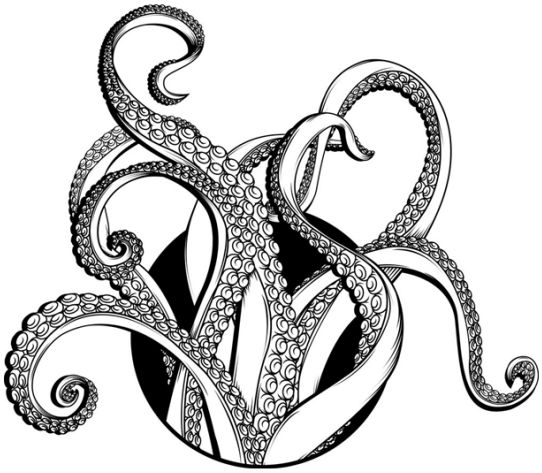

TENTACLE
Esophagus

TENTACLE - Esophagus

TreatmENT of AnastomotiC LeakagE after esophagectomy

Database cleaning, data verification and data validation protocol

Background

Anastomotic leakage remains a major complication after all types of esophagectomy and is associated with increased morbidity, mortality and a decrease in quality of life. The severity of anastomotic leakage can be very wide-ranging from a subclinical presentation to a life-threatening situation. Currently, the severity is graded according to how it is treated (1) and is therefore by definition not useful to guide decision making when anastomotic leakage is diagnosed in a clinical setting. Regarding the treatment of anastomotic leakage, evidence based treatment strategies are lacking (2, 3). From these studies, it became evident that the absence of an anastomotic leakage severity score complicates performing robust research on this topic. Therefore, the aim of the TENTACLE study is to investigate what factors contribute to anastomotic leakage severity and to compose an evidence based anastomotic leakage severity score. Furthermore, the aim of the TENTACLE study is to evaluate the effectiveness of different initial treatments for anastomotic leakages classified according to the severity. The TENTACLE study is an international multicenter retrospective cohort study. Currently, 70 centers from 20 different countries are participating. The samples size calculation showed that up to 680 patients were needed to be included. However, in December 2019 already 1500 cases have been entered in the online database. All participating centers have been instructed before and guided during data entry to promote high quality data. Nevertheless, performing data validation is crucial to ensure data quality and reliability.

Methods

The goal of database cleaning and data verification is to improve data quality and the described process is performed on all cases that are included in the study.

The goal of validation is to assess the quality of data. In total, 10% of all records will be validated. Two aspects of data quality and reliability will be quantitively assessed.

1) Case ascertainment will be assessed to identify a systematic difference in the selection of individuals included per center, defined as the proportion of cases included compared to the total amount of eligible cases.
2) Data accuracy which is the accuracy of data registration of included cases in the online database.

Database cleaning and data verification

A process of database cleaning and verification will take place to improve data quality and identify any faulty or inconsistent data entries. The study team will perform a structured verification based on data range, constraints and consistency. The whole database will be verified using prespecified variable conditions and queries. Identified data inconsistencies will be discussed with the center concerned. After consultation with the center, corrections will be performed if needed.

Validation process

Given the global nature of the TENTACLE study, an in-person validation process by the study team has logistical and practical limitations. The study team therefore chose to perform an on-site validation by an independent local validator of the participating centers as was previously done in other global surgical studies(4). After finalizing data entry, half of the participating centers will be selected for data

validation. To form a representative sample the centers will be selected on volume and location. These centers will be asked to recruit an independent validator at their hospital (e.g. doctor, nurse, researcher, student). This validator may not be previously involved with the patient inclusion and data registration and will be asked to sign a document confirming independence.

Case ascertainment validation

Case ascertainment will be evaluated qualitatively. First, at the end of inclusion and data registration all centers were asked whether they uploaded all their cases within the study period (i.e. 2011 – 2018) or whether they included a consecutive sample and for which period. In addition, all participating centers received a questionnaire which inquired about their years of experience with performing an esophagectomy and the annual number of patients undergoing an esophagectomy. The anastomotic leaking rate was conservatively estimated at 5% of all esophagectomies for the eight years study period (2011 – 2018). If the number of included cases was lower than the estimated number of patients suffering of an anastomotic leakage, the collaborators of that center were asked to substantiate this discrepancy.

Second, during the validation phase the independent validators of the centers selected for data validation will be asked the following questions to assess case ascertainment:

1. Have all anastomotic leakage cases between 2011 and 2018 been uploaded or has a sample been uploaded?
    - ☐ All cases within study period (2011 – 2018)
    - ☐ Sample within study period
2. If a sample has been uploaded, has a consecutive sample been uploaded, or has some other kind of sample been uploaded?
    - ☐ Consecutive sample of following years …… until ……..
    - ☐ Another sample (please describe sample): ……..

Response from the validators will be compared with the response from the center representatives. If any discrepancies are found, centers will be asked to elucidate their inclusion process. To prevent selection bias in the study, the study team may – after extensive consultation with the concerning center – decide to provide the center two weeks to complete a consecutive sample or exclude a center if their selection and inclusion has not proceeded according to the study protocol.

Data accuracy validation

The data accuracy assessment will consist of the validation of the key parameter in the validating centers. In total, 10% of all records will be validated. Records will be randomly selected for validation by the TENTACLE study team, with a minimum of 3 cases per center. Key parameters were selected by the TENTACLE study team to include baseline, as well as intervention and outcome parameters. The following parameters will be assessed in data accuracy validation.

Baseline:

1. Sex (male/female)
2. Age (years)
3. Year of surgery (2011-2018)
4. Baseline ASA (I-IV)

5. Operation type: abdominal phase (laparoscopic/robotic/open/converted)
6. Operation type: thoracic phase (thoracoscopic/robotic/open/converted)
7. Location of anastomosis (cervical/intrathoracic)

Leakage diagnosis and treatment:

7. Assessment that first diagnosed anastomotic leakage (endoscopic, contrast swallow esophagram, CT-scan, ingested fluids by drain, reoperation, other, unknown)
8. Location of leak (esophagogastric anastomosis, gastric tube, blind loop, other, unknown)
9. Extent of contamination at diagnosis (none, mediastinum, cervical, pleural, abdominal, unknown)
10. Leucocytes at leakage diagnosis (amount)
11. Primary treatment – Radiologic drainage (y/n)
12. Primary treatment – Re-operation (y/n)

Outcome:

13. Anastomotic leak Clavien-Dindo (grade I-V)
14. ICU (re)admission (yes/no)
15. 90-day mortality (yes/no)

The local validator will receive a list of the records to be validated from the study team. Key parameters will be retrieved from the local medical records and will be recorded in a validation Excel sheet provided by the study team. The local validator will not receive access to the Castor database to ensure that the parameters were retrieved from the local medical records. Before the validation deadline the local validators will send the completed validation sheet back to the TENTACLE study team. The coordinating investigator will compare the data retrieved by the validator with the data entered in Castor. The local validators will be asked to confirm any discrepancies found during the data accuracy assessment.

Subsequently, the center's data accuracy will be calculated, as well as the overall data accuracy. Depending on the results of data accuracy assessment, the study team may perform a heterogeneity analysis between centers with high and low data accuracy. The overall data accuracy will be described in the TENTACLE manuscripts.

Timeline

January 19th, 2020	–	Deadline for data entry
February 1st, 2020	–	Start of database cleaning and verification
		Initiation of data validation protocol, recruitment of validators
March 1st, 2020	–	Deadline for database cleaning and verification
		Start of actual data validation
April 15th, 2020	–	Deadline for data validation by validators at collaborating centers
May 1sth 2020	–	Validation analysis and results

Validator compensation

Centers will be offered compensation for their validation efforts. Centers will be offered either a place in the TENTACLE collaborative group for the independent validator or financial compensation. The

financial compensation is based on the effort and time of the validator assessing the data accuracy and ascertainment.

References

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4. GlobalSurg C. Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study. Lancet Infect Dis. 2018;18(5):516-25.