


# Trajectories of Health-Related Quality of Life, Health Literacy, and Self-Efficacy in Curatively-Treated Patients with Esophageal Cancer: A Longitudinal Single-Center Study in Italy

Journal of Patient Experience  
Volume 8: 1-10  
© The Author(s) 2021  
Article reuse guidelines:  
sagepub.com/journals-permissions  
DOI: 10.1177/23743735211060769  
journals.sagepub.com/home/jpx  


Arianna Magon, RN, MSN, PhD<sup>1</sup> , Rosario Caruso, PhD<sup>1</sup> ,  
Andrea Sironi, MD<sup>2</sup>, Sabrina Mirabella, RN, MSN<sup>3</sup>,  
Federica Dellafiore, PhD, RN<sup>4</sup>, Cristina Arrigoni, RN, MSc<sup>4</sup>,  
and Luigi Bonavina, MD, FACS<sup>2,5</sup>

## Abstract

This prospective longitudinal study aimed to describe the trajectories of HRQoL, health literacy, and self-efficacy in patients with esophageal cancer, which have been thus far poorly described. Data were collected at baseline (preoperative phase) and in the postoperative period (two weeks, and one, two, and three months after esophagectomy). The study hypothesis was that health literacy and self-efficacy might predict better health status and quality of life over time. Forty-five patients were enrolled between 2018 and 2019. HRQoL, health literacy, and self-efficacy were assessed using validated scales. The ability to analyze information to exert greater control over life events critically (critical health literacy) ( $\eta^2p = 0.660$ ) and the individual's confidence in dealing with challenging tasks (self-efficacy) ( $\eta^2p = 0.501$ ) strongly predicted the scores of general health status over time. Overall, the functional status improved at 3 months after surgery, and this trend paralleled the decline of cancer-specific and surgery-related symptoms. In conclusion, researchers and clinicians should pay greater attention to optimizing baseline health literacy and self-efficacy levels. Future educational and motivational interventions should be further tested and possibly integrated into the prehabilitation programs.

## Keywords

cancer, education, esophagectomy, esophageal cancer, health literacy, neo-adjuvant therapy, patient-reported outcome, prehabilitation, quality of life, self-efficacy

## Introduction

Esophageal cancer is the eighth most diagnosed type of cancer and the sixth most common cause of cancer-related mortality worldwide (1,2). About 30–40% of patients with esophageal cancer are eligible for a multimodality curative treatment, which typically includes neo-adjuvant chemotherapy or/and radiotherapy followed by esophagectomy. Overall, the multimodal approach is associated with a 10% to 15% greater survival advantage compared with a single-modality approach (3–6). This higher survival rate has led to a better appraisal of digestive symptoms and quality of life issues in the long-term survivors (7,8).

Health-related quality of life (HRQoL) is a multi-dimensional construct defined as patients' perception of the

<sup>1</sup> Health Professions Research and Development Unit, IRCCS San Donato Milanese, San Donato Milanese, Italy

<sup>2</sup> Division of General and Foregut Surgery, IRCCS Policlinico San Donato, San Donato Milanese, Italy

<sup>3</sup> Division of Surgery, ASST of Lodi, Lodi, Italy

<sup>4</sup> Department of Public Health, Experimental and Forensic Medicine, Section of Hygiene, University of Pavia, Pavia, Italy

<sup>5</sup> Department of Biomedical Sciences for Health, University of Milan, Milan, Italy

## Corresponding Author:

Arianna Magon, Health Professions Research and Development Unit, IRCCS Policlinico San Donato, Via Rodolfo Morandi, 30 | 20097 San Donato Milanese (Mi), Italy.

Email: arianna.magon@grupposandonato.it



effect of illness and treatment on their current level of physical, mental, and social functioning (9,10). Therefore, the HRQoL is the main proxy-reported outcome measure to assess the quality and effectiveness of care delivered, patients' needs, and treatment adherence (9,11). More specifically, several studies showed that HRQoL acts as a predictive factor of morbidity and mortality in curatively-treated patients with esophageal cancer; it has also become a core outcome measure to deliver comprehensive and patient-centered care and support clinical decision-making (4,11). In this regard, the European Organization for Research and Treatment of Cancer (EORTC) has developed specific measurement tools for measuring the overall perception of HRQoL and esophageal cancer-specific symptoms, which are respectively QLQ-C30 and QLQ-OES 18 (12–14).

Recent systematic reviews with meta-analyses have already described the clinical trajectories of HRQoL over time with different curative treatment strategies (15). Accordingly, neoadjuvant chemoradiotherapy followed by surgery provides better patients' HRQoL outcomes in the short-term follow-up compared to surgery alone; instead, no differences were identified between the curative treatment strategies after one year (4,15–17). In addition, other non-modifiable factors that could undermine the trajectory of HRQoL outcomes after esophagectomy, such as age, presence of comorbidities, tumor location and staging, and perioperative clinical complication (18). For this reason, beyond considering the predictive role of non-modifiable factors on HRQoL trajectories, integrating the assessment of patient-reported outcomes (PROs) in describing HRQoL is pivotal to have a precise overview of the patients' journey experiences (4,9,11,19).

Among PROs, health literacy and self-efficacy have been previously described to positively influence patients' engagement, facilitating their role as active players in the clinical pathway and symptom management and enhancing their HRQoL (20–22). Precisely, health literacy (HL) was defined as an individual's capacity to obtain, understand and function the essential information and services to best manage her/his health and engage in proper decision-making (22). Self-efficacy, defined as the individual's confidence in the ability to perform a challenging task under specific circumstances, is an important concept because it influences behaviors and outcomes (23). However, the potential role of health literacy and self-efficacy on the mid-long trajectory of HRQoL is poorly described in patients undergoing curative treatments for esophageal cancer (4,10,12,24). Therefore, describing health literacy and self-efficacy beyond a cumulative assessment of HRQoL is pivotal to precisely understanding patients' perceptions of their experience while receiving care and framing which elements might be susceptible to improvements through supportive and educational initiatives. For this reason, this study aimed to provide a longitudinal description of the trajectories of HRQoL, health literacy, and self-efficacy of esophageal cancer patients at baseline (preoperative phase) and in the postoperative period (2 weeks, and one, two, and three months after esophagectomy). As a secondary aim, this

study sought to explore whether health literacy and self-efficacy might predict better health status and quality of life over time.

## Methods

### Design

This study has an observational and longitudinal design performed in a single specialized Italian center treating esophageal cancer. The study protocol was approved by the Institutional Review Board (IRB) of the involved center.

### Sampling Procedure and Participants

Patients meeting the inclusion/exclusion criteria and treated between September 2018 and September 2019 were invited to participate in the study after receiving the information regarding the aim and methods of the study (one-year sampling strategy). The eligible patients were 51, and only 6 declined the invitation to participate due to lack of interest in the study. The inclusion criteria were age  $\geq 18$  years, a primary diagnosis of esophageal cancer, eligibility for esophagectomy, and willingness to participate in the study through the sign of informed consent form. The exclusion criteria were established in the study protocol to increase the homogeneity of the sample. Considering that the study focused on curatively-treated patients with esophageal cancer, patients in end-of-life status under palliative treatment were excluded. Given that the data collection was based on self-report measurements, patients with cognitive impairment (assessed using Six Item Screener, SIC) were also excluded. The last exclusion criterium was the presence of several comorbidities assessed using the Charlson Comorbidity Index (CCI), precisely when CCI was equal to or higher than 4, due to patients with  $CCI \geq 4$  might report more likely unfavorable health status for other morbidities than esophageal cancer. Overall, no patients were excluded from applying the exclusion criteria during the sampling procedure because no patients reported having these criteria. Patients were informed that they had the right to withdraw their consent at any time throughout the data collection period. There were no withdraws during the study; however, three patients died for complications during the postoperative period. Accordingly, 45 patients were enrolled, and 42 completed the data collection as per the study protocol.

### Data Collection and Measurements

The assessments for data collection for each time point were performed in paper form by a surgeon, and the data management process was lead by a research nurse. Data collection was guided by the esophageal cancer-specific core outcome set (COS) theoretical framework to measure HRQoL, self-efficacy, and health literacy (11). The baseline data collection

(T0) was performed before the surgical treatment during the pre-admission assessments. The postoperative data were collected two weeks after surgery (T1) and then after one (T2) and three months after the hospital discharge (T4). However, only for patients who underwent neoadjuvant chemo(radio)therapy treatment plan, the study protocol has scheduled an intermediate time point at the second month after discharge (T3) to obtain a more intense longitudinal description of HRQoL, self-efficacy, and health literacy (one data collection per month). The data collection timelines were designed to meet the follow-up visits of the enrolled patients, which were consistent with the best practice described in the literature (25).

The collected sociodemographic variables were sex (males vs. females), age (years), marital status (married vs. unmarried), educational level (primary school, high school, university), and working status (active worker, retired/unemployed). The collected clinical variables from the medical records were histological type (adenocarcinoma, squamous cell carcinoma, melanoma, other), anamnestic risk factors for esophageal cancer (i.e., alcohol and smoking habits, gastroesophageal reflux disease, Barrett's esophagus, obesity, achalasia, and history of certain other cancers, were categorized in "yes" vs. "no"), CCI (score categorized in no comorbidity, mild comorbidities that means one additional comorbidity, severe comorbidity that means two or three additional comorbidities as more than three were excluded), body mass index (BMI, kg/m<sup>2</sup>), surgical approach (transhiatal esophagectomy, transthoracic esophagectomy, minimally-invasive esophagectomy, and McKeown esophagectomy), length of hospital stay (days), complications (yes vs. no), chemotherapy (yes "neoadjuvant before surgery" vs. no), and radiotherapy (yes "neoadjuvant before surgery" vs. no).

The tools used to assess HRQoL were the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life questionnaire (EORTC QLQ-C30), the EORTC Quality of Life Questionnaire - Oesophageal Cancer Module (EORTC QLQ-OES18). The General Self-Efficacy Scale (GSE) and Health Literacy Questionnaire (HLQ) were respectively employed to assess general self-efficacy and health literacy (26,27). EORTC QLQ-C30 and EORTC QLQ-OES18 showed good evidence of validity and reliability, and both were available in Italian (13,14).

Precisely, EORTC QLQ-C30 aimed to measure the general quality of life (i.e., physical functioning, psychic/emotional, and social status) in patients undergoing any surgical cancer treatment (28,29). EORTC QLQ-C30 comprised both multi-item scales (i.e., five functional scales; three-symptom scale; a global health status/QoL) and single-item measures (six single items), using 4-point Likert and 7-point Likert scales. Finally, the raw score of each item and multi-item scales have to be standardized in a score ranging from 0–100 where the higher score for a functional scale or global QoL represented a healthier level of

functioning, whereas a high score for each symptom scale represents a high level of symptomatology or problems (30). EORTC QLQ-C30 also enables estimating health metrics, such as quality-adjusted life year, allowing researchers to compare health statuses between different conditions by using utility weights where the value one indicates an optimal health status, zero represents being dead and negative values represent health statuses perceived as worse than dead (31). A movement to worse levels of each problem for each EORTC QLQ-C30 dimension is generally associated with increasing utility decrements. The literature among patients with cancer presented the worst possible health status equal to  $-0.083$  (31).

On the other hand, EORTC QLQ-OES18 aimed to describe the symptoms and emotional problems referred to having oesophageal cancer in patients who underwent any treatment (13). EORTC QLQ-OES18 comprised 18 items using 4-point Likert scales divided in four subscales: eating (item 6 to 9); reflux (item 14,15); pain (item 16 to 18) and dysphagia (item 1 to 3) and six single items for other symptoms (item 4,5,10,11,12,13). The four subscales and the six single items have to be computed into symptoms and standardized functional scores ranging from 0 to 100 where a higher score for a functional scale represented a better level of functioning, whereas a high score for the symptoms represented a high score level of symptomatology.

GSE and HLQ were used in their validated Italian versions. GSE measured the confidence level of an individual to perform challenging tasks (self-efficacy) using ten items with a 4-point Likert measure, and the self-efficacy score was previously described as a predictor of achieving success in challenging processes (32). HLQ measured health literacy using 44 items divided into nine distinct subscales that theoretically match functional, communicative, and critical health literacy. Functional health literacy is given by sufficient basic skills in reading and writing to function effectively in everyday situations. Communicative health literacy is defined as more advanced cognitive and literacy skills, which, together with social skills, might actively participate in everyday activities, retrieving information and deriving meaning from several forms of communication. Critical health literacy is the more advanced cognitive skill, which, together with social skills, might be adopted to analyze information to exert greater control over critical life events. HLQ has 23 items with a 4-point Likert measure and 21 items with a 5-point Likert measure.

### Statistical Analysis

Descriptive statistics were performed for the collected variables before performing the scoring computations for each scale to identify possible errors, outliers, or missing data, including assessing skewness and kurtosis indices for the continuous variables for determining the shape of the distribution. Missing data were handled using a pairwise deletion

function. After computing scores for T0, T1, T2, T3, and T4, their means and standard deviations (SDs) were calculated for synthesizing the sample statistics of normally distributed variables and median with interquartile range (IQR) for non-normally distributed data.

The repeated measures ANOVA (within-subjects ANOVA) was used to test whether there were any differences between related population means for each self-report assessment (HRQoL, symptoms, self-efficacy, and health literacy); post hoc tests using the Bonferroni correction were employed to assess the comparisons between the 5 data collection time points. The  $F$ -statistic and the effect size using the partial eta-squared ( $\eta^2p$ ) were used to evaluate the models. The Greenhouse–Geisser correction was employed in case of

lack of sphericity to avoid overestimating the degrees of freedom and inflating the  $F$ -statistics.

Furthermore, the baseline measurements of health literacy and self-efficacy were included as predictors in a multivariate analysis of variance (MANOVA), considering the measurements of the general health status in T1, T2, T3, and T4 as the dependent variables for answering to the secondary aim of the study. Levene's test of equality of variance was used to examine the homogeneity of variance; in case of lack of homogeneity of variance, Pillai's trace has been employed as a more robust approach. The Box's M test was employed as a multivariate test of homogeneity of variance. Finally, the  $\eta^2p$  was used to report the effect size indicating how much variance was explained by the independent variables. All inferential tests employed two-tailed null hypotheses with  $\alpha = 0.05$  and were performed in IBM SPSS Statistics for Windows, Version 22.0 (IBM SPSS, Armonk, NY: IBM Corp.).

**Table 1.** Baseline Characteristics of the Enrolled Patients ( $n = 45$ ).

|                                   |   | N                            | %     |
|-----------------------------------|---|------------------------------|-------|
| Sex                               | Males   | 33                           | 73.3  |
|                                   | Females   | 12                           | 26.7  |
| Marital status                    | Married   | 15                           | 68.2  |
|                                   | Unmarried   | 7                            | 31.8  |
| Educational level                 | Primary school                                      | 4                            | 21.1  |
|                                   | High school   | 12                           | 63.2  |
|                                   | University  | 3                            | 15.8  |
| Working status                    | Active worker                                       | 7                            | 35    |
|                                   | Retired/unemployed                                  | 13                           | 65    |
| Age                               | Years (mean; SD)                                    | 63.02                        | 10.46 |
| Histological type                 | Adenocarcinoma                                      | 31                           | 68.9  |
|                                   | Squamous cell carcinoma                             | 13                           | 28.9  |
|                                   | Melanoma  | 1                            | 2.2   |
| Esophageal Cancer Risk Factors    | Yes   | 36                           | 87.8  |
|                                   | No  | 8                            | 17.4  |
| Comorbidities                     | Moderate Comorbidities                              | 22                           | 47.8  |
|                                   | Severe Comorbidities<br>(more than 3 comorbidities) | 7                            | 15.2  |
|                                   | BMI   | Kg/m <sup>2</sup> (mean; SD) | 25.5  |
| Neo-adjuvant chemo(radio) therapy | Yes   | 28                           | 62.2  |
|                                   | Surgical approach                                   |                              |       |
|                                   | Transhiatal esophagectomy                           | 3                            | 6.7   |
|                                   | Transthoracic esophagectomy                         | 35                           | 77.8  |
|                                   | Minimally-invasive esophagectomy                    | 6                            | 13.3  |
|                                   | McKeown esophagectomy                               | 1                            | 2.2   |

Legend: SD = standard deviation.

## Results

The baseline characteristics of the participants are shown in Table 1. They were mainly males ( $n = 33$ , 73.3%), married ( $n = 15$ , 68.2%), with a high school diploma ( $n = 12$ , 63.2%), retired ( $n = 13$ , 65%), having a mean age of 63.02 years (SD = 10.46). The most frequent histological type was adenocarcinoma ( $n = 31$ , 68.9%), and the majority of patients had at least one esophageal cancer risk factor ( $n = 36$ , 87.8%) and between one to three comorbidities ( $n = 22$ ; 47.8%). The mean BMI was 25.5 Kg/m<sup>2</sup> (SD = 2.96). The most frequent surgical approach was transthoracic esophagectomy ( $n = 35$ , 77.8%), and the median length of hospital stay was 11 days (IQR = 7–15 days). Twenty-eight patients (62.2%) received neoadjuvant chemotherapy before surgery.

Table 2 shows the longitudinal trajectory of HRQoL, symptoms, health literacy, and self-efficacy. Domains with significant changes over time are depicted in Figure 1.

### Functional Dimensions of HRQoL

The computed constructs of the EORTC QLQ-C30 regarding the functional profile of patients (physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning, and general health status/QoL) showed significant differences in their scores over time.

Physical functioning showed a large proportion of variance accounted for by changes over time ( $F_{(4,60)} = 20.583$ ,  $P < .001$ ,  $\eta^2p = .578$ ), where the lowest mean scores were recorded two weeks after surgery ( $\text{mean}_{(T1)} = 60 \pm 18.70$ ) and the scores after three months from hospital discharge ( $\text{mean}_{(T4)} = 93.13 \pm 7.55$ ) were significantly higher than the baseline scores ( $\text{mean}_{(T0)} = 88.3 \pm 14.29$ ). Likely, role functioning showed a large proportion of variance accounted for by changes over time ( $F_{(4,60)} = 13.48$ ,  $P < .001$ ,  $\eta^2p = .473$ ), reporting a significant improvement after three

**Table 2.** Longitudinal trajectory of HRQoL, symptoms, health literacy, and self-efficacy.

|                                  | T0    |       | T1    |       | T2    |       | T3    |       | T4    |       | $\eta^2p$ | <b>P</b>    |
|----------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-----------|-------------|
|                                  | Mean  | SD    | Mean  | SD    | Mean  | SD    | Mean  | SD    | Mean  | SD    |           |             |
| Physical functioning (PF2)       | 88.33 | 14.29 | 60.00 | 18.70 | 79.17 | 16.12 | 89.58 | 10.02 | 93.13 | 7.55  | .578      | <b>.001</b> |
| Role functioning (RF2)*          | 77.91 | 32.67 | 42.42 | 33.61 | 68.99 | 27.84 | 79.63 | 26.52 | 85.23 | 20.72 | .473      | <b>.001</b> |
| Emotional functioning (EF)       | 67.19 | 25.72 | 75.52 | 27.46 | 83.33 | 21.00 | 85.94 | 21.88 | 88.02 | 19.47 | .509      | <b>.001</b> |
| Cognitive functioning (CF)*      | 88.54 | 14.55 | 87.50 | 16.66 | 91.67 | 14.90 | 97.92 | 5.69  | 98.96 | 4.16  | .247      | <b>.009</b> |
| Social functioning (SF)          | 79.17 | 29.50 | 67.71 | 26.85 | 78.13 | 25.61 | 87.50 | 19.72 | 82.29 | 23.14 | .195      | <b>.010</b> |
| General health status/QoL (GHS)* | 60.42 | 17.87 | 52.08 | 15.95 | 65.63 | 14.23 | 69.79 | 16.35 | 72.92 | 13.43 | .317      | <b>.002</b> |
| Fatigue (FA)*                    | 27.78 | 27.51 | 50.00 | 25.33 | 29.17 | 22.54 | 22.92 | 23.11 | 15.97 | 19.01 | .379      | <b>.001</b> |
| Nausea vomiting (NV)*            | 10.42 | 17.07 | 20.83 | 23.96 | 10.42 | 20.06 | 9.38  | 20.15 | 8.33  | 21.08 | .122      | .138        |
| Pain (PA)                        | 6.25  | 11.98 | 38.54 | 19.92 | 17.71 | 17.01 | 13.54 | 16.35 | 6.25  | 10.31 | .538      | <b>.001</b> |
| Dyspnea (DY)                     | 4.17  | 11.38 | 33.33 | 24.34 | 14.58 | 20.97 | 14.58 | 17.07 | 8.33  | 14.90 | .345      | <b>.001</b> |
| Insomnia (SL)                    | 16.67 | 24.34 | 50.00 | 29.81 | 25.00 | 31.03 | 12.50 | 23.96 | 10.42 | 20.06 | .408      | <b>.001</b> |
| Appetite loss (AP)               | 17.78 | 27.79 | 37.78 | 27.79 | 22.22 | 29.99 | 17.78 | 17.21 | 11.11 | 20.57 | .211      | <b>.009</b> |
| Constipation (CO)*               | 8.33  | 14.91 | 16.67 | 21.08 | 10.42 | 20.06 | 6.25  | 13.43 | 0.00  | 0.00  | .156      | .066        |
| Diarrhea (DI)*                   | 8.33  | 22.77 | 25.00 | 19.24 | 12.50 | 20.63 | 10.42 | 20.06 | 6.25  | 18.13 | .153      | .082        |
| Financial difficulties (FI)*     | 6.25  | 13.43 | 14.58 | 17.07 | 14.58 | 17.07 | 14.58 | 20.97 | 10.42 | 20.06 | .067      | .364        |
| Eating (EAT)*                    | 20.54 | 21.92 | 29.47 | 19.19 | 22.56 | 16.05 | 17.13 | 17.26 | 14.57 | 12.15 | .113      | .142        |
| Reflux (RFX)*                    | 8.71  | 16.62 | 19.95 | 17.79 | 12.30 | 15.64 | 11.11 | 15.12 | 10.00 | 15.24 | .063      | .359        |
| Pain (PA)*                       | 10.10 | 18.99 | 11.38 | 14.20 | 8.47  | 10.64 | 5.56  | 10.26 | 3.95  | 7.54  | .151      | .065        |
| Dysphagia (DYS)*                 | 57.83 | 29.30 | 33.85 | 21.68 | 52.12 | 18.11 | 69.75 | 16.52 | 68.40 | 24.15 | .412      | <b>.001</b> |
| Swallowing saliva (SV)           | 15.91 | 26.40 | 17.83 | 22.24 | 4.76  | 15.74 | 9.26  | 15.36 | 4.44  | 15.24 | .099      | .149        |
| Choked swallowing (CH)           | 6.82  | 18.44 | 0.79  | 5.14  | 1.59  | 7.18  | 5.56  | 17.15 | 0.00  | 0.00  | .084      | .248        |
| Dry mouth (DM)*                  | 14.39 | 26.31 | 23.26 | 30.45 | 12.70 | 29.40 | 1.85  | 7.85  | 5.93  | 16.34 | .198      | <b>.020</b> |
| Taste (TA)*                      | 10.08 | 21.25 | 18.70 | 23.62 | 13.82 | 22.33 | 14.81 | 4.26  | 12.59 | 21.66 | .174      | <b>.038</b> |
| Coughing (CO)*                   | 8.33  | 17.79 | 22.48 | 23.81 | 15.87 | 23.55 | 7.41  | 10.77 | 5.93  | 14.71 | .273      | <b>.002</b> |
| Talking (SP)*                    | 9.09  | 18.13 | 10.85 | 18.85 | 7.94  | 20.57 | 3.70  | 23.55 | 6.06  | 14.86 | .060      | .398        |
| Critical Health Literacy*        | 2.99  | 0.39  | 3.03  | 0.435 | 3.005 | 0.47  | 3.08  | 0.393 | 3.1   | 0.397 | .156      | .103        |
| Communicative Health Literacy *  | 3.27  | 0.463 | 3.3   | 0.486 | 3.29  | 0.535 | 3.38  | 0.534 | 3.42  | 0.472 | .080      | .309        |
| Functional Health Literacy *     | 3.31  | 0.546 | 3.32  | 0.556 | 3.36  | 0.548 | 3.46  | 0.582 | 3.48  | 0.513 | .066      | .394        |
| General Self-Efficacy*           | 65.97 | 15.28 | 65.06 | 20.35 | 64.77 | 20.62 | 67.64 | 23.55 | 69.56 | 17.99 | .057      | .386        |

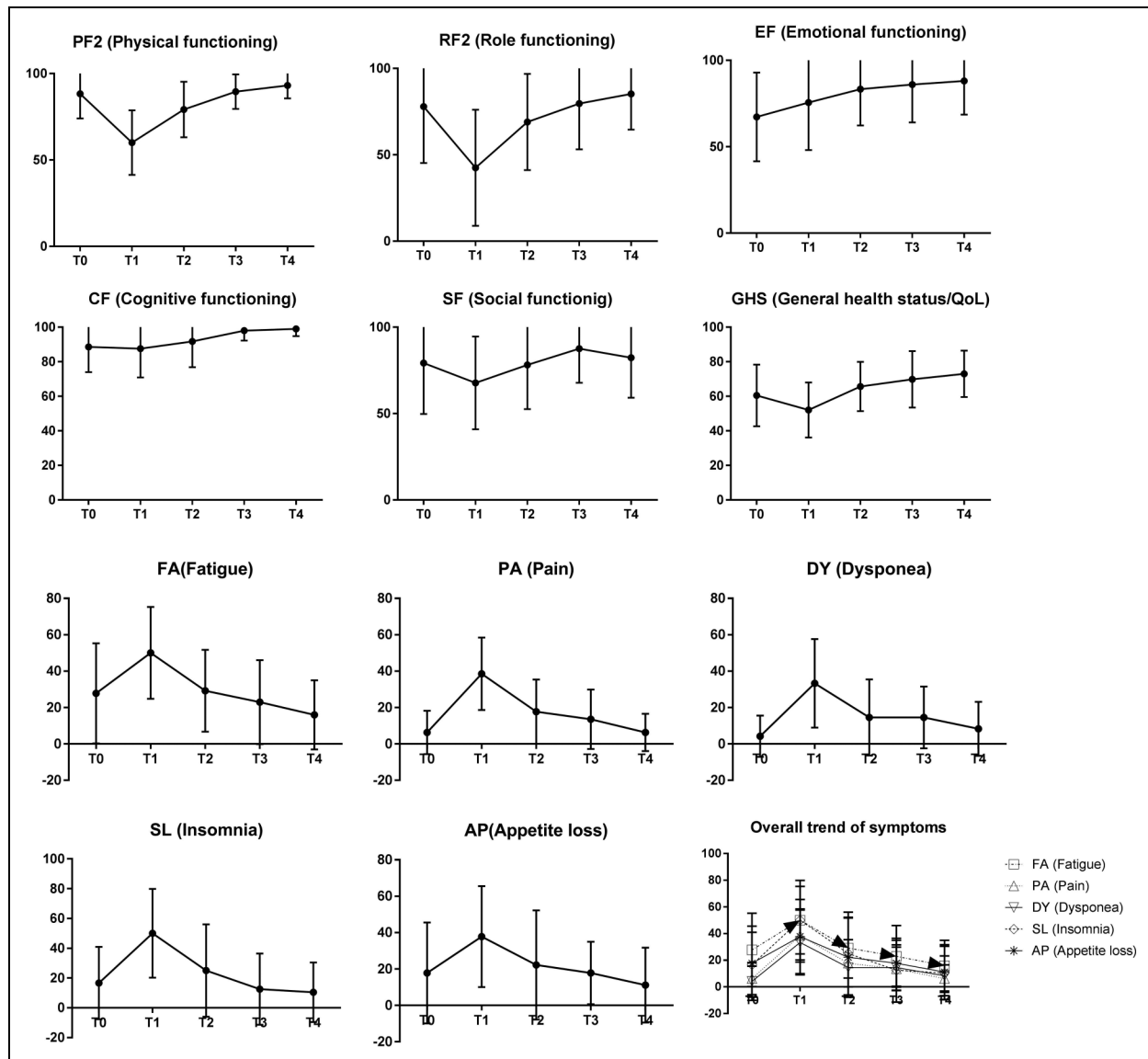
Note: \*Greenhouse-Geisser correction for lacking sphericity. P values in bold indicate significant changes of the measured variables over time.

months from hospital discharge ( $\text{mean}_{(T4)} = 85.23 \pm 20.72$ ) compared with scores of baseline ( $\text{mean}_{(T0)} = 77.91 \pm 32.67$ ). Emotional functioning showed a large proportion of variance accounted for by changes over time as well ( $F_{(4,60)} = 15.52$ ,  $P < .001$ ,  $\eta^2p = .509$ ). The scores of emotional functioning reported the larger mean difference from baseline assessment ( $\text{mean}_{(T0)} = 67.19 \pm 25.72$ ) and after three months from hospital discharge ( $\text{mean}_{(T4)} = 88.02 \pm 20.72$ ). Cognitive functioning showed a moderate proportion of variance accounted for by changes over time ( $F_{(2,4,36.5)} = 4.9$ ,  $P = .009$ ,  $\eta^2p = .247$ ). Cognitive functioning was roughly stable over time with only a slight decline in the mean scores collected two weeks after surgery ( $\text{mean}_{(T1)} = 87.50 \pm 16.66$ ) compared with the mean scores collected one month ( $\text{mean}_{(T2)} = 91.67 \pm 14.90$ ), two months (scores collected only in patients underwent neoadjuvant chemotherapy:  $\text{mean}_{(T3)} = 97.92 \pm 5.69$ ), and three months after hospital discharge ( $\text{mean}_{(T4)} = 98.96 \pm 4.16$ ). Social functioning showed a small proportion of variance accounted for by changes over time ( $F_{(4,60)} = 3.63$ ,  $P = .010$ ,  $\eta^2p = .195$ ). The scores of social functioning reported a slightly

significant improvement after three months from hospital discharge ( $\text{mean}_{(T4)} = 82.29 \pm 23.14$ ) compared to the mean scores collected two weeks after surgery ( $\text{mean}_{(T0)} = 67.71 \pm 26.85$ ) and the Bonferroni post hoc test ( $p = .058$ ) highlighted that the scores of obtained at T4 did not differ from scores collected at baseline (T0). Finally, the general health status/QoL showed a moderate proportion of variance accounted for by changes over time ( $F_{(2,5-36.8)} = 6.948$ ,  $P = .002$ ,  $\eta^2p = .317$ ), where a significant improvement after three months from hospital discharge ( $\text{mean}_{(T4)} = 72.92 \pm 13.43$ ) emerged in comparison with the baseline scores ( $\text{mean}_{(T0)} = 60.42 \pm 17.87$ ).

### Symptoms

The computed constructs of the EORTC QLQ-C30 regarding the general symptoms of patients with a significant effect size in their changes over time were fatigue, pain, dyspnea, insomnia, and appetite loss (Table 2). Constipation, diarrhea, and financial difficulties were roughly stable over time.



**Figure 1.** Longitudinal trajectories of domains with a significant score change over time (functional status, global Health, and symptoms).

Fatigue showed a moderate proportion of variance accounted for by changes over time ( $F_{(2.4,36.3)}=9.152$ ,  $P < .001$ ,  $\eta^2p = .379$ ), where the scores after three months from hospital discharge ( $\text{mean}_{(T4)} = 15.97 \pm 19.01$ ) were significantly lower than the baseline scores ( $\text{mean}_{(T0)} = 27.78 \pm 27.51$ ). Conversely, pain showed a large proportion of variance accounted for by changes over time ( $F_{(4,6)}=17.470$ ,  $P < .001$ ,  $\eta^2p = .538$ ), where its baseline scores were low at the baseline ( $\text{mean}_{(T0)} = 6.25 \pm 11.98$ ), with higher scores two weeks after surgery ( $\text{mean}_{(T1)} = 38.54 \pm 19.92$ ), and a progressive resolution which was reported to be fully obtained at three months after hospital discharge ( $\text{mean}_{(T4)} = 6.25 \pm 10.31$ ). Dyspnea reported a moderate proportion of variance accounted for by changes over time ( $F_{(4,6)}=7.89$ ,  $P < .001$ ,  $\eta^2p = .345$ ), where the scores after three months from hospital discharge ( $\text{mean}_{(T4)} = 8.33 \pm 14.40$ )

were significantly lower than the scores collected two weeks after surgery ( $\text{mean}_{(T1)} = 33.33 \pm 24.34$ ). Regarding insomnia, which showed a moderate proportion of variance accounted for by changes over time ( $F_{(4,6)}=10.32$ ,  $P < .001$ ,  $\eta^2p = .408$ ), the mean score after three months from hospital discharge ( $\text{mean}_{(T4)} = 10.42 \pm 20.06$ ) was significantly lower than the baseline mean score ( $\text{mean}_{(T0)} = 16.67 \pm 24.34$ ). Likely, appetite loss, which showed a small proportion of variance accounted for by changes over time ( $F_{(4,56)}=3.75$ ,  $P = .009$ ,  $\eta^2p = .211$ ), showed an improvement three months from hospital discharge ( $\text{mean}_{(T4)} = 11.11 \pm 20.57$ ) compared with scores collected two weeks after surgery ( $\text{mean}_{(T1)} = 37.78 \pm 27.79$ ).

The computed constructs of the EORTC QLQ-OES18 regarding the esophageal cancer-specific symptoms of patients with a significant effect size in their changes over

time were dysphagia, dry mouth, taste, and coughing. Eating, reflux, swallowing saliva, choked swallowing, and talking were roughly stable over time. Dysphagia showed a moderate proportion of variance accounted for by changes over time ( $F_{(2,28,36,64)} = 11.22$ ,  $P < .001$ ,  $\eta^2 p = .412$ ), where the scores after three months from hospital discharge ( $\text{mean}_{(T4)} = 68.40 \pm 24.15$ ) showed a higher adequate functionality than scores collected at baseline ( $\text{mean}_{(T0)} = 57.83 \pm 29.30$ ). Dry month showed a small proportion of variance accounted for by changes over time ( $F_{(2,45,39,24)} = 3.95$ ,  $P = .020$ ,  $\eta^2 p = .198$ ), where scores highlighted an improvement three months from hospital discharge ( $\text{mean}_{(T4)} = 5.93 \pm 20.57$ ) compared with scores collected at baseline ( $\text{mean}_{(T0)} = 14.39 \pm 26.31$ ). Likely, taste showed a small proportion of variance accounted for by changes over time ( $F_{(2,36,37,79)} = 3.371$ ,  $P = .038$ ,  $\eta^2 p = .174$ ), where scores reported an improvement after three months from hospital discharge ( $\text{mean}_{(T4)} = 12.59 \pm 21.66$ ) compared with scores collected two weeks after surgery ( $\text{mean}_{(T1)} = 18.70 \pm 23.62$ ). Coughing showed a moderate proportion of variance accounted for by changes over time ( $F_{(2,66,42,60)} = 6.017$ ,  $P = .002$ ,  $\eta^2 p = .273$ ), with scores indicating an exacerbation two weeks after surgery ( $\text{mean}_{(T1)} = 22.48 \pm 23.81$ ), an improvement starting from one month after hospital discharge ( $\text{mean}_{(T2)} = 15.87 \pm 23.55$ ), and a roughly complete resolution at scores collected three months after hospital discharge ( $\text{mean}_{(T4)} = 5.93 \pm 14.71$ ).

### Health Literacy, Self-Efficacy, and Their Relationship with General Health Status/QoL

The scores of critical health literacy ( $F_{(1,7,23,96)} = 2.581$ ,  $P = .103$ ,  $\eta^2 p = .156$ ), communicative health literacy ( $F_{(1,9,26,7)} = 1.220$ ,  $P = .309$ ,  $\eta^2 p = .066$ ), functional health literacy ( $F_{(2,4,33,84)} = 0.994$ ,  $P = .394$ ,  $\eta^2 p = .066$ ), and general self-efficacy ( $F_{(1,9,30,2)} = 0.970$ ,  $P = .386$ ,  $\eta^2 p = .057$ ) were roughly stable over time as no proportion of variance was accounted for by changes over time.

Considering the baseline scores of critical health literacy, communicative health literacy, functional health literacy, and general self-efficacy as independent variables and general health status/QoL scores in T1, T2, T3, and T4 as dependent variables (MANOVA), two significant predictors were detected. The critical health literacy ( $L = 0.34$ ,  $F_{(5,10)} = 3.87$ ,  $P = .033$ ,  $\eta^2 p = 0.660$ ) and the general self-efficacy ( $L = 0.31$ ,  $F_{(5,10)} = 3.67$ ,  $P = .035$ ,  $\eta^2 p = 0.501$ ) showed a large effect size in predicting the scores of general health status/QoL over time.

## Discussion

The present study provides new insights to assess HRQoL in curatively-treated esophageal cancer patients (15) by investigating health literacy and self-efficacy. A recent meta-analysis indicated that the levels of HRQoL achieved by

patients with esophageal cancer within three months from surgery tend to be stable also in long-term assessments (10,15,17,33). This evidence suggests that understanding which elements in the early assessment of patient needs might influence HRQoL over the first three months after surgery is particularly important to achieve long-term and stable positive outcomes regarding patient experiences and HRQoL (15,34).

The present study identified the baseline (preoperative) scores of critical health literacy and general self-efficacy as strong and positive predictors of the general health status/QoL over time. Considering that critical health literacy and general self-efficacy might be susceptible to improvements through educational and supportive initiatives for empowering patients and optimizing their confidence to deal with challenging situations (22), these results imply that focused educational, motivational, and supportive strategies in the preoperative period might be critical for achieving positive, short-, and long-term outcomes. In other words, these results enrich the framework of the prehabilitation programs for patients with esophageal cancer undergoing esophagectomy (35). Prehabilitation programs encompass multiple assessments and interventions, such as physical exercise, nutritional and psychological interventions, delivered through care pathways and bundle-based interventions across community care and hospital-based settings (36); however, the current bundle-based programs for delivering prehabilitation lack in identifying specific modifiable patient characteristics to guide the delivery of motivational interviewing and education (37,38). For this reason, focused interventions on increasing the levels of critical health literacy and self-efficacy bundle-based prehabilitation programs for patients undergoing esophagectomy might be strategic.

Another relevant result of this study was the longitudinal trends that emerged from the subscales highlighting functional capacity. The general trend, which was less marked for cognitive functioning, showed that after a functional decline in the immediate postoperative period (two weeks after surgery), recovery was achieved between one and two months after hospital discharge. Furthermore, the scores achieved at three months showed improvements compared to the baseline functional status of physical, role, emotional, cognitive functioning, and the general health status/QoL beyond the recovery. These results confirm and enrich with Italian-specific the findings of recent international studies (15,39,40).

Fatigue, insomnia, appetite loss, dysphagia, and dry mouth much improved at three months from hospital discharge. Other symptoms, such as pain, dyspnea, taste, and coughing, which were generally moderately relevant in the early postoperative period (two weeks after surgery), progressively deteriorated within three months from hospital discharge. These trends are consistent with previous studies (15,41).

### Limitations and Strengths

The results of this study have to be contextualized by considering several limitations. First, the single-center study design

limits a broad generalization of the results. However, the sampling approach considered the one-year, real-world experience of a specialized Italian center treating esophageal cancer. For this reason, the reported results are less subject to context-specific variations than extensive aggregate observational studies, which require specific endeavors to control confounders. Second, the limited sample size might have influenced two aspects: the study was not powered to examine survival or clinical outcomes, and subanalysis considering different treatments (e.g., “surgery alone” vs. “surgery plus neoadjuvant chemo(radio)therapy”), different surgical approaches (e.g., minimally invasive vs. open), and different clinical conditions (e.g., considering characteristics, such as BMI, nutritional status, age, sex, and comorbidities). For this reason, future larger studies and powered on specific outcomes are required to provide in-depth information on the relationships between health literacy, self-efficacy, and HRQoL in curatively treated patients with esophageal cancer.

## Conclusions

This study provided a short-term longitudinal trajectory of HRQoL, health literacy, and self-efficacy of cancer patients undergoing esophagectomy. HRQoL and PROs, such as health literacy, and self-efficacy, are generally underreported in curatively-treated patients with esophageal cancer. This study highlighted that baseline levels of health literacy and self-efficacy influence the overall trajectory of the general health status/QoL over three months. Furthermore, the functional patient status generally improved at three months from surgery, which was also the period where the majority of cancer-specific and surgery-related symptoms were declining. Given these results, clinicians and researchers need to identify strategies to optimize health literacy and self-efficacy before surgery and within the context of prehabilitation programs. Future outcome-powered studies and robust randomized controlled trials to test possible strategies, such as motivational interviewing and technology-based interventions crossing community and hospital-based services, are required to provide evidence-grounded prehabilitation pathways and bundles.

## Ethical Approval

This study was approved by the Ethical Committee of Ospedale San Raffaele, Italy (protocol *n.* 136/int/2018).

## Statement of Human and Animal Rights

All procedures performed in the study were following the ethical standards, Good Clinical Practice guidelines, and the 1964 Helsinki declaration and its later amendments.

## Statement of Informed Consent

Written informed consent was obtained from all patients before being included in the study.


## Declaration of Conflicting Interests


The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

## ORCID iDs

Arianna Magon  <https://orcid.org/0000-0003-0440-6940>

Rosario Caruso  <https://orcid.org/0000-0002-7736-6209>

## References

1. Malhotra GK, Yanala U, Ravipati A, Follet M, Vijayakumar M, Are C. Global trends in esophageal cancer. *J Surg Oncol.* 2017;115:564-79.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71:209-49.
3. Wildiers H, Mauer M, Pallis A, Hurria A, Mohile SG, Luciani A, et al. End points and trial design in geriatric oncology research: a joint European Organisation for research and treatment of cancer-alliance for clinical trials in oncology-international society of geriatric oncology position article. *J Clin Oncol.* 2013;31:3711-8.
4. Alghamedi A, Buduhan G, Tan L, Srinathan SK, Sulman J, Darling G, et al. Quality of life assessment in esophagectomy patients. *Ann Transl Med.* 2018;6:84-84.
5. Borggreve AS, Kingma BF, Domrachev SA, Koshkin MA, Ruurda JP, Hillegersberg R van, et al. Surgical treatment of esophageal cancer in the era of multimodality management. *Ann N Y Acad Sci.* 2018;1434:192-209.
6. Bernardi D, Asti E, Aiolfi A, Bonitta G, Luporini A, Bonavina L. Outcome of trimodal therapy in elderly patients with esophageal cancer: prognostic value of the Charlson Comorbidity Index. *Anticancer Res.* 2018;38:1815-20.
7. Boshier P, Klevebro F, Savva K, Waller A, Hage L, Hanna G, et al. Assessment of health related quality of life and digestive symptoms in long-term, disease free survivors after esophagectomy. *Ann Surg.* Epub ahead of print 14 February 2020. DOI: 10.1097/SLA.0000000000003829.
8. Griffin SM, Jones R, Kamarajah SK, Navidi M, Wahed S, Immanuel A, et al. Evolution of esophagectomy for cancer over 30 years: changes in presentation, management and outcomes. *Ann Surg Oncol.* 2021;28:3022.
9. Cella DF, Tulsky DS. Quality of life in cancer: definition, purpose, and method of measurement. *Cancer Invest.* 1993;11:327-36.
10. Darling GE. Quality of life in patients with esophageal cancer. *Thorac Surg Clin.* 2013;23:569-75.
11. Avery KNL, Chalmers KA, Brookes ST, Blencowe NS, Coulman K, Whale K, et al. Development of a core outcome set for clinical effectiveness trials in esophageal cancer resection surgery. *Ann Surg.* 2018;267:700-10.



12. Rosenbloom S, Victorson D, Hahn E, Peterman A, Cella D. Assessment is not enough: a randomized controlled trial of the effects of HRQL assessment on quality of life and satisfaction in oncology clinical practice. *Psychooncology*. 2007;16:1069-79.
13. Blazeby J, Conroy T, Hammerlid E, Fayers P, Sezer O, Koller M, et al. Clinical and psychometric validation of an EORTC questionnaire module, the EORTC QLQ-OES18, to assess quality of life in patients with oesophageal cancer. *Eur J Cancer*. 2003;39:1384-94.
14. Aaronson N, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez N, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85:365-76.
15. van den Boorn HG, Stroes CI, Zwinderman AH, Eshuis WJ, Hulshof MCCM, van Etten-Jamaludin FS, et al. Health-related quality of life in curatively-treated patients with esophageal or gastric cancer: a systematic review and meta-analysis. *Crit Rev Oncol Hematol*. 2020;154:103069.
16. Soriano TT, Eslick GD, Vanniasinkam T. Long-term nutritional outcome and health related quality of life of patients following esophageal cancer surgery: a meta-analysis. *Nutr Cancer*. 2018;70:192-203.
17. Schandl A, Johar A, Anandavadivelan P, Vikström K, Mälberg K, Lagergren P. Patient-reported outcomes 1 year after oesophageal cancer surgery. *Acta Oncol (Madr)*. 2020;59:613-9.
18. Chang Y, Tsai Y, Chao Y, Wu M. Quality-of-life measures as predictors of post-esophagectomy survival of patients with esophageal cancer. *Qual Life Res*. 2016;25:465-75.
19. Moons P, Budts W, De Geest S. Critique on the conceptualisation of quality of life: a review and evaluation of different conceptual approaches. *Int J Nurs Stud*. 2006;43:891-901.
20. Miller TA. Health literacy and adherence to medical treatment in chronic and acute illness: a meta-analysis. *Patient Educ Couns*. 2016;99:1079-86.
21. Peters M, Potter CM, Kelly L, Fitzpatrick R. Self-efficacy and health-related quality of life: a cross-sectional study of primary care patients with multi-morbidity. *Heal Qual Life Outcomes*. 2019;17:1-11.
22. Caruso R, Magon A, Baroni I, Dellafiore F, Arrigoni C, Pittella F, et al. Health literacy in type 2 diabetes patients: a systematic review of systematic reviews. *Acta Diabetol*. 2018;55:1-12.
23. Dellafiore F, Pittella F, Arrigoni C, Baroni I, Conte G, Pasquale CD, et al. A multi-phase study for the development of a self-efficacy measuring scale for ostomy care nursing management. *J Adv Nurs*. 2020;76:409-19.
24. Deshpande P, Sudeepthi BL, Rajan S, Abdul Nazir C. Patient-reported outcomes: a new era in clinical research. *Perspect Clin Res*. 2011;2:137.
25. Lordick F, Mariette C, Haustermans K, Obermannová R, Arnold D, on behalf of the ESMO Guidelines Committee. Clinical guidelines@esmo.org. Oesophageal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2016;27:v50-7.
26. Osborne R, Batterham R, Elsworth G, Hawkins M, Buchbinder R. The grounded psychometric development and initial validation of the Health Literacy Questionnaire (HLQ). *BMC Public Health*. 2013;13:658.
27. Luszczynska A, Scholz U, Schwarzer R. The general self-efficacy scale: multicultural validation studies. *J Psychol*. 2010;139:439-57. <https://doi.org/10.3200/JRLP1395439-457>
28. Weldring T, Smith S. Patient-reported outcomes (PROs) and patient-reported outcome measures (PROMs). *Heal Serv Insights*. 2013;6:6-61.
29. Macefield RC, Jacobs M, Korfage IJ, Nicklin J, Whistance RN, Brookes ST, et al. Developing core outcomes sets: methods for identifying and including patient-reported outcomes (PROs). *Trials*. 2014;15:1-12.
30. Fayer P, Aaronson N, Bjordal K, Groenvold M, Curran D, Bottomley A. EORTC QLQ-C30 Scoring Manual. 3rd ed. Brussels: European Organisation for Research and Treatment of Cancer, <https://abdn.pure.elsevier.com/en/publications/eorte-qlq-c30-scoring-manual-3rd-edition> (2001, accessed 21 July 2021).
31. Norman R, Mercieca-Bebber R, Rowen D, Brazier JE, Cella D, Pickard AS, et al. U.K. utility weights for the EORTC QLU-C10D. *Health Econ*. 2019;28:1385-401.
32. Panadero E, Jonsson A, Botella J. Effects of self-assessment on self-regulated learning and self-efficacy: four meta-analyses. *Educ Res Rev*. 2017;22:74-98.
33. Scarpa M, Valente S, Alfieri R, Cagol M, Diamantis G, Ancona E, et al. Systematic review of health-related quality of life after esophagectomy for esophageal cancer. *World J Gastroenterol*. 2011;17:4660-74.
34. Senkal M, Bonavina L, Reith B, Caruso R, Matern U, Duran M. Perioperative peripheral parenteral nutrition to support major gastrointestinal surgery: expert opinion on treating the right patients at the right time. *Clin Nutr ESPEN*. 2021;43:16-24.
35. Akiyama Y, Sasaki A, Fujii Y, Fujisawa R, Sasaki N, Nikai H, et al. Efficacy of enhanced prehabilitation for patients with esophageal cancer undergoing esophagectomy. *Esophagus*. 2020;18:56-64.
36. Minnella EM, Awasthi R, Loiselle S-E, Agnihotram RV, Ferri LE, Carli F. Effect of exercise and nutrition prehabilitation on functional capacity in esophagogastric cancer surgery: a randomized clinical trial. *JAMA Surg*. 2018;153:1081-9.
37. Belloni S, Arrigoni C, Dellafiore F, Diamanti O, Piredda A, Caruso R. Symptom clusters in cancer patients: an Italian survey to validate and describe unwarranted clinical variation, inequality in access to healthcare, knowledge, and risk of malpractice. *Acta Biomed*. 2021;92:e2021015.
38. Trimarchi L, Caruso R, Magon G, Odone A, Arrigoni C. Clinical pathways and patient-related outcomes in hospital-based settings: a systematic review and meta-analysis of randomized controlled trials. *Acta Biomed*. 2021;92:e2021093.
39. Yuan M, Bao Y, Ma Z, Men Y, Wang Y, Hui Z. The optimal treatment for resectable esophageal cancer: a network meta-analysis of 6168 patients. *Front Oncol*. 2021;0:362.
40. Irino T, Tsekrekos A, Coppola A, Scandavini CM, Shetye A, Lundell L, et al. Long-term functional outcomes after replacement of the esophagus with gastric, colonic, or jejunal conduits: a systematic literature review. *Dis Esophagus*. 2017;30:1-11.

41. Barbour AP, Cormack OMM, Baker PJ, Hirst J, Krause L, Brosda S, et al. Long-term health-related quality of life following esophagectomy: a nonrandomized comparison of thoracoscopically assisted and open surgery. *Ann Surg.* 2017;265:1158-65.

### Author Biographies

**Arianna Magon**, RN, MSN, PhD, is a doctorate student in Nursing Science and Public Health at the University of Rome Tor Vergata, Rome (Italy). She is currently a research nurse at IRCCS Policlinico San Donato (Italy).

**Rosario Caruso**, PhD, is the director of Health Professions Research and Development Unit at IRCCS Policlinico San

Donato, Italy. He holds a PhD in Nursing Science and Public Health from the University of Rome Tor Vergata.

**Andrea Sironi**, MD, is a general surgeon, Division of General and Foregut Surgery, IRCCS Policlinico San Donato (Italy).

**Sabrina Mirabella**, RN, MSN, is a clinical nurse working in the division of Surgery at the Hospital of Lodi, Italy.

**Federica Dellafiore**, PhD, RN, is a research fellow at the University of Pavia. She holds a PhD in Nursing Science and Public Health.

**Cristina Arrigoni**, RN, MSc, is a professor of Nursing Science at the University of Pavia. Her research focus is mainly on public health.

**Luigi Bonavina**, MD, FACS, is a full professor of General Surgery at the University of Milan and the director of the division of General and Foregut Surgery, IRCCS Policlinico San Donato (Italy).