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Titel onderzoek

A National Cohort Study To Evaluate The Prognostic Impact of Number of Retrieved Lymph Nodes In Gastric Cancer Surgery

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Beschrijving onderzoek

Many studies have shown that nodal metastasis in gastric cancer correlates with the overall survival of the patient.

The staging of Gastric cancer in patient determines the prognosis of the patient therefore requires accurate nodal metastasis evaluation.

Thus far, there are no single agreeable minimum lymph node retrieval that is accepted internationally^[1].

Depending on regions, there are different recommendations for the minimum lymph node yield in gastrectomy. NCCN guidelines stipulated a minimum of 15 nodes while the German S3 guidelines requires 25 lymph nodes yield in a curative gastrectomy for gastric cancer^[2,3,4]. On the other hand, our Eastern (Japanese/Korea/China) counterpart had suggested 15 lymph nodes for early gastric cancer and possibly up to 35 lymph nodes for advanced gastric cancer^[5,6].

This is partly contributed by the adoption of different approaches to the surgical approach between the regions that mandate dissimilar set of quality measures^[7,9]. However, a more extensive lymphadenectomy does not correlate with better survival as proven in previous Dutch and Italian study^[8]. However, more accurate staging is achieved with more lymph nodes examined thus potentially inducing a stage migration effect^[2,11].

Furthermore, the introduction and dissemination of neoadjuvant chemoradiotherapy has demonstrated to be effective for loco-regional tumour control. In comparison, by extrapolating from esophageal study, an analysis based on data from the CROSS trial, extensive lymph node dissection does seem to have potential survival benefits.

Even differences in histopathological evaluation method may influence the number of lymph nodes identified, as shown by De Marco et al. The total number of lymph node examined

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differed when the specimen was sent for reporting en-bloc (in most western country) compared to specimen sent as labelled sections (eastern counterpart). Higher number of lymph node retrieval requires more extensive lymphadenectomy during surgery and this created a paradox with our current evidence. There are evidence that showed increase survival benefit with higher number of lymph node yield^[4,5,6,7,17,18]. However, extensive lymphadenectomy had also failed to demonstrate survival benefit in Medical Research Trial UK, Italian and Dutch studies^[8,14,15,16]. The Dutch Upper GI Cancer Audit (DUCA) benchmarked 15 lymph nodes as a quality indicator for curative gastrectomy. There is a trend of an increasing lymph node yield seen in the data from the last 5 years^[13].

Onderzoeksvraag: *Hypothese, primaire en secundaire eindpunten*

This study is designed to:

1. evaluate the association of number of retrieved LNs with patient survival by comparing the survival of patients < 15 lymph nodes versus > 15 lymph nodes.
2. compare the pathological N staging between < 15 lymph nodes versus > 15 lymph node
3. compare lymph node yield between patients that received neoadjuvant treatment and patients without neoadjuvant treatment

Objectives:

1. Is the quality indicator of 'retrieval of at least 15 LNs' associated with long-term survival?
2. Is the quality indicator 'retrieval of at least 15 LNs' associated with more accurate staging?
3. Is neoadjuvant treatment associated with a reduced number of lymph nodes in the resection specimen?

Onderzoeksopzet:

Data are retrieved from Dutch national database on Upper GI Cancer retrospectively from years 2011 to 2016.

In this study, we collect the demographic details of the patients, tumor characteristics, pre-operative staging, treatment details, post-operative histopathological information and post-operative outcomes including survival (last moment of follow-up: September 2017)

However, patient personal details and treatment institute will remain anonymous.

Due to this reason, missing or incomplete data will be irrevocable.

Onderzoekspopulatie:

Inclusion criteria

Included in this study are all patients above 18 years old who underwent curative gastrectomy between 2011 to 2016 recorded in the national DUCA registry.

Exclusion criteria

Missing information on patient demographics

Missing information on neoadjuvant chemotherapy

Missing information on clinical N staging

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Unknown number of LNs retrieve
Missing information on follow-up up

Statistiek:

There are some statistical challenges associated with this study design.

- There is a bias that less extensive lymphadenectomy will be performed in more ill patients.
- There is a bias that more lymph nodes will be retrieved when clinical N staging pre-operatively is higher as surgeon will perform more meticulous lymphadenectomy.
- If long term survival is what we are looking into then there will be an over-estimation of survival for patient who are operated earlier in the study as compared to later as follow-up is shorter in the latter group.

Therefore we will use Propensity score matching (PSM) to create two cohorts of patients with comparable patient and disease characteristics and a comparable year of surgery. The group of patients with ≥ 15 retrieved LNs were matched to patients with < 15 retrieved LNs with the nearest neighbor method with a caliper of 0.20.

The selection of characteristics that are used for matching was based on the literature. The following characteristics were used: age, ASA score, Charlson comorbidity score, anamnestic weight loss, tumor location, cT-category, cN-category, cM-category, histological subtype, and, differentiation grade. Year of surgery is also used as a matching variable to avoid differences in the year of surgery between the groups since this may have influence on the impact of bias.

For sensitivity analyses, there were also groups matched for ≥ 10 , ≥ 20 , ≥ 30 LNs.

In the first part of this paper, the overall survival was compared between the groups ≥ 15 and < 15 LNs. For sensitivity analyses, also the overall survival was compared for the groups ≥ 10 versus < 10 , ≥ 20 versus < 20 , ≥ 30 versus < 30 LNs. In the second part of this paper, pathological N stage was compared for the groups ≥ 15 and < 15 LNs. To estimate the accuracy of pathological N staging, the survival was compared between the groups ≥ 15 and < 15 LNs in a subgroup of patients who were pathologically staged N0. These patients were chosen because the definition of N0 is uniform: no regional LN metastasis.

All outcomes were evaluated between the propensity score-matched groups.

Chi square test was used to compare the surgical outcomes between < 15 LNs yield and > 15 LNs yield.

Kaplan-Meier method was used to estimate survival curves for all stages and for each stage according to total number of lymph nodes examined. Log-rank test was used to detect survival differences.

Analysis of variance (ANOVA) was used to detect differences in the total lymph nodes examined among stages

Beoogde publicatie

A National Cohort Study To Evaluate The Prognostic Impact of Number of Retrieved Lymph Nodes In Gastric Cancer Surgery

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