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What is the best treatment option for head and neck cancers in COVID-19 pandemic? A rapid review

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ABSTRACT

With the onset of the COVID-19 crisis in late 2019, the health care systems of different countries are experiencing stressful conditions. Many patients need care in hospital wards and intensive care units (ICU). Head & neck cancers (HNC) are in a special condition in this pandemic. The main treatment in these patients is surgery. Most of these patients need care in the ICU, which is reduced in capacity in pandemic conditions. It's important to note that delays in the surgery of these patients make them non-operable and on the other hand increase mortality and morbidity. Numerous non-surgical alternative therapies have been proposed in these conditions, but there are fundamental questions about these suggestions. 1 How long should we look for alternative therapies? Because many countries are facing a second wave of the disease. 2 What's the effect of these alternative therapies and the delay in starting standard treatments in patients' survival?

Different countries have different financial resources; many countries, patients face restrictions on receiving alternative therapies to standard treatments, and in non-pandemic conditions, long queues are given for non-surgical treatments such as chemo-radiotherapy. There are numerous guidelines to guide head and neck surgeons to the best choice in this situation. It seems that different countries have to make individual decisions based on the prevalence of COVID-19 and the financial resources and facilities of the health care system.

In this review article, we have collected the opinions of world-renowned guidelines and institutions on how to treat HNCs during the pandemic.

1. Introduction

In December 2019 some pneumonia cases with an unknown source were reported in Wuhan, China. The causative micro-organism, a novel coronavirus, was named 2019-nCOV or COVID-19 by the World Health Organization (WHO) [1,2]. In January 2020 WHO announced the virus a Public Health Emergency of International Concern (PHEIC) [2]. The involvement of all countries around the world, more than 27 million people infected, and around 900,000 victims until September 8, show that the world is facing a disastrous pandemic [3].

The novel coronavirus is highly contagious and its transmission can occur via droplets or contact with nasal or oral mucosal surfaces. It has been also proposed that another way of virus dissemination could be aerosol, although to prove this needs more investigations [4,5]. The mean incubation period of the disease is 5.5 days and 14 days of isolation after the beginning of symptoms are sufficient for transmission control [6]. Fever, cough, dyspnea, and fatigue are the most common symptoms of the disease, however, about 18% of the patients are asymptomatic and can play a role in virus transmission [7,8]. The mortality rate of the infection is reported to be around 2.3% but can be significantly higher in patients above 70 years old. The mortality rate among patients suffering from cancer is 5.6% though it was anticipated

Abbreviations: WHO, World Health Organization; ICU, intensive care unit; HNC, head and neck cancer; MDT, multidisciplinary team; UADT, upper aero-digestive tract; AGP, aerosol-generating procedures; SCC, squamous cell carcinoma; OCC, oral cavity cancers; NAC, neoadjuvant chemotherapy; SFORL, French Society of Otorhinolaryngology, Head & Neck Surgery; PPE, personal protective equipment; ASTRO, American Society of Radiation Oncology; ESTRO, European Society for radiotherapy and oncology; HNSCC, head & neck squamous cell carcinoma; OCSCC, oral cavity squamous cell carcinoma; BAHNO, British Association of Head & Neck Oncologist; SSO, Society of Surgical Oncology; AHNS, American Head & Neck Society; AAES, American Association of Endocrine Surgeons; TC, thyroid cancer; ATC, anaplastic thyroid carcinoma; BAETS, British Association of Endocrine & Thyroid Surgeons; MTC, medullary thyroid carcinoma; PC, parathyroid carcinoma; PTC, papillary thyroid carcinoma; BCC, basal cell carcinoma; WLE, wide local excision; SLNB, sentinel lymph node biopsy; CCT, concomitant chemotherapy; NHS, national health service

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to be higher due to their immunosuppression [9]. The need for intensive care unit (ICU) admission and intubation was also reported higher in cancer patients compared to COVID-19 patients [10].

Deciding on the best treatment modality for head and neck cancer (HNC) patients is particularly complicated in the current situation due to the limited surgical and non-surgical resources. It necessitates utilizing multidisciplinary team (MDT) meetings to opt for the best treatment plan for any individual patient [11]. The possibility of infection with COVID-19 for patient and health care workers, the patient's comorbidities, the prognosis of the intervention, the effect of the treatment modality on quality of life, and the rate of acute complications are factors to be considered while choosing the best option of treatment [12]. Surgery is the main treatment for HNC patients. The surgeries are almost always prolonged, requiring ICU admission, mechanical ventilation, and the involvement of many health care workers both in the operation and in the pre-operative care. The use of ICU beds and ventilators for COVID-19 patents' care & the engagement of the medical staff in their treatment cause a delay in the treatment of HNC patients which may lead tumor progression, increase in the surgical resection field, complication, recurrences, and mortality [13]. Moreover, performing safe surgical operations faces many challenges in the current situation. The limitations in COVID-19 patients' screening, the possibility of transmission during the incubation period and by asymptomatic patients, the shortage of personal protective equipment (PPE), and the high viral load in upper aero-digestive tract (UADT) are some of these challenges [14]. Also, when the surgical procedure is done under general anesthesia, intubation and bag-valve mask ventilation may increase the chance of infection as aerosol-generating procedures (AGP). Tracheotomy, airway suctioning, and endotracheal tube substitution are other instances of AGP related to HNC surgeries [14]. Head & neck surgeons, too face a high risk of COVID-19 infection due to their surgical procedures on UADT which have a high viral load of COVID-19. [15]

Because of the above reasons and the unknown future of COVID-19 disease at present, we should change some of our previous treatment strategies of HNC and consider new strategies that may not necessarily follow the standard guidelines. Different countries of the world have different financial resources and this variation leads in turn to different strategy planning for the distribution of resources between the treatment of COVID-19 and other diseases. Moreover, HNC patients are diagnosed at different stages in different countries, which affects the decisions on their treatment. Since the beginning of the pandemic, several guidelines and recommendations for HNC management have been published by authoritative scientific centers around the world. Given that in many developing countries proposed alternative therapies such as chemoradiotherapy instead of radical surgery it is not affordable due to the limited accessibility of radiotherapy centers and their long waiting lists, therefore it isn't practical to use a single guideline in different conditions of the countries. As the second wave of the pandemic is expected these days, the present paper aims to review different opinions and studies on the subject which may be of help to different centers of the world to make the best decision in treating their patients based on their conditions & resources.

2. Surgical treatment

2.1. UADT mucosal squamous cell carcinoma (SCC)

The physicians of the University of Texas Southern Medical Center believe that in cases of primary mucosal SCC where the results of both surgical and nonsurgical treatment are the same, definitive nonsurgical modalities are preferable in the current pandemic situation. But the daily attendance of patients in radiotherapy centers and the immunosuppression that follows chemotherapy threaten the patients. It seems that in cases such as T1aN0 glottic or T1N0 tonsil SCC surgery is preferable to 7 weeks of undergoing radiotherapy [14].

The University of Texas Southwestern Medical Center's physicians believe the case is different with tumors for which surgery is the main treatment; These include oral cavity cancers (OCC), T4a laryngeal, advanced sinonasal and recurrent UADT cancers. The cost-benefit comparison is simple in low-risk patients (i.e. patients who have passed their 14 days of quarantine, have been asymptomatic during this period, and COVID-19 test negative 48 h before the surgery) with OCC or sinonasal cancer whose postoperative hospital stay is short. But in the case of advanced sinonasal and advanced laryngeal tumors, most of OCC and patients who require salvage surgeries a longer hospital stay and/or tracheostomy, laryngectomy, and/or free flap are required and the COVID-19 infection risk therefore increases. In such cases, alternative treatments seem to be more reasonable. We can use neoadjuvant chemotherapy (NAC) ± cetuximab or NAC ± immunotherapy to buy time for the health care system until the stabilization of the current situation when standard treatments can be provided. Induction chemotherapy could also be used to surmount the patients' symptoms and have the appropriate delay until the optimal surgical treatment [14].

Surgeons at the University of Pittsburgh, USA give the highest priority to mucosal SCC surgeries in the current situation [16]. When tracheostomy placement is not required, the French Society of Otorhinolaryngology, Head & Neck Surgery (SFORL) recommends surgical treatment for UADT SCC patients who will face poor prognosis if their treatment is delayed beyond one month. When tracheostomy is necessary, however, the recommendation is either to delay the surgery or to choose an alternative modality [17,18]. The study of the Stanford University Division of Head & Neck surgery; the mucosal SCC patients are ascribed the highest priority for surgery and is recommended to undergo surgical intervention without any delay. In the case of the limitation of resources, HPV negative patients are prioritized to positive ones [19].

Mehanna et al. published the opinions of 40 HNC experts from 35 scientific societies in a setting of severe resource limitation in the Lancet Oncology journal. More than 95% of these experts believe that a delay of above 8 weeks is unacceptable in the surgical treatment of early T1–T2 N0 oral cancers. In cases where surgery is anticipated within 4–8 weeks or after 8 weeks since diagnosis, 87.5% and 67.5% of the physicians (respectively) believe that the patient should undergo recurrent examinations and intervention should take place only in case of any tumor progression. 82.5% are against rapid initiation of non-surgical treatments such as radiotherapy in cases where surgery is anticipated within 4–8 weeks. 92.5% believe that surgery should not be delayed beyond 8 weeks in cases of early T1-N0 laryngeal cancer. 70% believe that radiotherapy could be initiated immediately as an alternative for surgery. In cases where a delay of 4–8 weeks is anticipated, 67.5% believe that radiotherapy should replace surgery, while a majority of 92.5% recommend radiotherapy in cases where more than 8 weeks of delay is anticipated. In advanced HNC cases where prolonged operation or admission is required (such as T4N1 cancer of the larynx, N2b OCC or cases where bone resection is mandatory) a strong agreement exists between more than 87.5% of experts that surgery should not be delayed beyond 4 weeks and if surgery is not feasible within this time, 90% recommend alternative treatments such as radiotherapy or chemo-radiotherapy. There is disagreement on using induction chemotherapy for these cases as long as the surgery is possible, and only 50% of respondents approved of this in cases where surgery is not possible within 4 weeks [20].

In another study, Brody et al. collected the opinions of 88 head & neck surgeons of different USA states about HNC treatments in the current pandemic situation. 85% of these surgeons approve of surgical treatment in locally advanced OCC; although in early OCC 93.3% of surgeons approve of surgical treatment. In early-stage OCCs, 53.3% of them prefer a 2–4 weeks delay, and around 12% prefer 6 weeks delay. In locally advanced OCCs, however, the majority of the surgeons believe that the minimum delay in surgery should occur compared to other tumors. About 50% of the surgeons recommend non-surgical

treatments for early glottic and HPV positive oropharynx cancers, and if surgical treatment has opted, the majority of them believe that it can be postponed for a maximum period of 4 weeks. This is also the case with advanced and recurrent laryngeal cancer [21]. The tragic result of this pandemic is the shutdown of operating theaters due to shortage of PPE & the priority of anesthesiologist & ventilators are for emergency care. In this situation, for HNC patients that usually undergo surgery, treating with radical (chemo-) radiotherapy is more logical that not receive any treatment. But radiotherapy for OCC is less efficient & more toxic in comparison to primary surgery. As a result, the experts of the American Society of Radiation Oncology (ASTRO) and the European Society for Radiotherapy and Oncology (ESTRO) have an agreement that for T1–T2 & T3–T4 OCC can wait up to 8 & 4 weeks for surgery, respectively. In these weeks serial monitoring is very important for understanding tumor progression [22].

MD Anderson Head and Neck Surgery Treatment Guidelines Consortium have also published a guideline for the HNC patients' treatment. This guideline advises early-stage OCC patients to delay the surgery for a short period during which they should have weekly telemedicine visits. It recommends to continue monitoring in stable cases and to stop monitoring and perform surgery in cases where progression or evidence of lymphadenopathy are observed although primary surgery is another option. Surgery and NAC are recommended for intermediate and advanced cases respectively. A short delay along with weekly telemedicine visits is also recommended for early & intermediate oropharynx tumors and non-surgical treatment is preferred. In advanced cases, too non-surgical treatment is recommended, as well as larynx/hypo-pharynx early & intermediate tumors. However, in advanced cases of larynx/hypo-pharynx that are accompanied by cartilage invasion, extra laryngeal expansion, recurrent tumor, or high probability of aspiration after chemotherapy surgical treatment is recommended. In the advanced cases where surgical treatment is indicated, NAC is advisable so that the patients undergo surgery after the COVID-19 peak. In intermediate sinonasal tumors, chemo-radiotherapy or radiotherapy are preferable and NAC is advisable for advanced cases of sinonasal undifferentiated or SCC [23].

A multi-institutional study in Hong Kong states that patients with head & neck squamous cell carcinoma (HNSCC), particularly small oral cavity squamous cell carcinoma (OCSCC) tumors that will need complicated reconstruction surgeries if the treatment is delayed, and large tumors of larynx and hypo-pharynx whose growths may result in the clogging of respiratory canals and necessitate tracheostomy must undergo surgery within 4 weeks. In cases such as small tumors of the larynx in which the endo-laryngeal method can be applied it is possible to wait for 8 weeks [24].

British Association of Head & Neck Oncologist (BAHNO) and Ansarian from Italy recommend local or pedicled flaps instead of a free flap or revascularized flap for reconstruction during the current situation [25,26]. BAHNO advises not to use microvascular free flap (as long as it is possible) and not to perform circumferential resection in patients who need laryngectomy or laryngectomy-pharyngectomy surgery so that using pedicled flaps such as major pectoralis or superficial cervical artery perforator flap become feasible [27]. France has reported a failed case of using chimeric double skin paddle free flap of fibula & thoracodorsal artery perforator flap for gingival mandibular SCC reconstruction in which no evidence of vascular thrombosis was observed in a patient that was infected by COVID-19. The authors of the paper believe disseminated intravascular coagulation to be a probable cause of the flaps' damage and considers it necessary to use Heparin for at least 15 days and to screen patients for COVID-19 before performing free flap surgeries [28].

2.2. Endocrine: thyroid & parathyroid

The physicians of the *University of Texas Southwestern Medical Center* believe that if sufficient hospital resources exist, thyroidectomy and neck dissection surgeries can be performed in the current situation as these surgeries are not concerned with UADG, have a low level of AGP and a low to medium risk [14].

The Society of Surgical Oncology (SS0), American Head & Neck Society (AHNS), and the American Association of Endocrine Surgeons (AAES) recommend surgery in the current situation for these patients: 1. Life-threatening thyroid cancer (TC), cases with local invasion such as invasion to the trachea or recurrent laryngeal nerve or aggressive biology tumors 2. Grave's disease with severe symptoms that do not respond to medical treatment, 3. Goiter that has a risk of clogging respiratory canals, 4. Open biopsy in suspected cases of ATC (Anaplastic thyroid carcinoma) or lymphoma, 5. Hyperparathyroidism is not controlled by medical treatment and has a life-threatening hypercalcemia, and 6. Endocrine diseases in pregnant women who are not controlled by medical treatment and is dangerous for either the mother or the fetus [29–32].

The British Association of Endocrine & Thyroid Surgeons (BAETS) advises performing surgery within 24 h on TC patients with severe clogging of respiratory canals. Stridor due to TC, operable poorly/undifferentiated TC, medullary thyroid carcinoma (MTC), TC spreads to the lymph node, uncontrollable thyrotoxicosis in cases where medical treatment or radioactive iodine are not feasible, and uncontrolled Grave's disease during pregnancy are the cases that must undergo surgery within 4 weeks. Surgery on other TC and benign masses of thyroid can be delayed up to 3 months or more than that respectively. Also, cases with parathyroid carcinoma (PC) suspicion, hyperparathyroidism that is not controlled by medical treatment, pregnant patients with high hypercalcemia (corrected calcium > 2.85 mmol·L), hypercalcemia after kidney transplant which threatens kidney function, and several hospitalizations because of hyperparathyroidism control are the cases that should undergo surgery within 4 weeks. Patients with recurrent, symptomatic kidney stones along with sepsis have up to 3 months to undergo parathyroidectomy [33].

Stanford University considers high-risk TC such as metastatic papillary thyroid carcinoma (PTC), locally aggressive PTC, ATC, MTC, follicular lesions greater than 4 cm, and PTC patients who need second surgery among cases for which urgent surgery is required and delaying in whose treatment result in prognosis reduction. Parathyroidectomy in patients with the reduction of kidney function is urgent as well. The surgical treatment of non-metastatic low-risk PTC can be postponed at least 30 days while surgery for cases such as goiter without respiratory symptoms, benign thyroid nodules, and parathyroidectomy in stable kidney function cases can be delayed 30–90 days [19].

SFORL believes that a delay of 6–8 weeks in the surgery of well-differentiated TC does not affect the patient's prognosis and that the patients should be visited after 6–8 weeks and the decision on his/her treatment should be made according to tumor growth speed and the pandemic situation [17,18]. However, Lee et al. from Hong Kong believe that in such cases the surgery can be delayed even up to 4 months [24]. This is while the physicians of the University of Pittsburgh Medical Center consider the highest priority of surgery for poorly differentiated TC and well-differentiated TC with local invasion [16].

82.5% of participants in the study of Mehanna et al. believe that the surgery can be delayed up to 12 weeks after the diagnosis of differentiated TC (e.g., T1–T3 or N0–N1b) in which no invasion to strap muscle, trachea, esophagus and the recurrent laryngeal nerve is observed and compression of airway not seen. 96.8% recommend serial monitoring of the patient if surgery is not expected during this period, and believe that surgery should be performed only in case of tumor progression. 96.8% disapprove of iodine therapy or radiotherapy as the first treatment in the current situation. 82.5% believe that a below 4 cm nodular T1–T2 differentiated TC that not invaded to the airway but abut to it has to operate in 4 weeks. Also, authors believe regional metastasis (92.5% of responders) and only extrathyroidal strap muscle invasion (85% of responders) is not an indication for accelerated surgery (in 4 weeks) [20].

In another study from The University of Texas MD Anderson Cancer Center, Jozaghi et al. offer recommended treatments of TC & PC based on the extent to which hospitals are engaged with Coronavirus. Provided that the number of COVID-19 patients is few and ICU and ventilators are available, they advise the following cases to undergo surgery as soon as possible: TC which is in severe need of airway management, progressive MTC or differentiated TC or large TC, large goiter which is likely to cause respiratory canal clogging, ATC or poorly differentiated TC without BRAFV600E mutation in which surgery is feasible, and symptomatic hypercalcemia in suspected cases of PC. In case of high numbers of COVID-19 patients and the limitation of ICU and ventilators the following cases have to surgery as soon as feasible: TC that has caused a problem in the respiratory canal, resectable ATC or rapidly progressive poorly differentiated TC without BRAFV600E mutations،clinically aggressive or rapidly progressive differentiated or medullary TC, and suspected cases of PC that are resistant to medical treatment. If the condition of the hospitals is more critical and all the ICUs and ventilators are being applied in the treatment of COVID-19 patients, only TC patients who need acute airway management should opt for surgery [34].

2.3. Salivary glands & skin cancers

SFORL puts aggressive salivary glands and aggressive skin cancers in the category of tumors that can lead to a decrease in survival in case of more than a month delay in treatments [17,18]. The risk of disease transmission during surgery in these patients is mild to moderate because UADT is not generally violated and AGP is low. These kinds of tumors should be treated without any delay if there is no limitation in hospital resources. In the few cases where surgery should be done in UADT (minor salivary gland tumors) or free tissue transfer is mandatory for reconstruction (mandibular resection in advanced skin or parotid tumor), MDT will decide on the surgical plan according to the high risk of transmission [14]. According to SFORL recommendation, in slow progressive salivary gland carcinoma and non-progressive skin cancers like basal cell carcinoma (BCC), the patient should be visited after 6–8 weeks. The decision will be made considering the tumor progression rate and the pandemic condition [17,18].

Stanford's university surgeons recommend that surgery should not be delayed in these cases: 1. Skin cancers such as Merkel cell carcinoma, melanoma with minimum 1 mm thickness, Advanced-stage cutaneous SCC (tumor size more than 4 cm, poorly differentiated tumors or tumors with deep invasion or perineural invasion), and BCC in critical areas such as periorbital BCC. 2. High-grade salivary carcinomas such as adenocarcinoma, salivary duct carcinoma, and other high-grade tumors. 3. Parathyroidectomy in cases that accompany impaired renal function; but surgery in low-grade salivary tumors and benign lesions of the salivary gland, parathyroidectomy in patients with normal kidney function also low-risk skin cancer could be delayed 30 and up to 90 days respectively [19]. Likewise, Lee et al. from Hong Kong recommend 8 weeks & 4 months of delay in surgery for high grade and low-grade salivary gland carcinomas respectively [24].

MD Anderson surgeons consider telemedicine visits for 8 weeks for low-grade salivary gland carcinoma is advisable. Intermediate cases should be evaluated individually. Rapidly progressive cases such as salivary duct carcinoma or carcinoma ex pleomorphic require surgery. For minor salivary gland tumors monitoring with imaging modalities is recommended. In general, surgery should not be done in the current situation unless the tumor progression rate is high. The center also recommends to postpone surgery in BCC and considers the use of Hedgehog inhibitors as an appropriate option if the tumor is advanced or symptomatic. They recommend 8–12 weeks of delay in wide local excision (WLE) or Mohs surgery in skin SCC. Local topical Imiquimod in early-stage cases and neoadjuvant treatments such as Cemiplimab in advanced cases are appropriate alternatives [23].

The advice of NCCN is that WLE should be postponed for 3 months in T1 & in situ melanoma. Surgery is preferable in T3/T4 rather than T1/T2 cases. Also, sentinel lymph node biopsy (SLNB) should be delayed for 3 months unless WLE is planned in which case SLNB should be done concurrently. In patients with palpable cervical lymphadenopathy, lymph node dissection is not recommended in the current situation and neoadjuvant treatments should be considered instead. If the metastatic lymph node invades vital areas such as the carotid artery or skull base, lymph node dissection should be performed. Metastatectomy (stages 3, 4) is also recommended if the patient is symptomatic or if the continuance of systemic treatment required [23,35].

3. Non-surgical treatment

ESTRO and ASTRO provide recommendations for HNC patients in the COVID-19 crisis [22]. The first recommendation is not to delay radiotherapy for more than 4 to 6 weeks; radical radiotherapy for HNSCC and adjuvant Radiotherapy for HNSCC with Involved margin has a high priority for treatment. But adjuvant radiotherapy is a lower priority for HNSCC with minor risk factors. During the early stages of the pandemic when the resources needed for radiotherapy are available (Scenario 1), it is recommended that radiotherapy be performed following the same protocol as before. However, during the later stages pandemic and when there is a severe decrease of available resources for radiotherapy (Scenario 2), there is a strong recommendation to perform hypo-fractionated radiotherapy (fewer sessions and higher doses per session) [22]. Reducing the number of surgeries will deprive a large number of patients of surgical treatment and radiotherapy will be chosen as an alternative treatment for them. The increase in the number of patients in radiotherapy centers and the decrease of the number of staff (due to the viral infection) result in considering hypo-fractionated radiotherapy as an alternative method during this particular situation to provide treatment for more patients and reduce the patients' referrals [36]. Also, Cisplatin at a dose of 80–100 mg/m^2 every 3 weeks or 30–40 mg/m^2 per week is the standard treatment for concomitant chemotherapy (CCT); in early pandemic conditions, CCT is more appropriate, but in late pandemic conditions, CCT will be removed. The members of these associations also recommend performing (chemo-) radiotherapy in OCSCC patients when surgery is not possible due to the closure of operating rooms [22].

The physicians of the University of Texas Southwestern Medical Center recommend replacing standard surgical treatment with primary radiation ± chemotherapy for limited and selected cases of OCSCC, T4a laryngeal SCC and advanced sinonasal malignancy; however, patients should be aware of the lower effectiveness of these treatments compared to standard treatments. Also, in cases that require salvage surgery and have been disease-free for a long time, re-irradiation ± chemotherapy is an appropriate alternative to surgery [14].

Chemotherapy should not be used in patients over 70 years of age due to its failure to improve survival, and neither in people under 70 with comorbidities due to the high risk of death from COVID-19. Induction chemotherapy with a cisplatin-based regimen is also not recommended [37].

The national health service (NHS) of England also categorized patients who need chemotherapy according to six priorities; Patients who have at least 50% chance of successful treatment by curative chemotherapy, and patients whose chance of successful treatment would be increased at least 50% by adjuvant chemotherapy or NAC along with surgery or radiotherapy have the highest priority for chemotherapy in the crisis. The lower the chance of successful treatment with chemotherapy is, the less would be the priority of the treatment. The priority also decreases in cases of palliative treatment. In radiotherapy treatment, the NHS has ascribed the highest priority to patients who have a high-growth mass and are currently undergoing curative radical (chemo) radiotherapy, or those who are currently undergoing external beam radiotherapy or have a brachytherapy plan following external beam radiotherapy. Radical radiotherapy in less aggressive cancers

where radiotherapy is definitive treatment or adjuvant radiotherapy in rapid proliferating cancers that have residue after surgery are the next priorities. Adjuvant radiotherapy in complete resection patients and also in cases of palliative radiotherapy has the lowest priority [38].

4. Treatment for COVID-19 positive patient

A study in China was conducted concerning 34 asymptomatic patients who underwent elective surgeries and began having symptoms after the surgery. The RT-PCR test was performed it was determined that all patients had COVID-19 and had been in the incubation stage at the time of surgery. 44% of these patients were transferred to the ICU and 20.5% died. Old age, prolonged surgery, and underlying diseases such as cardiovascular disease, cancer, and hypertension led to poorer outcomes for the patients [39]. It is therefore recommended to perform RT-PCR before surgery. Some centers even consider it necessary to have a second negative test before any surgery [16]. If the testing supplies are limited, a chest CT scan (that seems to be more accurate in diagnosing patients with COVID-19) can be used as well [40]. Considering the different pandemic situation in different countries and the limited diagnostic resources, it seems that patients who have UADT surgery, old age, or comorbidities should be prioritized for testing. If the patient tests positive for COVID-19, the surgery must be delayed unless the delay threatens the patient's life. The patient can be tested again 7 days after the disappearance of symptoms or 14 days after the last test, whichever is longer [19].

ESTRO and ASTRO suggest that radiotherapy treatment be delayed in patients with COVID-19 infection if treatment has not been initiated. In patients with mild symptoms who were infected during treatment, it is recommended to continue the treatment especially if they have completed 2 weeks of treatment. But in patients with Sever COVID-19, the treatment must be discontinued and delayed [22].

5. Conclusion

In deciding on the treatment plan we should take into consideration the importance of timely treatment of patients with HNC especially mucosal UADT SCC, the high probability of COVID-19 transmission especially in asymptomatic patients during surgery on UADT, and the difference in rates of COVID-19 infection and resource such as PPE, ICU, and operating rooms in different areas. It is recommended that centers examine each patient individually by MDT and determine the costs and benefits of delay in the standard treatment or alternative treatment. The risk of infection with the virus and its possible resulted complications for the patient should also be taken into account in the choice of treatment. Considering the reducing resources for cancer patients' surgery and the shift of large numbers of patients to alternative therapies, the limited therapeutic capacity of these treatments, and the postponement of diagnostic and follow-up measures even after the COVID-19 crisis, the challenges in the management of patients with cancer will continue to exist due to the overloading of health care because of the delayed treatments. Therefore, it will be necessary to share the experiences of different countries and medical centers to handle the situation.

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Abolfazl Salari: Conceptualization, Methodology, Writing - original draft, Validation. **Amirmohsen Jalaeefar:** Writing - original draft, Writing - review & editing, Validation. **Mohammad Shirkhoda:** Methodology, Writing - original draft, Writing - review & editing, Validation.

Declaration of competing interest

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