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Translocation of minimally invasive esophagectomy from the randomized controlled trial setting to national practice

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Beschrijving onderzoek
We have recently conducted a systematic review of 49 publications aimed to compare clinical outcomes from randomized controlled trials of minimal access surgery for gastrointestinal cancer to results from national cohort studies within the same study period (unpublished). The results suggest wide differences between the effect sizes for minimal access surgery seen in a randomized controlled trial setting and in real clinical practice as identified in national cohort studies. Minimal access surgery is an established example of surgical innovation into clinical practice with the IDEAL recommendations in place for this process. However the results of this review suggest limitations to the external validity of randomized controlled trials within surgical oncology, which may be secondary to bias in patient or surgeon selection.

Hypotheses:
(i) Adverse clinical outcomes observed within the Minimally Invasive Esophagectomy (MIE) group of the TIME RCT (1) will be reduced compared to those observed in the DUCA national audit.
(ii) Discrepancy in the effect sizes of clinical outcomes between open and MIE groups will exist between the TIME RCT and the DUCA national audit.
Primary endpoint:
(i) In-hospital mortality
Secondary endpoints:
(ii) Overall in-hospital morbidity

(iii) Anastomotic leak
(iv) Postoperative pulmonary morbidity
(v) Reoperation rate

Onderzoeksopzet:
Cohort study design.

Onderzoekspopulatie:
(i) Patients within the TIME RCT undergoing open and MIE for esophageal cancer (exposure cohort).
(ii) Patients within DUCA (2011 to 2017), who meet the following criteria
- Receiving Total MIE or Open esophagectomy for the treatment of esophageal cancer or gastro-esophageal junctional cancer (Siewert I and II).
- Histologically proven adenocarcinoma, squamous cell carcinoma, or undifferentiated carcinoma of the intrathoracic oesophagus and gastro-oesophageal junction.

Statistiek:
Comparison 1: Clinical outcomes from MIE groups in TIME RCT and DUCA
Initially univariate analyses will be performed to compare patient demographics between patients receiving MIE in TIME and in DUCA. Then univariate analyses will be performed to compare primary and secondary end-points between MIE procedures in TIME and in DUCA. Inverse probability weights (IPW) will be applied to correct for confounding and selection bias in the models. Firstly, a logistic model will be fitted to calculate the probability of having a MIE procedure and the predicted values will be used to calculate the inverse probability weights that will be afterwards applied in the logistic models for in-hospital mortality and secondary end-points.
Mediation analysis will be applied to investigate the direct effect of MIE upon in-hospital mortality and other secondary end-points, independent of other patient factors. The commonly called treatment in our mediation analysis is MIE. The mediator in this case is comorbidity, a disease that the patient presented before the surgery. The average causal mediation effects (ACME) are the difference between the potential outcome when the MIE has a value t and the expected value of the mediator when the patient has the MIE and the potential outcome when the expected value of the mediator when the patient does not have the MIE. When the ACME for the presence or absence of the MIE coincides the mean between both can be used. When they are different, an interaction term is introduced in the outcome model and the interpretation of the ACME is different for both binary stages of the MIE. The average direct effect (ADE) is calculated as the difference between the potential outcome with MIE present and absent. The value of the mediator for both terms comes from the expected value of the mediator when the value of the corrective surgery is t with t=0,1.

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References

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Beoogde publicatie

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