Treatment prioritization and risk stratification of head and neck cancer during COVID-19 pandemic: A systematic review

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ABSTRACT

Introduction: Treatment of head and neck cancer patients amidst the COVID-19 pandemic is challenging, whereas prolonged treatment initiation in head and neck squamous cell carcinoma may increase mortality and likelihood of recurrence. Special attention is needed to ensure safe and appropriate care of these patients. This article aims to review and discuss existing research on treatment prioritization and risk stratification of head and neck cancer patients during the pandemic.

Materials and Methods: The authors conducted literature search in three databases (PubMed, Cochrane, and Clinical Key) on July 15th, 2020. The keywords were ("Head and Neck Mucosal Malignancy" OR "Head and Neck Cancer") AND ("Management" OR "Head and Neck Surgery") AND ("COVID-19" OR "Pandemic"). The inclusion criteria were cancer in adult patients, published from 2020 in English, and with available access to full text. The exclusion criteria were comments, letters, and case reports. The articles were critically appraised using the Centre of Evidence-based Medicine (CEBM), University of Oxford and Duke University. The literature search strategy is illustrated using Preferred Reporting Items for Systematic review and meta-analysis (PRISMA) flow diagram.

Results: A total of 150 articles were identified; 21 articles were gathered from Clinical Key, 33 from Cochrane, and 96 from Pubmed. After screening abstracts and reviewing the full text, the authors determined five articles met the inclusion criteria. There are several key points of head and neck cancer management in the COVID-19 pandemic. Head and neck cancer management is considered a high-risk procedure; the clinician should use proper personal protective equipment. Before operative treatment, all patients should undergo a PCR test 14 days before surgery. In diagnosing head and neck cancer, laryngoscopy should be considered carefully; and cytology should be preferred instead. Medically Necessary, Time-sensitive (MeNTS) score is recommended for risk stratification and surgery prioritization; it has three domains: procedure, disease, and patient. However, it is not specified to head and neck cancer; therefore, it should be combined with other references. Stanford University Head and Neck Surgery Division Department of Otolaryngology made surgery prioritization into three groups, urgent (should be operated immediately), can be postponed for 30 days, and can be postponed for 30-90 days. Some urgent cases and should be operated on immediately include cancers involving the airways, decreased renal function, and metastases. For chemoradiation decision to delay or continue should refer to the goal of treatment, current oncologic status, and tolerance to radiation. In terms of patient's follow up, telephone consultation should be maximized.

Conclusion: MeNTS scoring combined with Guideline from Department of Otolaryngology at Stanford University prioritizing criteria can be helpful in decision making of stratifying Risk and prioritizing surgery in head and neck cancer management.

KEYWORDS:
COVID-19, head and neck cancer, head and neck surgery, surgical priority

INTRODUCTION

World Health Organization (WHO) declared the COVID-19 outbreak to be a global pandemic on March 11, 2020. As of June 2021, the number of COVID-19 cases exceeded 180 million cases. The speed and scale of the spread of COVID-19 have resulted in massive pressures on health services worldwide. COVID-19 can be transmitted from one person to another through droplets.[1] It has been reported that nasopharynx and oropharynx secretions have a high viral load, putting clinicians, especially otolaryngologists, at high risk for nosocomial transmission. Staff shortages due to illness and viral transmission concerns to healthcare workers and other patients have led to a limitation of healthcare capacity and resources. Otolaryngologists have had to adapt new strategies for care delivery.[2]

While many otolaryngology operations are elective and can be delayed, head and neck malignancy treatment cannot be delayed for long periods. Prolonged time to treatment initiation in head and neck squamous cell carcinoma lead to an increase in mortality and likelihood of recurrence. On the other hand, this group of patients is at increased risk for severe COVID-19 disease.[2] According to data from China, cancer patients faced an increased risk of death from COVID-19.[3] They are also more susceptible to COVID-19 infection and more likely to transmit the disease to otolaryngologists, due to repeated visits to health facilities, recurring diagnostic and treatment procedures, and immunosuppression caused

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by the malignancy and its therapy. It is recommended that the risk and benefits of treatment be assessed individually to identify patients eligible for treatment delay without serious consequences.[3] Therefore, Prachand wrote a medically necessary, time-sensitive (MeNTS) system that can be used as a reference for surgery prioritization during the pandemic. Higher score is associated with poorer outcome, meaning the procedure is not justified. However, this scoring system is not a specific guide for head and neck cancer.[4] Several studies have presented other stratification and prioritization strategies for head and neck cancer by its urgency, including surgery and chemoradiation.

This study aims to review existing research on treatment prioritization and risk stratification of head and neck cancer patients. In this pandemic era, it is important to be alert and assess the risk for the welfare of patients and health care providers. Priority of patients who must be treated immediately and when treatment can still be postponed with non-surgical therapy should be established.

MATERIALS AND METHODS

This study is a literature review. The authors conducted an article search using three databases, namely Pubmed, Cochrane, and Clinical Key on July 15th, 2020. The authors did advanced search used Boolean operator, and the keywords were ("Head and Neck Malignancy" OR "Head and Neck Cancer") AND ("Management" OR "Head and Neck Surgery") AND ("COVID-19" OR "Pandemic"). The keyword search above used the mesh term. The inclusion criteria used were studies in the English language, study on adult cancer patients, studies published from 2020 to 2021, and available full text.

The initial search found 150 articles. After doing a screening for studies found in more than one database, deduplication obtained 86 articles. The authors then screened all the studies title and abstract, 13 articles were appropriate with the study title. The exclusion criteria were then applied. The exclusion criterias were comments, letters, case reports study types. Five articles were included in the final literature review. The literature search strategy is illustrated using Preferred Reporting Items for Systematic review and meta-analysis (PRISMA) flow diagram (Figure 1.). After reading the full text, the articles were critically appraised using critical appraisal tool from Centre of Evidence-based Medicine (CEBM), University of Oxford and Duke University. In the critical study, an assessment is made based on validity, importance, and applicability. Critical review is carried out by all authors, an ENT surgeon and residents.

RESULTS

Based on the literature searches from three databases, 21 articles were obtained from Clinical Key, 33 from Cochrane, and 96 from Pubmed. A total of 150 articles were identified through database search, after screening abstracts and reviewing full text, the authors determined five articles appropriate with the study title. The procedure is illustrated in the flowchart (Figure 1). The five articles are "American Society of Clinical Oncology (ASCO) Special report: a guide to cancer care delivery during the COVID-19 pandemic" by ASCO[6], "Global radiation oncology's targeted response for pandemic preparedness" by Simcock et al[7], "Status and strategies for the management of head and neck cancer during COVID-19 pandemic: Indian scenario" by Gupta et al[11], "Practice recommendation for Risk-Adapted Head and Neck Cancer Radiation Therapy During the COVID-19 Pandemic: An American Society for Radiation Oncology and the European Society for Radiotherapy and Oncology (ASTRO-ESTRO) Consensus Statement" by Thomson et al[9], and "Framework for prioritizing head and neck surgery during the COVID-19 pandemic" by Topf et al[10]. All studies discussed in this article have been carried out and reviewed with critical appraisal of qualitative studies from CEBM University of Oxford. These journals discuss recommendations for the management of head and neck cancer in the pandemic era, some focus on surgery strategy, the rest provide complete strategies from infection prevention, teleconsultation, risk stratification to various therapeutic options, the study's results are summarized in Table I.

DISCUSSION

In the COVID-19 pandemic, protective measures must be followed by surgeons, especially in procedures that generate aerosol secretion. Any transmucosal head and neck procedure such as nasolaryngoscopy, endotracheal intubation, transnasal endoscopic surgery should be considered high risk. Personal protective equipment (PPE) should include an N95 respirator, face shield, surgical gown, and gloves.[5,6] The surge in COVID-19 cases in Indonesia has caused an increased demand for the health care system. Hospitals report shortages on equipment, personal protective equipment (PPE), healthcare workers, and ventilators. Prioritization and risk stratification for head and neck malignancy management is needed during the pandemic to conserve PPE, free up inpatient beds, and limit exposure of patients and staff. From the five articles obtained, the authors discussed key points to consider in dealing with head and neck cancer cases during the COVID-19 pandemic that will be further discussed in the subsections, including preoperative screening needed for patients undergoing surgery during the pandemic, increased risk of postoperative mortality in COVID-19 patients, risk stratification and prioritization for surgery and chemoradiation.

Preoperative Screening

In Wuhan, China, Patients scheduled to undergo head and neck surgery were required to have two negative COVID-19 polymerase chain reaction (PCR) swab examinations before surgery, and were asked to self-isolate for 14 days before surgery.[5] The decision is based on the incubation period of the SARS-CoV-2. The median incubation period is 5.1 days, and most patients became symptomatic within 14 days after exposure. Several other hospitals ensure patients have at least one negative COVID-19 PCR swab before surgery. In some centers, patients are screened with PCR and COVID-19 antibody tests 24 hours before surgery, and then the patients are being isolated. If the PCR shows positive results, they are isolated, and COVID-19 protocols are followed. If the PCR is negative while the antibody is positive, it will not require further testing. If both the PCR and antibody show negative results, they are tested weekly during their stay in the hospital.[5]

Table I: Previous Recommendations and Guidelines on Risk Stratification and Prioritization of of Head and Neck Cancer During COVID-19 Pandemic

S/N	Author (year)	Study design	Source	Recommendation	Annotation
1.	American Society of Clinical Oncology (2020)	Guideline	Committee members	Surgeries • Local resumption of elective surgery guidance: ○ COVID-19 awareness: screening, community numbers (prevalence, incidence) ○ Preparedness: bed capacities, intensive care units, and ventilators ○ Patient issues: testing policies, counselling, collaborative process, consider list of postponed cases, priority with MeNTS scoring, local strategy to increase operating room time availability, etc.	
2.	Simcock et al (2020)	Simcock et al (2020)	121 individuals from 17 countries	Consensus-based guideline • Minimising the risk of transmission: promote telephone consultation and remote monitoring, minimum family members attendance • Prioritising treatment by evidence, risk of COVID infection multiplied by risk of serious morbidity/mortality • Radical treatment • Adjuvant treatment: long term survival patient can avoid radiotherapy • Palliative treatment: smallest number of hospital visit	Head and neck cancer recommendation • Radiotherapy in patients with head and neck cancer is not recommended to be delayed. • Radical radiotherapy may be reduce from IMRT standard dose (evidence level II)
3.	Gupta et al (2020)	Literature review	16 major head and neck health care	Brief guidelines and recommendations given by FHNO during COVID • Diagnosis: avoid laryngoscopies, biopsies of benign lesions, FNACs should be preferred • Treatment: Surgery (consider if likelihood curing cancer), Radiotherapy (patients should be triaged and prioritized), Chemotherapy (judiciously on the expected benefit) • Follow up: minimize all follow-up appointments	Risky medical procedures should be avoided unless absolutely mandatory
4.	Thomson et al (2020)	Literature review	29 members from panel of international experts from ASTRO, ESTRO	• Treatment prioritization: Do not postpone initiation of HNSCC radiation, a very high priority. • Intercurrent SARS CoV-2 infection: Delay initiation until test is negative, do not interrupt after 2 weeks of radiation for mild symptoms, do not interrupt radiation for severe symptoms • Case-specific radiation therapy and chemotherapy practice: Continue to use concomitant chemotherapy, use a hypofraction radiation schedule • Operating room closures and the management of surgical cases: Radical chemoradiation therapy for oral tongue SCC (T3N2bM0) and sinonasal maxilla SCC (T4aN1M0), wait up to 4 weeks for oral tongue SCC (T3N2bM0), consider waiting for surgical within 4 weeks for locoregionally advanced oral cavity cancer • Adjustment to outpatient clinic appointments and supportive care: Reduce in-person consultation and replace with teleconsultation routine weekly	

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Table I: Previous Recommendations and Guidelines on Risk Stratification and Prioritization of of Head and Neck Cancer During COVID-19 Pandemic

S/N	Author (year)	Study design	Source	Recommendation	Annotation
5.	Topf et al (2020)	Literature review	Head and Neck Surgery in the Department of Otolaryngology at Stanford University	Stanford University Head and Neck Surgery Division Department of Otolaryngology Criteria for prioritizing patients requiring head and neck surgery • Urgent - proceed with surgery: HPV-negative HNSCC eps. with airways concerns, HPV-positive HNSCC with significant burden, HNSCC with complications of cancer treatment, Thyroid (anaplastic carcinoma, medullary carcinoma, >4 cm follicular lesion, etc), Skull base malignancy, etc. • Less urgent - consider postpone > 30 days: Low-risk PTC without metastasis, low-grade salivary carcinoma • Less urgent - consider postpone 30 to 90 days: Thyroid (goiter without airway/respiratory compromise, etc), Benign salivary lesions, skin cancer (melanoma ≤ 1 mm thickness, basal cell carcinoma where cosmetic impact, low-risk SCC)	All considerations are important looking at case by case basis, then follow the prioritization process during COVID-19 pandemic chart. If the patient is required to undergo surgery, preoperative screening is carried out following the pathway on wileyonlinelibrary.com.

Abbreviations: MeNTS; medically necessary, time-sensitive, IMRT; Intensity-Modulated Radiation Therapy, FHNO; Foundation for Head and Neck Oncology, FNACs; Fine needle aspiration cytology , HNSCC; Head and neck squamous cell carcinoma, SCC; Squamous cell carcinoma, HPV; Human papillomavirus, esp; especially, etc; et cetera, PTC; Papillary thyroid carcinoma

Table II: Medically Necessary Time Sensitive (MeNTS) Sugery Prioritization Scoring Developed by Prachand, et al4

Procedure	1	2	3	4	5
OR time	< 30 min	31-60 min	61-120 min	121-180 min	≥180 min
Anticipated length of stay	outpatient	23 hours	24-48 hours	≤3 days	>4 days
Post-operative ICU need	Very unlikely	<5%	5-10%	11-25%	≥25%
Bleeding risk	≤100cc	101-125 cc	251-500 cc	501-750 cc	≥750 cc
Number of surgical team	1	2	3	4	>4
Intubation probability	≤1%	1-5%	6-10%	11-25%	≥25%
Surgical site	None of the following	Abdominal MIS surgery	Abdominopelvic surgery, infraumbilical	Abdominopelvic open surgery, supraumbilical	OHNS, Upper GI, Thoracic
Disease	**1**	**2**	**3**	**4**	**5**
Non Operative effectiveness	None available	Available, <40% as effective as surgery	Available, 40-60% as effective as surgery	Available, 60-95% as effective as surgery	Available, equally effective
Non-operative treatment option resource use/exposure risk	Significantly worse	Somewhat worse	Equivalent	Somewhat better	Significantly better
Impact of 2 weeks delay in disease outcome	Significantly worse	Worse	Moderately worse	Significantly worse	Minimally worse
Impact of 2 weeks delay in surgical difficulty	Significantly worse	Worse	Moderately worse	Significantly worse	Minimally worse
Impact of 6 weeks delay in disease outcome	Significantly worse	Worse	Moderately worse	Significantly worse	Minimally worse
Impact of 6 weeks delay in surgical difficulty	Significantly worse	Worse	Moderately worse	Significantly worse	Minimally worse
Patient	**1**	**2**	**3**	**4**	**5**
Age	< 20 yo	21-40 yo	41-50 yo	51-65 yo	>65 yo
Lung disease (asthma, COPD, CF)	None			Minimal (rare inhaler)	>Minimal
OSA	Not present			Mild/moderate (non CPAP)	On CPAP
CV disease (HT, CHF, CAD)	None	Minimal (no meds)	Mild (1 med)	Moderate (2 meds)	Severe (≥3 meds)
Diabetes	None		Mild (no meds)	Moderate (PO meds only)	>Moderate (insulin)
Immunocompromised	No			Moderate	Severe
ILI symptoms	None (asymptomatic)				Yes
Exposure to known COVID-19 positive patients within 14 days	No	Probably not	Possibly	Probably	Yes

Morbidity and Mortality in COVID-19 Patient Undergone Surgery

Postoperative pulmonary complications occur in half of patients with COVID-19, and it is associated with increased risk of mortality. The overall 30-day mortality in patients undergoing surgery with perioperative COVID-19 infection was 23.8%, all-cause mortality rate 18.9% in elective patients, 25.6% in emergency patients, 16.3% in minor surgery, and 26.9% in major surgery.[8] This increased risk should be considered when planning surgery during COVID-19 pandemic. Postponing non critical surgery should be considered and the use of non-operative treatment should be maximized.[8]

Risk Stratification and Surgical Prioritization

Some factors are considered when deciding to proceed with medically necessary time-sensitive procedures (MeNTS); unfortunately, this scoring system is not specific to head and neck cancer cases, but the ASCO guideline still recommends its use for now.[4,6] There are twenty-one factors as significant contributors to MeNTS prioritization, grouped into 3 domains; procedure (7 factors), disease (6 factors), and patient (8 factors), total score ranging from 21 to 105 (Figure 2). Higher MeNTS score is associated with poorer outcomes, increased COVID-19 transmission, and increased hospital resources use.[6,9]

Each point of the MeNTS score can be scored from 1 to 5 (Table II). The procedure domain for MeNTS score includes operation duration, estimated length of stay, postoperative intensive care unit (ICU) needs, anticipated blood loss, number of the surgical team needed, probability of intubation, and surgical scale. Disease domain includes the effectiveness of other treatment options besides surgery, exposure risk of other treatment options, impact in disease outcome with a two-week delay, impact in surgical risk with a two-week delay, impact in disease outcome with six-week delay, and. Impact in surgical risk with six-week delay. Meanwhile, the patient domain includes: age, presence of lung disease, obstructive sleep apnoea, cardiovascular disease, diabetes, immunocompromised, influenza-like symptoms, and exposure to COVID within 14 days.[9]

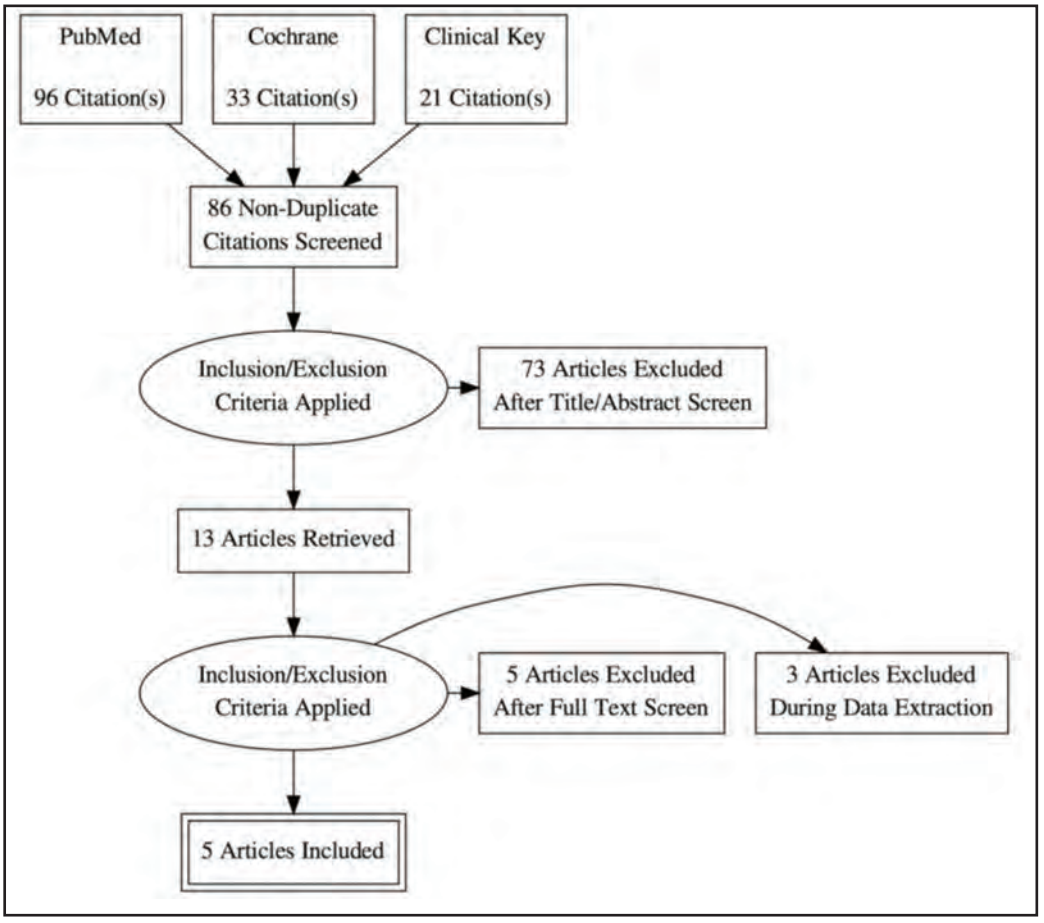

Fig. 1: Summary of procedure in this study.

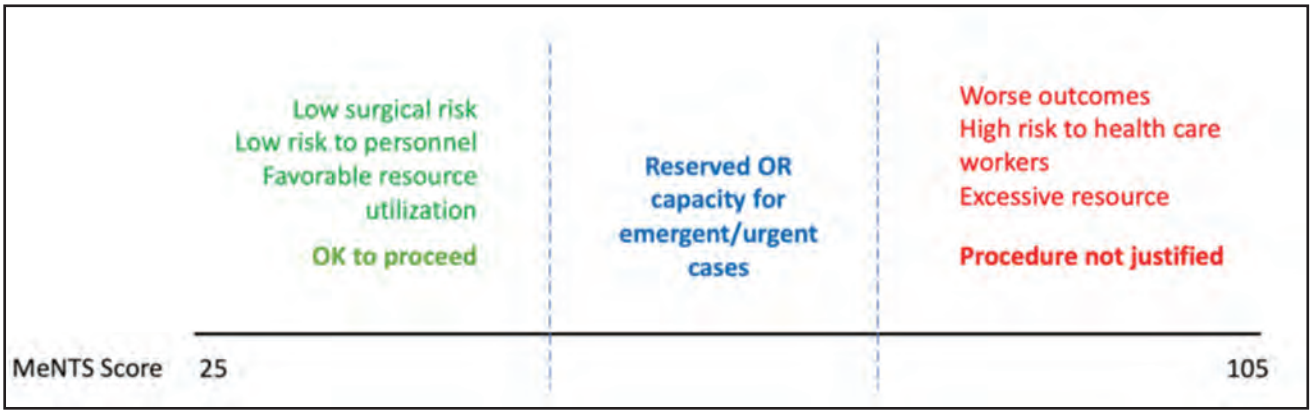

Fig. 2: MeNTS Score Range[11,12]

Surgical site on the head and neck gave a score of five on the procedure domain, giving a higher MeNTS score in procedural domain. However, delay of head and neck surgery causes worsening of outcome, giving a lower total score of MeNTS. Lower total MeNTS score indicates the surgery should be performed. There is no specific MeNTS score cut off to decide wheter the surgery should be performed or delayed, it should be adjusted based on resources availability and local condition.

Guideline from Department of Otolaryngology at Stanford University also prioritize surgery based on cancer's primary location. As mentioned before, any cancer involving the airways are considered urgent and need to be operated on immediately. Thyroid cancer, including anaplastic carcinoma, medullary carcinoma, and large follicular lesion, are also considered urgent cases. On the other hand, benign thyroid nodules, goitre, and thyroiditis can be postponed for > 30 days. Salivary cancers that are considered urgent include salivary duct carcinoma, high-grade mucoepidermoid

carcinoma, adenoid cystic carcinoma, and acinic cell carcinoma. Surgical management of benign salivary lesions can be postponed > 30 days. Advanced skin cancers are also considered urgent, meanwhile, melanoma < 1 mm thickness, basal cell carcinoma with low risk of morbidity, and low-risk squamous cell carcinoma can be postponed > 30 days.[10]

Meanwhile, Gupta et al. divide treatment criteria based on the choice of treatment to be given. They are divided as cancer prognosis, cancer type, and surgery type, and comorbidity. Surgical procedures are aimed at patients with the likelihood of curing cancer, but delay surgery in patients with low-grade tumours, avoid extensive surgery, avoid surgery for patients with low haemoglobin.[11] The discussion of therapeutic priorities by Simcock et al. is very interesting, which is explained through a simple model by multiplying the risk of COVID-19 infection by the mortality and morbidity of the patient.[7] Considering various references to determine management priorities, it is still important to consider each case itself.

Chemoradiation Prioritization

According to the American Society for Radiation Oncology (ASTRO), radiotherapy should be given as early as possible if it is used as a curative procedure.[10] Every month delay causes a 16% increased risk of mortality. For COVID-19 positive patients, the decision to delay or continue treatment should be individualized, based on the goal of treatment, current oncologic status, and tolerance. For palliative treatment, it is recommended to exhaust other options before undergoing radiotherapy. From ASCO advised postponing patient visits without delaying chemotherapy, especially patients with respiratory symptoms and fever. In order to reduce the frequency of hospital visits, it can be considered to change the treatment of the patients from intravenous to oral-systemic regimens and shorter radiotherapy fraction. Chemotherapy needs to be done wisely, considering its benefits, whilst also at the same time considering the risk of being exposed to the COVID-19.[11]

This topic is still relevant since the pandemic is still ongoing. Further study is still needed since the previous studies are based on expert opinions and then applied in daily practice as a guideline. There is also no further study regarding the success rate of these prioritization strategies when applied to clinical practice. Therefore, studies about effectivity of these strategies are recommended to figure out which one is the most appropriate recommendation for risk stratification and surgical prioritization of head and neck cancer patients during the pandemic.

CONCLUSIONS

Risk stratification and prioritization in treating head and neck malignancies should be individualized based on the diagnosis, patient, and procedure. The strategies to adopt this are by applying MeNTs scoring combined with the Stanford University Department of otolaryngology Head and Neck Surgery prioritizing criteria can be helpful in decision making; for chemoradiation, ASTRO recommendation can be used. Risk stratification in patients becomes important and will determine the next step of therapy. In limited resources, prioritization can help guide therapy flow in patients with head and neck cancer especially during this COVID-19 pandemic.

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