Outcome of antireflux surgery based on quality of life assessment

Ph.D. Thesis

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INTRODUCTION
Gastroesophageal reflux disease (GERD) is one of the commonest disorder in the gastroenterology, with a great impact on quality of life (QoL) of the GERD-patients, their everyday activity, emotional status and lifestyle. Health-related quality of life (HRQoL) is significantly affected by GERD, and its evaluation is emerging as a factor important to select treatment options for GERD and to assess the outcome of different treatment strategies. Since the introduction of laparoscopic fundoplication (LF) in 1991, there has been an exponential rise in the number of patients undergoing operation for GERD and in the number of centers performing these procedures. Laparoscopic antireflux surgery (LARS) has in recent years become the standard procedure for treating severe gastroesophageal reflux disease. Quality of life data and patient satisfaction are important issues in estimating the outcome of LARS. Several studies have demonstrated laparoscopic fundoplication can achieve an excellent surgical outcome including quality of life improvement in patients with GERD.

AIMS

1. The aim of our study is to evaluate the psychometric properties (reliability and validity) of a newly developed HRQoL questionnaire (QOLARS) containing both generic and disease-specific domains for use with patients with GERD who have undergone LF.
2. To report the mid-term results of the surgical management of GERD by laparoscopic fundoplication and to evaluate surgical outcome, including quality of life and patient satisfaction; and second, whether preoperative QoL measurement can predict which patients will be satisfied with antireflux surgery.

PATIENTS AND METHODS
My dissertation is based on two studies, which hypotheses were checked by. First, development and construction of a modular QoL questionnaire (QOLARS) suitable for the measurement of life quality will be detailed in this section. Then, participants of the follow-up study and statistic analysis will be displayed.
Development of the QOLARS questionnaire

In the 1st Department of Surgery, Semmelweis University laparoscopic antireflux operation of 252 patients with GERD was performed between April of 1994 and April of 2002. We have developed a 50 item Likert-type questionnaire including both generic and GERD-specific scales to measure patients’ quality of life, using widely applied and valid quality of life questionnaires.

The purpose of the construction of our questionnaire was to establish an instrument suitable for the measurement of efficacy and success of operation from the patient’s viewpoint, and impact on patient’s QoL. This questionnaire was developed to be more comprehensive than existing instruments. Recently, more GERD-specific quality of life questionnaire have been reported. These questionnaires concentrate on GERD symptoms and include questions concerning just the reflux-related symptoms, but these don’t involve items specific for the most frequent complications after operation (swallowing difficulties, belching and vomiting inability, excessive gas-bloating etc.), which have significant impact on the patients’ postoperative quality of life too. Most of studies ignore these factors and complaints.

We classified the items concerning the most frequently occurring symptoms following surgical treatment to a scale. Five more questions aiming subjective consideration of efficacy of operation by the patients and satisfaction with current status were added and involved in our instrument. However, several studies use disease specific or generic questionnaires but not both in combination. Generic instruments are comprehensive, designed to be applicable across disease, treatments and populations. The disadvantage of these instruments is that they may not be responsive enough. The disease-specific instrument is clinically more relevant, captures details about the disease activity and symptoms patterns and is likely to be more responsive to change than generic instrument. Taking into consideration the complementary nature of these different kinds of instruments, we used them in tandem, and combined the advantages of disease-specific and generic scales in our questionnaire. The QOLARS instrument is a 50-item Likert-type questionnaire including both generic and disease specific scales to measure patients’ quality of life (consist of Visick score, EORTC QLQ-C30, the modified GERD-HRQL and questions focused on the new complaints appearing after ARS and overall satisfaction with the results of fundoplication) [20].
Furthermore, five questions aiming subjective consideration of efficacy of operation by
the patients and satisfaction with current status were added. These new questions were
reviewed and confirmed by gastroenterologists and surgeons having experience in
laparoscopic fundoplication. Items were arranged to scales. Results (patients’ scores)
were transformed into scores from 0 to 100 by linear transformation (higher scores
represent more severe symptoms and greater impact on HRQoL). We have developed
two versions of the questionnaire: 45 question containing type for preoperative and a
50 question containing for postoperative use. These questionnaires are identical with the
exception of 5 added questions of the postoperative tool concerning surgical
complications and efficacy.

We performed retrospective analysis of patients who underwent laparoscopic
fundoplication. Each of the 252 operated patients a questionnaire was mailed, and were
requested to fill and return it in an enclosed envelope. 116 patients returned filled
questionnaire. These patients were the participants of our further study.

Translation of Visick score and EORTC QLQ-C30 into Hungarian language and
cultural validation has already been made. Language validation of the GERD-HRQL
was performed by four both native English and Hungarian speaking translators
(bilingual translation panel).

The psychometric properties were evaluated included internal-consistency reliability
(Cronbach $\alpha$), construct validity, known-groups validity. Results were expressed as
medians and ranges, unless otherwise stated. P values less than 0.05 were regarded
statistically significant. All reported P values are based on two-tailed tests. Statistical
analysis was performed with SPSS version 11.0, under Windows.

**Prospective evaluation of the QoL of GERD patients 3 years follow-up period after
LF**

Between 1. April 2002 and 31. May 2003, 41 consecutive patients underwent complete
“floppy” Nissen (n = 30) or partial Toupet (n = 11) laparoscopic fundoplication for
typical GERD in the 1st Department of Surgery, Semmelweis University. They were
assigned to either the Nissen or Toupet group depending on the descision of the
surgeon. Patients with a proven GERD were considered for surgery if the symptoms
persisted despite long-term adequate medical treatment with proton-pump inhibitors
(PPIs), need for “life-long therapy”, coexisting hiatal hernia. Five patients were truly “non-responders” to medical therapy. The mean duration of GERD symptoms was 4.5 years. The patients included 28 women and 13 men, with a mean age of 41 years (range, 17-68 years). All patients underwent preoperative physiological testing by upper endoscopy, oesophageal manometry, and 24-hour oesophageal pH monitoring, and some had contrast radiography and gastric emptying.

Quality of life was evaluated using a newly developed, standardized, validated quality of life questionnaire, the QOLARS. Patients were evaluated by QOLARS prior to surgery, 6 weeks, 1 year and 3 years after surgery.

Statistical analysis

Results were expressed as medians and ranges, unless otherwise stated. Preoperative and postoperative data were compared with use of the paired student t test. P values less than 0.05 were considered statistically significant. Statistical analysis was performed with SPSS version 11.0, under Windows.

RESULTS

My dissertation is based on two studies, which hypotheses were checked by. First, development and results of psychometric evaluation of a modular Qol questionnaire (QOLARS) suitable for the measurement of life quality will be detailed in this section. Then, results of a follow-up study for the efficacy of LF from the patients’ aspect and quality of life will be displayed.

Development of the QOLARS questionnaire

116 of 252 patients undergoing laparoscopic fundoplication (LF) filled the form and returned. These 116 patients were the participants of our further study. 85 of 116 patients recovered while 31 had complaints of different severity after operation. Filling time was 10 minutes approximately. The first 30 questions of our questionnaire consist of validated EORTC QLQ C30. The last 20 questions include GERD specific questions, questions concerning complications and efficacy from the patient’s perspective. This part of our questionnaire was psychometrically analyzed.
**Internal-consistency reliability**

For the GERD specific scale, we used a modified variation of GERD-HRQL (items: 32 to 45). If these 14 items are considered to be a single scale, its reliability is high, Cronbach $\alpha = 0.95$. We tested correlation amongst these 14 questions using the Pearson correlation coefficient. On the basis of these results we constructed 4 scales, targeting heartburn, swallowing complaints, drug taking and new complaints after operation. Between of the items of scales, most of cases high correlation was observed. Only the scale of new complaints occurring after the operation (belching or vomiting inability, gas-bloating) had relatively low correlation values (0.42; 0.47) between given scores. Explanation of this low correlation can be that not all patients suffering from gas-bloating had coexisting belching difficulties or vomiting inability. We classified these items to a scale, since these questions concern the most frequently occurring symptoms following surgical treatment.

The heartburn scale’s Cronbach $\alpha$ value is 0.96, gas-bloating, belching inability, inability to vomit scales have similarly high $\alpha$ value ($\alpha=0.86$). Question clusters concerning swallowing complaints and drug taking have high Pearson correlation value as well. It hadn’t sence to give Cronbach $\alpha$ of swallowing complaints or drug taking as they are consist of two items both. The swallow complaint question group’s $\alpha$ value is 0.74, and the drug taking group’s is 0.90.

Correlation is similarly high of items about subjective consideration of operation (satisfaction with current status), correlation level between op1 and op2 scores is: $r=0.80$.

Reliability of questionnaire is supported by high Cronbach $\alpha$ values and high correlation.

**Construct validity**

Using convergent and divergent validity, construct validity was evaluated by examining Pearson correlation coefficients between items and scales. Construct validity was demonstrated based on observed correlations.

Higher correlations were found between scales or items measuring the same construct (convergent validity) and lower correlations were found between different construct (divergent validity). Analyzing a correlation matrix, we found high correlation between the questions and scales in connected constellation, and low correlation if there were no
connections between examined items. We found tighter connection, that is higher correlation values between GERD specific part of questionnaire (convergent validity) than between items concerning GERD symptoms and general quality of life can be gained (divergent validity). The correlation between GERD symptoms and intensity of pain is higher (0.62), than the correlation between GERD symptoms and social function (0.46) or cognitive function (0.50). Similarly, between items of symptomatic scale (questions on heartburn, swallowing, gas-bloating, belching, inability to vomit, drug taking) and intensity of pain, the correlation was higher (0.56-0.65) (convergent validity), than that between pain intensity and item concerning diarrhoea (0.23) (divergent validity). A high correlation was observed between Visick scores and heartburn (0.70).

**Known-groups validity**

We divided patients into two groups based on a single question if they had any complaints when filling form or in the previous 4 weeks. Patients having no complaints displayed significantly better function and higher scores than patients with complaints (with the exception of DI score /diarrhoea/).

Patients were divided into 4 groups depending on their Visick score (VisickI-IV). Participants of higher Visick score reported significantly worse HRQoL to those having lower Visick score. Between the groups Visick I and Visick II, a significant differences concerning total quality of life, emotional factor, nausea-vomiting scores, heartburn, gas-bloating, vomiting inability and scores on efficacy of operation were found. Comparing groups Visick II and III all the items and scales showed significant difference except DI score. In consideration that group Visick IV involved only one patient, statistic comparison of Visick III and IV groups was not possible.

**Prospective evaluation of the QoL of GERD patients 3 years follow-up period after LF**

Before operation all of the patients (100%) completed the questionnaire. 28 of 41 patients (practicality of 68.29%) completed the QOLARS questionnaire at the 6 weeks by follow up visit. To each of 41 operated patients was posted the questionnaire 1 year and 3 years after surgery and was requested to fill and return in an enclosed envelope. 32 patients (practicality of 78.04%) answered questionnaire 1 year and 20 patients 3
years after operation. Patients who didn’t return questionnaire were contacted and requested to answer the questions by phone. Participant number of 3 years control raised to 27 (practicality of 65.85%) by phone interviews. Filling time was 10 minutes approximately.

Six weeks after operation nearly all QoL scores were improved comparing with the preoperative scores, except constipation and swallowing complaints. Scores of mentioned two items showed a worsening in QoL. There were no differences in physical functioning, dyspnoe, appetite, gasb/vomit scores between preoperative and 6 weeks after surgery assessment. The general quality of life score, emotional functioning, pain score, heartburn score, drug taking and satisfaction with current status scales improved statistically significantly. The mean values of 9 subdimensions improved 1 year postoperatively as follows: role functioning, social functioning, appetite, pain score, drug taking, general quality of life score, nausea and vomiting, heartburn, satisfaction with current status; the last four scores had significantly changed. The mean score of physical functioning, cognitive functioning, fatigue, sleep disturbance, constipation, diarrhoea, financial difficulty, swallowing complaints, gasb/vomit had not significantly changed by the end of the 1\textsuperscript{st} postoperative year. Patients had a slightly worse postoperative scores in emotional functioning and dyspnoe domains 1 year after LF. Three years after surgery the general quality of life score, role functioning, cognitive functioning, social functioning, fatigue, nausea and vomiting, pain score, appetite, heartburn score, drug taking and satisfaction with current status scales improved statistically significantly. Physical functioning, emotional functioning, dyspnoe, constipation, financial difficulty, swallowing complaints got better 3 years after operation. The scores of sleep disturbance, diarrhoea, gasb/vomit had not significantly changed.

Six weeks after operation 2 of the 28 patients (7%) were taking medications and 3 patients (10%) had moderate dysphagia, which cannot be perceived by the 1\textsuperscript{st} postoperative year. One patient (3%) has belching inability, two (7%) suffered from gas-bloating. Three patients (9%) suffered from minimal GERD symptoms for which they took occasionally antisecretory medication by the end of the 1\textsuperscript{st} postoperative year. Of the 8 patients (25%) who reported new symptoms after surgery, 3 (9%) reported belching inability, 5 reported excessive gas and abdominal bloating (15%). One patient
(3%) suffered from mild dysphagia not requiring dilatation. Three patients (11%) were adequately maintained on short-term proton pump inhibitor therapy because of reflux symptoms, four patients (14%) had gas-bloating and two (7%) belching inability there years after surgery. A minority (15%) of our patient population continued to use antisecretory medication three years after fundoplication. Epigastrial pain appeared among patients the three checking time in the same ratio.

The surgical success rate, as defined by Visick score of I-II, was 86% in the six weeks after operation, and 84% by the end of the first postoperative year and 85% three years after antireflux surgery. Regarding QoL and complications after surgery, almost identical results were found preoperatively and at the follow-up comparing the two groups operated on by Nissen or Toupet.

A group of patients becoming completely free from reflux-related symptoms after LARS both by objective measurements (ph monitoring, endoscopy), and by their answers on questions concerning GERD symptoms of questionnaire, even was surprisingly dissatisfied with the outcome and success of the operation. Patients were divided into 2 groups according to their satisfaction with the operative results. The dissatisfied patients has significantly worse OP1 and OP2 scores (subjective consideration of efficacy of operation by the patients) than satisfied ones, however their reflux-related symptoms disappeared (well reflected by their answers on questionnaire), and no physiologic or morphologic disorder could be found by objective tools.

For further investigations patients became symptoms-free were divided into two groups.

- group I, patients becoming completely free from reflux-related symptoms and satisfied with the success of operation.
- group II, patients becoming completely free from reflux-related symptoms and dissatisfied with the success of operation. No anatomic or physiologic disorder was found of dissatisfied patients.

The postoperative reflux-related symptoms were similar in both groups. There was no difference in the distribution of types of operations (Nissen or Toupet) between the satisfied and dissatisfied patients. The two patient groups were similar in terms of their demographic data, such as age, sex, duration of GERD and medical treatment. All
patients received PPI prior to surgery. None of patients had a previous antireflux procedure. Most of the dissatisfied patients had worse preoperative heartburn score and drug treatment score, and they did not respond to medical treatment. Patients who were dissatisfied with surgery had significantly worse median preoperative scores in four domains (satisfied/dissatisfied: physical functioning, 93,72 vs. 85,34; emotional functioning, 68,57 vs. 57,33; sleep disturbance, 35,92 vs. 24,92; constipation, 15,18 vs. 21,23) compared with patients who were satisfied with the procedure. Concerning other domains significant differences hasn’t been found.

**DISCUSSION**

Success of antireflux surgery can be measured in various ways. When physiologic endpoints have been used, it has repeatedly been shown to increase resting lower oesophageal sphincter (LES) pressure and decrease oesophageal exposure to acid. Objective measurement of physiologic outcome parameters does not always correlate with patient satisfaction or with improvement of QoL and symptomatology. With increasing recognition that physiologic measures alone may provide an inadequate basis for clinical decision making, QoL has become more important. Additionally, there is awareness that the validity, reliability and responsiveness of non-physiologic measures are excellent. Recently, more GERD-specific quality of life questionnaire have been reported however an instrument suitable for QoL measurements of GERD patients undergoing antireflux operation, involving items specific for the most frequent complications and subjective consideration of surgical treatment, has not been published to date.

The purpose of the construction of our questionnaire was to establish an instrument suitable for the measurement of efficacy and success of operation from the patient’s viewpoint, and impact of patient’s QoL.

In general, our results indicate that the questionnaire is reliable and valid. **Reliability:** in most cases, the HRQoL scales had reliability values (Cronbach-α) were above acceptable level (> 0.70). **Construct validity** was demonstrated based on the observed relationships between items and scales using convergent and divergent validity. The questionnaire also demonstrated **known-groups validity.** As expected, those who reported the least severe symptoms reported the highest functioning; in most cases, the
asymptomatic group reported better functioning than the symptomatic group. Additionally, those who had higher Visick-scores reported worse HRQoL than those with less Visick-scores. Since our questionnaire also contained items and scales not specific to GERD, we will be able to make comparisons with data from other studies. The primary objective of this study was to develop and test a new HRQoL questionnaire for use with individuals with GERD underwent laparoscopic fundoplication. Our results show that the questionnaire is a short and user-friendly instrument with excellent psychometric properties. It has been found valid and reliable.

In accordance with a number of previous studies, our results showed that laparoscopic fundoplication provides effective and durable relief of reflux in patients with GERD. The operation results in a high level of patient satisfaction, improved quality of life, and elimination of antisecretory medicines in the majority of patients. The QoL showed significant improvement after surgery. Before surgery all patients had a poor quality of life. The general quality of life score, heartburn score and the satisfaction with current status improved statistically significantly 6 weeks after and showed further improvement by the end of the 1st postoperative year and it remained stable 3 years after LARS.

Evaluation of HRQL could replace in most cases the objective postoperative testing. Quality of life response closely follows the clinical outcome of surgical treatment reflecting its side-effects as well. QOLARS is a sensitive tool to assess surgical outcomes after fundoplication. We must acknowledge the limitations of our study. First, our follow-up rate was a little bit poor 78.04 % at the 1st postoperative year and 65.85 % 3 years after surgery. If those who failed to return completed questionnaires were also the patients most dissatisfied with the results of the procedure, we would have dramatically less favourable results. Low follow-up rate can be explained by the poor compliance of our patients as only 68.29% presented themselves on the scheduled 6 weeks control. Other explanation can be the way of follow-up, as questionnaires were sent by post. Meanwhile some patients changed their address and so questionnaires couldn’t be delivered. A group of patients requested to answer by phone changed their phone number or refused participation in the study. Furthermore, patients have possibility not to respond to all the questions, but these questionnaires were excluded in this study. Second, despite the significant postoperative improvement in quality of life,
patient satisfaction and the effectiveness of fundoplication fell behind other reports of outcome at one or more years after LF. We observed that, despite accurately identifying patients having pathologic gastroesophageal reflux, still some patients are not satisfied with ARS. A possible explanation can be that LF is associated with an increased risk of some complications, and as well as the occurrence of new complications – gas-bloating, swallowing and belching difficulties or vomiting inability - specific to the procedure.

In our opinion patient satisfaction seems mainly to depend on the disappearance of clinical symptoms of GERD. However complaints appearing in the consequence of operation - swallowing and belching difficulties or vomiting inability excessive gas-bloating – can have significant negative impact on patients’ QoL and satisfaction with surgical treatment, such complaints appear more frequently among dissatisfied patients. Nevertheless patients with proven GERD should be informed before the operation that some symptoms related to dyspepsia are likely to persist after surgery. Our feeling is that the greater the spectrum of preoperative functional symptoms, the more the improvement of quality of life after surgery is questionable, but further investigations are needed in this matter.

It was found that among dissatisfied patients there were more non-responders to medical therapy and they had worse preoperative heartburn and drug treatment score. Our data demonstrates that patients being dissatisfied with surgery – however their reflux symptoms were controlled - had lower preoperative generic QoL scores in some domains (physical functioning, emotional functioning, sleep disturbance, constipation) comparing with satisfied ones. Nevertheless dissatisfied patients did not have an objectively documented postoperative physiologic or morphologic problem. Moreover there are many factors involved in patient satisfaction, it is known that several comorbidities, such as psychoemotional factors, chronic pain, psychiatric disease and personality will affect subjective outcome after LARS although there are not corresponding differences in the physiologic data.

Data obtained suggest that these patients should not generally be excluded from laparoscopic antireflux surgery but should be selected more carefully. This study suggest that a generic QoL scale can preoperatively identify patients with GERD who are likely to be dissatisfied with antireflux surgery, despite they being free from
objectively documented postoperative physiologic or morphologic problem and their reflux-related symptoms are controlled.

Our results shows that patient’s satisfaction is more complex than simply relief of symptoms of GERD, and that patients who may ultimately be dissatisfied with their symptoms outcome and success of surgery may preoperatively be identified. Thus we regard combined application of disease-specific and generic questionnaires important. We hope that QOLARS will identify patients who would benefit from ARS, and can predict less improvement and success after surgical treatment from the patient’s aspect. Our questionnaire (QOLARS) is presumably will be administered as a part of clinical trials with GERD patients who have undergone LF, and can contribute to the determination of indication for surgery, better patient selection, to draw up individual treatment strategy, and therefore to the success of ARS. Use of quality-of-life instruments as a predictive tool for surgical outcomes further long-term follow-up studies that include quality of life data and patient satisfaction reports after LARS are still required.

CONCLUSIONS

1. QOLARS is the first modular questionnaire developed for the measurement of QoL of GERD-patients treated by antireflux surgery. The QOLARS is a practical and user-friendly instrument, as it can easily be responded by the patients. Results of validity examinations verified the reliability and validity of questionnaire. Reliability of the questionnaire is proven. Chronbach α values are above acceptable level 0,70 for most scales. Construct validity were documented by using convergent and divergent validity, regarding of connections between scales and questions. Known-groups validity of the questionnaire is proven. Since our questionnaire (QOLARS) also contained items and scales not specific for GERD (questions on general QoL), we will be able to make comparisons with data from other studies.

2. Prospective study verified the long term and considerable improvement of QoL after LF of GERD-patients. Scores by questionnaire highly reflected subjective complaints of the patients. Course of disease and changes due to surgical process can be monitored by the data gained by analysis of questionnaire. Our
questionnaire complements well the information of objective measurements, and in certain cases can replace more expensive examinations. Patients’ satisfaction and the success of surgery from the aspect of patients is more complex than just eliminating reflux symptoms.

Further prospective studies of high number of patients need to make our questionnaire applicable as a predictive tool, and it would help us in the preoperative selection of patients and set up indication of surgery. However, study results make likely that questionnaire preoperatively is able to select patients who will be the most satisfied with the surgery. Simultaneously QOLARS can presumably indicate patients of surgical unsuccessful or predict less operative success from the patient’s aspect.

- Subjective success of surgery is less by those who had wide range of functional symptoms before the operation. Such patients, showing dyspeptic complains too, must be informed that some gastrointestinal symptoms can be remained after surgery.
- I observed, that drug treatment before the operation didn’t or in less degree relieve symptoms of patients were dissatisfied with surgical treatment.
- Among dissatisfied patients coexisting psychological disease and psychiatric disorders were more frequent. Multiple interactions between GERD and psyologic factors emphasize the importance of global therapeutic approach.

Quality of life measurement can be applicable for comprehensive analysis of surgical procedures.
PUBLICATIONS

