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Title

Treatment of Newly Diagnosed Gastroesophageal Reflux Disease in a National Population-based Cohort

Aim

To compare rate of surgery with medical treatment in patients with newly diagnosed gastro-esophageal reflux disease in a nationwide population based cohort over 15 years.

Background

Episodic reflux of gastric contents to the esophagus is physiological but is considered gastroesophageal reflux disease (GERD) when accompanied by bothersome symptoms, typically heartburn, regurgitation or retrosternal pain. Extra-esophageal symptoms such as asthma, laryngitis and chronic cough may also occur (1). GERD is a complex and multifaceted disease (2, 3), affecting 10-20% of the Western population (4) and has been shown to significantly reduce the quality of life (5). Worldwide, the prevalence of GERD has been increasing (6–8). Treatment of GERD consists of anti-secretory drugs, mainly proton pump inhibitors (PPI), or anti-reflux surgery. Laparoscopic anti-reflux surgery is considered standard of care in surgical treatment of gastro-esophageal reflux disease (9) and with careful patient selection based on thorough preoperative workup (10), symptom control and patient satisfaction are high compared to medical therapy. This has previously been demonstrated in metaanalysis (11, 12).

From 1990-2000 the utilization of anti-reflux surgery in the USA rose to 16.7 procedures per 100.000 inhabitants with a concomitant rise in the use of the transabdominal laparoscopic approach. This resulted in a decline of perioperative mortality and morbidity (13, 14). The rate of anti-reflux surgery dropped to 6.1 procedures per 100.000 inhabitants in 2010, when the patients were now older with significantly higher levels of comorbidity. Despite this, length of stay, morbidity and mortality was reduced even further. The laparoscopic approach is used in 80% of American procedures and the rate has not changed during the last ten years. It is unknown whether Denmark follows the same trends, as the popularity of anti-reflux surgery has been somewhat limited and the surgical setup is different with significantly fewer centers. In a Danish study, investigating the rate of reoperative anti-reflux surgery from 1997-2005, the rate of primary surgery was 5.2 per 100.000 inhabitants with a reoperation rate of 5% (15), however no data has been presented after 2005, and no Danish study has focused on treatment of newly diagnosed patients suffering from reflux disease.

As such, it is currently unknown how many patients each year are given the diagnosis GERD after upper endoscopy in Denmark and what treatment they receive. It is also unknown how the utilization of medical and surgical treatment has developed in this group of patients.

Methods

The study is a register-based cohort study with data from Danish national health registries (The National Patient Registry, The Danish National Prescription Register and The Civic Registry). The study period is 2000-2015.

The study population consists of all adult Danish patients diagnosed with GERD and GERD-related diagnosis identified with ICD-10 codes DK20.9B, DK21.0-21.9B & DK22.7 using The National Patient Registry).To

02.05.2018

validate GERD-diagnosis, upper endoscopy must have been performed no more than three months before time of diagnosis for the patient to be included. Endoscopy must have been performed during the study period 2000-2015.

Patients with GERD and GERD-related diagnosis up to four years before upper endoscopy are excluded from the study as are patients with any diagnosis of cancer of the gastrointestinal tract 4 years prior to upper endoscopy to the end of follow-up.

Age, sex and Charlson Comorbidity Index at date of primary upper endoscopy are derived from the National Patient Registry. From the same source, any anti-reflux surgery (Nomesco: KJBC00, KJBC01, KJBC02, KJBW96, KJBW97) performed within two years of inclusion are identified.

From The National Prescription Register, data on medical treatment with any antacid and anti-secretory treatment (ATC: MA02B) are identified from 4 years before inclusion to 2 years after. Data on anti-thrombotic drugs and non-steroid anti-inflammatory drugs (ATC: MB01A & MM01A) are also retrieved for the same period to adjust for possible preventive therapy with anti-secretory drugs. From the Civic Register, data on mortality in the follow-up period are retrieved.

Statistical analysis

Data will be analyzed using STATA15. Descriptive analysis of age, sex, Charlson Comorbidity Index, mortality and rate of anti-thrombotic treatment comparing patients treated pharmacologically (in defined daily dosages per year) or surgically (any anti-reflux procedure) for reflux disease using Student's t-test, Chi2-test and Mann-Whitney-U test.

Logistic and multinomial regression will be performed with treatment type (pharmacological, surgical or none) as primary outcome and age, sex, Charlson Comorbidity Index, pharmacological anti-reflux treatment prior to diagnosis, antithrombotic treatment and year of diagnosis as independent variables.

Secondary analysis will be performed using Cox-regression investigating time to initiation of any treatment with age, sex, Charlson Comorbidity Index, pharmacological anti-reflux treatment prior to diagnosis, antithrombotic treatment and year of diagnosis as independent variables. Change in treatment rates over time will also be investigated using national Danish census data and Poisson regression.

Sensitivity analysis excluded patients with anti-thrombotic treatment will be performed.

Funding and Ethical considerations

The study is part of a ph.d. thesis and is funded by The Region of Southern Denmark, The University of Southern Denmark, The Department of Surgery, Kolding Hospital and The Research Council at Little Belt Hospital.

The study requires no informed consent in Danish law as the study is register-based. However, permission from The Danish Data Protection Agency and The Danish Health Data Agency will be obtained before the study is commenced.

None of the involved parties have financial interests or conflicts of interest pertaining to this study.

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