

The Utility of a Specific Measure for Heart Transplant Patients: Reliability and Validity of the Kansas City Cardiomyopathy Questionnaire

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Background. Health-Related Quality of Life of patients with heart transplantation is an important variable; however, it has received little attention so far, and only two Spanish validated measurement instruments are available. The aim of our study was to validate the Spanish version of the Kansas City Cardiomyopathy Questionnaire (KCCQ) in heart transplant patients.

Methods. A prospective study was performed in 186 patients awaiting heart transplantation in nine transplant hospitals. Hundred transplant recipients filled out the KCCQ, the Euroqol 5-D (EQ5D), and the Short Form-36 (SF-36) Health Survey at pretransplant, after 3 months, 6 months, and 1 year of follow-up. A complete set of sociodemographic and clinical data were also collected. The validity, reliability, sensitivity to change, and effect size were studied. Two questionnaires, the SF-36 and EQ5D, were used to evaluate the validity.

Results. Mean age of patients was 56.0 years, and 80.5% were men. Twenty-six percent had acute rejection. A five-dimensional factorial structure could be discerned. The questionnaire presented a Cronbach's α coefficient of more than 0.7. Correlations between the KCCQ and the other questionnaires and clinical variables were satisfactory.

Conclusions. The KCCQ features adequate psychometric properties. The KCCQ offers several advantages over other questionnaires because it quantifies symptoms (frequency, severity, and stability) and it is much more sensitive to change, even when compared with the SF-36. The specific questionnaire for heart transplant patients is a useful and user-friendly instrument for measuring the Health-Related Quality of Life related to functional status, quality of life, and social limitation more accurately.

Keywords: Heart transplant, Health-Related Quality of Life, Kansas City Cardiomyopathy Questionnaire, Validation.

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There are 20 million people in the world with chronic heart failure (CHF); progressive deterioration would mean that many of these patients underwent heart transplantation. The aim of physicians is to perform transplant operations successfully but also to make the heart transplant patient's life as normal as possible. The improvements resulting from a successful transplantation are subject, however, to a variety of limiting factors, both physical and psychological (1, 2).

Generic Health-Related Quality of Life (HRQoL) questionnaires have been used in this group of patients (3), such as the Sickness Impact Profile (4) or the Short Form-36 (SF-36) (5). Specific evaluation tools are often more sensitive than generic health measures and enough to evaluate the impact of

specific diseases on HRQoL (6). HRQoL in heart transplantation has received little attention, and only a few validated specific measurement instruments are available, such as The Minnesota Living with Heart Failure Questionnaire (7), patients' perceptions of the effects of congestive heart failure on their lives, and the Kansas City Cardiomyopathy Questionnaire (KCCQ) (8) that was specifically developed to evaluate HRQoL in patients with CHF regardless of its origin. The KCCQ offers several advantages over the Minnesota Living with Heart Failure Questionnaire. The KCCQ quantifies symptoms (frequency, severity, and stability) and it is much more sensitive to change, even when compared with the SF-36 (9).

The aim of the present study was to assess the reliability and construct validity of the KCCQ in heart transplant recipients. In this sense, this study was undertaken to validate an appropriate, specific HRQoL tool of heart transplant patients for its routine use in the clinical practice in any Cardiology service. Two questions were specifically addressed: (1) "Is this questionnaire appropriate for measuring Spanish heart transplantations?" and (2) "Does this questionnaire enable us to gather more information than would be obtained relying only on the outcomes provided by a generic tool?"

MATERIALS AND METHODS

This study is part of the seven areas of the Research Network on Transplantation (RETIC C03/03), and it was an initiative for capturing HRQoL and clinical data for all patients undergoing heart transplantation in Spain. All patients 18 years or older (n=186) who were in the heart transplant

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waiting list in nine transplant hospitals in Spain and who had received their first cadaveric heart transplant between July 2004 and December 2006 ($n=100$) were included in this study for prospective pretransplant, after 3, 6, and 12 months posttransplantation ($n=98$).

Sociodemographic information and details of medical history were collected while patients were on the heart transplant waiting list and at 3 and 12 months after heart transplant. Data included age, sex, diagnostic, New York Heart Association (NYHA) functional degree, left ventricular ejection fraction, socioeconomic level, education level, occupation, comorbidities (measured by Charlson Index), immunosuppressor treatment (to evaluate whether there were any differences between HRQoL and side-effects associated to different immunosuppressive therapy regimens) and laboratory test. Also, two validated questionnaires were completed by the patients themselves or by trained interviewers (SF-36 Health Survey [SF-36] and Euroqol 5-D [EQ5D]).

The Questionnaires

The KCCQ is a self-administered, 23-item questionnaire measuring HRQoL in patients with CHF regardless of its origin. Each item has a 5-, 6-, or 7-point Likert scale. The questionnaire assesses six domains of HRQoL: Physical Limitation, Symptoms, Symptom Stability, Social Limitation, Self-Efficacy, and Quality of Life. Domain scores were transformed to 0–100 (highest level of functioning) scales. In addition, the KCCQ domains were aggregated into two summary scores: the Functional Status Summary Score and the Clinical Summary Score (8).

The SF-36 is a generic HRQoL assessment instrument (2–10) appropriately translated and validated in Spain (11), which includes eight dimensions and two summary scores (PCS, Physical Component Summary and MCS, Mental Component Summary). A standardization of these scores was applied, according to age and gender, using the Spanish population normative data (12). A standardized score more than 50 indicates better HRQoL than that of the general population of the same age and gender, whereas a score lower than 50 indicates worse HRQoL (13).

EuroQol (14, 15) describes the health status through five dimensions: mobility, personal care, daily-life activities, pain/discomfort, and anxiety/depression and also through a Visual Analog Scale (VAS).

Statistical Analysis

The statistical description of the clinical and socio-demographic variables was performed using frequencies, percentages, means, and standard deviations. The clinical mean values of the two time points were compared using a paired t test.

The validity, reliability, and sensitivity to change of the questionnaire were studied using the following analyses:

Step 1: an exploratory factor analysis (Varimax) was used to find if the responses of our patients were grouped in the same way as in the original questionnaire, analyzing the interrelationships between a set of variables. This step involved (a) determining the number of items and (b) identifying the number of meaningful factors to be retained based on the Scree test and the percentage of common

variance accounted for by a given factor (a minimum eigenvalue of 1.0 and the orthogonal rotation solution [Varimax] were used).

Step 2: internal consistency was studied by calculating Cronbach's α . This coefficient is acceptable when it is above 0.7, following the criteria expressed by Nunnally (16). Test-retest reliability was assessed by determining the intraclass correlation coefficient. It was therefore essential to include patients who would remain stable throughout the observation period (between 6 and 12 months posttransplantation). Requirements for stability were no hospitalizations, no change in NYHA classification, and a physician's assessment of stability.

Step 3: construct validity, studying the correlation coefficients between the KCCQ dimensions, and concept validity, analyzing the relationship between the KCCQ dimensions and the areas of SF-36 and EQ5D (VAS and health status preference value), using Pearson's coefficient of correlation corresponding to all data after heart transplantation.

Step 4: discriminant validity by comparing the scores of the KCCQ dimensions to the NYHA classification, diagnostic group, comorbidities, immunosuppressants (according to their primary calcineurin inhibitor regimen), left ventricle ejection fraction (LVEF) (<55% is considered as a reduce function), and according to the laboratory test and age. An analysis of variance was used, t test for simple comparison, and analysis of variance with Scheffe's test for multiple comparisons, and correlations for continuous variables.

Step 5: sensitivity to change, was estimated by means of a descriptive analysis of the KCCQ scores (at 3 and 12 months posttransplantation) using mean and standard deviation values. The mean values of the two time points were compared by a paired t test. The effect size was also assessed for each dimension of the Spanish KCCQ by dividing the difference between the mean score in the first interview and that of the last one by the standard deviation of the mean score in the first interview (17). The effect size is considered "small" if it is below 0.2; "moderate" if it is near 0.5; and "large" if it is above 0.8, according to Cohen's thresholds (17).

The statistical analysis was carried out with the SPSS 12.0 statistical software package. For all analyses, significance was taken as a P value less than 0.05.

RESULTS

The sample used for the validation study of the heart transplant version of the KCCQ was the 98 patients who received their first heart transplant and completed the year of follow-up, taking the personal interview when required.

Clinical and sociodemographic characteristics of the 98 patients are shown in Table 1. The comorbidity index changed during the different stages of the study: 1.29 ± 0.99 pretransplant; 1.0 ± 1.1 in the third posttransplant month; and 0.89 ± 0.76 after a year of follow-up. The analytic numbers with statistically significant improvements when comparing the initial values with those at the end of follow-up were hemoglobin, creatinine, and fasting glucose (Table 2).

Acute rejection episodes were experienced by 26% of patients during the first 3 months after transplantation and

TABLE 1. Respondents' characteristics (n=98), means and standard deviation, or proportions

Age, yrs (mean ±SD)	53.5 ± 9.5	Diagnosis (%)			
Male gender (%)	80.5	Ischemic cardiomyopathy		23	
Living with family (%)	96	Dilated cardiomyopathy		21	
Education level (%)		Cardiac valvulopathy		10	
Without primary	26.4	Others		31	
Primary	43.1	NYHA functional degree (%)			
Secondary or more	30.8	I (41)	II (43)	III (9)	IV (7)
Socioeconomic level (%) (<15,000 ₺/yr)	54.4	Diabetes (%)		33	
Smoking before transplant (%)	51	Chronic pulmonary disease (%)		3	
Alcohol before transplant (%)	23	Hypertension (%)		44	
Retired by illness (%)	69.3	Hyperlipidaemia (%)		44	

TABLE 2. Clinical data with means and standard deviation, or proportions at 3 and 12 months posttransplantation and statistical significance (P) between both moments with paired t test

	3 mos	12 mos	P
Acute rejection (%)	26	21	0.000
Body mass index, kg/m ² (mean ±SD)	26.5 ± 4.11	26.8 ± 4.4	NS
Biochemical analysis (mean ±SD)			
Hemoglobin (g/dL)	12.0 ± 1.5	12.5 ± 1.7	0.080
Creatinine (mg/dL)	1.48 ± 0.92	1.5 ± 0.91	0.701
Glucose (mg/dL)	96.4 ± 25.1	112 ± 51	0.020
Albumin (mg/dL)	4.05 ± 0.56	4.29 ± 0.34	0.000
Total cholesterol (mg/dL)	207 ± 49.2	175 ± 40	0.002
Triglycerides (mg/dL)	159.8 ± 74	135 ± 40	0.475
HDL (mg/dL)	117 ± 42	101 ± 39	0.026
LDL (mg/dL)	59.1 ± 18	51 ± 12	0.005
Immunosuppression (%)			
Cyclosporine+MMF+Prednisone	74	69	0.000
Cyclosporine+AZA+Prednisone	3	2	
Cyclosporine+Everolimus+Prednisone	4	3	
Tacrolimus+MMF+Prednisone	15	22	
Everolimus+MMF+Prednisone	4	64	

TABLE 3. Factor analysis—Rotated component matrix

Items	KCCQ				
	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
QoL and Social Limitation	0.704				
	0.545				
	0.705				
	0.571				
	0.604				
	0.569				
	0.493				
Moderate Physical Limitation		0.536			
		0.807			
		0.796			
		0.754			
Total Symptom Score			0.403		
			0.830		
			0.861		
			0.594		
			0.621		
			0.442		
			0.432		
			0.400		
Severe Physical Limitation				0.895	
				0.890	
Self-Efficacy					0.646
					0.808

by 21% 1 year after transplantation. With respect to hospital admissions throughout follow-up, 38% were admitted at least once; for these patients, the mean of hospitalized days was of 23 ± 20 days.

By the 12th month of follow-up, patients had used various immunosuppressive agents including prednisone (98%), cyclosporine (69%), mycophenolate mofetil (100%), tacrolimus (22%), azathioprine (2%), and sirolimus (4%). The predominant, mutually exclusive groups were those of patients on cyclosporine- and tacrolimus-based regimens with prednisone and others. Therefore, for the purpose of comparing patient/HRQoL, patients were grouped according

to their primary calcineurin inhibitor regimen: cyclosporine (n=81) and tacrolimus (n=15), with a 5% being crossovers between the two therapies.

Description of the Kansas City Cardiomyopathy Questionnaire

All the patients completed the Spanish version of KCCQ at all the stages of the study. Step 1 (factor analysis) yielded surprising results: (a) all 23 questions showed that the factor weights were higher than 0.40, except one question with 0.380. We found a new, stable, five-factor model (Table 3), which fits better than the original model (six factors); and

TABLE 4. Reliability: Internal consistency using Cronbach's α and test-retest using an intraclass correlation coefficient

KCCQ	Internal consistency	Test-retest
QoL and Social Limitation (QLSL)	0.87	0.84
Moderate Physical Limitation (MPL)	0.85	0.83
Total Symptom Score (TSS)	0.87	0.88
Severe Physical Limitation (SPL)	0.92	0.89
Self-Efficacy (SE)	0.46	0.45
Overall Summary Score (OSS)	0.93	0.91
Clinical Summary Score (CSS)	0.89	0.87

(b) the Scree test suggested that the first five factors were meaningful and hence worth keeping, as they explained the variance of 65.66% (eigenvalues 39.9; 9.7; 6.8; 6.1; 5.3) and the distributions of the items were similar (but not the same) to those in the original. The scales found through factor analysis were partly congruent with the original publication (15).

Step 2: the internal consistency reliability of the 23 questions was 0.92, measured by Cronbach's α (Table 4). For the dimensions: QoL and social limitation ($\alpha=0.87$), Moderate Physical Limitation ($\alpha=0.85$), Total Symptom Score ($\alpha=0.87$),

Severe Physical Limitation ($\alpha=0.92$), and Self-Efficacy ($\alpha=0.46$). The lower Cronbach's α for this domain reflects the different information of the two question's scale. In addition, the KCCQ domains were aggregated into two summary scores, the Overall Summary Score ($\alpha=0.93$) and the Clinical Summary Score ($\alpha=0.89$). Test-retests were higher than 0.7 for all dimensions, except for the Self-Efficacy dimension.

The results of step 3, the correlation coefficients among the dimensions of the KCCQ, are shown in Table 5. As can be observed, the coefficients ranged between the minimum of 0.18 and the maximum of 0.70 being, in most of the cases, moderate.

The correlation coefficients between the KCCQ and the SF-36 dimensions as well as EQ5D are presented in Table 5. Quality of Life and Social Limitation, Moderate Physical Limitation, Total Symptom Score, and the two summary scores of the KCCQ had high correlation coefficients with the physical dimensions of the SF36 and the two measures of EQ5D (EuroQol's health status preference value and EuroQol's VAS). Only QoL and Social Limitation and Overall Summary Score had modest correlations with the mental dimensions of the SF36. No adequate criterion standard is available for Self-Efficacy domain, and thus its acceptance could be decided based on its validity and reliability.

The last step of the validity process was the correlation of the KCCQ with sociodemographic and clinical variables.

TABLE 5. Validity: Correlation coefficients among the KCCQ dimensions, between the KCCQ dimensions and SF-36 and between the KCCQ dimensions and EuroQol-5D

	KCCQ						
	QLSL	MPL	TSS	SPL	SE	OSS	CSS
KCCQ autocorrelation							
QoL and Social Limitation (QLSL)							
Moderate Physical Limitation (MPL)	0.70 ^a						
Total Symptom Score (TSS)	0.65 ^a	0.61 ^a					
Severe Physical Limitation (SPL)	0.39 ^b	0.43 ^b	0.28 ^c				
Self-Efficacy (SE)	0.27 ^c	0.19 ^c	0.18 ^c	0.20 ^c			
Overall Summary Score (OSS)	0.95 ^a	0.81 ^a	0.80 ^a	0.48 ^b	0.26 ^c		
Clinical Summary Score (CSS)	0.76 ^a	0.86 ^a	0.87 ^a	0.53 ^b	0.20 ^c	0.92 ^a	
SF-36							
Physical functioning	0.63 ^a	0.64 ^a	0.52 ^b	0.37 ^b	0.18 ^c	0.69 ^a	0.65 ^a
Role-physical	0.63 ^a	0.61 ^a	0.54 ^b	0.40 ^b	0.18 ^c	0.70 ^a	0.66 ^a
Bodily pain	0.37 ^b	0.36 ^b	0.35 ^b	0.22 ^c	0.22 ^c	0.41 ^b	0.39 ^b
General health	0.57 ^a	0.45 ^b	0.49 ^b	0.24 ^c	0.11 ^c	0.59 ^a	0.51 ^b
Vitality	0.61 ^a	0.55 ^a	0.59 ^a	0.36 ^b	0.16 ^c	0.67 ^a	0.64 ^a
Social functioning	0.54 ^b	0.37 ^b	0.43 ^b	0.29 ^c	0.08 ^c	0.54 ^b	0.46 ^b
Role-emotional	0.52 ^a	0.35 ^b	0.41 ^b	0.28 ^c	0.09 ^c	0.52 ^b	0.45 ^b
Mental health	0.54 ^b	0.30 ^c	0.37 ^b	0.29 ^c	0.19 ^c	0.51 ^b	0.39 ^b
Physical Component Summary	0.54 ^b	0.58 ^a	0.50 ^b	0.35 ^b	0.17 ^c	0.61 ^a	0.60 ^a
Mental Component Summary	0.47 ^b	0.24 ^c	0.37 ^b	0.24 ^c	0.11 ^c	0.45 ^b	0.36 ^b
EuroQol-5D							
Visual Analog Scale	0.53 ^b	0.58 ^a	0.56 ^a	0.36 ^b	0.15 ^c	0.62 ^a	0.64 ^a
Health status preference value	0.59 ^a	0.56 ^a	0.52 ^b	0.32 ^b	0.08 ^c	0.64 ^a	0.61 ^a

All correlations were significant at the 0.01 level (two-tailed).

^a Moderate correlation ($r \geq 0.55$).

^b Modest correlation ($r \geq 0.32$ and $r < 0.55$).

^c Weak correlation ($r < 0.32$).

In general, the correlations of the seric hemoglobin were positive, although of a low degree, except for Moderate Physical Limitation ($P=0.019$). The seric creatinine and higher cholesterol levels correlated negatively, presenting low and moderate coefficients in some cases (QoL and Social Limitation, $P=0.036$ and 0.004 ; Moderate Physical Limitation, $P=0.060$ and 0.000 and Severe Physical Limitation, $P=0.000$ and 0.000). The NYHA classification of functional capacity presented moderate to high coefficients with Total Symptom Score and Severe Physical Limitation ($P=0.000$). For the Charlson's Scale, the correlation coefficients were low, being superior for the dimensions of the KCCQ that cover the physical area (Severe Physical Limitation, $P=0.015$ and Moderate Physical Limitation, $P=0.056$) than for those of the mental area (QoL and Social Limitation). The number of hospital admissions and days of hospital stay correlated negatively, with low coefficients, with the scores of the KCCQ dimensions, except for Moderate Physical Limitation ($P=0.056$) and Self-Efficacy ($P=0.002$) dimensions. These dimensions showed a moderate correlation with the days of hospital admission. Lower Total Symptom Scores were associated with increased age ($P=0.001$), whereas lower Severe Physical Limitation scores were associated with females ($P=0.046$) and reduced LVEF ($P=0.000$). There was no statistically significant association between the scores of the KCCQ dimensions

and the variables of "initial dysfunction of the graft," "acute rejection," and "immunosuppressor treatment."

In Table 6 the mean scores of the dimensions of the KCCQ and the SF-36 questionnaires are presented for the different stages of evolution. The KCCQ scores increased throughout the follow-up and also did those of the SF-36 and EQ5D, which means better HRQoL. In some cases, the increase is less important and not statistically significant (Self-Efficacy) whereas, in other cases, the increase is very clear (rest of the dimensions). PCS showed a little increase on follow-up and MCS a similar score to that at the start of transplantation. Only Physical Functioning, Role-Physical, Vitality, and Mental Health of the SF-36 experienced statistically significant changes within 3 and 12 months posttransplantation. Similarly, EuroQol's health status preference value and EuroQol's VAS were also better after 12 months when compared with the third month after transplantation, but only VAS was statistically significant.

Furthermore, along with the effect size coefficients for each of these score changes, the statistical significance based on " P " is shown in Table 6. The changes in the scores obtained in all dimensions of the KCCQ between the pretransplant and the 12-month follow-up were statistically significant, the mean scores improving throughout the first year. In SF-36, PCS, MCS, and all the dimensions (except for

TABLE 6. Health-Related Quality of Life scores and reliability assessments, statistically significant difference and effect size between mean scores at start (pretransplant) and at the end of follow-up (12 months)

Questionnaires	Moments of follow-up				P (3 mo vs. 12 mo)	Effect size
	Pretransplant	3 mo	6 mo	12 mo		
KCCQ (range 0–100)						
QLSL	32.3±21.6	69.1±23.9	78.3±17.7	83.1±18.9	0.000	2.37
MPL	25.3±24.1	60.4±29.0	71.3±25.3	79.0±22.1	0.000	2.23
TSS	51.6±25.7	80.5±21.2	85.1±19.4	85.7±19.7	0.049	1.33
SPL	73.7±32.4	86.5±21.1	94.7±12.8	95.1±15.5	0.001	0.66
SE	81.6±21.3	89.8±14.3	93.8±9.6	93.3±12.4	0.184	0.55
OSS	41.3±19.7	73.1±20.8	81.2±14.9	84.8±15.5	0.000	2.21
CSS	50.6±21.7	77.0±19.8	84.1±15.2	86.5±14.8	0.000	1.66
SF-36 (range 0–100)						
Physical functioning	16.7±26.5	39.3±15.4	42.3±14.9	45.3±11.9		
Role-physical	29.1±15.1	40.8±12.2	43.7±10.7	45.9±10.0	0.001	1.11
Bodily pain	42.3±14.5	43.2±11.9	44.7±12.5	44.6±12.3	0.999	0.16
General health	31.7±10.8	46.9±10.7	48.9±10.2	48.3±10.3	0.837	1.54
Vitality	32.7±12.0	49.2±11.2	51.2±10.9	52.3±10.5	0.033	1.63
Social functioning	12.8±45.3	34.3±28.1	40.2±19.7	37.8±28.3	0.207	0.55
Role-emotional	37.3±16.7	41.8±13.2	43.0±12.9	45.4±11.8	0.218	0.49
Mental health	39.5±13.1	46.8±13.3	51.3±11.1	51.9±12.4	0.021	0.95
PCS	22.7±20.2	39.1±14.3	41.6±12.0	42.9±12.4	0.060	1.00
MCS	39.0±17.2	46.7±15.4	49.8±12.6	50.0±14.6	0.225	0.64
EuroQol-5D						
Visual Analog Scale	38.3±19.3	67.9±16.1	72.0±16.4	75.3±17.1	0.006	1.92
Health status preference value	0.49±0.24	0.70±0.20	0.75±0.23	0.77±0.22	0.502	1.20

Dimensions of KCCQ: QoL and Social Limitation (QLSL), Moderate Physical Limitation (MPL), Total Symptom Score (TSS), Severe Physical Limitation (SPL), Self-Efficacy (SE), Overall Summary Score (OSS), and Clinical Summary Score (CSS). Physical Component Summary (PCS) and Mental Component Summary of the SF-36 (MCS).

Bodily Pain that scored almost the same as at the beginning of the study) were statistically significant. EuroQol's health status preference value and the VAS also had better scores, representing better perceived health ($P < 0.00$). EuroQol-5D results confirm the presence of impaired HRQoL in patients.

The effect size calculated for each dimension of the KCCQ was "high," except for Severe Physical Limitation and Self-Efficacy, for which it was "moderate." For the SF-36 and EQ5D, it was "moderate" to "high," except for Bodily Pain of the SF-36, for which it was "small."

DISCUSSION

In this section we will focus on answering the two main questions addressed in the article.

(1) Is this questionnaire appropriate for measuring Spanish heart transplants?

The results of this study support the psychometric properties of the KCCQ in patients with a heart transplant, and hence it has proved to be satisfactory. Every criterion to judge the interpretability and overall results was met on factor analysis (Table 3). We were able to show that factor weights were well above the minimum threshold required of 0.4, and they were grouped into five areas. In support of its reliability, most KCCQ scales were above 0.7, which is frequently cited as acceptable at group level (16). This indicates that the questionnaire is indeed reliable, even for its use in the individualized follow-up of heart transplant patients. The intraclass correlation coefficients calculated for the Spanish version of the KCCQ were also very good, above 0.7. One of the KCCQ scales, Self-efficacy, showed less consistent results in our population, than the other scales, and should be used with caution.

Also, the correlation coefficients between the dimensions of the KCCQ were moderate to high, conferring to the instrument the adequate construct validity. The positive correlation coefficients found between the dimensions of the KCCQ and the summary components of the SF-36 and EQ5D demonstrate that both instruments evaluate the same concept. We observed an adequate correlation of the questionnaire with SF-36 and the EQ5D areas, particularly for the domains of the physical component of the SF-36 and the EQ5D and, to a lesser extent, the mental domains (Table 5). However, the Bodily Pain dimension of the SF36 had weak correlations with KCCQ dimensions because patients did not report pain changes between the pre- and postheart transplantation scenarios. These results are consistent with the experience of other studies (18–21) using generic tools for HRQoL measurement, and confirm that HRQoL recovers after an adequate treatment.

Overall, correlations with the clinical variables were positive (the better the clinical value, the higher the HRQoL) and similar to those of previous studies (18–21), as were correlations with seric creatinine and higher cholesterol levels. We have found an important association between the HRQoL of transplanted patients and their degree of anemia in the initial stages, as previously described by other authors (22). Furthermore, the incidence of adverse posttransplantation events (initial graft dysfunction and acute rejection) was within the limits observed in other series of heart transplantations. The important association between KCCQ dimen-

sions and intensive care unit admissions or Charlson's Scale supported the validity of the KCCQ in heart transplantation.

(2) Does this questionnaire enable us to gather more information than would be obtained relying only on the outcomes provided by a generic tool?

The KCCQ offers several advantages over SF-36. The KCCQ provides more information about physical limitations and transplant symptoms than the SF-36 because it includes topics not assessed by the SF-36. In the present study, the score gradient between patients with normal and reduced LVEF or different functional classification of NYHA indicated that the scales of the disease-specific KCCQ discriminated better between patients with different levels of LVEF and NYHA than those of the generic SF-36. Also, this questionnaire is able to pinpoint significant differences between patients with different comorbidities using the Charlson's Scale. Therefore, the KCCQ was more responsive than the SF-36.

We did not find differences in HRQoL between a tacrolimus-based and a ciclosporin-based regimen on the dimensions of the KCCQ as reported in previous studies (23, 24). Additionally, KCCQ offers several advantages over other questionnaires, because not only does it capture physical limitations, but also quantifies symptoms independently of their immunosuppression treatment. On the other hand, the evolution of the scores in QoL and Social Limitation is centered on the evaluation of the emotional problems of heart transplanted patients, which are not included in the MCS score of the SF-36.

With respect to sensitivity to change, the differences between two mean values (3 and 12 months posttransplantation) and the effect size were very high, with a statistical significance lower than 0.01 and values over 0.80 (17) in almost every KCCQ dimension, thus demonstrating that the questionnaire is able to notice differences in health status between two specific periods, and that the change detected is indeed large.

Also, the improvement was partially confirmed, showing higher differences on the physical dimensions of the KCCQ and SF-36, than in the mental dimensions (Table 6) (18). As reported, the scores of the KCCQ dimensions showed a significant improvement in HRQoL between pretransplant and 3 months posttransplantation (scores increased significantly). Throughout the follow-up, HRQoL improved considerably with respect to scores at 3 months and it has been confirmed by the SF36; conversely, physical improvements were better determined by the KCCQ dimensions. Therefore, the KCCQ was more sensitive than the SF-36.

On the other hand, patients reported improvements in their mental condition in the first 3 months after transplantation, and physical and social improvements occurred after the third month posttransplantation. Also, this improvement in the mental condition was sustained consistently throughout the year, whereas the physical components continued to improve over the same period. To sum up, the absence of progress of the Bodily Pain dimension and the noteworthy improvement in the mental condition at 3 months (being similar to that of the general population) are significant occurrences.

However, the use of a questionnaire adapted to patients with a functioning heart transplant does not seem absolutely

correct when applied to other groups of different patients, as is the case of patients on the waiting list.

With regard to the effect size, the confirmed values showed the improvement on HRQoL in heart transplant. An effect size is a standardized, dimensionless number that allows the comparison of the results of different tests within one study (17). In short, effect size is a simple, quantitative measure that provides one useful index of the importance of an effect. The Moderate Physical Limitation, QoL and Social Limitation, and Total Symptom Score scales have the largest effect size ratio of any instrument used in these studies. The increase sensitivity of the KCCQ domains to clinical change, as compared with the baseline variability, should greatly increase the KCCQ's ability to detect important clinical changes in future clinical trials. However, we can conclude that a larger effect size may be associated with a more important clinical effect. Nevertheless, it is a limitation of this study that all patients were successful heart transplantees.

This is the second specific Spanish instrument translated and validated, and it can be used to measure symptoms and physical problems of patients with a functioning heart transplant.

The sample size of studies evaluating the psychometric properties of specific HRQoL assessment instruments, as is the case of the present study, can never reach the magnitude of the validations of generic instruments, given the shortage of patients available with a particular disease. The validation study of the original version of the KCCQ (8) was carried out with a sample of 98 heart transplant patients.

In summary, the KCCQ questionnaire provides a reliable way to know more about the HRQoL, especially about symptoms and physical and social limits on the heart transplant patient. We recommend the questionnaire for its use in clinical practice, mainly to study the physical domains difficulties in heart transplant patients. It has been elaborated through rigorous empirical development, it offers reliable psychometric properties, and it features an interpretable and rich factor structure. The study may provide a basis for future comparative assessments of heart transplantation and HRQoL. Specific measures to determine factors that intervene in HRQoL are essential to the development of new interventions that may modify their impact and, in the end, to improve the HRQoL of our transplanted patients.

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