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UK consensus recommendations on the management of oral epithelial dysplasia during COVID-19 pandemic outbreaks

Caroline Elizabeth McCarthy a,*, Stefano Fedele b,c, Michael Ho d, Richard Shaw a

Abstract

Objectives: Oral Epithelial Dysplasia (OED) is associated with an increased risk of oral cancer development. The SARS-CoV-2 pandemic is necessitating the suspension or dramatic reduction of face-to-face non-urgent elective services, including OED clinics. Little is known regarding the potential impact of elective services suspension upon the risk of OED progression, and whether alternative strategies (e.g. remote consultations) may be introduced to ensure OED surveillance. The aim of this paper is to provide expert-opinion consensus recommendations for the management of OED during the current and future pandemic outbreaks.

Materials and methods: A working group of nine UK-based senior clinicians and academics in Oral and Maxillofacial Surgery and Oral Medicine was created and twelve consensus statements were developed using a modified-Delphi process. Greater than 80% agreement was considered a consensus.

Results: Consensus was achieved for all twelve statements (89–100% agreement). The group agreed that, during the temporary suspension of elective services associated with COVID-19 pandemic outbreaks, patients with OED can be risk stratified to determine the length of accepted delay in face-to-face consultation. Remote consultations with patient-provided clinical photographs may be a useful way of maintaining a level of surveillance in this group of patients.

Conclusions: Using an expert working group methodology, we have developed consensus recommendations for the monitoring of individuals with OED during pandemic outbreaks associated with temporary suspension of elective services. This has identified areas of future research and highlighted the need for a stronger evidence base to inform the set-up and delivery of surveillance regimens for patients with OED.

Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is challenging health care systems across the globe beyond the demand for critical care of those who develop Coronavirus disease 2019 (COVID-19) clinical syndrome. A suspension or dramatic reduction in non-urgent elective services is implemented by the vast majority of health care systems worldwide in order to (i) maximise critical care capacity and (ii) reduce cross-infections among both health care providers and patients, when incidence levels of COVID-19 are high. An estimated 38.9% of all head and neck cancer surgical operations globally were cancelled during a 12-week period of peak disruption caused by COVID-19 [1], which has resulted in a backlog of patients in need of urgent operations. In addition, a significant drop in referrals of suspected cancers during April 2020 has been reported in England, with head and neck cancer referrals having dropped by 60% (n = 8,006) compared to April 2019 (n = 19,431) [2]. There are concerns that this decrease may result in diagnostic delay and a consequent increase in head and neck cancers diagnosed at a more advanced stage in the medium- and long-term [3], with the need for more complex and costly treatment and poorer outcomes for the affected individuals.

Oral epithelial dysplasia (OED) is a disorder of the oral mucosa...
associated with an increased risk of oral cancer development: approximately 10% of all OED patients experience disease progression and develop oral cancer with an average time-to-event of approximately 4 years from diagnosis [4]. The likelihood of disease progression increases with higher grades of dysplasia [5] and patients with OED on the lateral tongue [6,7] and non-smokers may be at higher risk [6,8]. Loss of heterozygosity, the superficial extension of the affected dysplastic mucosa (e.g. a large dysplastic lesion as opposed to a small one) and a previous history of oral cancer are also established risk factors [8-10]. There remains little robust evidence supporting any intervention in patients with OED that may reduce the risk of disease progression and ultimately the development of oral cancer. Individuals with OED regarded to be at lower risk of progression are often offered a surveillance programme of regular visual inspections with the option of re-biopsy where clinical manifestations suggest potential disease progression [11]. Surveillance intervals of 3, 6 or 12 months are commonly considered depending on the grade of dysplasia, clinical assessment of the lesion and previous medical history [11]. Although evidence remains weak due to the lack of well-designed clinical trials, some single-centre observational studies report notably positive outcomes when patients with OED are carefully monitored and surgical intervention offered at an appropriate stage in the disease process [12].

This is however difficult to achieve with the temporary suspension of elective services during pandemic outbreaks. Little is known regarding the potential impact of deferring regular monitoring upon the risk of OED progression, and whether alternative strategies (e.g. remote consultations) may be introduced so to ensure OED surveillance. Prevention and early detection of oral cancer is of paramount importance to avoid adding to the excess cancer mortality that is already expected as a result of the disruption to services caused by the SARS-CoV-2 pandemic [13,14]. The aim of this paper is to provide expert-opinion consensus recommendations for the management of OED during current and future pandemic outbreaks.

Methods

A modified Delphi process was used to develop the consensus guidelines. An expert working group of six Oral and Maxillofacial Surgeons and three Oral Medicine Consultants, all with an established specialist interest in the management of Oral Epithelial Dysplasia, was created. They were invited based on their track record of multidisciplinary clinical practice in this field, active research (publication and/or research grants), and contribution to national guidance and advisory panel for research in this area. The population of interest consists of specialist interest in the management of Oral Epithelial Dysplasia, was created. They were invited based on their track record of multidisciplinary, oral medicine and oral and maxillofacial surgery. The interviewer (CM) asked specific questions about the management of each case vignette including: the need for face-to-face examination, use of remote consultations, deferral and time intervals between consultations, and the decision to offer biopsy or surgery in relevant cases. Results were subsequently collated and a consensus document, consisting of twelve statements, was developed. All members of the group were asked to state their agreement or otherwise with each statement, with options for comments. Consensus was achieved if greater than 80% of respondents agreed with the statement. Where consensus was not achieved in the first round, statements were iteratively amended until consensus was achieved.

Table 1

<table>
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<tr>
<th>“Red flag signs and symptoms” of disease progression and/or oral cancer development in patients with OED [20].</th>
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<tbody>
<tr>
<td>Increasing size of lesion</td>
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<td>Increased thickness of lesion</td>
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<tr>
<td>New onset of paraesthesia</td>
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<td>New and persistent neck lump</td>
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deemed necessary and appropriate. The aim is to ensure that the relevant diagnosis is made available within 28 days at the very latest. This timeline is in accordance with the NHS long term plan to improve performance in the early diagnosis of cancer [21], with a new 28-day faster diagnosis target expected to be introduced in 2020 [22]. This approach also reduces the number of hospital appointments, thereby limiting exposure to SARS-CoV-2 [23].

Consensus statement 4

If deemed appropriate by the clinician and if patients are able, up-to-date photographs of the relevant oral lesions should be provided by the patient and sent for review by the clinical team. Usual consent, data storage and image-use guidelines and legislation apply (Consensus achieved: 89%).

Clinical photographs are important in the long-term monitoring of potentially malignant lesions of the oral mucosa [11]. The group agreed that photographs provided by patients, typically taken with a smartphone, can be a helpful adjunct to the remote consultation and can be stored in the patient records for future reference. The group discussed that not all patients may be able to take or send photographs for clinical review, or that the quality of the photographs may be poor and not informative (see below). Patients must be made aware that data security cannot be guaranteed when images are sent from their personal email account, as images are not subject to information governance and NHS data protection regulation until they have been received by the healthcare professional [24].

Consensus statement 5

Verbal or written guidance should be provided to patients for the purpose of achieving good-quality images suitable for surveillance (Consensus achieved: 89%).

There was consensus that verbal or electronic guidance should be provided for patients who are able and willing to take their own clinical images. The group suggested that the available UK guidance on the use of mobile photographic devices in dermatology [25] may also be relevant to the monitoring of oral mucosal disease. The recommendation is for clinicians to familiarise with the standards suggested in the guidance including consent, anonymisation, transfer and storage of patient-generated images. Poor quality images can compromise quality of care, therefore it is recommended that only patients with appropriate technology available and lesions amenable to clinical photography may be asked to provide images. Patients should be encouraged to take close-up images where possible, to avoid any identifying facial features.

Consensus statement 6

Patients with mild dysplasia, with no additional clinical risk factors, reporting no red flag signs or symptoms, can reasonably be delayed for six months, even without patient-provided photographs (Consensus achieved: 89%).

There was consensus that patients with a diagnosis of mild OED, a history of stable disease, no concerning feature at the most recent face-to-face consultation, can have their next face-to-face monitoring consultation deferred by up to six months from the date of the intended hospital appointment [26]. The group agreed that patients with mild OED are typically reviewed in hospital every 6–12 months, therefore a deferral of 6 months would translate, in the worst case scenario, into a maximum interval of 18 months between face-to-face assessments, which the group considered acceptable during a pandemic outbreak. Photographs provided by the patient may guide the clinicians’ decision: as per consensus statements 2 and 4, any evidence of disease progression on patient-generated clinical photographs should trigger the offer of a face-to-face urgent appointment within 2 weeks.

Consensus statement 7

Moderate Dysplasia: If the lesion/area appears stable on photographs, face-to-face review can be delayed by 6 months from the date of their scheduled review. If no photographs are available, the patient should be offered a face-to-face assessment within 3–4 months (Consensus achieved: 89%).

Considering the higher risk of progression to cancer of moderate OED (15% prevalence of oral squamous cell carcinoma development), [7,27] the group agreed that an individual risk stratified approach is required for all patients and the use of patient-generated clinical images is instrumental in stratifying patients with moderate OED into two groups. For those individuals with moderate OED that appears clinically stable and unchanged on patient-generated clinical photographs, it would be reasonable to defer their consultation by 6 months. However, should the patient be unable to provide clinical photographs, a face-to-face consultation within 3–4 months is recommended. As per consensus statements 2 and 4, any evidence of disease progression on patient-generated clinical photographs should trigger the offer of a face-to-face urgent appointment within 2 weeks.

Consensus statement 8

Patients with severe dysplasia but reporting no red flag symptoms or signs should be offered a face-to-face consultation within 4–6 weeks of their original, scheduled review (Consensus achieved: 100%).

There was strong consensus that any delay in face-to-face surveillance examination in cases of severe OED should be minimised, where possible, to within 4–6 weeks of the original, scheduled review. This reflects the annual incidence and prevalence of cancer development in individuals with severe OED being 3.6% [26] and 25% respectively, [7] with some authors suggesting an overall prevalence as high as 50% [27]. Photographs provided by the patient may guide the clinicians’ decision and, as per consensus statements 2 and 4, any evidence of disease progression on patient-generated clinical photographs should trigger the offer of a face-to-face urgent appointment within 2 weeks.

Consensus statement 9

Severe Dysplasia: Patients declining a 4–6 week rescheduled face-to-face appointment should be asked to send clinical images for review. They should be offered a new face-to-face appointment 4–6 weeks later (Consensus achieved: 89%).

The group recognised that, during a pandemic outbreak, individual risk perception may vary and some patients may decline the offer of a face-to-face consultation and ask for a remote consultation instead. Examples include individuals at higher risk of severe COVID-19 clinical syndrome due to medical history, ethnic background or age [28,29]. Therefore, the group agreed that patients with severe OED declining to attend a face-to-face consultation within 4–6 weeks from their original appointment should be reviewed remotely, with the benefit of clinical images if possible, and offered a new face-to-face consultation within an additional 4–6 weeks. As per consensus statements 2 and 4, any evidence of disease progression on patient-generated clinical photographs should trigger the offer of a face-to-face urgent appointment within 2 weeks.

Consensus statement 10

If local arrangements and capacity allow, patients with newly diagnosed severe OED who would normally be offered surgery (e.g. laser excision) may still undergo surgery with appropriate counselling regarding the risk of SARS-CoV-2 infection (Consensus achieved: 100%).

There was strong consensus from the group that the provision of surgical intervention for high risk OED should be resumed as soon as reasonably possible. The group agreed that, after prioritising time-
urgent trauma and cancer cases [23], where capacity allows, consideration should be given to the resumption of elective surgery for patients with newly diagnosed severe OED, especially during the phase of declining prevalence of the pandemic. The rationale for this recommendation is based on the reasonable intention to reduce the risk of disease progression and future oral cancer development, but also on the observation that in up to 10% of patients with biopsy-confirmed non-invasive lesion the definitive histological diagnosis is upgraded to squamous cell carcinoma following surgical excision [30].

Consensus statement 11

Patients in the ‘clinically vulnerable’ and ‘clinically extremely vulnerable group’ can be offered face-to-face appointments in line with the above recommendations and should be managed according to local arrangements (Consensus achieved: 100%).

NHS England recommends that individuals at risk of severe COVID-19 clinical syndrome should be offered remote consultation as first option, and required to attend face-to-face hospital consultations only for urgent reasons [31]. The group agreed that “clinically vulnerable” and “clinically extremely vulnerable” individuals with OED reporting red-flag signs or symptoms or providing clinical photographs suspicious for disease progression should be considered in need of an urgent consultation and offered a face-to-face appointment as per consensus statement 2.

Consensus statement 12

Patients who decline remote consultations and request a face-to-face appointment should be accommodated if capacity allows. Patients should be counselled on the risk and benefits of face-to-face appointments. (Consensus achieved: 100%).

The group recognised that some patients with OED may decline remote consultations and request to attend a face-to-face clinical review.

The Royal College of Surgeons (RCS) guidelines state that remote consultations should only be used for patients who are able and willing to communicate via telephone or video [23]. Accordingly, the group agreed that, where capacity allows, the request for a face-to-face consultation may be accommodated. Patients should be counselled on the potential risk of COVID-19 associated with hospital attendance and commuting [23].

Discussion

We have developed brief expert-opinion consensus recommendations for the management of patients with OED during pandemic outbreaks associated with temporary suspension of non-urgent elective hospital services. Figure 1 shows a flow chart to summarise these recommendations.

Patients with OED are at increased risk of developing oral cancer compared to the general population [10,32] and require close clinical monitoring and appropriately-timed surgical interventions [11]. As there will be a significant backlog of untreated cancer to be managed due to the disruption to cancer services caused by the current pandemic [33], it would be reasonable to suggest that careful management of OED may prevent disease progression and reduce the burden on already overstretched cancer services.

Evidence on the management of OED, follow-up periods and time intervals between monitoring reviews remains scarce, which prompted the use of a consensus approach in the development of these recommendations. Similar methodology has been successfully used to develop consensus recommendations for head and neck surgical oncology practice during the SARS-CoV-2 pandemic [34]. These consensus guidelines cannot cover every clinical situation and it is recognised that practice will need to respond to changing infection rates in the community.

Remote consultations have become routine practice within the NHS in the UK in recent months, in order to rationalise the need for travel to hospital and to limit the spread of SARS-CoV-2. Remote telephone triage

**Fig. 1.** Approach to Risk Stratification of Patients with Oral Epithelial Dysplasia during pandemic outbreaks requiring reduction of routine clinical services. a. Verbal or written guidance should be provided for the purpose of achieving good-quality images suitable for surveillance (CS 5). b. All patients, including ‘Clinically Vulnerable’ and ‘Clinically Extremely Vulnerable’ individuals should be offered face-to-face appointments where there is a clinical need for physical examination; likewise any patient who declines a remote consultation in preference of face-to-face examination should be accommodated where possible. (CS 11 & 12). c. Patients who initially decline a face-to-face consultation should be re-contacted in six weeks to offer an appointment.
should be arranged, within 1–2 weeks of the scheduled appointment, to identify patients reporting red flag symptoms and signs of oral cancer. Such patients should be offered an appointment for physical examination within two weeks, with provision for biopsy on the same day. The use of photographs provided by patients may aid decision-making about the need for a face-to-face consultation. However, the use of patient-provided photographs in the diagnostic and management pathway of OED is novel, requires evaluation, and further work will need to be done to establish the safety and efficacy of this approach. Patient-provided images have been successfully used to triage dental emergencies [35] and in dermatology consultations, with 76.5% (n = 124) of photographs provided by patients providing additional helpful information [36]. In the same study, 45.7% of patient-provided photographs were graded as good, 43.2% average and 11.1% were considered poor [36]; however, these patients had not been provided with guidance to aid in achieving diagnostic-quality images. We have recommended patients are provided with verbal or written guidance to support their photography.

The annual incidence and overall prevalence of oral squamous cell carcinoma development in individuals with mild OED is low (1.7% and 5% respectively) [4,26,37], therefore, in the context of a pandemic outbreak, physical examination can be reasonably delayed by up to six months, in the absence of red flag signs and symptoms. Moderate OED carries a higher risk of progression [5] (compared to mild OED) and, unless good quality clinical photographs demonstrate the lesion is stable, a physical examination should only be delayed for three to four months. In the case of a stable lesion of moderate OED, confirmed with photographs, a six-month delay is considered acceptable. It is recognised that some patients who are offered a remote consultation will decline in preference of physical examination. This should be accommodated wherever possible in accordance with RCS guidelines [23].

Patients with severe OED are at increased risk of developing oral cancer compared to lower grades of dysplasia [5,37], therefore only a short delay of 4–6 weeks in scheduled face-to-face examination can be accepted. The meta-analysis by Mehanna et al. suggests that 24.1% of patients with severe OED/Carcinoma in-situ progress to cancer, compared to 10.3% of those with mild-moderate OED. [4] Similarly, Warnakulasuriya et al. report a 35-fold increased risk of oral cancer development in individuals with severe OED (HR 35.44 95%CI 14.22–88.3) compared to non-dysplastic lesions. [5] The disruption to surgical services has been significant, however, as services resume priority should be given to patients with severe OED who are awaiting surgery, given their notably higher risk of progression to cancer [30]. It is acknowledged that a number of studies have demonstrated that grade of dysplasia is not predictive of cancer development [38,39], however, in the absence of well-established prognostic biomarkers, grade of dysplasia remains an important and the a widely used predictive marker.

Patients declining physical examination can be assessed via remote consultations with clinical photographs as an adjunct, however, there should only be a maximum six-week interval between patient contacts, at which time a physical examination should once again be offered. These recommendations apply to the general population, including clinically vulnerable and clinically extremely vulnerable patients (as defined by NHS England) [40]. Although it is recognised that remote consultations are helpful in limiting the need for physical appointments at a time when the rate of infection is high, practitioners should offer a physical examination if justified in line with these recommendations; local policies for protecting at-risk groups should be followed [41].

General Dental Practitioners (GDPs), who would normally be involved in the monitoring of patients with OED, have also been severely affected by the SARS-CoV-2 pandemic, with practices in the UK closed for a period of 12 weeks [42,43]. The backlog of urgent dental cases could mean that routine check-ups are further delayed in the short-term; this places the duty on secondary care to ensure patients with OED are optimally managed due to restrictions imposed upon GDPs. However, in the medium to long-term, collaboration with primary care and establishing managed clinical networks for the early diagnosis of oral cancer could be a key strategy in managing these cases [44]. GDPs could be involved in remote consultations with secondary care by providing up-to-date clinical images and details of their clinical assessment of the lesion; this form of supported remote consultation could be a strategy to enhance patient care whilst avoiding the need for hospital attendance.

The recommendations provided in the present paper are comparable to those published by societies representing Gastroenterology and Gynacology specialties [45,46]. The European Society for Gastroenterology have published a position statement regarding the management of patients scheduled for a GI endoscopy [45]; they suggest a case-by-case evaluation to risk stratify patients into high priority and low priority cases; the former should be managed within 12 weeks and the latter may be deferred beyond 12 weeks. Surveillance for Barrett’s oesophagus with or without low grade dysplasia is provided as an example of a low priority case. Endoscopic treatment of high-grade dysplasia is categorised as high-priority and management is indicated within 12 weeks of diagnosis, in line with our suggestion that severe dysplasia should be closely monitored, with surgical intervention in appropriate cases as soon as capacity allows.

The European Federation for Colposcopy (EFC) and European Society of Gynaecological Oncology (ESGO) have published consensus recommendations for the management of patients during the COVID-19 pandemic [46]. These recommendations concur with our own that patients with symptoms suspicious for cancer should be evaluated within two weeks. They also suggest a risk stratified approach and suggest patient’s with high grade (dysplastic) lesions should be offered proper surgical treatment within three months or a review appointment within six months if a conservative approach is warranted. Patient appointments for review of low-grade lesions can be postponed for 12 months.

The authors accept the evident limitations to the external validity of this Delphi process, as it lacks the context of real-world data. One parallel to illustrate this limitation would be the similarly constructed recommendations in the management of head and neck cancers [34]. The subsequent COVIdsurg data has demonstrated that some of the conclusions from the earlier consensus process have not been validated by real-world clinical outcome data [47]. The authors of the current manuscript would welcome the clinical validation of this consensus developed for OED.

We should strive to achieve the balance of minimising the risk of additional, preventable oral cancers whilst ensuring the risk of SARS-CoV-2 to staff and patients is sufficiently low to justify a physical examination. It is recognised that remote consultations have limitations when compared to clinical examination of patients with OED, therefore any delay in physical examination due to SARS-CoV-2 must be modest and risk-stratified.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. SF received salary support from the NIHR UCLH Biomedical Research Centre and the NIHR Clinical Research Network.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to thank all members of the working group: Dr Richard Cook, Mr. Jagtar Dhanda, Dr Deborah Holt, Mr Owais Khattak, Mr Michael Nugent and Mr Iain Varley, for their time, expertise and guidance in developing these recommendations.
Appendix A. Scenarios discussed by the expert panel to inform the development of consensus recommendations for the management of OED during pandemic outbreaks

Interviews were completed in June 2020

Case 1

A 60-year-old male patient, smoker with a background of ischaemic heart disease. He has a diagnosis of mild OED on the buccal mucosa from 4 years ago. Has been under 6-month review with OMFS; the most recent clinical photographs from 12 months ago show a homogenous leukoplakia which has reduced in thickness in comparison to initial photographs. He was scheduled for his 6-month review in April 2020 but this was cancelled due to the COVID-19 pandemic and you have been asked to reappoint him. Would you plan to see this patient face-to-face, if so, when? If not, how would you manage his review?

Case 2

A 50-year-old female with severe dysplasia on the left lateral tongue; non-smoker; 2.5cm x 1.5 cm lesion; mixed leukoplakia/erythroleukoplakia; diagnosed Feb 2020. She is under the care of oral medicine. She wasn’t sure about having surgery at the time so you agreed to arrange a review in 3 months (May 2020). This was cancelled due to the COVID-19 pandemic but you have been asked to review the notes and arrange her appointment. Would you plan to see this patient face-to-face? If yes, when and when? If not, how would you manage this situation?

Case 3

An 80-year-old male smoker, with hypertension, with a diagnosis of moderate OED on the lower left alveolar ridge, around 1.5 cm diameter, homogenous leukoplakia. The original diagnosis was made 2 years ago and the lesion has been stable on 6-monthly reviews in the Oral Medicine clinic. What will you do? Will you see this patient face-to-face?

Case 4

A 58-year-old male, non-smoker with a large area of moderate-severe dysplasia on the lateral tongue has been under review for 2 years on the Oral Dysplasia clinic (Oral Medicine dept with OMFS input). Surgery has been discussed but would require free-flap reconstruction and the patient has elected for a ‘watchful wait’ approach. He was scheduled for his 4-month appointment in May 2020 but this was cancelled due to COVID-19 and you have been asked to reschedule his appointment. You send a generic letter asking patients to report red flag symptoms and he reports that the lesion has become sore. You ask him to provide clinical photographs from 12 months ago show a homogenous leukoplakia which has reduced in thickness in comparison to initial photographs. He was scheduled for his 6-month review in April 2020 but this was cancelled due to the COVID-19 pandemic. Would you plan to review this patient face-to-face? If yes, when, and how would you manage this? If not, how would you manage this case?

Case 5

A 75-year-old female who completed treatment for breast ca (surgery, RT and chemotherapy) six months ago. She has a background of lichen planus and a diagnosis of severe OED in the lower left buccal sulcus from 3 years ago (excisional biopsy). She is under the care of OMFS. Mild dysplasia was evident at the margins and there is an area of that the lesion has become sore. You ask him to provide clinical photographs of the lesion in question, which appear to show more significant erythroplakia at the anterior edge of the lesion. Will you send a letter requesting you to review the lesion? If yes, when, and how would you manage this? If not, how would you manage this case?

Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joraloncology.2020.105110.

References