

ORIGINAL ARTICLE

# THE INCREASING NEED OF SALVAGE AND PALLIATIVE SURGERY WITH MICROVASCULAR FREE FLAPS FOR ADVANCED HEAD AND NECK CANCERS DURING COVID-19 ERA

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## ABSTRACT

Major head and neck oncologic surgery is a high resource-demanding activity. The aim of this manuscript was to highlight the challenges encountered in the management of oncologic head and neck patients undergoing large cancer resection and immediate reconstruction with microvascular free flaps, in a COVID-19 dedicated hospital.

We retrospectively analyzed data from patients admitted at A. Gemelli University Hospital Foundation, during the most acute COVID-19 emergency phase from February 2020 to June 2021, who underwent complex head and neck oncological surgery with immediate reconstruction using microvascular free flaps. We therefore reported clinical and management issues encountered during the hospitalization.

Forty-two patients were treated with extended surgical resection of the tumor and immediate reconstruction with microvascular free flaps, perforator or not, single or multiple in more complex reconstructions. No donor-site complications were recorded. The overall flap survival (OFS) rate was 95.2% after at least two weeks of follow-up; only in two patients we observed partial flap necrosis. Despite pandemic, the number of patients treated with large surgical tumor resection and reconstruction using microvascular or locoregional flaps did not diminished, but rather increased at our Institution. We also noticed a more advanced stage of the tumors at diagnosis, compared to pre-COVID

era, and an increasing need of salvage surgery after chemoradiotherapy failure or interruption, and palliative surgery. In fact, we observed several pa-

tients in which tumor expansion was so large to make them not suitable for a radical curative surgical treatment.

## KEY WORDS

*Head and neck advanced cancer; microvascular free flap; Surgical Oncology; COVID-19; salvage surgery; palliative surgery.*

## IMPACT STATEMENT

During COVID-19 era, the major head and neck surgery had an increasing demand, along with a more frequent palliative purpose for advanced and unresectable cancers.

## INTRODUCTION

The COVID-19 pandemic, with its impact over all the national health services, resulted in a radical reassessment of head and neck oncology, by requiring new security measures for patients, and a wide reorganization of the clinical and surgical management in almost all the hospitals. Both actors of the oncologic ENT scenario during pandemic changed their paradigms: the ENT surgeon, with his field of action including high-risk procedures for COVID-19 transmission (1, 2), and the patient affected by head and neck cancer, even more fragile due to older age, comorbidities and adverse outcomes that may influence and worsen a possible COVID-19 infection (3). In every hospital, several measures were applied to reduce transmission of virus, but in such a situation, the equilibrium between the clinician mission to care for patients and the need to protect them is fragile. Moreover, the unprepared health system had also to deal with hard ethical issues, due to a limited possibility to equally distribute resources among the population or the needs of individuals. All these difficulties lead to treatment delays, particularly risky in case of head and neck cancers, characterized by several peculiarities compared to all systemic tumors, such as slow growth, local intrinsic aggressiveness (4) with anatomic-functional impairment, disfiguring consequences, and agony. In our Head and Neck Oncology Unit, we treat hundreds of patients every year and the pandemic strained the most complex demolitive surgery we perform, for large cancer resection requiring an immediate reconstruction with microvascular free flaps or pedicled flaps. This kind of surgery, above all, suffered from a drastic reduction in economic resources, dedicated staff and time to spare with complex patients. However, while in our hospital all the outpatient clinics were closed, reducing the

activities to those strictly necessary, cancer patients represented the only case of non-delayable admission to our ward, and adequate treatment even during pandemic was guaranteed both for early and advanced stage tumors (5).

Together with these issues, for the ENT oncology surgeon there were other challenges showing-up in the management of a patient undergoing major cancer resection and reconstruction with microvascular free flap. These patients, in fact, usually present old age and several comorbidities, such as cardiac disease, peripheral vascular disease, chronic pulmonary disease (often associated to cigarette smoking), diabetes, previous cancer history and other factors, that can have a major impact in the management of these patients in the era of coronavirus pneumonia (6-8). Moreover, head and neck oncology surgery often requires a permanent or temporary tracheotomy, which represents one of the most dangerous aerosol-generating condition, with a high risk for an eventual coronavirus transmission (9, 10). The post-operative management of a patient who underwent major head and neck surgery is already rich of pitfalls for the clinician. Nevertheless, during COVID pandemic, the eventuality of post-operative cardiovascular and respiratory complications required a complex clinical management of these conditions, considering the shortage of resources in the field of radiology and pneumology. The aim of this manuscript was to highlight the challenges encountered in the management of oncologic patients undergoing extreme demolitive surgery and immediate reconstruction with microvascular free flaps, perforator or not, single or multiple in more complex surgical defects, during the COVID-19 era at A. Gemelli University Hospital Foundation, a COVID-19 dedicated hospital.

## MATERIALS, METHODS AND PERI-OPERATIVE CARE

### Setting and population

We retrospectively analyzed data from patients admitted at our Otolaryngology-Head and Neck surgical oncologic Unit, during the most acute COVID-19 emergency phase from February 2020 to June 2021, who underwent head and neck oncological surgery with immediate reconstruction using microvascular free flaps. The study was approved by the institutional ethical committee review board (protocol number: 0028911).

In this period, hospitalization at ENT department was prioritized, in accordance with the indications provided at that time (11), for patients affected by head-neck cancer (histologically proven by biopsy performed in Day Hospital regimen or during previous hospitalization) and after clinical evaluation by our multidisciplinary team (MDT). The latter, at our Institution, is composed by several specialists (12): head and neck surgeon, radiation oncologist, medical oncologist, supportive and palliative care specialist, nutritionist, neuroradiologist, speech pathologist, oncological dentist. All these health care providers, during COVID-19 pandemic, met via on-line platform (Microsoft Teams, Microsoft Corp., Washington, USA), where they could study imaging reproduced with screen sharing and discuss the peri-operative care.

### Admission to inpatient clinic

For each patient, a pre-operative anesthesiological evaluation was performed. The COVID-19 real-time reverse transcription polymerase chain reaction (rRT-PCR) test, for detection of viral nucleic acid, was obtained for all the patients through both nasopharyngeal and oropharyngeal swab (13). In case of anesthesiological eligibility for surgery and negativity to the COVID-19 test, patients were admitted to the inpatient clinic. From April 2020 patients underwent the COVID-19 IgM/IgG rapid test before admission. In case of absence of specific IgM, they were allowed to enter the hospital ward, where a confirmation COVID-19 RT-PCR swab test was therefore performed.

In case of positivity to the COVID-19 test and oncological indication to urgent surgery, our Institution provided a dedicated operatory room, with a post-operative hospitalization in a COVID-reserved

Department. Only one visitor for patient was allowed in specific visiting hours and with due regard for social distancing and wearing Personal Protective Equipment (PPE).

### Pre-operative procedures and major surgery management

In our practice, decision algorithms for head and neck cancer patients did not change. A weekly meeting with plastic and reconstructive surgeons was carried on with social distancing and pre-operative clinical evaluation of patients addressed to major demolitive surgery and immediate reconstruction with microvascular free flaps. Although this kind of reconstruction could require longer operating times and may increase post-operative complication, free flaps were always the first surgical choice and were preferred to loco-regional flaps, where clinical conditions were favorable. In some case, due to the extended anatomical defect resulting from the extreme demolitive surgery, free flaps were used in combination with a second free flap or a locoregional propeller flaps, such as the Internal Mammary Artery Perforator (IMAP) perforator flap (14), Supraclavicular Artery Island Flap (SCAIF), Delto-Acromial Perforator (DAP) Flap.

Every patient underwent head and neck magnetic resonance imaging (MRI), head-neck and chest computed tomography (CT), for a correct pre-operative staging. An expert radiologist using Doppler technique performed ultrasound assessment of donor and recipient vessels; this procedure selected the best pedicle vessel with the largest caliber. In case of planned osteocutaneous fibula flap, an angio-TC of leg vascularization is always performed in order to exclude atherothrombosis of peripheral vessels.

### Post-operative management

During the COVID-19 era, once the surgical and anesthesiological procedure was over the patient was monitored in a dedicated space adjacent to the operating room and then was transferred at the ENT inpatient clinic. During the post-operative period, for all patients the heightened risk of viral transmission was taken into account, especially in case of temporary or permanent tracheostomy (15). In cases of total laryngectomy, for example, patients were asked to wear a surgical mask (preferably an N95) over the stoma and an additional surgical mask or respirator over the nose and mouth; when decannulation was completed, a heat and moisture exchanger (HME) was always worn, according to other authors expe-

rience (16, 17). The weekly virtual multidisciplinary tumor board subsequently discussed all clinical cases, in order to plan an eventual adjuvant therapy. In our clinical practice, for all patients undergoing reconstruction with microvascular free flaps, prophylaxis with an angiotensin II receptor antagonist, statin, clopidogrel and low-molecular weight heparin was indicated, starting from a week before surgery (for statin only) and during the post-operative period, if not contraindicated (18-20).

### Data collection

We retrospectively collected data about oncologic patients admitted at our ENT department during COVID-19 era. Clinical data were obtained from clinical charts and from our institutional tumor board digital platform (SpeedRO, KDMS S. r. l., Italy), and we collected data about: demographics, oncologic diagnosis and staging, surgical procedures performed, length of hospitalization, complications of surgery and hospitalization, radiological studies, possible transfer to other hospital ward. We therefore documented the presence of patients with advanced stage of disease and considered by our multidisciplinary tumor board as not suitable for radical surgical treatment, but for a palliative surgery for ethical purposes.

## RESULTS

We included in this retrospective analysis 42 patients affected by advanced head and neck cancer and considered, by our multidisciplinary tumor board, eligible for extended surgical resection of the tumor and immediate reconstruction with microvascular or regional flap. In the same period of 2019, the total number of patients treated with the same kind of surgery was 37 patients, thus observing a 13.5% increase in this procedures. Demographics and characteristics of tumors and surgery are resumed in **table I**.

The oral cavity was the primary site of tumor in 22/42 patients (52.4%), larynx and tracheal stoma in 11/42 cases (26.2%), oropharynx in 5/42 patients (11.8%), two patients (4.8%) were affected by hypopharyngeal cancer and two patients (4.8%) by locally extended facial skin cancer. Surgery with palliative intention was performed in 8/42 patients (19%), while salvage surgery after prior surgery or chemo-radiotherapy failure was performed in 12/42 patients (28.6%). In the same period of ob-

	NO. PATIENTS (%)
<b>Sex</b>	
Males	31 (73.8 %)
Females	12 (16.2 %)
<b>Age at diagnosis</b>	
Mean (range)	59.6 (34-79)
> 50	39 (92.8%)
< 50	3 (7.2%)
<b>Primary site of tumor</b>	
Oral cavity	22 (52.4%)
Larynx and tracheal stoma	11 (26.2%)
Oropharynx	5 (11.8%)
Hypopharynx	2 (4.8%)
Skin	2 (4.8%)
<b>Histology</b>	
Squamous cell carcinoma	38 (90.5%)
Adenoid cystic carcinoma	3 (7.1%)
Ameloblastoma	1 (2.4%)
<b>Stage</b>	
III	10 (23.8%)
IVA	24 (57.1%)
IVB	8 (19.1%)
<b>Type of surgery</b>	
Upfront	22 (52.3%)
Salvage	12 (28.6%)
Palliative	8 (19.1%)

**Table I.** Demographics, cancer characteristic and type of surgery in the studied population.

servation, before COVID pandemic, the rate of palliative and salvage surgery was respectively 8% and 14%. We tried to limit trans-mandibular approach to oral cavity cancer, in order to reduce the operating time, when technically possible and safe for oncological radicality. Bilateral neck dissection was performed in 37/42 cases (88.1%), including all the oral cavity and oropharyngeal cancers, while a revision or unilateral neck dissection was performed in 5/42 cases (11.9%). In case of neck node positivity, we always perform a modified radical neck dissection, including level Va; in case of cN0 oral cancers, we usually perform an elective and selective neck dissection, including level I and submandibular gland.

We performed an immediate reconstructive surgery with microvascular or regional flaps. **Table II** resumes the characteristics of adopted flap. Mean length of flap used was 11.5 cm, while mean width was 6.7 cm. In two cases, we adopted a double non-chimeric ALT flap to obtain a neo-pharynx and to resurface the neck, after a large neck cancer resection. The ALT flap was also used as second flap, in combination with osteocutaneous

Fibula flap, for cheek and soft tissue defect after segmental mandibulectomy. Finally, three patients underwent nerve reconstruction; in one of them, who underwent resection of the base of the tongue, we performed the anastomosis of lateral femoral cutaneous nerve of ALT flap with residual lingual nerve, not involved by tumor invasion. Another patient underwent anastomosis of femoral nerve with residual facial nerve, after facial skin cancer resection and total parotidectomy.

No donor-site complications were recorded. The overall flap survival (OFS) rate was 95.2% after at least four weeks of follow-up; only in two patient (4.8%) we observed partial flap necrosis within the first week after surgery, which required a second reconstructive surgery, using ALT flap with successful results. Mean duration of hospital stay was 37.8 days (range 14-88); decannulation was performed after a mean time of 21.5 days. At the exit from the hospital, 5/42 patients (11.9%) were feeding with gastrostomy-tube, while the other 37/42 patients (88.1%) showed a valid oral intake.

Finally, at the end of most acute emergency phase of pandemic, we discussed the clinical cases of seven patient that were considered not eligible for radical oncologic surgery by our multidisciplinary tumor board. Those patients had been addressed to surgery for local recurrence after prior surgery failure, just before the pandemic, but during the lock-down period they voluntarily postponed the hospitalization.

## DISCUSSION

In a COVID-dedicated center, as it was in our experience, modification in the prioritization of surgical procedures, redistribution of human and economic resources, reduction of non-COVID-19-related health care, were just some of the challenges that upset our everyday clinical practice, similarly to other experiences described in Italy (21, 22). All the health providers experienced clinical, managing and ethical issues that are still burdening their everyday activity. In such a setting, major head and neck oncologic surgery is a high resource-demanding activity, due to large PPE use, complex care support, risk of surgical complication and long hospitalization (23). However, this kind of surgery is usually the best or the only opportunity for patient with advanced cancer, requiring extreme oncological surgery with immediate reconstruction. In our experience, as the first European country hit and extensively involved by the pandemic, with high number of deaths, the A. Gemelli University Hospital Foundation tried to preserve the standard of care for non-COVID oncologic patients and for emergencies (24). Nevertheless, our hospital was one of the few COVID-centers of Rome and the central part of Italy, with a great impact over its internal organization. One of the costs paid to prevent the loss of any possible infected patient, was a particular attention to admission in the hospital ward, that in many cases led to delays in the process of hospitalization, for example in case of pre-operative imaging suspicious for initial interstitial pneumonia, even in absence of fever. Moreover, these patients often present respiratory comorbidities, old age and post-operative fever, thus representing another challenging issue. Some authors described the difficulties encountered in the management of complex head and neck cancer patients, both from surgical and multidisciplinary point of view, and they evidenced how the limited resource affected the oncological practice, reducing the number of non-priority procedure and

	NUMBER
<b>Flap</b>	
ALT	21/42 (50%)
Fibula	6/42 (14.3%)
FFRF	5/42 (11.9%)
IMAP	4/42 (9.5%)
SCAIF	4/42 (9.5%)
DAP	1/42 (2.4%)
PM	1/42 (2.4%)
<b>Arterial microanastomosis (receiving vessel)</b>	
External carotid artery	27/32 (84.4%)
Superior thyroid artery	5/32 (15.6%)
<b>Venous microanastomosis (receiving vessel)</b>	
Internal jugular vein	30/32 (93.7%)
TLF trunk	2/32 (6.3%)
Double microanastomosis	9/32 (28.1)
<b>Partial flap necrosis</b>	
Mean days after surgery	2/42 (4.8%)
Mean age of patient	5.5
Mean no. comorbidities	65
Hypercholesterolemia	2.5
Diabetes	2/2 (100%)
Sepsis	1/2 (50%)
Local infection	0/2 (0%)
	1/2 (50%)

**Table II.** Type of surgical reconstruction and its complications.

ALT: Antero-Lateral Thigh free flap; FFRF: Free Forearm Radial Flap; IMAP: Internal Mammary Artery Perforator; SCAIF: Supraclavicular Artery Island Flap; DAP: Delto-Acromial Perforator; PM: Pectoralis Major.

the usage of distant free tissue transfer in oncological reconstruction, when non strictly necessary (25-27). In our head and neck oncological practice, before COVID-19, we performed major surgery and reconstruction with microvascular flaps at least once a week, in cooperation with plastic and reconstructive surgeons. Despite pandemic, in most acute emergency phase, the number of patients treated with large surgical tumor resection and reconstruction with microvascular free flaps did not decrease, but rather presented a 13.5% increase, compared to the previous year. This increasing need for oncological surgery seems to be in counter-trend compared to the diminished rate of ENT emergencies, as described by Gelardi *et al.* (28). A possible explanation could be the prioritization of hospital admissions for the oncological patients, along with a higher operatory room availability due to the absence of non-oncological surgical procedures. Moreover, several neighboring hospitals addressed their oncological patients to our Institution, due to their impossibility to guarantee a safe flow of incoming patients. In our oncology practice during pandemic, we did not register an increased rate of post-operative complications (*i.e.*, dehiscence, fistula, infection, flap failure due to thrombosis or ischemia); only two patients, in fact, showed a distal partial necrosis of the flap, and underwent surgical revision.

On the other side, as described by other authors (29-31), in the conclusive phase of the emergency in Italy, we faced with the ethical and clinical issue represented by patients with advanced, disfiguring and painful malignancies of head and neck district, sometimes considered as not suitable for a radical surgical demolition. This was direct consequence of both a diagnostic and a therapeutic delay. In fact, several patients declared to be extremely afraid of contagion risk during lockdown, so they decided to postpone follow-up visits and radiological examinations, even when they were necessary and safe; moreover, some patients interrupted chemo-radio treatments on course, for fear of contagion in the hospital setting. As result, in the last weeks we documented an increased number of more advanced tumors. Unfortunately, for some of them it was impossible to achieve oncological radicality, even with a complex surgery and reconstruction, and a palliative surgical resection was invoked by the patient and then performed. Probably, in our oncological experience, these last patients represent the most severe consequence of COVID-19 era. Magaldi *et al.* (32) described a standardized procedure to per-

form virtual follow-up visits and telephone counselling, in order to monitor patients and establish "in-person" visits for a restricted number of them. This protocol resulted to be highly effective in case of patients presenting new or alarming symptoms, such as dysphonia, dyspnea and dysphagia, thus leading to a reduced number of delayed diagnosis. In conclusion, the changes in the whole health system that have been put in place during the COVID-19 pandemic, have largely impacted over management of patients with advanced head and neck cancer. In our experience, the use of microvascular free flaps, single or multiple, allowed the surgeon to treat many patients who postponed the follow-up and whose tumor presented a large growth during the lockdown. Unfortunately, we observed an increasing number of patients in which tumor expansion was so large to make them not suitable for surgery with a curative intent and were therefore treated with palliative surgery in order to reduce pain, restore form and function and to improve the quality of residual life and death. We definitively considered this condition as the main burden of COVID-19 era on the head and neck oncology.

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## ETHICS

### Fundings

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

### Conflict of interests

The authors declare that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patient-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

### Availability of data and material

Data available on reasonable request from the authors.

### Authors' contribution

All the authors contributed equally to conception, data collection, analysis and writing of this paper.

## Ethical approval

The study was approved by the institutional ethical committee review board (protocol number: 0028911).

## Consent to participate

Informed consent was obtained from all individual participants included in the study.

## REFERENCES

- Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *New Eng J Med* 2020;382(12):1177-9.
- Balakrishnan K, Schechtman S, Hogikyan ND, Teoh AYB, McGrath B, Brenner MJ. COVID-19 Pandemic: What Every Otolaryngologist-Head and Neck Surgeon Needs to Know for Safe Airway Management. *Otolaryngology-Head and Neck Surgery* 2020;162(6):804-8.
- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet (London, England)*. 2020;395(10229):1054-62.
- Shuman AG, Campbell BH. Ethical framework for head and neck cancer care impacted by COVID-19. *Head & Neck* 2020;42(6):1214-7.
- Galli J, Settini S, Tricarico L, Almadori G, Paludetti G. Clinical and surgical management of patients with head and neck cancer in a COVID-19 dedicated centre in Italy. *Head & Neck* 2020;42(7):1466-70.
- Silverman DA, Lin C, Tamaki A, et al. Respiratory and pulmonary complications in head and neck cancer patients: Evidence-based review for the COVID-19 era. *Head & Neck* 2020;42(6):1218-26.
- Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *International Journal of Infectious Diseases* May 12, 2020;94:91-5. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32173574>. Last access: Apr 11, 2020.
- Mo P, Xing Y, Xiao Y, et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. *Clinical Infectious Diseases* Mar 16, 2020. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32173725>. Last access: Apr 15, 2020.
- Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PloS one* 2012;7(4):e35797.
- Tay JK, Khoo ML-C, Loh WS. Surgical Considerations for Tracheostomy During the COVID-19 Pandemic. *JAMA Otolaryngology-Head & Neck Surgery* Mar 31, 2020.
- Mehanna H, Hardman JC, Shenson JA, et al. Recommendations for head and neck surgical oncology practice in a setting of acute severe resource constraint during the COVID-19 pandemic: an international consensus. *The Lancet Oncology* 2020;21(7):e350-9.
- Heineman T, St John M, Wein R, Weber R. It Takes a Village: The Importance of Multidisciplinary Care. *Otolaryngol Clin of North Am* 2017;50(4):679-87.
- Falsey AR, Formica MA, Walsh EE. Simple method for combining sputum and nasal samples for virus detection by reverse transcriptase PCR. *J clin microbiol* 2012;50(8):2835.
- Almadori G, Di Cintio G, De Corso E, et al. The usefulness of the IMAP propeller flap for trachea and tracheostome reconstruction after resection of parastomal recurrence of squamous cell carcinoma following salvage total laryngectomy. *European Archives of Oto-Rhino-Laryngology* 2020.
- Kligerman MP, Vukkadala N, Tsang RKY, et al. Managing head and neck cancer patients with tracheostomy or laryngectomy during the COVID-19 pandemic. *Head & Neck* 2020;42(6):1209-13.
- Smith JD, MacDougall CC, Johnstone J, Copes RA, Schwartz B, Garber GE. Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis. *Can Med Assoc J* 2016;188(8):567-74.
- Brook I, Bogaardt H, van As-Brooks C. Long-Term Use of Heat and Moisture Exchangers among Laryngectomees: Medical, Social, and Psychological Patterns. *Annals of Otol, Rhinol*

- Laryngol 2013;122(6):358-63.
18. Gupta A, Stokes W, Eguchi M, et al. Statin use associated with improved overall and cancer specific survival in patients with head and neck cancer. *Oral oncol* 2019;90:54-66.
  19. Karsenti G, Le Manach Y, Bouvier S, Chaine A, Bertolus C. Statins: A new pharmacological agent for free flap surgery? *J Plastic, Reconstruct Aesth Surg* 2010;63(5):870-4.
  20. Fichter AM, Ritschl LM, Robitzky LK, et al. Impact of different antithrombotics on the microcirculation and viability of perforator-based ischaemic skin flaps in a small animal model. *Sci Rep* 2016;6(1):35833.
  21. Longo F, Trecca EMC, D'Ecclesia A, et al. Managing head and neck cancer patients during the COVID-19 pandemic: the experience of a tertiary referral centre in southern Italy. *Infect Agents Cancer* 2021;16(1):9.
  22. Monroy-Iglesias MJ, Tagliabue M, Dickinson H, et al. Continuity of Cancer Care: The Surgical Experience of Two Large Cancer Hubs in London and Milan. *Cancers* 2021;13(7):1597.
  23. Pawlik TM, Tyler DS, Sumer B, et al. COVID-19 Pandemic and Surgical Oncology: Preserving the Academic Mission. *Ann Surg Oncol* 2020;27(8):2591-9.
  24. Hwang ES, Balch CM, Balch GC, et al. Surgical Oncologists and the COVID-19 Pandemic: Guiding Cancer Patients Effectively through Turbulence and Change. *Ann Surg Oncol* 2020;27(8):2600-13.
  25. Ranasinghe V, Mady LJ, Kim S, et al. Major head and neck reconstruction during the COVID-19 pandemic: The University of Pittsburgh approach. *Head & Neck* 2020;42(6):1243-7.
  26. Rassekh CH, Jenks CM, Ochroch EA, Douglas JE, O' Malley BW, Weinstein GS. Management of the difficult airway in the COVID-19 pandemic: Illustrative complex head and neck cancer scenario. *Head & Neck* 2020;42(6):1273-7.
  27. Patel RJ, Kejner A, McMullen C. Early institutional head and neck oncologic and microvascular surgery practice patterns across the United States during the SARS-CoV-2 (COVID19) pandemic. *Head & Neck* 2020;42(6):1168-72.
  28. Gelardi M, Iannuzzi L, Trecca EMC, Kim B, Quaranta NAA, Cassano M. COVID-19: what happened to all of the otolaryngology emergencies? *Eur Arch Oto-Rhino-Laryngol* 2020;277(11):3231-2.
  29. Werner MT, Carey RM, Albergotti WG, Lukens JN, Brody RM. Impact of the COVID-19 Pandemic on the Management of Head and Neck Malignancies. *Otolaryngol-Head Neck Surg* 2020;162(6):816-7.
  30. Brody RM, Albergotti WG, Shimunov D, et al. Changes in head and neck oncologic practice during the COVID-19 pandemic. *Head & Neck* 2020;42(7):1448-53.
  31. Arduino PG, Conrotto D, Broccoletti R. The outbreak of Novel Coronavirus disease (COVID-19) caused a worrying delay in the diagnosis of oral cancer in north-west Italy: The Turin Metropolitan Area experience. *Oral Diseases*.2020;odi.13362.
  32. Magaldi L, Salzo AE, Trecca EMC, Iannuzzi L, Fortunato F, Cassano M. The importance of head and neck counselling in the COVID-19 era. *Acta Otorhinolaryngologica Italica* 2021;41(2):192-4.