diagnosis-related stress, ANOVA was used for both categorical (gender, educational level, marital status, route of transmission, antiviral therapy, and histological severity of liver disease) and continuous variables (age, perceived disease severity and trait anxiety). For the later, patients were divided into two groups according to the median value. Multivariate analysis was performed including variables significantly associated with diagnosis-related stress (*P* < 0.10).

RESULTS

Study population

The characteristics of the 185 patients are shown in Table 1. There were 111 men and 74 women with a mean age of 45 \pm 11 years. The study group had a broad distribution of educational background. Seventy-four (40%) patients were infected through blood transfusion, whereas 48 (26%) were infected through intravenous drug use. The mean time since CHC diagnosis was 2.9 \pm 2.6 years. Fifty-nine (32%) patients were receiving antiviral therapy at the time of the study. Of the 169 patients with available liver biopsy data, 28 (17%) had evidence of cirrhosis. The mean STAI-Y score for trait anxiety was 45 \pm 11 (range 22-80). This score did not differ from measures obtained in a community sample^[24].

VAS scores for diagnosis-related stress and perceived disease severity

Mean \pm SD scores for diagnosis-related stress were 72 \pm 25 (range: 5-100). Mean \pm SD scores for perceived disease severity were 74 \pm 19 (range: 15-100). Three months later, the second assessment in a subgroup of 30 randomly selected patients showed that all VAS scores were reproducible over time (no difference was observed for

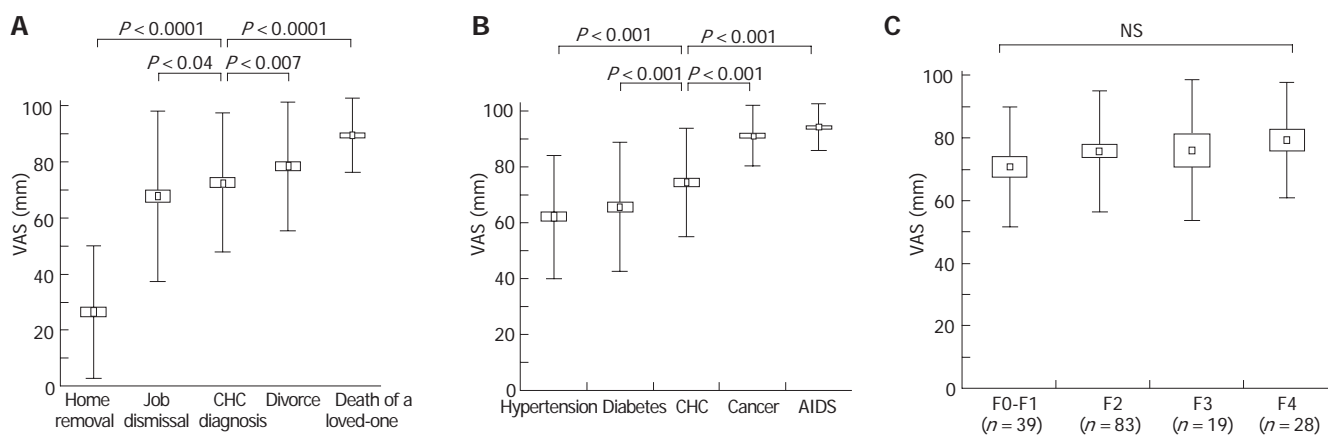


Figure 1 (A) Comparison between mean visual analogue scale (VAS) scores for chronic hepatitis C (CHC) diagnosis-related stress and four other stressful life events (i.e., home removal, job dismissal, divorce, and death of a loved-one) selected from the Paykel life-event scale^[23] in the 185 patients. *P* values are for post-hoc comparisons made after significant one-way ANOVA ($F=249.32$, $P<0.0001$). (B) Comparison between mean visual analogue scale (VAS) scores for perceived chronic hepatitis (CHC) severity and four other common chronic diseases carrying a risk of life-threatening complications (i.e., hypertension, diabetes, cancer and AIDS) in the subgroup of 185 patients. *P* values are for post-hoc comparisons made after significant one-way ANOVA ($F=173.81$, $P<0.001$). (C) Mean visual analogue scale (VAS) scores for perceived chronic hepatitis (CHC) severity according to actual severity of liver disease assessed using METAVIR fibrosis score (F0: no fibrosis; F1: portal fibrosis without septa; F2: portal fibrosis and few septa; F3: numerous septa without cirrhosis; F4: cirrhosis) in the 169 patients with available liver specimen. In Figures A, B and C, the upper and lower limits of the boxes and the middle square indicate the standard error and the mean, respectively. The upper and lower horizontal bars indicate the standard deviation.

any item, using a paired *t* test).

Comparison with other stressful life events and chronic diseases

Mean ±SD scores for stress were as follows: death of a loved-one (89 ± 13), divorce (78 ± 23), CHC diagnosis (72 ± 25), job dismissal (68 ± 30) and home removal (26 ± 24) (Figure 1A). CHC diagnosis was significantly more stressful than job dismissal ($P<0.04$) and home removal ($P<0.0001$) but less than divorce ($P<0.007$) and death of a loved-one ($P<0.0001$).

Mean VAS scores for perceived disease severity were as follows: AIDS (94 ± 08), cancer (91 ± 11), CHC (74 ± 19), diabetes mellitus (66 ± 23) and hypertension (62 ± 20) (Figure 1B). CHC was considered significantly more severe than diabetes mellitus ($P<0.0001$) and hypertension ($P<0.0001$) but less than cancer ($P<0.001$) and AIDS ($P<0.001$).

Relationship between perceived disease severity and actual severity

Mean VAS scores for perceived disease severity did not differ according to the Metavir fibrosis stages in the 169 patients in whom a liver specimen was available (Figure 1C).

Factors associated with diagnosis-related stress

In univariate analysis, diagnosis-related stress was associated with female sex ($P<0.003$), infection through blood transfusion ($P<0.002$), high perceived disease severity ($P<0.001$) and high trait anxiety ($P<0.001$) (Table 2). Stress tended to be higher in patients with low education level, although the difference did not reach statistical significance ($P=0.07$). Scheffé post hoc tests revealed that stress scores were significantly higher in

Table 2 Factors associated with diagnosis-related stress in univariate analysis in the 185 patients

	Diagnosis-related stress (mean VAS scores)	<i>P</i>
Age (yrs)		
< 46	73 ± 25	
≥ 46	72 ± 24	NS
Gender		
Male	66 ± 26	
Female	79 ± 22	< 0.003
Educational level		
< High school	75 ± 24	
≥ High school	69 ± 25	0.07
Marital status		
Single/divorced	73 ± 25	
In couple	72 ± 24	NS
Routes of transmission for HCV		
Blood transfusion	80 ± 20	
Intravenous drug use	65 ± 27	
Others	68 ± 26	< 0.002
Antiviral therapy		
Ongoing	69 ± 25	
Untreated	74 ± 25	NS
Histological severity of liver disease (n=169)		
F0-F1-F2 (n=122)	74 ± 23	
F3-F4 (n=47)	70 ± 29	NS
Time since diagnosis (yrs)		
< 2	71 ± 26	
≥ 2	73 ± 24	NS
Perceived disease severity (VAS)		
< 75	59 ± 23	
≥ 75	83 ± 21	< 0.001
Trait anxiety (STAI)		
< 45	64 ± 27	
≥ 45	81 ± 19	< 0.001

For continuous variables (age, time since diagnosis, perceived disease severity and trait anxiety) patients were divided into two groups according to the median value.

Table 3 Factors associated with diagnosis-related stress in multivariate analysis in the 185 patients

	Diagnosis-related stress (100mm VAS score) ²	
	β^1	P
Gender : (male: 1, female: 2)	0.02	0.76
Routes of transmission: (drug user =1; other =2, blood transfusion =3)	0.17	<0.01
Educational level: (< high school:1, \geq high school:2)	-0.03	0.58
Anxiety (STAI-Y score)	0.30	<0.001
Perceived disease severity (100mm VAS score)	0.43	<0.001

¹regression coefficient.

²Regression model: R=0.60, R²=0.36, adjusted R²=0.35, F(5, 171)=19.65, P<0.001.

patients infected through blood transfusion than in those infected through intravenous drug use ($P<0.001$). No difference was observed for patients infected through other routes of transmission. Stress did not differ between untreated and treated patients. In the latter patients, stress did not differ according to virological response.

In multivariate analysis, stress was related only to perceived disease severity ($P<0.001$), trait anxiety ($P<0.001$) and infection through blood transfusion ($P<0.01$). These parameters accounted for 36% of the variance of diagnosis-related stress (R²=0.36; $P<0.001$; Table 3).

DISCUSSION

Our results show that learning one has contracted HCV infection, with its implications for future health and behaviour, is a major stressful event (with mean scores of 72 ± 25 on a 100-mm visual analogue scale). By comparison with other stressful life events selected from the Paykel life-event scale^[23], ranging from minor (i.e., home removal) to major (i.e., death of a loved one), CHC diagnosis was considered less stressful than death of a loved one (89 ± 13 , $P<0.0001$) and divorce (78 ± 23 , $P<0.007$), but more than job dismissal (68 ± 30 , $P<0.04$) and home removal (26 ± 24 , $P<0.0001$). These results emphasize the considerable emotional and psychological burden that CHC diagnosis represents in patients' life. So far, the psychological issues that CHC patients face remain poorly understood. In the studies having reported clinically significant emotional distress and depressive disorders in patients with CHC^[2,13-15], the psychological impact of diagnosis knowledge was not taken into account. However, it is important to distinguish between psychological reactions to the knowledge that one has been infected with HCV and the direct effects of the virus itself as evidenced by the results of the present study. Our findings are consistent with those of Rodger *et al*^[6] who compared 15 patients who were aware of having HCV infection with 19 subjects who were unaware of having HCV infection, and found that the former had significantly poorer HRQOL scores. More recently, Dalgard *et al*^[17] have confirmed these results in a cohort of 199 Swedish active drug user patients, showing that those who

believed they were infected had a lower HRQOL scores than those who believed they were not infected. Taken together, these results provide evidence of the considerable negative impact of the knowledge of the diagnosis of CHC on patients' perception of their psychological well-being, known for other chronic diseases as the "labeling" effect^[25]. Such an effect has recently been illustrated in a study by Zickmund *et al*^[26], showing that stigmatization was common in patients with CHC and was associated with a lower quality of life and with a deterioration of social support.

There are increasing evidences that CHC infection may be associated with significant cerebral dysfunction. Several authors have reported cognitive impairment and central nervous system functional abnormalities in CHC patients compared with uninfected controls, using P300 event-related potentials, a sensitive electrophysiologist test of cognitive processing^[27] or magnetic resonance spectroscopy^[28-31]. Such findings suggest a direct biological effect of HCV infection on cerebral function. Whether cognitive dysfunction is an important determinant of impaired HRQOL in CHC remains to be determined.

As natural history of chronic HCV infection remains poorly defined^[32], it is not surprising that CHC diagnosis, a disease with uncertain outcome, raises significant concerns about future health status. Indeed, CHC was perceived as a severe disease (74 ± 19), after AIDS (94 ± 08 , $P<0.001$) and cancer (91 ± 11 , $P<0.001$), but before diabetes (66 ± 23 , $P<0.001$) and hypertension (62 ± 20 , $P<0.001$). Interestingly, perceived CHC severity was not related to the actual severity of the disease, as assessed by the severity of liver histological lesions. This finding is consistent with the results of Foster *et al*^[3] who showed that the significant impairment of HRQOL experienced by CHC patients could not be attributed to the histological severity of liver disease. It is also in keeping with studies^[33-35] conducted in patients with hypertension or chronic respiratory diseases, showing that perception of a disease usually correlates poorly with its medically defined characteristics. In addition, the patients' perception of CHC severity seemed to have a more significant impact on their psychological status than did the histological severity of their liver disease as evidenced by multivariate analysis, showing that diagnosis-related stress was mainly related to perceived CHC severity, trait anxiety and infection through blood transfusion. An explanation for that latter finding may be the fact that patients infected through blood transfusion had no reason to expect such a health problem. By contrast, former drug users likely knew, given their past lifestyle, they were at risk of contracting severe diseases, such as HIV/AIDS, hepatitis B or C, with related-consequences for their future health.

Although our patient population does not represent a random sampling of CHC patients, we believe that it is representative of the general population of CHC patients. The demographic and clinical characteristics of our study population, including routes of transmission and proportion of patients with cirrhosis at the time of diagnosis, are similar to that reported in large surveys of patients with CHC in France^[36,37]. In addition, all

VAS scores were reproducible over time in a sample of randomly selected patients. Although some of our patients received antiviral therapy (32%), diagnosis-related stress and perceived disease severity mean VAS scores did not differ between treated and untreated patients.

Finally, our findings may have important implications for clinicians who take care of patients with CHC. They highlight the importance of communication between patients and their physician and the crucial role of the specialist in providing adequate and accessible information for patients to cope with their condition^[38].

In conclusion, our results show the considerable psychological and emotional burden that a diagnosis of CHC represents, even in the absence of significant liver disease. They should be taken into account when announcing a diagnosis of CHC in order to reduce its negative effects.

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