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ORIGINAL ARTICLE

Strategy for the practice of digestive and oncological surgery during the Covid-19 epidemic☆☆☆

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KEYWORDS

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Summary The Covid-19 pandemic is changing the organization of healthcare and has a direct impact on digestive surgery. Healthcare priorities and circuits are being modified. Emergency surgery is still a priority. Functional surgery is to be deferred. Laparoscopic surgery must follow strict rules so as not to expose healthcare professionals (HCPs) to added risk. The question looms large in cancer surgery—go ahead or defer? There is probably an added risk due to the pandemic that must be balanced against the risk incurred by deferring surgery. For each type of cancer—colon, pancreas, oesogastric, hepatocellular carcinoma—morbidity and mortality rates are stated and compared with the oncological risk incurred by deferring surgery and/or the tumour doubling time. Strategies can be proposed based on this comparison. For colonic cancers T1-2, N0, it is advisable to defer surgery. For advanced colonic lesions, it seems judicious to undertake neoadjuvant chemotherapy and then wait. For rectal cancers T3-4 and/or N+, chemoradiotherapy is indicated, short radiotherapy must be discussed (followed by a waiting

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☆☆ The objectif of this paper is to allow the surgeons to adapt their practices during the first phase of the epidemic until the peak is reached. When the peak is over our systems will have to adapt, but patient management will have to become optimal again.

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period) to reduce time of exposure in the hospital and to prevent infections. Most complex surgery with high morbidity and mortality—oesogastric, hepatic or pancreatic—is most often best deferred.

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Introduction

We are today in an unprecedented situation that is putting all the world's healthcare systems to the test. On 11 March 2020 the World Health Organization (WHO) declared that the epidemic of Covid-19 had become a pandemic. Everywhere in the world, public authorities are recommending strengthened preventive hygiene measures that call on the public's civic responsibility. Epidemiological peaks and the seriousness of the acute respiratory distress syndromes threaten to swamp our resuscitation and intensive care provision. Our governments are taking necessary measures to 'flatten the curve' and spread out over time the influx of cases requiring hospitalization. Meanwhile, they are taking measures to increase our conventional hospital and intensive care capacities.

The French Health Minister Olivier Véran set in action an early plan at the national scale to 'avert a stranglehold'. On 12 March the government instructed "all hospitals to promptly de-schedule all non-urgent surgery requiring post-operative recovery and resuscitation or continuous monitoring, without adversely affecting patients' life-chances. Special attention is required for patients in care for cancer. The purpose of this measure is both to free up beds in recovery and resuscitation wards, and to avoid exposing patients recently operated on to a harmful virus infection."

A recent article published by our Chinese colleagues [1] suggests that patients with cancer are more likely to be infected by the virus because of their immunodepressed state induced by their cancer, their chemotherapy and their surgery. The article also emphasizes that these patients are at higher risk of developing severe episodes (39% vs. 8%). Patients who have been operated on or who have undergone anticancer chemotherapy in the month preceding the appearance of the virus had a higher risk (75%) of developing a severe episode than those who had not undergone surgery or chemotherapy (43%). This study admittedly concerns only a small number of patients, and its scientific soundness can be easily criticized, but decisions will have to be made before more powerful scientific findings become available.

Our focus here is on how the oncological impact of deferring surgical care can be balanced against the added mortality risk of a severe respiratory infection with Covid-19.

Our intention is to pool thinking and propose strategies to be implemented to help manage, at our scale, the unprecedented health crisis that is facing us today. The thinking includes not only patient care but also the protection of healthcare professionals (HCPs) whose work entails added exposure to contamination.

General strategy for visceral surgery during the Covid-19 epidemic

Digestive and parietal disorders are the reason for large numbers of surgical operations, accounting for 12% of surgical hospitalizations in 2015.

The Covid-19 epidemic is still in its early stages in France, but the situation is already serious and has commanded mobilization at an unprecedented scale. The situation is straightforward for emergency cases (infection, ischaemia, obstruction, trauma), which must be dealt with promptly.

Health disorders that cannot be deferred for longer than one month must also be dealt with, if possible, by laparoscopy to minimize postoperative impact on respiratory function. In all cases, patients must be considered as possibly infected, and so cross-infection must be prevented.

It is recommended not to carry out elective surgery for benign disorders, because such surgery can be performed without jeopardizing the result once the epidemic has subsided. It is important to inform patients and their families of the medical reasons for deferring surgery, namely collective welfare (freeing both ordinary and recovery and resuscitation hospital beds, relieving the HCPs) and individual precaution (preventing a more serious respiratory infection after surgery). It is also useful to inform patients that the intervention they need will probably be deferred until well after the epidemic has abated, because there will be many other patients awaiting treatment, whose numbers will depend on how long the epidemic lasts.

A special case is that of patients who are or may be infected by Covid-19 and who require emergency surgery. In this situation, two factors are to be considered:

- protection of HCPs;
- minimization of the respiratory impact of the intervention. Ample communication must be the rule, with the operating theatre team, anaesthetists and other related HCPs, and the operation must be performed with stringent protection.

The operating theatre must if possible be under negative pressure to prevent outward diffusion and contamination of personnel and surfaces outside. The choice of approach must first be discussed case by case with the anaesthetist: laparoscopy is to be preferred if the causal condition permits it and if the patient's cardiorespiratory status is stable; otherwise, laparotomy is indicated.

Precautions concerning laparoscopy (appendectomy, exploratory, etc.)

Laparoscopy has many advantages, essentially its favourable impact on respiratory function and length of hospital stay. However, caution is required when performing laparoscopy because of the risk of exposure and infection of the personnel present. The main risk arises from the presence of pathogens in the peritoneal cavity, which is favoured by dissection. The aerosol released into the room during surgery (leaks) or after the operation (exsufflation), can contaminate personnel and all the furniture and surfaces in the room via airborne particles. If the laparoscopic approach is chosen, surgeons must:

- make sure all the instruments are in order and the aspiration system operates correctly; this last must be used systematically, before incision via a check list;

- make appropriate openings to introduce trocars without leakage and use balloon trocars if available;
- not create a leak if smoke is hindering surgery, but instead use the aspirator to remove the smoke;
- aspirate the whole peritoneal cavity before making an auxiliary incision and when the operation is completed before the trocars are removed.

If in doubt or if experience in laparoscopy is scant, laparotomy is to be preferred.

Adaptation of the post-operative period

After every surgical intervention, the medical, paramedical and cleaning personnel must take the most stringent protection measures in line with national and local recommendations (French nosocomial infection control committees, CLIN). Like precautions must be taken for the recovery room or post-anaesthesia care unit (PACU).

Post-operatively, patients will be admitted to a hospital ward adapted to their respiratory condition. It is advisable for hospital wards to be sectioned off into individual rooms during the epidemic to forestall cross-infection with other patients or visiting relatives. Individual rooms would also facilitate isolation management if this proved necessary. It is important to clearly inform patients and their families that visits are not allowed. This ban is designed to protect patients, visitors and hospital staff. When care times per patient are longer than usual owing to the especially strict precautions taken to prevent cross-infections, it is advisable to put in place electronic means of communication (telephone, email, etc.) with family members so they can be informed of their relative's state of health. The impossibility for relatives to come and visit patients in hospital generates stress and anxiety. In addition to taking phone numbers, it would therefore be useful to take email addresses of family contacts.

Adaptation of the consultation system

All non-essential consultations must be cancelled or deferred. They can best be replaced by distance consultations using telemedicine applications or the telephone. Reducing the number of consultations will reduce the risk of cross-infection.

If a consultation is essential, it must be scheduled, and patients asked whether they feel any respiratory discomfort. Patients must be told to come alone or with only one other person to reduce the numbers of possible contacts.

Consultations must be scheduled with long intervals between successive consultations to prevent crowding in waiting rooms.

Contacts with patients must be limited. If a clinical examination is essential, then it must be carried out with gloved hands. HCPs must change their gloves immediately after coming into contact with patients, body fluids or contaminated materials. Quick-drying water-alcohol gel must be used for hands. The relevant nosocomial infection control committees (CLIN in France) guidelines for HCPs must be strictly adhered to, including schedules for changing masks.

Consulting rooms must be regularly ventilated and aired. Surfaces must be disinfected between successive patients.

Strategy for oncological digestive surgery practice during the Covid-19 epidemic

The Covid-19 epidemic is disrupting not only our daily lives but also how we manage patients, especially those with cancer. This new coronavirus is passed on mainly in breath droplets, but possibly also by contact and oro-faecally. The infection has an incubation time of 1–14 days. Asymptomatic infected patients may be contagious during the incubation period, and negative tests do not rule out infection. Cancer patients are fragile, often malnourished and with an immune system compromised by both the cancer and its treatment. There seems to be an increase in cases of severe ARDS in such patients. In addition, in the current situation it is judicious to conserve medical resources, though without compromising patient prognosis.

In non-urgent cases, non-surgical treatments are to be preferred. Surgery can be done once the epidemic is quelled. However, even after the epidemic is over, the return to normal will take place only gradually, because the HCPs, especially anaesthetists and resuscitation teams, will be exhausted by several weeks of unstinting efforts to battle the infection. There will also be more patients awaiting care owing to the deferral of surgery during the epidemic.

Hence we must draw up a reasonable care strategy that takes into account both management of the epidemic and treatment of the cancer. Saving time, while curbing the spread of the illness during the epidemic and hastening the return to normal is the challenge we all have to meet.

Care provision must be adapted to the regional health situation, forecasted evolution of the epidemic, and the risk that our healthcare systems may be overwhelmed. It is advisable to plan for the risk of overload and be ready to switch to a degraded work mode. A patient needing post-operative respiratory assistance after major surgery or a complication might not receive it if our systems were saturated.

Care for cancer patients has several common imperatives:

- combat malnutrition by favouring a balanced diet, providing nutritional supplements or by enteral tube feeding;
- avoid serious adverse effects on the immune system caused by aggressive treatments;
- avoid hospitalizations, visits, and hospital stays that favour contamination by the virus;
- prefer a therapeutic sequence that does not require strictly timed surgery that might not be feasible;
- discuss care provision in multidisciplinary meetings to draw up an individual care plan best adapted to the patient and to the epidemic setting. These meetings are to take place virtually (virtual multidisciplinary consultation meetings) or in small groups (segmentation of teams) to prevent the virus spreading through the various medical staff;
- offer psychological assistance to patients who have to cope with managing cancer and measures to shelter them and others from the epidemic.

Our Chinese colleagues have published several articles suggesting changes to practice and adaptation of strategies [2–5].

Specific features of care by cancer type

Two questions are essential in our thinking on care strategy:

- what are the known operating risks and the new added risks of respiratory infection? The latest research findings show that patients with tumours are more prone to infection by Covid-19 owing to their systemic immunodeficient status caused by the disease, oncological treatment (radiotherapy, chemotherapy) and surgery. Patients operated on or undergoing chemotherapy in the months preceding the infection had a serious form of infection in 75% of cases, representing a relative risk calculated by multivariate analysis of 5.34 (CI95% 1.80–16.18, $P=0.0026$) [1]. In this light, exposure of patients to added risk of post-operative morbidity and mortality must be considered and factored into the choice of strategy made;
- what would be the oncological impact of a long deferral (6–12 weeks) due to the epidemic? Time-to-surgery is often considered a measure of care quality. However, when waiting time is most often due to overloaded operating schedules, it has been shown that this time lapse can also be gainfully used to select the “best candidates” for surgery (true resectables) and prepare them for intervention (prehabilitation, management of anaemia if needed, preoperative nutrition). In the current situation, and given the risks incurred, it is essential to consider the oncological impact of deferral imposed by the exceptional demands made on care provision.

These questions will now be detailed by organ.

Specific features of care for colorectal cancers

Morbidity and mortality

In colorectal surgery, post-operative mortality and morbidity were estimated at respectively 3.4% and 35% in the French surgery association (AFC) trial [6]. This prospective trial included 1421 patients, and mortality at 3 months was 6.3%. Four mortality risk factors, accessible before surgery, were isolated: the urgency of the surgery (relative risk 4.42), neurological antecedents (relative risk 3.85), weight loss above 10% of initial weight (relative risk 3.42) and age above 70 years (relative risk 2.16). This study showed that the greater the number of mortality risk factors, the higher the mortality rate. For rectal surgery, the most feared complication is anastomotic fistula, with a frequency of 15–26% (Greccar 5) and an associated mortality of 6–39% [7].

Oncological impact of deferral

This impact has not often been measured in colonic surgery. In advanced forms of rectal cancer, a neoadjuvant treatment is necessary, with a time lapse between the end of chemoradiotherapy and surgery of 8 weeks, extendable to 12 weeks with no harmful consequences (Greccar 6 trial) [8]. Hence is it not the patients at the start or in the middle of treatment who will be causing us problems, but the patients who have finished their treatment and whose surgery has already been scheduled.

Summary

- For pre-cancerous lesions with good prognosis (T1-2, N0), it is advised to defer surgery according to the stage of the epidemic.
- For advanced colonic lesions, it is judicious to recommend neoadjuvant chemotherapy and wait until the peak of the epidemic has passed before proposing radical surgery. These situations will have to be discussed case by case to take into consideration the oncological risk, the risk of evolution towards occlusion, and the risk of induced immunodepression, which could be extremely harmful.
- For cancers T3-4 and/or N+, chemoradiotherapy is indicated, short radiotherapy is to be discussed (followed by a waiting period) to reduce the exposure time in hospital and avoid infections. Induction chemotherapy can also be discussed case by case.
- For cancers with obstruction, a stoma will be performed followed by chemotherapy. Special attention will be paid during stoma care (contaminating act) to prevent infection of HCPs.
- For cancers at end of treatment, where surgery must be scheduled, the strategy will be adapted to the duration of the epidemic, its peak, and the available medical resources. In some cases, interim chemotherapy can be proposed [9].

Specific features of care for pancreatic cancers

Morbidity and mortality

Despite cumulated surgical, anaesthesiological and resuscitation efforts, and peri-operative optimization measures (improved rehabilitation, prehabilitation), morbidity and mortality for cephalic duodenopancreatectomies remain high. The latest review of data from the French medical information programme (PMSI) estimated the mortality rate at 8.2% [10]. Overall and severe complication rates were respectively 75% and 30% with, in order of frequency, specific complications (pancreatic fistula, haemorrhage) and infectious complications [11].

After left splenopancreatectomy, although mortality rates were lower (3%), the rate of severe complications was about 25%.

Oncological impact of deferral

Two retrospective cohort studies of North American national register data [12,13] evaluated the impact of waiting time before pancreatectomy for cancer. Mirkin et al. [12] suggested that long-term survival was unaffected by waiting time. In the study published by Swords et al. [13] time-to-surgery was short (1–14 days) for 4.4%, medium (15–42 days) for 51.6%, and long (43–120 days) for 14% of patients. Mortality rates were lower for patients with medium waiting times (hazard ratio 0.94, CI95% 0.90–0.97) and long waiting times (hazard ratio 0.91, CI95% 0.86–0.96). There

was no difference in rate of ganglion invasion, locoregional non-resectability, discovery of metastatic extension on exploration, or positive margins. Mortality at 90 days was lower in the group with medium waiting time (odds ratio 0.75, CI95% 0.65–0.85) and in the group with the long waiting time (odds ratio 0.72, CI95% 0.60–0.88).

Summary

If there is no histological documentation:

- For peri-ampullary tumours, deferral of surgery will be proposed according to the operative risks as the epidemic unfolds.
- For corporocaudal lesions, according to possibilities of access to surgery and how the epidemic is evolving, surgery can be proposed to patients at low operative risk but must otherwise be deferred.
- If there is histological documentation pointing to pancreatic adenocarcinoma:
 - Interim chemotherapy can be proposed for cephalic lesions. These situations will be discussed case by case to take into consideration the oncological risk and the risk of induced immunodepression, which could be extremely harmful (biliary drainage and malnutrition in particular).
 - For lesions requiring left splenopancreatectomy, surgery can be proposed in patients at low operative risk (comorbidities, nutritional state), but must otherwise be deferred, with possible interim chemotherapy. These situations will be discussed case by case to take into consideration the oncological risk and the risk of induced immunodepression, which could be extremely harmful.

Specific features of care for oesogastric cancers

Morbidity and mortality

Surgery of oesogastric cancers carries a high risk of complications. Rates of major complications after upper polar oesophagectomy are high, at 36–64% in the MIRO trial, with rates of major respiratory complications of 18–30% [14]. After total gastrectomy, rates of major complications are lower, but still 10–15%, mostly respiratory and septic complications [15,16].

Oncological impact of deferral

Localized oesogastric cancers generally progress quite slowly (whatever the histological subtype). The average progression time from localized to locally evolved or metastatic is 34–44 months, based on Asian literature data. The doubling time of a locally advanced gastric cancer is 6.2 months [17,18]. The epidemiology of oesogastric cancers in France and in Europe are different, so that these data need to be analysed with some clinical circumspection. Tumours diagnosed at an early stage make up fewer than 5% of patients operated on, and for a cancer of the oesophagus to be symptomatic, 80% of the lumen must be functionally blocked.

Summary

- In the light of these considerations and current strategies for pre-operative treatments (neoadjuvant chemotherapy (FLOT regimen in particular), neoadjuvant chemoradiotherapy) except for superficial forms, gastrectomies and oesophagectomies must be deferred, with discussion of how to pursue pre-operative treatment if it ends during the epidemic (maintenance chemotherapy according to modes discussed in multidisciplinary concertation meetings and adapted case by case, taking into account the non-negligible risk of chemo-induced immunosuppression).
- For cancers requiring partial gastrectomy, given the lower risk of complications, surgery can be proposed to patients at low operative risk, but must otherwise be deferred.

Specific features of care for liver tumours

Morbidity and mortality

The risks of post-operative complications must be estimated according to the status of the underlying liver tissue (cirrhosis, steatosis) and the surgical act planned (minor or major hepatectomy, liver segments/sectors concerned). Overall complication rates are 15% and 45% after minor and major hepatectomy respectively, and 4% and 20% for severe complications [19]. On cirrhotic livers, the latest retrospective AFC study recorded overall and severe complication rates of 44% and 11% respectively [20].

Oncological impact of deferral

For hepatocellular carcinoma, the risk of tumour growth leading to non-resectability is low and is not life-threatening in the short term. An et al. retrospectively analysed the data of 175 patients with hepatocellular carcinoma without treatment. The median tumour volume doubling time was 85.7 days with an upper extremum of 851.2 days [21]. Few similar data are available for intrahepatic cholangiocarcinoma.

Summary

Given the low risk of tumour growth over the duration of the epidemic, surgery must be deferred for patients with early liver tumours.

- In the case of a lesion amenable to minor hepatic exeresis, according to the possibilities of access to surgery and how the epidemic unfolds, surgery can be proposed to patients at low operative risk but must otherwise be deferred.
- In the case of a lesion requiring major hepatic exeresis, surgery must be deferred, with possible preparation by portal embolization if necessary, and nutritional preparation. Special attention will be paid to hilar cholangiocarcinoma, as regards septic and nutritional risk.
- Patients who are candidates for tumour destruction by thermal ablation can be treated according to the possibilities of access to surgery and interventional radiology facilities and how the epidemic unfolds.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020;21(3):335–7.
- [2] Zhang Y, Xu JM. [Medical diagnosis and treatment strategies for malignant tumors of the digestive system during the outbreak of novel coronavirus pneumonia]. *Zhonghua Zhong Liu Za Zhi* 2020;42(0):E005.
- [3] Chen YH, Peng JS. [Treatment strategy for gastrointestinal tumor under the outbreak of novel coronavirus pneumonia in China]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2020;23(2):I–IV.
- [4] Hu XH, Niu WB, Zhang JF, et al. [Thinking of treatment strategies for colorectal cancer patients in tumor hospitals under the background of coronavirus pneumonia]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2020;23(3):E002.
- [5] Wu F, Song Y, Zeng HY, et al. [Discussion on diagnosis and treatment of hepatobiliary malignancies during the outbreak of novel coronavirus pneumonia]. *Zhonghua Zhong Liu Za Zhi* 2020;42(0):E004.
- [6] Alves A, Panis Y, Mathieu P, et al. Postoperative mortality and morbidity in French patients undergoing colorectal surgery: results of a prospective multicenter study. *Arch Surg* 2005;140(3):278–83 [discussion 84].
- [7] Denost Q, Rouanet P, Faucheron JL, et al. To Drain or Not to Drain Infraperitoneal Anastomosis After Rectal Excision for Cancer: The GRECCAR 5 Randomized Trial. *Ann Surg* 2017;265(3):474–80.
- [8] Lefevre JH, Mineur L, Kotti S, et al. Effect of Interval (7 or 11 weeks) Between Neoadjuvant Chemoradiotherapy and Surgery on Complete Pathologic Response in Rectal Cancer: A Multicenter, Randomized Controlled Trial (GRECCAR-6). *J Clin Oncol* 2016;34(31):3773–80.
- [9] Habr-Gama A, Perez RO, Sabbaga J, Nadalin W, Sao Juliao GP, Gama-Rodrigues J. Increasing the rates of complete response to neoadjuvant chemoradiotherapy for distal rectal cancer: results of a prospective study using additional chemotherapy during the resting period. *Dis Colon Rectum* 2009;52(12):1927–34.
- [10] El Amrani M, Lenne X, Clement G, et al. Specificity of Procedure volume and its Association With Postoperative Mortality in Digestive Cancer Surgery: A Nationwide Study of 225,752 Patients. *Ann Surg* 2019;270(5):775–82.
- [11] Schwarz L, Bruno M, Parker NH, et al. Active Surveillance for Adverse Events Within 90 Days: The Standard for Reporting Surgical Outcomes After Pancreatectomy. *Ann Surg Oncol* 2015;22(11):3522–9.
- [12] Mirkin KA, Hollenbeak CS, Wong J. Time to Surgery: a Misguided Quality Metric in Early Stage Pancreatic Cancer. *J Gastrointest Surg* 2018;22(8):1365–75.
- [13] Swords DS, Zhang C, Presson AP, Firpo MA, Mulvihill SJ, Scaife CL. Association of time-to-surgery with outcomes in clinical stage I-II pancreatic adenocarcinoma treated with upfront surgery. *Surgery* 2018;163(4):753–60.
- [14] Mariette C, Markar S, Dabakuyo-Yonli TS, et al. Health-related Quality of Life Following Hybrid Minimally Invasive Versus Open Esophagectomy for Patients With Esophageal Cancer, Analysis of a Multicenter, Open-label, Randomized Phase III Controlled Trial: The MIRO Trial. *Ann Surg* 2019.
- [15] Bartlett EK, Roses RE, Kelz RR, Drebin JA, Fraker DL, Karakousis GC. Morbidity and mortality after total gastrectomy for gastric malignancy using the American College of Surgeons National Surgical Quality Improvement Program database. *Surgery* 2014;156(2):298–304.
- [16] Wang WJ, Li R, Guo CA, et al. Systematic assessment of complications after robotic-assisted total versus distal gastrectomy for advanced gastric cancer: A retrospective propensity score-matched study using Clavien-Dindo classification. *Int J Surg* 2019;71:140–8.
- [17] Fujiya K, Irino T, Furukawa K, et al. Safety of prolonged wait time for gastrectomy in clinical stage I gastric cancer. *Eur J Surg Oncol* 2019;45(10):1964–8.
- [18] Oh SY, Lee JH, Lee HJ, et al. Natural History of Gastric Cancer: Observational Study of Gastric Cancer Patients Not Treated During Follow-Up. *Ann Surg Oncol* 2019;26(9):2905–11.
- [19] Kawaguchi Y, Fuks D, Kokudo N, Gayet B. Difficulty of Laparoscopic Liver Resection: Proposal for a New Classification. *Ann Surg* 2018;267(1):13–7.
- [20] Hobeika C, Fuks D, Cauchy F, et al. Impact of cirrhosis in patients undergoing laparoscopic liver resection in a nationwide multicentre survey. *Br J Surg* 2020;107(3):268–77.
- [21] 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;21(3):279–86.