

DRAFT  
10 October 2013

## **BOWEL ADVISORY GROUP**

### **Working group on Quality of Life following Intestinal Transplantation**

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#### **Remit**

To advise on an appropriate instrument to evaluate quality of life and performance following intestinal transplantation.

To agree items for data collection to measure outcomes following transplant.

#### **Introduction**

Simple metrics of graft or patient survival following intestinal transplantation are too crude a measure to determine the value or appropriateness of the procedure. This affects the advice available and offered to prospective patients and their families. Consequently a measure of the quality of life (QoL) before and after intestinal transplantation is needed. Such a measure should be validated, comparable, sensitive and responsive. This means quantifying intra- and inter-observer variation, enabling comparisons with other conditions (most notably so that Quality Adjusted Life Years (QALYs) can be calculated by the National Institute of Health and Clinical Excellence, NICE), being sensitive enough to collect disease-specific data for intestinal transplantation or intravenous nutrition, and responsive enough to detect differences before and after transplantation at pre-determined time points.

No single index can meet all these criteria. Furthermore, the evaluation of paediatric and adult QoL are very different, not least because children are often confined to hospital prior to intestinal transplantation with conditions not uncommonly from birth and resulting in transplantation that is often multivisceral, in contrast to adults who usually have experience of a normal QoL prior to the illness or event that precipitated intestinal failure [1,2].

The purpose of this paper is to review available indices and to give guidance to the Bowel Advisory Group of the NHSBT on appropriate data collection. Paradoxically, there may be an advantage in having a small number of patients (19 intestinal transplants, in the UK 2012/13), compared to heart (126), pancreas (406), liver (733), or kidney (1977) transplantation, simply because the data can be expected to be collected in all patients to give a true measure of the value with regard to QoL. The goal of evaluating QoL is to compare measures in patients receiving home parenteral nutrition who are listed for intestinal transplantation and in those same patients after transplantation. Only in this way will the impact of impact transplantation on quality of life be properly evaluated.

#### **Methods**

A working group (authors) was established by the Bowel Advisory Group of National Health Service Blood and Transplant (NHSBT) in October 2011. A draft paper was written by SPLT who consulted Dr Loris Pironi (Bologna, author of only paper comparing intestinal transplantation and parenteral nutrition); Dr Janet Baxter (Dundee, author of only validated index of quality of life and home parenteral nutrition); Professor Crispin Jenkinson (Oxford,

DRAFT  
10 October 2013

authority on quality of life and patient-related outcome measures); and Marion O'Connor (Oxford, intestinal transplant dietitian introducing pre- and post-transplant application of

HPN-QOL index). The paper was amended by co-authors before being finalised and submitted to BAG for consideration and adoption.

A PubMed/Medline search was conducted using MeSH terms: intestinal transplant(ation); quality of life; intestinal transplant and quality of life; intestinal transplant and quality of life and score; intestinal transplant and quality of life and score and validation or operating characteristics; intestinal transplant or home parenteral nutrition or intestinal failure and patient related outcome measures or performance.

Generic and parenteral-nutrition disease-specific indices were summarised and broadly compared, with consideration of generic and potential disease-specific patient-related outcome measures. Discussion and recommendations were placed in the context of the UK intestinal transplant programme, likely assessment by the National Institute of health and Clinical Excellence (NICE) and the need to inform all parties contributing to the programme, so that patients can be better informed with regard to treatment choices

## Results

### *Literature search on quality of life and intestinal transplantation*

A search of PubMed (MeSH terms 1. intestinal transplant(ation) (6834); 2. quality of life (128118); 3. 1 and 2 (275); 4. 1 and 2 with 'score' (21); 'validation' (0) or 'operating characteristics' (0), revealed one original article [3]. In this paper from Bologna, 18 patients on home parenteral nutrition (HPN) and 12 who underwent intestinal transplantation were studied using the non-disease specific Short Form-36. Scores were standardized for sex- and age-matched group scores of the healthy population by calculating the Z-score. Patients on HPN and intestinal transplant were well matched for primary intestinal disease, presence of a stoma, body mass index, employment and marital status. The values of all the physical components of SF-36 were reduced in HPN, but only in physical functioning after transplant. Subjective physical health was better after transplant than on stable HPN.

### *Review of potential indices*

A review of the instruments used to assess the quality of life of adult patients with chronic intestinal failure receiving parenteral nutrition at home [4] identified 34 reports, 19 of which used non-specific generic instruments, 8 non-validated questionnaires, 4 a combination of both and 3 did not use any formal instrument. The lack of systematic study led the authors to develop and validate a questionnaire (HPN-QOL) [5]. A brief description of candidate scoring systems is appropriate.

### Generic

**EQ-5D™** (EuroQol) is a standardised instrument for use as a measure of health outcome. Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status [6]. EQ-5D is primarily designed for self-completion by respondents and is ideally suited for use in postal surveys, clinics or face-to-face interviews. It is simple, taking only a few minutes to complete. The EQ-5D-5L developed in 2005 consists of 2 pages – the **EQ-5D-5L** descriptive system (page 2) and the EQ visual Analogue scale (EQ VAS) (page 3). The descriptive system comprises the same 5 dimensions as the EQ-5D-3L (mobility, self care, usual activities, pain/discomfort, anxiety/depression). However, each dimension now has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. EQ-5D is used by NICE to calculate Quality Adjusted Life Years. It has been applied to children. [7]

DRAFT  
10 October 2013

**SF-36®** is a multi-purpose, short-form health survey with only 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index. It is the most widely evaluated generic patient assessed health outcome measure in a bibliographic study of the growth of “quality of life” measures [6]. Its value in estimating disease burden and comparing disease-specific benchmarks with general population norms is illustrated in articles describing more than 200 diseases and conditions. An amended version (**SF-36v2®**) with 5 response levels for the 8 descriptive components was developed in 1998 and an **SF-12®** is a one page questionnaire that takes a couple of minutes to complete.

#### Disease specific

**HPN-QOL.** The questionnaire was developed in Scotland, published in 2010 and administered to 100 patients receiving HPN [5]. It used psychometric testing to examine reliability and validity, was then refined through scaling analysis, leading to a final questionnaire of 48 items. This is the only validated disease-specific score of QoL for intestinal failure, but it has not yet been validated after intestinal transplantation.

The Cambridge-Miami (**CaMi**) score was developed as a pre-operative scoring system to help quantify the likelihood of survival after transplantation of the small intestine either alone or as a composite graft, to help assess patients. [8] The score combines risk factors for early-, medium-, and long-term survival, including loss of venous access and impairment of organs or systems not corrected by transplantation, each scored 0-3. Initial validation examined the preoperative scores of 20 patients who had received intestinal transplants either isolated or as part of a cluster graft, who had either been followed up postoperatively for at least 10 years, or died within 10 years and compared with their survivals. A CaMi score <3 was associated with survival ≥3 years (12/12 patients) and >3 with survival <6 months (4/4). It is simple, disease-specific and is undergoing prospective validation, but does not examine QoL.

#### *Strengths and weaknesses of relevant indices*

Index	Validation	Comparability	Disease specificity	Responsiveness	Practicality	Ref
<b>EQ-5D</b>	++	++ many disease areas	-	+	++	6
<b>SF-36</b>	++	++ many disease areas	-	++	++	6
<b>HPN-QOL</b>	+	-	+/- not for transplant	+	++	5
<b>CaMi</b>	+/-	-	+	+/-	++	8

#### *Outcome measures*

Patient-related outcome measures (PROMS) are intended to be understandable, robust criteria against which treatment response can be evaluated, in contrast to generic or disease-specific indices [9]. As with QoL, however, PROMS can be generic (such as working capacity, hospitalisation, mortality) or disease-specific. None, other than mortality, have been systematically evaluated in intestinal transplantation. It is, however, possible to create a short list of appropriate outcomes that should be subject to consensus.

DRAFT  
10 October 2013

## Discussion

It is self-evident that the impact of a major intervention such as intestinal transplant on QoL should be measured, primarily to evaluate treatment success in a more sophisticated manner than the crude metrics of mortality or graft survival, so that patients and health care professionals can be better informed about treatment choices.

There is no single validated index for measuring QoL before and after intestinal transplant, but independent expert advice (Professor Crispin Jenkinson) recommends that both a generic index (EQ-5D or SF-36) and a disease-specific index be used. The generic index means that the intervention can be compared across disease areas – of crucial importance for national decision-making (eg by NICE) and that the disease-specific index be used to capture information of relevance to the condition. Whilst either EQ-5D or SF-36 might be used (or, indeed, both for a small population size such as intestinal transplantation), NICE base decisions on EQ-5D and the impact of data collection on paper and subsequent data entry if both generic indices are used needs to be considered. With regard to a disease-specific index, there is only one that has been validated in intestinal failure (HPN-QOL) and this is best applied (and if necessary adapted) for use in intestinal transplantation. A substantial advantage of the HPN-QOL is that it has been validated for the pre-transplant population under study, since all of these patients (with rare exceptions) will be on stable HPN before transplant.

The CaMi score is a separate index that is set to have particular value in predicting mortality based on pre-transplant assessment. It is complementary to QoL assessment. Furthermore, it is designed to evaluate short (6 months), medium (1 year) and long-term (3 year) survival. This, therefore, sets time points against which QoL can be applied.

There remains the challenging question of how to assess the impact of intestinal transplantation on QoL in the paediatric population. The generic EQ-5D has been shown to be transferrable to children [7]. The HPN-QOL has not been validated in children, but it seems reasonable for it to be applied and adapted until its operating characteristics in children can be evaluated.

## Recommendations

1. All patients undergoing intestinal transplantation should have an EQ-5D-5L recorded before, 6m, 12m and 3y after transplant as a generic QoL index against which QoL can be compared with other disease areas.
2. All patients undergoing intestinal transplantation should have an HPN-QOL recorded before, 6m, 12m and 3y after transplant as a disease-specific QoL index against which QoL can be compared with other patients on stable HPN.
3. Generic patient-related outcome measures that should be collected after intestinal transplant should include:
  - Mortality
  - Hospitalisation (days/year)
4. Disease-specific patient-related outcome measures that should be collected after intestinal transplant should include
  - HPN-free (yes or no)
  - IV Fluid-free (yes or no)
  - Enteral-feed free (yes or no)

DRAFT  
10 October 2013

5. The role of other measures that might help make the pharmacoeconomic case for intestinal transplantation merit discussion by BAG and might include working capacity (Work Performance Activity Index, WPAI); a comparable paediatric index that applies to schooling; a generic performance index (Karnofsky index); or social benefit support.

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