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## **Goedgekeurde aanvraag gegevens ten behoeve van wetenschappelijk onderzoek** DUCA201805

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### **Titel onderzoek**

Risk factors for incomplete resections after neoadjuvant chemoradiotherapy in esophageal cancer: a population-based study

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### **Beschrijving onderzoek**

The addition of chemoradiotherapy prior to esophagectomy has significantly improved survival of patients with esophageal cancer<sup>1</sup>. One of the objectives of neoadjuvant chemoradiotherapy is to reduce the size of the primary tumor to increase the chance of a complete resection<sup>2</sup>. However, despite the decrease of positive resection margins since the introduction of neoadjuvant chemoradiotherapy, positive resection margins are found in 4.1% to 26%<sup>3-7</sup> of patients according to the definition of the College of American Pathologists<sup>8,9</sup>.

Positive resection margins are associated with poor outcomes such as local recurrence, distant metastasis and reduced overall survival<sup>4</sup>. Knowledge of patient, tumor, and treatment characteristics that increase the risk of positive resection margins could potentially help surgeons to anticipate the need for taking larger margins or changing their surgical approach when removing the tumor.

Tumor location, surgical approach (transhiatal versus transthoracic) and pathological stage have previously been identified as independent risk factors for positive resection margins in patients that were treated for esophageal cancer<sup>4,10</sup>. However, so far these risk factors were mainly determined in patients that underwent primary surgery. With the widespread implementation of neoadjuvant chemoradiotherapy (CROSS) as integral part of a curative treatment strategy and the developments in minimal invasive surgery, the influence of these risk factors might have changed.<sup>1,11,12</sup>

2017.1

Therefore, the aim of this study is to re-evaluate risk factors of positive resection margins in patients that undergo esophagectomy for esophageal cancer following neoadjuvant chemoradiotherapy on a population level.

**Onderzoeksopzet:**

Study population: All patients undergoing an elective esophagectomy for esophageal cancer after neoadjuvant chemoradiotherapy (CROSS) between 2011 and 2017, and registered in the DUCA registration. Patients undergoing salvage esophagectomy for recurrent esophageal disease will be excluded.

Outcome measures: Positive resection margin

Predictors: The primary predictors for our analysis will include all perioperative patient, tumor and treatment related characteristics that are recorded in the DUCA that may clinically be associated with the primary study outcome. Candidate predictors for incomplete resection as selected according to evidence from literature review and expert opinion are: pre-operative BMI, weight loss<sup>4</sup>, tumor histology, interval between nCRT and surgery, cT-stage, cN-stage<sup>13</sup>, tumor location<sup>4</sup>, type of surgery<sup>14</sup>, type of reconstruction (intrathoracic or cervical<sup>15</sup>) and hospital volume ( $\leq 20$ , 21-40, 41-60,  $>60$  esophagectomies a year<sup>16</sup>).

**Statistiek:**

Continuous variables will be expressed as mean  $\pm$  standard deviation or as median with interquartile range (IQR), where appropriate. Missing data will be imputed with the iterative Markov chain Monte Carlo method<sup>17</sup>. To assess the independent association of predictors with a positive resection margin all prespecified predictors will be included in a multivariable logistic regression model. The initial logistic regression model will be reduced using backward stepwise elimination based on Akaike Information Criterion. Also, we will include interactions of tumor location with surgical approach (transhiatal versus transthoracic) to model the potential differential impact of surgical approach on proximal versus distal tumors. For internal validation, the model will be subjected to 200 bootstrap resamples to calculate the optimism of the model and the shrinkage factor, after which the beta-regression coefficients will be adjusted.

**Beoogde publicatie**

Risk factors for incomplete resections after neoadjuvant chemoradiotherapy in esophageal cancer: a population-based study

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