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Development and Validation of a New Questionnaire for the Evaluation of Upper Gastrointestinal Symptoms in the Elderly Population: A Multicenter Study

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Background. Several diagnostic questionnaires for evaluating upper gastrointestinal symptoms have been described; none of these, however, has been validated in older individuals.

Objectives. To develop and validate a diagnostic tool for evaluating upper gastrointestinal symptoms in older patients.

Methods. A cohort of 206 older patients who underwent a upper gastrointestinal endoscopy (development cohort) was used for developing a 15-item upper gastrointestinal symptom questionnaire for the elderly population (UGISQUE), including five symptom clusters: (a) abdominal pain syndrome, (b) reflux syndrome, (c) indigestion syndrome, (d) bleeding, and (e) nonspecific symptoms. The questionnaire was then validated in a cohort of 326 older patients selected from those who underwent an upper gastrointestinal endoscopy in 15 gastroenterological centers in Italy (validation cohort).

Results. The endoscopic diagnoses in the development and validation cohorts were esophagitis (E) 15.5% and 29.4%, erosive gastritis (EG) 24.8% and 24.8%, peptic ulcer (PU) 26.2% and 14.7%, and without organic lesions (WOL) 31.0% and 33.5%, respectively. In both the cohorts, patients with upper gastrointestinal disorders showed significantly more symptoms than WOL patients. The predictive value of UGISQUE for any pathological condition (E, EG, or PU) was good, with areas under the receiver-operating characteristic curve of .80, 95% confidence interval (CI) 0.743–0.864, and of .78, 95% CI 0.73–0.83, in the development and validation cohorts, respectively. The accuracy of UGISQUE was significantly higher than that for the individual clusters of symptoms in predicting the presence of E ($p = .004$), PU ($p < .0001$), or any pathological condition ($p < .0001$).

Conclusion. UGISQUE is an accurate diagnostic tool for evaluating symptoms in elderly patients with upper gastrointestinal disorders.

Key Words: Gastrointestinal symptoms—Esophagitis—Peptic ulcer—Gastritis—Elderly population.

CLINICAL features of upper gastrointestinal disorders, including gastroesophageal reflux disease (GERD) and peptic ulcer (PU), in elderly patients are quite different from those of young or adult individuals (1,2). Moreover, the intensity of symptoms may be less severe in older individuals and therefore may not receive the full attention by physicians or the patient himself or herself. Thus, the diagnosis of upper gastrointestinal disorders may be missed or delayed in the elderly individuals (3,4).

Several scales and questionnaires for diagnostic, epidemiological, and clinical trial investigation of patients with GERD (5–11) or dyspepsia (12–17) have been recently developed. None of these instruments, however, has been validated specifically in elderly individuals (18).

The aims of this study were to develop and validate a diagnostic questionnaire for the evaluation of upper gastrointestinal symptoms in older patients.

Methods

Study Population

The study was conducted according to the Declaration of Helsinki and the guidelines for Good Clinical Practice and was approved by our institutional ethics committee. Written informed consent was obtained from the patients or from relatives prior to participation in the study.

Two cohorts of elderly patients were included. The first cohort (development cohort) was included for developing the upper gastrointestinal symptom questionnaire for the elderly population (UGISQUE); the second cohort (validation cohort) was involved in the study to validate the questionnaire in a multicentric population in the frame of the IPOD project (*i*dentification of sym*pto*ms and risk factors to detect reflux *d*isease in elderly populations).

For inclusion in the development cohort, all patients aged 60 years or older who underwent an upper gastrointestinal

endoscopy at the geriatric unit of the Casa Sollievo della Sofferenza hospital (IRCCS, San Giovanni Rotondo, Italy) from January to June 2007 were screened. For inclusion in the validation cohort, all patients aged 60 years or older who underwent an upper gastrointestinal endoscopy in 15 gastroenterological centers in Italy, selected by number of examinations as regional representative, during a 1-month study period between February and April 2007, were screened.

Exclusion criteria were as follows: (a) a cognitive impairment of grade moderate to severe as evaluated by a Short Portable Mental Status Questionnaire score of 7 or higher (19), (b) previous surgery of the gastrointestinal tract, (c) presence of gastrointestinal tumors, (d) presence of other tumors at late stages, and (e) use of antisecretory treatments during the previous 4 weeks.

Measurements

Information on sociodemographic characteristics (age, gender, marital status), anthropometric measurements (body mass index [BMI]: body weight/height^2), smoking status, alcohol consumption, physical functional status (according to the Barthel index (20)), comorbidity, and drug assumption was collected from all participants.

The UGISQUE

For developing the UGISQUE, an analysis of symptoms in the development cohort population was initially done for identifying the most relevant symptoms that could predict the endoscopic outcome. Symptoms were collected just before the endoscopy; both the patients and the investigators were not aware of the results. Our starting point was the Gastrointestinal Symptom Rating Scale (GSRS), as modified for patients with upper gastrointestinal disorders (21). The GSRS questionnaire included eight items (items 1–8) for the description of upper gastrointestinal symptoms and seven items (items 9–15) that described diarrhea and constipation; only the first eight items were evaluated in the present study. Other symptoms were recorded when they were indications for performing the endoscopy. In particular, the following symptoms were recorded: hematemesis, melena, anemia defined as a loss of 3 g or more of hemoglobin during the past 3 months (22), anorexia (23), weight loss of 3 kg or more during the past 3 months (24), vomiting, and dysphagia (25). Thus, the UGISQUE included 15 items for the description of symptoms divided into five symptom clusters: (a) abdominal pain syndrome (stomach ache/pain, hunger pains in stomach or belly), (b) reflux syndrome (heartburn, acid reflux), (c) indigestion syndrome (nausea, rumbling in the stomach [ie, vibrations or noise in the stomach], bloated stomach [ie, swelling in the stomach], burping [ie, bringing up air or gas through the mouth]), (d) bleeding (hematemesis, melena, anemia), and (e) nonspecific symptoms (anorexia, weight loss, vomiting, dysphagia).

The UGISQUE included a response scale with four grades: (a) absent = no symptoms are reported by patient; (b) mild = awareness of symptoms, but they are easily tolerated; (c) moderate = symptoms interfering with the normal activities; and (d) severe = symptoms that induced inability to perform normal activities or symptoms requiring health intervention. Symptomatic patients were defined as those who reported moderate or severe discomfort in at least one item.

Endoscopic Diagnoses

At study entry, an endoscopy was performed. Reflux esophagitis (E) was endoscopically defined and classified according to the Los Angeles classification (26). Hiatus hernia was diagnosed when the Z-line and the gastric folds extended 2 cm or more above the diaphragmatic hiatus (27). Gastric and duodenal lesions were defined according to the Cotton and Williams' criteria (28). According to their endoscopic diagnoses, in both cohorts, four groups of individuals were considered: (a) individuals without organic lesions (WOL), (b) individuals with E), (c) individuals with erosive gastritis (EG), and (d) individuals with PU.

Helicobacter pylori infection was studied histologically using the Sydney classification (29) and by the rapid urease test performed on both gastric antral and body biopsies (CLO test; Delta West, Bentley, Australia). Patients were considered infected with *H. pylori* if at least one method was positive for the infection; patients were considered not infected if both methods were negative for the infection (30).

Statistical Analysis

The association among general characteristics, symptomatology, and groups of individuals was studied using the chi-square test or Fisher exact test. Group mean values were compared through the generalized linear model procedure, after testing for homoschedasticity (Levene's test). In case of heteroschedasticity, Welch's analysis of variance was performed. The goodness of fit of prediction models based on the UGISQUE was evaluated defining logistic regression models for both development and validation cohorts, with binomial outcomes in relation to endoscopic diagnosis (E vs WOL; EG vs WOL; PU vs WOL; E, EG, or PU vs WOL), adjusting for age and sex. Area under the receiver-operating characteristic curves (ROCs) were compared using Delong's test (31), and Hanley and McNeil's method (32).

Power analysis was calculated on ROC curves in both development and validation cohort samples, achieving a power of .98 and .64, respectively.

All statistical analyses were performed using SAS, version 9.1.3 package (SAS Institute, Cary, NC), and PASS 2008, version 08.0.5 (NCSS, LLC, Kaysville, UT).

Results

Development Cohort

Two hundred six patients were included: 89 men and 117 women, mean age = 76.2 ± 7.1 years, range = 62–96 years. The endoscopic diagnoses were as follows: E = 32 patients (15.5%), EG = 51 patients (24.8%), PU = 54 patients (26.2%), and WOL = 69 patients (33.5%). Characteristics of patients stratified by endoscopic diagnoses are reported in Table 1. As shown in Figure 1, patients with E showed significantly more abdominal pain ($p = .0028$), reflux symptoms ($p < .0001$), indigestion syndrome ($p = .0004$), and nonspecific symptoms ($p = .0001$) than WOL patients. PU patients demonstrated significantly higher frequency of abdominal pain ($p = .02$), bleeding ($p < .0001$), and nonspecific symptoms ($p < .0001$) than WOL patients. Patients with EG had significantly higher frequency of abdominal pain ($p < .02$) and nonspecific symptoms ($p = .0039$) than WOL patients.

The predictive value of UGISQUE was good, with an area under the ROC curve of .80 (95% confidence interval [CI] 0.743–0.864) in patients with any pathological feature at endoscopy (E, PU, or EG). The accuracy of UGISQUE was significantly higher in patients with E (ROC area = .87, 95% CI 0.80–0.94) and in patients with PU (ROC area = .87, 95% CI 0.81–0.93) than in patients with EG (ROC area = .74, 95% CI 0.65–0.83; E vs EG, $p = .001$ and PU vs EG, $p = .0008$). Moreover, using the Delong's test, we found that UGISQUE had significantly higher diagnostic accuracy than the individual clusters of symptoms in predicting the presence of E ($p = .004$), PU ($p < .0001$), or any pathological condition (E, PU, or EG, $p < .0001$) as diagnosed by endoscopy.

Validation Cohort

The validation cohort included 326 patients: 169 men and 157 women, mean age = 72.0 ± 7.2 years, range = 60–93 years (Table 1). The endoscopic diagnoses were as follows: E = 96 patients (29.4%), EG = 81 patients (24.8%), PU = 48 patients (14.7%), and WOL = 101 patients (31.0%). As shown in Figure 1, patients with E showed significantly more abdominal pain ($p = .0009$), reflux symptoms ($p < .0001$), indigestion syndrome ($p < .0001$), bleeding ($p = .04$), and nonspecific symptoms ($p = .05$) than WOL patients. Patients with PU had more abdominal pain ($p = .02$), reflux symptoms ($p = .006$), bleeding ($p < .0001$), and nonspecific symptoms ($p = .0003$) than WOL patients. Finally, patients with EG had significantly more abdominal pain ($p = .002$), bleeding ($p = .0002$), and nonspecific symptoms ($p = .0229$) than WOL patients. The area under the ROC curve of UGISQUE in patients with any pathological condition at endoscopy (E, EG, or PU) was also good (ROC area = .78, 95% CI 0.73–0.83). Diagnostic accuracy of UGISQUE was higher in patients with E (ROC area = .86, 95% CI 0.81–0.91) and with PU (ROC area = .78, 95% CI 0.70–0.86) than in those

Table 1. Characteristics of Participants in the Development and Validation Cohorts, Stratified by Endoscopic Diagnoses

	Development Cohort ($n = 206$)					Validation Cohort ($n = 326$)				
	WOL ($n = 69$)	E ($n = 32$)	EG ($n = 51$)	PU ($n = 54$)	*p* Value	WOL ($n = 101$)	E ($n = 96$)	EG ($n = 81$)	PU ($n = 48$)	*p* Value
Gender (% male)	36.2	53.1	41.2	48.2	ns	48.5	61.1	50.6	41.7	ns
Age (y, $M \pm SD$)	75.7 ± 6.1	74.2 ± 7.0	76.8 ± 7.4	77.6 ± 8.0	E vs PU .0336	73.3 ± 7.1	69.5 ± 7.1	72.9 ± 6.5	73.4 ± 7.4	E vs WOL .0002
Marital status (% married)	56.5	62.5	62.8	59.3	ns	63.6	69.2	66.7	62.2	ns
BMI (kg/m^2, $M \pm SD$)	26.7 ± 4.5	25.0 ± 3.6	28.5 ± 4.7	28.0 ± 6.3	E vs EG .0008; E vs PU .0297	25.1 ± 3.1	25.4 ± 3.0	26.5 ± 3.3	26.2 ± 4.2	EG vs WOL .0052
Alcohol (% daily)	12.3	9.4	9.3	8.9	ns	31.5	29.7	29.7	27.9	ns
Smoking status (% smokers/former)	22.0	18.8	17.8	17.4	ns	13.9	22.9	12.4	10.4	ns
Comorbidity (n, $M \pm SD$)	2.21 ± 1.59	2.63 ± 1.56	2.59 ± 1.29	3.20 ± 1.86	PU vs WOL .0025	2.54 ± 1.45	1.66 ± 1.68	3.22 ± 2.22	2.73 ± 1.86	E vs WOL .0002; EG vs WOL .0274
Drugs (n, $M \pm SD$)	3.24 ± 2.78	3.40 ± 2.57	3.53 ± 1.94	4.16 ± 2.29	PU vs WOL .0434	2.30 ± 1.65	1.31 ± 1.82	2.26 ± 1.86	2.02 ± 1.60	E vs WOL <.0001
Physical functioning (%, need of assistance)	20.6	29.0	18.4	55.1	.0001	16.1	17.1	21.7	27.9	ns
Helicobacter pylori (%)	15.9	31.3	43.1	51.9	E vs WOL ns; EG vs WOL .002; PU vs WOL .0001	17.4	28.0	48.9	41.9	E vs WOL ns; EG vs WOL .01; PU vs WOL .05

Note: BMI = body mass index, E = esophagitis, EG = erosive gastritis, ns = not significant, PU = peptic ulcer, WOL = without organic lesions.

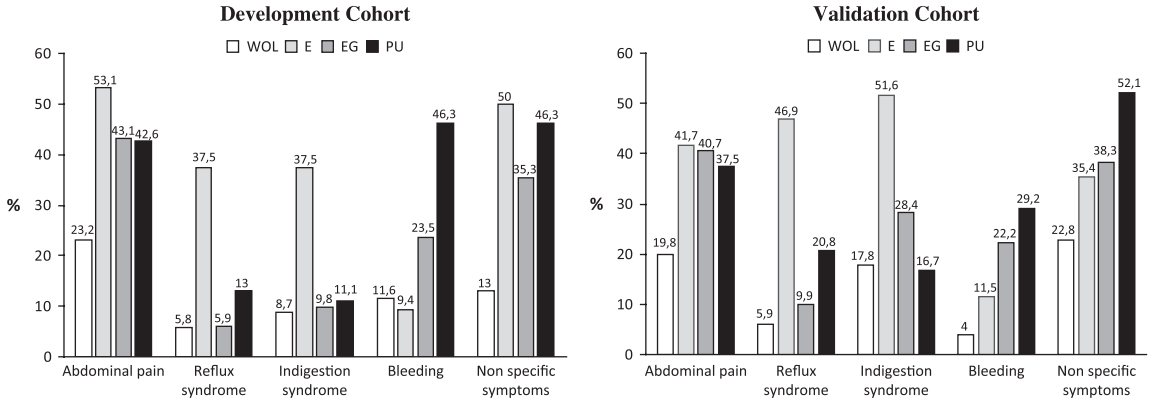

Figure 1. Distribution of class of symptoms (%) in the elderly individuals, stratified by cohort and endoscopic diagnosis outcomes.

with EG (ROC area = .73, 95% CI 0.66–0.80; E vs EG, $p < .0001$ and PU vs EG, p = not significant).

As observed in the development cohort, also in the validation cohort UGISQUE had significantly higher diagnostic accuracy than the individual clusters of symptoms in predicting the presence of E ($p = .0001$), PU ($p < .0001$), or any pathological condition (E, PU, or EG, $p < .0001$).

Discussion

The study reports the development and validation of a new questionnaire for the evaluation of symptoms in two independent cohorts of elderly individuals with endoscopic diagnoses of E, PU, or EG. The findings of the study demonstrated that elderly patients with gastrointestinal disorders had significantly higher rates of abdominal pain, reflux symptoms, indigestion syndrome, bleeding, and also nonspecific symptoms, than those without endoscopic lesions. Because the presence of nonspecific symptoms has been reported as one of the most important reasons for late diagnoses (1) or even severe complications (3) in elderly patients, the findings of the study support the concept that the use of a comprehensive diagnostic tool specifically developed for elderly patients may be useful in reducing misleading and underrecognized diagnoses.

The heterogeneity of symptoms reported by the patients of both the cohorts indirectly confirms that the elderly patient may have a different clinical expression of the upper gastrointestinal diseases compared with young or adult individuals (1,2).

The predictive value of UGISQUE in identifying older patients with upper gastrointestinal disorders was good in both the cohorts. Moreover, the diagnostic accuracy of UGISQUE was higher in patients with E and PU than in patients with EG. Indeed, the analysis of clinical characteristics of patients with different pathologies failed to find any significant role of comorbidities, drug use, or functional disability that may explain these discrepancies.

To our knowledge, this is the first diagnostic questionnaire for the evaluation of upper gastrointestinal disorders specifically developed for and validated in elderly patients. The different physicians involved in the study did not encounter problems with the administration of the UGISQUE or with the collection of data. Moreover, no significant problems were reported by the patients in the understanding of the questionnaire or by the investigators in the evaluation of responses.

The study has some limitations. Because UGISQUE was developed and validated in elderly patients who underwent an upper gastrointestinal endoscopy in selected centers, it is likely that the instrument may not be so accurate for the evaluation of elderly patients from different settings. Moreover, the absence of assessment of lower gastrointestinal symptoms as well as of reliability and validity of individual items may limit the clinical usefulness of the UGISQUE. Finally, all patients who were in treatment with antisecretory drugs were excluded; because it has been reported that these treatments may significantly influence the symptomatology in older patients with upper gastrointestinal disorders (33,34), we cannot exclude the fact that a specific validation of UGISQUE is needed in these patients.

In conclusion, we developed and validated a new questionnaire for the evaluation of elderly patients with upper gastrointestinal disorders. Further studies are needed to explore its efficacy and clinical usefulness in clinical trials.

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