

Ontario's Adult Referral and Listing Criteria for Liver Transplantation

PATIENT REFERRAL CRITERIA

The patient referral criteria are criteria which a Health Care Provider would utilize to refer a patient to a transplant centre for assessment. The criteria identified below are the currently agreed upon conditions for which a patient should be considered for referral for liver transplant assessment.

- 1) **Chronic Liver Disease:** Referral for adult liver transplantation should be considered for patients with decompensated chronic liver disease. Such patients generally have one or more of the following:
 - End-stage of chronic liver disease with hepatic decompensation
 - Ascites or complications thereof such as hepatic hydrothorax and (resolved) spontaneous bacterial peritonitis, jaundice, coagulopathy, hepatic encephalopathy or portal hypertensive GI bleed. These patients will typically have a Model of End-stage Liver Disease score (MELD 3.0) of greater than or equal to 11
 - Other complications of end-stage liver disease or portal hypertension such as:
 - Hepatopulmonary syndrome (HPS)
 - Hepatocellular carcinoma (HCC)
 - Portopulmonary Hypertension (PoPH)
- 2) Fulminant Hepatic Failure
- 3) **Metabolic Disorders:** Referral for adult liver transplantation may also be considered for patients with metabolic disorders of hepatic origin. This may include conditions such as hereditary transthyretin amyloidosis, hyperoxaluria type I and others.
- 4) **Selected Malignancies:** Referral for adult liver transplantation may also be considered for patients with selected malignancies listed below.
 - Colorectal Liver Metastases (CRLM), please see the Patient Listing Indications for further information.
 - Selected neuroendocrine liver tumours
- 5) **Alcohol Associated Liver Disease (ALD):** Referral for adult liver transplantation may also be considered for patients with ALD. Please see the Patient Listing Indications for further information on this condition.

Early referral is essential to allow the patient to be evaluated and to survive (in a condition that still allows major surgery) until a suitable organ becomes available.

PATIENT LISTING INDICATIONS

Each patient is assessed individually for suitability for liver transplantation by one of the two provincial liver transplant programs (London or Toronto). The criteria identified below are the currently agreed upon general and specific conditions for which a patient may be eligible to be waitlisted for liver transplantation in Ontario.

1) General: Listing for liver transplantation may be considered for patients if the following requirements are met:

- Therapeutic options, other than liver transplantation, have been exhausted;
- Absence of obvious contraindication for transplant; and,
- Expected 5-year survival \geq 60% (co-morbidity, compliance).

2) End-Stage Chronic Liver Disease: Listing for liver transplantation may be considered for patients with decompensated cirrhosis with a MELD 3.0 score of greater or equal to 15. Patients with MELD 3.0 scores less than 15 may be considered only with the presence of factor(s) indicating poor prognosis that is/are not adequately captured by their MELD 3.0 score (e.g. recurrent cholangitis, refractory ascites).

*MELD 3.0 is a scoring system for assessing the severity of chronic liver disease; the higher the score, the more severe the liver disease and the lower the patient's 90-day survival without a liver transplant.

3) Hepatocellular Carcinoma (HCC): Patients with hepatocellular carcinoma, including those that are downstaged, may be considered for liver transplantation. However, they must be carefully selected to minimize the chance of recurrence after surgery. Of note, exception points for allocation purposes will be granted only if the HCC meets the following criteria: one HCC nodule greater than or equal to 2cm, or multiple HCC nodules greater than or equal to 1cm, or one HCC nodule greater than 1cm and less than or equal to 2cm that cannot be treated by intent to cure other than liver transplantation, or any recurrent HCC nodule greater than or equal to 1cm. In addition to meeting one of the aforementioned criteria, patients must meet all of the following criteria to be granted exception points for allocation: Total Tumour Volume (TTV) less than or equal to 145cm³ and Alpha Fetoprotein (AFP) less than or equal to 1,000, diagnostic imaging for HCC (if imaging not diagnostic than a biopsy is required), no evidence of vascular invasion or extrahepatic spread, and no HCC mixed with predominance of cholangiocarcinoma features on histology.

- Candidates undergoing downstaging treatment will be eligible for exceptions points if the HCC falls within or below the minimum criteria 90 days post procedure. HCC patients not fulfilling the specified criteria (outlined above) do not receive exception points but can be actively listed as per their calculated MELD 3.0 score.

4) Alcohol-Associated Liver Disease (ALD): Patients with alcohol-associated liver disease may be considered for liver transplantation. These patients must be carefully assessed for higher risk of return to problematic alcohol use to help ensure optimal outcomes in addition to meeting standard transplant

listing and contraindication criteria. The transplant team should be guided in its assessment by the following criteria:

- a) The patient does not meet criteria for moderate to severe Alcohol Use Disorder (AUD) likely to result in a return to problematic drinking in the post-transplant period;
- b) The patient is willing to commit to abstinence from alcohol;
- c) The patient is willing to commit to AUD treatment pre/post-transplant when recommended by transplant psychosocial team;
- d) History of no more than one previously failed AUD treatment where failure is defined as a return to problem drinking that would meet criteria for AUD;
- e) Absence of comorbid active substance use disorder, excluding cannabis use ;
- f) Absence of untreated and refractory severe psychiatric co-morbidity (including personality disorder) likely to interfere with treatment adherence;
- g) Other than in relation to alcohol use, no history of recurrent problems with adherence to medical treatment and repeated inability to follow up with/unable to contact patient;
- h) The patient has a dedicated support person available to assist them throughout the process and stable housing.

In addition to the above, patients identified as having Chronic ALD should have the ability to engage in the ALD psychosocial assessment and demonstrate capacity to consent to protocol requirements. For those patients who are diagnosed as having Severe Alcoholic Hepatitis (SAH) they must meet the additional criterion as having SAH as their first liver-decompensating event leading to diagnosis of acute liver disease.

If an ALD patient does not meet the above criteria, they may be re-assessed when there is a change (including a change in their psycho-social profile) that in the transplant team's opinion would merit re-considering whether they meet the above criteria.

- 5) **Fulminant Hepatic Failure:** Patients with fulminant hepatic failure may be considered for liver transplantation if they meet the Kings College Criteria or other validated criteria and have no contraindication (see *Patient Listing Contraindications* below) for transplant. Conditions that may result in fulminant hepatic failure requiring transplantation include both acetaminophen and non-acetaminophen induced liver injury.
- 6) **Metabolic Diseases:** Liver transplantation may be offered as therapy for patients with certain metabolic diseases of hepatic origin (e.g. hereditary transthyretin amyloidosis, Maple Syrup Urine Disease, hyperoxaluria type I, etc.).
- 7) **Re-Transplantation Due to Failed Primary Graft or Hepatic Artery Thrombosis:** Patients who received a previous liver transplant which has failed may be considered for re-transplantation. Such conditions leading to re-transplantation include:
 - Non-function of primary graft within 7 days of transplant, and includes the following lab parameters*:
 - Aspartate aminotransferase $\geq 3,000$

- INR \geq 2.5
- Lactate \geq 4 mmol/L
- Arterial pH \leq 7.30
- Venous pH \leq 7.25
- Hepatic artery thrombosis within 24 hours to 7 days of transplant

** All lab value results reported for the required tests must be from the same blood draw taken 24 hours to 7 days after the initial transplant.*

8) Other Conditions: Selected patients with certain rare conditions may be considered for liver transplantation. Such conditions may include:

- Selected cholangiocarcinoma (within the Mayo Clinic protocol)
- Selected neuroendocrine liver tumours
- Selected unresectable colorectal liver metastases (CRLM) may be considered pending review and approval by the CRLM Patient Review Committee (see Colorectal Liver Metastases Transplant Exception Application Form for criteria considerations)
- Fibrolamellar HCCs
- Selected hepatoblastomas
- Hepatopulmonary syndrome with PaO₂ <60 mmHg
- Hepatorenal syndrome may be considered for combined liver-kidney transplantation
- Portopulmonary hypertension with mean pulmonary arterial pressure (MPAP) <35 mmHg and portal vascular resistance <5 Wood units or MPAP between 35 to 45 mmHg and portal vascular resistance <3 Wood units.

PATIENT LISTING CONTRAINDICATIONS

The contraindications for liver transplantation identified below are the currently agreed upon conditions in which the presence of one or more may result in the patient not being eligible to be waitlisted for liver transplantation in Ontario.

- 1) Co-Morbidities:** Patients with any co-morbidity that decreases the likelihood of surviving 5 years post- transplant to below 60% or for whom the peri-operative risk is deemed unacceptably high are not candidates for liver transplantation.
- 2) Nutritional State:** For a patient with a calculated body mass index (BMI) [estimated dry weight (kg) divided by height (cm)] that exceeds 45 kg/m², liver transplantation is a relative contraindication due to excessive morbidity and potential excess mortality. For patients with a BMI > 45 kg/m², liver transplantation may still be considered pending a medical evaluation.

For a patient with a body mass index (BMI) < 18.5 kg/m², liver transplantation is a relative contraindication, and aggressive nutritional support should be implemented. Transplant programs may consider a patient's frailty when assessing their suitability for listing.

- 3) Infections:** Patients are not candidates for liver transplantation if they display the following:
- Active or uncontrolled extrahepatic infection (including sepsis)
 - Uncontrolled HIV infection (i.e. detectable viral load and/or CD4 count <100) or AIDS.
- 4) Malignancy:** Patients with extrahepatic malignancy are not candidates for liver transplantation. In general, patients must be cancer free for at least 2 – 5 years after curative therapy, depending on the cancer type. This may be assessed on an individual patient basis depending on the type and stage of the tumour.
- 5) Vascular Abnormalities:** Patients who display any of the following are not candidates for liver transplantation:
- Extensive thrombosis of the portal vein, superior mesenteric vein and splenic vein, or other extensive vascular anomalies or pathologies precluding sufficient revascularization of the graft. These patients may be considered for multivisceral transplant.
 - A mean pulmonary arterial pressure >45 mmHg despite vasomodulator treatment is an absolute contraindication in patients with portopulmonary hypertension.
- 6) Psychosocial Considerations:** Patients who display any of the following are not candidates for liver transplantation:
- Unstable psychiatric disorder, especially one likely to interfere with compliance;
 - Ongoing or current illicit drug misuse;
 - Previous documentation or current unwillingness or inability to follow the advice of health professionals;
 - Social support/compliance issues prohibiting adherence to post-operative medications and/or follow-up care.
- 7) Tobacco Use:** Tobacco use is a relative contraindication. Patients that use tobacco may still be eligible for liver transplantation pending a medical evaluation and with full informed consent regarding their increased risk. However, smoking cessation should be strongly encouraged before liver transplantation.

Version Control

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