HHS Public Access

Author manuscript

Clin Gastroenterol Hepatol. Author manuscript; available in PMC 2019 March 01.

Published in final edited form as:

Clin Gastroenterol Hepatol. 2018 March ; 16(3): 305–310. doi:10.1016/j.cgh.2017.11.049.

Patient-Reported Outcomes in Esophageal Diseases

Craig C. Reed, MD and **Evan S. Dellon, MD MPH**

Center for Esophageal Diseases and Swallowing, and Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine; University of North Carolina School of Medicine, Chapel Hill, NC

Introduction

Patients seek medical care for symptoms affecting their quality of life,[1] and this is particularly true of digestive diseases where many common conditions are symptom predominant. However, clinician and patient perception of symptoms often conflict,[2] and formalized measurement tools may have a role for optimizing symptom assessment. Patient reported outcomes (PROs) directly capture patients' health status from their own perspectives and can bridge the divide between patient and provider interpretation. The US Food and Drug Administration (FDA) defines PROs as 'any report of the status of a patient's health condition that comes directly from the patient without interpretation of the patient's response by a clinician or anyone else.'[3]

For the clinical assessment of esophageal diseases, existing physiologic and structural testing modalities cannot ascertain patient disease perception or measure the impact of symptoms on healthcare associated quality of life. In contrast, by capturing patient-centric data, PROs can provide insight into the psychosocial aspects of patient disease perceptions, capture health-related quality of life (HRQL), improve provider understanding, highlight discordance between physiologic, symptom, and HRQL measures, and formalize follow-up of treatment response.[1,4] Following symptoms such as dysphagia or heartburn over time in a structured way allows clinically obtained data to be used in pragmatic or comparative effectiveness studies. PROs are also now an integral part of the FDA's drug approval process.

In this paper, we review the available PROs capturing esophageal symptoms with a focus on dysphagia and heartburn measures that were developed with rigorous methodology; it is beyond the scope of this paper to do a thorough review of all upper GI PROs or quality of life PROs. We then discuss how esophageal PROs may be incorporated into clinical practice now, as well as opportunities for PRO use in the future.

Corresponding Author: Evan S. Dellon MD, MPH, CB#7080 Bioinformatics Building, 130 Mason Farm Rd. UNC-CH, Chapel Hill, NC 27599-7080, Phone: (919) 966-2513, Fax: (919) 843-2508, edellon@med.unc.edu.

Disclosures: Dr. Reed has no potential conflicts of interest pertinent to the content of this paper.

Esophageal symptoms-specific PROs

The literature pertinent to upper gastrointestinal and esophageal-specific PROs is heterogeneous, and the development of PROs has been variable in rigor. Two recent systematic reviews identified PROs pertinent to dysphagia and heartburn (Table 1) and both emphasized rigorous measures developed in accordance with FDA guidance.[3]

Patel et. al. identified 34 dysphagia-specific PRO measures of which 10 were rigorously developed (Table 1). These measures encompassed multiple conditions including *esophageal cancer* [Functional Assessment of Cancer Therapy Esophageal Cancer Subscale (FACT-E), European Organization for Research and Treatment of Cancer Quality-of-Life with esophageal Cancer 25 items (EORTC QLQ-OG25), European Organization for Research and Treatment of Cancer Quality-of-Life with esophageal cancer 18 items (EORTC QLQ-OES18)], *upper aerodigestive neoplasm-attributable oropharyngeal dysphagia* [M.D. Anderson dysphagia inventory (MDADI)], *mechanical and neuromyogenic oropharyngeal dysphagia* [swallow quality of life questionnaire (SWAL-QOL), Sydney Swallow Questionnaire (SSQ), [swallowing quality of care (SQAL-CARE)], *achalasia* [Measure of Achalasia Disease Severity (MADS)], *eosinophilic esophagitis* [Dysphagia Symptom Questionnaire (DSQ)], *general dysphagia symptoms* and *gastroesophageal reflux* [Patient-Reported Outcomes Measurement Information System Gastrointestinal Symptom Scales (PROMIS-GI)]. PROMIS-GI, produced as part of the NIH PROMIS program, includes rigorous measures for *general dysphagia symptoms* and *gastroesophageal reflux* in addition to lower gastrointestinal symptom measures.

The systematic review by Vakil et. al found 15 PRO measures for GERD symptoms that underwent psychometric evaluation (Table 1). Of these, 5 measures were devised according to the developmental steps stipulated by the US Food and Drug Administration and the European Medicines Agency, and each measure has been utilized as an endpoint for a clinical trial. The 5 measures include the GERD Symptom Assessment Scale (GSAS), the Nocturnal Gastro-oesophageal Reflux Disease Symptom Severity and Impact Questionnaire (N-GSSIQ), the Reflux Questionnaire (ReQUEST), the Reflux Disease Questionnaire (RDQ), and the Proton Pump Inhibitor Acid Suppression Symptom Test (PASS) (Table 1). Additional PROs capturing esophageal symptoms include the eosinophilic esophagitis symptom activity index (EEsAI), Eckardt score (used for achalasia), Mayo dysphagia questionnaire (MDQ), and GERD-Q (Table 1).

While HRQL measures exist for esophageal symptoms, a thorough discussion of these measures exceeds the scope of this paper. The utilization of many HRQL instruments may be problematic, as they either may not be disease-specific or they may poorly translate across disease processes. The Northwestern Esophageal Quality of Life (NEQOL) instrument, a rigorously developed measure that has recently been introduced, addresses these concerns and may be utilized for a variety of diseases and symptoms affecting the esophagus.[5]

Utilization of Esophageal PROs in Practice

Before incorporating a PRO into clinical practice, providers must appreciate the construct(s), intent, developmental measurement properties, validation strategies, and responsiveness characteristics associated with the measure.[4] PROs can be symptom and/or condition specific. For example, this could include dysphagia associated with achalasia or eosinophilic esophagitis, post-operative dysphagia from spine surgery, or general dysphagia symptoms regardless of the etiology (Table 1). Intent refers to the context in which a PRO should be utilized and is generally stratified into three areas: population surveillance, individual patient-clinician interactions, and research studies.[4] A thorough analysis of PRO developmental properties exceeds the scope of this paper. However, several key considerations are worth discussing. Each measure should clearly delineate the construct, or outcome, in addition to the population used to create the measure (e.g. patients with achalasia). PROs should be assessed for reliability, construct validity, and content validity. Reliability pertains to the degree in which scores are free from measurement error, the extent to which items (i.e. questions) correlate, and test-retest reliability. Construct validity includes dimensionality (evidence of whether a single or multiple subscales exist in the measure), responsiveness to change (longitudinal validity), and convergent validity (correlation with additional construct-specific measures). Central to the PRO development process is the involvement of patients and content experts (content validity). PRO measures should be readily interpretable, and the handling of missing items should be stipulated. The burden, or time required for administering and scoring the instrument, and the reading level of the PRO need to be considered.[6] In short, a PRO should measure something important to patients, in a way that patients can understand, and in a way that accurately reflects the underlying symptom and disease.

While PROs traditionally represent a method for gathering data for research, they should also be viewed as a means of improving clinical care. The monitoring of change in a particular construct represents a common application of PROs in clinical practice. This helps quantify the efficacy of an intervention can provide insight into the comparative effectiveness of alternative therapies. For example, in a patient with an esophageal stricture, a dysphagia-specific measure could be used at baseline prior to an endoscopy and dilation, in follow-up after dilation, and then as a monitoring tool to determine when repeat dilation may be needed. Similarly, the Eckardt score has been commonly used to monitor response to achalasia treatments. Clinicians may also utilize PROs in real time to optimize patient management. The data gathered from PROs may help triage patients into treatment pathways, trigger follow-up appointments, supply patient education prompts, and produce patient and provider alerts.[6] For providers engaging in clinical research, PROs administered at the point of patient intake, whether electronically through a patient portal or in the clinic, provide a means of gathering baseline data.[7] A key question, however, is whether it is practical to use a PRO routinely in the clinic, esophageal function lab, or endoscopy suite.

These practical issues include cultivating a conducive environment for PRO utilization, considering the burden of the measure on the patient, and utilization of the results in an expedient manner.[7] In order to promote seamless use of a PRO in clinical work-flows, a multi-modal means of collecting PRO data should be arranged. Electronic PROs (ePROs)

available through a patient portal, designed with a user-friendly and an intuitive interface, facilitate patient completion of PROs at their convenience, and ideally prior to a clinical or procedure visit. For patients without access to the Internet, tablets and/or computer terminals within the office are convenient options. Nurses or clinic staff could also help patients complete a PRO during check-in for clinic, esophageal testing, or endoscopy. The burden a PRO imposes on patients also limits the utility of a measure. For instance, PROs with a small number of questions are more likely to be completed, while scales consisting of 30 of more items are infrequently finished. Clinicians should also consider how they plan to utilize the results of a PRO prior to implementing one; if the data will not be used, then the effort to implement and collect it will be wasted. Moreover, patients will anticipate that the time required to complete a PRO will translate to an impact on their management plan and will more readily complete additional PROs if previous measures expediently affected their care.[7]

Barriers to PRO implementation and future directions

Given the potential benefits to PRO use, why are they not routinely implemented? In practice, there are multiple barriers that thwart the adoption of PROs into both healthcare systems and individual practices. The integration of PROs into large healthcare systems languishes partly due to technological and operational barriers.[7] For instance, the manual distribution, collection, and transcription of hand-written information requires substantial investitures of time, which is magnified by the number of patients whose care is provided within a large health system. One approach to the technological barrier includes the creation of an electronic platform integrating with patient portals. Such a platform would obviate the need to manually collect and transcribe documents, and could import data directly into provider documentation and flowsheets. However, the programming time and costs are substantial upfront, and without clear data that this could lead to improved outcomes or decreased costs downstream there may be reluctance to devote resources to this. In clinical practice, the already significant demands on providers' time mitigates enthusiasm to add additional tasks. Providers could also face annual licensing agreements, fees on a per study basis, or royalties associated with particular PROs, and at the individual practice level, there may not be appropriate expertise to select and implement routine PRO monitoring. To address this, efforts are being made to simplify the process of incorporating PROs. For example, given the relatively large number of heterogeneous PROs, the PROMIS project[1] endeavors to clarify which PROs constitute the best measure for each construct and condition.[7] The PROMIS measures are also provided publicly and available without license or fee.

Areas particularly well situated for growth in the use of PRO measures include comparative effectiveness studies and pragmatic clinical trials. PRO-derived data may promote a shift from explanatory RCTs to pragmatic RCTs, as this data emphasizes patient-centered care and is more broadly generalizable to clinical settings. Furthermore, the derivation of data directly from the healthcare delivery system through PROs, such as two-way text messages, increases the relevance and cost-effectiveness of clinical trials. Given the current medical climate, pressures continue to mount toward the identification of cost efficient and efficacious medical therapies.[8] In this capacity, PROs facilitate the understanding of changes

in HRQL domains subject to treatment choices. PROs further consider the comparative symptom burden and side effects associated with competing treatment strategies.[9] Finally, PROs have also enabled the procurement of data from patient-powered research networks. While this concept has not yet been applied to esophageal diseases, one example of this in GI is the Crohn's and Colitis Foundation of America (CCFA) Partners project, which has built an internet cohort consisting of approximately 14,200 IBD patients who are monitored with a series of PROs.[10] An endeavor such as this should be a model for esophageal conditions in the future.

Conclusion

PROs, as a structured means of directly assessing symptoms, help facilitate a provider's understanding from a patient's perspectives. Multiple PROs have been developed to characterize constructs pertinent to esophageal diseases and symptoms. These vary in methodological rigor, but multiple well-constructed PROs exist for symptom domains such as dysphagia and heartburn, and can be used to monitor symptoms over time and assess treatment efficacy. Implementation of esophageal PROs, both in large health systems and in routine clinical practice is not yet standard and faces a number of barriers. However, the potential benefits are substantial and include increased patient-centeredness, more accurate and timely disease monitoring, and applicability to comparative effectiveness studies, pragmatic clinical trials, and patient-powered research networks.

Acknowledgments

Dr. Dellon is a consultant for Adare, Alivio, Allkalos, Banner, Enumeral, GSK, Receptos/Celegene, Regeneron, and Shire, receives research funding from Meritage, Miraca, Nutricia, Receptos/Celegene, Regeneron, and Shire, and has received an education grant from Banner.

Grant Support: This research was supported, in part, by NIH awards T32DK007634 (CCR) and R01DK101856 (ESD).

References

1. Spiegel B, Hays R, Bolus R, Melmed G, Chang L, Whitman C, et al. Development of the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) Gastrointestinal Symptom Scales. Am J Gastroenterol. 2014; 109(11):1804–14. [PubMed: 25199473]
2. Chassany O, Shaheen NJ, Karlsson M, Hughes N, Rydén A. Systematic review: symptom assessment using patient-reported outcomes in gastroesophageal reflux disease and dyspepsia. Scand J Gastroenterol [Internet]. 2012; 47(12):1412–21. Available from: http://www.tandfonline.com/doi/full/10.3109/00365521.2012.712999.
3. U.S. Department of Health and Human Services FDA Center for Drug Evaluation and Research USD of H and HSFC for DE and, U.S. Department of Health and Human Services FDA Center for Biologics Evaluation and Research USD of H and HSFC for BE and, U.S. Department of Health and Human Services FDA Center for Devices and Radiological Health USD of H and HSFC for D and R. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. Health Qual Life Outcomes [Internet]. 2006; 4:79. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17034633%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC1629006.
4. Lipscomb J. Cancer Outcomes Research and the Arenas of Application. J Natl Cancer Inst Monogr [Internet]. 2004; 2004(33):1–7. Available from: https://academic.oup.com/jncimono/articlelookup/doi/10.1093/jncimonographs/lgh038.

5. Bedell A, Taft TH, Keefer L. Development of the Northwestern Esophageal Quality of Life Scale : A Hybrid Measure for Use Across Esophageal Conditions. Am J Gastroenterol. 2016 Apr; 111(4): 493–9. [PubMed: 26881974]

6. Farnik M, Pierzchala W. Instrument development and evaluation for patient-related outcomes assessments. Patient Relat Outcome Meas. 2012 Jul.(3):1–7.

7. Neil, W., Wagle, MDM. Implementing Patient-Reported Outcome Measures (PROMs); NEJM Catal [Internet]. 2016. p. 1-2.Available from: http://catalyst.nejm.org/implementing-proms-patient-reported-outcome-measures/

8. Richesson RL, Hammond WE, Nahm M, Wixted D, Simon GE, Robinson JG, et al. Electronic health records based phenotyping in next-generation clinical trials: a perspective from the NIH Health Care Systems Collaboratory: Table 1. J Am Med Informatics Assoc [Internet]. 2013; 20(e2):e226–31. Available from: https://academic.oup.com/jamia/article-lookup/doi/10.1136/amiajnl-2013-001926.

9. Coon CD, McLeod LD. Patient-Reported Outcomes: Current Perspectives and Future Directions. Clin Ther. 2013; 35(4):399–401. [PubMed: 23541709]

10. Chung AE, Sandler RS, Long MD, Ahrens S, Burris JL, Martin CF, et al. Harnessing person-generated health data to accelerate patient-centered outcomes research: The Crohn's and Colitis Foundation of America PCORnet Patient Powered Research Network (CCFA Partners). J Am Med Informatics Assoc. 2016; 23(3):485–90.

Table 1

Overview of esophageal-PROs for measuring dysphagia or heartburn[†]

Condition or symptom and instrument	Target population	Longitudinal validity	Plan for scoring measure & missing data	Reference
Esophageal cancer				
FACT-E [*]	Cohort A: adults with resectable squamous or adenocarcinoma of the esophagus or GEJ[1] Cohort B: esophageal cancer patients with planned neoadjuvant chemoradiation before surgery	Yes	Yes / No	Cancer 2006; 107: 854–63.
EORTC-QLQ-OG25	Esophageal or gastric cancer including tumors of the GEJ	No	Yes / No	Eur J Cancer 2007; 43: 2066–73.
EORTC-QLQ-OES18	Newly diagnosed squamous cell or esophageal adenocarcinoma	No	Yes / No	Eur J Cancer 2003; 39: 1384–94.
Cancer-attributed OP[2] dysphagia				
MDADI	Neoplasm of the upper aerodigestive tract	No	Yes / No	Arch Otolaryngol Head Neck Surg 2001; 127: 870–6.
Mechanical and neuromyogenic OP dysphagia				
SWAL-QOL	Mechanical or neurologic OP dysphagia due to multiple causes	Yes	Yes / No	Dysphagia 2000; 15: 122–33.
SSQ	Neuromyogenic or OP dysphagia with 3 months of stable symptoms	Yes	Yes / No	Gastroenterology. 2000; 118(4): 678–87.
SWAL-CARE	Mechanical or neurologic OP dysphagia due to multiple causes	No	Yes / No	Dysphagia 2002; 17: 97–114.
Achalasia				
MADS	Achalasia patients	No	Yes / Yes	Am J Gastroenterol 2005; 100: 1668–76.
Eckardt score [*]	Newly diagnosed achalasia patients undergoing pneumatic dilatation	No	Yes / No	Gastroenterology 1992;103:1732–1738.
Eosinophilic esophagitis				
DSQ	Adolescents and adults with EoE	No	Yes / Yes	Aliment Pharmacol Ther 2013; 38:634–42.
PEESS v2.0 [*]	Pediatric patients with EoE	No	No / No	BMC Gastroenterol 201 1 Nov 18;11:126
EEsAI	Adults with EoE	No	No / No	Gastroenterol 2014 Dec;147(6):1 255–66.e21.
General dysphagia				

Condition or symptom and instrument	Target population	Longitudinal validity	Plan for scoring measure & missing data	Reference
PROMIS-GI *	Multiple GI disorders and symptoms	No	Yes / No	Am J Gastroenterol 2014; 109: 1804–14.
MDQ	Adults with dysphagia	No	No / No	Dis Esophagus 2007;20:202–5.
Heartburn				
GSAS *	Patients with GERD	Yes	Yes / Yes	Dig Dis Sci 2001;46:1540–1549
N-GSSIQ	Patients with GERD confirmed with pH monitoring, endoscopy, imaging, physician diagnosis, or PPI response with symptoms over previous 3 months	Yes	No / Yes	Aliment Pharmacol Ther 2010;32:591–602
ReQuest	Patients with GERD	Yes	No / No	Aliment Pharmacol Ther 2004;20:891–898
RDQ	GERD in primary care and clinical trials	Yes	Yes / No	Aliment Pharmacol Ther 2007;25:1087–1097
PASS	Patients in clinical practice taking a PPI	Yes	Yes / No	Gastroenterol. 2009;136(Suppl 1):M1870
GERD-Q *	Diagnosis of GERD in primary care	No	Yes / No	Aliment Pharmacol Ther *2009;30(10): 1034*.

† adapted from Patel et al and Vakil et al:

Patel DA, Sharda R, Hovis KL, et al. Patient-reported outcome measures in dysphagia: a systematic review of instrument development and validation. Dis esophagus. Dis Esophagus. 2017 May 1;30(5):1–23.

Vakil NB, Halling K, Becher A, Rydén A. Systematic review of patient-reported outcome instruments for gastroesophageal reflux disease symptoms. Eur J Gastroenterol Hepatol. 2013 Jan;25(1):2–14.

1: gastroesophageal junction;

2: oropharyngeal

* Publicly available