

Relationship between psychiatric disorders and physical status during the course of a heart transplantation program: a prospective, longitudinal study

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Background. Evidence of a lack of relationship between psychiatric disorders and physical status during a heart transplantation (HT) program would configure mental well-being as an independent endpoint deserving specific interventions.

Methods. We report a prospective, longitudinal study on patients (n = 127) undergoing HT in order to investigate the relationship between psychiatric disorders and physical status.

Results. At pre-HT evaluation, at least one psychiatric disorder according to the DSM-IV diagnoses was present in 27 patients (21%); the prevalence of psychiatric disorders was not related ($p \geq 0.150$) to physical status (assessed by clinical, electrocardiographic, echocardiographic, and hemodynamic parameters). At post-HT evaluation 1 year after HT, all clinical-instrumental parameters significantly improved ($p \leq 0.016$), but not the prevalence of psychiatric disorders, which were diagnosed in 34 patients ($p = 0.016$ vs pre-HT).

Conclusions. During the HT program, no significant relationship exists between physical status and prevalence of psychiatric disorders, which increases after the operation. This finding indicates the need for the mandatory provision of adequate psychological support during all of the phases of the HT experience.

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Since patients with chronic heart failure (CHF) might be interested in quality of life more than length of life in absolute terms, their mental status deserves special attention¹. Conflicting reports exist on the effect of heart transplantation (HT) on mental status^{2,3}. The studies reported in the literature do not include a prospective, longitudinal exploration of the relationship between physical status and prevalence of psychiatric disorders during the course of an HT program^{4,5}. If such a study demonstrated a lack of correlation between the physical and mental dimensions, this would indicate that mental well-being should be considered as an independent therapeutic endpoint^{6,7}. Conversely, evidence of direct correlation between physical and psychiatric disorders would imply that interventions aimed at improving physical status can also benefit mental status⁸⁻¹⁰. Accordingly, we designed a prospective, longitudinal study to investigate the relationship between psychiatric disorders and physical status during the course of an HT program.

Methods

All consecutive patients with CHF who underwent HT at our Institution from January 1993 to December 2001 were considered eligible for the study. The single inclusion criterion was the availability of a concomitant mental and physical status assessment at the time of listing (pre-HT evaluation) and 1 year after HT (post-HT evaluation). All patients who did not complete the pre- and post-HT evaluations were excluded from the study. Physical status evaluation included a complete physical examination, electrocardiography (ECG), two-dimensional standard transthoracic echocardiography, and right heart catheterization. The authors prospectively collected clinical and instrumental parameters at the time of psychiatric evaluations. All patients underwent detailed semistructured interviews by clinical psychologists with extensive experience in psychosomatic research; the Italian version of the SCID leading to DSM-IV diagnoses was used⁴. DSM-IV di-

agnoses considered were: post-traumatic stress disorder, generalized anxiety disorder, specific phobia, agoraphobia, major depressive disorder, adjustment disorder, panic disorder, social phobia, dysthymic disorder, schizophreniform disorder. DSM-IV psychiatric diagnoses were eventually grouped in diagnostic categories⁴.

Continuous variables are expressed as mean \pm SD, and categorical data as number (percentages). Comparisons between groups with or without at least one DSM-IV diagnosis were performed with unpaired Student's t-test or χ^2 test. Effects of HT on DSM-IV diagnoses and clinical-instrumental parameters were analyzed using the McNemar's and paired Student's t-test. Identification of predictors of survival was accomplished by performing Cox proportional hazards analysis on candidate variables. A p value $<$ 0.05 was considered as statistically significant.

The local Institutional Committee on human research approved the study, which has been performed and reported according to national legal requirements, and the Declaration of Helsinki. Informed consent was obtained from every patient.

Results

The inclusion/exclusion criteria were fulfilled by 127 patients (Table I). The mean time from pre-HT evaluation to HT was 5 ± 5 months. It should be noted that the vast majority of patients enrolled in the study were young males who underwent HT because of severe CHF due to non-ischemic dilated cardiomyopathy (Table I). As shown in table II, anxiety-related disorders turned out to be the most frequent psychiatric diagnostic category at pre-HT evaluation.

Table I. Clinical and instrumental characteristics of 127 patients before and after heart transplantation (HT).

	Before HT	After HT	p
Age (years)	52 \pm 11		
Male gender	112 (88%)	–	–
Ischemic etiology	46 (36%)	–	–
NYHA class III-IV	108 (85%)	2 (2%)	$<$ 0.001
SBP (mmHg)	104 \pm 15	139 \pm 16	$<$ 0.001
HR (b/min)	80 \pm 15	77 \pm 10	0.133
LVEDD (mm)	75 \pm 12	45 \pm 5	$<$ 0.001
LVEF (%)	26 \pm 8	61 \pm 8	$<$ 0.001
RAP (mmHg)	7 \pm 4	5 \pm 3	0.016
PCWP (mmHg)	20 \pm 9	10 \pm 3	$<$ 0.001
PAP (mmHg)	29 \pm 10	16 \pm 4	$<$ 0.001
CI (l/min/m ²)	2.3 \pm 0.6	3.4 \pm 0.8	$<$ 0.001

CI = cardiac index; HR = heart rate; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; RAP = right atrial pressure; SBP = systolic blood pressure.

Table II. Prevalence of diagnoses of psychiatric disorders (DSM-IV diagnostic categories) in 127 patients with chronic heart failure undergoing heart transplantation (HT).

DSM-IV diagnostic categories	Before HT	After HT	p
Anxiety disorders	25 (19%)	26 (20%)	$>$ 0.999
Mood disorders	2 (2%)	6 (5%)	0.219
Somatoform disorders	1 (1%)	1 (1%)	$>$ 0.999
Adjustment disorders	1 (1%)	3 (2%)	0.500
Psychotic disorders	0 (0%)	1 (1%)	$>$ 0.999
At least one DSM-IV diagnosis	27 (21%)	34 (26%)	0.016

Two patients before HT and 3 patients after HT had two diagnoses.

At pre-HT evaluation, patients with at least one DSM-IV diagnosis (n = 27) and those with no DSM-IV diagnosis (n = 100) were similar as regards clinical parameters (age p = 0.167, male gender prevalence p = 0.899, CHF etiology p = 0.654, NYHA class p = 0.594, systolic blood pressure p = 0.483), ECG parameters (heart rate p = 0.156, presence of right/left intraventricular conduction delay p \geq 0.476, sinus rhythm prevalence p = 0.195), echocardiographic parameters (left ventricular end-diastolic diameters p = 0.477, and ejection fraction p = 0.218), and hemodynamic parameters (right atrial pressure p = 0.923, pulmonary artery pressure p = 0.460, capillary wedge pressure p = 0.267, cardiac index p = 0.604). As regards the physical effects of HT, a striking improvement of clinical-instrumental physiological parameters was evident at post-HT evaluation (12 ± 4 months after HT) (Table I). However, this was not accompanied by any evidence of improvement in prevalence of diagnoses of psychiatric disorders (Table II) (note that "anxiety disorders" continued to be the most frequent diagnostic category). All the 27 patients who presented at least a DSM-IV diagnosis at pre-HT evaluation maintained it after HT, and 7 patients developed *de novo* psychiatric disorder after HT (p = 0.016). Patients with or without at least one DSM-IV diagnosis continued not to show after HT significant differences in the vast majority of the clinical and instrumental parameters (all p values \geq 0.139); the single exception was mean right atrial pressure (7 ± 4 vs 5 ± 3 mmHg in patients with and without DSM-IV diagnosis, respectively; p = 0.048). Regarding variables strictly related to post-HT status, no differences in biopsy score (p = 0.998), use of steroids (p = 0.633), or presence of malignancy (p = 0.548) was observable between patients with and without at least one DSM-IV diagnosis. The survival at 1 year after HT was not influenced by the presence of psychiatric disorders diagnosed neither before (p = 0.448 at univariate analysis using Cox proportional hazards analysis) nor after HT (p = 0.668).

Discussion

Our prospective longitudinal study provides evidence that no significant relationship exists between physical status and prevalence of psychiatric disorders during the course of the HT program. Moreover, we found that the already high prevalence of psychiatric disorders encountered in patients with CHF candidates for HT increases after the operation.

In our series, the prevalence of psychiatric disorders prior to HT was not related to objective parameters of CHF severity. This finding is in line with our previous observation that the objective indicators of disease severity that largely determine physicians' care appear to have little relationship on the mental status of CHF patients in general, raising the question as to whether accepted treatments for CHF may – by themselves – fail to satisfy patients' perceived needs¹¹. For example, the SOLVD study, which launched the use of angiotensin-converting enzyme inhibitors, indicated that these drugs lead, at best, to only modest improvements in quality of life¹².

We found that the improvements generated by HT in physical status did not coincide with any significant improvement in the prevalence of psychiatric disorders, which actually increased after HT. These findings underscore the relevance of patients' subjective perceptions¹³. Moreover this concept is further underlined by the general distance between prevalence of psychiatric disorders and physical status in our patients even at post-HT evaluation (the single recorded association between mental status and right atrial pressure has been previously reported¹). No relationship between DSM-IV diagnoses and episodes of severe rejections (possibly mediated by higher doses of steroids¹⁴) was confirmed in the present study; further data are needed to clarify these issues^{15,16}.

Should psychiatric disorders become a specific target for therapeutic interventions before and after HT? Patients waiting for HT undergo constant psychological stress, and usually present a compromised mental status at the time of intervention^{4,5,17,18}. Furthermore, the physical improvements after HT rely on maintenance of a demanding lifestyle, and compliance with complex therapeutic protocols and frequent check-ups and tests^{2,19,20}. In view of the psychological stress experienced during the HT program²¹, the higher prevalence of psychiatric disorders is scarcely surprising^{4,5,14,20}. While the effectiveness of any intervention should be carefully assessed before valuable resources are invested⁷, the unique nature of the transplantation discipline does seem to merit separate cost-effectiveness guidelines²², especially in the light of the life-saving nature of the procedure, society's goodwill toward organ donors, and the current organ shortage. Even though the present study does not address the question as to whether psychological support can improve mental status before or after HT, our findings further under-

line the importance of considering mental well-being as an independent endpoint deserving specific therapeutic interventions. Thus, appropriate forms of psychological support during HT programs need to be searched for without further delay^{4,14,21,23,24}.

Since a formal program of psychological support is not available at our Institution, for practical reasons, not all our HT recipients could be included in the present study. However, selection bias seems unlikely, since the study sample shows no differences in terms of etiology of CHF, age at the time of HT, or male gender prevalence (all $p \geq 0.410$) from the entire historical population of HT recipients at our Institution ($n = 285$). The possibility should also be noted that patients who do not fulfill DSM-IV criteria may also present psychological problems requiring clinical attention. Further studies using a combination of different diagnostic criteria are needed to reach optimal diagnostic accuracy.

In conclusion, during the HT program no significant relationship exists between physical status and prevalence of psychiatric disorders, which increases after the operation. This finding indicates the need for the mandatory provision of adequate psychological support during all of the phases of the HT experience.

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