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Original article

The first wave of COVID-19 did not cause longer wait times in head and neck cancer. Experience of a French expert center

T. Vanderhaegen [a], A. Pierache [b], G. Mortuaire [a], B. Rysman [a], R. Nicot [c], D. Chevalier [a,d], F. Mouawad [a,d,*]

[a] ENT and Head and Neck Department, Huriez Hospital, Lille University, CHU Lille, rue Michel-Polonovski, 59037 Lille cedex, France
[b] METRICS: Evaluation des Technologies de Santé et des Pratiques Médicales – ULR 2694 – University Lille – CHU Lille, 59000 Lille, France
[c] Service de stomatologie et de chirurgie maxillo-faciale, hôpital Roger Salengro, université de Lille, CHU de Lille, rue Michel-Polonovski, 59037 Lille cedex, France
[d] CANTHER "Cancer Heterogeneity, Plasticity and Resistance to Therapies", UMR9020 CNRS – U1277 Inserm – Université de Lille – CHU de Lille–COL, 59037 Lille cedex, France

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ABSTRACT

Background: Head and neck cancers (HNC) have poor survival prognosis, as tumors are often diagnosed at advanced stages in patients consulting late. The first lockdown linked to the 1st wave of COVID-19 (Coronavirus Disease 2019) disrupted consultation schedules in France.
Objective: The principal aim of the present study was to analyze consultation wait time in HNC during and after lockdown, in our university expert oncology reference center, to disclose any increase in treatment wait time.
Methods: A single-center retrospective study included patients with a first diagnosis of HNC. Three groups were distinguished: "lockdown", "post-lockdown", and a "control" group (corresponding to a reference period 1 year earlier). Intervals between first oncologic consultation and multidisciplinary tumor board (FC-MTB) and between MTB and first treatment (MTB-T) were assessed.
Results: One hundred and seven patients were included in the control group, 60 in the lockdown group and 74 in the post-lockdown group. There was no increase in median FC-MTB interval (respectively 35, 29 and 28 days) between the lockdown and post-lockdown groups compared to the control group (respectively $P = 0.2298$ and $P = 0.0153$). Likewise, there was no increase in MTB-T interval (27, 20 and 26 days respectively) ($P = 0.4203$).
Conclusion: No increase in wait times was observed during the lockdown and post-lockdown periods in our center.

1. Introduction

The first French COVID-19 (Coronavirus disease-2019) victims were managed on January 24, 2020 [1]. The infection, with a high level of respiratory transmission, began to spread worldwide from the Chinese city of Wuhan [2]. With the exponential rise in contamination and mortality and the saturation of health services in France, notably in certain regions including ours (Fig. 1), exceptional measures were taken on March 17 to break the chain of contamination, with several weeks' nationwide lockdown [3]. At the same time, medical consultations and non-urgent surgery were limited or cancelled, to control contamination of patients in hospital and to free up personnel, beds and ventilators for patients with severe SARS-CoV-2 (Severe Acute Respiratory Syndrome induced by Coronavirus 2) [4,5].

Good practice guidelines were drawn up by the French ENT Society (SFORL) [5,6]. As of May 11, when lockdown was lifted, surgery was no longer to be postponed, to avoid treatment delay and loss of chance [6]. Even so, Laccourreye et al. reported a drop in the number of patients dealt with in their multidisciplinary tumor board meetings, perhaps due to the difficulty of consulting during this period or of organizing imaging assessments. This state of affairs could delay treatment, with risk of local, lymph node and/or remote extension, jeopardizing survival and aggravating morbidity associated with heavier treatments [7–9].

* Corresponding author. Service d'ORL et de chirurgie cervico-faciale, université de Lille, hôpital Huriez, CHU de Lille, ONCOLille, Institut du cancer. CANTHER "Cancer Heterogeneity, Plasticity and Resistance to Therapies", UMR9020 CNRS – U1277 Inserm – Université de Lille – CHU de Lille – COL, 59037 Lille Cedex, France.
E-mail address: francois.mouawad@chru-lille.fr (F. Mouawad).

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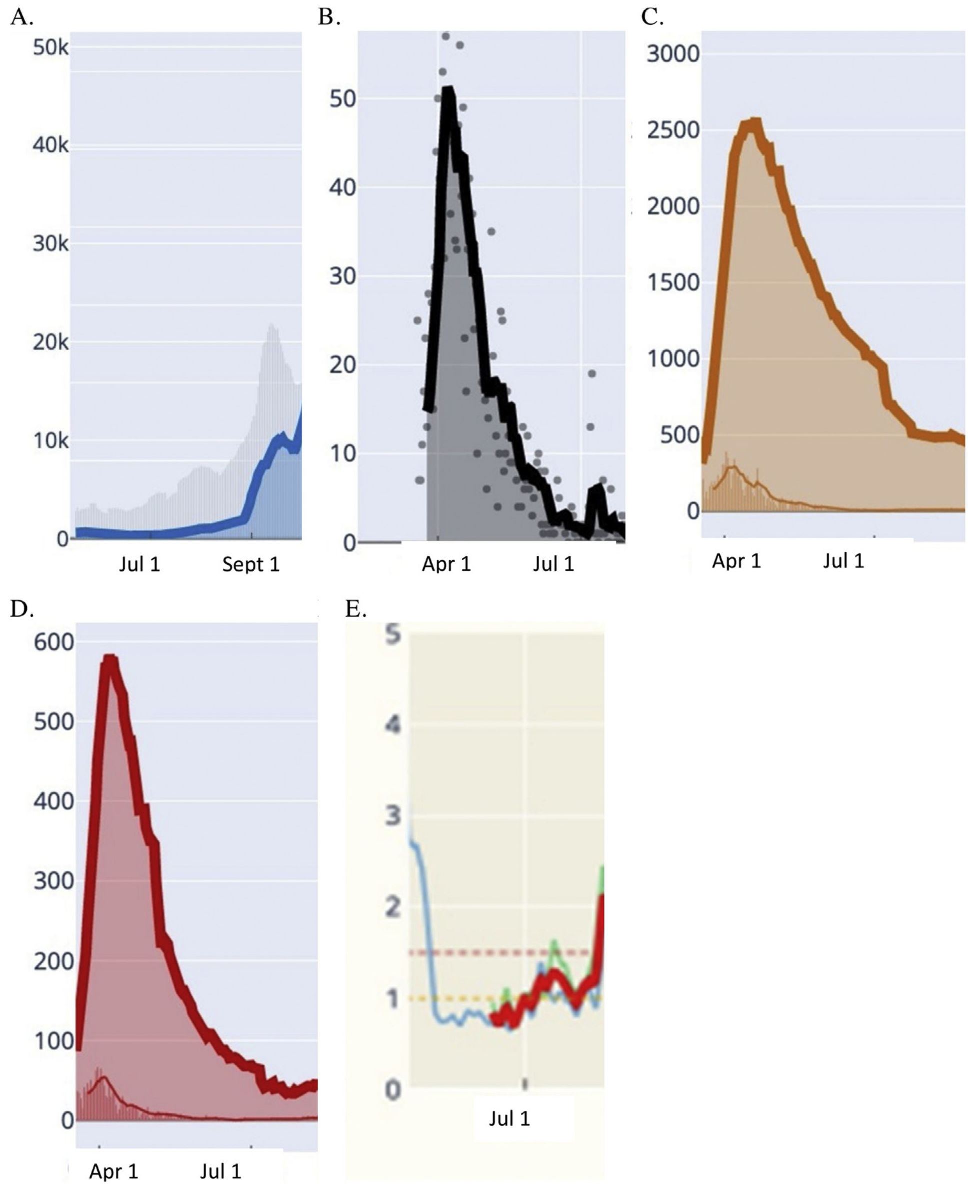

Fig. 1. A. Number of Covid-19+ patients in the Hauts de France administrative region. Numbers are not exhaustive for the 1st wave, as testing was not systematic; therefore curves were not plotted. B. Daily Covid-19-related in-hospital deaths in the Hauts de France region. C. Hospital admissions for Covid-19 in the region. D. ICU admissions for Covid-19 in the region. E. R0 curve in the region during the 1st wave. All graphs were taken from the covidtracker.fr website, based on Public Health France data.

The main aim of the present study was therefore to assess two principal time intervals in diagnostic and therapeutic management during 3 periods: lockdown, post-lockdown, and a control period (i.e., the corresponding period in 2019). This assessment concerned head and neck cancer patients dealt with in multidisciplinary tumor board meetings in the framework of initial management. Secondary objectives comprised comparison of clinical stages and associated synchronous tumors at initial treatment.

2. Patients and methods

This was a single-center retrospective study of 3 cohorts of patients treated for a first head and neck cancer, conducted in our regional university oncology reference center in France.

The first cohort was a control group of patients presented in head and neck cancer multidisciplinary tumor board meetings in the year prior to lockdown, between June 1 and August 31, 2019 (i.e., a period of 13 weeks). The second cohort comprised patients presented during the lockdown period (extended to the end of May): March 17 to May 31, 2020 (i.e., a period of 11 weeks). The third cohort comprised patients presented after lockdown, between June 1 and September 6, 2020 (i.e., a period of 14 weeks).

Inclusion criteria comprised presentation in our head and neck cancer multidisciplinary tumor board meetings for a first head and neck cancer, age >18 years, and consent to use of medical data for research purposes.

Exclusion criteria comprised age < 18 years, prior history of head and neck cancer, non-consent to use of medical data, presentation for persistence or local or locoregional recurrence or metastasis, skin or thyroid cancer (dealt with by other team meetings in our institution), and presentation for assessment of treatment efficacy and/or discussion of possible adjuvant treatment.

Epidemiologic data comprised age, gender, WHO (World Health Organization) general health status score, Charlson comorbidity score [10], and percentage weight-loss over 3 months. Oncologic data comprised tumor location, tumor stage (TNM 8th edition) [11], and histologic diagnosis. Daily consumption of or withdrawal from alcohol and tobacco at diagnosis were recorded. Any synchronous

Table 1
Epidemiology (age, gender, WHO score, Charlson score, weight-loss and severity, tumor location, stage, alcohol intake and smoking) in the 3 groups.

	Control $n = 107$	Lockdown $n = 60$	Post-lockdown $n = 74$	P
Male gender (%)	86 (80.4)	46 (76.7)	56 (75.7)	0.72
Age (years) ± standard deviation	63.2 ± 10.4	61.6 ± 9.1	63.4 ± 9.8	0.52
WHO score > 2 (%)	8 (7.5)	3 (5)	1 (1.4)	0.19
Charlson score > 4 (%)	55 (51.4)	33 (55)	37 (50)	0.84
Weight-loss (%)	23 (38.3)	11 (27.5)	22 (47.8)	0.15
Severity of weight-loss (%)				
< 5%	4 (17.4)	2 (18.2)	8 (36.4)	0.63
5–10%	9 (39.1)	5 (45.4)	8 (36.4)	
> 10%	10 (43.5)	4 (36.4)	6 (27.2)	
Tumor location (%)				
Oral cavity/oropharynx	56 (52.3)	35 (58.3)	44 (59.5)	0.86
Larynx/hypopharynx	37 (34.6)	19 (31.7)	23 (31.1)	
Other	14 (13.1)	6 (10)	7 (9.4)	
Stage (%)				
I/II	33 (30.8)	15 (25.9)	14 (18.9)	0.20
III/IV	74 (69.2)	43 (74.1)	60 (81.1)	
Alcohol (%)				
Consumption > 20 g/d continued	34 (41.4)	22 (46.8)	25 (43.1)	0.95
> 20 g/d ceased	18 (22)	8 (17)	13 (22.4)	
< 20 g/d	30 (36.6)	17 (36.2)	20 (34.5)	
Smoking (%)				
Active	48 (55.8)	27 (50)	41 (62.1)	0.64
Withdrawal	26 (30.2)	21 (38.9)	18 (27.3)	
Non-smoker	12 (14)	6 (11.1)	7 (10.6)	

Data shown as number (%).

tumor, the treatment recommended in the team meeting (surgery, radiotherapy, chemotherapy, support care, palliative care, and associations) and any infection and/or COVID-related complications during the diagnostic and therapeutic process were recorded.

To assess the main endpoint, 2 management intervals were analyzed: the time between first consultation (ENT, maxillofacial surgery, etc.) and the multidisciplinary tumor board meeting (FC-MTB), and the time between the meeting and initiation of treatment (MTB-T). Specific intervals for MTB to surgery (MTB-S) or MTB to radio- and/or chemo-therapy (MTB-RTCT) were also measured. For secondary endpoints, tumor stage at treatment and any synchronous tumors were recorded.

Statistical analyses were performed by the institution's methodology and biostatistics unit. Qualitative variables were reported as number and percentage. Numerical variables were reported as mean and standard deviation when normally distributed, or else as median and interquartile range; normality was checked graphically and on Shapiro-Wilk test. Data were reported for the 3 groups (2019 control, 2020 lockdown, and 2020 post-lockdown) and compared by logistic regression for binary variables or linear regression for time intervals (FC-MTB, MTB-T, MTB-S and MTB-RTCT). Intervals were transformed logarithmically to check normal residue distribution. Comparisons were adjusted on predefined confounding factors: WHO score (dichotomized as ≤2/>2), Charlson score (dichotomized as ≤4/>4), tumor location (oral cavity and oropharynx; larynx and hypopharynx; other) and tumor stage at arrival (dichotomized as early (I and II)/advanced (III and IV)). Odds ratios (OR) for binary values and difference in mean value for time intervals were derived from regression models as size effect with 95% confidence interval (CI).

MTB-T interval was compared between groups on a competitive risk model with death without treatment as competitive event. Cumulative incidence was estimated following Kalbfleisch and Prentice, and comparison used the Fine-Gray test. Comparisons were adjusted on the predefined confounding factors. The significance threshold was set at $P < 0.005$, in line with the methodological improvements implemented in the European Annals of Otorhinolaryngology, Head & Neck Diseases [12–14]. Analyses used SAS® software (SAS Institute, version 9.4). The article was drawn up following STROBE guidelines [15].

3. Results

3.1. Description of the 3 cohorts

Data were analyzed for 241 patients. The 3 groups comprised: 107 patients for 12 MTBs during the 2019 control period (mean 8.9 patients per MTB), 60 patients for 10 MTBs during the lockdown period (mean 6 patients per MTB) and 74 patients for 14 MTBs during the post-lockdown period (mean 5.3 patients per MTB).

Intrinsic characteristics were similar between groups. There was a clear male predominance in all groups. Mean age was 63.2 ± 10.4 years in the control group, 61.6 ± 9.1 in the lockdown group, and 63.4 ± 9.8 years in the post-lockdown group. WHO score was ≤ 2 in more than 90% of cases. Charlson score was ≤ 4 in almost half, in all groups. All 3 groups showed predominance of the 4 tumor locations most frequently encountered in the head and neck: 28–39.2% for the oral cavity, 20.3–28.3% for the oropharynx, 18.3–21.6% for the larynx, and 9.5–13.3% for the hypopharynx. Tumor stage at treatment initiation showed predominance of advanced stages (III/IV) in all groups: 69.2% in controls, 74.4% in the lockdown period, and 81.1% in the post-lockdown period. More than 40% of patients in all 3 groups showed alcohol intake above the recommended daily maximum of 20 g/day, and 50–60% of patients were active smokers (Table 1).

3.2. Main endpoint: time intervals

3.2.1. Median FC-MTB interval

Median FC-MTB interval was 35 days [23; 50] in the control period, 29 days [17; 43] in the lockdown period, and 28 days [17; 37] in the post-lockdown period. On univariate analysis, the control and post-lockdown periods differed significantly, with shorter intervals in the latter ($P = 0.0047$); this difference was not significant on multivariate analysis after adjustment on dichotomized WHO score, dichotomized Charlson score, and tumor location and

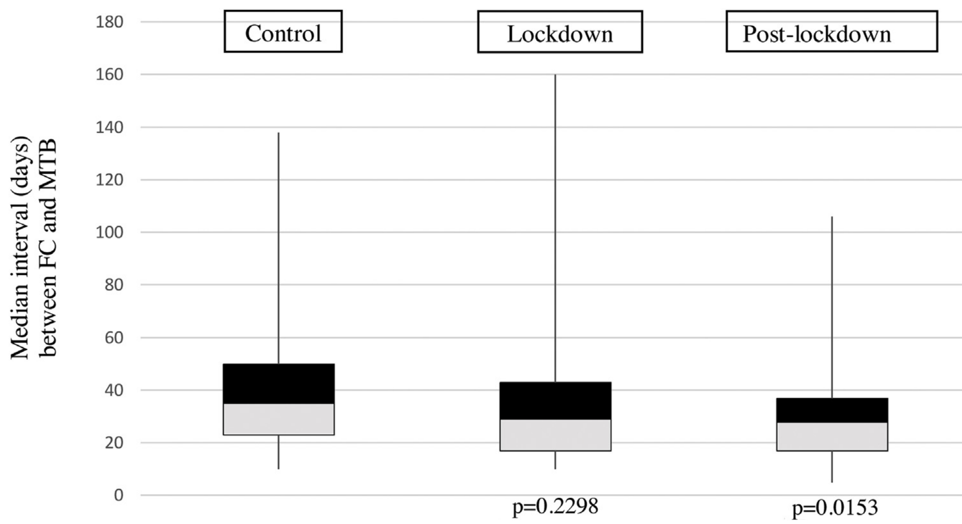

Fig. 2. Median interval between first specialist consultation and the multidisciplinary tumor board meeting (FC-MTB). Boxplots: left, control (35 days [23;50]); center, lockdown (29 days [17;43]); right, post-lockdown (28 days [17;37]). Comparison (*P*-values) versus control (*P* = 0.2298 for lockdown; *P* = 0.0153 for post-lockdown).

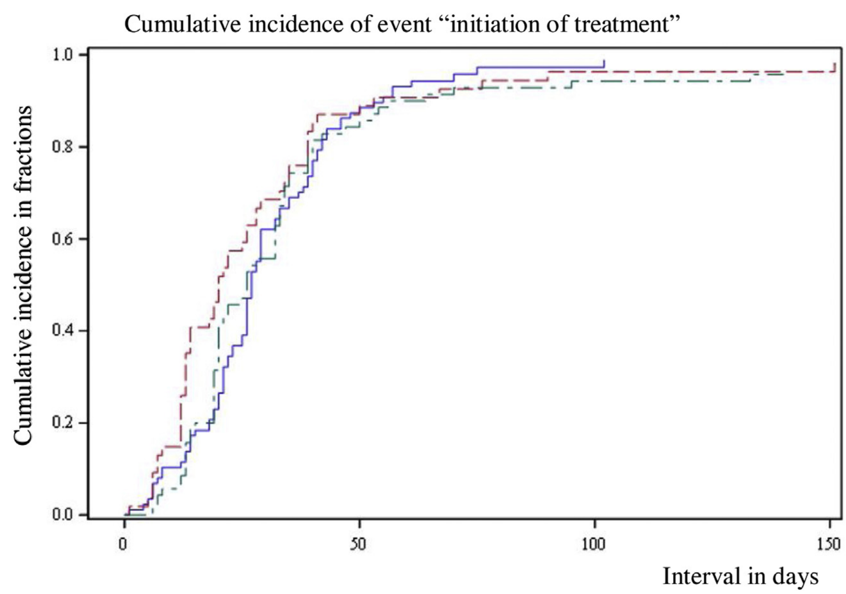

Fig. 3. Median interval between MTB and treatment (MTB-T). Cumulative incidence curves for the event "first treatment") with comparison versus control (*P*-values). Blue curve, control (27 days); red curve, lockdown; green curve, post-lockdown. Comparison between lockdown and control shows a *P*-value of 0.4203.

dichotomized stage (*P* = 0.0153). The control and lockdown periods did not significantly differ (univariate analysis, *P* = 0.1694; multivariate analysis, *P* = 0.2298); nor did the lockdown and post-lockdown periods (univariate analysis, *P* = 0.2011; multivariate analysis, *P* = 0.2191) (Fig. 2).

3.2.2. Median MTB-T interval

The median MTB-T interval on cumulative incidence was 27 days in the control period, 20 days in the lockdown period, and 26 days in the post-lockdown period, with no significant differences on univariate (*P* = 0.5102) or multivariate analysis (*P* = 0.4203) (Fig. 3).

3.2.3. Specific MTB-S interval

Median MTB-S interval was 20 days [13; 27] for controls, 13 days [12; 19] in the lockdown period, and 19 days [14; 26] in the post-lockdown period, with no significant differences between lockdown and control (*P* = 0.1597) or post-lockdown (*P* = 0.3682) (Fig. 4).

3.2.4. Specific MTB-RTCT interval

Median MTB-RTCT interval was 42 days [32; 50] for control, 39 days [34; 50] in the lockdown period, and 34.5 days [32.5; 40] in the post-lockdown period, with no significant differences between lockdown and control (*P* = 0.9369) or post-lockdown and control (*P* = 0.3955) (Fig. 5).

3.3. Secondary endpoints

3.3.1. Clinical stage at treatment and association with synchronous tumor

In the control group, 33 patients (30.8%) presented early-stage cancer (I or II) and 74 (69.2%) advanced stages (III or IV). In the lockdown group, 15 patients (25.9%) presented early-stage cancer and 43 (74.1%) advanced stages. In the post-lockdown group, 14 patients (18.9%) presented early-stage cancer and 60 (81.1%) advanced stages. There was no significant difference between control and lockdown on univariate (*P* = 0.5019) or multivariate

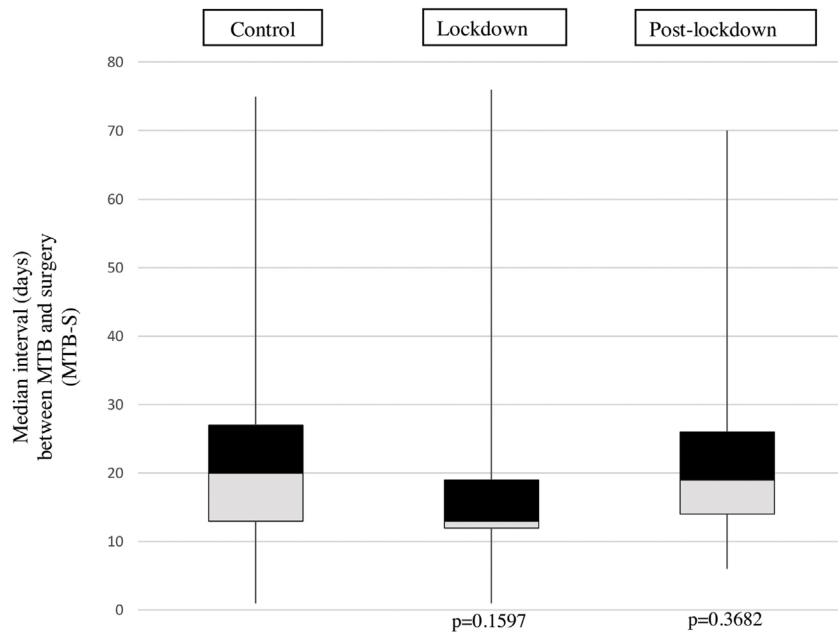

Fig. 4. Median interval between MTB and surgery (MTB-S) Boxplots: left, control (20 days [13;27]); center, lockdown (13 days [12;19]) right, post-lockdown (19 days [14;26]). Comparison (*P*-values) versus control (*P* = 0.1597 for lockdown; *P* = 0.3682 for post-lockdown).

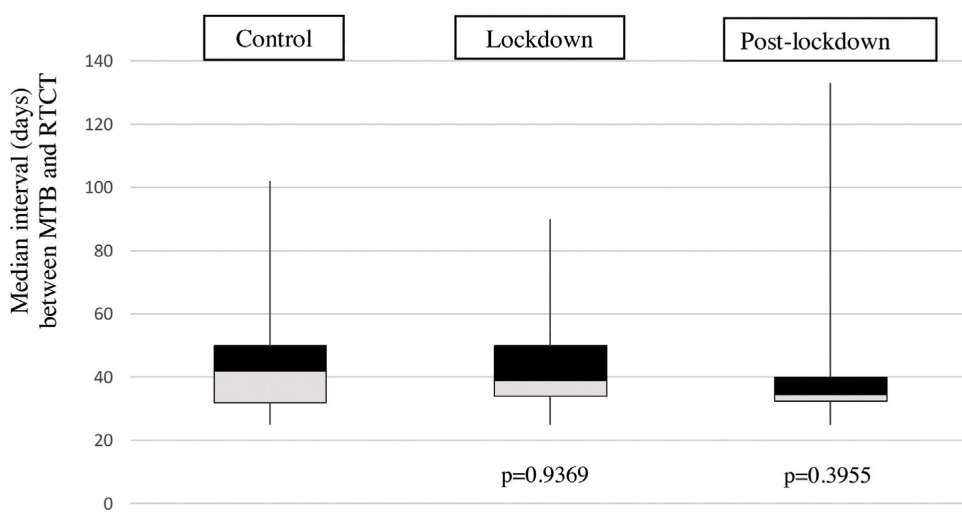

Fig. 5. Median interval between MTB and radio- and/or chemotherapy (MTB-RTCT). Boxplots: left, control (42 days [32;50]); center, lockdown (39 days [34;50]); right, post-lockdown (34.5 days [32,5;40]). Comparison (*P*-values) versus control (*P* = 0.9369 for lockdown and *P* = 0.3955 for post-lockdown).

analysis (*P* = 0.5123), or between control and post-lockdown (*P* = 0.0745, and *P* = 0.0622).

Synchronous cancer was present in 10 of the 107 control patients (9.3%), 10 of the 60 patients in the lockdown group (16.7%), and 8 of the 74 patients in the post-lockdown group (10.8%), with no significant differences between control and lockdown (*P* = 0.1673) or control and post-lockdown (*P* = 0.7463) (Table 2). One patient in the lockdown group (1.6%) presented severe COVID-related pneumopathy requiring postponement of hemostatic radiotherapy, and 1 patient (1.6%) presented pulmonary embolism following COVID-19 infection, contraindicating the original MTB proposal for neck dissection, replaced by radiotherapy. There were no cases of COVID-19 infection during treatment in the post-lockdown group. No patients contracted COVID-19 during hospital stay.

4. Discussion

The FC-MTB interval (i.e., diagnostic work-up) showed no significant inter-group difference, but was shorter in absolute terms in the post-lockdown situation. This suggests optimization of management, based on priority accorded, even before the COVID epidemic, to cancer patients. It also suggests priority accorded to oncology, at the expense of other activities, during lockdown, reducing oncology wait time, even if not significantly. Even so, the situation could be further improved, as the interval of 28 days was at the upper limit of the SFORL recommendations [16]. For the MTB-T interval, the study found no significant inter-group difference. The original hypothesis of possible lengthening of wait times during the first wave thus was not confirmed.

Table 2
Synchronous cancer; early (I/II) and advanced stages (III/IV) in control, lockdown and post-lockdown period.

	NA Controls *n* (%)	Lockdown *n* (%)	Post-lockdown (%)	*P*-value lockdown versus control	*P*-value Post-lockdown versus control
Synchronous cancer (%)	10 (9.3)	10 (16.7)	8 (10.8)	0.1673	0.7463
Stage *n* (%)					
I/II	33 (30.8)	15 (25.9)	14 (18.9)		
III/IV	74 (69.2)	43 (74.1)	60 (81.1)	0.5123	0.0622

Data shown as number (%).

Minimizing diagnostic and therapeutic wait times is an imperative in head-and-neck oncology: longer wait times are an independent factor for increased mortality [17], with 5% greater risk per 30 days' lengthening of the diagnosis-to-treatment interval [18] and 0.09–0.17% decrease in local control per day between surgery and radiotherapy [19]. Tevetoglu et al. found no increase in wait time between specialist consultation and surgery between March 15 and September 15, 2020; there was, however, a significant increase in the interval between symptom onset and specialist consultation: 19.01 ± 4.6 weeks, versus 16.6 ± 5.9 weeks in the control period [20]. However, it was not sure that this was related to the epidemic, as these intervals were often reported only roughly by patients, with declaration bias. That time to treatment did not increase in our center, despite the health crisis and associated hospital management restrictions, may have been due to various factors. The priority accorded by the official recommendation to urgent activity, including oncology, and the postponement of functional or less urgent surgery, eased access to theater. The same effect was felt in consultation [5,6]. We also found a decrease in the mean number of patients presented in MTBs in the lockdown and post-lockdown periods compared to the control period: respectively 6 and 5.3 patients on average, versus 8.9. This trend was also reported by Laccourreye et al. [7]. It may have been due to patients deliberately hesitating to consult or to difficulties in accessing care. The closure of many community offices during lockdown, reducing the number of nasal endoscopies, was one reason. De Luca's team reported 35–40% fewer patients between February and November 2020 compared to the same period in the 5 previous years [21]. This decrease was seen not only in head-and-neck cancer but also in all types, as shown by a recent Dutch report [22].

The secondary endpoints (tumor stage at treatment and rate of synchronous tumor) indirectly assessed treatment delay. The underlying study hypothesis concerned a difference in the patient population compared to the control situation, in terms either of increased tumor stage at diagnosis or of synchronous tumor rate. Both points may result from longer wait times or to patients consulting for advanced stages only. The present results showed no increase in advanced stages or synchronous tumors in the lockdown and post-lockdown groups as compared to control. A study of breast-cancer patients in Northern Italy, which was one of the early hotspots of SARS-CoV-2 in Europe, reported increased rates of lymph node involvement associated with more advanced tumor in the high-grade subgroup. The authors attributed this to the suspension of mammography for 2 months during lockdown [23]. In head-and-neck cancer, preliminary data from another Italian study showed a 3-fold increase in advanced stages (stages III and IV) in April and May 2020 as compared to the same period in 2019 [24]. These results are comparable to those of Tevetoglu et al., who reported a significant increase in the number of high-grade tumors (T3/T4), especially in the larynx, in patients treated between March 15 and September 15, 2020 compared to the same period in 2019: 53% versus 28% ($P = 0.024$). Even so, according to tightened statistical criteria, the difference is not significant [20]. It is difficult to draw any conclusion about the rate of advanced-stage consultation. More than half of head-and-neck cancer patients are diagnosed at an advanced stage, usually due to delayed consultation even prior to the COVID crisis [25]. The three groups in the present study showed fairly comparable epidemiological characteristics in terms of gender, age, comorbidity and tumor location and, above all, stage. Patients managed in our center mostly (> 60%) presented with advanced stages even before the epidemic, which may account for the lack of difference in terms of stage and synchronous locations, in contrast to other countries in Europe and worldwide. Moreover, countries differ in health-care organization (cost borne by the patient, ease of access to reference centers) and there are differences according to the organ involved that may impact time to treatment, and these effects may or may not have been amplified by lockdown [26,27]. Finally, in the present study, onset of COVID infection did not seem to lengthen wait time or modify management protocols. Only 2 patients in the lockdown group developed COVID infection; in 1 case time to radiotherapy was lengthened, and in the other surgery was replaced by radiotherapy. As well as issues of wait time, lack of consensus on oncologic treatment is sometimes an obstacle to optimal care. A questionnaire sent to 36 American heck-and-neck oncologic surgery centers revealed differences in protocol between centers. Precise protocols were available for 31% of centers, while in 47% treatment decisions were at the surgeon's discretion. In respectively 14% and 19% of centers there was a decision-making committee or designated individual to guide decision-making [28]. In France, various protocols have been drawn up by scientific societies, but do not amount to personalized care plans [5,6,29].

The present study had several biases. The retrospective design could lead to incomplete or missing data. The interval between symptom onset and first consultation is of particular importance, but could not be analyzed due to many missing data points, approximate timing in consultation letters and considerable memory bias in patients. This item was also lacking in other reports [25,26]. The selection of the control period, in summer, is also open to discussion; it was not a good period for consultations or for short wait times, with physicians on vacation. However, we wished to conduct the study shortly after the first wave so as to be able to study time intervals as soon as the epidemic set in. Three periods were chosen, with a control period in the previous year; admittedly it was during the summer, but this allowed comparison with the post-lockdown period, which was also in summer, and seemed the most relevant for analyzing any delay, as it showed whether there was any lengthening in diagnostic wait time. Diagnosis was 4 to 8 weeks prior to the post-lockdown period, during lockdown itself. Thus, in the lockdown period, diagnosis had usually already been made and would be unaffected. This methodology was discussed with our statisticians, and seemed the most robust in terms of comparability between periods. In the "continuity of care" concept applied in our health system, diagnostic procedures continue even in summer, especially in oncology, and thus should not impact time to treatment. The study did not investigate survival, which should be the focus of subsequent studies to determine any post-pandemic peak in mortality. Reports of the impact of the pandemic on oncology are important, analyzing consequences in terms of severity at diagnosis, assessing the mathematical models predicting a post-pandemic "oncologic epidemic peak" [30].

Despite the resilience of the heath system, oncology wait times will need to be analyzed in successive waves (2nd, 3rd, and more...) to assess the consequences of repeated stress. Shaw et al. showed a 58% decrease in oncologic surgery during the 2nd wave in the UK in January–February 2021, compared to pre-pandemic levels, suggesting the difficulty of adapting to health crises despite 1st-wave experience [31]. In France, oncologic surgery activity was stable during the 1st wave, whereas functional surgery collapsed [32].

5. Conclusion

The present study focused on certain time intervals in the management of head-and-neck cancer during 3 precise periods, and found no increase in wait times during the 2020 lockdown and post-lockdown periods compared to the 2019 control period. Medium-to long-term analyses of overall survival and of the effect on wait times during successive waves will be needed to assess the final impact of health-care measures on head-and-neck cancer patients.

Disclosure of interest

The authors declare that they have no competing interest.

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