

Reshape and secure HCC managing during COVID-19 pandemic: A single centre analysis of four periods in 2020 versus 2019

1 | INTRODUCTION

The COVID-19 pandemic threatened to completely change the priorities of our health systems. However, the diagnosis and timely treatment of patients with cancer should never be compromised: the interruption or delay of cancer surveillance or treatments schedules, because of pandemic, may significantly impact patients' survival.¹ This is particularly true for HCC: despite the task of guaranteeing the safety of our patients, facing a new infection with increased mortality risk in patients with cirrhosis, we needed to maintain treatments of HCC and in the adequate timeframe.²⁻⁴ While studies had shown how deep the pandemic has changed the management of HCC with respect to surveillance, diagnosis and treatment, none has evaluated the effectiveness of the measures taken to cope with COVID-19.^{1,5-7} To evaluate the impact of new measures deployed for HCC management during the pandemic, we compared the efficiency and clinical quality key performance indicators (KPI) generated from 2020 to 2019.

2 | PATIENTS AND METHODS

This is a single centre, retrospective study, including patients with HCC managed by our multidisciplinary team. To assess if the modified strategies adopted to manage HCC during the COVID-19 pandemic allowed us to maintain the standard of care, we compared selected KPI in 2020 with those generated in 2019, in patients with HCC discussed in a weekly multidisciplinary team meeting (MDTM). According to the SARS-CoV-2 incidence in Italy, four different periods were compared: the prepandemic phase (January–February), the first-wave phase (March–May), the low-incidence phase (June–September) and the second-wave phase (October–December).

In our centre, treatment for each patient is decided by MDTM according to international guidelines. In 2017, we formally adopted

as quality control of care the maximum acceptable timeframe for HCC management, selected on the basis of both tumour doubling time and expected survival benefit.⁸⁻¹⁰

To face the pandemic, percutaneous microwave thermal ablation (MWTA) was preferred to surgical resection and laparoscopic MWTA to reduce both the needs of postoperative stays in the intensive care unit and the hospital stay duration.⁷ We considered surgery case-by-case, whenever percutaneous ablation was judged inappropriate. Transarterial chemo(radio) embolization (TACE and TARE) was maintained whenever the risk/benefit ratio was judged appropriate. Systemic treatments were maintained as per clinical practice.

To face SARS-CoV-2 spread, admissions for HCC treatment in our department were managed as follows: (i) dedicated COVID-19-free areas of the hospital (ward, angiographic suite and operating theatre); (ii) healthcare personnel dedicated only to COVID-19-free areas, using protective equipment and bimonthly SARS-CoV-2 tested by nasopharyngeal swabs; (iii) telephone survey designed to detect possible contact or infection by SARS-CoV-2 and mandatory SARS-CoV-2 test performed 24 hours before admission for patients.

The selected KPI were as follows:

1. Number of procedures performed (liver transplant [LT], surgical procedures, percutaneous ablations, TACE and TARE sessions, systemic treatments).
2. Duration of timeframes for HCC management: (a) interval between the outpatients' visit and MDTM (expected <15 days); (b) interval between the MDTM and HCC treatment (<30 days); (c) interval between treatment and first radiological evaluation (<45 days); (d) complete timeframe from outpatients' visit to first radiological evaluation (<90 days). According to quality procedures, we evaluated all delays to identify actionable interventions to improve HCC management.
3. Rate of complete responses after percutaneous ablations at first radiological evaluation. This KPI is intended to measure both accuracies of MDTM decisions and the effectiveness of treatment.
4. Prevalence of patients positive for SARS-CoV-2 before admission and incidence of symptomatic COVID-19 7-14 days following discharge, to detect the effectiveness of procedures to reduce nosocomial transmission of SARS-CoV-2.

Abbreviations: BCLC, Barcelona clinic liver cancer; COVID-19, coronavirus disease 2019; CT, computed tomography; HCC, hepatocellular carcinoma; KPI, key performance indicators; LT, liver transplantation; MDTM, multidisciplinary team meeting; MRI, magnetic resonance; MWTA, microwave thermal ablation; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; TACE, transarterial chemoembolization; TARE, transarterial radioembolization.

2.1 | Statistical analysis

Continuous variables were expressed as median and range, and categorical variables were presented as frequency and percentages. Student's t test for continuous variables and χ^2 test for categorical variables were used to compare performances in 2020 to 2019 and the four periods of the year.

3 | RESULTS

The first documented case of COVID-19 in our hospital occurred on 23 February 2020. Thereafter, the hospital's organization was quickly modified: specific clinical pathways for patients with COVID-19 were created and internal guidelines were implemented and periodically updated. In 2020, in our hospital, 2154 patients entered for COVID-19, with the peak in November (560 patients) and the nadir in July 2020 (20 patients).

During 2020, 18 LTs for HCC (-35.7%), 23 surgical resections (+43.8%), 9 laparoscopic MWTA (-52.6%), 51 percutaneous ablations (+108.3%), 146 TACE/TARE sessions (-20.2%) were performed and 186 systemic treatment drugs (+11.4%) dispensed (Table 1). Out of a total of 1416 visits performed in HCC outpatients' clinic, 82 (7.2%) were conducted by videocalls.

In 2020, 208 treatments were decided amongst 579 cases discussed in MDTM compared with 231/555 in 2019: these were the subject of the comparative analysis. The new diagnosis of HCC discussed in MDTM and subsequently treated in our centre was

homogeneously distributed over the four periods both within each year and between each period of the 2 years under analysis (Table 1). Durations of the different timeframes are presented in Table 2 according to the four periods of COVID-19 pandemic. Overall, considering the whole course of a single HCC management, the median time was significantly longer in 2020 compared with 2019 (69 [20-198] vs 64 [26-161] days, $P = .0006$). However, when we stratified the results for the four periods, this delay was statistically significant only in the first two periods of 2020. During 2020, the interval between outpatients' visit and MDTM was >15 days in 8 (3.8%) cases vs 10 (4.3%) in 2019 ($P = .07$), while the interval between MDTM and HCC treatment was >30 days in 58 (27.9%) cases in 2020 vs 70 (30.3%) in 2019 ($P = .48$). The interval between treatment and radiological assessment was >45 days in 57 (27.5%) cases in 2020 vs 20 (8.7%) in 2019, $P < .0001$, and the whole course of HCC management was >90 days in 45 (26%) cases in 2020 vs 20 (10%) in 2019 ($P < .0001$). In 2019 and 2020, no patient was lost on follow-up.

The rate of complete response of target lesion after ablations at first radiological evaluation was 22/24 (91.7%) in 2019 vs 44/50 (86%) in 2020 ($P = .48$) for percutaneous MWTA and 17/19 in 2019 (89.5%) vs 8/9 (88.9%) in 2020 ($P = .96$) for laparoscopic MWTA, respectively.

Finally, all patients were tested for SARS-CoV-2 24 hours before admission *per protocol* and 6/162 (3.7%) turned positive (three were hospitalized for severe COVID-19, no one died) and their procedure was postponed accordingly. Following hospitalization for HCC treatment, no one of the other 156 patients reported COVID-19 7-14 days after discharge from our ward.

TABLE 1 Visits and procedures for HCC management performed in our Unit in 2019 and 2020 according to the four predefined periods

	Year	Period 1 (Jan-Feb)	Period 2 (March-May)	Period 3 (June-Sept)	Period 4 (Oct-Dec)	Overall
Outpatients' visits	2019	261	413	437	444	1555
	2020	301 (+15%)	213 (-48%)	475 (+9%)	427 (+4%)	1416 (-8.9%)
Cases discussed in MDTM	2019	77	135	180	163	555
	2020	105 (+36.4%)	89 (-34.1%)	186 (+3.3%)	199 (+22.1%)	579 (+4.3%)
New diagnosis of HCC discussed in MDTM	2019	15/77 (19%)	19/135 (14%)	23/180 (13%)	18/163 (11%)	82/555 (15%)
	2020	14/105 (16%)	16/89 (18%)	17/186 (9%)	23/199 (12%)	69/579 (12%)
Liver transplantations for HCC	2019	5	6	7	10	28
	2020	7 (+28.6%)	2 (-66.7%)	7 (+0%)	2 (-80%)	18 (-35.7%)
Surgical resections	2019	2	5	4	5	16
	2020	2 (+0%)	4 (-20%)	8 (+100%)	9 (+80%)	23 (+43.8%)
Laparoscopic ablations	2019	8	4	3	4	19
	2020	2 (-75%)	5 (+25%)	1 (-16.7%)	2 (-75%)	9 (-52.6%)
Percutaneous ablations	2019	3	4	8	9	24
	2020	5 (+66.6%)	18 (+350%)	16 (+100%)	11 (+22%)	50 (+108.3%)
TACE/TARE procedures	2019	27	45	69	42	183
	2020	33 (+18.2%)	18 (-60.0%)	53 (-23.2%)	42 (+0%)	146 (-20.2%)
First-/second-line dispensed drugs	2019	34	47	54	32	167
	2020	34 (+0%)	47 (+0%)	58 (+7.4%)	47 (+46.8%)	186 (+11.4%)

Abbreviations: MDTM, multidisciplinary team meeting; TACE, transarterial chemoembolization; TARE, transarterial radioembolization.

Bold indicates the overall columns for friendly reading.

TABLE 2 Timeframes of different activities related to HCC management in our Unit according to the four periods of 2020 compared with 2019

Timeframe, days	Year	Period 1 (Jan-Feb)	P-value	Period 2 (March-May)	P-value	Period 3 (June-Sept)	P-value	Period 4 (Oct-Dec)	P-value	Overall	P-value
Outpatients' visit-MDTM	2019	2 (0-43)	.457	3 (0-27)	.297	3 (0-35)	.403	3 (0-30)	.065	3 (0-43)	.657
	2020	3 (0-20)		3 (0-45)		2 (0-30)		6 (0-16)		3 (0-45)	
MDTM-HCC treatment (percutaneous ablations and TACE)	2019	18 (6-49)	.008	20 (4-64)	.007	27 (4-84)	.0009	25 (4-84)	.0009	22 (4-84)	.876
	2020	23 (4-140)		28 (4-104)		15 (3-49)		15 (2-65)		19 (2-140)	
MDTM-percutaneous ablations	2019	28 (20-36)	.08	25 (21-63)	.863	40 (4-84)	.170	45 (27-84)	.03	39 (4-84)	.604
	2020	55 (25-116)		28 (14-84)		36 (8-49)		34 (8-65)		37 (8-116)	
MDTM-TACE	2019	15 (6-49)	.134	20 (4-64)	.024	27 (4-69)	.004	21 (4-68)	.0001	20 (4-69)	.042
	2020	21 (8-112)		27 (4-104)		15 (3-46)		13 (2-46)		15 (2-112)	
HCC Treatment-Radiological evaluation of response	2019	32 (10-66)	.0006	34 (26-71)	.421	33 (14-69)	.0008	34 (4-77)	.001	34 (4-77)	<.0001
	2020	42 (21-162)		34 (27-66)		42 (16-115)		42 (19-69)		41 (16-162)	
Outpatients' visit-Radiological evaluation of response	2019	54 (26-95)	<.0001	62 (43-108)	.006	70 (29-119)	.411	69 (36-161)	.949	64 (26-161)	.0006
	2020	101 (33-198)		73 (36-182)		66 (20-119)		60 (20-119)		69 (20-198)	

Abbreviations: MDTM, multidisciplinary team meeting; TACE, transarterial chemoembolization.
 Bold indicates the overall columns for friendly reading.

4 | DISCUSSION

This is the first study to evaluate the efficiency and quality of the measures implemented to tackle the challenges for HCC management owing to the SARS-CoV-2 pandemic. In general, there are a few papers addressing the measurement of quality of care in patients with cirrhosis in the field of hepatology, generally evaluating HCC surveillance only.⁸⁻¹¹ We showed that these strategies were able to safely ensure continuity of care to our HCC patients, highlighting some negative effects in terms of procedures not performed or delayed during the first wave but also the improved performances in the subsequent periods of the year compared with 2019.

The decreased number of LT in 2020 was determined by a complex series of external factors that changed the number of LT in northern Italy and worldwide.¹² On the other hand, the number of percutaneous ablations significantly increased in 2020, and it was not detrimental for patients in terms of radiological response as shown by our data. This increase was the direct consequence of our strategy favouring percutaneous ablations to reduce the need for operating theatres, beds in intensive care and days of hospitalization, whenever possible.⁴ Nonetheless, the number of surgical resections progressively increased during 2020, initially because of the temporary reduction of pandemic and later on thanks to the reorganization of the hospital aimed at favouring non-postponable interventions in oncological patients, during the second wave of pandemic. A significant decrease of TACEs was both a direct result of the pandemic in the first wave and the consequence of a personalized risk/benefit approach: the measures implemented allowed us to carry out the same number of TACEs during the second wave performed in 2019. These findings differed from the results of a survey conducted in 43 Italian hospitals, reporting that both surgical and locoregional treatments were reduced or even stopped in a significant number of centres, with similar rates during the first and second waves.¹² Finally, the slight increase of systemic treatments in 2020 was limited to the fourth period of 2020 and mainly attributable to the progressive use of lenvatinib in the first line and above all cabozantinib in the second and third line, which were not available in 2019 in Italy.

The whole management of a single HCC case generally lasted <90 days despite the pandemic, achieving our internal indicator of quality. We were able to maintain a performance comparable with the previous year as far as the timeframe between visit and MDTM, while the timeframe between MDTM and HCC treatment was even shorter during the second wave of pandemic compared with the same period of 2019. Only the timeframe between HCC treatment and radiological evaluation significantly increased in the first two periods of 2020. However, after having brought all the radiological examinations back to our centre, the waiting time has returned to the timeframes of the previous year. The low number of video calls testifies to the fact that at our centre, we favoured telemedicine, especially for non-oncological outpatients visits.¹²

All measures taken to reduce the risk of nosocomial SARS-CoV-2 infection allowed us to identify a few positive cases before admission

thus preventing the in-hospital spread of the virus and avoiding symptomatic COVID-19 development after hospital discharge.

The study has some limitations: it is a retrospective and single centre study thus limiting the applicability of our results. Amongst the strengths of our study, we opened a new perspective in HCC management, promoting standardization of quality and efficiency of care during the routine management of our patients, not only during the pandemic, by the analysis of clinical quality KPI.

In conclusion, this study demonstrated that HCC can be appropriately and timely managed even during the COVID-19 pandemic by implementing strategies aimed at both tailoring the most cost-effective solution on a case-by-case basis and reducing the risk of SARS-CoV-2 infection.

KEYWORDS

efficiency, key performance indicator, liver cancer, quality, SARS-CoV-2

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CONFLICT OF INTEREST



MI: speaking/teaching, consultant and advisory board for Bayer, Gilead Sciences, BMS, Janssen, Ipsen, MSD, BTG-Boston Scientific, AbbVie, Guerbet, Eisai. AS: Speaker Bureau: Bayer, Gilead Science, Janssen, BTG, AbbVie, Novartis; Advisory board: Tiziana Life Sciences. PL: Advisory Board/Speaker Bureau for BMS, Roche, Gilead Sciences, GSK, AbbVie, MSD, Arrowhead, Alnylam, Janssen, Sbring Bank, Myr, Eiger. Authors have no conflict of interest to disclose.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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