



Cutoff values of major surgical complications rates after gastrectomy

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Received: 30 October 2017 / Accepted: 2 March 2018 / Published online: 31 March 2018
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Abstract

Gastric cancer is one of the most frequent cancers worldwide, and surgical resection remains the mainstay of the therapeutic pathway. Gastrectomy for cancer is still performed in many hospitals, and centralization remains limited to a small number of health systems. Morbidity and mortality after surgery for gastric cancer are surprisingly high. However, while mortality is obviously defined, major morbidity definitions still present some critical points. The aim of this study is to underline the need for universally accepted definitions of major complications and to describe the research agenda of a multicenter, European-based, prospective project launched by the European Chapter of the International Gastric Cancer Association (IGCA), with the goal of providing a list of complications related to gastrectomy for cancer with their definitions.

Keywords Gastric cancer · Gastrectomy · Complications · International consensus

Introduction

Although it is no longer the most frequent cancer in Western countries, gastric carcinoma remains one of the leading causes of death from cancer worldwide [1, 2]. The only hope for definitive care should include radical surgery, eventually with chemo- and/or radiotherapy. Subtotal and total gastrectomies are the most commonly performed operations, by open, laparoscopic and robotic approaches. In the majority of countries centralization of gastric cancer surgery into high-volume centers is not yet widely accepted [3]. 30 days postoperative mortality rate has been reported at about 5% in many Western series, while Eastern centers usually report no more than 2% mortality rates. Some recent national health system surveys have stated a 6.3% (Italy, Agenas PNE study, 2015) and a 2–7% (EU, Eurecca study, 2016) mortality rate

in Europe [4, 5]. Low-volume centers have greater mortality rates, up to 20%, but also in high-volume centers 3–5% mortality 30-days after surgery is claimed, eventually related to high surgical risk cases. Moreover, 90-days mortality rates are even greater, including patient's death after prolonged ICU stay.

Countermeasures should be taken toward these postoperative mortality rates. They include reducing or eliminating the risk factors, early complications recognition by a pro-active attitude, and effective treatment. However, some preliminary assessments should be done: from one side, defining the incidence of complications is of uppermost importance, with the aim of focusing the postoperative actions toward the most frequent clinical scenarios; on the other side, investigating the risk factors may allow a better pre- and intraoperative prophylactic approach. Finally, only by a reliable check of the postoperative course, assessment of the countermeasure effectiveness is possible. Both risk factors, incidence of complications, and outcome analysis are not easily recorded in the absence of clear definitions.

Indeed, postoperative morbidity rates are reported in a very confusing way. From the most cited randomized controlled trials performed in the 1990s, and from the institutional US datasets (NCS-NSQIP, VA-NSQIP), major morbidity is reported in a range of 21–46, 24 and 33%, respectively [6, 7]. Some recent series, including extended interventions, reported about 15% postoperative morbidity rate [8–10]. The range is wide because some different

The article is part of topical collection on Gastric Cancer Surgery.

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definitions have been utilized. This is the rule in the vast majority of the literature, where no reference to a standard list of definitions is provided [10]. For instance, a systematic review published in 2001 retrieved a total of 40 different definitions of anastomotic leakage from 107 studies [11].

Therefore, it is time for a consensus on commonly accepted definitions of complications following surgery for gastric cancer. This paper describes the preliminary steps of a project launched by the European Chapter of the International Gastric Cancer Association (IGCA) in November 2015 to define a comprehensive list of surgery-related, gastric cancer specific complications.

Methods

On November 27, 2015, an informal meeting was held in Verona, Italy, under the auspices of the Italian Research Group for Gastric Cancer (GIRCG), to set the foundations for the establishment of the European Chapter of the International Gastric Cancer Association. The meeting was attended by 20 experts from several countries across Europe. During the meeting, five research projects were launched, the first of which was entitled “Complications after Gastrectomy for Cancer. A European Perspective”.

A Restricted Working Group was appointed during December 2015 and by the beginning of February 2016, 33 European experts were invited to take part in the Enlarged Working Group (EWG). The list of these experts was formed starting from the participants in the EURECCA project and the GIRCG membership, and taking into account a well-documented commitment to surgical treatment of gastric cancer and the availability of a reliable gastrectomy database in their home institutions. By mid-February, 31 invited experts (Table 1) confirmed their participation and the acceptance of the rules of the project, designed to be mainly Web based.

Six rounds of questions were administered and then examined (Table 2). In every round, each expert was asked to answer specific questions rather than commenting and suggesting modifications to a statement. The questions enabled the experts to analyze both the list of complications and their definitions. The answers to the questions in each round were then made available to the other experts, more frequently in a blinded fashion, for a series of discussion rounds (we adopted the modified Delphi-method), over a period of 6 months. When a strong agreement (with more than 80% of the experts agreeing) was achieved, the RWG moved to the subsequent round of questions. When the answers of the experts were different, the RWG summarized the various opinions and then rephrased the question into a dichotomic form. In some cases, the answers of some experts that turned out to be particularly significant for the discussion were made available to all EWG experts; then, a

Table 1 European experts participating in the project

Country	Experts
Denmark	Lone Susanne Jensen
France	Christophe Mariette Guillaume Piessen
Germany	Ines Gockel Arnulf H. Hölscher Hans-Joachim Meyer Daniel Reim
Ireland	Thomas Murphy John V. Reynolds
Italy	Maurizio Degiuli Giovanni De Manzoni Uberto Fumagalli Paolo Morgagni Franco Roviello
The Netherlands	Wobbe O de Steur Suzanne S. Gisbertz Henk Hartgrink Johanna W. van Sandick
Poland	Wojciech Kielan Piotr Kołodziejczyk Wojciech Polkowski
Portugal	Paulo Matos da Costa Lucio Lara Santos
Russia	Mikhail Ter-Ovanesov
Spain	Manuel Pera
Sweden	Jan Johansson
Switzerland	Stefan Mönig Paul M. Schneider
UK	William Allum Richard Hardwick Shaun R. Preston

further round of answers was obtained, until an increasing convergence of opinions occurred such that a strong agreement was deemed to be reached.

We considered only gastrectomy performed by abdominal way (esophageal–gastric junction, Siewert type 2 and 3 treated by laparotomy or laparoscopy were included). The definitions of complications were based on clinical experience rather than literature review. Preliminary results of this project were presented in Lisbon, Portugal, on June 16, 2016, during the “Esophageal and Gastric Cancer Initiative” conference.

Results

In round 1, preliminary questions were discussed. First of all, most experts agreed that postoperative general complications should be recorded and included in the list, being frequently the main cause of failure of the therapeutic path. A lot of discussion was devoted to the optimal timing for postoperative assessment. Initially, the day of discharge

Table 2 Question rounds and complication topics

Round 1 preliminary	Should general complications be included? When should the “Complications recording sheet” be filled in? (at discharge, 30 days, 90 days, etc....) Should complications be categorized into subgroups?
Rounds 2, 3, 4 general complications	Do you prefer “General” or “Medical” Complications? Simple list of generic dysfunctions subdivided by system vs detailed list with all complications for each system? Sepsis and infection in general vs surgical subgroup?
Round 5 intraoperative complications	Do you believe that intraoperative complications should be included in the list of surgical complications? (1) Damage to vessels and organs (2) Intraoperative bleeding
Round 6 postoperative complications	(1) Postoperative bleeding (2) Postoperative occlusion (3) Postoperative bowel perforation (4) Duodenal leak (5) Anastomotic leak (6) Pancreatic fistula (7) Postoperative pancreatitis (8) Collections without fistula (9) Postoperative biliary leakage (10) Postoperative chylous ascites (11) Postoperative lymphorrhea (12) Delayed gastric emptying

of the patient was suggested as the most intuitive and simple by many experts. However, after a number of blinded resubmissions, an agreement was obtained according to which 90 days after surgery was deemed to be the proper timing for evaluation. In this round, it was also decided not to categorize complications into separate subgroups (at first, the RWG had proposed the following subgroups: intraoperative/early postoperative/septic complications/late postoperative).

In rounds 2, 3, and 4, it was decided that the term “general” was better than “medical” for nonsurgical complications, and those adverse events were classified as a complete list of all major neurologic, cardiovascular, respiratory, liver, kidney, and infectious diseases. A clear definition was offered for each complication. Round 5 was devoted to intraoperative complications. First, the experts were asked if they believed that intraoperative damage to vessels and organs and intraoperative major bleeding should be included in the list (the answers were positive). Next, the experts were asked to answer questions geared to providing a precise definition of such complications. Round 6 was the most challenging, as it involved analyzing postoperative surgical complications. Starting from a list of 12 main complications outlined by the Italian Research Group for Gastric Cancer in a previous multicentric work [12], the experts were asked to comment and modify this list and their definitions.

Final confirmation rounds were then necessary for the approval of the final list (rounds 7, 8, and 9) and for drafting and checking this paper (rounds 10 and 11). Overall, the project involved a 14-month, multicentric, work.

Discussion

While mortality data, notwithstanding lack of agreement over 30- or 90-day, or in-hospital reporting, are unequivocal, the definition of morbidity and complications lacks rigor and consistency. Postoperative complications specifically related to gastrectomy have never been clearly defined, and thus they are listed with a wide range of percentages in the existing literature. Hence, the time is ripe for finding a consensus on commonly accepted definitions of major complications after gastric cancer surgery under the auspices of scientific societies whose mission is gastric cancer research and care. A successful completion of this task would enable the standardized comparisons between published clinical data, with a potentially positive impact on the effective management of gastric cancer after gastrectomy.

The goal of facilitating comparison of outcomes between different series, and finally to determine standards of care, is further supported by recent Asian studies which have highlighted the benefit of standardized reporting for detailed comparisons of the differences between Western and Eastern surgeons [13, 14]. Some other classifications of postoperative complications are available in the literature. The Common Terminology Criteria for Adverse Events (CTCAE) published in 2009 by the NIH (USA) defines adverse events as “any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure” [15]. However, CTCAE definitions are of limited clinical value, being

based on physiopathological more than clinical parameters. For instance, “Intra-abdominal hemorrhage” is defined as “a disorder characterized by bleeding in the abdominal cavity”. This sentence clearly does not allow to define if a given clinical picture should be considered or not a major complication: a patient with bloody drainage, hemodynamically stable, without lowering of the red blood cells count nor need for transfusion, enters in this definition in the same way that a patient with massive hemorrhage, taken to the operating room for emergent operation in haemorrhagic shock. The task of grading the severity of complications was fully answered by the most common and universally recognized classification of postoperative complications, the “Clavien–Dindo” (C–D) classification [16, 17]. C–D is treatment related, scores between 1 and 5, and easy to use and to share; thus, it has been broadly employed for postoperative outcome reporting. C–D has been recently translated into a Comprehensive Complications Index (CCI), which is a Web-based calculator combining multiple complications and giving a final score from 0 to 100 [18, 19]. C–D and CCI should be the basis for the EGCA project. However, both are not specific for gastric cancer surgery; most important, both do not give a definition of complications. A number of clinical pictures should be reported in the postoperative course, eventually without need for direct intervention, thus belonging to the C–D class 1 or 2, even though they involve some heavy and costly clinical consequences. For example, anastomotic leak conservatively treated, without possibility of endoscopic treatment or need for percutaneous or surgical drainage, for which a patient remains in ICU for long time, is actually only C–D grade 1 or 2, but clearly represents a major complication that should be recognized and reported. Furthermore, a patient vomiting for 20 days and being unable to eat clearly has a delayed gastric emptying of clinical relevance, but still it is considered C–D 1 or 2.

A very important study was done by Low and colleagues in the field of esophageal surgery [20]. Starting from the acknowledgement that “... *there were marked differences in the way in which complications were described and documented (...)* Lack of standardization has hampered outcome assessment after esophagectomy”, this work listed 49 items subdivided into 9 groups, including both general and specific adverse events. Four complications specific to esophagectomy were precisely defined (anastomotic leak, conduit necrosis, chyle leak, recurrent nerve palsy). Esophageal surgery is actually centralized in a small number of centers with medium and high volume, due to the rarity of the disease and to the high complexity of the surgical procedure. Because gastrectomy is performed in a greater number of centers, sometimes with very low caseload, this may have a greater impact on clinical practice.

Another study was published by the Japanese Clinical Oncologic Group (JCOG), assessing complications after

surgery for nine different cancers, including gastric cancer [21]. The Clavien–Dindo grading of severity was the basis of this paper, which does not aim at defining each complication. Seventy-two adverse events were included, some of which may be observed after gastrectomy (but also after other abdominal oncological procedures). The list published by the JCOG is difficultly handled, making a total of about 400 possible combinations. It does not provide a clear definition, resulting in possible variability of interpretation, and maintains the limitations of the C–D classification.

In conclusion, a project is ongoing under the auspices of the European Chapter of the International Gastric Cancer Association, with the aim of identifying complications related to gastrectomy for cancer and to make an agreement on clear and precise definitions. Further possible developments include the setting of a “complications recording sheet”, and an official assessment of the incidence of complications across specialized centers. This will finally allow determination of a benchmark for complications.

Compliance with ethical standards

Conflict of interest and source of funding For all authors, none was declared.

Research involving human participants and/or animals The current study does not involve human participants or animals. Hence, no Institutional Review Board’s prior approval was required.

Informed consent The current study does not involve human participants. No informed consent was therefore necessary.

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