REVIEW

Thyroid cancer in the age of COVID-19

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Abstract

COVID-19 has modified the way we practice medicine. For thyroid cancer, there have been several significant impacts. First, the diagnosis has been delayed due to social isolation, reduced access to investigations and staff redeployment. Secondly, treatment planning has needed to take into account the risk to patients and/or staff of nosocomial transmission of the virus. Finally, there are some specific concerns with respect to interactions between the virus, its treatments and cancer. This mini-review aims to address each of these impacts and to provide some guidance and confidence to our patients and colleagues during this challenging time.

Key Words

- thyroid cancer
- COVID-19
- tyrosine kinase inhibitor
- radioactive iodine

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Introduction

COVID-19 has quickly overwhelmed medical practice, albeit that most cases will recover uneventfully. The risk of death from COVID-19 is clearly related to older age and the presence of key comorbidities (Wang *et al.* 2020). Many patients with thyroid cancer will have these high-risk features; and many thyroid cancer specialists may also be deemed, vulnerable workers. Our usual algorithms of care based upon risk-stratified treatment modalities have acquired the ordinal variable of COVID-19 risk. Ordinarily, the choice for treatment of differentiated thyroid cancer is straightforward with surgery at the earliest opportunity followed, where indicated, by radioactive iodine (I^{131}). Now, however, the risk of morbidity or mortality from thyroid cancer competes against the risk of COVID-19 exposure (to patients and staff) in medical settings and the availability of operative and post-operative care.

Early data from China suggests that COVID19 *per se* does not worsen the outcome of cancer, but as the pandemic continues, with investigations and treatment

delay, morbidity and mortality from thyroid cancer may increase (Liang *et al.* 2020). Experience from other disasters is informative and may predict outcomes for thyroid cancer patient. Following Hurricane Katrina, breast cancer patients had a 15% increase in mortality compared to matched patients at the same stage, which remained significant after adjustment for sociodemographic characteristics and cancers stage (Bell *et al.* 2020). A meta-analysis looking at the impact of natural disasters to oncology care identified infrastructure disruptions, health care workforce disruptions including delay in medical training, disruption to follow up, and medication stock shortages to be factors contributing to disruption in continuity of oncology care (Man *et al.* 2018). Although we lack much of the data required to best manage each cancer scenario, some generic principles have at least become apparent over the past few months.

In this review, we discuss some clinical challenges that clinicians could consider during this pandemic.

Figure 1

Impact of COVID-19 on outpatient clinic presentations, ultrasound-guided fine needle biopsy, and in-patient radioactive iodine ablation numbers at Royal North Shore Hospital, Sydney Australia. (A) The numbers of patients presenting for outpatient review via face to face and telehealth consultation (phone and video), at the Department of Endocrinology, Royal North Shore Hospital (RNSH), Sydney, Australia, in March, April, and May, in 2019 compared to 2020. Numbers in 2019. Though the total numbers of patients seen on all platforms, in 2019 ($n = 2167$) and 2020 ($n = 2179$) are the same in these two periods, the majority of patients were seen face to face in 2019, and via telehealth in 2020. (B) The numbers of patients undergoing ultrasound-guided fine needle biopsy aspirate in 2019 compared to 2020, in March, April and May at RNSH. The lower numbers in April in 2019 and 2020 likely reflect holidays during this period. Despite this, there has been a consistent reduction in numbers in 2020 compared to 2019, at 59% for March, 62% for April, and 63% for May in 2020. (C) Numbers of patients having inpatient admission for radioactive iodine ablation in 2019 compared to 2020 at RNSH. Numbers are mostly maintained in March 93% and April 100% but reduced to 62% in April.

We will reference experience with other coronaviruses where possible but the scale of COVID-19 is unprecedented and published experience is limited.

Effect of COVID-19 risk mitigation strategies on thyroid cancer diagnosis

Delay in thyroid cancer diagnosis due to fewer medical assessments

Social distancing and/or social isolation are now recognized as two of the most important protections against the spread of COVID-19 (Koo *et al.* 2020). However, both have resulted in changes to usual medical care. Within primary care, there was a rapid transfer from face-to-face consultation to telehealth from March 2020. Health care systems developed strategies to assess patients remotely (Greenhalgh *et al.* 2020, Kidd 2020) with greater than 80% of all consultations becoming virtual in published series (Gilbert *et al.* 2020). While clinicians and patients have been reasonably satisfied with video consultations, assessment for thyroid nodules or cancer recurrence is inadequate without physical examination and ultrasound (Greenhalgh *et al.* 2020, Hollander & Carr 2020). Similarly, availability of fine needle biopsies for thyroid nodules has been restricted by concerns about COVID-19 (Huang *et al.* 2020a, Kooraki *et al.* 2020). Since fewer than 10% of all thyroid nodules will be malignant (Haugen *et al.* 2016), it has been reasonable to delay most thyroid biopsies during the pandemic, except for those nodules with highly concerning sonographic features as per TIRADS scoring system (Grant *et al.* 2015), or clinical features of obstruction (Huang *et al.* 2020a, Vrachimis *et al.* 2020).

Our own experience of the impact of COVID-19 on clinical practice is shown in Fig. 1; most of our consultations from March have been by telehealth, driven in part by institutional policy (Fig. 1A); whereas only 4.9% of consultations in 2019 was via telehealth, for the same period in 2020 it was 72% of consultations (41% in March, 95% in April, and 83% in May), despite similar total consultation numbers (2019 $n = 2167$, 2020 $n = 2179$). There has been a considerable decline in the number of thyroid biopsies performed in this time period (Fig. 1B); only 59%, 62% and 63% of biopsies were being done in March, April, and May 2020 compared to 2019. Nevertheless, to date, we have been able to maintain our treatment for high-risk thyroid cancers, including I¹³¹ ablation for March (93%) and April (100%) but a

slight decline in May (62%) (Fig. 1C). Urgent surgery for proven thyroid cancer has not been delayed, with similar numbers in 2019 and 2020 (73% of cases in April 2020 compared to 2019). Table 1 offers a proposed matrix for the management of thyroid cancer during COVID-19 based on our experience and the current risk level for local COVID-19 community transmission, including how to screen patients, triaging treatment including surgery, I-131, and systemic treatment, and outpatient follow up.

Effect of COVID-19 risk mitigation strategies on thyroid cancer treatment

Balancing timing of cancer treatment against the risk of COVID-19 exposure (to patients and healthcare workers) in medical settings

Thyroid cancer outcomes vary widely according to patient age, gender, histological subtype, extrathyroidal extension, nodal involvement and the presence or absence of distant metastases (Grant *et al.* 2015, Cabanillas *et al.* 2016). It is arguable that most papillary thyroid cancers occurring in younger subjects (e.g. <50 years) would not suffer from a delay in either diagnosis or treatment for the duration of the COVID-19 pandemic (Perrier *et al.* 2018); whereas treatment of advanced thyroid cancers may be time-critical particularly in the presence of airway compromise (Cabanillas *et al.* 2019). Where patients have space occupying lesions within the brain or spinal cord, extensive lung metastases, or neck lesions in close proximity to the trachea, prompt surgical,

and systemic treatment may be time critical. This would include, where appropriate, I¹³¹, external beam radiotherapy (ERBT), and tyrosine kinase inhibitor (TKI) therapy. The benefit of these treatments has to be balanced against the risk of nosocomial transmission within the hospital setting. During the peak of the pandemic, where COVID-19 transmission rates were high, the significant risk of contracting COVID-19 during hospitalisation entails that treatment is justified if there is likely imminent progression. The utilisation of resources for patients to be admitted and use of personal protective equipment (PPE) to complete treatment is an additional consideration. In particular, in the aerosol generating head and neck surgeries, there is increased risk for health care workers (HCW) for contract COVID-19 and increased PPE is required to reduce HCW transmission (Couloigner *et al.* 2020, Cui *et al.* 2020, Kowalski *et al.* 2020, Mick & Murphy 2020).

Where possible, oncology surgery has continued, but options, where this is not possible, include active surveillance; deferring those who have the stable disease who cannot undergo immediate surgery; and increasing PPE for patients who must undergo treatment (Huang *et al.* 2020b). Triaging of resources puts an additional strain on the clinicians and patients, and may need to be performed by a separate committee, to balance public health concerns and adequate management of thyroid cancer (Civantos *et al.* 2020). Balancing the need for surgery with the risk of both the patient and staff to asymptomatic COVID-19 needs to be carefully assessed (von Lilienfeld-Toal *et al.* 2020).

Table 1 Proposed matrix for management of thyroid cancer during COVID-19.

Risk level*	Screening	Surgery	I ¹³¹	Systemic treatment	Follow up
Low	As per usual protocol. Consideration of minimising repeat biopsies and FNA in non-suspicious nodules	Consider delay in surgery if possible, with operating theatre rationalisation and reduced use of non-critical AGP (e.g. VCC)	Adjuvant, recurrence and palliative treatment as per usual guidelines, consideration of delaying adjuvant treatment in low risk cases	As per usual guidelines	Telemedicine preferred but face-to-face consultation acceptable
Medium	Reduction in USS and FNA to minimise health care services interaction	All non-urgent elective surgery postponed. Only cases likely to cause morbidity within 30 days indicated (category 1)	Continuation of treatment for recurrence or metastatic PTC	Metastatic DTC, all PDTC, all MTC, all ATC to receive usual care	Telemedicine preferred
High	Minimal	Proceed for imminent mortality airway compromise, space-critical metastases	Considered on case by case basis	Cautious initiation, generally avoid if ECOG>1	Telemedicine required

*Risk level: low-low community case load, low risk of patient having COVID and low risk of nosocomial acquisition; medium, moderate community case load; high-high community case load and high risk of community transmission
AGP, aerosol generating procedures; VCC, vocal cord check.

The European Society of Medical Oncology (ESMO) guidelines for COVID-19 have highlighted two patient groups to consider, those 'off' therapy and those on 'active' therapy. Common to both groups are enforcing social distancing methods, PPE, and hand hygiene. In those on active treatment activities such as dispensing oral chemotherapy for 3 months at a time should be encouraged, delay follow up visits, telemedicine where possible and performing all pathology close to home to minimise nosocomial transfer (ESMO 2020). 'Active therapy' patients include newly diagnosed patients who need surgery and/or RAI; and patients with recurrent or metastatic disease. These patients will usually require physical attendance for assessment and treatment. 'Off active therapy' includes those DTC patients with low risk of recurrent and/or metastatic disease. These patients would be suitable for follow-up by virtual consultation. Patients with stable minimal residual disease might in selected cases also be managed by virtual consultation.

Operating theatre and/or intensive care unit availability

Thyroid cancer surgery is preferentially performed at specialist centres, with patients often having to travel from their homes to different locations, which may not be possible during the pandemic. In our institution, surgical clinic visits were reduced by approximately 80% during the height of our 'first wave' of COVID-19. In addition, surgical staff and/or operating theatres may be redeployed to manage COVID-19 cases. In Australia, elective surgery was furloughed to protect PPE availability until such a time as COVID-19 cases decreased and protect patients and staff from Aerosol generating procedures (AGP) and unintended exposure to COVID-19 (Brat *et al.* 2020). Surgery in the head and neck and intubation for anaesthesia is classified as a high risk of AGP and thus changes in theatre management have been introduced to mitigate this risk. These changes include the use of specialised PPE and changes to intubation protocols which have increased case time and further reduced theatre availability (Howard 2020).

In addition, the work-up of patients with thyroid cancer has changed with limited availability of vocal cord checks (VCC) using laryngoscopy due to the risk of generating aerosols in an uncontrolled environment, due to this in our institution, VCC were not able to be conducted for any patients including those with suspected vocal cord palsies (Thamboo *et al.* 2020).

Due to these issues, many surgical societies issued guidelines as to which patients should proceed

with surgery, many of these guidelines divide presentation by urgency of the predicted harm if the patient's pathology was not treated (<https://www.generalsurgeons.com.au/covid-19>). A common system used in Australia is to classify patients who will come to harm if surgery is delayed more than 4–6 weeks (Category 1) and those which will come to harm if delayed more than 12 weeks (Category 2), and cases assessed as being able to be delayed longer than 12 weeks (Category 3).

During the initial stages of the COVID-19 pandemic, only category 1 cases were recommended to proceed (Royal Australian College of Surgeons 2020).

Thus, patients with thyroid cancer were classified as Category 1 if the size and location of cancer posed an immediate threat of harm if left untreated; patients with smaller cancers were delayed. With the re-opening of semi-elective surgery in Australia, many of these patients with smaller cancers who were initially delayed have now been able to have surgery. However, a substantial number of patients with atypical nodules were delayed and who are only now proceeding with surgery for diagnostic hemithyroidectomy. It is likely that many patients have also delayed presentation for assessment and surgery, the effect of which will become apparent in the coming months to years.

Availability of radioactive iodine resources

Management of intermediate- and high-risk differentiated thyroid cancer includes post-surgical administration of I¹³¹. This usually requires admission to hospital, and thus there has been a decrease in nuclear medicine services for diagnosis (reduced by 58.4% for thyroid) and therapy (reduced by 41.8%) noted in Europe after the pandemic has reached a peak (Freudenberg *et al.* 2020). Depending on the location, nuclear medicine procedures may also uncover asymptomatic patients with COVID-19, found in 9% of a series of asymptomatic patients in Italy in March 2020 (Albano *et al.* 2020). Local centres must carefully assess risk to patients with delay of diagnostic scans where possible, and mitigate risks of admission by risk assessment and utilize outpatient treatment where possible. The American Thyroid Association (ATA) has released guidelines on when it is possible to delay I¹³¹ and surgery for thyroid cancer, however, this largely depends on local COVID-19 transmission rates and the ability of the health systems to manage (American Thyroid Association 2020).

One additional point to note is the effect of I¹³¹ on smell. Olfactory function is reported to deteriorate in early

stages of I¹³¹ with mild and moderate anosmia occurring in the first year post I¹³¹ (Suat *et al.* 2016). Anosmia or hyposmia is also a characteristic complication of COVID-19 (Gane *et al.* 2020). It is vital to recognise this crossover to avoid causing unnecessary alarm in patients following I¹³¹ treatment.

Overall, patient communication is critical to stratify risk and manage appropriately those with severe disease. Utilisation of telemedicine and continuation of remote multidisciplinary meetings will assist with difficult decision making (Hennessey 2020, Hollander & Carr 2020). Although thyroid cancer is mostly slow growing, there are those with advanced disease whose prompt treatment should remain a priority despite the global pandemic (Wang & Zhang 2020, Xia *et al.* 2020).

Initiation and monitoring of tyrosine kinase inhibitor therapy

Radioactive iodine refractory differentiated thyroid cancer and metastatic medullary thyroid cancer are often managed with tyrosine kinase inhibitor (TKI) systemic therapy, including lenvatinib, cabozatinib, and vandetanib (Gild *et al.* 2011, Wells *et al.* 2015, Haugen *et al.* 2016, Tsang *et al.* 2016). Treatment initiation even in non-pandemic times is challenging and when there is rapidly progressive disease a pandemic environment further complicates the situation. The decision to commence TKIs must balance the risks of regular clinic visits for clinical review, ECG and pathology tests on treatment, against the risk of cancer progression if left untreated. Generally, systemic therapy is recommended when patients develop symptomatic and/or progressive disease.

TKIs have a myriad of adverse effects, which usually present in the first few months of treatment (Cabanillas & Takahashi 2019). They are well described and as such can be anticipated, monitored and managed remotely (Supplementary Table 1, see section on [supplementary materials](#) given at the end of this article). Of note, hypertension is common, and may be a positive sign that the patient will respond to treatment (Wirth *et al.* 2018). Ideally, patients should be provided with their own sphygmomanometer to monitor blood pressure remotely where possible and plan to escalate treatment within the first few weeks, including the use of increased doses of antihypertensive agents. The use of either angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) appears to be safe in patients at risk for COVID-19 (Guo *et al.* 2020, Rico-Mesa *et al.* 2020, Vaduganathan *et al.* 2020, Zhang *et al.* 2020).

Other symptoms of TKIs can mimic COVID-19, including fatigue, nausea, vomiting, and diarrhoea. Palmar plantar erythrodysesthesia is a common and often severe adverse effect, and having pre-emptive supply of potential treatment such as topical urea and corticosteroids may be useful to allow continuation of treatment. Use of smartphones to send clinicians high-resolution photographs of skin lesions may be a sensible method for follow up and assessing grades of severity. Some TKIs cause prolongation of the QT interval, particularly vandetanib. Utilisation of remote monitoring, such as with ECG apps on smartphones, may prompt earlier reviews where required (Garabelli *et al.* 2017).

As most follow up consultations will be by telemedicine, utilisation of prefilled adverse effects list prior to consultation will streamline the consultation (Supplementary Table 1).

Heritable thyroid cancer syndromes

As much as COVID-19 impacts on the practice of individual clinicians, its disruptive effects are magnified in conditions that require complex systems-based care. This is exemplified by the example of Multiple Endocrine Neoplasia syndrome type 2 (MEN2) and other heritable thyroid cancer syndromes. In ordinary circumstances, recognition and management of MEN2 follows a highly co-ordinated routine involving surgeons, physicians, pathologists, genetic testing facilities, family cancer centres, imaging facilities (both structural and PET) and, in some cases, fertility services. Thus, patients diagnosed with MTC should generally be referred for genetic counselling and germline *RET* testing; if MEN2 is confirmed, then cascade testing of first-degree relatives should be accompanied by appropriate genetic counselling. Familial *RET* mutation carriers will then be considered for prophylactic thyroidectomy (Wells *et al.* 2015); all MEN2 patients also require periodic screening for pheochromocytoma (Brandi *et al.* 2001, Tsang *et al.* 2015, Wells *et al.* 2015). Prenatal counselling is appropriate for an MEN2 patient planning a family (Tsang *et al.* 2015). MEN2 patients with metastatic MTC may be suitable for targeted therapies.

COVID-19 will disrupt this 'supply chain' of MEN2 management at every step: patients with MTC may face delays in seeing a Genetics Service; *RET* genetic testing may be delayed due to reduced pathology services; family member tracing and testing will be compromised by disrupted Clinical Genetics services; referrals for prophylactic thyroidectomy will be delayed by restrictions

on surgical services described previously; prenatal counselling may be more difficult to obtain; and diagnosis of metastatic MTC may be delayed if patients are reluctant to attend routine follow-up visits and/or oncology clinics and imaging facilities are restricted. These disruptions may have a multiplier effect on adverse outcomes: MEN2 may not be appropriately diagnosed; family members may not be traced and offered genetic testing; the benefits of prophylactic thyroidectomy may be lost; and metastatic disease may progress beyond the benefit of targeted therapy. There is no easy solution other than prioritising coordinated service delivery as best as possible.

Impact of thyroid cancer on COVID-19

Increased risk of COVID-19 complications

The initial data from Wuhan confirmed that harbouring malignancy increases the risk of ICU admission and death, HR 3.50 (95% CI 1.60–7.64) (Guan *et al.* 2020).

Predilection for thyroid cancer in COVID-19 patients

To investigate a relationship between thyroid cancer and COVID-19, we examined first the effect of having thyroid cancer and the potential increased risk for COVID-19 acquisition and second, whether COVID-19 can predispose patients to cancers, including thyroid. As discussed above the spectrum of thyroid cancer patients is broad and those patients with small well-differentiated tumours are likely to do well regardless and these 'off active treatment' patients are unlikely to be immunosuppressed secondary to their cancer diagnosis. The 'active therapy' cohort thyroid cancer patients comprise immunocompromised cancer patients that are recognised to have an increased risk for community-acquired respiratory viruses (Whimbey *et al.* 1997). The cause of the increased risk is multifactorial, including cellular and humoral immunity compromise, invasive vascular lines and local tumour effects. It is estimated that patients with cancer are ten times more likely to acquire sepsis than those without (Thirumala *et al.* 2010). Indeed, a majority of thyroid cancer patients die from non-cancer related illnesses including infection (Zaorsky *et al.* 2017).

Treatment can further impact the likelihood of COVID-19 infection and complications. I¹³¹ is used in both adjuvant and metastatic settings for DTC. I¹³¹ has short- and long-term effects on immune function that may affect patients' COVID-19 outcome. Transient reductions

in myeloid and lymphoid cell lineages are common after ablative therapy which can continue out to 1 year (Molinaro *et al.* 2009). The nadir is usually 5–9 weeks. Bone marrow suppression following prolonged high dose I¹³¹ is well described, and when used in conjunction with ERBT or in the presence of bony metastases it can lead to a more severe suppression (reviewed in Lee 2010). The CDC has indicated that patients with bone marrow suppression are at higher risk for COVID-19 severity and complications (US Department of Health & Human Services 2020). I¹³¹ itself can modulate the immune system with cytokines dysregulation observed following I¹³¹ treatment for Graves' disease (Du *et al.* 2017). In those thyroid cancer patients with thyroid autoimmunity, treatment with I¹³¹ can increase IL-6, a cytokine implicated in severe respiratory disease and death from COVID-19. Patients who did particularly poorly had a surge of IL-6 and ferritin which correlated with mortality (Ruan *et al.* 2020).

It is controversial whether high-dose corticosteroids should be avoided in patients at risk of COVID-19. In previous coronavirus pandemics (MERS-CoV and SARS) corticosteroids were associated with worse outcomes in patients (Li *et al.* 2020). In thyroid cancer, corticosteroids are often used in patients with brain metastases or high volume lung metastases at the time of I¹³¹ treatment (McWilliams *et al.* 2003). From early data on COVID-19, some patients were found to be COVID-19 positive at the time of receiving I¹³¹ therapy (Albano *et al.* 2020). All these issues whilst unknown could be considered in deciding timing of I¹³¹ in the COVID-19 pandemic.

In the last decade, TKIs have become standard treatment for advanced thyroid cancers particularly those with anaplastic or radioiodine refractory components (Gild *et al.* 2017). Whether these agents increase the risk of COVID-19 infection and/or complications is unknown. Patients on lenvatinib in the SELECT trial were more likely to develop pneumonia, sepsis and other lower respiratory tract infections than the placebo group 6 (Schlumberger *et al.* 2015).

Drug interactions are also critical to consider for those on TKIs as the consequence can be fatal. Current experimental therapies for COVID-19 and potential thyroid cancer treatments interactions is Table 2. Some TKIs used in the treatment of thyroid cancers including Dabrafenib, Trametinib and Selumetinib could be considered for repurposing as they have in vitro activity against other coronaviruses SARS and MERS-CoV (Kindrachuk *et al.* 2015).

In our cancer patients, the decision to treat progressive metastatic disease must be balanced against the risk of

Table 2 Interaction between COVID-19 and systemic thyroid cancer treatments.

Treatment	Mechanism/theory	Outcome	Thyroid cancer drug interaction
Ivermectin	Inhibit viral repair	Reduced viral cell RNA <i>in vitro</i>	N/A
Convalescent plasma	IgG or IgM SARS-CoV-2 antibodies as infusion	Patients improved and viral load negative	
Lopinavir-Ritonavir	Antiviral	Mixed outcome, 1 study clinical improvement, 2 nil	
Tocilizumab/Siltuximab	Anti-IL6 receptor antibody	Reduced CRP levels in small group	Lenvatinib – increase risk of abnormal heart rhythm Cabozatinib – will potentiate drug concentration
Hydroxychloroquine	Inhibited viral replication	Effective <i>in vitro</i> and promising viral clearance in patients	
ACE inhibitors	SARS-CoV2 binds to ACE2 receptor for cell entry	Lower mortality	Nil reaction

complications familiar to cancer patients such as infection compounded by frailty.

Long-term risks

Whether COVID-19 will ultimately lead to increased incidence of any cancer is highly speculative. However, viruses do play a role in the development of some cancers, including thyroid cancer. There is no data suggesting that other coronaviruses have affected thyroid cancer incidence, but these also had much lower worldwide infection rates compared with COVID-19. Certain viruses are established carcinogens including human papilloma virus, hepatitis B and C and Epstein Barr virus (EBV). EBV is a highly contagious and ubiquitous virus which can cause several cancers but the vast majority of those who contract it will have minor symptoms. EBV together with Parvovirus B19 have been associated with increased inflammation in thyroid tissue upregulating IL6 and TNF α and the presence of EBV and its gene products have also been associated with thyroid tumorigenesis (Etemadi *et al.* 2017, Moghoofei *et al.* 2019). EBV has also been shown to activate the ERK pathway which we know is dominant in thyroid cancer (Kakavandi *et al.* 2018). Whether this extends to COVID-19 is unknown nor the increase in incidence following prolonged COVID inflammation, an established cancer risk.

Inflammation

Infection leading to inflammation is an important consideration for the long-term effects of COVID-19. COVID-19 induces a proinflammatory generation and secretion of cytokines including IL-6. Chronic inflammation increases the risk and progression of cancer. Recent studies have shown how in a murine model,

acute lung infection can augment tumour metastases by supporting a metastatic-niche like environment (Yan *et al.* 2013). Pneumonia with lung injury occurred in 16% of patients with SARS (Ruuskanen *et al.* 2011). Potential future effects of such widespread lung inflammation on our metastatic thyroid cancer patients is concerning and the extent unknown.

Immunosuppression

Long-term immunosuppression is linked with various complications including cancer incidence. In patients following renal transplants, there is a higher incidence of thyroid cancer thought to be due to the prolonged immunosuppression (Karamchandani *et al.* 2010, Veroux *et al.* 2019). The synchronous appearance of Hashimoto's thyroiditis and thyroid cancer has long connected a dysfunctional immune system with the development of malignancy (Ehlers & Schott 2014). In other dysfunctional immune system diseases such as inflammatory bowel disease and SLE, thyroid cancer is more common and in those on immunosuppressive therapy had an increased risk (Antonelli *et al.* 2010, Cao 2018). Furthermore, the immunomodulatory effect of statins may also contribute to an increase in thyroid cancer prevalence in women in a case-control study (Hung *et al.* 2015).

Academic setbacks

The consequences for the thyroid cancer research community is grim and the impact on a thyroidologist is already lamented (Hennessey 2020). Several conferences have been postponed including the International Thyroid Congress, the Endocrine Society meeting in San Francisco, the ATA spring meeting. It is likely that more academic congresses in 2020 and beyond will be affected. The deceleration of research, and the lack of opportunity

to share ideas in international meetings will take time to recover and regain momentum.

Conclusions

The impact of COVID-19 is unprecedented and this mini-review aims to highlight the changes in risk management and practice for thyroid cancer. The generally indolent nature of many thyroid cancers may withstand delayed treatment, but this subtlety should be carefully communicated to patients. While we have attempted to anticipate some of the longer-term effects, vigilance is required in monitoring patients together with the frequently changing literature to remain up to date on the myriad of complications of this novel coronavirus.

Supplementary materials

This is linked to the online version of the paper at <https://doi.org/10.1530/ERC-20-0279>.

Declaration of interest

B R reports personal fees from Loxo Oncology, during the conduct of the study. B R, R C B and V T report personal fees from Eisai, outside the submitted work. The other authors report no conflict of interest.

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All co-authors reviewed and approved the final manuscript.

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