Validation of the Data Quality and Early Outcomes of the Spanish EURECCA Esophagogastric Cancer Registry

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SUMMARY

Objective. The objective of the study is to verify and validate the data collected in the Spanish EURECCA (EUropean REgistry of Cancer CAre) Esophagogastric Cancer Registry between January 2014 and December 2017 through an audit process. It is also intended to describe the initiation and implementation of this Registry as well as its early outcomes.

Methods. An audit of registered cases (esophageal, esophagogastric junction and gastric cancer resectable patients undergoing surgery) from 01/01/2014 to 12/31/2017 and a descriptive analysis of these data will be performed.

Expected results. The study could show that the Spanish EURECCA Esophagogastric Cancer Registry is a reliable source of information, valid for carrying out specific and exhaustive analysis that may lead to high quality publications in indexed journals. It is also expected to generate a high impact based on the large number of cases included in the Registry, favoring new research projects.

Relevance. The standardization of the data collection is essential to compare outcomes between different centers, regions and countries. This study will allows us to verify the integrity of the collected data as well as its accuracy, a critical aspect to gain credibility for future studies using the Registry data.

Audit project and Background

The overall objective of the project is to verify and validate the data collected in the Spanish EURECCA Esophagogastric Cancer Registry through an audit process.

The project is divided into two sub-studies.

For sub-study 1 (data audit) the specific objectives are:
- To verify the integrity of the cases.
- To check the accuracy of the data.

For sub-study 2 (descriptive analysis) the specific objectives are:
- To perform a descriptive analysis of the outcomes of the Registry.
- To compare our information and outcomes with the outcomes of other European registries.

The EURECCA project (European Registration of Cancer Care) began in 2007 with the aim of improving the quality of care for patients with rectal cancer in different European countries. The EURECCA Upper GI Cancer Registry was created in 2013, focusing exclusively on esophagogastric cancer. At first, a consensus was reached among several European registries (England, Ireland, Denmark, Sweden, France, Germany, Poland and Italy), about a basic list of data that any esophagogastric cancer registry needs to collect (de Steur 2014). Since then, two studies developed within the EURECCA Project have been published analyzing and comparing the data of these registries (Messager M: 116-122, 2016; Messager M: 1432-47, 2016) and showing variations within countries. A review of the literature shows how the implementation of the registries has evolved over the years, for example, Denmark initiated the national registry of esophagogastric cancer in 2003 (Jensen 2010; Kjaer 2017) and Sweden in 2006 (Linder 2016). In 2007, the Dutch Cancer Society concluded that by analyzing and auditing the data collected in the registries it is possible to minimize the variation between centers, leading to an improvement in the overall quality of patient care (Wouters 2010). In 2011, the National Oesophagogastric Cancer Audit (NOGCA) of England started collecting prospective information of every diagnosed and treated case of esophageal and stomach cancer, and since then has reported its results annually (https://digital.nhs.uk/catalogue/PUB21561). In 2011, the Dutch Upper Gastrointestinal Cancer Audit (DUCA) initiated a national registry of all patients with esophageal and stomach cancer undergoing surgery with curative intent. Participation in this registry is mandatory since 2012 and represents a quality standard whose preliminary results have allowed the optimization of cancer diagnosis and treatment (Busweiler 2016).

The centralization of esophageal and gastric cancer surgery in Spain is now a reality in Catalonia and Navarre since 2011 and 2012 respectively. Since 2013, the Spanish EURECCA Esophagogastric Cancer Registry has been collecting data in both Autonomous Communities (Allum 2016) and, furthermore, it is important to point out that since the beginning there has been a consensus on the required variables with their respective definitions. An example of this has been the description and reporting of post-operative complications following the recently validated recommendations of the Esophageal Complications Consensus Group (ECCG) (Low 2015; Low 2018).

Verifying and validating the collected data is crucial to ensure the reliability of the information (Bray 2009; Parkin 2009). In Norway, an audit of the data collected in the Norwegian Registry of Rectal Cancer (NRCR) created in 1993 (Sunniva 2015) has been published, demonstrating a high degree of validity and an improvement in the quality of the treatment over the years. Since June 2012, this registry also has an electronic version. In relation to esophagogastric cancer surgery, periodic audits on the diagnostic process and the results of the treatment are carried out in England, Sweden (Linder 2016), and the Netherlands (Busweiler 2016). All these publications conclude that audits are an important strategy used in health care to maintain quality standards and improve patient care. Audits provide a way to identify deficiencies in clinical practice, to assess trends and provide constructive feedback to surgeons and others health care workers. The validity of any audit is based on the accuracy of its data. For this reason, is considered vital to carry out an "in situ" audit of the data collected in the EURECCA on-line Registry.

Methodology

The EURECCA Registry

The EURECCA online Registry collects data of esophageal, esophagogastric junction and gastric cancer resectable patients undergoing surgery. It was launched with the initial participation of 2 Spanish Autonomous Communities, Catalonia and Navarra, with 21 participating centers. In March 2017, the Basque Country joined the Registry, incorporating other 9 hospitals. More recently La Rioja joined as well with a single hospital. It is important to highlight that, to date, there are 30 participating centers in the Spanish EURECCA Esophagogastric Cancer Registry, which collect information of more than 10 million people.
For this specific project, only the cases of the two first Autonomous Communities that initiated the project will be analyzed: Catalonia and Navarre.

Quality measure and data set

For this specific study the data collection was closed on December 31, 2017.

The online form contains 93 variables distributed in 4 categories of data:

- Patient characteristics: Patient data (7) and Comorbidities (5).
- Care process: Diagnosis and staging (10), Preoperative optimization (4), Neoadjuvant treatment (3).
- Surgery and histopathology: Surgery (17), Histopathology (24).
- Postoperative period: Hospital stay and Complications (14), Follow-up (9).

The selection of these variables was established in accordance with a general consensus of the Spanish EURECCA group. Multidisciplinary quality standards have been introduced (surgery, oncology and histopathology) and all the PIs (Principal Investigators) were sent the definitions of many of the variables: for instance lymphadenectomies (D0, D1, D1+, D2) and complications (Pneumonia, Acute respiratory distress syndrome, myocardial infarction, acute delirium, generalized sepsis, pancreatic fistula). In addition, pathologists from all Units participating in the EURECCA project agreed to follow standardized histopathology protocols for esophageal, esophagogastric junction and gastric cancer in order to describe and report their findings.

Audit and validation

The on-line form itself is considered as an internal filter/audit for data collection. Several data fields inform if they seem implausible when saving them, according to previously established ranges.

In addition, the Data Manager (DM) monthly provides a feedback to each center, summarizing the missing variables (blank) and potentially erroneous ones, to be reviewed by the PIs.

Based on the experience of the Dutch Upper Gastrointestinal Cancer Audit (DUCA) (Busweiler 2016), the validation of the data collected in our Registry will be carried out at two levels:

- First level: Integrity.
To ensure that patients are collected consecutively (non-selected) and the Registry includes all cases of resectable Esophageal, Esophagogastric junction and Stomach Cancer operated on, a cross-check with the data from the Clinical Documentation Service of each center will be carried out. Each Clinical Documentation Service will be requested to perform a search in its hospital discharge database of all cases codified by the International Classification of Diseases (ICD-9-CM International Classification of Diseases, Ninth Revision, Clinical Modification for Catalonia and ICD-10-CM International Classification of Diseases, Tenth Revision, Clinical Modification for Navarra) with the main diagnosis associated with Esophageal, Esophagogastric junction and Stomach Cancer.

- Second level: Accuracy.
A small group of researchers (2 doctors or 1 doctor + 1 Data manager), from a different center to the one evaluated, will visit the audited center and will carry out an exhaustive review of a list of selected

variables included in the Registry. A random sample of patients will be selected in each participating center.

- For those centers where the total number of cases is less than or equal to 20, the entire sample (100%) will be analyzed.
- For those centers where the total number of cases is between 21 and 100, a sample of 20 patients will be taken, randomly chosen (minimum 20%).
- For those centers that exceed 100 cases, a sample of 20% of the total number of patients included in that hospital will be selected, up to a maximum of 50 patients.

The following variables will be analyzed:

- Comorbidities: ASA (American Society of Anesthesiologists) score, Charlson Comorbidity Index.
- Diagnosis and stage: Date of diagnosis, Location of the tumor.
- Neoadjuvant treatment: Start date.
- Surgery: Date of the surgery, Access, Surgical technique (type of gastrectomy and esophagectomy).
- Histopathology: Histological type, Radicality of the resection (R0, R1, R2), No. of lymph nodes examined, Pathological stage (pTNM).
- Postoperative period: Complications, Transfusion, Pneumonia, Anastomotic leak, Clavien-Dindo classification.
- Follow-up: Last follow up, Readmission, Recurrence, Date of recurrence, Patient status, Date of death.

A concordance process between the extracted data during the "in situ" review and the data contained in the EURECCA Registry will be established. The reviewers will prepare an audit report with the errors and/or blank fields detected and this will be sent to the PIs of this audit for its analysis.

Statistical analysis plan

Univariate descriptive analysis will be performed, presenting the results as means (with standard deviation and range) for the continuous variables and as numbers and percentages for the categorical variables. In addition, bivariate analysis will be carried out among the variables of interest to describe their level of correlation and evaluate the possible differences between them. To evaluate the differences between the continuous variables, the comparison of means based on the T-Student will be used, and for the comparison of differences in the categorical variables, the Chi-square test will be used. Finally, linear regression models and generalized linear models (as appropriate depending on the response variable) will be used to study the dependence of the variables of interest, with other factors of study. Statistical analysis will be carried out using the SPSS (Statistical Package for the Social Sciences) Software (IBM SPSS Statistics 22). All tests will be bilateral with a level of significance of 5%. 100% of the data recorded from 01/01/2014 to 06/30/2017 will be analyzed, and the proportion of values lost in the variables of interest will be evaluated.

In particular, it is proposed to carry out the following descriptive and comparative analysis between hospitals:

- Tumor location: Stomach, Esophagus, Esophagogastric junction.
- Patients characteristics and comorbidities: Age (≤70 o >70), Sex (Ratio M:F), BMI (<20, 20-24, 25-29, ≥30), Weight loss %, ECOG (Eastern Cooperative Oncology Group) score, ASA score (1-2 or ≥3), Charlson Comorbidity index (0, 1, ≥2).
- Tumor characteristics: Tumor localization, Histological type, Clinical tumor stage, CEA (carcinoembryonic antigen), Ca 19.9, Preoperative study.
- Treatment: Preoperative optimization (transfusions, hemoglobin (Hb) at diagnosis, preoperative Hb, iron therapy), Neoadjuvant treatment, Surgery (type, approach, type of anastomosis, etc.)
- Histopathology.
- Postoperative period and follow-up: Length of hospital stay, Complications (types and Clavien-Dindo classification), Readmission, Adjuvant treatment, In-hospital mortality, 30 and 90 days mortality, Recurrence.

Limitations

The Registry requires an effort by all researchers to correctly fill in the data collection form. It is a large number of variables, but validated variables by almost all the PIs and by international consensus have been chosen.

To reduce errors in filling in the data, the open data collection fields have been minimized (which accept any type of character) and closed fields variables have been preferred (drop-down lists and calendars to select the dates).

Another limitation is the variability in the coding used between the participating centers. To reduce this variability to a minimum, the group of researchers developed an exhaustive protocol for defining the variables, which was agreed upon and approved by the research team prior to the start of data collection.

The centralization of the data, leads to the requirement of a secure Internet connection, with an updated browser.

Work plan

The entire project will be carried out at the Hospital del Mar in Barcelona (PSMar), except for the "in-situ" audit of the collected data, which requires a visit of the audit team to each of the participating centers in the project.

The project is structured in two different sub-studies developed in 3 research periods:

1st Period: First 3 months of the study.
During the first period of the study, all cases registered in the online form EURECCA, which underwent surgery from 01/01/2014 until 12/31/2017, will be closed. Each one of the responsible investigators should review the cases before its closing:

- Month 2: Closure of cases operated on from 01/01/2014 until 12/31/2015.
- Month 3: Closure of cases operated on from 01/01/2016 to 12/31/2017.

2nd Period: Next 4 months of the study.
During the second period of the study, the data will be audited for verification and validation at the two levels detailed in the methodology section:

- Months 4 and 5: Extraction of data from the Clinical Documentation Services of each center to check their completeness.
- Months 6 and 7: On-site verification of the data.

3rd Period: Last 5 months of the study.

- Month 8: Statistical analysis.
- Month 9: Conclusions sub-study 1.

With all the data recorded and closed, the Data Manager of the study, will be responsible for carrying out the export and final review of the entire database and will proceed to the descriptive statistical analysis, task in charge of all the researchers of the study in collaboration with the Epidemiology and Biostatistics of the Epidemiology Service of the Hospital del Mar in Barcelona.

- Month 10: Exportation and Descriptive Analysis of the data.
- Month 11: Conclusions sub-study 2 descriptive.

Ethical considerations

The EURECCA register was presented and approved by the Parc de Salut MAR Clinical Research Ethics Committee in 2013 in its initial version (nº 2013/5047/I) and the amendment to the version has been subsequently approved, dated 9 June 2016 in the Ethic committee (CEIC) PSMar and in the respective CEICS of the participating centers.

Can Antaviana SL (www.antaviana.cat) is the external company contracted for the creation, in 2016, of the on-line form for the centralized collection of data. The Spanish EURECCA Esophagogastric Cancer Registry collects the anonymized data through a secure environment, which is accessed from any computer with Internet connection, but with restricted access, a username and password are required, assigned to each IP by the Data Manager (DM), in order to access it.

The patient is identified with a 6-digit ID code that the web system automatically generates as a new case is introduced. Each center maintains ownership of their data with a source document that links the case ID with the clinical history number. Each center can choose when to complete the data, there is a responsible surgeon for each Unit or a designated assistant. The DM reviews all the anonymized data to discover inconsistencies, errors and omissions. In this way, the national and international guidelines (declaration of Helsinki) is fulfilled and the confidentiality of the data is ensured, in accordance with the Spanish Organic Law 15/1999 of December 13 on the Protection of Personal Data.

For sub-study 1, it will be necessary for the PIs and/or DM to travel to an audit center to verify the data, accept and sign the specific Confidentiality Document of each Clinical Documentation Service.

Budget

It is planned to apply for a Grant from a Scientific Society, which will make it possible to cover the expenses related to the Audit of data (visit of the audit team), the statistical analysis of the data and the publication of the results.

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