

Recommendations of the BSSO for patients with hepatobiliary cancers in the context of COVID-19 epidemic 2020

Recomendações da SBCO para pacientes com câncer hepatobiliar no contexto da epidemia de COVID-19 em 2020 pedido de mudança.

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ABSTRACT

Since the first report in Hubei, China, COVID-19 rapidly spread throughout the world and the World Health Organization (WHO) declared COVID-19 as global Pandemic on March 11, 2020. The first confirmed case in Brazil was on February 26, 2020. These outbreaks pose a greater threat to patients with cancer in terms of morbidity and mortality as well as for the healthcare system professionals. The purpose of this editorial/letter is to provide specialist based recommendations for the treatment of hepatobiliary tumors during the pandemic period.

Keywords: Coronavirus infections; Liver; Biliary tract neoplasms.

RESUMO

Desde o primeiro relatório em Hubei, China, a COVID-19 se espalhou rapidamente pelo mundo e a Organização Mundial da Saúde (OMS) declarou a COVID-19 como pandemia global em 11 de março de 2020. O primeiro caso confirmado no Brasil foi em 26 de fevereiro de 2020. Esses surtos representam uma ameaça maior para os pacientes com câncer em termos de morbimortalidade e também para os profissionais do sistema de saúde. O objetivo deste editorial/carta é fornecer recomendações baseadas em especialistas para o tratamento de tumores hepatobiliares durante o período de pandemia.

Descritores: Melanoma; Terapia de modalidade combinada; Sistemas de saúde; Sistema único de saúde; Metástase neoplásica.

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INTRODUCTION

COVID-19 infection is caused by the novel coronavirus, named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), that was first reported in Hubei, Wuhan province of China, in December 2019.^[1] This illness is rapidly spreading throughout the world and the World Health Organization (WHO) declared COVID-19 as global pandemic on March 11, 2020. The first confirmed case in Brazil was on February 26, 2020 and so far there are 19,638 cases and 1,056 deaths (5,4 % of lethality).^[2] As testing for COVID-19 for the asymptomatic population has not been possible so far, there is chance that under notification is a fact and lethality overestimated.

According to National Institute of Cancer of Brazil (INCA), 685,960 new cases of cancer are expected in 2020.^[3] Patients with cancer are immunocompromised and therefore more vulnerable to infection for COVID-19 in theory, which can often end in fatality. The vulnerability of patients with cancer was evident by the high risk of mortality during the previous Middle East respiratory syndrome-coronavirus (MERS-CoV) outbreaks.^[4]

These outbreaks pose a greater threat to patients with cancer in terms of morbidity and mortality, as well as for the healthcare system professionals. To expose a cancer patient to a multimodal treatment or surgery, specifically, may be a potential threat under the circumstances of COVID-19 epidemic, therefore recommendations are necessary regarding who could wait. But another potentially harmful situation is the postponement of surgery in cancer patients, not only for common sense, but otherwise due to temporary adaptations in cancer hospitals logistics upon the shortage of intensive care unit (ICU) beds and resources.

Numerous organizations (SSO, NCCN, ESO, and ASCO) are publishing guidelines and recommendations for the best treatment of this population in order to reduce the exposure of the patient and the assistant team without compromising the cancer prognosis.

The purpose of this editorial/letter is to provide specialist based recommendations for the treatment of hepatobiliary tumors during the pandemic period. We understand that it is a very heterogeneous group of tumors and patients, so each case must be individualized with the multidisciplinary team.

CONSIDERATIONS

Colorectal liver metastases (CRLM):

- The mean tumor volume doubling time (TVDT) for metastases vary 86-155 days.^[5]
- Surgery is the best treatment for colorectal liver metastases.^[6]
- Radiofrequency (RFA) and microwave ablation are superior than chemotherapy alone for CRLM treatment.^[7]

- RFA show a significantly lower rate of complications and length of hospital than surgery.^[8]
- There is no difference between disease-free survival in patients undergoing neoadjuvant chemotherapy and those who undergoing upfront surgery for resectable CRLM. Upfront surgery should not be proposed to patients at high risk of postoperative complications or those requiring complex hepatectomies.^[9]

Hepatocellular carcinoma (HCC):

- The median TVDT for HCC in patients with chronic liver disease is 85.7 days (11-851.2 days).^[10]
- There was no difference in overall survival, treatment-related complication or recurrence-free survival at 3 years between RFA or surgical resection for HCC Barcelona-clinic liver cancer (BCLC) A.^[11]
- Transarterial chemoembolization (TACE) is commonly used as a bridging therapy prior to liver transplantation (LT).^[12] The role of TACE in the neoadjuvant setting prior to resection remains unclear and is not routinely recommended.

Intrahepatic cholangiocarcinoma (iCCA):

- The median TVDT for iCCA is 70 days (14.5-512.9 days).^[13]
- High-powered microwave ablation (MWSA) seems to be a good option for treatment in small iCCA nodules (up to 4cm), even better than RFA.^[14]

Hilar cholangiocarcinoma (hCCA):

- Surgery is the best treatment for resectable hilar cholangiocarcinoma.^[15]
- Percutaneous biliary drainage in selected patients are recommended to reduce the risk of operative complications.^[16]
- Portal vein embolization (PVE) should be considered preoperatively for patients in whom the functional liver remnant (FLR) is estimated to be less than 20-30% of the total liver volume after major liver resection.^[17,18]
- Brazilian law does not allow transplantation LT for hCCA.

Gallbladder cancer:

- It's a very aggressive tumor and the only chance for a complete cure is by surgical resection; however, at initial presentation, only 10% of patients are candidates for surgery with a curative intent.^[19]

General recommendations

We consider the COVID mass testing of patient with cancer important, but this amount of testing is not yet available in Brazil.

The health system of each region should try to create "COVID free pathways" at the 3 levels of assistance - basic, secondary, and tertiary.^[20] Through a screening system, it would be possible to select units that would not treat patients suspected of COVID-19, prioritizing certain serious diseases, such as cancer, if possible.

We believe all cases should be discussed in the multidisciplinary team based manner, and the team should consider the information provided by the infection control commission. No surgery should be postponed in the presence of sufficient resources (ICU beds, staff...).

It is important to stratify the patient according to their surgical gravity.^[21]

Priority level 1A: Emergency - operation needed within 24 hours to save life.

Priority level 1B: Urgent - operation needed with 72 hours.

Based on:

Urgent/emergency surgery for life threatening conditions such as obstruction, bleeding and regional and/or localised infection permanent injury/clinical harm from progression of conditions such as spinal cord compression.

Priority level 2: Elective surgery with the expectation of cure, prioritised according to:

- within 4 weeks to save life/progression of disease beyond operability based on; urgency of symptoms;
- complications such as local compressive symptoms;
- biological priority (expected growth rate) of individual cancers.

Local complications may be temporarily controlled, for example with stents if surgery is deferred and/or interventional radiology.

Priority level 3: Elective surgery can be delayed for 10-12 weeks will have no predicted negative outcome.

*Classification of procedures according to priority.

| Classification | Time | According to pathology |
|--------------------|-------------------|---|
| Emergency | whithin 1 hours | Tumor rupture with bleeding and instability |
| Urgency | whithin 24 hours | Cholangitis (biliary drainage)/ Tumor rupture with bleeding and instability - Embolization by radiointervention |
| Relative urgency | whithin 2 weeks | Preoperative biliary drainage for hilar cholangiocarcinoma / Preoperative portal vein embolization / Neoadjuvant chemoembolization |
| Essential elective | Between 3-8 weeks | Resections of malignant liver tumors after neoadjuvance / Resections of gallbladder tumor / Treatment of hilar cholangiocarcinoma after portal vein embolization and / or biliary drainage / Treatment of intrahepatic cholangiocarcinoma |
| Elective | more than 8 weeks | Resections of benign tumors (adenomas, large cysts, etc.) |

Specific recommendations

Colorectal liver metastases (CRLM):

- Initiate neoadjuvant chemotherapy for rapidly growing metastases; synchronous or metastatic to more than one site, in resectable cases.
- Avoid unnecessary prolongation of chemotherapy, only due to the epidemic.
- If the patient has finished neoadjuvant treatment consider delay surgery for 4-6 weeks on major hepatectomies.
- RFA and MWSA can be offered to 1-3 nodules < 3cm.

Hepatocellular carcinoma (HCC):

- RFA for patients BCLC A group.
- TACE as a bridge for transplantation.
- In patients who have had TACE and are at risk of drop out of Milan criteria consider LT. Intrahepatic cholangiocarcinoma (iCCA).
- MWSA should consider to treatment single nodule <4cm.
- Patients not suitable for MWSA consider surgery, give preference to laparoscopic or robotic techniques.

Hilar cholangiocarcinoma (hCCA):

- In the case of potentially resectable hilar cholangiocarcinoma biliary drainage and portal vein embolisation should be considered.

Gallbladder cancer:

- Surgery should not be delayed because it is an aggressive tumor that does not respond to other therapies.

*Classification of procedures according to priority.

CONFLICTS OF INTEREST

The authors have no conflicts to disclose.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020 Feb;382(8):727-33.
2. Ministério da Saúde (BR). COVID-19 - Painel coronavírus [Internet]. Brasília, DF: Ministério da Saúde; 2020; [access in 2020 Apr 10]. Available from: <https://covid.saude.gov.br/>
3. Ministério da Saúde (BR). Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Estimativa 2020: incidência de câncer no Brasil [Internet]. Rio de Janeiro, RJ: Ministério da Saúde/INCA; 2019; [access in 2020 Apr 10]; Available from: <https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//estimativa-2020-incidencia-de-cancer-no-brasil.pdf>
4. Jazieh AR, Alenazi TH, Hejazi A, Al Safi F, Al Olayan A. Outcome of oncology patients infected with coronavirus. *J Glob Oncol*. 2020 Mar;1(6):471-5. DOI: <https://doi.org/10.1200/GO.20.00064>
5. Finlay IG, Meek D, Brunton F, McArdle CS. Growth rate of hepatic metastases in colorectal carcinoma. *Br J Surg*. 1988 Jul;75(7):641-4. DOI: <https://doi.org/10.1002/bjs.1800750707>
6. Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. *Ann Surg*. 1999 Sep;230(3):309-18;discussion:318-21.
7. Meijerink MR, Puijk RS, Van Tilborg AAJM, Henningsen KH, Fernandez LG, Neyt M, et al. Radiofrequency and microwave ablation compared to systemic chemotherapy and to partial hepatectomy in the treatment of colorectal liver metastases: a systematic review and meta-analysis. *Cardiovasc Intervent Radiol*. 2018 Apr;41(8):1189-204. DOI: <https://doi.org/10.1007/s00270-018-1959-3>
8. Van Amerongen MJ, Jenniskens SFM, Van Den Boezem PB, Fütterer JJ, Wilt JHW. Radiofrequency ablation compared to surgical resection for curative treatment of patients with colorectal liver metastases - a meta-analysis. *HPB (Oxford)*. 2017 Sep;19(9):749-56. DOI: <https://doi.org/10.1016/j.hpb.2017.05.011>
9. Allard MA, Nishioka Y, Beghdadi N, Imai K, Gelli M, Yamashita S, et al. Multicentre study of perioperative versus adjuvant chemotherapy for resectable colorectal liver metastases. *BJS Open*. 2019 Oct;3(5):678-86. DOI: <https://doi.org/10.1002/bjs5.50174>
10. An C, Choi YA, Choi D, Paik YH, Ahan SH, Kim MJ, et al. Growth rate of early-stage hepatocellular carcinoma in patients with chronic liver disease. *Clin Mol Hepatol*. 2015 Sep;21(3):279-86. DOI: <https://doi.org/10.3350/cmh.2015.21.3.279>
11. Lu MD, Kuang M, Liang LJ, Xie XY, Peng BG, Liu GJ, et al. Surgical resection versus percutaneous thermal ablation for early-stage hepatocellular carcinoma: a randomized clinical trial. *Zhonghua Yi Xue Za Zhi*. 2006 Mar;86(12):801-5.
12. Pompili M, Francica G, Ponziani FR, Iezzi R, Avolio AW. Bridging and downstaging treatments for hepatocellular carcinoma in patients on the waiting list for liver transplantation. *World J Gastroenterol*. 2013 Nov;19(43):7515-30.
13. De Rose AM, Cucchetti A, Clemente G, Ardito F, Giovannini I, Ercolani G, et al. Prognostic significance of tumor doubling time in mass-forming type cholangiocarcinoma. *J Gastrointest Surg*. 2013 Jan;17(4):739-47. DOI: <https://doi.org/10.1007/s11605-012-2129-6>
14. Giorgio A, Gatti P, Montesarchio L, Santoro B, Dell'Olio A, Crucinio N, et al. Intrahepatic cholangiocarcinoma and thermal ablation: long-term results of an Italian retrospective multicenter study. *J Clin Transl Hepatol*. 2019;7(4):287-92. DOI: <https://doi.org/10.14218/JCTH.2019.00036>
15. Jarnagin WR, Fong Y, DeMatteo RP, Gonen M, Burke EC, Bodniewicz J, et al. Staging, resectability, and outcome in 225 patients with hilar cholangiocarcinoma. *Ann Surg*. 2001 Oct;234(4):507-17;discussion:517-9.
16. Rerknimitr R, Angsuwatcharakon P, Ratanachu-ek T, Khor CJL, Ponnudurai R, Moon JH, et al. Asia-Pacific consensus recommendations for endoscopic and interventional management of hilar cholangiocarcinoma. *J Gastroenterol Hepatol*. 2013 Jan;28(4):593-607. DOI: <https://doi.org/10.1111/jgh.12128>
17. Abdalla EK, Barnett CC, Doherty D, Curley SA, Vauthey JN. Extended hepatectomy in patients with hepatobiliary malignancies with and without preoperative portal vein embolization. *Arch Surg*. 2002;137(6):675-81. DOI: <https://doi.org/10.1001/archsurg.137.6.675>
18. Hemming AW, Reed AI, Howard RJ, Fujita S, Hochwald SN, James C, et al. Preoperative portal vein embolization for extended hepatectomy. *Ann Surg*. 2003 May;237(5):686-93. DOI: <https://doi.org/10.1097/01.SLA.0000065265.16728.C0>
19. Kanthan R, Senger JL, Ahmed S, Kanthan SC. Gallbladder cancer in the 21st century. *J Oncol*. 2015 Sep;2015:967472. DOI: <https://doi.org/10.1155/2015/967472>
20. Sociedade Brasileira de Cirurgia Oncológica (SBCO). Vias livres de COVID-19 [Internet]. Rio de Janeiro, RJ: SBCO; 2020; [access in 2020 Apr 20]. Available from: <https://www.viaslivresdecovid.com/>
21. National Health Service (NHS). Speciality guides for patient management during the coronavirus pandemic Clinical guide for the management of non-coronavirus patients requiring acute treatment: cancer [Internet]. London, UK: NHS; 2020; [access in 2020 Apr 20]. Available from: <https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/cancer-and-COVID-19.pdf>