The Organ Transplant Symptom and Well-Being Instrument – Psychometric Evaluation

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Abstract: *Background:* There is a need for instruments combining measurements of symptom distress and well-being in the organ transplant population.

Objectives: The aim of this study was to describe the development and initial psychometric evaluation of a measure of symptoms and well-being in organ transplant recipients labelled the Organ Transplant Symptom and Well-being instrument (OTSWI) and to provide descriptive data on these matters.

Method: In this cross sectional survey, the study sample (n=185) completed several measures including demographic information, the Short form- 36 items (SF-36), and the OTSWI to assess concurrent validity by exploring relationships between OTSWI and measures of health related quality of life (HRQOL). The expected scale dimensionality of the OTSWI questionnaire was examined both by the confirmatory multi-trait analysis program and by explorative principal component analysis (with oblique, varimax rotation). Scale reliability was further estimated using the Cronbach's alpha.

Results: There were eight factors built up from twenty of the initial fifty one items and were labelled *fatigue*, *joint and muscle pain*, *cognitive functioning*, *basic activities in daily life*, *sleeping problems*, *mood*, *foot pain* and *economy*. For the remaining twenty-one items no consistent and meaningful factors could be found leading to relevant symptoms acting as single items. All eight factors had satisfying internal convergent validity as well as good item-scale discriminatory validity or 'success rate'.

Discussion: Results support the internal consistency, reliability and concurrent validity of the OTSWI as an instrument to measure symptom distress and well-being in relation to organ transplantation. (Word count 244).

Keywords: Organ transplantation, symptoms, psychometric evaluation, health related quality of life, well-being, nursing.

INTRODUCTION

Health related quality of life (HRQOL) in organ transplant recipients has been extensively assessed since it has emerged as an important outcome measure to quantify the success of transplantation in the long term [1-4]. Forsberg [5] reported the experienced meaning of health and quality of life among liver transplant recipients, one year after the transplantation, as "*the sense of freedom to choose to do what ever you want to do and being able to do it*"[p 9]. Health was experienced as physical as well as mental well-being. Factors in support of experiencing the essence of health and quality of life were; courage to live, hope for the future, having a job and feeling mentally well. Health was not considered being totally medically healthy. The meaning of quality of life (QoL) sometimes was expressed as equal to experiencing health in general and in particular in strong conjunction with stable economy. Bad economy was considered to be a strong obstacle to reach QoL.

A systematic approach to incorporate symptoms and the impact of side-effects from medication is however seldom documented [6-7]. In an extensive review of symptom experience after solid organ transplantation [8] symptoms were related to health related quality of life and non-adherence. Based from their review of 135 references and 18 specific reports on symptom experience after organ transplantation Kugler *et al*., [8] concluded that further research should focus on the evaluation of symptom experiences using longitudinal designs to assess changes of occurrence and severity of symptoms over time. Also the interrelatedness between symptom experience and its potential impact on quality of life as well as on non-adherence need further clarification. Special attention should be paid to the level of perceived symptom distress and its impact on the daily life of the patient as a high level of distress might lead to non-adherence and worse HRQoL, as experienced in kidney, heart and lung transplant recipients [9]. Kugler *et al*., [8] argue that little evidence is given on the impact of symptom experience on outcomes in terms of HRQoL, including emotional and functional status and comorbidities.

Neurological complications are common after organ transplantation and can be divided into such of those common to all types of transplant and others of those specific to transplanted organ [10]. These complications are associated with significant morbidity involving neurotoxicity

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attributable to immunosuppressive drugs, followed by seizures, opportunistic central nervous system (CNS) infections, cardiovascular events, encephalopathy and de novo CNS neoplasms. Calcineurin inhibitors are the main drugs involved in neurotoxicity, leading to complications, which ranges from mild symptoms, such as tremors and parasthesia to severe symptoms, such as disabling pain syndrome and leukoencephalopathy [10-11]. Most of the instruments available aimed at assess symptom experiences are only focused on symptoms, and are predominantly based on clinical experience and expert panels [12-14]. There is a need for instruments combining measurements of symptom distress and well-being by the means of health related quality of life. Therefore the aim of this study was to describe the development and initial psychometric evaluation of a measure of symptoms and well-being in organ transplant recipients labelled the Organ Transplant Symptom and Well-being instrument (OTSWI) and to provide descriptive data on these matters.

FRAMEWORK

Symptom experience is a critical post-transplant outcome. A symptom is defined as a physical or mental feature, which is regarded as indicating a condition of disease, particularly such a feature that is apparent to the patient [15]. Symptoms are a regular part of the human experience. According to Kleinman [16], severe symptoms manifest as illness, which refers to how the sick person lives with and respond to the symptoms and disability. Symptoms are the most common reason why people seek health care and they are of vital importance in the treatment and care of the patients [17]. Behind the development of OTSWI there is a distinction between disease and illness. Disease is defined as an abnormality in the structure and functions of body organs and systems and can often be identified by signs of bodily disorder such as oedema or dyspnoea [18]. Illness means experienced reduction in states of well-being and social function manifesting as symptoms [18]. Disease and illness do not have a one-to-one relationship. Signs can be identified without experiences of symptoms and similar degrees of organ pathology can generate quite different symptoms i.e. graft rejection after organ transplantation. Illness may occur in the absence of detectable disease.

Symptoms might be defined as an experience reflecting changes in the biopsychosocial functioning, sensations or cognition of an individual. In contrast a sign is defined as any abnormality, indicative of disease that is detectable by the individual or by others [19]. Sometimes the symptoms occur in the absence of signs or they are poorly related to the severity of the disease [20].

Symptom experience can be conceptualized by two different related concepts symptom occurrence and symptom distress [21]. Symptom occurrence can be quantified by frequency, severity and duration of a given symptom. Symptom distress refers to the emotional burden caused by a symptom and might be defined as the degree of discomfort, physical and mental upset, anguish or suffering experienced from a specific symptom or symptom cluster [21-22]. In OTSWI symptom distress is measured by degree of discomfort. When there are three or more concurrent and multiplicative symptoms related to each other they are called symptom cluster e.g. fatigue. The symptoms in a cluster must not have the same aetiology in that they can have a physical as well as a psychological or cognitive origin.

Patients suffering from symptoms need care. A comprehensive assessment of the symptoms experienced from patients perspective, followed by identification of strategies for interventions and evaluation of the outcomes is the most common way to plan and accomplish care for the patients [23]. The effect or outcome criterion of the interventions is often assessed as changes in performance, health related quality of life, disease progression and survival [24-25]. The goal of organ transplantation is not merely survival, but to give the individual the best HRQoL possible. In the OTSWI the outcome criterion is well-being by the means of health related quality of life involving physiological, emotional, social and behavioural components. The basic assumption behind OTSWI is that well-being is present in the absence of fatigue, joint and muscle pain, sleeping problems, mood problems, foot pain and worries about economy as well as in the absence of impairments regarding cognitive functioning and basic activities in daily life. In this instrument well-being and health related quality of life are viewed synonymously. Health related quality of life (HRQoL) refers to a person's subjective evaluation of the influence of their current health status, health care, and health promoting activities on their ability to achieve and maintain a level of overall function that allows them to pursue valued life goals and that is reflected in their general well-being [26]. HRQoL is determined by emotional well-being and social, physical and cognitive functioning. Forsberg [5] have suggested the application of this HRQoL-definition on liver transplant recipients as follows. The transplant recipient's current health status, i.e. presence of graft rejection, infection or surgical complication influences, and is influenced by the health care provided such as medication, patient education or mental support. The individual ability to perform health-promoting activities, for example physical exercise and adherence with medication, affects the ability to achieve and maintain a level of overall functioning. The result of this process finally affects the person's ability to pursue valued life goals that in the end reflects their general well-being. Factors that determine HRQoL are emotional and social well-being as well as physical and cognitive functioning. Spiritual and socio-economic dimensions may affect the whole concept of HRQoL. The OTSWI doesn't include spiritual dimensions however; physical and cognitive functioning, emotional well-being as well as socio-economic dimension that determine HRQoL are covered. Social well-being and physical functioning will be included in the instrument during further development.

METHODOLOGY

Subjects and Procedures

In this cross sectional survey, questionnaires were mailed in February 2008 to organ transplant recipients (OTRs), transplanted at the Sahlgrenska University Hospital in Gothenburg, Sweden. Participants were included through an existing register including all OTRs. The invited study group included 229 OTRs between 19-65 years old, transplanted with a kidney (n=147), a liver (n=50) or a heart and/or a lung

(n=32). This distribution between organ transplantation reflects the reality at this centre; kidney transplant recipients (KTRs) are the largest group of transplanted patients and then liver transplant recipients (LTRs) and the smallest group are heart transplant recipients (HTRs) and lung transplant recipients (LUTRs). All patients with a recovery period of 1year +/- 3 months and 3 years +/- 3 months after transplantation were included. This criterion was applied in order to catch those with a relatively recent transplantation and those who have had their transplant for a longer time. Clinical and demographic data were collected in the set of questionnaires. Data included type of organ transplanted and date of transplantation, number of graft rejections, age, sex, marital and occupational status. After the first mailing, 162 participants responded. A reminder was mailed in May 2008, increasing the number of responders to 185 participants. This means a final response rate of 81% (185 of 229).

Questionnaires

Organ Transplant Symptom and Well-Being Instrument (OTSWI)

The development of the questionnaire OTSWI, which is developed to measure symptom prevalence, symptom distress and level of well-being, has followed the steps described by Juniper, Guyatt and Jaeschke [27] in Table **1**. Each response relates to how much the problem or situation discomforts you, assessed on a five-point scale ranging from "not at all"(0), "a little"(1), "somewhat"(2), "quiet a bit"(3) and "very much" (4). Time was specified to a time frame of one week.

Short Form Health Survey SF-36

The Swedish version of the SF-36 questionnaire, which measures health status, was used to validate the OTSWI questionnaire [28]. The SF-36 measures eight health domains: *Physical functioning* (PF), *Role limitations due to physical problems* (RP), *Bodily pain* (BP), *General health* (GH), *Vitality* (VT), *Social functioning* (SF), *Role limitations due to emotional problems* (RE) and *Mental health* (MH). The scores range from 0-100 on all scales with higher scores indicating a better HRQoL. The SF-36 also provides two summary measures; Physical Component Score (PCS) and Mental Component Score (MCS) [28].

Determining Validity of the OTSWI

Data was analysed with SPSS version 15.0 and the Multi-trait Analysis Program – version 2 [29]. The expected scale dimensionality of the OTSWI questionnaire was examined both by the confirmatory multi-trait analysis program and by

Table 1. The Steps of Development and Testing the Instrument Organ Transplant Symptom and Wellbeing Instrument (OTSWI) Suggested by Juniper, Guyatt and Jaeschke [27]

A. Development		
Step	***Task***	***Performance***
1	Specifying measurement goals	OTSWI was developed to be used for adult persons waiting for or have undergone solid organ transplantation (OT). They should be able to read and write Swedish or any other relevant language that the instrument is translated to. The primary purpose of the instrument is to be discriminative and evaluative. All areas of dysfunction associated with solid OT are included. The instrument is supposed to be self -administered, but will also be suitable for telephone interviews.
2	Item generation	Item pool was chosen from unstructured interviews, studies regarding health related quality of life (HRQOL), review of the transplant specific literature; discussions with transplant professionals and finally a review of generic HRQOL instruments.
4	Item reduction	The initial version included in a total 51 items. There were 28 items focused on symptoms, 8 items on physical functioning, 8 on emotional aspects and 7 items on social and financial aspects. The items were reduced by factor analysis based at 185 organ transplant recipients reported in Table 2. Finally the items were grouped into domains and labelled by a combination of their content, clinical experience and common sense.
4	Questionnaire formatting	Words were used that apply to the widest range of cultures and geographic areas in order to facilitate translation and widespread use. Each response relates to how much the problem or situation discomforts you, assessed on a five-point scale ranging from "not at all"(0), "a little"(1), "somewhat"(2), "quiet a bit"(3) and "very much" (4). Time was specified to a time frame of one week.
B. Testing		
5	Pretesting	A small pretest was performed involving ten organ transplant recipients (OTR).
6	Reliability	Scale reliability was estimated using the Cronbach's alpha. Reliability in terms of the relationship between the signal, in this case the difference between subjects, and the noise, the difference within a subject when the clinical state is stable will be tested by further research.
7	Responsiveness	To test if the instrument is responsive to the true change occurring in a patient over a period of time further research will be needed.
8	Validity	Validity was determined by the confirmatory multi-trait analysis program and by explorative principal component analysis (with oblique, varimax rotation). Construct validity was determined by examining the relation between OTSWI and the generic HRQOL-instrument SF-36.
9	Interpretability	We will use the so called anchor-based approach, where the changes in quality of life measures are compared, or anchored to other clinically meaningful outcomes. This will be tested further. In this study clinically meaningful outcomes were considered to be time since transplantation, number of graft rejections, type of organ and graft function at the time of the data collection.

explorative principal component analysis (with oblique, varimax rotation). In the multi-trait analysis program the hypothesized internal item-scale structure is examined, i.e. convergent and discriminatory validity. Convergent validity refers to the consistency of the items expected to measure a scale (factor). This was tested by computing the item correlations with their expected factor, corrected for overlap. A common criterion is item-scale correlations of at least 0.40 [29] Discriminatory validity was tested by computing the proportion of items that correlated higher or significantly higher with their expected (hypothesized) scale compared with the other scales (success rate). In the explorative principal component analysis, three strategies were used interactively to determine the number of tentative factors to retain - Cattell's scree plot, absorption of variance and meaningfulness of factors [30]. The item-scale structure that was the best compromise between the results of the multi-trait analysis and the explorative factor analysis was finally retained. Scale reliability was further estimated using the Cronbach's alpha. According to conventional rule this coefficient should at least exceed 0.70 [31]. Construct validity was tested by examining the relation between scores on the OTSWI and the generic HRQoL-instrument SF-36.

When analysing differences between two unpaired groups independent t-test were performed, and between three unpaired groups one-way ANOVA was performed. To investigate relationships Pearson correlations were calculated. The Ethics committee of Gothenburg University approved the study and the participants gave their written consent to participate.

RESULTS

Clinical and Demographic Variables

A majority of the participants were male (62%) and most of the total group were working (46%) or on disability pension (35%). A total of 66% were cohabitant or married. According to the selection, the distribution between the organ transplanted recipients reflected the reality at our center with 63% KTRs, 21% LTRs and 15% receiving a heart or a lung. Detailed demographics of the study participants are shown in Table **2**.

Obtained Factors in the OTSWI Questionnaire

There were eight factors verified by the psychometric tests developed to measure well-being. These eight factors were built up from twenty of the fifty-one items and were labelled *fatigue* (3 items), *joint and muscle pain* (3 items), *cognitive functioning* (2 items), *basic activities in daily life (BADL)* (3 items), *sleeping problems* (3 items), *mood* (2 items), *foot pain* (2 items) and *economy* (2 items). For the remaining twenty-one items no consistent and meaningful factors could be found leading to relevant symptoms acting as single items. In the explorative principal component analyses this eight-factor solution was supported by the following tests. Together the eight factors accounted for 86 % of the variance of the initial fifty-one items. Cattell's scree plot flattened out after the eighths factor and the items with the highest loadings on each factor were homogenous and meaningful in content. All eight factors also had eigen-values above one [28]. In the tests of convergent and discriminatory validity with the multi-trait analysis program it was found that all eight factors had satisfying internal convergent validity as well as good item-scale discriminatory validity or 'success rate'. Item scale correlations, corrected for overlap, ranged from 0.66 to 0.98 as shown in Table **3**. The related measure of item consistency, the Cronbach's alpha coefficient, was good for all scales (Table **3**).

Table 2. Demographics Among 185 Organ Transplant Recipients

Male	62 % (n=114)
Female	38 % (n=71)
Age < 50 yr	42 % (n=77)
Age > 50 yr	58 % (n=108)
Working	46 % (n=85)
Studying	2 % (n=3)
Retired	1 % (n=2)
Disability pension	35 % (n=64)
Sick-leave	12 % (n=22)
Unemployed	2 % (n=4)
Other	2 % (n=4)
Single	34 % (n=61)
Co-habitant/Married	66 % (n=122)
Kidney Transplant Recipients (KTR)	63 % (n=117)
Liver Transplant Recipients (LTR)	21 % (n=39)
Heart/Lung Transplant Recipients (HLTR)	16 % (n=29)
Time since tx; 1year +- 3 month	58 % (n=107)
Time since tx; 3 year +- 3 month	42 % (n=78)
Number of patients having a rejection	38 % (n=70)

Results of the test for construct validity are given in Table **4** where reasonable relations were found between the eight factors in OTSWI and SF-36 in all relevant areas except between basic activities in daily life and physical functioning (Table **4**). After reduction of 11 items that showed no meaningful correlation to any of the other items, in a total twenty single items remained measuring symptom prevalence and symptom distress as reported in Table **5**. When measuring relations between single symptoms and SF-36 (Table **6**) we only report correlations where at least one value is of .40 and above since this cut off represent a moderate correlation. The symptoms in Table **6** were selected since median level was reported as a little bit (median 1) indicating slight distress. Regarding the rest of the symptoms, also maintained in the instrument, the median level was 0 (not at all) and therefore not reported in the table.

Descriptive Data Regarding OTRs Experienced Well-Being

The data were skewed in all areas reported by OTSWI where descriptive data are given in Tables **7** and **8**. The reason for this descriptive part is to provide data for future comparison when further testing and using the OTSWI.

Table 3. The Factor Structure by the Use of Oblique Varimax Rotation

Factors in OTSWI	Item	Item Scale Correlation	Cronbach's Alfa
1. Fatigue (F)	I am physically tired	.81	.90
	I have no energy	.82	
	I feel lazy and listless	.83	
2. Joint and muscle pain (JMP)	My muscles are aching	.81	.87
	My joints are aching	.79	
	My legs are aching	.72	
3. Cognitive functioning (CF)	I have difficulties to remember	.89	.84
	I find it hard to concentrate	.66	
4. Basic ADL (BADL)	Due to my physical condition I can't get dressed by myself	.98	.92
	Due to my physical condition I can't take a bath or shower	.96	
	Due to my physical condition I can't buy food by my self	.84	
5. Sleeping problems (SP)	I have difficulties with falling asleep	.87	.89
	I sleep poorly	.88	
	I wake up during the night	.83	
6. Mood (M)	I feel irritated	.74	.82
	I feel angry	.86	
7. Foot pain (FP)	There is a burning ache in my feet	.86	.81
	There is a numb and stabbing feeling in my feet	.88	
8. Economy (E)	I worry about not being able to keep my job due to my health condition	.88	.81
	I worry about my economy due to my health condition	.84	

Table 4. Pearson Correlations Between the Factors of Organ Transplant Symptom and Wellbeing Instrument (OTSWI) and Short Form Health Survey SF-36 Measuring Eight Health Domains

OTSWI / SF-36	Fatigue	Joint and Muscle Pain	Cognitive Functioning	Basic ADL	Sleeping Problems	Mood	Foot Pain	Economy
PF	-.60**	-.46**	-.25**	-.26**	-.35**	-.23**	-.36**	-.37**
RP	-.67 **	-.41**	-.39**	-.18*	-.35**	-.33**	-.31**	-.44**
BP	-.39**	-.61**	-.34**	-.14	-.34**	-.29**	-.36**	-.30**
GH	-.55**	-.35**	-.43**	-.08	-.28**	-.35**	-.22**	-.46**
VT	-.76**	-.40**	-.54**	-.11	-.39**	-.42**	-.30**	-.46**
SF	-.60**	-.36**	-.49**	-.12	-.38**	-.46**	-.29**	-.51**
RE	-.57**	-.29**	-.41**	-.17*	-.29**	-.38**	-.25**	-.33**
MH	-.50**	-.28**	-.50**	-.05	-.38**	-.53**	-.22**	-.44**
PCS	-.60**	-.55**	-.29**	-.21**	-.35**	-.22**	-.36**	-.40**
MCS	-.57**	-.24**	-.54**	-.06	-.35**	-.53**	-.21**	-.42**

Physical functioning (PF), Role limitations due to physical problems (RP), Bodily pain (BP), General health (GH), Vitality (VT), Social functioning (SF), Role limitations due to emotional problems (RE) and Mental health (MH) and two summary measures; Physical component Score (PCS) and Mental component score (MCS).
*= Significance at .05-level.
** = Significance at.01-level.

There were three areas where the whole group reported worst well-being. In the first area, sleep problems (median 3= quite a bit) 79% reported the symptom and of those 27% were severely bothered. In the second area, fatigue (median 2= some what) 67% reported the symptom and among those 29% had severe problems. Finally 68% reported muscle and joint pain (median 2) where 16% had severe pain. The symptoms where median level was reported as a little bit (median 1) were dyspnoea (51%), trembling hands (53%), increased appetite (56%), and decreased libido (58%).

Table 5. Twenty Items Measuring the Prevalence of Symptoms and Level of Symptom Distress in the Organ Transplant Symptom and Well-Being Instrument (OTSWI)

	Symptoms	Not at All 0	A Little Bit 1	Some What 2	Quite a Bit 3	Very Much 4
1	I am breathless	0	1	2	3	4
2	I need to rest because I am breathless	0	1	2	3	4
3	I'm swollen	0	1	2	3	4
4	I feel nauseous	0	1	2	3	4
5	I have oral fungus	0	1	2	3	4
6	I have oral herpes	0	1	2	3	4
7	I have increased appetite for food	0	1	2	3	4
8	I have decreased appetite for food	0	1	2	3	4
9	I have dyspepsia	0	1	2	3	4
10	I'm constipated	0	1	2	3	4
11	I have diarrhea	0	1	2	3	4
12	My skin is itching	0	1	2	3	4
13	I have headache	0	1	2	3	4
14	There is a burning pain in my hands	0	1	2	3	4
15	There is a numb and stabbing pain in my hands	0	1	2	3	4
16	My hands are trembling	0	1	2	3	4
17	I feel dizzy	0	1	2	3	4
18	I feel sad	0	1	2	3	4
19	My looks makes me embarrassed	0	1	2	3	4
20	My libido is decreased	0	1	2	3	4

Each response relates to how much the problem or situation discomforts you, assessed on a five-point scale ranging from "not at all"(0), "a little"(1), "somewhat"(2), "quiet a bit"(3) and "very much" (4).

Table 6. Pearson Correlations Between Selected Symptoms Measured by Organ Transplant Symptom and Wellbeing Instrument (OTSWI) and Short Form Health Survey SF-36 Measuring Eight Health Domains

OTSWI / SF-36	Dyspnoea	Oedema	Dizzieness	Sadness	Decreased Libido	Embarrassed by Looks
PF	-.63**	-.48**	-.38**	-.35**	-.37**	-.29**
RP	-.53 **	-.33**	-.36**	-.48*	-.43**	-.32**
BP	-.35**	-.39**	-,20**	-.28**	-.29**	-.16*
GH	-.46**	-.25**	-.25**	-.46**	-.42**	-.22**
VT	-.58**	-.44**	-.44**	-.56**	-.45**	-.33**
SF	-.49**	-.33**	-.35**	-.57**	-.50**	-.36**
RE	-.32**	-.26**	-.35**	-.64**	-.39**	-.33**
MH	-.34**	-.28**	-.32**	-.70**	-.36**	-.40**
PCS	-.60**	-.43**	-.30**	-.27**	-.39**	-.20**
MCS	-.32**	-.25**	-.35**	-.75**	-.42**	-.39**

Physical functioning (PF), Role limitations due to physical problems (RP), Bodily pain (BP), General health (GH), Vitality (VT), Social functioning (SF), Role limitations due to emotional problems (RE) and Mental health (MH) and two summary measures; Physical component Score (PCS) and Mental component score (MCS).
*= Significance at .05-level.
** = Significance at.01-level.

Regarding the rest of the 16 symptoms the median level was 0 meaning not at all.

Differences in Perceived Well-Being Between Organ Transplants

When analysing differences in well-being between the various organ groups there were no differences found in the eight factors in the OTSWI. Regarding symptoms, measured by single items, liver transplant recipients (LTR) were significantly more sad (p=.005) than those receiving a kidney or a heart and/or lung. There were also some tendencies noticed were LTRs reported more fatigue (p=.07) than the other two groups as well as more pain in the joints

Table 7. Descriptive Data on Well-Being Measured by the Organ Transplant Symptom and Wellbeing Instrument (OTSWI) Among 185 Organ Transplant Recipients.

	Factors of Well-Being							
	Fatigue	**Joint and Muscle Pain**	**Cognitive Functioning**	**Basic ADL**	**Sleeping Problem**	**Mood**	**Foot Pain**	**Economy**
Mean	2,64	2,41	1,73	0,72	3,32	1,01	1,03	1,91
Median	2,00	2,00	1,00	0	3,00	0	0	1
SD	2,92	2,84	1,93	2,25	3,30	1,49	1,79	2,36
Skewness	1,25	1,58	1,27	3,70	1,16	1,88	2,20	1,40
Min	0	0	0	0	0	0	0	0
Max	12	12	8	12	12	7	8	8

Each response relates to how much the problem or situation discomforts you, assessed on a five-point scale ranging from "not at all"(0), "a little"(1), "somewhat"(2), "quiet a bit"(3) and "very much" (4).

(p=.06). LTRs also reported more headache (p=.09) and dizziness (p=.09) however not significant.

Differences in Well-Being Due to Age, Gender, Time Since Transplantation and Having a Rejection or Not

Patients younger than 50 years reported significantly more problems with irritation and aggressive mood (p=.03) as well as with heart burn (p=.03). Tendencies in differences due to age were noticed regarding basic activities in daily life where patients older than 50 years reported more problems (p=.06) as well as regarding decreased libido (p=.07). Patients below 50 years, tended to report more tremor (p=.09).

When comparing differences due to gender, women reported more sleep problems (p=.004) and joint pain (p=.01). Female OTRs had more oedema (p=.006), were more nauseas (p=.02) and more dizzy (p=.000) than male OTRs. Finally the women were significantly more sad (p=.03), had less libido (p=.01) and were more bothered by their physical appearance (p=.006) than the male OTRs.

There were no differences between the OTRs with a follow up of one year and those transplanted more than three years except for two symptoms. The patients with a short follow-up reported more diarrea (p=.05) and those with a longer follow-up reported more itching (p=.03). No differences were found in any area or any single symptom between those who had experienced one or more graft rejections and those who hadn't.

DISCUSSION

Methodological Considerations

In the literature there are eight attributes for instrument properties to be used in the evaluation regarding sustainability for distribution to the target population. These eight attributes are: conceptual and measurement model, reliability, validity, responsiveness, interpretability, respondent and administrative burden, alternative forms and cultural and language adaptations [32]. Other researchers have defined similar, but less comprehensive quality criteria [33-34]. A part from evaluation of validity and reliability, a clear description of measurement aims, target population, the concept of interest (theoretical framework), item selection, item reduction and the workload required from respondents to complete the questionnaire should be provided when developing a new questionnaire [35]. We argue that the above mentioned quality criteria are fulfilled regarding OTSWI with the exception of reliability which is not yet fully tested. As mentioned in Table **1**, reliability in terms of the relationship between the signal, in this case the difference between subjects, and the noise, the difference within a subject when the clinical state is stable will be tested by further research. Also to test if the instrument is responsive to the true change occurring in a transplanted patient over a period of time further research will be needed.

A methodological or a psychometrical error was noticed when finding out the weak correlation values between the domain physical functioning in SF-36 and Basic Activities in daily life in OTSWI. At first we hade viewed the domain BADL as similar to PF, however when scrutinizing the items in the BADL-domain they are not at all similar to PF. Instead they measure factors completely related to activities in daily life functioning. Items regarding actual physical functioning were removed during the test using Cronbach's Alfa since the alfa-values were so high that only a few items were needed. When further test will be performed a domain comprising physical functioning will be added and tested. Also a domain more explicitly comprising the social well-being dimension will be developed by further test. In the present version the social well-being are more implicit involving ability to work and libido. Despite these errors we conclude that the development procedure, which has lasted for over five years, has been successful so far and that the OTSWI might be used in the target population for various longitudinal follow-up.

Discussion Regarding Descriptive Findings

The patients were bothered somewhat (median 2) by fatigue and quite a bit (median 3) by sleeping problems. Today we don't know enough about fatigue after organ transplantation, whether the sleeping problems cause fatigue or about how the patients master this symptom. In other patient groups with chronic heart failure and myocardial infarction it has been shown that other variables i.e. low haemoglobin levels, depressed mood, anxiety and uncertainty were associated with different dimensions of fatigue [36-37]. Falk [36] also showed that nausea, poor appetite and bodily pain associated with fatigue even if they were not the most dominating symptoms. Further studies are

Table 8. Descriptive Data on Symptoms Measured by the Organ Transplant Symptom and Wellbeing Instrument (OTSWI) Among 185 Organ Transplant Recipients

Symptoms								
	Dysponea	**Oedema**	**Nausea**	**Oral Fungus**	**Oral Herpes**	**Increased Appetite**	**Loss of Appetite**	**Heart Burn**
Mean	0,78	0,68	0,25	0,13	0,09	0,94	0,26	0,43
Median	1	0	0	0	0	1	0	0
SD	0,97	0,91	0,52	0,46	0,28	1,12	0,68	0,82
Skewness	1,36	1,60	2,29	4,20	2,94	1,42	2,86	2,42
Min	0	0	0	0	0	0	0	0
Max	4	4	3	3	1	6	4	4
Symptoms								
	Diarrea	**Itching**	**Headache**	**Burning Hands**	**Tremor**	**Dizzy**	**Sad**	**Decreased Libido**
Mean	0,42	0,43	0,51	0,11	0,76	0,41	0,59	1,26
Median	0	0	0	0	1	0	0	1
SD	0,78	0,80	0,81	0,46	0,90	0,69	0,89	1,4
Skewness	1,99	2,19	2,06	4,64	1,34	2,01	1,80	0,82
Min	0	0	0	0	0	0	0	0
Max	4	4	4	3	4	4	4	4

Symptoms	
	Physical Appearance
Mean	0,44
Median	0
SD	0,97
Skewness	2,5
Min	0
Max	4

Each response relates to how much the problem or situation discomforts you, assessed on a five-point scale ranging from "not at all"(0), "a little"(1), "somewhat"(2), "quiet a bit"(3) and "very much" (4).

needed regarding the relationship with fatigue and other conditions and symptoms.

Fatigue in healthy individuals was decribed by Grandjean [38] as a non-specific state indicative of decreased level of vitality, which is supported by our study, where fatigue were associated with low physical functioning, role-physical, vitality and social functioning as reported in Table **4**. This state has a protective function of forcing the body to avoid further stress, with exhaustion being the end of the fatigue continuum. This temporary form of fatigue is identified as acute and characterized as protective and identifiably linked to a single and obvious cause. In our study the patients had been transplanted for quite a while. According to Piper [39] chronic fatigue is referring to a state where the fatigue is accompanied by diseases. It then becomes a symptom that is complex, multicausal and multidimensional that is difficult to characterize and define. Fatigue is one of the most frequently reported symptoms in many chronic illnesses, including cancer [40], renal failure [41], chronic pulmonary disease [42], multiple sclerosis [43] and rheumatoid arthritis [44]. The point regarding organ transplant recipients is that their previous chronic disease is managed and improved although not always cured by the transplantation. The organ transplant recipients are able to live a normal life although with a chronic medical treatment to prevent rejection of the transplanted organ and other medication to manage co-morbidities e.g. hypertension. The findings in our study emphasizes the importance of comprehensive assessment and a broad approach to interventions during follow-up visits in the out patient clinic, because reduction of fatigue may get through alleviation of more manageable influencing symptoms i.e. possible anxiety and depression. One might start with assessing and treating the sleeping problems reported as something that affects daily life, and not look away from the fact that fatigue is reported as a key factor leading to decreased quality of life in patients with chronic diseases [20].

Dysponea as a single symptom correlated strongly with decreased physical functioning as well as the physical component score measured by SF-36. In return, sadness correlated strongly with low mental health as well as the mental component summary (Table **6**). However, these symptoms were reported as minor distressing, dysponea (median 1, a little bit) and sadness (median 0, not at all). A reasonable explanation might be that these symptoms strongly affect HRQoL for those who are suffering, however in general these symptoms are not an issue for the whole transplant population.

There were only weak relationships between the dimensions measured by SF-36 and the symptom embarrassed by looks. In another study [45] involving 108 liver transplant recipients, the most frequent symptom in male and female recipients were increased hair growth. Women with a long-term follow up (5-18 years) reported more cosmetic side-effects and over all symptom distress was more serious in women than in men. In our study the symptom physical appearance was not at all (median 0) distressing in the whole group, but the female patients were more embarrassed by their looks than the male patients (p=.006). Also several other symptoms were more distressing among females i.e. nausea, oedema and decreased libido. Regarding decreased libido, sexual dysfunction and sex hormone disturbances are widely reported in men and women before organ transplantation e.g. patients with chronic liver disease. Successful liver transplantation leads to improvements in sex hormone disturbances in both men and women, but immunosuppressive drugs may interfere with hormone metabolism [46]. Health issues, medications, aging and psychological and social issues, might affect post transplant sexual health. In a study by Ho, Ko, Schaeffer *et al*., [47] 23% of males and 26% of females reported decreased libido. This picture that women overall experience more symptoms than men is supported by numerous studies reported in the extensive review by Kugler *et al*., [8], however no conclusive discussion about why female organ transplant recipients experience more symptom distress than males are presented. Thus, this is an area for further research.

Besides problems with sleep and fatigue the most prominent symptom causing distress was muscle and joint pain. This is in line with a previous study [48] reporting that 53% of the organ transplant recipients reported pain to some extent and that the most common pain locations were hands and feet followed by the back. This symptom might be caused by the so called Calcineurin Inhibitor Pain Syndrom reported by Grotz *et al*., [11] and further discussed as neurological complications by Senzolo, Ferronato and Burra [10].

Drawing firm conclusions from this single study on symptom experience, symptom distress and well-being is of course difficult. In line with previous knowledge, the results indicate that few symptoms actually cause distress in daily life among organ transplant recipients. New information involve that sleeping problems were most disturbing followed by fatigue and muscle and joint pain. Dyspnoea, increased appetite, decreased libido and tremor affected the patients only a little bit. Fatigue correlated moderately or strongly with almost all dimensions of importance in HRQoL reported by SF-36. Further studies should focus on the fatigue in particular as well as the relationship between symptom distress and HRQoL.

CONCLUSION

Fatigue might be a key factor leading to a decreased HRQoL not only in patients with chronic diseases, but also for organ transplant recipients with prerequisites to be well and experience good HRQoL. The newly developed instrument labelled the Organ Transplant Symptom and Well-being Instrument offer a possibility to include both symptoms occurrence, symptom distress and health related quality in the measurements. Now transplant nurses have a useful tool to assess post transplant patients and plan their goal directed nursing interventions in collaboration with the patients concerned.

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CONFLICTS OF INTEREST

There are no conflicts of interest to declare.

APPENDIX

The Organ Transplant Symptom and Wellbeing Instrument (OTSWI)

Below there is a list of statements that other persons, with the same health condition as you, consider important. Please state how well each statement reflects your situation during **the last seven days.** Please mark the most suitable figure at each line.

		Not at All 0	A Little 1	Somewhat 2	Quiet a Bit 3	Very Much 4
1	I have difficulties with falling asleep	0	1	2	3	4
2	I sleep poorly	0	1	2	3	4
3	I wake up during the night	0	1	2	3	4
4	My muscles are aching	0	1	2	3	4
5	My joints are aching	0	1	2	3	4
6	My legs are aching	0	1	2	3	4
7	There is a burning ache in my feet	0	1	2	3	4
8	There is a numb and stabbing feeling in my feet	0	1	2	3	4
9	I am physically tired	0	1	2	3	4
10	I have no energy	0	1	2	3	4
11	I feel lazy and listless	0	1	2	3	4

(APPENDIX) contd…..

		Not at All 0	A Little 1	Somewhat 2	Quiet a Bit 3	Very Much 4
12	I have difficulties to remember	0	1	2	3	4
13	I find it hard to concentrate	0	1	2	3	4
14	Due to my physical condition I can't take a bath or shower	0	1	2	3	4
15	Due to my physical condition I can't get dressed by myself	0	1	2	3	4
16	Due to my physical condition I can't buy food by myself	0	1	2	3	4
17	I feel irritated	0	1	2	3	4
18	I feel angry	0	1	2	3	4
19	I worry about not being able to keep my job due to my health condition	0	1	2	3	4
20	I worry about my economy due to my health condition	0	1	2	3	4
21	I'm breathless	0	1	2	3	4
22	I need to rest because I am breathless	0	1	2	3	4
23	I'm swollen	0	1	2	3	4
24	I feel nauseous	0	1	2	3	4
25	I have oral fungus	0	1	2	3	4
26	I have oral herpes	0	1	2	3	4
27	I have increased appetite for food	0	1	2	3	4
28	I have decreased appetite for food	0	1	2	3	4
29	I have dyspepsia	0	1	2	3	4
30	I'm constipated	0	1	2	3	4
31	I have diarrhea	0	1	2	3	4
32	My skin is itching	0	1	2	3	4
33	I have headache	0	1	2	3	4
34	There is a burning pain in my hands	0	1	2	3	4
35	There is a numb and stabbing pain in my hands	0	1	2	3	4
36	My hands are trembling	0	1	2	3	4
37	I feel dizzy	0	1	2	3	4
38	I feel sad	0	1	2	3	4
39	My looks makes me embarrassed	0	1	2	3	4
40	My libido is decreased	0	1	2	3	4

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