Postoperative outcome after oesophagectomy for cancer: Nutritional status is the missing ring in the current prognostic scores

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Abstract

Background: Several prognostic scores were designed in order to estimate the risk of postoperative adverse events. None of them includes a component directly associated to the nutritional status. The aims of the study were the evaluation of performance of risk-adjusted models for early outcomes after oesophagectomy and to develop a score for severe complication prediction with special consideration regarding nutritional status.
Methods: A comparison of POSSUM and Charlson score and their derivates, ASA, Lagarde score and nutritional index (PNI) was performed on 167 patients undergoing oesophagectomy for cancer. A logistic regression model was also estimated to obtain a new prognostic score for severe morbidity prediction.
Results: Overall morbidity was 35.3% (59 cases), severe complications (grade III—V of Clavien—Dindo classification) occurred in 20 cases. Discrimination was poor for all the scores. Multivariable analysis identified pulse, connective tissue disease, PNI and potassium as independent predictors of severe morbidity. This model showed good discrimination and calibration. Internal validation using standard bootstrapping techniques confirmed the good performance.
Conclusions: Nutrition could be an independent risk factor for major complications and a nutritional status coefficient could be included in current prognostic scores to improve risk estimation of major postoperative complications after oesophagectomy for cancer.
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Introduction

Surgery remains the best curative option for oesophageal cancer despite the use of neoadjuvant radiochemotherapy with complete pathological responses between 20 and 30%.[1,2] Due to the high morbidity and mortality rates after oesophagectomy there is a tendency for centralisation of surgical treatment in high volume centres. The centralisation leaded to a reduction in postoperative mortality, with rates below 5%,[3] but overall morbidity still varies between 40 and 50%.[4] Thus, the preoperative selection of patients suitable for oesophagectomy is one of the main tasks of the multidisciplinary team involved in decision making.

Several preoperative prognostic scores based either on physiology of the patient or on the operative findings were designed in order to give a good estimation of the risk of postoperative adverse events.[5—10] Most of the prognostic scores were designed for general or oncological surgery and were validated for different malignancies. Many studies focused on the postoperative mortality and few ones on morbidity for oesophageal cancer, but they obtained conflicting results in terms of observed/predicted ratio.

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Preoperative nutrition status received minor interest in risk analysis; none of the above mentioned scores includes a parameter linked to nutrition (albumin, percentage of weight loss or BMI). These parameters had already been included in some prognostic scores[11,12] but they had never been used for oesophageal cancer. Quite often, patients with oesophageal cancer have a particular comorbidity pattern: impaired cardiovascular function in patients with adenocarcinoma and impaired pulmonary and hepatic function due to smoking and alcohol consumption in patients with squamocellular cancers.[13] The common feature is the impaired nutritional status due to the dysphagia with the consequent metabolic alteration caused by weight loss.

The aim of the present study was to evaluate the different scores in the prediction of post-operative outcome in patients undergoing resection for oesophageal cancer and to develop a clinical scoring system to predict the risk of severe complications.

Materials and methods

Study design

We performed a retrospective study using a prospective collected database of consecutive patients operated for histological confirmed oesophageal or gastro-oesophageal junction cancer in a single institution (Surgical Oncology Unit, Veneto Institute of Oncology) between January 2008 and October 2012. Only Siewert type I and II tumours were included, type III tumours were considered gastric cancers and not included in the analysis. The study was performed according to Helsinki's principles and it was notified to the Ethical Committee of the Veneto Institute of Oncology.

Preoperative evaluation

All patients underwent preoperative staging, which included: upper gastrointestinal endoscopy with biopsy and endoscopic ultrasonography, high resolution computed tomography of the neck, chest and upper abdomen, integrated fluorodeoxyglucose positron emission tomography/computed tomography and staging laparoscopy (where indicated). Functional status was assessed in all patients by routine blood tests, electrocardiogram, pulmonary function tests and cardiac ultrasound at admission for surgery. Based on preoperative staging and according to the recommendations of the multidisciplinary team work-up, patients with tumours staged above T2N0 were considered suitable for neoadjuvant therapy.

Neoadjuvant therapy

The most common preoperative chemotherapy regimen consisted of 5-fluorouracil and a platinum agent (the standard regimen was 100 mg/m^2 cisplatin (DDP) on Day 1 and 1000 mg/m^2 fluoruracile (5-FU) per day in continuous infusion from Day 1 to Day 5 for 3−4 cycles), but taxanes were also prescribed as part of the treatment regimen for some of the patients. Chemotherapy was administered concurrently with radiation therapy, but the exact sequence depended on the clinical protocol or on the physician's preference. Standard radiotherapy was usually performed in 1.8-Gy daily fractions for a total dose of 45−50 Gy. The planned target volume included the primary tumour, with 5-cm longitudinal margins; metastatic nodes, with 2-cm margins; supraclavicular fovea; and mediastinum. This involved an initial phase using anteroposterior−posteroanterior fields to a total dose of 30.6 Gy. The radiation portals were then modified to encompass the primary tumour and metastatic nodes with 2-cm margins, using an oV-cord conformal oblique weld to a dose of 45−50.4 Gy.

Surgery and post surgical follow up

Surgery was performed by two experienced surgeons (C.C. and E.A.). Types of surgery included: open radical transthoracic oesophagectomy with cervical or mediastinal anastomosis, transhiatal or minimally invasive oesophagectomy. Pathological staging was based on latest edition of the TNM classification.[14] Postoperative morbidity was defined as any complication occurring within 90 days form surgery. Postoperative complications were graded according to the Clavien−Dindo classification[15] based on therapeutic consequences of the complications: grade I as a deviation form the normal postoperative course without need for therapy and grade II, complications requiring pharmacological treatment, considered as minor complications; grades III, complications requiring surgical, endoscopic or radiologic interventions, grade IV, life-threatening complications requiring intensive care, as major complications and grade V, death. If a patient developed a major complication associated with one or many minor ones it was considered having only the major complication.

Prognostic scores

The postoperative mortality risk for POSSUM,[5] Portsmouth-POSSUM and Oesophago-gastric POSSUM[6,16] were calculated using calculation sheets available on www.sfar.org and on www.riskprediction.org.uk. The POSSUM morbidity score was calculated for each patient using a scoring system which includes a physiologic score and an operative score.[5] The following variables were investigated as indicators of immune and nutritional status of the patients: BMI (body mass index), weight loss (in percentage), total lymphocyte count, haemoglobin, platelet count, total protein, albumin, prealbumin and the prognostic nutritional index (PNI)[11] calculated as $10 \times$ albumin (g/dl) $+ 0.005 \times$ total lymphocyte count (per mmc). The Charlson Comorbidity Index (CCI)[8] calculation involves