Head and neck cancer surgery during the COVID-19 pandemic

COVIDSurg Collaborative

Published in:
Cancer

DOI:
10.1002/cncr.33320

Publication date:
2020

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
COVIDSurg Collaborative (2020). Head and neck cancer surgery during the COVID-19 pandemic: An international, multicenter, observational cohort study. *Cancer*. https://doi.org/10.1002/cncr.33320

Original Article

Head and Neck Cancer Surgery During the COVID-19 Pandemic: An International, Multicenter, Observational Cohort Study

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BACKGROUND: The aims of this study were to provide data on the safety of head and neck cancer surgery currently being undertaken during the coronavirus disease 2019 (COVID-19) pandemic. **METHODS:** This international, observational cohort study comprised 1137 consecutive patients with head and neck cancer undergoing primary surgery with curative intent in 26 countries. Factors associated with severe pulmonary complications in COVID-19–positive patients and infections in the surgical team were determined by univariate analysis. **RESULTS:** Among the 1137 patients, the commonest sites were the oral cavity (38%) and the thyroid (21%). For oropharynx and larynx tumors, nonsurgical therapy was favored in most cases. There was evidence of surgical de-escalation of neck management and reconstruction. Overall 30-day mortality was 1.2%. Twenty-nine patients (3%) tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) within 30 days of surgery; 13 of these patients (44.8%) developed severe respiratory complications, and 3.51 (10.3%) died. There were significant correlations with an advanced tumor stage and admission to critical care. Members of the surgical team tested positive within 30 days of surgery in 40 cases (3%). There were significant associations with operations in which the patients also tested positive for SARS-CoV-2 within 30 days, with a high community incidence of SARS-CoV-2, with screened patients, with oral tumor sites, and with tracheostomy. **CONCLUSIONS:** Head and neck cancer surgery in the COVID-19 era appears safe even when surgery is prolonged and complex. The overlap in COVID-19 between patients and members of the surgical team raises the suspicion of failures in cross-infection measures or the use of personal protective equipment. ***Cancer* 2020;0:1-13**.

LAY SUMMARY:
- Head and neck surgery is safe for patients during the coronavirus disease 2019 pandemic even when it is lengthy and complex.
- This is significant because concerns over patient safety raised in many guidelines appear not to be reflected by outcomes, even for those who have other serious illnesses or require complex reconstructions.
- Patients subjected to suboptimal or nonstandard treatments should be carefully followed up to optimize their cancer outcomes.
- The overlap between patients and surgeons testing positive for severe acute respiratory syndrome coronavirus 2 is notable and emphasizes the need for fastidious cross-infection controls and effective personal protective equipment.

KEYWORDS: coronavirus, coronavirus disease 2019 (COVID-19), head and neck cancer, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), surgery.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coronavirus infection, has led to a rapid reduction of elective surgery due to a lack of capacity and concerns over patient safety.[1] The problems are highlighted in surgical oncology, where a delay or cancellation of surgery may directly lead to poor outcomes or, at worst, increased loss of life. Recent international data from 1128 patients known to be suffering from COVID-19 at the time of surgery showed a severe pulmonary complication rate of 51.2% and a mortality rate of 23.8%.[2] Surgeons operating in the upper aerodigestive tract are at particularly high risk of contracting COVID-19, with many severe cases and some fatalities reported.[3-5]

In head and neck cancer surgery, published guidelines for the COVID-19 pandemic[3,5-21] have been formulated on the basis of reasonable assumptions, experience from severe acute respiratory syndrome (SARS),[7] and consensus reached with the Delphi method[16] rather than patient-level data. For squamous cell carcinomas (SCCs) of the oropharynx (OP) and larynx (L), there is equipoise between the effectiveness of primary surgery and (chemo)radiotherapy; avoiding surgery has been recommended. A delay of surgery appears pragmatic for more indolent thyroid malignancies. For other head and neck tumors such as oral cavity (OC) SCCs and salivary gland malignancies, it is of considerable importance that nonsurgical management is frequently suboptimal, and considerable dilemmas remain. New guidelines have recommended the

Collaborating authors are listed in the supporting information.

Additional supporting information may be found in the online version of this article.

DOI: 10.1002/cncr.33320, **Received:** July 30, 2020; **Revised:** September 26, 2020; **Accepted:** October 8, 2020, **Published online** Month 00, 2020 in Wiley Online Library (wileyonlinelibrary.com)

avoidance of procedures presumed to be high-risk, such as tracheostomy and free-flap reconstruction, and de-escalation to palliative treatment for the elderly or those with a poor performance status.[16]

Typically, SCCs of the head and neck have a short tumor volume doubling time,[22] so delays in diagnosis and treatment engender a high risk of upstaging. Surgery can be prolonged, can involve direct airway manipulations and aerosol-generating procedures, and can necessitate complex reconstruction such as microvascular free tissue transfer. Routine reliance on critical care for postoperative recovery is common to many institutions, and this may increase the risk of cross-infection with the SARS-CoV-2 virus. However, in oral SCCs, salivary malignancies, and other such cases, the opportunities for a cure are reliant on surgery, and without evidence-based alternative modalities, the imperative is to schedule surgery without delay. Anecdotally, the perceived risk of uncontrolled locoregional disease in patients with advanced SCC of the head and neck has led many services to preserve head and neck oncology despite the huge resource constraint, whereas most other oncology services have been paused.

Among these pragmatic assumptions, there is a paucity of data to inform practice. Tangible opportunities exist to capture real-world data that might affect cancer surgery through the COVID-19 pandemic iteratively and with immediate effect. With this rationale, the Global Health Research Unit of the National Institute for Health Research launched COVIDSurg for oncology (https://globalsurg.org/covidsurg/), with head and neck cancer–specific fields incorporated early in its evolution and with an international collaborative group designing it. The objective of this first output for the head and neck data from COVIDSurg is to describe surgical practice and safety during the early period of the pandemic.

The aims are 1) to describe the range of surgeries performed within the first 3 months of the pandemic and to estimate the extent of therapeutic migration and surgical de-escalation by comparison with historical data, 2) to determine patient safety regarding 30-day outcomes for mortality and severe pulmonary complications attributable to COVID-19, and 3) to determine the 30-day incidence of COVID-19 in the surgical team.

MATERIALS AND METHODS

Design

This international, observational cohort study included patients with a diagnosis of head and neck malignancy who underwent primary surgery with curative intent during the COVID-19 pandemic. Only routine, anonymized data were collected, and ethics and data release were managed though an ethics committee and an independent data monitoring committee. The study was registered at each site as either a clinical audit or a service evaluation; this reflected that the regulatory permissions required varied from country to country.

Inclusion Criteria

Patients were eligible for study inclusion from the date of that hospital's first admission of an individual testing positive for a SARS-CoV-2 infection up to 3 months from that date or the data lock on June 17, 2020, whichever came first. Each participating hospital included consecutive adult patients undergoing head and neck cancer surgery with curative intent. Surgery was defined as a procedure performed by a surgeon in an operating theater under general or local anesthesia. Head and neck cancer was defined as any malignant diagnosis above the clavicle excluding localized nonmelanoma skin, hematopoietic, intra-ocular, and primary brain malignancies. The study was publicized globally through the International Federation of Head and Neck Oncological Societies, the International Academy of Oral Oncology, the European Association of Craniomaxillofacial Surgery, and other national associations.

Outcome Measures

Outcome measures were mortality, complications, and a SARS-CoV-2 infection within 30 days of surgery. Specifically, the primary measure of interest for patient safety was the diagnosis of severe pulmonary complications with either a positive SARS-CoV-2 diagnosis or a clinical diagnosis of COVID-19. Secondary outcome measures included the TNM stage, tumor subsite, histology, and specific ablative and reconstructive surgery undertaken to evaluate the impact of the COVID-19 pandemic on case selection and treatment pathways. The diagnosis of a SARS-CoV-2 infection within 30 days of the operation in any member of the operating team was also recorded.

Diagnosis of SARS-CoV-2 Infection

Laboratory testing for SARS-CoV-2 infection was based on viral RNA detection by quantitative reverse transcription–polymerase chain reaction. Sampling, including nasal swabs and/or bronchoalveolar lavage, and analyses were performed according to local hospital protocols. Because quantitative reverse transcription–polymerase chain reaction testing was not available at all participating hospitals at all times, patients were also included on the basis of alternative laboratory tests or clinical or radiological findings. This was done by a senior physician and was based on the clinical presentation of symptoms highly suspicious for a SARS-CoV-2 infection, including cough, fever, and/or a myalgia diagnosis, or was based on computed tomography (CT) of the chest according to local protocols. This composite diagnostic criterion was applied to both head and neck patients and health care workers on the index operating team.

Data Collection and Follow-Up

REDCap was used to record all data through its web application. Recorded demographic variables included the country and hospital of operation, age, sex, and American Society of Anesthesiologists (ASA) physical status classification. Cardiac comorbidity was reported with the Revised Cardiac Risk Index.[23] Head and neck data included the tumor subsite, neck metastasis management (elective or therapeutic), flap or other reconstruction, airway management, and location of postoperative care. The status of the clinical environment (hot vs cold) was recorded, and this reflected the relative mixing or separation of known or suspected COVID-19 admissions with oncology cases. Cold sites were defined as those hospitals that did not admit patients with COVID-19 or in which there was complete segregation of wards and operating and critical care environments. Hot sites were defined as those in which there was incomplete or no segregation of services. The magnitude of surgery was categorized[24,25] as minor (minor/intermediate) or major (major/complex major). Screening was defined as a preoperative SARS-CoV-2 swab or CT scan in the 72 hours before surgery. The community SARS-CoV-2 incidence was categorized as low (<25 cases per 100,000) or high (≥25 cases per 100,000) during February, March, and April 2020 and was derived from the relevant registries.[26-28]

Complications at 30 days were categorized with the Clavien-Dindo grade,[29] and reconstructive outcomes were recorded. Before the locking of the data set for analysis, the senior local principal investigator for each hospital was asked to confirm data completeness and that all eligible patients had been entered into the database.

Statistical Analysis

Continuous data were summarized as medians and interquartile ranges, and categorical data were described as frequencies of counts and percentages. Proportions were compared with a 2-sided Fisher exact test, and a significance level of 5% was used to determine statistical significance. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated with univariate logistic regression. All statistical analyses were performed with R version 3.6.1. The detailed protocol is available at https://globalsurg.org/cancercovidsurg/.

RESULTS

Patient Data

Data were collected for 1137 patients from 133 hospitals in 26 countries who were undergoing primary surgery with curative intent. The greatest numbers of cases were ascertained from the United Kingdom (350 patients [31%]), the United States (220 patients [19%]), Italy (165 patients [15%]), and Spain (84 patients [7%]). The number of cases per week was highest from March 16 to 23 (188 surgeries).

Baseline Characteristics of the Patients

The baseline characteristics of the patients and tumors are shown in Table 1. Fifty-seven percent of the patients were male, and 62% were 60 years old or older. Thirty-three percent of the patients had an ASA score ≥ 3, and 11% had an Eastern Cooperative Oncology Group performance status ≥ 2. Patients had T3/T4 tumors in 31% of cases and positive neck disease in 32%. OC was the commonest cancer site in 38% of cases (n = 433), and it was followed by the thyroid (21% [n = 235]) and cutaneous (14% [n = 157]). Notably, L and OP accounted for only 8% and 6%, respectively (87 and 73 cases). Subsequent analyses are presented with categorization into OC and non-OC groups. Seventy-eight percent of the hospital sites were categorized as hot, and 15% of the patients were in high SARS-CoV-2 incidence areas. Fifty-one percent of the patients (579 of 1127) were screened for COVID-19 by laboratory tests or CT chest imaging. There was an equal split between major and minor surgery. The commonest comorbidities were hypertension (40%), diabetes mellitus (14%), and respiratory problems (11%: chronic obstructive pulmonary disease [6%] and asthma [5%]; Table 2).

Surgery

Eighty-nine percent of the operations (1015 of 1137) included surgical excision of a primary tumor, and 50% (567 of 1137) included a neck dissection. The proportions of patients with OC tumors undergoing neck dissection were as follows: T1, 30% (40 of 133); T2, 74% (87 of 118); T3, 88% (44 of 50); T4, 83% (87 of 105); and unknown T stage, 27 (total, 63% [271 of 433]). This is less than would normally be expected and

TABLE 1. Characteristics of Patients and Tumors

Characteristic	Value	Oral, No. (%)	Oropharynx, No. (%)	Hypopharynx, No. (%)	Larynx, No. (%)	Salivary, No. (%)	Skin, No. (%)	Thyroid, No. (%)	Other, No. (%)	Total, No. (%)
Total		433 (38)	73 (6)	12 (1)	87 (8)	54 (5)	157 (14)	235 (21)	86 (8)	1137
Age	20-29 y	6 (1)	0 (0)	0 (0)	1 (1)	0 (0)	1 (1)	24 (10)	0 (0)	32 (3)
	30-39 y	12 (3)	1 (1)	0 (0)	2 (2)	5 (9)	2 (1)	38 (16)	4 (5)	64 (6)
	40-49 y	37 (9)	8 (11)	0 (0)	6 (7)	3 (6)	5 (3)	44 (19)	6 (7)	109 (10)
	50-59 y	94 (22)	23 (32)	1 (8)	15 (17)	11 (20)	19 (12)	52 (22)	22 (26)	237 (21)
	60-69 y	135 (31)	21 (29)	8 (67)	33 (38)	17 (31)	37 (24)	42 (18)	26 (30)	319 (28)
	70-79 y	97 (22)	16 (22)	3 (25)	23 (26)	14 (26)	44 (28)	32 (14)	20 (23)	249 (22)
	80-89 y	46 (11)	4 (5)	0 (0)	7 (8)	4 (7)	39 (25)	3 (1)	6 (7)	109 (10)
	≥90 y	6 (1)	0 (0)	0 (0)	0 (0)	0 (0)	10 (6)	0 (0)	2 (2)	18 (2)
Sex	Female	186 (43)	20 (27)	5 (42)	18 (21)	24 (44)	43 (27)	151 (64)	35 (41)	482 (42)
	Male	246 (57)	53 (73)	7 (58)	69 (79)	30 (56)	113 (72)	83 (35)	51 (59)	652 (57)
	Unknown	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	1 (0)	0 (0)	3 (0)
ASA physical status score	1	79 (18)	15 (21)	2 (17)	11 (13)	9 (17)	15 (10)	54 (23)	12 (14)	197 (17)
	2	206 (48)	30 (41)	7 (58)	45 (52)	29 (54)	60 (38)	141 (60)	50 (58)	568 (50)
	3	136 (31)	28 (38)	3 (25)	30 (34)	15 (28)	78 (50)	39 (17)	22 (26)	351 (31)
	4	12 (3)	0 (0)	0 (0)	1 (1)	1 (2)	3 (2)	1 (0)	2 (2)	20 (2)
	Unknown	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	1 (0)
ECOG/WHO PS	0	248 (57)	51 (70)	7 (58)	47 (54)	40 (74)	65 (41)	180 (77)	49 (57)	687 (60)
	1	123 (28)	18 (25)	3 (25)	33 (38)	8 (15)	58 (37)	46 (20)	25 (29)	314 (28)
	2	52 (12)	1 (1)	1 (8)	7 (8)	5 (9)	24 (15)	6 (3)	9 (10)	105 (9)
	3	8 (2)	2 (3)	0 (0)	0 (0)	1 (2)	6 (4)	1 (0)	3 (3)	21 (2)
	4	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	4 (3)	0 (0)	0 (0)	5 (0)
	Unknown	2 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	2 (1)	0 (0)	5 (0)
T stage	T1	133 (31)	23 (32)	2 (17)	38 (44)	10 (19)	37 (24)	111 (47)	10 (12)	364 (32)
	T2	118 (27)	21 (29)	3 (25)	11 (13)	17 (31)	50 (32)	52 (22)	7 (8)	279 (25)
	T3	50 (12)	2 (3)	3 (25)	17 (20)	6 (11)	22 (14)	19 (8)	6 (7)	125 (11)
	T4	105 (24)	4 (5)	4 (33)	15 (17)	7 (13)	8 (5)	9 (4)	12 (14)	164 (14)
	Unknown	27 (6)	23 (32)	0 (0)	6 (7)	14 (26)	40 (25)	44 (19)	51 (59)	205 (18)
N stage	N0	294 (68)	14 (19)	6 (50)	67 (77)	33 (61)	99 (63)	127 (54)	38 (44)	678 (60)
	N1	51 (12)	38 (52)	2 (17)	7 (8)	3 (6)	14 (9)	58 (25)	17 (20)	190 (17)
	N2/3	64 (15)	17 (23)	4 (33)	9 (10)	6 (11)	9 (6)	12 (5)	13 (15)	134 (12)
	Unknown	24 (6)	4 (5)	0 (0)	4 (5)	12 (22)	35 (22)	38 (16)	18 (21)	135 (12)
M stage	M0	364 (84)	64 (88)	12 (100)	79 (91)	34 (63)	113 (72)	184 (78)	64 (74)	914 (80)
	M1	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (1)	7 (3)	1 (1)	10 (1)
	Unknown	69 (16)	9 (12)	0 (0)	8 (9)	19 (35)	43 (27)	44 (19)	21 (24)	213 (19)
RCRI	0	326 (75)	57 (78)	10 (83)	61 (70)	39 (72)	104 (66)	200 (85)	69 (80)	866 (76)
	1	81 (19)	14 (19)	2 (17)	21 (24)	12 (22)	34 (22)	30 (13)	11 (13)	205 (18)
	2	19 (4)	1 (1)	0 (0)	5 (6)	2 (4)	14 (9)	5 (2)	6 (7)	52 (5)
	≥3	7 (2)	1 (1)	0 (0)	0 (0)	1 (2)	5 (3)	0 (0)	0 (0)	14 (1)
Hot vs cold unit	Cold	59 (14)	11 (15)	3 (25)	28 (32)	10 (19)	47 (30)	79 (34)	16 (19)	253 (22)
	Hot	374 (86)	62 (85)	9 (75)	59 (68)	44 (81)	110 (70)	156 (66)	70 (81)	884 (78)
Community SARS-CoV-2 incidence	Low	371 (86)	63 (86)	8 (67)	70 (80)	43 (80)	146 (93)	189 (80)	75 (87)	965 (85)
	High	62 (14)	10 (14)	4 (33)	17 (20)	11 (20)	11 (7)	46 (20)	11 (13)	172 (15)
Grade of surgery	Major	151 (35)	28 (38)	9 (75)	71 (82)	7 (13)	20 (13)	225 (96)	51 (59)	562 (49)
	Minor	280 (65)	45 (62)	3 (25)	16 (18)	47 (87)	137 (87)	10 (4)	35 (41)	573 (50)
	Unknown	2 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0)

Abbreviations: ASA, American Society of Anesthesiologists; ECOG, Eastern Cooperative Oncology Group; PS, performance status; RCRI, Revised Cardiac Risk Index[23]; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

TABLE 2. Baseline Comorbidities

Comorbidity	Oral (n = 433), No. (%)	Not Oral (n = 704), No. (%)	Total (n = 1137), No. (%)
Current smoker	106 (24)	95 (13)	201 (18)
Asthma	19 (4)	43 (6)	62 (5)
Chronic kidney disease	14 (3)	28 (4)	42 (4)
COPD	26 (6)	43 (6)	69 (6)
Congenital cardiac abnormality	1 (0)	4 (1)	5 (0)
Congestive heart failure	10 (2)	18 (3)	28 (2)
Dementia	6 (1)	7 (1)	13 (1)
Diabetes mellitus	60 (14)	95 (13)	155 (14)
Hypertension	180 (42)	271 (38)	451 (40)
Myocardial infarction	31 (7)	44 (6)	75 (7)
Peripheral vascular disease	17 (4)	26 (4)	43 (4)
Stroke/TIA	26 (6)	26 (4)	52 (5)
Other	182 (42)	265 (38)	447 (39)

Abbreviations: COPD, chronic obstructive pulmonary disease; TIA, transient ischemic attack.

indicates a significant de-escalation of neck management. Thirty-one percent of the patients (355 of 1137) had reconstruction, but only around half of those received free flaps requiring microvascular anastomosis (17% [191 of 1137]). Of the operations for OC tumors, 52% (223 of 433) included some form of reconstruction: a free flap in 33% (143 of 433), a local flap in 7% (32 of 433), a regional pedicled flap in 9% (39 of 433), and obturation in 2% (8 of 433). In 13% of OC cases (57 of 433), surgeons stated that their reconstructive choice had been compromised in comparison with normal practice.

Airway Management

Airway management was extubation in 72% (822 of 1137), tracheostomy in 17% (192 of 1137), and overnight intubation in 3% (39 of 1137). Three percent (32 of 1137) reported a change in airway technique in comparison with their normal practice, and this was mostly attributable to changes in airway management for 6% of OC tumors (26 of 433). Overall, 11% (120 of 1137) reported some change or compromise to their surgical management related to the effect of the COVID-19 pandemic, but this was approximately doubled for OC tumors at 20% (80 of 433).

Postoperative Complications

The 30-day complications for 1130 patients are described in Table 3. The commonest complications were wound dehiscence/infection, which was seen in 11% (119 of 1130), and pneumonia, which was seen in 4% (40 of 1130). The 30-day postoperative mortality rate was 1.2% (14 of 1130). Among the 351 patients who underwent flap reconstruction and had 30-day outcomes, there were 4 total flap failures (1%) and 14 partial failures (4%); 12 patients had a viable reconstruction with a persistent fistula (3%).

Incidence of Postoperative SARS-CoV-2/COVID-19 and Severe Pulmonary Complications

A diagnosis of COVID-19 or a positive test for SARS-CoV-2 was found for 29 of 1127 patients (3%) within 30 days of surgery; 25 were laboratory diagnoses. Severe pulmonary complications attributed to COVID-19 occurred in 13 patients (44.8% of the positive patients). For these 13 patients, the 30-day outcome was discharge (n = 10) or death (n = 3). COVID-19–related deaths within 30 days of surgery occurred, therefore, in less than 0.3% of all operated patients but in 10.3% of those infected. Factors associated with severe pulmonary complications in COVID-19–positive patients were determined by univariate analysis (Table 4 and Fig. 1). There were significant correlations with an advanced T stage (OR for T4, 11.5; 95% CI, 1.33-99.2), node-positive disease (OR for N2/3, 6.94; 95% CI, 1.53-31.36), and admission to critical care (OR, 3.85; 95% CI, 1.28-11.58). There were trends that did not reach statistical significance for patients undergoing surgery in hot surgical units (P = .084) and for patients who were screened for SARS-CoV-2 preoperatively (P = .092). Notably, there were not significant associations with age; ASA score; Eastern Cooperative Oncology Group performance status; Revised Cardiac Risk Index; tumor site; or any aspect of surgery, including free-flap reconstruction, or airway management, including tracheostomy.

COVID-19 Diagnosis in the Surgical Team

Members of the surgical team developed COVID-19 within 30 days in 3.5% of operations (40 of 1130; Table 5 and Fig. 2). There was a significant association with operations in which the patient subsequently tested positive for SARS-CoV-2 within 30 days (OR, 10.3; 95% CI, 4.1-25.8); remarkably, after 24% of the procedures in which a patient tested positive, a member of the head and neck surgical team developed COVID-19 within 30 days. There were also associations with a high community SARS-CoV-2 incidence (OR, 4.0; 95% CI, 2.1-7.7), with patients who had been screened for SARS-CoV-2 preoperatively (OR, 2.9; 95% CI, 1.4-6.1), with

TABLE 3. 30-Day Complications and Outcomes

	Oral (n = 427), No. (%)	Not Oral (n = 703), No. (%)	Total (n = 1130), No. (%)
Complication			
Acute kidney injury	5 (1)	1 (0)	6 (1)
ARDS	2 (0)	1 (0)	3 (0)
Bleeding requiring transfusion	18 (4)	6 (1)	24 (2)
Cardiac arrest requiring CPR	3 (1)	2 (0)	5 (0)
Deep vein thrombosis	0 (0)	2 (0)	2 (0)
Graft/flap failure	12 (3)	1 (0)	13 (1)
Myocardial infarction	2 (0)	0 (0)	2 (0)
Pneumonia	21 (5)	19 (3)	40 (4)
Pulmonary embolism	0 (0)	2 (0)	2 (0)
Sepsis	3 (1)	4 (1)	7 (1)
Septic shock	1 (0)	1 (0)	2 (0)
Stroke	0 (0)	2 (0)	2 (0)
Urinary tract infection	4 (1)	2 (0)	6 (1)
Wound sepsis or dehiscence	74 (17)	45 (6)	119 (11)
Other complication	69 (16)	91 (13)	160 (14)
30-d outcomes			
Alive: discharged home	404 (95)	681 (97)	1085 (96)
Alive: discharged to a rehabilitation center	2 (0)	4 (1)	6 (1)
Alive: remained admitted to hospital	11 (3)	13 (2)	24 (2)
Alive: transferred to another hospital	1 (0)	0 (0)	1 (0)
Died	9 (2.1)	5 (1)	14 (1.2)
Highest Clavien-Dindo grade as inpatient up to 30 d[a]			
None	314 (74)	557 (79)	871 (77)
Grade 1: deviation from postoperative course without pharmaceutical intervention	16 (4)	60 (9)	76 (7)
Grade 2: pharmaceutical intervention only	42 (10)	56 (8)	98 (9)
Grade 3A: surgical, endoscopic, or radiological reintervention (not under general anesthetic)	19 (4)	13 (2)	32 (3)
Grade 3B: surgical, endoscopic, or radiological reintervention (under general anesthetic)	23 (5)	10 (1)	33 (3)
Grade 4A: life-threatening complication requiring intensive care management (single-organ dysfunction)	5 (1)	4 (1)	9 (1)
Grade 4B : life-threatening complication requiring intensive care management (multiple-organ dysfunction)	1 (0)	1 (0)	2 (0)
Unknown	2 (0)	1 (0)	3 (0)

Abbreviations: ARDS, acute respiratory distress syndrome; CPR, cardiopulmonary resuscitation.
[a]Clavien-Dindo grade 5 is death; it is reported under 30-day outcomes.

oral tumor site operations (OR, 5.3; 95% CI, 1.24-22.7), with the use of tracheostomy (OR, 2.6; 95% CI, 1.3-5.1), and with surgical complication (OR, 3.5; 95% CI, 1.7-7.1). The data for the community incidence of COVID-19 typically showed 100 to 200 infections per 100,000 population per month for high-risk regions in the period of case ascertainment. The frequency of infections that we have demonstrated in members of the surgical teams reflects an at least 1 order of magnitude higher risk than the community incidence, and this suggests that occupational exposure was the predominant mechanism.

DISCUSSION

These data allow a unique international perspective on the safety of head and neck cancer surgery during the COVID-19 pandemic and on changes in practice brought about in response to perceived risk. Although observational, the data reflect significant changes in practice arising from concerns about the perceived vulnerability of patients with cancer, cancelled surgery, and published guidelines. Although the first COVID-19 peak has passed in Europe and New York at the time of this writing, it is evident that Europe faces a significant second peak. These data have lasting international significance and will inform practice for future outbreaks and for other regions with a rising incidence of COVID-19.

There are several limitations to the methodology used that limit interpretation of the data. Regarding the case definition, these observational data take a pragmatic approach to the diagnosis of COVID-19 and reflect shifting standards and resources of hospitals and health systems and at the national level in the early months of this pandemic. Prospective interventional studies would doubtless involve a more rigorous testing protocol to define COVID-19 cases. It is possible that undiagnosed SARS-CoV-2 infections or infections causing only minor symptoms may be underreported at the 30-day endpoint. The data show some noteworthy associations but cannot be conclusive about causation and mechanism

TABLE 4. Univariate Correlations Between Severe Pulmonary Complications of COVID-19 and Patient, Operation, and Hospital Characteristics

		Severe COVID-19 Pulmonary Complication, No. (%)			
Covariate	Value	No	Yes	Total, No.	*P*-value
Age	<40 y	95 (99)	1 (1)	96	.829
	40-69 y	650 (99)	9 (1)	659	
	≥70 y	372 (99)	3 (1)	375	
Sex	Female	475 (99)	5 (1)	480	1
	Male	639 (99)	8 (1)	647	
ASA grade	1 or 2	751 (99)	7 (1)	758	.374
	3 or 4	365 (98)	6 (2)	371	
ECOG/WHO PS	0/1	983 (99)	11 (1)	994	.656
	≥2	129 (98)	2 (2)	131	
Smoker	No	919 (99)	11 (1)	930	1
	Yes	198 (99)	2 (1)	200	
Tumor subsite	Larynx, hypo/oropharynx	171 (99)	1 (1)	172	.903
	Oral	421 (99)	6 (1)	427	
	Other	294 (99)	3 (1)	297	
	Thyroid	231 (99)	3 (1)	234	
Reconstruction	Free flap	185 (98)	4 (2)	189	.69
	Other reconstruction	162 (99)	2 (1)	164	
Airway management	Extubation at completion of procedure	810 (99)	7 (1)	817	.202
	Other	118 (98)	2 (2)	120	
	Tracheostomy	188 (98)	4 (2)	192	
Care in ITU from theater	No	912 (99)	7 (1)	919	**.02**
	Yes	203 (97)	6 (3)	209	
Clinical T stage	T1	361 (100)	1 (0)	362	**.037**
	T2	274 (99)	3 (1)	277	
	T3	123 (98)	2 (2)	125	
	T4	157 (97)	5 (3)	162	
Clinical N stage	N0	671 (100)	3 (0)	674	**.004**
	N1	184 (97)	5 (3)	189	
	N2/3	129 (97)	4 (3)	133	
Clinical M stage	M0	898 (99)	10 (1)	908	1
	M1	10 (100)	0 (0)	10	
General anesthetic	No	76 (99)	1 (1)	77	.602
	Yes	1041 (99)	12 (1)	1053	
Screened preoperatively	No	546 (99)	3 (1)	549	*.092*
	Yes	571 (98)	10 (2)	581	
Surgical complications[a]	No	1001 (99)	10 (1)	1011	.149
	Yes	116 (97)	3 (3)	119	
Grade of surgery	Major	552 (99)	8 (1)	560	.418
	Minor	563 (99)	5 (1)	568	
Community SARS-CoV-2 incidence	High	169 (98)	3 (2)	172	.432
	Low	948 (99)	10 (1)	958	
RCRI	0	852 (99)	10 (1)	862	.671
	1	201 (99)	2 (1)	203	
	2	50 (98)	1 (2)	51	
	≥3	14 (100)	0 (0)	14	
Hot vs cold unit	Cold	250 (100)	0 (0)	250	*.084*
	Hot	867 (99)	13 (1)	880	

Abbreviations: ASA, American Society of Anesthesiologists; COVID-19, coronavirus disease 2019; ECOG, Eastern Cooperative Oncology Group; ITU, intensive therapy unit; PS, performance status; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

P

A severe pulmonary complication of COVID-19 was defined as a diagnosis of COVID-19 or a SARS-CoV-2–positive test and pneumonia, acute respiratory distress syndrome, or a pulmonary embolism.

[a]A surgical complication was defined as either a deep or superficial wound infection or wound dehiscence.

(particularly the direction of cross-infection or whether patients were infected pre-, peri-, or postoperatively). Finally, the data reflecting changes in, or the avoidance of, surgery can be only best estimates against historical data.

Case ascertainment aligns well with global geographic regions experiencing the highest incidence of COVID-19 during this period; the United Kingdom, Italy, Spain, and New York City were particularly well represented.

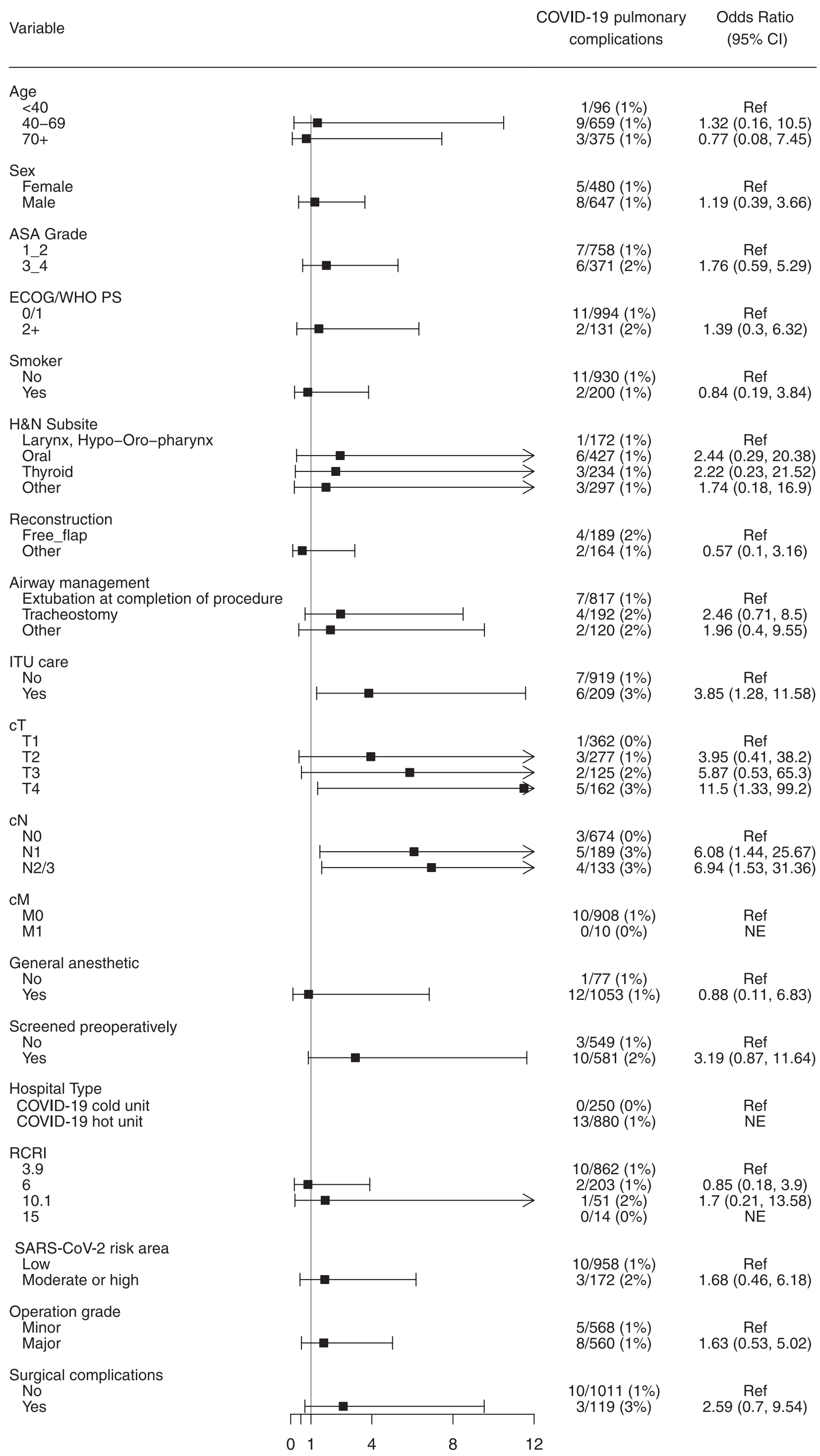

Figure 1. Forest plot of associations with severe pulmonary complications of COVID-19 in patients. ASA indicates American Society of Anesthesiologists; CI, confidence interval; COVID-19, coronavirus disease 2019; ECOG, Eastern Cooperative Oncology Group; H&N, head and neck; ITU, intensive therapy unit; NE, not evaluable; PS, performance status; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

TABLE 5. Univariate Correlations Between COVID-19 Developing in a Member of the Surgical Team Within 30 Days and Patient, Operation, and Hospital Characteristics

		Member of Surgical Team Diagnosed With COVID-19 Within 30 d, No. (%)			
Covariate	Value	No	Yes	Total, No.	*P*
Age	<40 y	91 (97)	3 (3)	94	1
	40-69 y	635 (96)	24 (4)	659	
	≥70 y	361 (97)	13 (3)	374	
Sex	Female	463 (97)	16 (3)	479	.871
	Male	621 (96)	24 (4)	645	
ASA grade	1 or 2	726 (96)	31 (4)	757	.174
	3 or 4	360 (98)	9 (2)	369	
ECOG/WHO PS	0/1	956 (96)	36 (4)	992	1
	≥2	127 (97)	4 (3)	131	
Smoker	No	899 (97)	30 (3)	929	.207
	Yes	188 (95)	10 (5)	198	
Tumor subsite	Larynx, hypo/oropharynx	170 (99)	2 (1)	172	**<.001**
	Oral	400 (94)	25 (6)	425	
	Other	295 (99)	2 (1)	297	
	Thyroid	222 (95)	11 (5)	233	
Reconstruction	Free flap	176 (94)	12 (6)	188	.823
	Other	154 (94)	9 (6)	163	
Airway management	Extubation	791 (97)	24 (3)	815	**.012**
	Other	118 (98)	2 (2)	120	
	Tracheostomy	177 (93)	14 (7)	191	
Care in ITU from theater	No	887 (97)	31 (3)	918	.533
	Yes	199 (96)	9 (4)	208	
Clinical T stage	T1	345 (96)	16 (4)	361	.285
	T2	269 (97)	8 (3)	277	
	T3	120 (96)	5 (4)	125	
	T4	150 (93)	11 (7)	161	
Clinical N stage	N0	646 (96)	27 (4)	673	.2
	N1	185 (98)	4 (2)	189	
	N2/3	124 (94)	8 (6)	132	
Clinical M stage	M0	869 (96)	37 (4)	906	1
	M1	10 (100)	0 (0)	10	
General anesthetic	No	77 (100)	0 (0)	77	.106
	Yes	1010 (96)	40 (4)	1050	
Screened preoperatively	No	538 (98)	10 (2)	548	**.003**
	Yes	549 (95)	30 (5)	579	
Patient positive for SARS-Cov-2/COVID-19[a]	No	1065 (97)	33 (3)	1098	**<.001**
	Yes	22 (76)	7 (24)	29	
Hot vs cold unit	Cold	245 (98)	5 (2)	250	.174
	Hot	842 (96)	35 (4)	877	
Surgical complications[b]	No	980 (97)	29 (3)	1009	**.002**
	Yes	107 (91)	11 (9)	118	
Grade of surgery	Major	533 (96)	24 (4)	557	.199
	Minor	552 (97)	16 (3)	568	
Community SARS-CoV-2 incidence	Low	931 (97)	24 (3)	955	**<.001**
	Moderate or high	156 (91)	16 (9)	172	
RCRI	0	831 (97)	30 (3)	861	.837
	1	192 (96)	9 (4)	201	
	2	50 (98)	1 (2)	51	
	≥3	14 (100)	0 (0)	14	

Abbreviations: ASA, American Society of Anesthesiologists; COVID-19, coronavirus disease 2019; ECOG, Eastern Cooperative Oncology Group; ITU, intensive therapy unit; PS, performance status; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

P-values in bold are <.05, statistically significant, and in italics are between .05 and <.1.

[a]Positivity for SARS-Cov-2/COVID-19 was defined as a diagnosis of COVID-19 or a SARS-CoV-2–positive test and pneumonia, acute respiratory distress syndrome, or a pulmonary embolism.

[b]A surgical complication was defined as either a deep or superficial wound infection or wound dehiscence.

Postoperative COVID-19/SARS-CoV-2 and severe pulmonary complications were seen in 3% and 1% of patients, respectively. The overall 30-day postoperative mortality rate was 1.2%, which is similar to pre-COVID data.[30,31] Patients were more likely to develop severe pulmonary complications of COVID-19 if they had an advanced tumor stage or if they had been admitted to critical care. However, the absolute risks were approximately 3%, and this should

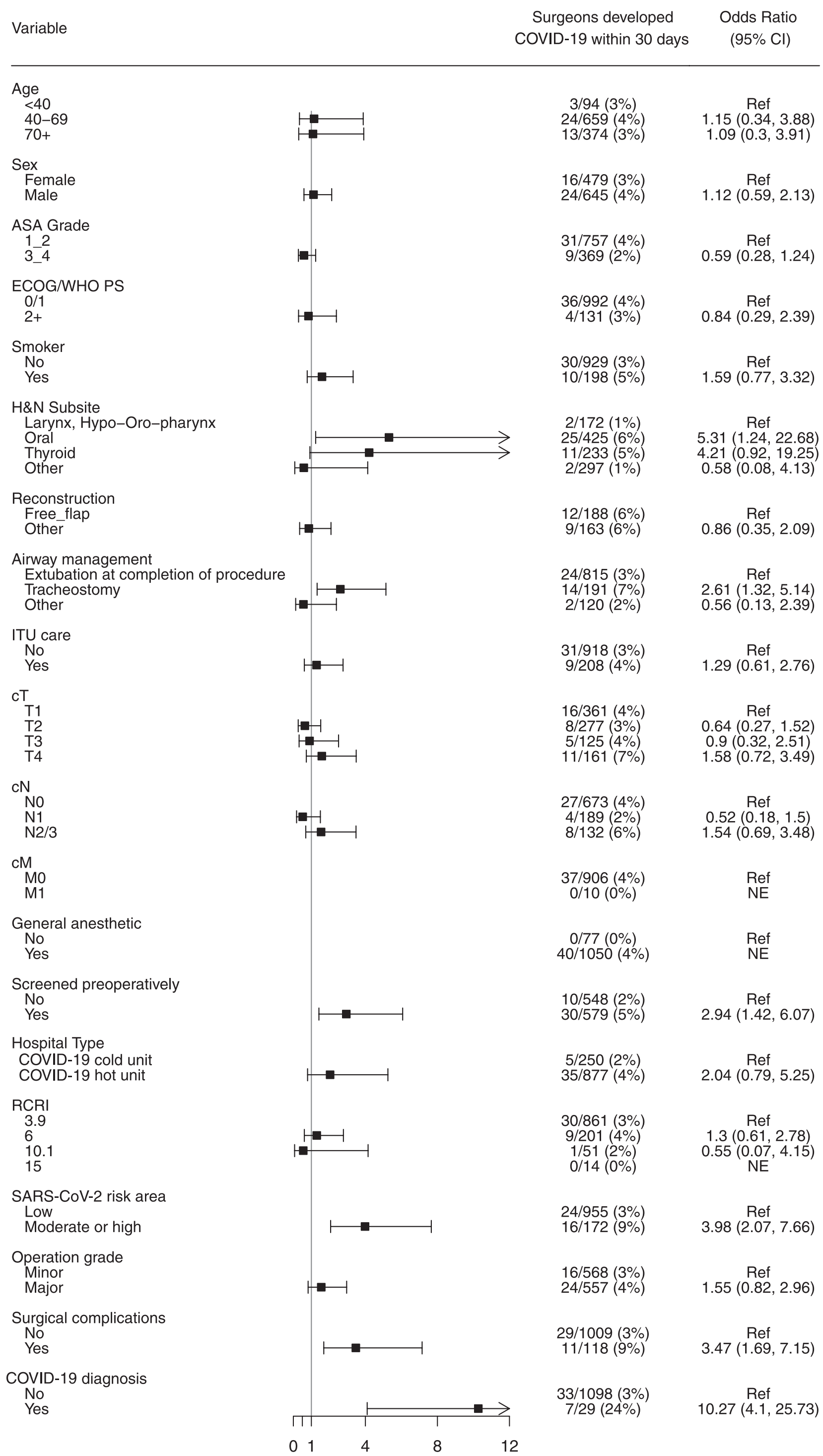

Figure 2. Forest plot of associations with the diagnosis of COVID-19 in members of the surgical team. ASA indicates American Society of Anesthesiologists; CI, confidence interval; COVID-19, coronavirus disease 2019; ECOG, Eastern Cooperative Oncology Group; H&N, head and neck; ITU, intensive therapy unit; NE, not evaluable; PS, performance status; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

be considered from the perspective of the dismal prognosis for these patients if appropriate cancer treatment had been withheld. The rates of severe respiratory complications and mortality among those developing postoperative COVID-19 were 44% (13 of 29) and 10.3% (3 of 29), respectively. It is speculated that these might have been avoided by the uniform adoption of patient segregation, screening, and use of personal protective equipment (PPE). There were nonsignificant trends toward higher patient risk if surgery was performed in hot units and in areas with a higher community SARS-CoV-2 incidence, although it is recognized that such dichotomization of risk is imprecise. Many head and neck surgery teams could not relocate to cold sites because of their requirement for specialist skills and other equipment. It is reassuring that even for high-risk areas and hot units, the risk of severe COVID-19 pulmonary complications was relatively modest. Medical and surgical complications were within the ranges normally seen for the cohort as a whole. Head and neck surgery was safe for patients, and it was noteworthy that this safety extended to surgeries that were prolonged, involved complex surgery, or involved free-flap reconstruction.

It is particularly concerning that 40 members of the surgical teams developed COVID-19 within 30 days of surgery within this cohort. In 24% of the operations in which the patient developed COVID-19 or tested positive for SARS-Cov-2, a member of the operating team later developed COVID-19. This high incidence of infection cannot be easily attributed merely to community transmission because even for regions of high community transmission, the risk to members of the surgical team was typically an order of magnitude higher than this background rate. The outcome of these surgeons' illnesses has not been sought in this study, nor have the details of the PPE used or the additional clinical roles performed for inpatients with COVID-19 in the same period. It is not possible to clarify a mechanism or direction of transmission; this is at least circumstantial evidence of some deficiency in the adoption or application of PPE. These data are unique and confirm previously expressed concerns that head and neck cancer surgical teams are vulnerable, potentially highly so, to acquiring COVID-19 during aerosol-generating procedures.

The distribution of cases operated by site was oral cavity (OC) 38%, larynx (L) 8% and oropharynx (OP) 6%. Within countries submitting the majority of cases, the distribution of cases by anatomical site differs significantly from the predicted incidence, most notably for L and OP. The analysis of these data is imprecise because it relies on historical comparisons, but estimates of therapeutic migration away from surgery to radiotherapy-based protocols are possible. The Global Cancer Observatory indicates that OC accounts for 45% of squamous carcinomas worldwide (the United Kingdom, 58%; the United States, 49%; and Spain, 50%). OP accounts for 12% (the United Kingdom, 29%; the United States, 25%; and Spain, 13%), and L accounts for 22% (the United Kingdom, 24%; the United States, 11%; and Spain, 30%).[32] The low inclusion of L and OP cases receiving primary surgery reported here suggests a significant change in the treatment pathway in comparison with historical data from the United Kingdom, the United States, and Europe. Among UK patients having major head and neck surgery in 2004-2009, 70% of OC cancers, 35% of OP cancers, and 43% of L cancers were treated with primary surgery.[33] Data from 2013-2015 (OC, 76%; OP, 43%; and L, 45%)[34] and 2016 (OC, 75%; OP, 35%; and L, 48%)[35] were similar. In the United States, 2009 data from the Surveillance, Epidemiology, and End Results database showed that 82% of OC cancers, 28% of OP cancers, and 32% of L cancers were treated with primary surgery.[36] An analysis of National Cancer Data Base figures from 2004 to 2013 shows that for T1/T2 OP cancers, the rate of primary surgery rose from 56% in 2004 to 82% in 2013.[37] In Spain, data from Madrid illustrate that in 2017, 74% of OC cancers, 34% of OP cancers, and 71% of L cancers were treated with surgery.[38] Data from the Netherlands Cancer Registry in 2008 are similar (OC, 88%; OP, 27%; and L, 28%).[39]

There are several explanations for the observed changes in the proportions of patients undergoing surgery. It is possible that specific cohorts of patients may not have been presented; however, the preservation of OC cases treated with surgery makes this less likely. It is more probable that the treatment modality may have changed. It has been estimated that 37% of cancer surgeries have been cancelled during the COVID-19 pandemic.[1] It is, therefore, probable that patients amenable to surgery were treated at a higher rate with primary radiotherapy or chemoradiotherapy instead. This may be due to the perceived risk of surgery for patients and health care workers or due to a lack of capacity. It is unclear what impact this will have on cancer outcomes or if there will be any increased risks of COVID-19 for those receiving chemoradiotherapy, and longer follow-up for this cohort may clarify these potential risks.

Primary surgery is a standard of care for OC malignancies and usually extends to surgical neck staging because occult metastases are very common. Neck dissection was omitted in 70% of T1 cases, 26% of T2 cases, 12% of T3 cases, and 17% of T4 cases (37% overall). Nine percent of the cases for which neck dissection was omitted had clinical or radiologically evident nodal metastases (cN1-3); therefore, the management of the clinically N0 neck was substantially more conservative in comparison with historical norms of 19% to 28% for all-stage oral cancer series,[40,41] and this may have significant oncological consequences.[42,43] The use of reconstruction and free-flap microvascular reconstruction also appears to be less frequent than historical norms. In this cohort, 45% of oral cancer cases had some form of reconstruction, and the 74 free flaps represented only 25% of these cases. These data indicate fewer patients receiving free flaps in comparison with other recent series[40] and greater reliance on more basic techniques that avoid microsurgery to offer simpler and shorter operations.

The presented data support the idea that head and neck cancer surgery can be executed safely even in high-incidence communities. This safety extends to more complex and prolonged procedures, including those requiring free-flap reconstruction. The rate of severe pulmonary complications of COVID-19, although not high, might yet be reduced by rigorous screening, demarcation of hot and cold inpatient sites, regular staff testing, and effective PPE. Notwithstanding the low rate of infection, the consequences for affected patients were high rates of serious pulmonary complications and mortality. There was a concerning overlap in COVID-19 between patients and their surgeons; one explanation would be some failure of cross-infection measures. Along with early data on the safety of chemotherapy,[44] it appears that with some mitigations, standard cancer therapy for head and neck cancers need not be withheld during the COVID-19 pandemic even in high-incidence regions.

FUNDING SUPPORT

This report was funded by a National Institute for Health Research (NIHR) Global Health Research Unit Grant (NIHR 16.136.79), the British Association of Surgical Oncology, the Association of Coloproctology of Great Britain and Ireland, the Association of Upper Gastrointestinal Surgeons, the Bowel Disease Research Foundation, Yorkshire Cancer Research, Sarcoma UK, the Vascular Society for Great Britain and Ireland, and the European Society of Coloproctology. The funders had no role in the study design; the data collection, analysis, and interpretation; or the writing of this report. The views expressed are those of the authors and not necessarily those of the National Health Service, the NIHR, or the UK Department of Health and Social Care.

CONFLICT OF INTEREST DISCLOSURES

Christian Simon reports personal fees from Pfizer, Merck, MSD, and Seattle Genetics and grants from Roche and Intuitive outside the submitted work. The other authors made no disclosures.

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