



Emerging Concepts Impacting Head and Neck Cancer Surgery Morbidity

Ohad Ronen · K. Thomas Robbins · Ashok R. Shaha ·
Luiz P. Kowalski · Antti A. Mäkitie · Ewa Florek · Alfio Ferlito

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ABSTRACT

All treatment modalities for head and neck cancer carry with them a risk of adverse events. Head and neck surgeons are faced with significant challenges to minimize associated morbidity and manage its sequelae. Recognizing situations in which a surgical complication is an

adverse event inherent to the procedure can alleviate the psychologic impact a complication might have on the treatment team and minimize external and internal pressures. Focusing on the complications that can be effectively modified, future complications can be avoided. Also, some surgical morbidities may not be preventable, necessitating the option to reconsider whether the incidents should be labeled toxic reactions rather than a complication. This discussion highlights some of the areas in which additional research is needed to achieve

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O. Ronen (✉)
Head and Neck Surgery Unit, Department of
Otolaryngology-Head and Neck Surgery, Affiliated
With Azrieli Faculty of Medicine, Galilee Medical
Center, Bar-Ilan University, POB 21, Nahariya, Safed
2210001, Israel
e-mail: Ohadr@gmc.gov.il

K. T. Robbins
Department of Otolaryngology-Head and Neck
Surgery, Southern Illinois University School of
Medicine, Springfield, IL, USA

A. R. Shaha
Head and Neck Service, Department of Surgery,
Memorial Sloan Kettering Cancer Center, New York,
NY, USA

L. P. Kowalski
Department of Otorhinolaryngology-Head and
Neck Surgery, A.C. Camargo Cancer Center, São
Paulo, Brazil

L. P. Kowalski
Department of Head and Neck Surgery, University
of São Paulo Medical School, São Paulo, Brazil

A. A. Mäkitie
Department of Otorhinolaryngology-Head and
Neck Surgery, University of Helsinki and Helsinki
University Hospital, Helsinki, Finland

E. Florek
Laboratory of Environmental Research, Department
of Toxicology, Poznan University of Medical
Sciences, Poznan, Poland

A. Ferlito
Coordinator of International Head and Neck
Scientific Group, Padua, Italy

the goal of minimizing the impact of surgical morbidity.

Keywords: Head and neck; Cancer; Complication; Morbidity; Toxicity

Key Summary Points

Head and neck surgeons are faced with significant challenges to minimize associated morbidity and manage its sequelae.

In some situations, a surgical complication is an adverse event inherent to the procedure and may not be preventable.

These incidents should be labeled “toxic” reactions rather than a “complication.”

Often ignored are the psychological stresses imposed on the surgical team.

The morbidity and mortality rounds are cornerstone for addressing surgical complications and quality improving, and it is recommended they use the SBAR tool and root-cause analysis model.

INTRODUCTION

Surgery remains the mainstay for treatment of most head and neck cancers [1]. Other modalities play important roles as well, particularly radiation therapy. While all treatment options carry with them a risk of adverse events, the morbidity associated with surgery is most common. Thus, the head and neck surgeon is faced with significant challenges to minimize associated morbidity and manage its sequelae.

While there is an abundance of reports that focus on operative procedures and patient characteristics as causative factors for surgical morbidity, there remain overarching considerations that are important to consider. These include issues of differentiating morbidity that

is considered a toxicity versus a complication; existential factors that increase the risk of surgical morbidity; and abrogating measures that impact the personal well-being of the patient and treatment team.

The notable progress in reconstruction with free flaps has made it possible for head and neck surgeons to perform a wide range of radical procedures with high rates of local disease control and usually acceptable cosmetic and functional results. However, in a specific group of patients with even more advanced-stage disease, such procedures can be associated with significant functional deficits. Although surgery could be a curative option, it could be impossible to rehabilitate function. This dilemma was the origin of the idea of “functional inoperability.” In the opinion of the group of Dutch experts, operations such as those involving bilateral hypoglossal nerve resection should be avoided [2].

Recognizing situations in which a surgical complication is an adverse event inherent to the procedure can alleviate the psychologic impact a complication might have on the treatment team and minimize external and internal pressures. Focusing on the complications that can be effectively modified, future complications can be avoided. In this way, the medical system as a whole may benefit. Also, multidisciplinary team discussion can be less biased, and the patient-informed consent process can become more direct and realistic.

MORBIDITY COMPARISONS BETWEEN CHEMOTHERAPY AND SURGERY: TOXICITY VERSUS COMPLICATION

To examine the issue of toxicity on a basic level, it is insightful to consider the inherent quality of the therapeutic agent such as a drug or a molecule interacting with the body. Given that it has to be delivered according to a specific protocol, the dose must be adjusted to the patient’s age, weight, and surface area, as well as to renal and liver functions. Most drug metabolism reactions take place in the liver. Disease

states can significantly impair these processes. The condition of the kidneys is important in the case of drugs that are excreted mainly in the urine. Impaired function of these organs may increase the risk of formation of significant concentrations of the drug or its metabolite and may reveal the drug's toxic effects. A stringent adherence to protocols should be kept; otherwise, any unwanted consequences might be considered as negligence and cannot be related only to the drug's inherent potential toxicity [3]. The same human factor applies to surgery. As in drug delivery, the surgeon should "deliver" the surgical procedure to the patient, adhering to accepted protocols, while adjusting for patient habitus and specific anatomy, comorbidities, and possible interactions with other medications. Again, deviations from accepted practices can lead to unwanted consequences.

SURGICAL MORBIDITY: COMPLICATION VERSUS TOXICITY

As noted above, if surgery is performed according to accepted practices, and if an unwanted consequence occurs, the morbidity may be interpreted as a toxicity rather than a complication. In comparison with nonsurgical treatment, it is interesting to note that the morbidity related to head and neck cancer treated with radiation and/or chemotherapy is more often considered a toxicity [4]. Thus, the implication is that morbidity encountered when delivering nonsurgical interventions is less related to the therapist and more to the inherent adverse reactions of the therapy itself. While this denotation may be partly explained because surgery tends to be more variable relative to its nonsurgical counterparts, the sequence of events of surgery often clouds the ability to categorize morbidity as a complication versus a toxic reaction.

Additional insights as to why surgically associated morbidities are generally considered as complications may be gained by examining the subject of causality. Thus, for radiation and chemotherapy, a clear demarcation appears to exist between the morbidity from accepted

consequence of the therapy versus that which is operator dependent. In other words, there are well-documented side effects from chemotherapy agents and therapeutic doses of radiation therapy, most of which are defined as toxicities. Such toxicities can range from mild to life threatening and categorized as grades 1–5 [4]. Also, most toxicities can be predicted, while only a minority is unpredictable. Nevertheless, there remains a clear division and conscious separation between the intended treatment effect and the unwanted side effect or toxicity. In contrast, surgery can result in immediate and sometimes devastating morbidity. Although not intended, it is more often linked to the surgical procedure and to the treatment team. Thus, the team, and more specifically the operator performing the procedure, is usually recognized as being the instigator of the complication rather than the nature of the surgery itself. Less commonly, the event may be labeled a toxicity when the surgeon has limited control over its development. Even when a treatment plan is decided in a multidisciplinary manner, unlike chemotherapy, which is given in a standard protocol by any member of the treating team, surgery treatment is delivered through the surgeon and is not standardized by nature.

The informed consent process adds an additional layer of complexity when denoting surgical morbidity. For example, in situations when a specific complication is expected, and its known incidence has been discussed with the patient preoperatively, ironically, the informed consent process highlights the issue of causality. In other words, even in situations where surgeons have discussed a specific morbidity, they still may not have prevented it. This contrasts with delivering a drug where, although its toxicity is known, and patients are informed of it, the expected and unwanted side effect is perceived as happening by chance and is not caused by physicians delivering it. In a systematic review of patients' recollection and understanding of informed consent a wide range was found, with some articles reported as low as 21% of patients' recall of potential risks and complications of their medical procedure [5].

In terms of related factors that may distinguish between complications and toxicities, there are a number of considerations. While surgical morbidities occur under a variety of circumstances [6], they can arise as a mere “undesirable result of surgery” or related to the general illness of the patient including postoperative care [7]. The latter situation has an important timeframe distinction that defines a surgical complication as an event that occurs in the postoperative setting and related to the surgical procedure. Thus, late surgical morbidities can be seen days and even weeks after the surgical procedure itself. An example of a late complication is the patient with comorbidity who experiences a postoperative undesirable complex course in the intensive care unit, such as prolonged mechanical ventilation with failed weaning off the respirator, with accompanied undesired pressure ulcers, sepsis, etc. Nevertheless, it is possible in scientific reports to compare surgical complication rates more accurately provided that definitions factor in the timing and extent of the complication event.

Hospitals in the USA are required to report their 30-day mortality rate as one of the outcome measures used to evaluate surgical safety and compare hospital quality. When a mortality case within a 30-day period is linked to a surgical procedure, it is often difficult to relate it to a reliable, measurable, and actionable event during the surgical procedure and to isolate it from other related medical causes. For example, preoperative anemia was found to be a risk factor for 30-day postoperative mortality in head and neck microsurgical reconstruction in a database of over 2300 patients [8]. It is difficult to decide whether the anemia is directly linked to the death or rather the blood transfusions and general condition of the patient were the culprit.

A necessary distinction should be made between an undesirable “complication” and an expected “sequela” that is inherent to the procedure [9]. Since surgery, as opposed to radiation and chemotherapy, is a treatment that has a limited and short time range, complications and sequela can often be interchanged. Thus, as long as an event is expected, it should be considered as a sequela and not a complication.

However, this distinction is rather vague, as patients are preoperatively informed of many possible events that might occur during surgery, and although all of them can be expected at a specific rate, if they occur they are still considered a complication and not a sequela. This distinction calls for self-assessment of any complication rate, as different surgeons and facilities present different surgical complication rates of the same procedure.

A suggested classification of the treatment sequelae based on the casual factor might be useful both in alleviating the burden of liability as well as to decrease future complications. Such a possible classification might be to divide the sequelae into (1) patient-related (comorbidities, etc.), (2) tumor-related (site, stage, infiltration, etc.), and (3) treatment-related complications (adverse surgical complication, combined treatment modalities, preoperative radiotherapy (RT), etc.)

MAJOR VERSUS MINOR COMPLICATION

There is no clear definition to distinguish between major and minor complications in head and neck surgeries. While some differentiate major and minor complications on the basis of the treatment needed to address the consequences caused by the complications [10], others assessed whether the complication involved the surgical field directly or other organs [11].

In 2004, Dindo, Clavien et al. from Zurich, Switzerland proposed a surgical complication five-grade classification based on the intervention needed to manage the complication [12]. Grade I is defined as any deviation from the surgery that does not need a pharmacologic or other intervention, while grade V is defined as death of the patient. A letter “d” suffix denotes a long-lasting disability after patient’s discharge, such as paralysis of the vocal cord following a recurrent laryngeal nerve injury. The Clavien–Dindo classification was assessed on hypothetical cases as well as real-life cases and was found to have a moderate to high interobserver reliability with a statistically significant association with length of hospital stay [13, 14].

The American College of Surgeons initiated a National Surgical Quality Improvement Program (ACS NSQIP) that resulted in an online risk calculator based on real data from 585 hospitals, and uses patient predictors to predict the chance that patients will have any of 18 different outcomes within 30 days following surgery [15]. The ACS-NSQIP calculator provides estimated length of stay, serious complications, pneumonia, renal failure, cardiac complication, surgical site infection, and death, among other complications. Although there is no definition for serious complication, this category includes both direct surgical outcome (surgical site infection, wound dehiscence, return to the operating room) as well as other medical complications (cardiac arrest, myocardial infarction, pneumonia, progressive renal insufficiency, pulmonary emboli). With regard to head and neck surgeries, studies found that this online calculator did not demonstrate efficacy for predicting postoperative complications in head and neck that require microvascular reconstruction [16, 17].

There were efforts by other disciplines to categorize major and minor complications in specific situations using the Delphi technique in an international cooperation. In the above Delphi round, the authors used a specific key question of the influence of the complication on the decision to abandon an indicated adjuvant radiotherapy [18]. This perspective on a major complication might be extremely relevant in patients undergoing complex head and neck surgeries, as radiotherapy is advocated for many indications (positive margins, extracapsular lymph node extension, advanced T and N classification, lymphovascular involvement, and perineural spread), and a delay of more than 6 weeks can reduce the beneficial effect radiotherapy has.

ROOT-CAUSE ANALYSIS

Several studies estimated that around half of surgical complications are preventable [19, 20]. This has led to a root-cause analysis of surgical complication identifying the cause of it and suggesting prevention measurements [21].

According to Donabedian, who coined this term, potential factors for any adverse event are human fatigue, communications, proficiency, environment/equipment, protocols, and barriers. Preventive measures targeting communication, checklists, reporting systems, and the use of evidence-based medicine can decrease surgical complications [22].

PREEMPTIVE STRATEGIES FOR RISK REDUCTION

In recent years, additional efforts have been made to reduce surgical morbidity through interventions that are overarching or general. For example, preoperative checklists done prior to and upon entering the operating room have become more widely used [23]. These checklists help reduce unwanted morbidities such as wrong-site/wrong-side surgery and other anticipated problems during surgery.

Categorization of surgical patients through assigning comorbidity indices that correlate with high surgical risks has also had an impact. Also, high-risk operations have been defined as those that carry a mortality rate of 5% or more [24]. Preoperative evaluations with anesthesiologists and other consultants such as internal medicine help to prepare patients for the physical stress associated with oncologic head and neck surgery. A recent systematic review of evidence-based optimal perioperative care for patients undergoing head and neck surgery with free flap reconstruction cited a variety of interventions to reduce morbidity. These include preoperative carbohydrate treatment, pharmacologic thromboprophylaxis, perioperative antibiotics in clean-contaminated procedures, corticosteroid and antiemetic medications, short-acting anxiolytics, goal-directed fluid management, opioid-sparing multimodal analgesia, frequent flap monitoring, early mobilization, and the avoidance of preoperative fasting, which can enhance recovery [25].

Surgical complications, or adverse events, are traditionally divided into early and late. Both complications can be anticipated to a greater degree when patients head and neck area were exposed to radiation, the patient is

malnourished, is obese, or has diabetes [26–28]. Body habitus and general fitness represent additional factors in which the risk of morbidity is influenced. Studies show that more than one-third of Americans are obese or significantly overweight and at increased surgical risk [29]. Older age by itself, however, does not seem to increase surgery-related complication [30–32]. A recent systematic review conducted by Garip et al. demonstrated that tobacco smoking was significantly associated with an increased risk of overall surgical complications and hematoma formation [33]. Another prevalent comorbidity that is associated with postoperative complications is sleep apnea that can be sometimes an unrecognized morbidity [34]. Thus, patient-related factors should also be taken into consideration preoperatively as they can increase complications and even mortality [35–38].

Guidelines and index scoring also represent preemptive approaches to identify high-risk patients for surgical morbidity in order to implement preventive measurements. Two commonly used methods are American Society of Anesthetists (ASAS) grading and Physiological and Operative Severity Score for the enumeration of Mortality and morbidity (POSSUM) score [39, 40]. The POSSUM score integrates several physiologic and operative parameters into a predicted mortality and morbidity rate. A similar risk calculator based on real big data was constructed by the American College of Surgeons “National Surgical Quality Improvement Program” [41], yet its use in microvascular free flap transfer reconstruction may be less substantiated [16, 17, 42]. Application of these tools can assist in patient counseling and multidisciplinary decision-making for various surgical interventions [43].

A recent study by Taylor et al. investigated over 92,000 patients undergoing a thyroidectomy and parathyroidectomy in the USA between 2015 and 2018. They compared the performance of the American Society of Anesthesiologists (ASA) classification and the modified five-point frailty index (mFI-5) for predicting complications and found the former to be more accurate in predicting mortality and serious postoperative morbidity [44].

Sanabria et al. proposed a score to predict postoperative complications in patients with head and neck cancer aged > 70 years: male sex (2 points), two or more comorbidities (2 points), clinical stage IV (3 points), bilateral neck dissection (2 points), and the need for reconstruction (2 points) [45]. The higher the score, the higher the risk of complications (> 50% of risk for scores higher than 6). Fancy et al. also proposed a risk stratification system for patients older than 80 years: ASA II [odds ratio (OR) 1.87] or III (OR 4.50), need for additional operations (OR 5.04), and duration of surgery (OR 1.08) as predictors for 30-day severe complications [46].

Patients should be carefully selected for complex head and neck surgeries on the basis of comorbidities and patient characteristics. A study by Piccirillo et al. compared two different comorbidity indices (Charlson Comorbidity Index and the Klabunde Index) and disease-specific indices (the Washington University Head and Neck Index and the Head and Neck Cancer Index) for outcome [47]. While the investigated indices provided useful prognostic information, there was no advantage of one index over the other in overall survival prediction. However, a study that used a combined Charlson-Age Comorbidity Index found that it had an independent relative risk of 1.43 for death within a year in patients undergoing salvage surgery for recurrent head and neck surgery cancer [48].

Surgical complications can be measured specific to the organ or tissue that has been affected, such as a neurologic deficit or according to the patient quality of life (QoL). Measuring QoL fields allows for comparison between different treatment modalities and enables a nondichotomic labeling of the complication [49]. Evaluating QoL parameters also has the benefit of comparing new surgical technologies with other techniques and with other treatment modalities [50].

Extensive head and neck cancer tissue, in either the primary or regional sites, also increases complication risk. In these circumstances, the so-called complications are done “intentionally” during surgery to achieve better tumor extirpation. Examples can be

intentionally excision of involved motor or sensory nerves, major veins and arteries, muscles, or even partial or complete resections of the cartilaginous framework of the larynx or trachea. Surgeons should observe preoperative imaging for such possible surgical consequences and alert the patients in advance during the informed consent process. It remains an ethical and medicolegal issue whether to label these events as complications since they were very likely to happen, or as surgical toxicity, and part of this treatment modality.

Enhanced recovery after surgery (ERAS) protocols were developed in colorectal vascular, gastric, orthopedic, and other surgery fields and addressed pre- and intraoperative care elements. Implementation of ERAS protocols can be challenging, so key elements for successful implementation were suggested by Huber et al. [51] These key elements include engaging clinicians, focusing on patients undergoing major resection with free-flap reconstruction, having individuals with quality improvement expertise embedded in clinical teams, and a measurement audit and feedback system.

Blood transfusion is associated with higher risk for postoperative medical and surgical complications and hospital readmission in head and neck reconstruction surgeries, although it is unclear whether they serve as a surrogate marker or a direct cause [52].

RECOGNITION OF ACCEPTABLE RATES OF SURGICAL MORBIDITY

Even at the hands of the most experienced surgeon, complications occur at an accepted rate. Surgeons should constantly monitor their data and calculate their surgery success rates and complications sequelae. Deviation from the published rates can be differ from one facility to another, dependent on several factors. Among such factors can be the population that is being treated. A referral center that specializes in treating complex cases, reoperated surgeries, recurrences, post-radiation surgical fields, failures, patients with severe and complex comorbidities, disease that necessitate

multidisciplinary surgical teams, and challenging postoperative caring teams are expected to present higher “complication” rates. Misunderstanding and negative bias is expected if data from different centers who treat patients with different characteristics are wildly publicized. To avoid such a problem, detailed patient characteristics, including the above parameters, are needed whenever complications are reported. In turn, this will allow better communication and comparison between centers and improved research quality investigating outcomes in such complex head and neck cancer cases.

Physicians should be well trained in managing both chemotherapy-induced toxicities as well as surgical complications. How complications or toxicity is managed very much determines outcome, as poorly managed complications are associated with worse outcomes. There is a paucity of manuscripts that compare management options of complications. One example is the nonsurgical treatment of pharyngocutaneous fistula after laryngectomy. A recent systematic review on this topic by Locatello et al. found only seven manuscripts that included 27 patients altogether [53]. This is in contrast to management of chemotherapy-induced neutropenic sepsis, where there are national protocols on proper handling of these life-threatening situations [54].

MORBIDITY AND MORTALITY ROUNDS

The morbidity and mortality (M&M) rounds are cornerstone for addressing surgical complications and quality improvement. These M&M rounds, as they are often called, should be conducted in an introspective and nonjudgmental atmosphere with participation of the surgical team and use of a root-cause analyses resulting in preventive measures. In a recent study, Laury et al. investigated a proposed otolaryngology-specific M&M curriculum [55]. The authors found a significant improvement in the quality and educational value of the M&M presentation after the implementation of the

situation, background, assessment, and review/recommendations (SBAR) tool. A national multispecialty survey that was conducted in the USA has found that all otolaryngology programs conducted M&M rounds, but it was not uniform in its content [56]. The rounds did not vary largely from other disciplines, and they were regarded as contributing to improved patient care, residents' education, and culture change.

An example of expected success rates of an elective surgery can be found in the recent publication of quality indicators for the diagnosis and management of primary hyperparathyroidism published this year by an international expert panel. One of their quality indicators states that patients undergoing surgery for primary hyperparathyroidism should have a cure rate approaching 98% [57]. Obviously, a medical group or a single surgeon should calculate personal data for comparison with accepted success rates. In situations where the rate of an adverse events is similar to published data, or whether the difference is related to other factors as discussed previously, there is a rationale to denote the adversity as a toxicity rather than a complication of the surgery.

Surgical skills and volume are related to complication rates. In a study of over 30,000 total thyroidectomies performed by over 1000 surgeons in NY, a higher rate of hypocalcemia and temporary tracheotomy was found in low-volume surgeons [58]. A prospective trial conducted in Italy has shown that residents enrolled in a dedicated and programmed training could perform total thyroidectomy with an operative time similar to senior surgeons after 25–30 procedures with no increase in perioperative complications [59].

Other ways of improving surgical skills and reducing complication are the use of simulators and dissection labs. In a randomized double-blinded study on a small group of general surgery residents, virtual reality training has shown to reduce operative time and reduce complications [60]. In another trial, assessing 955 trivial cataract cases, residents whose training involved simulators had half the complication rates compared with residents who did not complete a simulation training [61].

THE PSYCHOLOGICAL IMPACT OF SURGICAL MORBIDITY

While much emphasis is given to the physical impact whenever morbidity occurs related to surgical intervention, the emotional stress imposed on the patient should not be ignored. This can be related to psychological reactions of the patient. More recent qualitative analyses have been performed to improve the specific aspects of this [62]. Patients who experienced surgical complications had worse physical and mental well-being as well as significantly worse postoperative psychosocial outcomes at 12 months or longer following surgery [62].

More often ignored are the psychological stresses imposed on the surgical team, particularly the operating surgeon. They are often considered to be “second victims” in the event of surgical complications, during or after the surgery [63]. These incidents can have significant, deep, and long-lasting effects on the health professionals involved. Despite this, team members including surgeons usually receive limited support from their medical workplace [64]. Key factors in developing a second victim syndrome include: experience; attribute complication of poor judgment or concentration, lack of knowledge or skills, or errors in the health system; female surgeon, “exhausted” or tired; feeling demoralized or unrewarded; and perceive an imbalance between professional and personal life [63]. Some of these factors could be addressed by use of a flat hierarchy within the department and good leadership, which plays an essential role. Understanding these factors allows us to appreciate the vulnerability of the “second victim” and their responses, and in turn coping mechanisms they adopt. For major complications, the emotions are sometimes so strong that surgeons are at high psychological risk. Pinto et al. found that 36.2% of surgeons experienced acute traumatic stress levels following poor patient outcomes, and following major surgical complications, surgeons have double the risk of developing major depression [65]. Shifting the term “complication” to a more subtle, less accusing and libeling term might

have a significant effect on surgeon's well-being that can eventually be transferred back to better managing their patients later on.

CONCLUSIONS

The morbidity related to head and neck cancer surgery remains an important problem. While much research has been done to identify and ameliorate causative factors, additional emerging strategies focusing on overarching measures are needed. Also, some surgical morbidities may not be preventable, necessitating the option to reconsider whether the incidents should be labeled toxic reactions rather than a complication. This discussion highlights some of the areas in which additional research is needed to achieve the goal of minimizing the impact of surgical morbidity.

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