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Introducing national guidelines on perioperative chemotherapy for gastric cancer in Norway: A retrospective audit

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Abstract

Background: In 2006, perioperative chemotherapy with epirubicin, cisplatin/oxaliplatin, and capecitabine was recommended in the National Guidelines for patients with resectable gastric cancer in Norway. We conducted a national audit related to clinical aspects, local organisation and the implementation of this multimodal treatment.
Patients and methods: All Norwegian departments of oncology were asked to submit aggregated data on gastric cancer patients who had started perioperative chemotherapy for cure; departments of surgery were asked to report on patients undergoing resection after preoperative chemotherapy. Data were retrospectively collected.
Results: All 20 departments of oncology and 20 of 21 departments of surgery responded. Of 336 patients operated on for gastric cancer and reported by surgeons, 144 (43%) received preoperative chemotherapy. 169 patients were reported by departments of oncology. 152 (90%) completed the preoperative cycles; 92 (54%) started the postoperative cycles; and 68 (40%) completed all cycles. Toxicity grade ≥ 3, overall and haematological, increased during postoperative compared to preoperative cycles, 50 vs. 34% ($P = 0.012$) and 35 vs. 20% ($P = 0.012$), respectively. Surgical morbidity and mortality were 26 and <2%, respectively. R0 resection was achieved in 86% of surgically treated patients. Five per cent had a complete pathological response (ypT0) and 48% were node negative (ypN0). Within the first year, the National Guidelines were implemented in 19 of 25 hospitals (76%).
Conclusions: In this population-based series, the tolerability of perioperative chemotherapy reported in the MAGIC trial was reproduced. Toxicity grade ≥ 3 was considerable and significantly increased related to postoperative cycles. The National Guidelines were rapidly adopted.

Keywords: Gastric cancer; Perioperative chemotherapy; Guidelines; Surgery; Toxicity

Introduction

In 2006, The Norwegian Gastrointestinal Cancer Group (NGICG) recommended the introduction of perioperative chemotherapy for patients with resectable gastric cancer (GC). The MAGIC trial, published earlier the same year, had demonstrated a significant survival benefit for patients with gastro-oesophageal cancer treated perioperatively with epirubicin, cisplatin and 5-fluorouracil (ECF) compared to those treated with surgery alone.[1] In Norway, the MAGIC regimen was modified by replacing 5-fluorouracil by capecitabine (ECX) and offered the possibility of replacing cisplatin by oxaliplatin (EOX). These recommendations were later adopted in the National Guidelines by the Norwegian Directory of Health.[2]

Based on a single randomised controlled trial,[1] these guidelines transferred the treatment of resectable GC from the surgical to the multidisciplinary domain. Two and a half years after their introduction, NGICG conducted

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a retrospective audit. We wanted to report our experiences with the implementation of perioperative chemotherapy for GC on a national basis, including local organisation, how the guidelines are interpreted and the degree of compliance, and to assess the tolerability of chemotherapy and surgery. Such an investigation would add population-based evidence to a regimen already widely adopted but so far sparsely documented.

Patients and methods

The Norwegian population is 4.8 million. The incidence of GC has been steadily decreasing and the age-adjusted (world) incidence rate per 100 000 person-years is currently 6.6 for men and 3.3 for women.[3] In the Northern Region, GC surgery is centralised to the university hospital in Tromsø, and in the Central Region, to St. Olav's Hospital in Trondheim. In the Western and South-Eastern Regions, many GC patients are treated in low-volume district hospitals. Yet none of the Norwegian university departments would be considered high-volume centres by international standards.[4]

In June 2009, a questionnaire related to the treatment of GC and the implementation of perioperative chemotherapy was sent to all Norwegian departments of surgery and oncology. Those who did not reply within two months were reminded by telephone calls or E-mail. Surgeons were asked to report data on patients operated on with a preoperative curative intent for cancer of the stomach and gastro-oesophageal junction after neoadjuvant chemotherapy. They were also asked to state the number of patients treated without neoadjuvant chemotherapy during the same period and the reason why such therapy had been declined. The questionnaire included a survey on preoperative, multidisciplinary assessment of GC patients and on indications for perioperative chemotherapy.

Surgical patients were identified by diagnosis (ICD-10), and/or surgical procedure (Nordic Classification of Surgical Procedures, NCSP). The majority of data were collected retrospectively from hospital records; three departments provided data from prospective databases.

Oncologists were asked to report on patients who had started preoperative chemotherapy as treatment for cure: the chemotherapy regimens, the number of pre- and postoperative cycles for each patient, haematological and non-haematological toxicity, and treatment related complications were registered. The questionnaire included the same survey on indications for perioperative chemotherapy as the one distributed to surgeons. In departments of oncology, patients were identified by diagnosis, and/or the specific regimen code, according to the Norwegian classification, applied to every cycle of chemotherapy given within the public health system, and/or Cytodose®, an administrative electronic tool for prescribing chemotherapeutic regimens. Patients who for any reason only received chemotherapy postoperatively were not included, nor were patients who received other regimens than ECX, ECF, EOX, and EOF. All departments of oncology provided retrospectively collected data.

Norwegian legislation imposes limitations on the collection and publication of information that may infer with personal integrity without an explicit consent. Accordingly, information on individual patients could not be supplied, and each department aggregated their data.

By dividing the total number of annual resections, with and without chemotherapy, by the mean number of patients with adenocarcinoma and undifferentiated carcinoma reported to The Norwegian Cancer Registry for the years 2007 and 2008, an approximate resection rate was estimated.

As information on individual patients was not registered, continuous data were not available for statistical analysis. Categorical data were analysed using the chi-square test, employing the Yates' correction for expected values less than five.[5] P values less than 0.05 were considered to indicate statistical significance.

Results

One hundred and sixty-nine patients, 109 men (64%) and 60 women (36%), aged 33–79 years, started preoperative chemotherapy. Chemotherapy was administered in 28 localities: in seven university departments of oncology, in 13 departments of general internal medicine or oncology, in two local surgical departments instructed by oncologists, and in six satellite out-patients clinics (Table 1). All departments submitted data. In one district hospital perioperative chemotherapy had not been introduced.

From departments of surgery, information was obtained for 144 patients operated on after preoperative chemotherapy, 92 men (64%) and 52 women (36%), aged 33–79

Table 1
The organisation and logistics of multimodal treatment of gastric cancer in Norway.

Number of patients (%)		
Chemotherapy and surgery in the same hospital	112	(66)
In university hospitals	86	
In district hospitals	26	
Chemotherapy and surgery in different hospitals	32	(19)
Chemotherapy in district hospital, surgery in university hospital	27	
Chemotherapy in university hospital, surgery in district hospital	5	
Missing data on surgery	9	(5)
Chemotherapy in university hospital, no data on surgery	5	
Chemotherapy in district hospital, no data on surgery	4	
No resection after preoperative chemotherapy	16	(9)
University hospital	12	
District hospital	4	