

Health related quality of life and associated symptoms in barrett's esophagus patients

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Impact paragraph

Gastroesophageal reflux is common in western countries with a prevalence of 18.1%–27.8% in North America and 8.8%–25.9% in Europe. Barrett’s esophagus (BE) is known to be a result of longstanding gastroesophageal reflux disease (GERD). However, only a small proportion (10-15%) of patients with GERD are at risk of developing BE¹. The diagnosis of BE is made if the distal esophagus is lined with columnar epithelium with a minimum length of 1cm (tongues or circular) containing intestinal metaplasia at histopathological examination². BE affects 2–7% of adults in Western countries³ and is predominantly diagnosed in middle-aged white men^{4,5,6}. Other factors associated with the development of BE is a family history with BE, current or past smoking and being overweight. BE is a pre-malignant condition that places patients at risk for developing esophageal adenocarcinoma (EAC). The relative risk of EAC in patients with non-dysplastic BE is 30–125 times higher compared to the general population. Patients therefore undergo regular endoscopic surveillance for early detection of malignant transformation. Although early detection may lead to improved survival, the absolute risk for malignant transformation is low (approximately 0.3–0.5% per year)^{7,8}. When diagnosed with a pre-malignant condition, the message can cause anxiety and uncertainties to the patient. The importance of patient perceptions on the impact of the disease and response to treatment is being widely recognized. Illness perception is described by Broadbent as a patient’s cognitive appraisal and personal understanding of a medical condition and its potential consequences⁹. This may include both positive and negative illness beliefs that can influence the ability to cope with the disease and to perceive it as manageable or threatening¹⁰.

The main goal for this thesis was to gain more insight into health-related quality of life (HRQoL) and perceptions of patients with a Barrett’s esophagus on associated symptoms, cancer risks and the use of artificial intelligence. Furthermore, to provide healthcare professionals knowledge on how to measure HRQoL in patients with BE. The perceptions of patients were investigated using a variety of research techniques (focus groups, cross-sectional self-administered questionnaire studies, a multi-center study and a literature review). The results of the studies outlined in this dissertation have been published or submitted in international peer-reviewed journals in gastro-enterology or quality of life. In addition, the study findings were presented at (inter)national congresses including Digestive Disease Days (DDD, Veldhoven, The Netherlands), Digestive Disease Week (DDW, Washington, USA) and the United European Gastroenterology Week (UEGW, Vienna, Austria)

Implications for patients

Patient perceptions have been the main focus in this thesis. Gaining more insight into which factors are influencing the lives of BE patients will benefit the patients through a more patient centered care. The identification of patient's perceptions can be helpful to healthcare professionals in better understanding patient's needs and delivering more patient centered care. Results of the focus group discussions (chapter 2) and its systematic review (chapter 3) found that BE patients perceive having trust in their healthcare professionals and receiving adequate information on the diagnosis are highly important. It was even indicated that having a good relationship with healthcare professionals reduced their cancer worry. We, therefore, encourage patients to ask their physician the questions: "What are my treatment or surveillance options?", "What are the advantages and disadvantages of these options?", "What does this mean for my situation?" These questions will invite the physician to provide adequate information and leads to an more open conversation. Shared decision making starts with the realization by the medical specialist and the patient that they need each other. The medical specialist has the medical knowledge, and patients are specialized on their personal situation.

Patients with a good reflux symptom control were found to report less negative illness perceptions on the diagnosis of Barrett (chapter 5), higher (e.g. better) HRQoL scores (chapter 5), a lower cancer risk perception (chapter 2 and 4) and low cancer worry (chapter 6). Furthermore, results from the focus group study confirmed that taking proton pump inhibitors and a good reflux symptom control was perceived as an important factor for improving HRQoL. To prevent reflux related symptoms we would advise patients to use their proton pump inhibitors and to avoid certain foods (such as mint, fatty foods, spicy foods, tomatoes, onions, garlic, coffee, tea, chocolate, and alcohol). Furthermore, it is advised to sleep on an incline and if necessary lose weight and /or quit smoking.

Implications for healthcare professionals

Healthcare professionals caring for patients with BE should be aware of the implications of this diagnosis. This thesis provides insights on the perceptions of the diagnoses of BE. These findings can be used for counselling in daily clinical practice. We would like to make healthcare professionals aware of the importance of communicating with patients on gastroesophageal reflux symptoms and treat with adequate medication as needed. Experiencing symptoms of gastroesophageal reflux in BE patients is related to overestimating their cancer risk (chapter 4), more cancer worry (chapter 6), lower generic HRQoL and worse illness perceptions on the diagnosis BE (chapter 5). This underlines the importance of awareness amongst physicians that less burden of gastroesophageal reflux symptoms will enhance quality of life and decrease cancer worry (chapter 6) in BE patients. When communicating with patients it is essential to provide BE patients information tailored to their personal needs. We recommend that physicians offer an easy and approachable contact opportunity for BE patients to discuss symptom flares or fear of cancer. Our results

have shown that overall cancer worry scores were lower in BE patients who had undergone endoscopic treatment. These scores, however, were not correlated to time from treatment or histology. Therefore, it is a misconception that eliminating BE with endoscopic treatment may reduce cancer worry.

Previous studies have shown it is difficult for individual patients to accurately estimate their cancer risk, these findings were confirmed in chapter 4. None of the patients accurately estimated their annual cancer risk (59% underestimated and 41% overestimated), the lifetime risk was overestimated by 25% and 26% underestimated their cancer risk. Physicians should keep on communicating with patients about the actual low cancer risk. On the contrary, with the patients who underestimate their risk it is advised to discuss the importance of endoscopic surveillance. This will lead to greater patient understanding and may therefore positively affect health outcomes. In addition to the presence of cancer worry and gastroesophageal reflux symptoms, we found that anxiety and depression symptoms and the female gender were also associated with a negative illness perception of the diagnosis of BE.

Physicians, nurse practitioners, nurses and physician assistants should be aware that patients' trust in their healthcare professionals and endoscopic surveillance is perceived by BE patients as very important. BE patients rely on endoscopic surveillance for the early detection of EAC. Trust in the medical team and expertise of the physician in endoscopic procedures was reported as an imported factor improving HRQoL (chapter 2), which was most prominent in patients endoscopically treated for Barrett's neoplasia. However, patients are possibly too reliant on this reassurance and therefore healthcare professionals must, for this exact reason, be aware that discontinuing EGD at 75 years of age can make patients feel anxious. Patients interviewed in the focus groups found it important to receive information about guidelines and arguments for the intervals or discontinuation of the surveillance endoscopies.

Artificial intelligence (AI) is new development in clinical medicine and especially in gastrointestinal (GI) endoscopy. AI has the potential to improve the quality of GI endoscopy. We found that patients with gastrointestinal symptoms hold positive perceptions towards Artificial Intelligence (AI) and the implementation of AI in healthcare. The majority of GI-patients were not anxious about AI and thought the implementation of AI in healthcare will increase the quality of care. One third of patients was unfamiliar with AI, those patients stated a less positive perspective towards AI. Half of the GI patients reported beneficially to a virtual nurse, a technique that performs tasks normally conducted by nurses and is available at any time. AI will only play a significant role in healthcare if patients and physicians are knowledgeable and supportive towards AI.

Implications for research

Patient-reported outcomes (PROs), including HRQoL, measure the patient's health status from the patient's perspective. For the selection of PROMs, we encourage physicians and researchers measuring HRQoL to choose their PRO from a patient perspective and not strictly based on relevance according to health professionals' definitions. Using PROMs that are more patient-centered will enhance knowledge of the true impact of surveillance and endoscopic treatment on the (perceived) functioning of BE patients. In chapter 3 we have developed a conceptual framework on factors influencing HRQoL according to Barrett patients. This framework can be used by researchers to determine which construct to be measured. Within qualitative studies, the following factors influencing HRQoL were addressed by patients, namely: fear of cancer, anxiety, trust in physician, sense of control, uncertainty, worry, burden of endoscopy, knowledge and understanding, GI symptoms, sleeping difficulties, diet and lifestyle, use of medication, and support of family and friends. Furthermore, this thesis provides insights on how HRQoL has been measured in BE patients and provides healthcare professionals with an advice on which PROM's to choose. A combination of the disease-specific PROMs: GIQLI or GERD-HRQOL, with the CWS, TPS, the B-IPQ would be appropriate. However, this would necessitate a large number of questions to be addressed by patients. Using the "Patient-Reported Outcomes Measurement Information System" (PROMIS®) databank may be an appropriate solution for this problem. PROMIS is an easily accessible set of person-centered measures (www.promishealth.org), using computerized adaptive testing from large item banks for over 70 domains relevant to a wide variety of chronic diseases. PROMIS enables comparisons across populations and studies and can be integrated in several electronic health records. We advise clinicians to use the items: PROMIS GI (disrupted and swallowing, reflux and gas and bloating), PROMIS Anxiety, and PROMIS Self-Efficacy (Managing medications and treatment, Managing Symptoms). Our study on translation and validation of the Dutch-Flemish version of the PROMIS Gastrointestinal symptom scales (chapter 8) found good psychometric properties for the use in Barrett patients, but not only Barrett patients. Further research is required to validate the item bank against objective tests such as upper GI endoscopy, motility studies, or other diagnostics.

The studies in this thesis were almost entirely based on research with a cross-sectional design. Therefore, the associations and correlations that were found must be interpreted with some caution, because no causality has been investigated. Further research should be undertaken to investigate the causal factors that influence the HRQoL in BE patients. We advise to perform studies with a longitudinal design to develop a prediction model in HRQoL. Furthermore, we hope investigators in the field of endoscopic treatment of BE would integrate PROMs in their study protocol for randomized control trials. Further longitudinal research in patients treated with ET is needed to measure cancer worry and burden over time. Finally, it would be interested to perform a RCT in patients with negative illness

perception on the diagnosis BE and determine the effect of treatment optimisation or counseling.

The findings of this dissertation resulted in a collaboration between Mirjam van der Ende-van Loon and a group of researchers from the University of Cambridge. They are currently working on the project: 'Psychological and behavioral aspects of Cytosponge screening for Barrett's esophagus'. Cytosponge-trefoil factor 3 (TFF-3) testing is effective at identifying Barrett's esophagus in people with acid reflux and heartburn. Within clinical trials, participants have reported high acceptability of the Cytosponge. However, past trials have not examined barriers to uptake or the psychological impact of a Barrett's diagnosis in this context. Moreover, this project aims to understand the psychological outcomes and information needs of the potentially large numbers of people who may be diagnosed with Barrett's, leading to long-term surveillance. Based on current clinical and research work, the PhD student Mirjam van der Ende- van Loon has been invited as an expert in the field of quality of life in BE patients to contribute to this project.

Implications for society

In addition to reporting important patient-reported outcome measures in studies presented in this thesis, the PhD student is dedicated to promoting research conducted by nurses. Florence Nightingale stated more than 150 years ago: "Let us never consider ourselves finished nurses.... we must be learning all of our lives". Research from the nursing perspective will provide more deepening in the advancement of healthcare. The findings from nurse led research can help shape health policy and global healthcare. The use of evidence-based practices by nurses improves standards of care. Patients rely on nurses for information to make informed decisions about their health. Furthermore, research helps to professionalize the nursing profession as it evolves with the needs of society and advances in medical science, and helps nurses provide effective, evidence-based care. The PhD student has given several lectures on nursing research to (inter)national nurses and donors of the Catharina Research Fund. In addition, an article was published in the Eindhovens Dagblad entitled, "Doctor maar geen arts" (Doctor but not a physician), and an interview with the PhD student about the nursing research was published in a magazine of the Catharina Hospital titled 'trots' (pride). By spreading her enthusiasm for research, the doctoral candidate hopes to inspire other nurses or Nurse Practitioners to start their own research project.

List of publications

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Quirine Eunice Wennie van der Zander, Ramon M. Schreuder, Ayla Thijssen, Carolus HJ Kusters, Nikoo Dehghani, Thom Scheeve, Bjorn Winkens, **Mirjam CM van der Ende - van Loon**, Peter HN de With, Fons van der Sommen, Ad AM Masclee and Erik J Schoon. Artificial Intelligence for Characterization of Diminutive Colorectal Polyps: A Feasibility Study Comparing Two Computer-aided Diagnosis Systems

Scientific presentations

MCM van der Ende-van Loon, W. Rosmolen, EJ Schoon, S. Houterman, WL Curvers. Barrett patients overestimating their esophageal cancer risk have more reflux symptoms and a decreased quality of life.

- Digestive Disease Days, Veldhoven, Netherlands, 2017 (oral presentation)
- Digestive Disease Week, Washington, United states of America, 2018 (poster presentation)

MCM van der Ende-van Loon

Inschatting van het kanker risico door patiënten met een Barrett slokdarm

- Digestive Disease Days, Veldhoven, Netherlands, 2017 (invited speaker)

MCM van der Ende-van Loon, M Brouwers, S de Munnik, P Nieuwkerk, W Curvers, E Schoon. Factors influencing health-related quality of life in patients with Barrett's esophagus: a qualitative focus group study.

- Digestive Disease Days, Online congres, Netherlands, 2021 (oral presentation)

MCM van der Ende-van Loon, PT Nieuwkerk, RAB Oude Nijhuis, SHC van Stiphout, RCH Scheffer, RJJ de Ridder, RE Pouw, A Alkhalaf, BLAM Weusten, WL Curvers, EJ Schoon.

Factors associated with health related quality of life in patients with Barrett Esophagus.

- 30th UEGW, Vienna, Austria, 2022 (moderated poster presentation)

MCM van der Ende- van Loon. Quality of life in patients with a Barrett Esophagus – what nurses need to know-

- 30th UEGW, Vienna, Austria, 2022 (invited speaker)

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