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EXPERT FORUM

Incidental liver and pancreatic lesions: triage, diagnosis and referral

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About the speakers



Associate Professor Adam Bartlett

Associate Professor Adam Bartlett is an experienced general surgeon specialising in the comprehensive management of conditions affecting the liver, gallbladder, bile ducts, pancreas, stomach and spleen, including cancer. He collaborates with a multidisciplinary team and is skilled in different surgical approaches, including open, laparoscopic and robotic-assisted surgeries. Adam prioritises continuous learning and development, and brings a wealth of international expertise to his work. Adam continues to hold a position at the University of Auckland, and runs both a public and private practice. He is based in Auckland, but provides consultations and support in Queenstown, and engages in pro bono surgery in Rarotonga annually.



Mr Michael Chu

Mr Michael Chu is a highly trained general surgeon specialising in HPB (hepato-pancreato-biliary) and renal transplant surgery. With a deep commitment to his field, Mr Chu boasts a rich education background, including training in Australia and New Zealand. As the only surgeon in New Zealand with post-fellowship sub-specialisation training in both liver/pancreas/biliary surgery and renal transplant surgery, his surgical repertoire includes both open and laparoscopic (key-hole) procedures. Michael is noted for his meticulous approach to patient care, ensuring that all his patients receive comprehensive, tailored treatment plans. His multilingual abilities in English, Mandarin, and Cantonese, further allow him to connect and communicate effectively with a diverse patient demographic, embodying a patient-centric approach to healthcare. He also actively participates in teaching and is involved in various research projects – demonstrating a commitment to advancing surgical techniques and patient outcomes. He is based primarily in Auckland for his General and HPB work while regularly travelling to Wellington and Christchurch for renal transplant surgeries.

Abbreviations used in this review

AFP = alpha-feto protein
CA = cancer antigen
CEA = carcinoembryonic antigen
CT = computed tomography
ERCP = endoscopic retrograde cholangiopancreatography
EUS = endoscopic ultrasound
FDG PET-CT = fludeoxyglucose positron emission tomography with computed tomography
MRCP = magnetic resonance cholangiopancreatography
MRI = magnetic resonance imaging

This publication summarises a Goodfellow Unit webinar by general, liver and pancreatic surgeons - Associate Professor Adam Bartlett and Mr Michael Chu who spoke about incidental liver and pancreatic lesions. They discussed the different types of lesions commonly encountered in primary care, key factors in assessing such findings, including patient history, risk factors, and clinical presentation, and guidance on when to refer to a specialist for further evaluation. They also addressed the likelihood of malignancy.

The webinar and this review are sponsored by Allevia Hospitals, formerly MercyAscot.

The webinar is available from: <https://www.goodfellowunit.org/events-and-webinars/incidental-liver-and-pancreatic-lesions-triage-diagnosis-and-referral>

THE INCIDENTAL LIVER LESION

— Associate Professor Adam Bartlett

A/Prof. Bartlett explained that as a result of patients undergoing a lot more imaging than they have in the past, incidental liver lesions are being diagnosed with much greater frequency. It is important to understand which lesions should be further investigated and which ones can be ignored.¹ A/Prof. Bartlett presented the following case of a patient with an incidental liver lesion.

CASE REPORT:

A 35-year-old fit and well woman presented with one episode of mild right upper quadrant discomfort, but no other symptoms and no family history of note. She was taking the oral contraceptive pill. There were no significant findings on physical examination or blood tests. An ultrasound scan revealed a solid hyperechoic lesion in the liver (**Figure 1**). The lesion was solitary, well demarcated and heterogeneous.

What should you do?

1. Ignore it completely
2. Repeat the ultrasound in 6 months
3. Refer for biopsy of the liver lesion
- 4. Request further imaging – CT or MRI**
5. Refer to a hepato-pancreato-biliary (HPB) surgeon

A/Prof. Bartlett explained that at this stage, further imaging should be requested and that a contrast-enhanced CT would be the first imaging modality. In this case, CT findings suggested that the lesion was a hepatic adenoma (**Figure 2**).

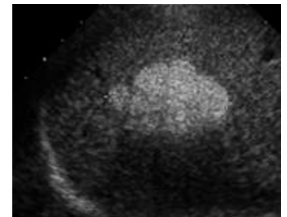


Figure 1. Solitary well demarcated solid heterogeneous liver mass seen on ultrasound imaging.



Figure 2. CT imaging showing a focal liver lesion likely in keeping with a hepatic adenoma.

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A/Prof. Bartlett explained that the focus of this discussion is on incidental liver lesions identified in imaging in asymptomatic patients. He emphasised that the overwhelming majority of these incidental lesions are benign but that the risk of the lesion being malignant increases with:

1. Age
2. Patients with a history of cancer, especially those tumours that have a high propensity to metastasise to the liver, such as colorectal, gastric or pancreatic cancer.
3. In patients with chronic liver disease.

It is important to acknowledge that the finding of any liver lesion is likely to cause a significant degree of patient anxiety.

Diagnostic approach

The first question in assessing an incidental liver lesion is to determine if it is solid or cystic.

Solid Liver lesions:

In evaluating the nature of an incidental solid liver lesion, one needs to determine whether the patient has cirrhosis or other risk factors for hepatocellular carcinoma (HCC), such as a history of chronic hepatitis B, hepatitis C, exposure to aflatoxins, haemochromatosis, or excessive alcohol consumption (**Figure 3**). A/Prof. Bartlett explained that patients with chronic liver disease or cirrhosis experience a repeated cycle of liver injury and repair, increasing their likelihood of developing liver cancer. He emphasised that when one finds a solid liver lesion in a patient with cirrhosis, it is hepatocellular carcinoma until proven otherwise.

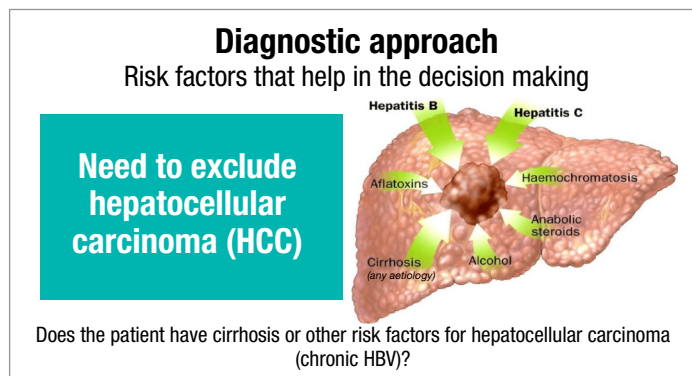


Figure 3. Risk factors for hepatocellular carcinoma.

A/Prof. Bartlett explained that hepatocellular carcinoma may be excluded by first undertaking blood tests to check liver enzyme profile and serum alpha-feto-protein (AFP); AFP is positive in 80% of patients with hepatocellular carcinoma. The next step is to perform a contrast-enhanced CT or MRI of the liver. **Figure 4** demonstrates the characteristic appearance of hepatocellular carcinoma on contrast imaging, with arterial phase enhancement and portal venous phase washout.

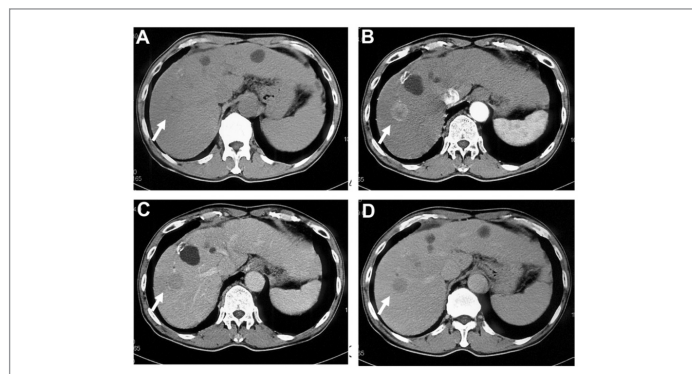


Figure 4. A hepatocellular carcinoma prior to contrast (A), with contrast in the arterial phase (B), in the venous phase with contrast starting to wash out (C), and in the delayed phase with washout (D).

A/Prof. Bartlett emphasised that metastatic liver cancer (secondary cancer to the liver) is far more common than primary liver cancer. The most common primary cancer found in those with a secondary liver metastasis is colorectal cancer, which predominantly spreads to the liver due to its venous drainage via the portal vein. Other types of cancer that may spread to the liver include skin melanoma, breast cancer, ovarian cancer, small cell lung cancer, gastric cancer and pancreatic cancer.

A/Prof. Bartlett explained that in a patient with a history of malignancy presenting with a liver lesion, the first thing is to check their tumour markers and undertake contrast-enhanced cross-sectional imaging (CT or MRI). He added that certain cancers can also be staged using FDG PET-CT. FDG is taken up by all cells in the body, but certain tumour cells lack the ability to excrete FDG, enabling localisation of the tumour as a focal area of uptake (**Figure 5**). This functional imaging can help confirm the diagnosis and extent of the cancer.

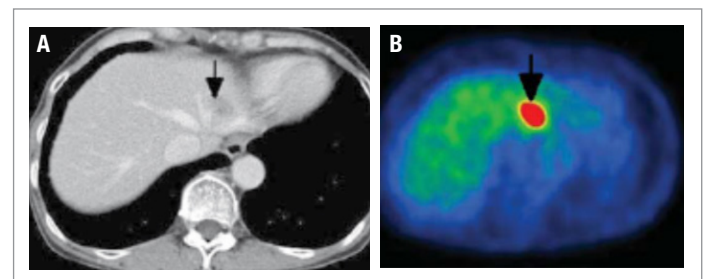


Figure 5. CT of the liver (A) and FDG PET-CT (B) showing uptake of FDG by the malignant liver mass.

Types of benign liver lesions

Benign liver lesions can be broadly classified as either solid or cystic.

Solid liver lesions

There are three common benign solid liver lesions: hepatic haemangioma; focal nodular hyperplasia (FNH); and hepatocellular adenoma. When a solid liver lesion is seen on ultrasound, blood tests investigating liver function should be undertaken. Depending on the certainty of ultrasound diagnosis, further imaging (CT or MRI) may be required.

Hepatic haemangioma is a benign liver lesion consisting of clusters of blood vessels lined by normal endothelial cells and fed by a hepatic artery. These lesions are an aberration of normal development within the liver. The reported incidence of hepatic haemangioma is 7%, but A/Prof. Bartlett believes they are more common, partly due to identification with improved imaging. Hepatic haemangioma are more common in females, with a ratio of 5:1 and the majority are <3 cm in diameter. On ultrasound they typically appear as a homogenous, hyperechoic well-defined solid mass. These lesions are rarely symptomatic, but may become symptomatic if they involve the liver capsule and cause capsular stretch.

A/Prof. Bartlett explained that the management of hepatic haemangioma primarily involves reassurance once other lesions have been excluded, and he stressed that no further imaging or investigations are necessary if typical features are seen on ultrasound, the lesion is <3 cm, the patient is female, and there are no other risk factors for malignancy. However, if there is uncertainty on the ultrasound then further contrast-enhanced imaging may be required, by either CT or MRI. Recently, contrast-enhanced ultrasound (CEUS) has become available which is very specific in confirming the diagnosis of hepatic haemangioma.

Focal nodular hyperplasia (FNH) is a benign liver lesion that is composed of a proliferation of hyperplastic hepatocytes surrounding a central stellate scar. These lesions are incidentally seen on ultrasound or CT in 0.2% and 1.6% of patients, respectively. Typically, FNH is a solitary lesion that is more commonly seen in women than in men. FNH does not require surveillance, except when it is atypical or >5 cm. According to A/Prof. Bartlett, the vast majority of FNH are very small and can be easily categorised.

Hepatocellular adenoma is an uncommon solid, benign liver lesion that develops in an otherwise normal-appearing liver. These lesions are typically solitary and found in young women that have been taking exogenous oestrogen in the form of the oral contraceptive pill or in patients that have used anabolic



steroids. Depending on the subtype, there may be a possible risk of malignant transformation or bleeding.

All adenomas require specialist follow-up and possible treatment. Blood tests, including AFP and liver function tests, should be undertaken along with contrast-enhanced ultrasound, CT or MRI, to confirm the diagnosis.

A/Prof. Bartlett explained that the treatment for hepatocellular adenoma in female patients is complex. Patients should avoid exogenous oestrogen. If the lesion is <5cm then one could consider either short-interval surveillance imaging or biopsy to define the subtype, which determines the risk to the patient. Long-term it is likely that the patient will require ongoing surveillance, or surgical resection. He added that a hepatic adenoma in a male always requires surgical resection.

Cystic liver lesions

A/Prof. Bartlett explained that cystic liver lesions are more common than solid liver lesions and are almost always benign. It is extremely rare for a cystic liver lesion to be malignant. Benign cystic liver lesions are categorised as simple hepatic cysts, polycystic liver disease, abscess, hydatid or hamartoma. He pointed out that ultrasound imaging is very good at characterising cystic structures because they contain fluid. While most cysts are simple cysts, complex cysts require additional imaging and multiple cysts are often difficult to follow with ultrasound. The more complex a cyst is, the more likely it may be associated with an underlying condition that requires surveillance or treatment.

A/Prof. Bartlett presented a useful algorithm for the management of patients presenting with incidental liver cysts on ultrasound (Figure 6). He explained that symptomatic liver cysts are rare, and their symptoms are often vague, including pressure from the cyst pushing on the liver capsule manifesting as a fullness, pressure under the ribcage or early satiety. He added that if the patient is asymptomatic, then irrespective of how big the cyst is, it can be left alone; however, if symptoms are present, then referral for consideration of treatment is appropriate. Historically, cysts were drained by percutaneous needle aspiration, but with this technique the cyst tends to return quickly. The treatment of choice is cyst fenestration, which is an operation usually performed laparoscopically, that involves removal of the cyst wall. This not only enables histological confirmation that the cyst is benign, but also is associated with a much lower incidence of recurrence.

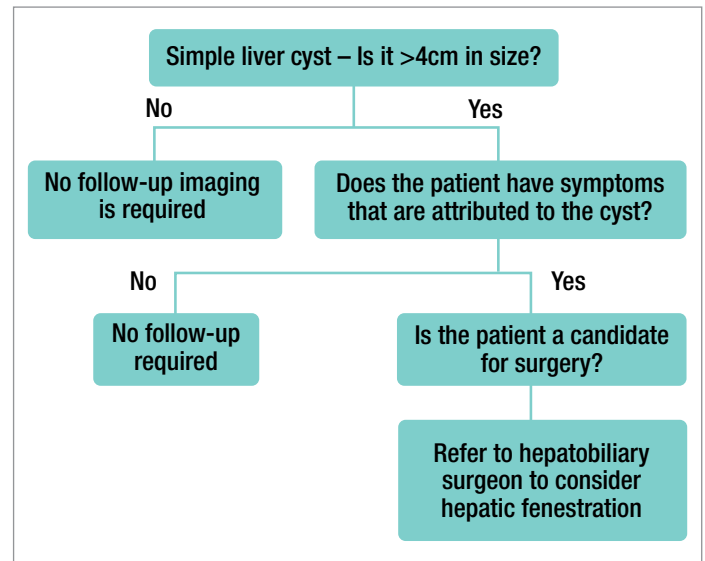


Figure 6. Algorithm for the management of patients presenting with ultrasound evidence of an incidental liver cyst.

The indeterminate liver lesion

A/Prof. Bartlett explained that with current modern-day imaging, the percentage of liver lesions that remain indeterminate is very low. The options for managing the indeterminate liver lesion are either surveillance (if the lesion does not change over time, then it is unlikely to be of concern), or biopsy to obtain histological confirmation. A/Prof Bartlett's preference is surveillance, and he typically reassesses the lesions at 6 months, and if there has been no change, increasing the interval to 12-monthly. He emphasised that the preferred approach will come down to a discussion with the patient about the perceived risk of malignancy, the patients other risk factors for malignancy, and the patient's level of comfort to just monitor the lesion. He added that liver biopsy is an invasive procedure, which is not always definitive and is to be avoided if possible.

TAKE-HOME MESSAGES:

- Liver lesions are commonly seen on imaging performed for an unrelated reason
- Management is primarily around evaluation of malignant risk and obtaining further imaging
- Cystic liver lesions are relatively common and are almost always benign
- Only a minority of solid lesions are malignant
- Biopsy of liver lesions is rarely required
- Uncharacterised liver lesions are increasingly rare, and often require ongoing surveillance.

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THE INCIDENTAL PANCREATIC LESION

— Mr Michael Chu

CASE REPORT:

A 50-year-old, fit and well male, presented with vague right upper quadrant discomfort and reduced appetite. He also reported passing dark urine and pale stools. There was no family history of note. On examination, he appeared jaundiced, but there were no other abnormal findings. His blood tests showed an elevated bilirubin level of 90, mildly deranged liver function and an INR of 1.4. His CA 19-9/CEA/CA125 tumour marker levels were all normal.

Mr Chu explained the next steps and types of investigations that one could undertake to diagnose the case above, but pointed out that not all of these tests are available in primary care. Initially, one should repeat the patient's bloods at 24-48 hours. Possible imaging studies include ultrasound scan (USS) of the upper abdomen, CT of the abdomen and pelvis, magnetic resonance cholangiopancreatography (MRCP)/MRI of the pancreas, endoscopic retrograde cholangiopancreatography (ERCP), or endoscopic ultrasound (EUS). The simplest and most cost-effective imaging would be a USS.

On ultrasound, sludge was evident in the patient's gallbladder, while the common bile duct was dilated at 13 mm and his pancreatic duct was dilated at 4 mm. Mr Chu pointed out that the pancreatic duct is not normally seen on ultrasound, but when it is seen, it is cause for concern. When both the common bile duct and the pancreatic duct are seen due to dilatation, it is referred to as the 'double duct sign'. The next imaging modality is ideally a MRCP/MRI of the pancreas, but this can be hard to achieve in primary care and usually the patient will end up having a CT pancreas and subsequently, an MRCP/MRI after referral.

On MRI, a mass was evident in the head of pancreas, along with dilated common bile duct and pancreatic duct. Mr Chu explained that this mass was considered likely to be malignant. Ideally this patient would undergo an urgent Whipple procedure (Figure 7) within 1-2 weeks, but this is not always possible.

Mr Chu explained that pancreatic incidentaloma seen on imaging studies for an unrelated reason are becoming increasingly common because so many scans are being performed and the quality of the scans have significantly improved over the years. He pointed out that pancreatic lesions vary widely in size, from small cysts to large solid invasive tumours.² Fortunately, the majority of these incidentaloma are benign. Mr Chu added that the risk of the lesion being malignant increases with age and subtype of pancreas lesions.

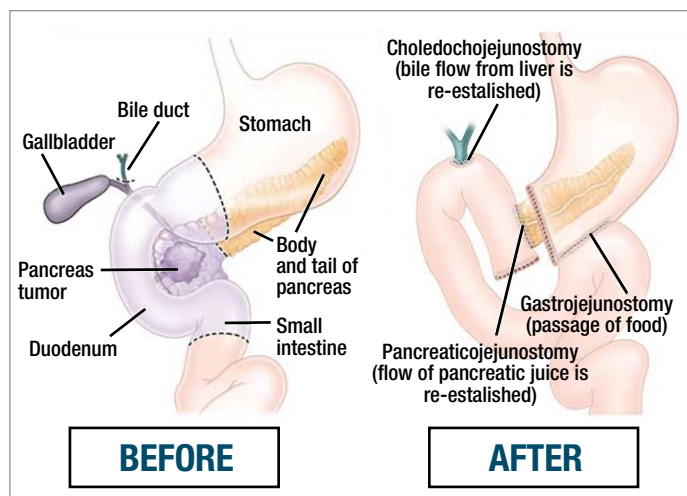


Figure 7. Whipple procedure for the treatment of head of pancreas cancer.

Risk factors for pancreatic cancer

Mr Chu explained that chronic inflammation of the pancreas due to chronic pancreatitis, family history of smoking, diabetes and obesity increases the risk of pancreatic cancer (Figure 8). Furthermore, African Americans and Ashkenazi Jews have been identified as a group at higher risk of pancreatic cancer.

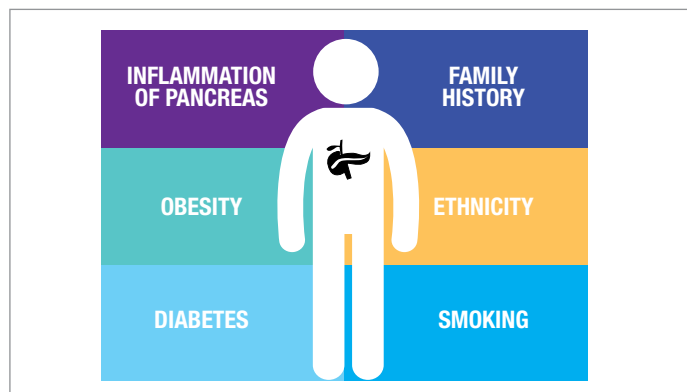


Figure 8. Risk factors for pancreatic cancer.

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Types of benign pancreatic lesions

Cystic pancreatic lesions

Cystic pancreatic lesions are fluid-filled structures and can be either mucinous or non-mucinous. Mucinous lesions are more common, and are further sub-typed into mucinous cystic neoplasms (MCN) or intraductal papillary mucinous neoplasms (IPMN). The most common type of non-mucinous lesion is a serous cystic neoplasm (SCN).

Worrisome features of cystic pancreatic lesions are: size >3 cm; dilatation of the main pancreatic duct (>5mm); presence of mural nodule; pancreatic atrophy distal to the lesion; elevated CA 19-9; and rapid growth of the lesion. Mr Chu stressed that CA 19-9 is not secreted in all patients with pancreatic cancer and therefore a normal CA 19-9 can be falsely reassuring.

MCN lesions in the pancreas are distinct lesions with an ovarian-like stroma. They occur infrequently, almost exclusively in females (20:1), and carry the potential for malignant transformation.

IPMN lesions are commonly found on imaging and exhibit varying degrees of risk. These lesions typically occur in the 5th to 7th decade of life and carry no difference in incidence between males and females. Malignant risk for IPMN depends on the morphologic type and whether the lesion involves the main pancreatic duct. IPMN are sub-divided into side-branch and main-duct IPMN. Side-branch IPMN are mostly benign, but should be monitored. Main-duct IPMN have malignant potential and should be treated if the patient is fit for major pancreatic surgery. Mr Chu pointed out that these lesions cause a lot of anxiety, including for surgeons, and surveillance is resource intensive with world-wide guidelines recommending imaging every 6 months and EUS every 12 months. Mr Chu emphasised that in New Zealand, such surveillance is not feasible. He believes scans undertaken every 12 to 24 months are appropriate for these types of lesions.

SCN lesions are generally benign. They occur most commonly in patients in their late 60's and can slowly grow to become very large. These lesions can be left alone unless they become symptomatic due to size.

Solid pancreatic lesions

Solid pancreatic lesions are the most concerning as they are more likely to be malignant. Solid pancreatic lesions are divided into pancreatic ductal adenocarcinoma (PDAC), pancreatic neuroendocrine tumours (PNET), and solid pseudopapillary neoplasm (SPN), which is a pre-malignant lesion.

SPN lesions are rare and predominantly occur in young females in the 2nd and 3rd decade of life. These lesions are thought to be pre-malignant with a good prognosis. They may be confused with neuroendocrine tumours.

PNET lesions are the second most common solid pancreatic tumours. Incidental PNET are characterised by size <2 cm with Grade 1 differentiation on biopsy. These tumours are further sub-typed into functioning and non-functioning tumours. Monitoring via repeat imaging is appropriate for non-functioning PNET <2 cm with low tumour activity (Ki-67 <2%).

PDAC lesions are the most common cause of solid pancreatic incidentaloma. These tumours carry a poor prognosis despite advancements in chemotherapy and surgery. Early diagnosis of these tumours is challenging. In Japan, 40% of asymptomatic PDAC are found to be at Stage III or IV, but their 5-year survival is 30.6%, which as Mr Chu points out is remarkable given that 10 years ago, the 5-year survival of pancreatic cancer was approximately 7% in the US and approximately 10% in Australia.³⁻⁵ The type of surgery for PDAC depends on the location of the lesion.

Mr Chu explained that solid pancreatic lesions are the main reason that pancreatic surgery is undertaken given their high malignancy potential and that definitive diagnosis can be very difficult, especially for small lesions.

Diagnosing pancreatic lesions

Common blood tests include liver function and CEA/CA 19-9. Mr Chu explained that contrast-enhanced CT or MRI are the scans of choice for pancreatic lesions. He added that the pancreas is not usually well visualised on ultrasound due to bowel gas. CT scans are excellent for assessing the relationship between the pancreatic lesion and the major blood vessels. Mr Chu explained that the majority of pancreatic lesions can be diagnosed from a CT scan. If the diagnosis is not clear from the CT scan, then an MRI will be necessary.

Mr Chu explained that pancreatic biopsies are very rarely performed and only undertaken in certain cases, such as (1) uncertainty on the type of pancreatic lesion, (2) to determine the type of cancer for the oncologists to provide the most appropriate form of chemotherapy prior to surgery, or (3) determine the most appropriate palliative treatment options. He added that laparoscopy is also rarely performed, undertaken usually if one is concerned about peritoneal disease, as this is hard to see on imaging. Mr Chu explained that two different endoscopic manoeuvres are undertaken for pancreatic lesions, the EUS (an ultrasound probe at the end of an endoscope) or ERCP.

EUS is used when the nature of the pancreatic mass is uncertain or if tissue biopsy is required. Mr Chu explained that there are only four indications for ERCP in pancreatic cancer: cholangitis, biliary drainage prior to chemotherapy, severe pruritus, and malabsorption. He added that ERCP is not often performed, due to the risk of pancreatitis.

Mr Chu presented a useful diagnostic flow chart for the diagnosis of pancreatic lesions (**Figure 9**).

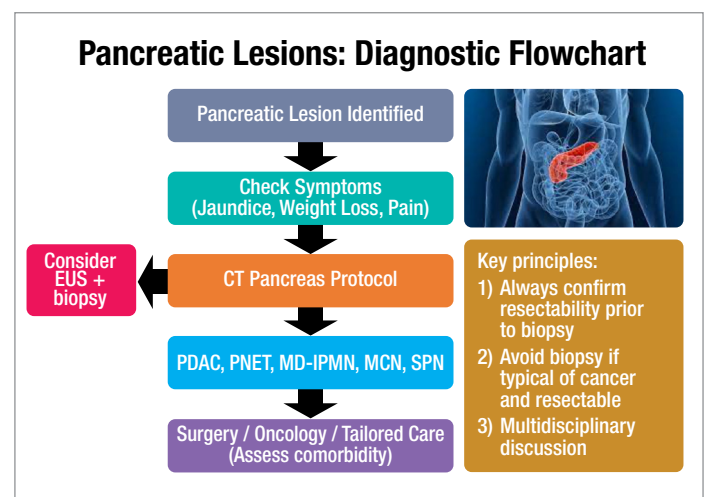


Figure 9. Diagnostic flow chart for the diagnosis of pancreatic lesions.

TAKE-HOME MESSAGES:

- Pancreatic lesions are becoming more commonly seen on imaging studies due to advancement in imaging
- Diagnosis is generally made on imaging alone with evaluation of malignant risk
- The majority of solid lesions are malignant
- Cystic pancreatic lesions can be divided into mucinous and non-mucinous
- Biopsy of pancreatic lesions is generally performed via EUS
- The management of pancreatic lesions hugely depends on patient fitness and co-morbidity.





QUESTIONS AND ANSWERS SESSION

Q. What is the most common age group for liver lesions?

A. Almost all of the benign liver lesions (e.g., hepatic haemangioma, benign cysts) are seen in younger age groups, as they are developmental. A solid liver lesion in an older person is a red flag. With stored digital images available back to the 1990s, there is an ability to check if a lesion may have been present on a previous scan and if it's been present for a number of years, it is unlikely to be malignant. Solid organs such as the pancreas and liver are ideally suited for imaging.

Q. Should tumour marker testing for pancreatic cancer be undertaken in primary care?

A. If there are no pancreatic lesions, then tumour marker testing should not be undertaken. Tumour marker testing is not a screening tool and it would not be expected that a patient presenting to primary care with symptoms of pancreatic cancer would have had such testing before referral. Some people with malignant lesions do not secrete CA 19-9. Therefore, a normal CA 19-9 level in a person with a pancreatic lesion does not rule out malignancy. Also, the CA 19-9 level may be elevated due to jaundice. The most useful place for tumour markers is in monitoring treatment.

Q. Is metabolic disease a risk factor for pancreatic cancer?

A. For both the liver and pancreas, repeated injury and repair can predispose a patient to malignant changes. Metabolic disease causes stress to the pancreas as it tries to secrete more insulin, and obesity is a risk factor for pancreatic cancer. Genetics probably plays a larger role in predisposition to injury to the pancreas. Furthermore, if a patient has chronic pancreatitis, they should have annual imaging and blood tests.

Q. How useful are liver function tests?

A. Liver function tests give an indication of the injury or what might be occurring, but they don't actually provide information about the function of the liver. If a lesion is present and the liver function test levels are elevated, it is more likely that it may be something sinister, but metastases may also present with normal liver function test.

Q. Should pancreatic biopsy be performed endoscopically or laparoscopically?

A. This is surgeon dependent, but endoscopic biopsy is preferable, as it is easier and provides a direct route to the pancreas.

EXPERTS' CONCLUDING REMARKS

Most incidental liver and pancreatic lesions are benign, and patients don't need to be referred. Radiology is becoming more definitive with regard to diagnosing these lesions. It is very easy to share any queries on imaging with the appropriate specialists for further advice. Lesions can be totally normal and benign and we need to avoid anxiety around their discovery where possible.

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