Provincial Health Services Authority

Cystic Fibrosis

STANDARDS OF CARE FOR BRITISH COLUMBIA

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CYSTIC FIBROSIS CARE BC
Provincial Health Services Authority

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7.2 Liver transplantation

Purpose

The intent of this document is to provide guidance for decision making related to liver transplantation in cystic fibrosis (CF) and is not intended to replace the knowledge and assessment of the skilled practitioner. Comprehensive recommendations and guidelines for referral and care of liver transplantation can be found in the BC Transplant ***Clinical Guidelines for Liver Transplantation***, with additional information found in the ***Cystic Fibrosis Foundation (CFF) Consensus Liver Transplantation Guidelines***.

Background

Cystic fibrosis is a multi-system disorder primarily affecting the lungs and digestive tract. 30 per cent of CF patients develop CF-related liver disease (CFLD) which can lead to progressive cirrhosis, portal hypertension and the need for liver transplantation[9].

Liver transplantation can offer significant benefits to those with severe CFLD. Fortunately, only about 3 to 7 per cent of those with evidence of CFLD go on to develop cirrhosis[10] and need for liver transplantation. Choosing the optimal time for liver transplantation remains a difficult problem but the trend has been to consider the option before severe liver decompensation develops. Evidence has demonstrated that survival post-liver transplantation is as good if not slightly better than after lung transplantation, and can result in weight gain and improvement in lung function.

Diagnosis of CFLD

CFLD may not be clinically apparent until pronounced pathological changes have occurred. In most cases, patients remain asymptomatic (without appearance of jaundice or pruritus) even when progressing to multilobular cirrhosis. There are two peak ages of presentation: the first around 10 years of age and the second in early adulthood.

Commonly, the diagnosis occurs when hepatomegaly is identified at routine physical examination, with or without the presence of abnormal liver biochemistry. The rate of progression of disease will vary by patient[2]. Most people with CF who are referred for liver transplantation have either progressive liver failure or intractable bleeding from esophageal or gastric varices.[1] Due to a lack of specific and sensitive tests to evaluate biliary cell function, early diagnosis of CFLD relies on clinical examination, biochemical testing and imaging.

Diagnostic criteria for CFLD

When considering if CFLD is present, at least two of the following variables should be present:

1. Abnormal physical examination (hepatomegaly and/or splenomegaly)
2. Increase of transaminases (AST and ALT) and GGT above upper normal limits at 3 consecutive samples over 12 months (excluding other causes)
3. Ultrasonographic evidence of liver involvement (steatosis, heterogenous parenchyma and surface nodularity of the liver and findings suggestive of portal hypertension (ascites, mesenteric edema, splenic enlargement).
4. Abnormal histology on liver biopsy.[2]

When to refer/referral process

Recommendations of when to refer can vary between individuals and providers;, however, literature has indicated that liver disease severity in CF can be masked until later stages of disease. It is therefore of paramount importance to be attuned to indicators of progressing disease and consider that the ***work up, referral process and wait time to transplantation can be lengthy – therefore erring on the early side of referral***. In circumstances where referral occurs at an early stage in the disease process, the transplant clinic can assess the patient, then continue ongoing monitoring in conjunction with the supporting clinic.

Liver function scoring is commonly used for determining severity of disease and to guide transplant referral. Frequently used severity scoring systems in hepatology include the MELD-Na+ and Child-Pugh scores (see details below). These tools can underestimate liver disease severity in CFLD due to focal biliary cirrhosis, which can cause complications of portal hypertension prior to the development of end-stage cirrhosis and alterations in liver synthetic function. Therefore, CF-specific considerations should also guide referral.

MELD-Na^+ Score

MELD-Na^+ scoring is used in Patients >12 years of age to estimate the chance of survival of their disease over the next three months. It is based on results of four laboratory tests, which together, help to indicate how well the body is functioning. These tests include INR, Creatinine, Bilirubin, Serum Sodium[4], with a scoring range from 6 to 40, a higher number indicating more severe disease.

MELD-Na^+ scoring can remain low, then quickly increase. It is generally recommended that liver transplant referral should occur with any score that is equal to or greater than 14.[5]

CHILD -Pugh Scoring

CHILD – Pugh has been one of the most widely applied scoring systems for liver disease.[6] The five clinical scoring measurements include total bilirubin, serum albumin, prothrombin time, ascites and hepatic encephalopathy.

It is recommended that referral should occur when scoring is greater than or equal to 8.[3]

PELD Score

Pediatric End-Stage Liver Disease (PELD), is a numeric scale for transplant candidates younger than 12. It was developed as an objective method of prioritization, while accounting for children's growth and development needs.[11] It may range higher or lower than MELD. In most instances, given the natural history of CFLD, children under 12 would not be referred for transplant and is therefore not commonly used.

Due to the stealthy nature of CFLD progression and the fact that MELD-Na^+ and Child-Pugh scoring systems are primarily focused on liver synthetic function, which tends to only worsen with very advanced CFLD, it is also important to consider additional indicators in conjunction with the MELD-Na^+ or CHILD-Pugh scores, especially in cases where the typical threshold for referral is not met. These indicators include:

- Patients with moderate or severe ascites, particularly those with intractable or diuretic resistant ascites
- Variceal bleeding
- Hepatocellular carcinoma (within Milan criteria)
- Cholangiocarcinoma (selected cases with low tumour burden)
- Hepatic encephalopathy [1,3]

Additional CF considerations

In addition to the previous factors, the supplemental indicators that should be reviewed include:

- Growth failure as a result of liver disease
- FEV1 <70 per cent or evidence of FEV1 declining of >5 per cent per year[7]

Preserved lung function is also a requirement for liver transplantation, and needs to be a factor within the process, although there is no consensus minimum lung function threshold. Referral should be initiated at an early stage when declining lung function is present in association with liver disease, regardless if strict criteria has been met. In cases of moderate to severe lung disease, a lung transplant assessment might also be warranted. Whenever possible, the goals include avoiding liver and lung transplants at the same time.

In all cases, communication between the cystic fibrosis team, the transplant team, and the hepatologist remain paramount in the process. Regular and ongoing discussions with patient-focused care will ensure any gaps are bridged or concerns managed. Mechanisms to achieve this will vary depending on the situation, but responsibility falls to all participants to ensure communication and patient centred care is maintained.

Who can refer

Referral to the outpatient liver transplant program must be from a specialist, such as hepatologist, surgeon, internal medicine specialist, or gastroenterologist. Referral from family doctors are generally not accepted[3].

In most cases, the hepatologist will make the referral for assessment to the transplant clinic. However, in some circumstances, the CF clinic may refer to minimise lag time. In these cases, the hepatologist will need to remain involved and communication between the three groups remain strong.

Most importantly, for reasons outlined in the when to refer section, referral should NOT be delayed for sake of specific party inclusion, or for discipline-specific concerns. Delaying the process can negatively impact patient outcomes, and should be avoided whenever possible.

Where to refer

All adult liver transplant assessments are co-ordinated through the Liver Transplant Clinic at Vancouver General Hospital (VGH). The referral, assessment, and waiting list processes are similar to those described for lung transplant (section 7.1), and can also be found in the BC Transplant Clinical Guidelines for Liver Transplantation. Surgery is also completed at VGH.

Liver transplant for the pediatric age group is currently referred out of province to Alberta's Transplant program. This is facilitated through a similar process as the out-of-province referrals for lung transplant (section 7.1).

Pre-transplant assessment

Assessment for transplant is conducted by the BC liver transplant team. It commonly involves multiple visits, and some may be conducted virtually. The majority of the testing can be completed in the patient's home community.

The assessment process includes careful evaluation for both medical and psychological suitability and may include review by those with expertise in respirology, nursing, psychology, transplant surgery, pharmacology, social work, nutrition, anesthesiology and physiotherapy. All immunizations should be up to date. Once all of the evaluations have been completed, each case is discussed at a multidisciplinary conference to determine the appropriate option.[3]

In situations when a liver transplant is needed urgently and there is insufficient time for the social worker, dietitian, and/or physiotherapist to complete their assessments, further history and collateral information should be sought from the corresponding allied health member of the CF team.

Transplantation timing

Transplantation suitability and timing remains at the discretion of the transplantation team. Transplantation occurs when BC Liver Transplant deems appropriate for the patient, and a suitable organ is available.[3]

Post-transplant complications

While there are many potential post-transplant complications, the most important are related to infections due to the medications needed to suppress the immune system and prevent rejection of the transplanted organs.

As part of the assessment process, the BC Liver Transplant team reviews in detail the post-transplant treatment regimen as well as surgical and other potential complications. This is augmented with post-transplant support from the CF team[3].

Defining care team roles

Throughout the process, it remains important to understand the roles and responsibilities of each of the participants. This will help to manage expectations and assist in defining responsibilities. It is essential to consider that, in some circumstances, the outlined parameters are not hard lines, but may flow between parties to ensure safe and efficient care.

1. CF care team

Once the patient has been referred and received a consultation with the BC Liver Transplant team, they are then supported by their referring specialist or general practitioner. For CF patients, this care generally falls to their CF team, who work to arrange investigations and testing as required, along with supporting the patient in their daily care. The CF team should also regularly communicate changes in patient status to BC Liver Transplant.[5]

2. BC Liver Transplant

BC Liver Transplant team receives the patient referral and assesses for suitability. When required, it preforms transplant and conducts follow-up care. Once the liver transplant has been completed and the patient has stabilized, they will return to their home community with follow-up from both the Liver Transplant Clinic and their CF team.

3. Gastroenterologist/hepatologist

This physician works in a consultation role, and in most instances makes the referral to transplantation. Ongoing communication from all parties should include the gastroenterologist/hepatologist. It is important to note that the patient's location in the province will likely affect if the patient is followed by a hepatologist or gastroenterologist.

4. Patient

Patients should work to remain in the best health possible and work to follow care plans as determined in conjunction with their BC transplant gastroenterologist and CF clinic. Any concerns or issues should be expressed to any of the parties and be addressed as readily as possible.

Conclusion

As outlined in this document, timing of referral as well as liver transplantation remains a challenging decision. In general, is it recommended that practitioners aim for early referral and reduction of delays to ensure the best possible outcomes for the patient. It is also paramount that all participants employ open and regular communication to minimize any barriers that may impede the process. Focusing on these factors will allow for the best outcomes for CFLD patients during the transplant process.

References

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