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## Correspondence

### Five recommendations for loco-regional treatments of hepatocellular carcinoma during the COVID-19 pandemic



With the rapid increase of COVID-19 infected patients, doctors from all specialties are recruited to tackle this problem. Planned surgeries are postponed, operating rooms and wards are converted to treat COVID-19 patients, thus diverting resources away from cancer patients [1]. Given these limitations, it is necessary to consider changes from the current guidelines. Particularly, for patients with early/very early hepatocellular carcinoma (HCC), the treatment strategy should be maintained according to the guidelines, considering that systemic therapies are not a valid alternative [2]. In our Center, which is dedicated to the mini-invasive surgery, we drew up a protocol based on 5 recommendations in order to adapt the therapeutic algorithm proposed by the actual guidelines [2,3] to the new emergency situation and to select the safer treatment (ablation or surgery) for Child A patients with HCC in BCLC A staging and, at the same time, to reduce the risk of COVID-19 infection for patients as well as health professionals. Indications for liver transplantation have not changed: we referred to transplant centers patients with high risk of drop-out due to progression of HCC or to a liver failure Fig. 1.

#### 1. Do not touch

During the pandemic emergency, planned outpatient visits have been almost totally canceled. Hence, when hepatologists, oncologists or family doctors during the follow-up identify patients with evidence of new or recurrent HCC nodules, they send clinical files by e-mail and CT or MRN images by a file sharing service (for example WeTransfer) to our team, in order to evaluate images using an open source dedicated medical image viewer (for example Osirix or Horos for Mac). If outpatient visits cannot be postponed, patients are queried on phone about their clinical status (fever, respiratory distress, contact with suspected COVID-19+ family members), then they come alone or with only a caregiver to reduce the risk of possible contacts, using personal protective equipment.

If the patients are candidates for a surgical procedure, they are firstly contacted by phone for a quick triage on their clinical condition: no access can be allowed in case of respiratory symptoms and/or fever. We have organized limiting points of entry to the hospital with separated paths for accessing the hospital for these patients. Surgical masks and handwashing with hydroalcoholic gel are provided to all patients at the entrance. Preoperative tests including physical examination, routine laboratory tests, and anesthesiologist's evaluation, in order to develop a definitive plan of care, are performed in an outpatient COVID- free clinic. In addition to this, nasal and pharyngeal swabs and a chest X-Ray need to be performed 48-hours before the hospital admission for the surgical procedure, as suggested by Welfare of Lombardy (Protocollo

G1.2020.0016173). Only patients with completely negative findings can be hospitalized. This strategy reduces the risk of false-negative patients, as shown in previous studies [4]. In suspected cases with negative Covid-tests, we have prudently postponed the surgery and repeated the diagnostic tests after 15 days. Only negative patients are admitted to dedicated rooms in a COVID-free department of our Hospital, repeating temperature tests. When it is possible, hospitalized patients stay in single rooms. Patients and their families are informed that visits are not allowed. Asymptomatic patients with positive tests must be deferred to surgery until two consecutive naso-pharyngeal swabs have negative results. During the hospitalization, patients have been regularly monitored for temperature and respiratory symptoms: in the case of suspected symptoms, a naso-pharyngeal swab and chest X-ray or thoracic CT scan must be performed.

When discharged, patients are informed to respect a 20-day isolation period with social distancing and restricted family interactions. We chose this 20-day isolation period in the early stage of the COVID-19 emergency, when a patient died due to COVID-19 pneumonia: symptoms started 21 days after the patient's discharge. It is not clear if the patient got the infection at the time of surgery or after hospital discharge in the community, because three days before her first symptoms appeared, her husband was hospitalized for COVID-19 pneumonia. Patients are monitored at home with regular contacts by phone, electronic text transmission, e-mail or smartphone Apps and they are invited to contact us in case of fever and/or respiratory symptoms.

#### 2. Do not work alone

Normally, disease staging is assessed by a multidisciplinary tumor board, according to the Barcelona Clinic Liver Cancer (BCLC) criteria and the Italian Multisocieties Recommendations [2,3]. Deviation from these guidelines due to the COVID-19 emergency should be discussed in a multidisciplinary meeting with surgeons, radiologists, and hepatologists in order to decide the patient's eligibility to an invasive treatment and a treatment strategy should be drawn up that takes into account both the problem of the COVID-19 infection risk and the treatment of cancer. Meetings take place either virtually by conference calls or in small groups to avoid transmission of the virus among the medical staff. In candidates to an invasive treatment, liver function (according to the Child-Pugh classification) and routine laboratory tests are evaluated. Only patients with a Child-Pugh A score are considered for an invasive treatment. Furthermore, concomitant diseases and age are particularly considered to evaluate the surgical risk in terms of prioritization and type of procedure. Child-Pugh B patients have been evaluated for liver transplantation: patients who are most likely to die on the waitlist should be prioritized and those who can wait longer should be deferred.

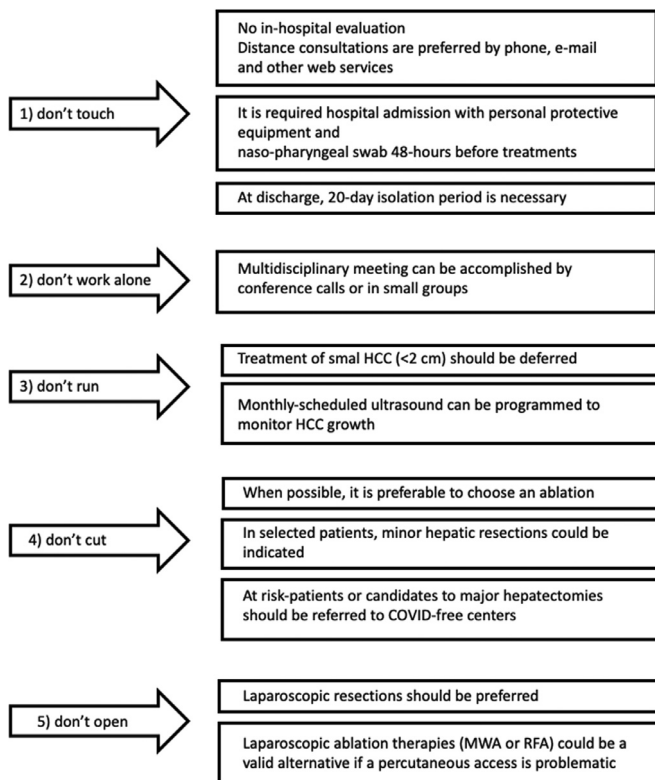


Fig. 1. Five recommendations for the treatment of HCC patients in COVID-19 era  
MWA: microwave ablation; RFA radiofrequency ablation

### 3. Do not rush

Patients are evaluated weighing the risk of post-operative complications against the need of Intensive Care Unit (ICU) assistance, being aware of the paucity of resources available and knowing that most ICU departments are COVID19-dedicated and that the ICU team is mostly involved in the emergency COVID-19 setting. In patients with small HCC requiring a surgical approach, the risk of tumor growth leading to an untreatable stage is low. In this situation, treatment can be deferred [5] and an active monitoring is offered, including a monthly-scheduled ultrasound examination in order to prevent the risk of progression beyond treatment criteria and only growing tumors are scheduled for surgery. In this situation, it is important to consider the oncological impact of deferral: HCC diameter larger than 3 cm could make the ablation choice unavailable and vascular infiltration could prevent the possibility of a minor hepatic resection (HR).

### 4. Do not cut

If the HCC nodule diameter is less than 3 cm, thermoablation should be preferred as a minimally invasive procedure with low impact on patient's condition: the chosen approach (percutaneous or laparoscopic) is evaluated according to the tumor position [6] and patients with superficial lesions adjacent to abdominal viscera, which could be easily displaced during laparoscopy or with deep-sited lesions undetectable at ultrasound, are referred to our center for a laparoscopic approach. Only patients with low risk of liver failure and without severe comorbidities are evaluated for HR which is recommended for single HCC nodules with a diameter >3 cm, when sufficient remnant liver volume is maintained [7]. In this period the capacity on the operating room and/or ICU is limited and, therefore, in the case of HCC requiring a major hepatectomy, the patient must be referred to a "COVID-free" insti-

tution in order to reduce the postoperative risks and to optimize the healthcare resources, according to "Decreto Regione Lombardia n. 3353 del 15-3-2020" (<https://www.regione.lombardia.it/wps/wcm/connect/af6d2303-9212-433e-abcb-ac5a77b48fe5/Decreto%203353.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-af6d2303-9212-433e-abcb-ac5a77b48fe5-n3DP1AT>)

### 5. Do not open

When HR is indicated, a laparoscopic approach should be preferred for its advantages in respiratory function and hospital length of stay. However, caution is required while performing laparoscopy for the risk of virus aerosol, by leaks or during deflation [8]. It is necessary to use balloon trocars to avoid dislocation with appropriate trocar incisions without leakage. Aspiration system is used to remove the smoke and when procedure is finished, it is mandatory to completely aspirate the peritoneal cavity before making the auxiliary incision and/or remove trocars. Absorbable sutures can be used to reduce the need of postoperative outpatient visits. Laparoscopic thermoablation is a safe and effective treatment for tumors not amenable to HR, especially when the percutaneous approach is deemed very problematic [9].

In the group of patients submitted to ablation therapies (8 laparoscopic microwave ablations) or HR (2 laparoscopic and 1 open resections) in this period, none developed positivity or COVID-19 symptoms during the hospitalization. In our Department, in the early period of the emergency, two patients were admitted with acute surgical pathologies and developed COVID-19 pneumonia during the postoperative period. Our team has been trained to isolate early these patients and to ensure that individuals at risk of exposure are tested rapidly.

In our hospital, even if many Departments have been dedicated to the COVID-19 infection, the recommendations adopted in our protocol of surgical treatment allowed the active management of patients with HCC without increasing the risk of COVID-19 infections, both for patients and healthcare personnel.

### Declaration of Competing Interest

The authors indicate no potential conflicts of interest.

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