

Considerations for HPB Surgeons in a Complex Triage Scenario COVID-19

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Summary

The ANZHPBA trusts the judgement of its members to make individual patient management decisions. These are not rigid guidelines, and will not be able to consider every clinical scenario. The ANZHPBA aims to support our members in making the clinical decision appropriate for their patient in their particular clinical situation recognising that circumstances vary around the country and will continue to change.

COVID-19 Response phases

The ACS has provided a sensible division of three phases that reflect the acuity of the local COVID-19 situation:

Phase I. Semi-Urgent Setting (Preparation Phase) — few COVID-19 patients, hospital resources not exhausted, institution still has ICU ventilator capacity and COVID-19 trajectory not in rapid escalation phase

Phase II. Urgent Setting — many COVID-19 patients, ICU and ventilator capacity limited, operating room supplies limited

Phase III - “Wartime” footing - Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, operating room supplies exhausted; only patients in whom death is likely within hours if surgery is deferred

Of course such categorisation can fail to capture the nuance of individual hospital resourcing and the surge capacity of different institutions will be variable..

Under Phase I conditions

1. Resectable Pancreatic Carcinoma

- a. Consider up front resection if local resources allow
- b. MUST consider “biological” not just “technical” resectability
- c. Neoadjuvant therapy remains an option

2. BR/Locally advanced PDAC

- a. Clarify decision rules PRIOR to initiating neoadjuvant/palliative chemotherapy
- b. Prolonged neoadjuvant therapy may be a safe alternative
- c. Upfront resection unlikely to be most appropriate option

3. Hepatocellular Carcinoma

- a. Outpatient based liver directed and ablative therapies may be preferential
- b. Resection may be appropriate up front in selected patients

4. Metastatic Colorectal Cancer

- a. Where limited progression will not compromise inflow/outflow structures or future resectability - surgery should be deferred
- b. Short interval (3 month) followup
- c. Chemotherapy may be considered for these patients when it can be given safely
- d. Delay with watchful waiting may not impact outcomes in select cases
- e. Patients with extensive bilobar metastases or those requiring complex resection strategies may be better treated with ongoing outpatient chemotherapy and bridging liver directed therapies if available

5. Pancreatic neuroendocrine tumours

- a. Observation, medical suppression therapy and delaying radical surgery may be most appropriate
- b. Consider radiological investigations for diagnosis over invasive endoscopic procedures

6. Biliary disease

- a. Single staged operative gallstone management avoiding ERCP may be safest for patients and staff
- b. Most biliary colic cases can safely be delayed
- c. Early acute cholecystectomy for cholecystitis remains preferred treatment

7. Therapeutic Upper Gastrointestinal Endoscopy/ERCP/EUS

- a. Likely to be performed for luminal obstruction or significant biliary sepsis

- b. Should be considered urgent/essential and not delayed
- c. In patients with non-pruritic jaundice secondary to advanced/metastatic malignancy discussion must be had regarding the utility of any intervention¹
- d. Interventional EUS for pancreatitis complications should be carefully considered against the option of non-aerosolising percutaneous measures

8. Diagnostic Upper Gastrointestinal Endoscopy/EUS

- a. Where obtaining a diagnosis cannot be achieved with alternate means AND
- b. A tissue diagnosis will lead to significant alteration in clinical decision making
- c. Such procedures should be considered
- d. Delay is likely to push the cancer diagnosis peak forwards and may result in cancer progression

Introduction

There is an extraordinary situation unfolding worldwide as COVID-19 impacts the population. Whilst the disaster in China, Italy, Spain and the USA has crippled their health systems, in many countries the future hangs on a knife edge as we wait to see the degree of community transmission. It is possible that despite avoiding a complete overwhelming of our available resources, we may remain significantly constrained in our ability to deliver standard care for a period of many months due to material and personnel shortages.

The impact of COVID-19 on HPB practice will be profoundly felt from access to theatre for acute cholecystitis to chemotherapy complications for advanced cancer patients. As personal protective equipment (PPE) and ICU support becomes more scarce, we must take the opportunity to review our decision making processes. The choice to set limits is a necessary response. It is important that we systematically address those decisions based on best available evidence, ethical values and prioritisation guidelines². We must advocate for our vulnerable patient population and not lose sight of the fundamental requirement for equitable access to health care for COVID-19 and non COVID-19 associated illness.

Prioritisation

The past weeks have seen several guidelines and government directives published emphasising a shift to focus on urgent surgery^{3,4}. Implementing these directives in the setting of complex, multimodal hepatopancreaticobiliary diseases is not always straight-forward.

The American College of Surgeons have published several guidelines regarding cancer care in the COVID setting, and advise using the Elective Surgery Acuity Scale (ESAS) available on the ACS Website⁵. There is currently no ACS guidance available specifically for HPB cases. The American College of Physicians published a broad guideline for cancer care and emphasise the need to continue to diagnose and manage treatable conditions at this time⁶. The Royal College of Radiologists (UK) have produced pancreas cancer specific guidelines⁷, although some components represent a significant deviation from current practice in Australia.

Whilst brief delays in treatment and diagnosis may not result in worsening outcomes⁸ it is imperative that we do not unnecessarily delay cases, creating a perfect storm in which an iatrogenic ‘cancer peak’ coincides with the COVID peak, ICUs begin to fill and cases become inherently more urgent and complex as diseases progress.

The factors we must consider when deciding on urgency of investigation and intervention include:

1. risk of progression with delay;
2. impact of such a progression;
3. available alternatives;
4. likely outcomes with and without intervention
5. available resources and potentially competing cases.

How each of these factors is weighed and measured and how and the needs of an individual patient are weighed against those of another, is highly complex and fraught with ethical dangers.

In the COVID setting, we should generally aim to select options that have:

1. the shortest hospital stay with the fewest complications;
2. the least likelihood of needing critical care or shortest duration in critical care;
3. the highest life expectancy and return to best functional capacity;
4. the lowest combined utilization of hospital resources;
5. the lowest risk of transmitting SARS-Cov2 to healthcare workers.

Treatment of HPB conditions - malignancy

General considerations

COVID-19 has poor outcomes in patients over the age of 70 with comorbid conditions, a group over-represented among patients with HPB malignancies. Malignancy alone constitutes a significant risk of poor outcome when COVID-19 is contacted (Case Fatality Rate 6%). Chemotherapy compounds the risk for worse outcomes if infection with Sars-CoV-2 is contracted.

Resectable pancreatic adenocarcinoma (PDAC), ampullary cancer and distal cholangiocarcinoma

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| Risk of progression | <ul style="list-style-type: none"> ● Significant, treatment to commence within timeframe ● PDAC time to metastasis is shorter in tumours > 2cm (3 months) as compared to <2cm (7 months) ● Ampullary intestinal type carcinoma tend to have a slower progression time |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Individual-significant – 5yr survival ~50 down to <5% if metastasis occurs during delay ● Systemic-limited – may not alter resource requirement significantly |
| Treatment options | <p>Phase 1</p> <ul style="list-style-type: none"> ● Resection is advocated ● May allow 12-20 weeks post-op before adjuvant therapy |
| | <p>Phase 2 - risk of contraction of COVID-19 increased due to population incidence</p> <ul style="list-style-type: none"> ● Prioritise early cancers to surgery (<Stage IIA) ● Carefully consider surgery in N1 patients in view of the poor long term survival. ● NAC has the added risk of neutropenia |
| | <p>Phase 3 (Crisis)</p> <ul style="list-style-type: none"> ● Neoadjuvant chemotherapy for N1 disease |

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| | <ul style="list-style-type: none"> • Early stage close observation is warranted but prioritise surgery as early as possible. Add chemotherapy if progression in 6 weeks. |
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Recommendation

- *Consider up front resection if local resources allow procedures should be considered*
- *MUST consider “biological” not just “technical” resectability*
- *Neoadjuvant chemotherapy remains an option*

Locally advanced PDAC

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| Risk of progression | <ul style="list-style-type: none"> • Variable – may be scope to continue for 6 months of up front chemotherapy if tolerating well. May be scope for switch to chemoradiotherapy in selected cases |
| Consequence of disease progression | <ul style="list-style-type: none"> • Individual – variable – progression on chemotherapy generally portends poor prognosis. Immunosuppression with chemotherapy may increase COVID-19 related complications • Systemic – variable – local chemo/radiotherapy resources to be weighed against theatre, ICU and ward access |
| Alternatives | <ul style="list-style-type: none"> • As above, consider prolonged neoadjuvant vs resection |
| Treatment options | <p>Phase1 and 2</p> <ul style="list-style-type: none"> • Individual – variable – progression on chemotherapy portends poor prognosis. Immunosuppression with chemotherapy may increase COVID-19 related complications • Systemic – variable – local chemo/radiotherapy resources to be weighed against theatre, ICU and ward access <p>Phase 3</p> |

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| | <ul style="list-style-type: none"> ● Palliation might be appropriate as quality of any treatment will be hampered by lack of supportive resources to deliver safe chemo and radiotherapy. |
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Recommendation

- Clarify decision rules *PRIOR* to initiating neoadjuvant/palliative chemotherapy
- Prolonged neoadjuvant therapy may be a safe alternative
- Upfront resection unlikely to be most appropriate option

Hepatocellular Carcinoma

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| Risk of progression | <ul style="list-style-type: none"> ● Variable – depends highly on tumour size, grade, underlying liver reserve, comorbidities ● Smaller tumours < 2 cm have slow progression rate > 3 months |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Individual – variable – tumours may breach size limits for percutaneous and liver directed therapies ● Systemic – variable – local theatre/Interventional Radiology/hepatology access needs to be considered |
| Alternatives | <ul style="list-style-type: none"> ● Near equipoise exists for HCC resection and ablative measures in chronic liver disease patients, resection may be best option in well, non CLD patients with an anticipated short hospital stay⁹ |

Recommendations

- Outpatient based liver directed and ablative therapies may be preferential - either definitive or as a bridge to surgery
- Resection may be appropriate up front in selected patients

Metastatic Colorectal Cancer

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| Risk of progression | <ul style="list-style-type: none"> ● Variable |
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| | <ul style="list-style-type: none"> ● Patients with well and moderately differentiated tumours have a very slow progression time (> 6 months) ● Poorly differentiated tumours progress rapidly (survival in months) ● Tumours with threatened margins need special consideration |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Individual <ul style="list-style-type: none"> ○ Unresectable disease ○ Prolongation of chemotherapy past 3 months increases complications of future liver surgery ● Systemic – variable – local chemo/radiotherapy resources to be weighed against theatre, ICU and ward access |
| Alternatives | <ul style="list-style-type: none"> ● Phase 1 <ul style="list-style-type: none"> ○ Consider surgery for good prognosis tumours needing simple resections ● Phase 2 and 3 <ul style="list-style-type: none"> ○ Patients with limited, peripheral hepatic metastases may be observed with comparable survival to resected disease over 10-12 months¹⁰ ○ Tumours at critical locations should be treated ● Chemotherapy can be considered, but risks of prolonged therapy require discussion |

Recommendation

- Where limited progression will not compromise inflow/outflow structures or future resectability - surgery should be deferred
- Short interval (3 month) followup should be performed
- Chemotherapy may be considered for these patients when it can be given safely
- Patients with extensive bilobar metastases or those requiring complex resection strategies may be better treated with ongoing outpatient chemotherapy and bridging liver directed therapies if available.
- Prognosis should be in the range of 40-60% 5yr survival projected.

Pancreatic NETs

Where there is diagnostic uncertainty, Ga-68 DOTATE-PET may be considered an alternative diagnostic modality to EUS/endoscopic biopsy to avoid risk to the treating teams and limit patient complications.

Rare presentations including resectable, non-metastatic high grade tumours may be resected or potentially offered neoadjuvant therapies in an experimental setting pending resources.

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| Risk of progression | <ul style="list-style-type: none"> ● NF-pNETs and small functioning NETs have a slow progression rate. ● High grade pNETs have rapid progression and poor survival. |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Individual - limited ● Systemic-limited – may not alter resource requirement significantly |
| Treatment options | <ul style="list-style-type: none"> ● NF-pNETs < 2cm can be safely observed in accordance with existing international guidelines <p>Well Differentiated - All phases</p> <ul style="list-style-type: none"> ● Some functional GI-NETs can be safely suppressed with medication (diazoxide for insulinoma, proton pump inhibition for gastrinoma, somatostatin analogues for all functional lesions) and this may be appropriate especially in high risk groups. <p>High grade non metastatic NET</p> <p>Phase 1 and Phase 2</p> <ul style="list-style-type: none"> ● Surgery should be considered for Grade 2 and 3 tumours that are not locally advanced. <p>Phase 2-3</p> <ul style="list-style-type: none"> ● Chemotherapy and palliation are options to consider |

Treatment of HPB conditions - acute biliary emergencies

Biliary colic

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| Risk of progression | <ul style="list-style-type: none"> ● Risk of progression with delay – low – 50% may not require operative intervention even with prolonged follow up¹¹ |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Individual - limited – small increase in perioperative risk with colic progressing to cholecystitis ● Systemic-limited – may not alter resource requirement significantly |
| Alternatives | <ul style="list-style-type: none"> ● Weigh acute cholecystectomy vs outpatient management with antispasmodics |

Recommendation

- *Simple biliary colic should be managed conservatively in the current environment*
- *Patients with crescendo or severe recurrent symptoms; or those with significant derangement of liver function tests or imaging suspicious for choledocholithiasis may be considered for urgent surgery*

Acute Cholecystitis

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| Risk of progression | <ul style="list-style-type: none"> ● Moderate – perforation / gangrenous GB, cholangitis |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Individual - moderate <ul style="list-style-type: none"> ○ Increased perioperative risk with cholecystitis progressing to complicated cholecystitis ● Increase hospital stay and readmission risk with patient and staff exposures |
| Alternatives | <ul style="list-style-type: none"> ● acute cholecystectomy remains standard of care ● delayed cholecystectomy is potentially suitable pending timing with pandemic peak ● home oral antibiotic may be required in setting of severe resource restriction¹² |

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| | <ul style="list-style-type: none"> percutaneous cholecystostomy is an appropriate delay strategy in select cases |
| COVID Risk (HCW) | <ul style="list-style-type: none"> Low risk |

Recommendations

- *Early acute cholecystectomy remains standard of care¹³*
- *Percutaneous cholecystostomy can be an effective temporising measure*
- *Outpatient antibiotic therapy is not recommended*

Choledocholithiasis (without cholangitis)

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| Risk of progression | <ul style="list-style-type: none"> Variable depending on symptoms, stone size etc |
| Consequence of disease progression | <ul style="list-style-type: none"> Individual - moderate pancreatitis, cholangitis Systemic - moderate May require prolonged admission, ICU admission depending on systemic response to sepsis/pancreatitis |
| Alternatives | <ul style="list-style-type: none"> Acute cholecystectomy with duct exploration and ERCP are both appropriate Single anaesthetic laparoscopic cholecystectomy with duct exploration may be preferable and convey reduced risk Acute surgical units should involve HPB specialists when possible to expedite patient care and facilitate single procedure options |
| COVID Risk (HCW) | <ul style="list-style-type: none"> Upper GI endoscopic procedures have high potential for aerosolisation |

Recommendations

- *Single staged operative gallstone management avoiding ERCP may be safest for patients and staff*

Investigation of HPB Conditions

Upper gastrointestinal endoscopy (including ERCP and EUS) are considered high risk, aerosol generating procedures in patients with confirmed or suspected COVID-19. GESA currently strongly recommends limiting endoscopy services to Emergency and Urgent cases only, and deferral of elective and semi-elective cases¹⁴.

Interventional upper gastrointestinal endoscopy/EUS- diagnostic

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| Risk of progression | <ul style="list-style-type: none"> ● Moderate |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Moderate/Severe |
| Individual | <ul style="list-style-type: none"> ● Cancer progression |
| Systemic | <ul style="list-style-type: none"> ● Risk of aligning cancer peak with pandemic peak |
| Alternatives | <ul style="list-style-type: none"> ● Resection/treatment without confirmed diagnosis may be considered in some cases ● Interventional radiology may be appropriate |
| COVID Risk (HCW) | <ul style="list-style-type: none"> ● Upper GI endoscopic procedures are AGPs ● Local anaesthetic based IR procedures have limited potential for aerosolisation |

Recommendation:

Where obtaining a diagnosis cannot be achieved with alternate means AND a tissue diagnosis will lead to significant alteration in clinical decision making, such procedures should be considered.

Interventional upper gastrointestinal endoscopy/ERCP/EUS - therapeutic

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| Risk of progression | <ul style="list-style-type: none"> ● High |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Moderate/Severe |
| Individual | <ul style="list-style-type: none"> ● Luminal obstruction +/- aspiration / Cholangitis |

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| | <ul style="list-style-type: none"> ● Potentially fatal |
| Systemic | <ul style="list-style-type: none"> ● High resource utilisation ● Critical care required |
| Alternatives | <ul style="list-style-type: none"> ● Surgical and percutaneous interventions may be available, but in general the side effect profile would favour endoscopic management |
| COVID Risk (HCW) | <ul style="list-style-type: none"> ● Upper GI endoscopic procedures are AGPs |

Recommendation:

- *Interventional upper gastrointestinal endoscopy and ERCP are likely to be performed for luminal obstruction or significant biliary sepsis, these procedures should be considered urgent/essential and not delayed*
- *In patients with non-pruritic jaundice secondary to advanced/metastatic malignancy discussion must be had regarding the utility of any intervention¹*
- *Interventional EUS for post-pancreatitis complications should be carefully considered and weighed against the option of non-aerosolising percutaneous measures*

Interventional radiological techniques - diagnostic and therapeutic

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| Risk of progression | <ul style="list-style-type: none"> ● Moderate |
| Consequence of disease progression | <ul style="list-style-type: none"> ● Moderate/Severe |
| Individual | <ul style="list-style-type: none"> ● Cancer progression/Cholangitis/Sepsis ● Potentially fatal |
| Systemic | <ul style="list-style-type: none"> ● Risk of aligning cancer peak with pandemic peak ● Risk of significant ICU resource utilisation |
| Alternatives | <ul style="list-style-type: none"> ● Resection/treatment without confirmed diagnosis may be considered in some cases |
| COVID Risk (HCW) | <ul style="list-style-type: none"> ● Local anaesthetic based IR procedures have limited potential for aerosolisation ● When general anaesthesia is required, local protocols should be observed |

Recommendation

- *Where obtaining a diagnosis cannot be achieved with alternate means AND a tissue diagnosis will lead to significant alteration in clinical decision making, such procedures should be considered*
- *Delay is likely to push the cancer diagnosis peak forwards and may result in cancer progression*

Laurence Webber, Mohammed Ballal and David Cavallucci for the ANZHPBA

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