

Impact of Covid-19 pandemic for patient care in an Interventional Radiology Unit

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Method Article

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Abstract

Purpose: Assess the impact of Covid-19 pandemic in work volume in an Interventional Radiology Unit during the “State of Emergency” (16th March - 30th April) in 2020 and to analyse the short-term consequences for oncology patients.

Materials and Methods: Single-centre retrospective analysis. The number and type of procedures performed during the “State of Emergency” was compared with the homologous period in 2019. The second analysis compared the impact on disease progression for oncology patients after the “State of Emergency”. All patients that had a scheduled loco-regional treatment (LRT) (74 hepatocellular carcinoma (HCC); 10 liver metastases) between 2nd May - 16th July 2020 were compared with the homologous period in 2019 (68 HCC; 11 liver metastases). The compared outcome measures included: baseline data, time from diagnostic imaging to LRT, LRT performed as planned, change in LRT.

Results: There was a 55.2% reduction of procedures during the “State of Emergency” (n=77 in 2020; n=172 in 2019) with a significant increase in urgent procedures (48.1% in 2020; 33.1% in 2019; p=0.0120). Post-“State of Emergency”, in 2020, HCC patients had higher model of end-stage liver disease (MELD) scores (p=0.0124) and larger tumours (mean difference of 8.7 mm, p=0.0071). Mean time from diagnostic imaging to LRT increased 14.1 days (p=0.0439). More patients received different or no LRT due to disease progression (15.5% in 2020; 3.8% in 2019; p=0.0061).

Conclusion: There was a reduction in interventional oncology treatments during the “State of Emergency” with more patients experiencing disease progression precluding LRTs in the following months.

Introduction

On the 11th March 2020, World Health Organization declared Covid-19, the disease caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), a pandemic. The worldwide spread of the disease changed the organization of the healthcare units and patient care. The “State of Emergency” was declared in Portugal from the 18th March until the 2nd May [1], which caused a reduction/suspension of non-urgent medical care during this period. This might have had an impact in patient care for oncology patients with hepatocellular carcinoma (HCC) and liver metastases referred to Interventional Radiology (IR) for loco-regional treatments (LRTs). However, the magnitude of this reduction/suspension in patient care on disease progression for oncology patients treated by interventional radiologists is largely unknown. Thus, the purpose was to compare the volume and type of procedures in an IR unit during the “State of Emergency” period in 2020 with the homologous period in 2019 and its short-term consequences on the disease progression in patients approved for LRTs of HCC and liver metastases.

Material And Methods

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. The first analysis compared

the number of procedures, type and elective/urgent nature of the procedures performed during the “State of Emergency” (16th March - 30th April 2020) with the homologous period in 2019. To have a better idea on the impact of the “State of Emergency”, a larger timeframe was also compared between 2019 and 2020: all oncology LRTs (TACE - trans-arterial chemoembolization, TAE - trans-arterial embolization and MWA - microwave ablation) performed for HCC and liver metastases, from 1st March to 30th June 2020 were compared with the homologous period in 2019.

The impact on disease progression for oncology patients was assessed in the following months to the “State of Emergency”. All patients that had a scheduled LRT (74 HCC and 10 liver metastases) between 2nd May and 16th July 2020 (post-“State of Emergency”) were compared with the homologous period in 2019 (68 HCC and 11 liver metastases). Patients who had inadequate procedure-day laboratory findings were excluded. The compared outcome measures included: time from diagnosis imaging to multidisciplinary team meeting (MDTM) and scheduled LRT, LRT performed as planned, change in LRT type due to progression and progression of disease precluding LRT. For patients with HCC, clinical, imaging and laboratory data were recorded: sex, age, aetiology of chronic liver disease, Child-Pugh and model of end-stage liver disease (MELD) scores on the procedure day, alpha-fetoprotein level, Barcelona Clinic Liver Cancer (BCLC) staging, number of tumours, size of index tumour and sum of tumours’ size on the last diagnostic imaging, planned treatment, previous treatments, last diagnostic imaging date, multidisciplinary meeting date and scheduled LRT date. For patients with liver metastases, clinical and imaging data were also recorded: sex, age, primary tumour, number of metastases, size of index metastasis and sum of metastases’ size on the last diagnostic imaging, planned LRT, previous treatments, last diagnostic imaging date, multidisciplinary meeting date and scheduled LRT date. Descriptive statistical analysis plan was used to compare 2019 and 2020 data. The Kolmogorov Smirnov test was used to assess normality of data distribution. The chi-square test was used to compare nominal (categorical) data whereas the Student's t-test was used for continuous variables. Significance was set at $p < 0.05$. The statistical software package used was Stata 15 (StataCorp, College Station, Texas).

Results

Comparing the number of procedures between 16th March and 30th April 2019 (n=172) and 16th March and 30th April 2020 (n=77) there was a volume reduction of 55.2%. When comparing the type of procedures (elective/urgent) there was a significant difference, with 33.1% urgent procedures in 2019 versus 48.1% urgent procedures in 2020 ($p=0.0120$) (Figures 1 and 2). The volume reduction in procedures performed was more pronounced for liver TACE (80.0% reduction), MWA (75.0% reduction) and percutaneous biopsies (65.2% reduction) (Figure 3). There was also a reduction in the overall number of urgent procedures performed between 2019 and 2020 with the exception of trans-arterial embolizations that had a slight (25%, n=2) increase (Figure 4). When comparing the number of procedures between 2019 and 2020 through the different weeks of the analysed timeframe, one can note the immediate effect of the “State of Emergency” after 16th March (Figures 5 and 6). The greatest

reduction in oncological loco-regional treatments was noted during the “State of Emergency” (16th March - 30th April 2020), with a gradual recovery after that.

The second analysis of the study aimed to assess the impact on disease progression for all oncology patients treated with LRTs after the “State of Emergency”. Table 1 compares the baseline data of HCC patients treated at this IR unit between 2nd May and 16th July 2020 (post-“State of Emergency”), with the homologous period in 2019. In 2020, HCC patients had significantly higher MELD scores ($p=0.0124$), reflecting more decompensated liver cirrhosis. The Child-Pugh score difference was marginally insignificant with a trend for higher scores in 2020 ($p=0.0556$). In 2020, HCC patients had 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 time from imaging diagnosis to 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 4 shows the mean time from diagnosis to LRT for those patients with disease progression precluding the planned LRT in 2020 ($n=13$; 117.23 ± 58.31 days). There was a mean increase of 29.1 days for these patients when compared with 2019 (88.11 ± 56.04 days; $p=0.0561$).

Discussion

This study highlights the impact on non-Covid-19 patient care due to the restraints imposed by the Covid-19 pandemic. Recently, this impact has also been assessed in an IR unit in the United States of America [2], where the elective outpatient procedures were responsible for over 60% of the workload before the pandemic, which reduced to less than 40% during the pandemic. There was a shift to urgent and emergent procedures. Although, there was an intention to maintain interventional oncology, there was also a gradual reduction in volume of procedures as the pandemic progressed. We observed the same findings, with a high reduction in the overall number of procedures performed, and a significant shift from elective to urgent procedures. The oncological IR procedures were the most affected. The “State of Emergency” lasted approximately one and a half month, delaying most oncological IR procedures during this timeframe. This led to a significant delay in treatment response of approximately 2 weeks. As a likely consequence, HCC patients had more decompensated liver cirrhosis. The fact that there was higher tumour burden in the 2020 patients’ group may also be due to the patients’ selection bias. Patients with higher disease burden were prioritized in the post-“State of Emergency” period.

Finally, this had an obvious impact on planned treatments, with many ablation procedures being changed to TACE or even to systemic therapy due to disease progression. This delay in treatment response in IR units has also been described previously [3]. According to the experience from an IR Unit in Milan, Italy [3],

there was a delay of 2 months in the treatment of 26% of the patients due to the pandemic and three patients underwent thermal ablation instead of the pre-planned surgical resection. However, LRTs were encouraged as bridge treatment before liver transplantation, in order to reduce disease progression. LRTs were also preferred over surgical resection to reduce the need of intensive care unit beds and hospitalization time. Palliative treatments (TACE and radioembolization) were maintained, but they were postponed in elderly and in patients with comorbidities. In 2020, the absolute number of liver transplants, surgical resections and TACE was inferior to the same 4-week period in 2019. However, the absolute number of radioembolizations, microwave and radiofrequency ablations was superior [3], contrary to the present report. In a cross-sectional survey conducted to assess the impact of Covid-19 on hepato-pancreato-biliary surgery [4], it was shown that chemotherapy and ablation were more utilised for colorectal liver metastases whereas TACE and ablations were more utilised for HCC in Covid-High countries compared to Covid-Low countries.

One study [5], which analyzed 175 HCCs growth rate showed that total volume doubling time (TVDT) of the tumors increased with increasing tumor size, which meant that HCCs do not grow exponentially. They suggested a sigmoidal growth model, as in other human cancers, and the explanation for this was that only the tumor cells near the tumor boundaries have access to enough nutrients. Another study focusing on liver transplantation for HCC [6], concluded that the probabilities of waiting list dropout due to disease progression at 6, 12 and 24 months were 7.3%, 25.3% and 43.6%, respectively. The dropout rate increased exponentially in the first 15 months, with the greatest rates between 9 and 15 months. Thus, timing of treatment for patients with HCC matters, with a high probability of disease progression when left untreated for more than 6 months.

On 23rd of March 2020 the Society of Surgical Oncology (SSO) [7] recommended ablation or stereotactic radiosurgery instead of resection for liver metastases where possible and ablation or embolization over resection for HCC. This emphasises the importance of IR as an alternative option in moments of crisis and resources scarcity. A position paper from the European Association of the Study of the Liver (EASL) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) [8], stated that the care of patients with HCC should be maintained according to guidelines, including continuing systemic treatments and evaluation for liver transplant. Thus, it is important and recommended that IR LRTs for oncology patients are kept within reasonable timeframes to avoid treatment delays that could preclude planned procedures due to disease progression.

The limitations in this study were its retrospective analysis, the lack of similar studies for comparison and the relatively small sample size. The difference in HCC size between 2019 and 2010 might also be due to a selection bias. There was prioritization for larger tumours to be treated sooner after the “State of Emergency”. However, we cannot exclude that the Covid-19 pandemic might also have played a role in disease progression. We were not able to measure the time before the diagnostic imaging which could be greater in 2020, delaying the diagnosis and respective treatments. This could also have been influenced with the Covid-19 pandemic with many oncology patients opting to stay home and not performing the standard imaging exams for disease surveillance. The type of activity at this specific IR unit may not

represent all IR units as the major activity relies on oncology liver treatments that were analysed. No specific analysis was performed on other frequently performed IR procedures that may be more representative of volume load in other IR units.

Conclusion

During the “State of Emergency” there was a significant reduction in the number of procedures performed in the IR Unit, mainly interventional oncology treatments. There was a relative increase in emergency procedures. As a consequence, when interventional oncology treatments were resumed post-“State of Emergency”, there was a mean increase of 14 days from the diagnostic imaging to the LRT date. This delay was even higher, 29 days, for those patients with disease progression precluding planned LRTs. This delay in LRTs was associated with larger tumours and more patients experiencing disease progression precluding planned LRTs when comparing 2020 with the homologous period in 2019. In the post-“State of Emergency” period, HCC patients also had greater MELD scores in comparison with 2019, which suggests more decompensated liver disease. Interventional Radiology has a key role in the treatment of HCC and liver metastases, particularly in times of resource scarcity. This role should be taken into consideration during the 2nd wave and future pandemics, as recommended by many medical societies [7,8]. The long-term effects of “State of Emergency” plans in the treatment and prognosis of oncology patients remains unknown. These results should orientate Hospital Units when deciding how to prioritize patient care in the setting of the Covid-19 pandemic.

Declarations

Statement of ethics approval: 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.

Competing interests:

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.

References

1. Decreto do Presidente da República n.º14-A/2020. Diário da República n.º55/2020, 3º Suplemento, Série I de 2020-03-18.
2. Manna S, Voutsinas N, Maron SZ, et al. Leveraging IR's Adaptability During COVID-19: A Multicenter Single Urban Health System Experience. *J Vasc Interv Radiol* 2020;31(7):1192-1194. doi: 10.1016/j.jvir.2020.04.030.

3. Iavarone M, Sangiovanni A, Carrafiello G, Rossi G, Lampertico P. Management of hepatocellular carcinoma in the time of COVID-19. *Ann Oncol* 2020;31(8):1084-1085. doi: 10.1016/j.annonc.2020.04.007.
4. Balakrishnan A, Lesurtel M, Siriwardena AK, et al. Delivery of hepato-pancreato-biliary surgery during the COVID-19 pandemic: an European-African Hepato-Pancreato-Biliary Association (E-AHPBA) cross-sectional survey. *HPB (Oxford)* 2020;22(8):1128-1134. doi: 10.1016/j.hpb.2020.05.012.
5. An C, Choi YA, Choi D, et al. Growth rate of early-stage hepatocellular carcinoma in patients with chronic liver disease. *Clin Mol Hepatol* 2015; 30;21(3):279–86.
6. Yao FY, Bass NM, Nikolai B, et al. Liver transplantation for hepatocellular carcinoma: Analysis of survival according to the intention-to-treat principle and Dropout from the waiting list. *Liver Transpl* 2002;8(10):873-83. doi: 10.1053/jlts.2002.34923.
7. Society of Surgical Oncology (SSO). Resource for management options of GI and HPB cancers. <https://www.surgonc.org/wp-content/uploads/2020/03/GI-and-HPB-Resource-during-COVID-19-3.23.20.pdf>[Internet]. Society for Surgical Oncology. 2020
8. Boettler T, Newsome PN, Mondelli MU, et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. *JHEP Rep* 2020;2(5):100169. doi: 10.1016/j.jhepr.2020.100169.

Tables

Table 1 - Patients baseline data with hepatocellular carcinoma scheduled for LRT between 2nd May and 16th July 2019 versus 2nd May to 16th 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			0.0124
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
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)	0.0071
Sum of tumours size (mm), mean (SD)	35.94 (30.56)	50.92 (40.73)	0.0070
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)	

LRT - loco-regional treatment; 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 2nd May and 16th July 2019 versus 2nd May to 16th July 2020

	2019 (n=11)	2020 (n=10)	p-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 treatment; SD - standard deviation; NET - neuroendocrine tumour; MWA - microwave ablation; N/A - not applicable.

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

	2019 (n=79)	2020 (n=84)	p-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)	0.0186
Time from last diagnostic imaging to LRT (days), mean (SD)	88.11 (56.04)	102.18 (47.94)	0.0439
Endpoints			0.0061
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)	

HCC - hepatocellular carcinoma; LRT - loco-regional treatment; MDTM - multidisciplinary team meeting; SD - standard deviation.

Table 4 - Compared outcomes from patients with HCC and liver metastasis from 2nd May to 16th July 2020 with procedure performed as planned versus change in procedure and no LRT due to disease progression

	Procedure as planned (n=71)	Change/no LRT (n=13)	<i>p</i> -values
Time from last diagnostic imaging to MDTM (days), mean (SD)	36.94 (35.49)	64.54 (67.24)	0.0859
Time from MDTM to LRT (days), mean (SD)	62.48 (34.95)	52.69 (34.62)	0.8190
Time from last diagnostic imaging to LRT (days), mean (SD)	99.42 (45.74)	117.23 (58.31)	0.1564

HCC - hepatocellular carcinoma; LRT - loco-regional treatment; SD - standard deviation.

Figures

Loco-regional treatments

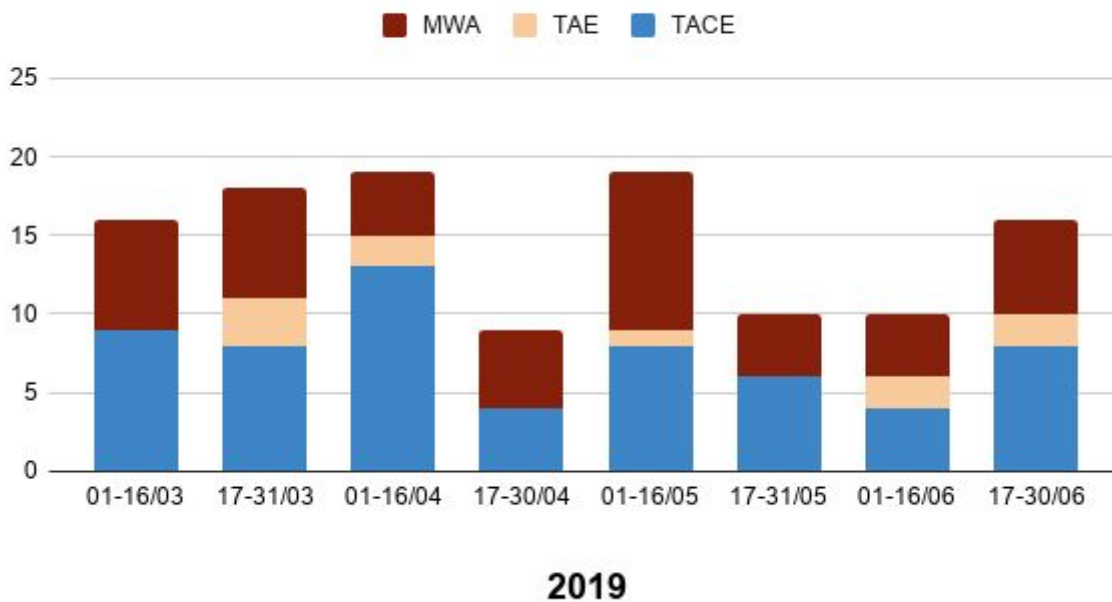


Figure 1

Comparison of percentages between urgent and elective procedures performed at the Interventional Radiology Unit between 16th March and 30th April 2019 (homologous period to the 2020 “State of Emergency” period).

Loco-regional treatments

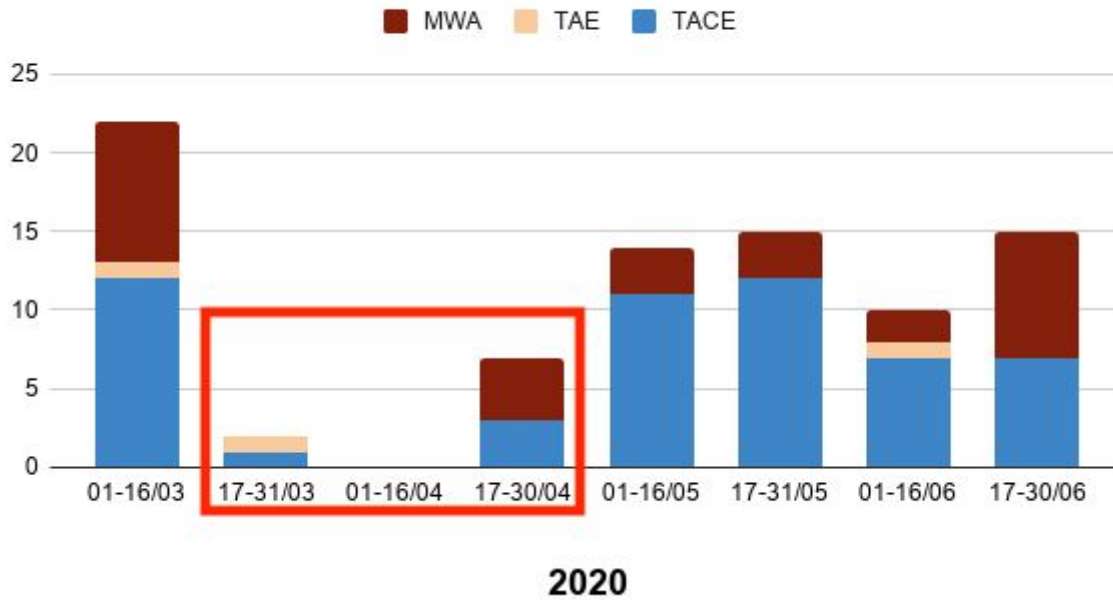


Figure 2

Comparison of percentages between urgent and elective procedures performed at the Interventional Radiology Unit between 16th March and 30th April 2020 ("State of Emergency" period).

All procedures 16/03 - 30/04/2019 (n=172)

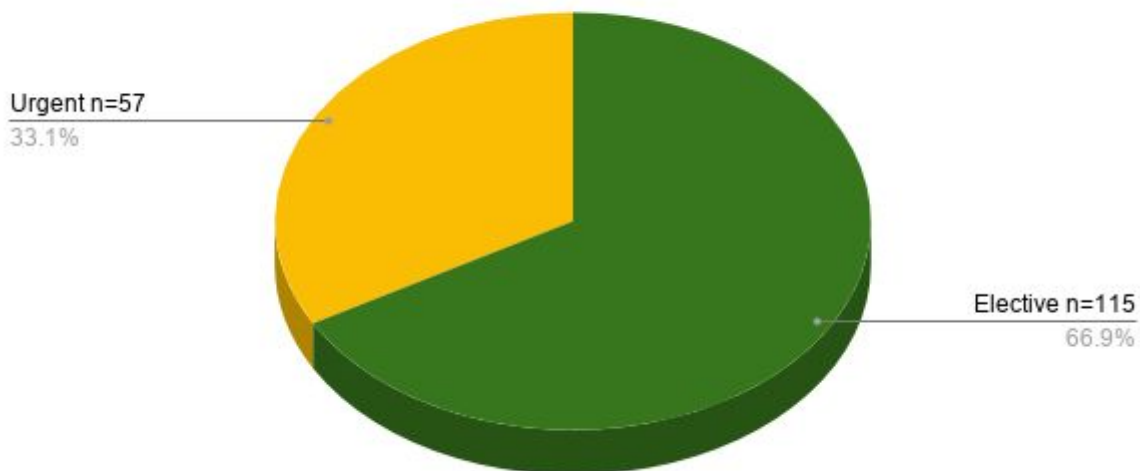


Figure 3

Comparison between 2019 and 2020 in terms of elective procedures between 16th March and 30th April, subdivided by procedure type. TACE – transarterial chemoembolization; TAE – transarterial embolization; MWA – microwave ablation; PTC – percutaneous transhepatic cholangiography.

Elective procedures 16/03 - 30/04 (n 2019=115; n 2020=40)

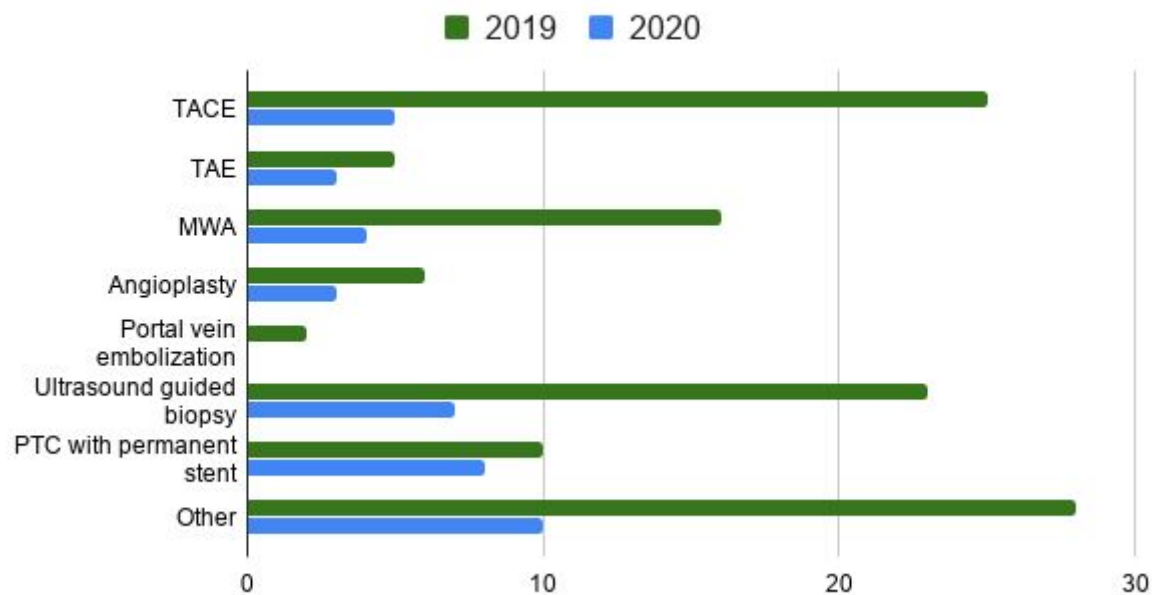


Figure 4

Comparison between 2019 and 2020 in terms of urgent procedures between 16th March and 30th April, subdivided by procedure type. PTC – percutaneous transhepatic cholangiography.

Urgent procedures 16/03 - 30/04 (n 2019=57; n 2020=37)

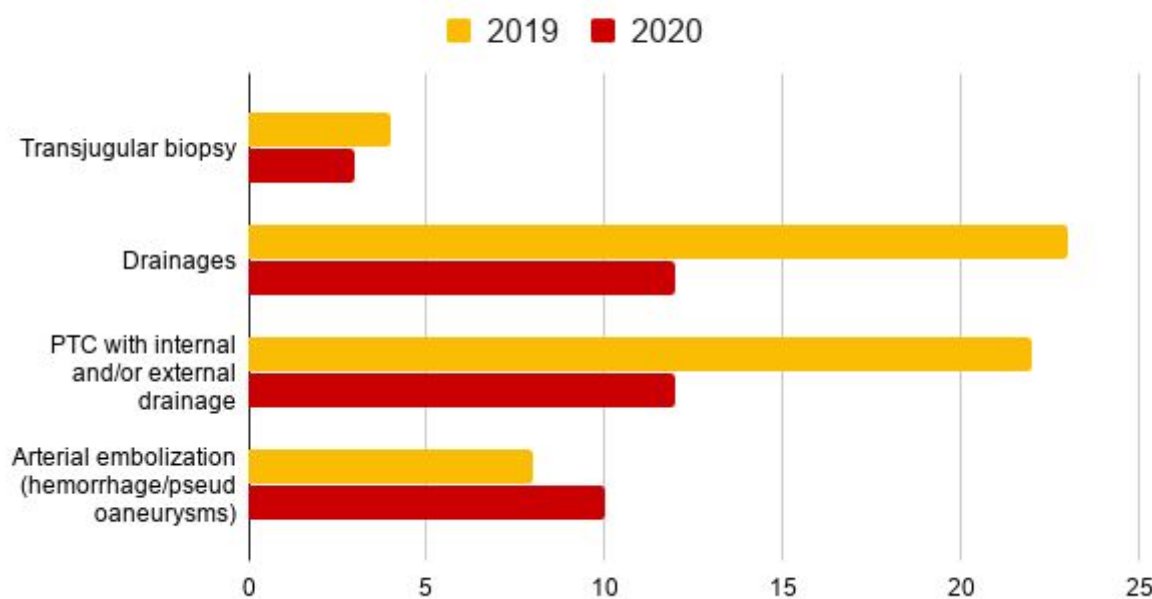


Figure 5

Distribution of loco-regional treatments for hepatocellular carcinoma and liver metastases (microwave ablation – MWA; TAE – transarterial embolization; TACE – transarterial chemoembolization) from 1st March to 30th June 2019, subdivided in 2-week periods.

All procedures 16/03 - 30/04/2020 (n=77)

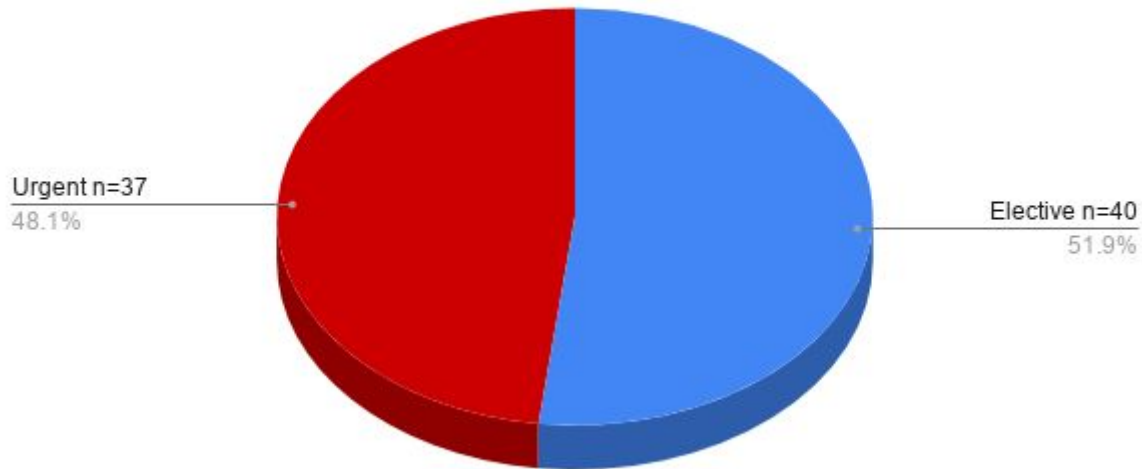


Figure 6

Distribution of loco-regional treatments for hepatocellular carcinoma and liver metastases (microwave ablation – MWA; TAE – transarterial embolization; TACE – transarterial chemoembolization) from 1st March to 30th June 2020, subdivided in 2-week periods. Red box – “State of Emergency” period.