

Development of the Functional Assessment of Chronic Illness Therapy – Liver Transplant (FACT-LT) Scale

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ABSTRACT

Background: This study aims to propose an initial development of the FACT-Liver Transplant (FACT-LT) scale to assess the major physical and emotional concerns of patients before and after Orthotopic Liver transplant (OLT) due to acute and chronic liver failure and hepatocellular carcinoma.

Methods: The FACT-LT was developed in two phases. In Phase I, items were generated: 1) through interviews with 10 OLT experts and 15 candidates for or recipients of both oncological and non-oncological OLT which identified relevant topics; 2) from the FACIT item bank. In Phase II, a questionnaire to assess item frequency, applicability, and comprehension was administered to 20 OLT experts and, to assess item difficulty, embarrassment and content irrelevance, to 30 transplant recipients or candidate patients (15 oncological, 15 non-oncological).

Results: In Phase I, 44 items were formulated/reviewed, and 30 items were maintained. All the healthcare professionals interviewed rejected the recommendation to develop two different modules for cancer and non-cancer patients. In Phase II, the majority of the experts and patients expressed an overall satisfaction with the questionnaire, indicating that the items were relevant, comprehensible and not embarrassing (range 75% - 99%). The first version of the FACT-LT includes 28 items defining four QOL domains: 5 items relating to Physical Well-Being, 8 to Functional Well-Being, 13 to Emotional Well-Being, and 2 to Social/Family Well-Being.

Conclusion: The preliminary results obtained were promising; however further studies are needed, in order to proceed with a FACT-LT validation process.

KEYWORDS: Hepatocellular carcinoma; Liver transplant; Quality of life; Well-being

INTRODUCTION

Over the last two decades, orthotopic liver transplant (OLT) has become an established worldwide clinical treatment for acute and chronic liver failure and for hepatocellular carcinoma (HCC) [1]. OLT represents an unique opportunity to remove

both the tumor and the underlying cirrhosis surgically and is associated with excellent long-term survival rates reaching over 70% after 5 years [2]. OLT suggests a multitude of complex physical and psychological implications, in particular during the waiting period for the donor organ and when the organ is received as well.

This procedure is different from traditional surgery where the “diseased part” may be removed because the transplant implies a substitution of the organ with an explanted-one

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from an individual who is no longer alive. This implies a symbolic relationship between patient and donor. The waiting period is characterized by a lower level of personal control, physical functioning, mental health, satisfaction with health, optimism, religious/spiritual beliefs, perceived social support and high level of anxiety compared with the general population. Moreover, it is highly associated with high rates of morbidity and mortality [3].

A large number of studies have shown that OLT markedly improves physical and psychological functioning principally in patients with end-stage liver disease [4-8]. Conversely, more recent research reported the presence of various psycho-physical issues after the transplant procedure. In fact, a decline registered in well-being may be an expression of difficulties in the patients' adaptation to the post-transplant condition, when they may face medical complications of OLT or recurrent liver disease; other reasons could also be related to psychological complications due to dependent relationships with medical staff or dependence on chronic immunosuppressive drugs taking [5]. Furthermore, many patients may find it difficult to return to the workforce not only because of this major surgery, but also because of their age [6-8].

Therefore, OLT impacts not only survival, but also affects health domains related to quality of life (HRQOL) [9-12]. HRQOL is a multidimensional construct comprising the physical domain, which includes: independence in activities of daily life and symptoms of disease, psychological domain, involving both emotional, cognitive and behavioural status and the Social/Family domain, pertaining to how people perceive their role and relationships with other people [13]. Assessment of Quality of Life (QOL) can provide crucial information on the impact of a disease [14, 15, 16], with QOL considered to be an independent predictor of survival and response to therapy in cancer patients [17]. For these reasons, it is important to have a specific questionnaire able to gather the characteristics of OLT condition in patients.

At the present time, QOL after transplant is evaluated through nonspecific instruments, i.e. the Short Form Health Survey (SF-36) [18] or the World Health Organization Quality of Life (WHO-QOL) [19] or liver disease specific questionnaires: Liver Disease Quality of Life (LDQOL) [20] and Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep) [21], which are predominately focused on physical aspects related to the underlying disease cirrhosis or other liver disease; they dedicate limited attention to the above aspects strictly related to the OLT experience.

The aim of the current study was to start developing the FACT-Liver Transplant (FACT-LT) scale that assesses and identifies the major physical and emotional concerns of patients before and after OLT due to acute and chronic liver failure and HCC. The FACIT validation protocol include 5 phases [21]. In the present work we focused on the first two: 1) item generation; 2) item review and reduction. Please see Appendix 1 for FACIT presentation.

MATERIALS AND METHODS

Phase I – Item Generation

Items were generated in Italian through two integrated procedures:

1) Following FACIT subscale development guidelines, some semi-structured interviews were conducted with 15 candidates for oncological and non-oncological recipients of OLT (Participant details can be seen in Table 1), and 10 experts i.e. oncologists, hepatologists, transplants surgeons, nurses and psychologists working in the field of OLT. All candidates and healthcare professionals were asked to list elements topics related to numerous aspects of the disease e.g. symptoms, concerns, treatments, QOL, patient behaviour etc. Experts were also asked about the necessity of developing different modules: one cancer specific and one non-cancer specific. LG and MB also provided assessment of interviews through thematic analysis [23]. Eligibility criteria for the healthcare professionals were the following: MD, MS or RN

Table 1: Demographic and clinical characteristics of the patients participating in phase I and II.

	Phase I		Phase II	
	N= 15	%	N= 30	%
Gender				
Male	13	86.7	25	83.3
Female	2	13.3	5	16.7
Disease				
HCC + Cirrhosis	6	40.0	13	43.3
NET	3	20.0	3	10.0
Cirrhosis no HCC	5	33.4	13	43.3
Others	1	6.7	1	3.4
Time from OLT				
<1 year	5	33.3	10	33.3
>1 year	5	33.3	13	43.3
In list	5	33.3	7	23.3
Virus				
No virus	4	26.7	9	30.0
HCV	6	40.0	15	50.0
HBV	5	33.3	6	20.0

Notes: HCC: hepatocellular carcinoma, NET: neuroendocrine tumor, HCV: Hepatitis C virus, HBV: Hepatitis B virus.

degree minimum of 3 years' experience treating LT patients and fluency in Italian. Eligibility criteria for patient candidates were: 18 years of age or older, candidate for OLT or having already received OLT, fluent in Italian, ability to complete the questionnaires and participate in a brief semi-structured interview, no severe mental disorder or dementia and written informed consent. Patient and specialist responses were combined. Two judges, LG and MB, psychologists with twenty years of experience in the field of OLT, reviewed the item list for overlap and/or irrelevance to the purpose: initially they did this separately, then met together to review the item, reaching an agreement by discussion.

2) A list of FACIT Item bank [22], as exhaustive as possible and pertinent to QOL in patients undergoing OLT (both candidates and liver recipient patients) was provided to two independent judges. Over 300 items from the FACIT item bank were examined by them with the same procedure as previously discussed. Only items considered to be distinct from those in the general version of FACT

(FACT-G) and potentially relevant to patients undergoing or candidates for OLT were included.

The work team analyzed the two lists of items to avoid overlap between patients/healthcare personnel and the FACIT item bank. The full-body text of the final candidate items was examined, so that items could be substituted with previously validated equivalent FACIT items, if available, formatted with response choices compatible with a 5-point Likert-type scale and eventually modified. Discordant results were discussed until a common result was achieved. The selected items were included for Phase 2.

Phase II - Item Review and Reduction

A convenience sample of twenty experts recruited in four different Italian cancer facilities were asked to rate how frequent, pertinent and comprehensible each item was on a 3-point scale, ranging from 0 (indicating rare/not pertinent/difficult to understand) to 2 (indicating very frequent/very relevant/very easy to understand). Open-ended questions

Table 2: Summary of liver transplant specific aspects as reported by experts and patients in the interviews.

PHYSICAL WELL-BEING	<ul style="list-style-type: none"> Treatment side effects / Immunosuppressive drugs side effects Tremors Back pain Sexual impotence Difficulty in breathing Heartburn Hallucinations Memory and/or concentration difficulties Fever Problems with digestion Fatigue Pain Physical function
EMOTIONAL WELL-BEING	<ul style="list-style-type: none"> Increase in emotionality Change in the hierarchy of personal values / give value to life / joy to be alive Euphoria Symbolic relationship with the donor Psychological Coping Need to be reassured / encouraged Feeling insecure / More reassurances (need of information) Feeling commiserated Consciousness of the transplantation meaning Psycho-physical expectations after transplantation Change in mood Fear that the disease returns Fear of infections or of that the virus returns Plans for the future Anxiety disorders Fear of not being able to manage alone Sense of guilt-depression Liver duration Fear of going back home after transplantation Feelings regarding the new liver
SOCIAL-FAMILY WELL-BEING	<ul style="list-style-type: none"> Capability to return to work / professional role Relationship with the caregivers Closeness to the family Ability to enjoy oneself Social relationship modification Curiosity and nosiness of other people To feel useful and busy / social role
FUNCTIONAL ASPECTS	<ul style="list-style-type: none"> Life style (nutrition, smoking habits, alcohol consumption...) Organizational problems for the patient and the family (transfers, sleeping away from home...) Financial problems Difficulties in maintaining compliance with therapies Autonomy

Table 3: Expert and patient evaluation of FACT Liver Transplant Subscale.

FACT Item Code	Items	Dimensions	% of experts deemed questions			% of patients deemed questions		
			Frequency	Applicability	Comprehensible	Difficult	Embarrassing	Irrelevant
BR7	I feel independent	FA	100%	100%	100%	0%	4%	0%
LT1	The treatment for my health problems causes organizational difficulties for me or my family	FA	89%	100%	89%	0%	4%	8%
LT2	I feel anxious	EWB	100%	100%	89%	0%	0%	4%
BMT14	I have tremors	PWB	78%	89%	100%	0%	8%	0%
ES12	I have mood swings	EWB	89%	100%	100%	4%	8%	0%
LT3	I get emotional easily	EWB	89%	100%	100%	0%	0%	0%
LT4	I often think about the donor	EWB	78%	89%	100%	4%	8%	4%
LT5	When I think to the donor I feel uneasy	EWB	56%	89%	100%	8%	4%	4%
FT10	My cancer or treatment has reduced my satisfaction with my present financial situation	FA	100%	100%	100%	0%	21%	4%
LT6	The disease experience has influenced or modified my personal values	EWB	100%	100%	78%	16%	0%	0%
BR3	I can remember new things	FA	68%	78%	100%	4%	4%	4%
LT7	Thinking about having someone else's liver makes me feel uneasy	EWB	66%	89%	89%	4%	4%	4%
LEU5	I feel uncertain about my future health	FA	100%	100%	100%	13%	4%	4%
LT8	I am satisfied with my relationship with medical staff	SFWB	89%	100%	100%	8%	17%	4%
LT9	I feel insecure	EWB	89%	100%	100%	0%	4%	4%
LT10	I have difficulty having sex	PWB	89%	100%	100%	4%	26%	8%
LT11	It's hard to have a healthy lifestyle (abstinence from smoking, from alcohol consumption, etc.)	FA	89%	100%	100%	0%	17%	4%
BR1	I am able to concentrate	FA	78%	100%	100%	4%	0%	4%
LT12	I am worried about how long my new liver will last	EWB	100%	100%	78%	8%	4%	0%
LT13	I have difficulty complying with treatment	FA	45%	100%	100%	0%	4%	4%
BR6	I have trouble with my eyesight	PWB	56%	78%	100%	8%	4%	8%
LT14	I have swelling in the legs and/or abdomen	PWB	89%	100%	100%	4%	0%	4%
GF5	I am sleeping well	FA	89%	100%	100%	8%	0%	0%
BMT2	I feel distant from other people	SFWB	32%	89%	100%	4%	8%	4%
LT15	I have daytime sleepiness	FA	67%	100%	100%	4%	0%	0%
HEP4	I have had itching	PWB	66%	89%	100%	0%	0%	0%
LT16	I'm afraid of the liver being rejected	EWB	100%	100%	100%	8%	0%	0%
LT17	I am worried the liver will not arrive in time*	EWB	100%	100%	100%	0%	0%	4%

Notes: FA: functional aspects, EWB: emotional well-being, PWB: physical well-being, SFWB: social/family well-being,
*This item can be applies only to pre-transplantation.

were used to identify additional QOL issues. Expert evaluation was collected, and frequencies of responses summarized. Further refinement was considered ensuring the inclusion of all potentially clinically relevant items and the elimination of redundant ones.

Thirty transplant recipients or candidate patients (15 oncological, 15 non-oncological) were asked to participate in an Internal Review Board (IRB) approved pilot study evaluating the pilot questionnaire (for candidate details, please see Table 1). Patients were recruited at the time of a prescheduled follow-up appointment at the Clinical Psychology, Istituto Nazionale dei Tumori of Milan, in Italy. After written informed consent was obtained from the patients, researchers gave them the pilot questionnaire and asked them to rate each item for difficulty, embarrassment and irrelevance of content. Patients were also asked open-ended questions to allow them to comment on each item and to add potentially relevant themes, not specifically covered by the module during a semi-structured interview in Phase I. Items identified as frequent, pertinent and comprehensible by at least 65% of the participants were retained.

Ethical Considerations

All procedures followed were in accordance with the ethical standards of the committees responsible for human experimentation, both those of the Institute and National, and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all participants for inclusion in the study. All enrolled patients provided written informed consent. Protection of the patients' identities was guaranteed by assigning study-specific, unique patient numbers. The project was approved by the hospital's Ethics Committee of Fondazione IRCCS Istituto Nazionale dei Tumori, Milan (Italy) (N. INT 26/10).

RESULTS

Phase I

The interviews conducted in the first phase permitted the identification of 44 topics which can be classified into 4 macro areas: Physical

Well-being (N= 13), Emotional Well-being (N= 20), Social/Family Well-being (N= 7) and Functional Aspects (N= 4) (Table 2).

Out of a total of 44, some topics also were to be present in the FACIT item bank. Therefore, these topics were replaced with existing items. The topics not present in the FACIT item bank were transformed into items by the team. This process resulted in the selection/creation of 30 items overall. Of these 30, 11 topics were also present in the FACIT item bank and 19 are new.

All the healthcare professionals interviewed rejected the suggestion of developing two different modules for cancer and non-cancer patients as unreasonable.

Phase II

The 30 items were evaluated by the 20 experts (100% response rate) as frequent, pertinent and comprehensible with the exception of the items "I feel that other people pity me" which was judged as uncommon (63%) and non-pertinent (33%) and "Other people avoid me because of my health condition" which was judged to be infrequent (63%). As a result, both items were removed.

A majority of the patients who participated in the pilot study expressed overall satisfaction with the questionnaire, indicating that the questions were not difficult, embarrassing or irrelevant (range 75% - 99%). The items "Due to my health problems I have financial troubles," "I have difficulty having sex" and "I am satisfied with my relationship with medical staff" were judged to be embarrassing by 21%, 26% and 17% of the patients respectively; however they were maintained in the questionnaire at the recommendation of the experts (Table 3).

The current version of the FACT-LT includes the FACT-G plus the 28-item liver transplant-specific sub-scale, encompassing four QOL domains: 5 items relate to Physical Well-Being, 8 to Functional Well-Being, 13 to Emotional Well-Being, and 2 to Social/Family Well-Being. Appendix 2 shows the final questionnaire

in Italian and English. All items are relevant to both the waiting period for the transplant and after the transplant has taken place, with the exception of item "I am worried the liver will not arrive in time", relevant only in the first case.

DISCUSSION

In Phase I, we started the initial development of a OLT-specific sub-scale that consisted of 30 items encompassing four QOL domains (Physical Well-being, Emotional well-being, Social/family Well-being and Functional aspects), 29 of which are applicable both to the waiting period and after transplant and 1 is relevant to the waiting period only, they comprise Functional and Emotional domains predominantly. Phase II confirmed the results obtained in Phase I. The content of the instrument was derived from liver transplant patients, both cancer and non-cancer, and clinical experts to ensure that appropriate QOL concerns were included; all the items in the instrument were considered fully relevant to liver transplant patients.

Specific OLT topics such as new organ integration and the symbolic relationship with the donor can influence coping processes after transplant, as already highlighted by the literature. The concern that the liver will not arrive in time is also specific to the OLT condition [16, 17]. These aspects have never been contemplated in other existing tools but they are fundamental for setting up correct counseling actions. These results confirm the relevance of having a health-related QOL specific module (FACT-LT).

The impact of liver disease and medical complications on QOL and psychological distress before and after OLT is a topic of growing interest. However, at the state of the art there are no known tools specifically designed for this particular clinical condition. The strong point of this work is that it will start to fill this gap. Our work is a first step of a longer and more complex process, but it has the merit of opening a cultural reflection on the specificity of living patients with liver transplants.

This work has some limitations that must be taken into account. First, the study was conducted in Italy, and it is possible that the formulation of the items was affected by the characteristics of the National Health System of this country. It is possible to find differences in other countries with different systems of care and welfare and different needs, expectations, and fears may emerge. Secondly, we focused only on item generation and item review and reduction. Further changes may be needed during step 3, "Scale Construction/Piloting".

FACT-LT can have interesting applicative implications on clinical and research field. As for the first aspect, a tool that allows an in-depth knowledge of the physical, psychological or social aspects of the reality of people with liver transplants is important because it allows health professionals to gain elements for correct counseling action. From a research point of view, a tool like FACT-LT will allow us to explore aspects that until now, have remained completely unexplored due to the lack of tools specifically created for liver transplant patients e.g. the symbolic relationship with the donor.

In conclusion, although further steps are needed, as required by the protocol, the results of this work are encouraging.

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