








# The Covid-19 Pandemic Constraints May Lead to Disease Progression for Patients with Liver Cancer Scheduled to Receive Locoregional Therapies: Single-Centre Retrospective Analysis in an Interventional Radiology Unit

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## Introduction

The lockdown period (LDP) due to the Covid-19 pandemic was declared in Portugal from the 18 March until the 2 May 2020 [1], causing a reduction/suspension in non-urgent medical care during this period. Previous studies have confirmed the negative impact of the LDP in the workload at different Interventional Radiology (IR) units across Europe [2, 3]. However, the potential impact on disease progression for oncology patients scheduled for loco-regional therapies (LRT) is mainly unknown, hence this

report, which is a single-centre retrospective analysis on the impact of Covid-19 pandemic in an IR Unit. Institutional Review Board approval for the retrospective analysis of data was obtained. Descriptive statistical analyses were used to compare 2019 (non-COVID) and 2020 (COVID) data.

Comparing the total procedure numbers in the LDP ( $n = 77$ ) with the homologous time-period in 2019 ( $n = 172$ ), there was a reduction in the overall number of procedures by 55.2%. When comparing the type of procedures (elective/urgent), there was a significant difference, with 33.1% ( $n = 57$ ) urgent procedures in 2019 versus 48.1% ( $n = 37$ ) urgent procedures in 2020 ( $p = 0.0120$ ). The volume reduction in procedures performed was more pronounced for liver transarterial chemoembolization (TACE) (80.0% reduction), microwave ablation (MWA) (75.0% reduction) and percutaneous biopsies (65.2% reduction). The greatest reduction in oncological loco-regional treatments was noted during the LDP [1], with a gradual recovery after that (Fig. 1).

The main analysis of this study was to assess the impact on disease progression for all liver oncology patients treated with LRTs after the LDP. All patients that had a scheduled LRT (74 hepatocellular carcinoma, HCC and 10 liver metastases) between 2 May and 16 July 2020 (post LDP) were compared with the homologous period in 2019 (68 HCC and 11 liver metastases). Tables 1 and 2 compare the baseline data of HCC and liver metastases patients treated at this IR unit in the post LDP with the homologous period in 2019. In 2020, HCC patients had significantly higher model of end-stage liver disease (MELD) scores ( $p = 0.0124$ ) and significantly larger tumours (mean difference of 8.7 mm,  $p = 0.0071$ ), reflecting more disease burden on the diagnosis. Also, the number of HCCs was higher in 2020 ( $p = 0.0503$ ). Table 3 shows that the mean

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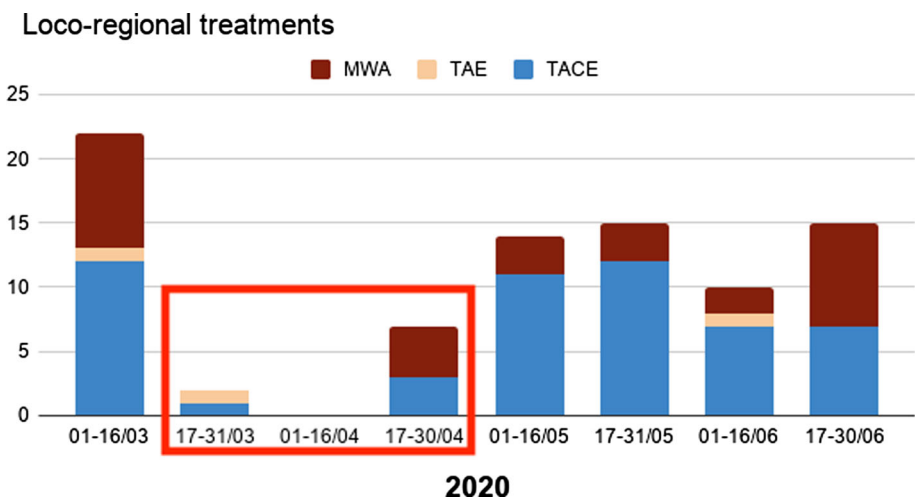
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**Fig. 1** Distribution of loco-regional therapies for hepatocellular carcinoma and liver metastases (microwave ablation—MWA; TAE—transarterial embolization; TACE—transarterial chemoembolization) from 1 March to 30 June 2020, subdivided in 2-week period. Red box—lockdown period (LDP)



**Table 1** Patients baseline data with hepatocellular carcinoma scheduled for LRT between 2 May and 16 July 2019 versus 2 May to 16 July 2020

	2019 (n = 68)	2020 (n = 74)	p values
Sex			0.5666
Male	89.70% (61)	90.54% (67)	
Female	10.29% (7)	9.46% (7)	
Age (years), mean (SD)	66.25 (10.35)	66.84 (9.75)	0.6361
Aetiology			0.8752
Non-identified	13.24% (9)	8.11% (6)	
Alcohol	33.82% (23)	43.24% (32)	
HCV	22.06% (15)	24.32% (18)	
HBV	2.94% (2)	5.41% (4)	
Mixed	17.65% (12)	12.16% (9)	
Other	4.41% (3)	4.05% (3)	
Non-cirrhotic	4.41% (3)	2.7% (2)	
Child–pugh			0.0556
A	97.06% (66)	90.54% (67)	
B	2.94% (2)	9.46% (7)	
C	0% (0)	0% (0)	
Meld			<b>0.0124</b>
1–9	64.71% (44)	45.95% (34)	
10–19	35.29% (24)	52.70% (39)	
> 20	0% (0)	1.35% (1)	
Alpha-fetoprotein (ng/mL)			0.4950
< 200	82.35% (56)	82.43% (61)	
> 200	17.65% (12)	17.56% (13)	
BCLC			0.1147
0	29.41% (20)	18.92% (14)	
A	54.41% (37)	55.41% (41)	
B	16.18% (11)	24.32% (18)	
C	0% (0)	1.35% (1)	
D	0% (0)	0% (0)	
Number of tumours			0.0503

**Table 1** continued

	2019 ( <i>n</i> = 68)	2020 ( <i>n</i> = 74)	<i>p</i> values
1	66.18% (45)	62.16% (46)	
2	23.53% (16)	17.57% (13)	
≥ 3	10.29% (7)	20.27% (15)	
Size index tumour (mm), mean (SD)	27.94 (18.71)	36.62 (22.88)	<b>0.0071</b>
Sum of tumours size (mm), mean (SD)	35.94 (30.56)	50.92 (40.73)	<b>0.0070</b>
Planned treatment			0.0731
TACE	61.76% (42)	75.68% (56)	
TAE	1.47% (1)	1.35% (1)	
MWA	32.35% (22)	20.27% (15)	
PEI	4.41% (3)	2.70% (2)	
Previous treatments			0.7633
No	42.65% (29)	48.65% (36)	
Yes	57.35% (39)	51.35% (38)	

Bold values indicate statistically significant differences

*LRT* loco-regional therapies, *SD* standard deviation, *HCV* hepatitis C virus, *HBV* hepatitis B virus, *MELD* model of end-stage liver disease, *BCLC* Barcelona Clinic Liver Cancer staging, *TACE* transarterial chemoembolization, *TAE* transarterial embolization, *MWA* microwave ablation, *PEI* percutaneous ethanol injection

**Table 2** Patients baseline data with liver metastases scheduled for LRT between 2 May and 16 July 2019 versus 2 May to 16 July 2020

	2019 ( <i>n</i> = 11)	2020 ( <i>n</i> = 10)	<i>p</i> values
Sex			0.8917
Male	54.55% (6)	80% (8)	
Female	45.45% (5)	20% (2)	
Age (years), mean (SD)	69.82 (13.68)	67.60 (12.15)	0.3488
Primary tumour			0.4578
Colon	81.82% (9)	80% (8)	
Rectum	0% (0)	10% (1)	
Pancreas NET	9.09% (1)	0% (0)	
Urothelium	0% (0)	10% (1)	
Breast	9.09% (1)	0% (0)	
Number of metastases, mean (SD)	1.36 (0.67)	2.10 (2.13)	0.8424
Size index metastasis (mm), mean (SD)	26.09 (10.35)	22.40 (11.07)	0.2202
Sum of metastases size (mm), mean (SD)	30.09 (10.89)	40.10 (38.31)	0.7787
Planned treatment			N/A
MWA	100% (11)	100% (10)	
Previous treatments			0.7359
No	36.36% (4)	50% (5)	
Yes	63.64% (7)	50% (5)	

*LRT* loco-regional therapies, *SD* standard deviation, *NET* neuroendocrine tumour, *MWA* microwave ablation, *N/A* not applicable

time from imaging diagnosis to multidisciplinary team meeting (MDTM) was not significantly increased in 2020 ( $p = 0.7422$ , mean difference of 4.8 days). However, the mean time from MDTM to the LRT increased by 9.3 days ( $p = 0.0186$ ), with an overall increase in time from diagnosis to LRT of 14.1 days ( $p = 0.0439$ ). This delay had an

impact on the planned LRTs, with significantly more patients receiving different LRTs (TACE instead of ablation for HCC) or not being able to receive any kind of LRTs due to disease progression (15.5% in 2020 versus 3.8% in 2019;  $p = 0.0061$ ).

**Table 3** Compared outcomes measures from patients with HCC and liver metastases scheduled for LRT between 2 May and 16 July 2019 versus 2 May to 16 July 2020

	2019 ( <i>n</i> = 79)	2020 ( <i>n</i> = 84)	<i>p</i> values
Time from last diagnostic imaging to MDTM (days), mean (SD)	36.41 (50.78)	41.21 (42.63)	0.7422
Time from MDTM to LRT (days), mean (SD)	51.71 (19.54)	60.96 (34.88)	<b>0.0186</b>
Time from last diagnostic imaging to LRT (days), mean (SD)	88.11(56.04)	102.18 (47.94)	<b>0.0439</b>
Endpoints			<b>0.0061</b>
LRT as planned	96.20% (76)	84.52% (71)	
Change in LRT	1.27% (1)	4.76% (4)	
Progression precluding LRT	2.53% (2)	10.71% (9)	

Bold values indicate statistically significant differences

HCC hepatocellular carcinoma, LRT loco-regional therapies, MDTM multidisciplinary team meeting, SD standard deviation

As noted with prior studies [2–5], the LDP induced an overall reduction in the number of elective IR procedures, with a relative increase in emergency procedures. The present study showed that this interruption in IR procedures may have a negative impact for liver oncology patients. Interruption of the elective IR oncological procedures was planned based on the Portuguese declaration of the LDP and local Hospital constraints [1]. Our IR unit is located at a COVID-referral hospital, so all priorities were given to optimize response to COVID patients. However, the 2-week delay in IR response hardly justifies itself the disease progression of liver tumors and the higher MELD scores observed in 2020 when compared to 2019. There was also a prioritization of patients with more advanced liver tumors to be immediately treated after the LDP that may partially justify these differences. Also, delays in diagnostic imaging studies, missed or delayed clinical appointments due to the COVID-19 pandemic are likely to have contributed to these differences but were not quantified with the available data. All efforts should be made to maintain IR oncology service lines during this COVID-19 pandemic to avoid disease progression that may have a negative impact on overall survival for these patients.

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#### Compliance with Ethical Standards

**Conflict of interest** Tiago Bilhim is a paid consultant for Merit Medical and has received speaker fees for Philips Medical, Cook Medical, Terumo and is a stock holder for EmbolX. Nuno Vasco Costa is a paid consultant for Merit Medical. Filipe Veloso Gomes is a paid consultant for Terumo.

**Ethical Approval** Institutional review board approval was waived to perform this retrospective analysis.

**Informed Consent** Written informed consent was obtained from all patients.

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