



Liver transplantation for alcohol-related liver disease in the UK: revised UK Liver Advisory Group recommendations for referral

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Liver disease, of which liver cirrhosis is the most advanced stage, constitutes the fourth most common cause of life-years lost in men and women younger than 75 years in England, where mortality rates from liver disease have increased by 25% in the past decade. Alcohol consumption is the most common modifiable risk factor for disease progression in these individuals, but within the UK, there is substantial variation in the distribution, prevalence, and outcome of alcohol-related liver disease, and no equity of access to tertiary transplantation services. These revised recommendations were agreed by an expert panel convened by the UK Liver Advisory Group, with the purpose of providing consensus on referral for transplant assessment in patients with alcohol-related disease, and clarifying the terminology and definitions of alcohol use in liver injury. By standardising clinical management in these patients, it is hoped that there will be an improvement in the quality of care and better access to liver transplant assessment for patients with alcohol-related liver disease in the UK.

Introduction

Liver disease is the fourth most common cause of life-years lost in individuals under the age of 75 years in England.^{1,2} Alcohol-related cirrhosis is the most frequent cause of liver failure in the UK and a reduction in rates of harmful drinking presents a key target to improve the nation's health.³ Rates of alcohol-specific hospital admission vary by up to seven times across England, with a disproportionate number of cases in deprived regions of the country.⁴ The UK underperforms in the management of chronic liver disease when compared with other European countries,^{5,6} with high levels of liver-related morbidity and alcohol-related disease. The rising incidence of obesity and other risk factors for liver injury (eg, diabetes) suggest that deaths from cirrhosis will be unacceptably high in the UK unless effective public health interventions are used.⁷

Liver transplantation for alcohol-related liver disease is a successful treatment option in carefully selected patients with end-stage cirrhosis,⁸ and the existing recommendations for identifying suitable transplant candidates were first agreed in 2005.⁹ These new recommendations are an update to the original UK Liver Advisory Group advice published in 2005, and define the UK position on referral of patients with alcohol-related liver disease for liver transplantation.

Background and methods

A multidisciplinary working group representing liver transplant centres in the UK was commissioned in early 2018 by the UK Liver Advisory Group on behalf of the UK National Health Service Blood and Transplant (NHSBT) to review the evidence used for selecting suitable patients with alcohol-related liver disease for liver transplantation. Individuals with expertise in addiction psychiatry, transplant nursing, and liver disease were invited to convene a writing group representing the seven UK

transplant centres and included representation from the British Liver Trust charity.

This multidisciplinary working group, chaired by AH, convened a series of consensus meetings at the University of Birmingham, UK, and produced draft recommendations that were agreed by the UK Liver Advisory Group. The working group reviewed the existing recommendations for referral and included guidance from the National Institute for Health and Care Excellence (NICE) and the National Confidential Enquiry into Patient Outcome and Death with the results of a detailed literature search before producing updated recommendations for referral, with the objective of increasing access to liver transplant services and improving outcomes for patients with alcohol-related liver diseases.⁹⁻¹²

The recommendations were approved by the UK Liver Advisory Group and components were presented at the British Liver Transplant Group annual meetings in 2018 and 2019. Further revisions were made in the light of comments made by the wider audience, including the Substance Misuse Specialists in Liver Transplant group; these were approved by UK Liver Advisory Group and the recommendations submitted for publication. These recommendations represent expert consensus opinion on behalf of the UK Liver Advisory Group and a summary of the key changes is provided in panel 1.

Assessing a patient with alcohol-related disease for liver transplantation

Different diagnostic systems define disorders relating to alcohol consumption, including alcohol use disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders-5, hazardous and harmful use, and alcohol dependence.^{13,14} These diagnostic terms are used in the UK and are preferable to what has traditionally been called alcoholism. Although the details and relative merits of

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Panel 1: What is new in the UK Liver Advisory Group recommendations

- The requirement for a patient to solely complete a defined period of alcohol abstinence before referral for liver transplantation has been superseded by multidisciplinary specialist evaluation of a patient's suitability for transplantation
- Clinicians should refer patients with alcohol-related liver disease to specialist addiction clinics in liver transplant centres or satellite units
- Patients who do not recover from alcohol-related liver disease despite 3 months of validated alcohol abstinence and optimal clinical management should be referred for transplant assessment, including patients who have been treated for alcohol-related hepatitis
- Multidisciplinary assessment of patients with alcohol-related liver disease should comprise an evaluation by experts in addiction psychiatry, nutritional therapy, and liver transplantation
- All patients should undergo detailed nutritional assessment before they are sent for transplant work up, but this process should not be allowed to delay referral

these diagnostic categories are beyond the scope of these recommendations, they are defined in the NICE guidance,¹⁰ and their application in the management of alcohol-related liver disease is reviewed extensively.^{15,16} In all cases, the pattern of alcohol consumption for patients with liver disease should be routinely assessed. This assessment should include a comprehensive history of the pattern of alcohol consumption, including duration and volume. In addition, consideration should be given to the use of screening tools such as the Alcohol Use Disorders Identification Test (AUDIT) to screen individuals with liver disease for alcohol use disorder or alcohol dependence.¹⁷ Individuals with alcohol use disorder have a high prevalence of psychiatric comorbidity, particularly anxiety and affective disorders, and other substance use disorders, and we recommend that they should be referred to specialist addiction or mental health treatment services, where available.^{18,19}

In individuals with alcohol use disorder, alcohol dependence, or in whom alcohol use has contributed to the development of liver disease, the objective of management is to establish and maintain alcohol abstinence. Indeed, alcohol abstinence is the foundation of management and a crucial goal in alcohol-related liver disease as abstinence improves clinical outcomes at all stages of alcohol-related liver disease.²⁰ The clinical endpoints should aim to achieve improved insight into drinking behaviour and trigger factors, and to teach assertive alcohol avoidance and skills to prevent relapse (ie, return to drinking alcohol). Assessment should consider which patients will need professional help to achieve these endpoints. In patients with alcohol-related

Panel 2: Assessing patients for a liver transplant

- Alcohol assessment should include biochemical testing and an assessment of the use of other drugs of addiction
- Patients with alcohol-related liver disease should be offered access to specialists in the treatment of alcohol use disorders and encouraged to engage with peer-support and mutual aid groups, such as Alcoholics Anonymous and Self-Management and Recovery Training; access to specialists in nutritional therapy is also important
- Refer patients with decompensated alcohol-related liver disease for consideration of liver transplantation if they still have decompensated liver disease after optimal management and 3 months' validated abstinence from alcohol, with evidence of engagement with local specialist addiction treatment services if appropriate, and they are otherwise suitable candidates for liver transplantation; or if a patient requests a second opinion they should be referred to a specialist addiction clinic in another transplant centre, where a multidisciplinary assessment of the individual's suitability for transplantation can be made

liver disease, or those in whom harmful alcohol use has contributed to their liver disease (alcohol-contributory liver disease), abstinence from alcohol must be established before referral for consideration of liver transplantation (panel 2).

Obtaining a comprehensive alcohol history is key to understanding the drivers for problematic alcohol use and assessing the likelihood that abstinence will be achieved and maintained. In many cases, alcohol plays a contributory part in the evolution of other liver diseases, such as hepatitis C, hepatocellular cancer, and non-alcohol steatohepatitis. If there is evidence of an alcohol use disorder (even if the influence of alcohol is thought to be subordinate to other liver pathology), the patient should be managed in the same way as individuals with alcohol-related liver disease. All patients referred for liver transplantation, irrespective of their underlying disease, should be assessed for signs of alcohol and substance use disorders due to the prevalence of alcohol use disorders across the full diagnostic spectrum,^{21,22} and this assessment should include identification of dependence on prescribed analgesics and sedatives. Transplant candidates with mild-to-moderate alcohol use disorder should undergo the same process of psychosocial evaluation as patients with a severe alcohol use disorder.

Patients with decompensated cirrhosis related to alcohol use should be assessed in specialist multidisciplinary liver clinics in which they can benefit from early evaluation in a multidisciplinary setting. Referrers should encourage engagement with specialist addiction treatment services located within their region. NICE has published guidelines for the specialist treatment of alcohol use disorder¹¹ and there is now a good evidence base for the benefits of engagement with specialist

services.²³ Engagement with specialist addiction treatment services might provide further corroborative evidence of abstinence from alcohol, demonstrates an individual's commitment to behavioural change, and ensures that the patient has received appropriate counselling and education.

Timing of referral for transplant assessment

Liver transplantation is a well established treatment for individuals with chronic liver disease, including alcohol-related liver disease, who have a likelihood of poor survival or impaired quality of life.^{24,25} Alcohol-related liver disease is now the leading indication for liver transplantation in the UK and USA,²⁶⁻²⁸ and one of the most frequent indications in Europe.²⁰ In the UK, the over-riding principles of liver transplantation are that the projected life expectancy for a patient after receiving a liver transplant must exceed their life expectancy without undergoing transplantation.^{24,25} Referral for liver transplantation should be considered when a patient with established alcohol-related liver disease develops any of the typical features of decompensation (eg, jaundice, ascites, variceal bleeding, or hepatic encephalopathy), which are not reversible with abstinence.²⁹ A UK Model for End-Stage Liver Disease (UKELD) score of 49 is the equipoise at which the predicted 1-year mortality without liver transplantation (9%) matches that after liver transplantation, and is therefore the threshold of minimum listing criteria for elective liver transplantation in those with irreversible decompensation in the UK.^{24,30}

We recommend that patients with decompensated alcohol-related liver disease should be referred to consider their suitability for liver transplantation if they still have evidence of decompensation after best management and 3 months abstinence from alcohol and are otherwise suitable candidates for liver transplantation in line with NICE guidance (panel 2).¹⁰ This period of evaluation will typically be based in an outpatient setting while the individual is receiving treatment for their liver disease. A patient's suitability for transplantation should be judged by the assessing team at the time of referral.

Although all patients with alcohol-contributory liver disease should have shown their capacity to maintain abstinence from alcohol at the time of referral, there is no defined period of abstinence that a patient must achieve before referral for assessment, and referral should not delay assessment if it would compromise a patient's outcome. As a rule, if there is no evidence of clinical improvement after 3 months of alcohol abstinence with intensive and ongoing therapeutic input from medical, alcohol, and dietetic services, it would be appropriate to refer the patient to a transplant centre. This referral is in line with NICE clinical guidelines¹⁰ which conclude, on the basis of clinical consensus and published data,³¹ that if there is to be any substantial improvement in liver function with abstinence from alcohol, it will usually be evident within 3 months. In cases in which further delay would

Panel 3: Recommendations for referral for liver transplantation in alcohol-associated liver disease

- Assessment for liver transplantation should be made in a specialist multidisciplinary clinic
- Contraindications to liver transplantation include active ongoing alcohol use, drinking alcohol while on the waiting list and during the period of transplant evaluation, and a history of repeated non-adherence to advice to abstain from alcohol
- Relative contraindications to liver transplantation:
 - Evidence of apparently deliberate poor adherence to medication or clinical care, including frequent missed medical appointments
 - Inadequate patient support or social network, which is likely to undermine the patient's ability to maintain abstinence and engage with treatment
 - Evidence of severe and enduring mental health problems that, in the opinion of the transplant team, will undermine the likelihood of a good clinical outcome and graft survival despite optimal psychiatric input
 - Two or more episodes or periods of alcohol relapse within 2 years, despite clinical advice to abstain and in the knowledge of harm
 - History of cross dependence (ie, stopping one substance of addiction but replacing it with another)
 - Refusal to engage in a smoking cessation programme before and after transplantation

compromise a patient's outcome, a favourable psychosocial evaluation of relapse risk can supersede the conventional 3-month observation period in exceptional cases, although patients must be abstinent at referral (panel 3).

Short periods of abstinence (usually ≤ 6 months) are thought to be associated with increased rates of postoperative relapse.³²⁻³⁵ Other studies did not find a correlation between length of abstinence and a return to drinking,³⁶⁻³⁸ and a structured interview by an addiction specialist during the pre-operative evaluation is likely to be more effective than time-based qualification.^{38,39} For these reasons, the 6-month rule (ie, at least 6 months of abstinence are required pre-transplantation) that many clinicians believe governs criteria for transplant assessment is of no practical use, as achieving abstinence through ill health with periods of hospitalisation is not a robust predictor of future abstinence from alcohol. For these reasons, an exact period of abstinence from alcohol is not required to qualify for transplant evaluation in the UK. Indeed, rather than a specified duration of abstinence, several other factors have shown an association with a return to drinking alcohol after liver transplantation (panel 4) albeit in heterogeneous, often retrospective analyses. The presence of these factors should be considered in referral and assessment.

We recommend that individuals being assessed for transplantation in which alcohol has contributed to their

Panel 4: Factors reported to influence risk of return to drinking alcohol after liver transplantation

- A longer duration of abstinence before liver transplantation predicts reduced rates of alcohol relapse^{32-35,40-44}
- The duration of abstinence before liver transplantation does not predict alcohol reinstatement^{36-38,45}
- Poor social support increases the likelihood of alcohol relapse^{32,33}
- A family history of alcohol use disorders increases the risk of alcohol relapse^{32,44,46}
- Alcohol dependence and withdrawal before liver transplantation increases the risk of alcohol reinstatement post-transplant^{41,44,47,48}
- Psychiatric comorbidities^{40,42,44,49,50} or personality disorder³⁷ make alcohol relapse more likely
- Co-existing substance use disorders⁴⁸ or smoking^{42,49} increase the likelihood of alcohol use after transplant
- Continued drinking despite the knowledge of harm and in the presence of complications of liver disease predicts an increased likelihood of alcohol use after transplant^{37,51}
- Non-compliance or non-attendance at clinic and non-concordance with medication schedule increases the likelihood of post-transplant complications^{37,49}
- Previous failed attempts at rehabilitation or specialist alcohol treatment denotes an increased likelihood of alcohol reinstatement after transplant^{37,48,51,52}
- The high-risk alcoholism relapse score (ie, duration of heavy drinking, usual number of daily drinks, and number of previous alcoholism inpatient treatments) predicts the likelihood of postoperative alcohol relapse^{40,44}
- Younger age increases the likelihood of post-transplant alcohol relapse^{41,47}
- Marriage^{42,52} or the presence of a supportive life partner³³ and young children³³ reduce the risk of alcohol relapse after transplantation

liver disease should undergo a psychosocial assessment to establish the likelihood of maintaining long-term abstinence after liver transplantation. This assessment should be undertaken by a suitably qualified alcohol or addictions specialist health-care professional. Every UK liver transplant centre has specialist input from a clinical nurse specialist in alcohol and substance misuse, or an addictions psychiatrist, constituting the Substance Misuse Specialists in Liver Transplant network, which is affiliated with the British Liver Transplant Group. Assessment should include careful attention to risk factors associated with prediction of return to drinking and should provide advice for the transplant team on monitoring, support, and follow-up arrangements to help prevent return to drinking. Given the high prevalence of psychiatric comorbidity among individuals with alcohol use disorder, further psychiatric evaluation could be required. Overall, a multidisciplinary approach evaluating not only medical suitability, but also psychosocial suitability, for liver transplantation is the key element in ensuring that good candidates for transplantation are not turned away and that individuals deemed to pose increased risk are offered the support that they need.

Discussions in which the clinician has explicitly recommended abstinence in patients with liver disease are important and should be carefully documented in clinic letters and notes. Repeated failure to follow clinical advice or continued drinking despite the knowledge of

harm is a negative prognostic factor for transplantation.^{37,49} Moreover, recommendations to merely moderate alcohol consumption in patients with alcohol liver disease are inadequate, although in some patients, complete abstinence might not be immediately achievable. In these individuals, alcohol dose reduction with the goal of abstinence is a realistic compromise and patients should be supported in their endeavours by referral to specialist services, even though this trajectory would preclude transplantation until alcohol abstinence is secured.

Few patients have their abstinence from alcohol validated biochemically by the time they are referred for assessment and only a minority are engaged with addiction services. Any failure of engagement is concerning, especially as ongoing treatment and support from specialist services is an important component in achieving good long-term outcomes after transplantation. With specific reference to liver transplantation, there is evidence to suggest that people who engage with alcohol treatment services have better outcomes than those who do not access treatment,^{53,54} and liver transplant centres in the UK should provide access to specialists who can evaluate patients for transplant assessment and listing. Peer recovery support services that offer mutual aid, such as Alcoholics Anonymous, are widely available and accessed. These services do not offer formal treatment but many find the support in achieving and maintaining abstinence helpful and they can facilitate and support engagement in treatment services.⁵⁵

Failure to engage with alcohol services at the point of referral for transplantation should not preclude assessment for transplantation. The variation in provision of alcohol services in the UK means that some patients are unable to access alcohol support services in their locality and this discrepancy should not be allowed to prejudice an individual's opportunity for assessment.

Although the use of an alcohol-abstinence agreement does not necessarily reduce the likelihood of an individual returning to drinking,⁵⁶ it enshrines an agreed code of behaviours between the transplant unit and the patient, and routine use of these documents is encouraged. All patients accessing care after receiving a transplant should be subject to regular enquiry about recent alcohol use (ie, drinking alcohol since their previous appointment) by members of the clinical team. Biochemical markers of alcohol consumption should be sent when appropriate and there should be consistency in practice at satellite and regional specialist clinics (panel 3). Ongoing monitoring is essential; alcohol use disorders have a relapsing and remitting course, and alcohol use is reported in up to 15–25% of patients on transplant waiting lists.^{57–59}

Early liver transplantation for alcohol-related hepatitis

Early liver transplantation has been shown to improve survival in carefully selected patients with severe alcohol-related hepatitis that is unresponsive to medical

management.⁶⁰ Since the initial study of early liver transplantation in severe alcohol-related hepatitis, several other centres have reported improved survival,^{61,62} with a multicentre US observational study reporting 3-year survival of 84%.⁶³ However, although the original study had a strict inclusion criterion of patients being non-responsive to corticosteroids (ie, a Lille score >0.45) to alcohol-related hepatitis in biopsy-proven alcohol-related hepatitis,⁶⁰ the larger US study cohort was more heterogeneous, with just over half of patients receiving steroids and 40% of patients having had evidence of cirrhosis with no steatohepatitis on the explant liver histology.⁶³

In the UK, the largest ever clinical trial (STOPAH) in alcohol-related hepatitis (n=1053) reported that 90-day mortality among patients with a Lille score of more than 0.45 was 43.6%,⁶⁴ which suggests that if the strict inclusion criteria for early liver transplantation were applied to UK patients, approximately half of the individuals who would have had a transplant for alcohol-related hepatitis would have survived without liver transplantation. Moreover, there has been a subjective relaxation of the original requirement for a strict unanimous favourable psychosocial evaluation, with reports suggesting that patient selection is now applied less stringently,^{61,63,65} and the consequences on longer-term outcomes are awaited. More generally, it has been suggested that early liver transplantation for alcohol-related hepatitis could lead to broader acceptance of alcohol-related liver disease for liver transplant, particularly in the USA.²⁸

The UK consensus is that, as yet, there are no sufficiently defined, robust, objective, and validated criteria to select individuals with severe alcohol-related hepatitis who might benefit most from early liver transplantation, while also ensuring optimal donor graft utility. Further studies are warranted and we anticipate that, as further data emerge, this recommendation will be reviewed. However, the position in the UK at present recommends that if liver insufficiency persists after 3 months of documented alcohol abstinence in individuals with an index presentation of severe alcohol-related hepatitis, consideration should be given to referral for liver transplantation if their psychosocial risk profile is favourable.

Preventing alcohol relapse after transplantation and improving outcomes

Clinical experience suggests that a liver allograft is more susceptible to alcohol injury than is the native liver. Liver transplant recipients who do not have evidence of alcohol-contributory liver disease or alcohol-related liver disease should have this clearly explained and be encouraged to observe strict alcohol moderation, with their alcohol usage evaluated on a regular basis at outpatient review. Intermittent alcohol use has been reported in up to 82% of general liver transplant

recipients, with heavy drinking recorded in 9% of patients transplanted for non-alcohol-related liver disease.²² This finding suggests that all patients should be carefully screened for alcohol use disorders, irrespective of their original cause of disease.

The likelihood of alcohol relapse after liver transplantation increases with time,⁶⁶ although an early return to heavy alcohol use is unusual. Usually, a return to regular alcohol consumption after liver transplantation for alcohol-related liver disease is insidious and occurs between 2 years and 5 years after surgery.^{37,66,67} This relapse can be hard to identify without specific questioning, and identification is heavily reliant on patient self-reporting, although there are occasions in which family members will voice concerns. The proportion of patients who return to regular alcohol consumption after liver transplantation is approximately 20%,^{37,67} although few patients die from recurrent alcohol-liver disease after transplantation.⁶⁶

The use of prescribed opiate replacement in patients with a history of drug use should not preclude transplantation, but these drugs must be prescribed in conjunction with appropriate engagement with specialist addiction treatment. Likewise, for patients receiving pharmacotherapy for alcohol relapse prevention (eg, acamprosate, baclofen, disulfiram, naltrexone) this should not preclude their consideration of suitability for liver transplantation. However, it should be stated that most of the drugs approved in the UK to treat alcohol use disorders¹¹ have not been specifically tested in individuals with advanced alcohol-related liver disease. In particular, clinical practice guidelines do not recommend the use of either disulfiram or naltrexone in patients with advanced alcohol-related liver disease but there is a small amount of data suggesting that acamprosate and baclofen might be useful. Further data, particularly regarding baclofen in alcohol-related liver disease, is likely to emerge.

If there is evidence of alcohol consumption by patients with alcohol-related liver disease while they are on the transplant waiting list, they should be removed from the list. If there are extenuating circumstances, a period of further intensive monitoring could permit re-assessment, assuming the individual has made the life changes necessary to reduce the risk of further alcohol use (panel 3).

Although a return to alcohol use has a minimal effect on outcome in the first 5 years after transplantation, there is a clear demarcation between survival at 10 years in transplant recipients who return to drinking and those who remain abstinent.^{45,68,69} The increase in mortality noted in these studies is not primarily related to alcohol-induced graft failure, but rather reflects an increased incidence of cardiovascular disease and solid organ malignancy (especially aerodigestive cancers). The incidence of solid organ and lymphoproliferative malignancy are already significantly increased in transplant recipients compared with patients who

have not received a transplant, and clinical outcomes (ie, poor response to chemotherapy and reduced survival) are usually worse in the patients who received a transplant. In addition, psychiatric morbidity is more common in patients who receive a transplant for alcohol-related liver disease, although a diagnosis of a mental illness is not a contraindication to transplantation.^{70,71}

The increased rates of cardiovascular disease and upper gastrointestinal and lung malignancy infer a symbiotic relationship with smoking, which is more prevalent in individuals with alcohol-related liver disease than in the general population. Active smoking at the time of transplant assessment is associated with increased all-cause mortality after transplantation, particularly from cardiovascular disease and sepsis,⁷² and other studies suggest that smoking withdrawal after liver transplantation might have a protective effect against the development of cancer.⁷³ Active smokers being assessed for liver transplantation must understand that they will be expected to engage with a smoking cessation programme before surgery and commit to stopping smoking after transplantation.

Monitoring patients for alcohol use

All patients undergoing assessment for liver transplantation should undergo urine testing for illegal and non-prescribed drug use at their first visit to the assessment clinic, or on admission to the ward. Alcohol use should be ascertained, and samples tested for blood alcohol or alcohol metabolites (when available) at the point of assessment.

Because alcohol use disorders follow a relapsing and remitting clinical course, ongoing monitoring for alcohol use is mandatory both before and after transplantation. It is important for patients to understand that abstinence will be biochemically verified as part of their routine management at the transplant centre and referring centre.

Routinely used blood tests (including γ -glutamyl transferase, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and mean corpuscular volume) are the most frequently used indirect biomarkers for the detection of alcohol consumption.⁷⁴ Although the pattern of biochemical disarray (eg, markedly elevated γ -glutamyl transferase, and AST values greater than ALT levels) can be suggestive of alcohol excess, they have a low sensitivity and specificity in advanced liver disease.^{75,76} Carbohydrate-deficient transferrin, an additional indirect biomarker of alcohol excess, is often used to detect concealed or under-reported alcohol consumption in a range of scenarios.⁷⁷ However, the use of carbohydrate-deficient transferrin has fallen out of favour in the context of liver transplantation due to a growing recognition that it is less reliable in patients with advanced liver disease than in individuals without liver disease,^{78–80} nor is it universally available.

By comparison, direct biomarkers of alcohol consumption, which detect the presence of alcohol or its

metabolites, have a much higher specificity and are therefore more reliable than indirect biomarkers, even in advanced liver disease. Established direct markers include blood alcohol concentration, breathalyser analysis (for exhaled alcohol), or detection of the alcohol conjugate ethyl glucuronide in urine or hair samples. Data for urinary ethyl glucuronide show a high sensitivity and specificity in its ability to reliably detect alcohol consumption before and after liver transplantation.^{59,81} Although ethyl glucuronide assays are used in some UK centres, they are not widely available. Emerging data for other biomarkers, including hair ethyl glucuronide,⁸² and other alcohol metabolites (eg ethylsulfate, fatty acid esters, and phosphatidylethanol)⁸³ in defining alcohol avoidance in potential liver transplant candidates could clarify their role and utility.

When used properly, random blood alcohol testing is a powerful tool for assessing adherence, which requires very little in the way of laboratory resources. Each transplant centre should seek consent from patients listed for alcohol-related liver disease to embark on this process and provide written guidance for general practitioners and local hospitals detailing how the testing is to be done, including timing and frequency. Patients should be made aware that repeated failure to attend testing when requested could be construed as a potential indicator of non-engagement and possible concealment. Biological confirmatory testing is particularly useful in circumstances in which hepatic encephalopathy can lead to an erroneous assumption that a patient has been drinking. Patients on the liver transplant waiting list typically require monthly review in the outpatient clinic to identify any further deterioration, nutritional assessment, blood sampling, and UKELD calculation. These blood tests will include indirect biomarkers of alcohol consumption in addition to blood alcohol testing, although random blood alcohol testing must be done less predictably, and at shorter notice, than routine clinic follow up will usually permit.

Conclusions

There are worrying variations in the provision of treatment services for alcohol use disorders and referral for transplantation assessment within the UK.^{4,26} Multidisciplinary pre-assessment and post-transplant monitoring are a prerequisite to prevent late onset alcohol relapse and the complications associated with a return to regular alcohol use in liver transplant recipients.

Patients considered eligible for liver transplantation should be assessed and followed up in specialised liver clinics, both at referring centres and within transplant units. These clinics should provide the clinical and support services necessary to manage the complex psychological and clinical comorbidities associated with these disorders.

Referral and transplant centres need to ensure that suitable candidates for liver transplantation are not overlooked and that they provide the support and

Search strategy and selection criteria

References for the recommendations were identified through searches on PubMed and Web of Science from Jan 1, 2000, to Oct 1, 2019, using the MeSH terms “alcoholic liver disease”, “liver transplantation,” and “alcohol relapse”. Articles were also identified through searches of the authors’ own files. Only papers published in English were reviewed. The final reference list was generated on the basis of relevance to the scope of these recommendations.

expertise that will allow high-risk individuals to compete effectively with other candidates for a liver transplant. The importance of timely referral cannot be overstated, and it is incumbent upon clinicians who treat patients with alcohol-associated liver disease to have a thorough understanding of these recommendations.

Contributors

AH chaired the UK Liver Advisory Group (LAG) advisory group on behalf of the UK LAG, led the writing group, and wrote and edited the manuscript. SM and ED wrote and edited the manuscript and were members of LAG. KA helped edit the document and prepare the manuscript for submission. HA, JAL, CP, LS, and KW were members of LAG and contributed to the writing and editing the final manuscript. AL is the previous chief executive of the British Liver Trust, and PH is the current chief executive of the British Liver Trust. AL contributed to the content of the recommendations. JO’G and DT commissioned the advisory group on behalf of LAG, and DT edited the final manuscript.

Declaration of interests

We declare no competing interests.

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