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Alcohol-Associated Liver Disease in Women: Clinical Considerations and Strategies to Improve Outcomes

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Abstract

Although alcohol-related liver disease (ALD) has traditionally been viewed as predominantly affecting men, its burden has increased substantially among women. This trend is particularly concerning because women may develop severe liver injury at lower levels of alcohol exposure, and some populations have shown a greater risk of subsequent disease progression. Women may also encounter stigma, caregiving responsibilities, financial constraints, psychiatric comorbidity, and interpersonal violence that complicate access to addiction treatment and transplant evaluation. Despite these differences, women remain underrepresented in ALD research, and clinical recommendations continue to rely largely on evidence derived from male populations. This narrative review examines why women require specific consideration across the spectrum of ALD. We synthesize current evidence on sex-related biological vulnerability, changing epidemiologic patterns, inequities in access to alcohol use disorder treatment, and disparities in transplant evaluation. We also discuss management strategies that may improve outcomes, including earlier recognition, integrated hepatology and addiction care, pharmacotherapy tailored to liver function and pregnancy considerations, nutritional and psychosocial support, and timely transplant referral. Finally, we highlight critical evidence gaps and priorities for women-centered research and clinical care.

Categories: Transplantation, Internal Medicine, Gastroenterology
Keywords: alcohol misuse, alcohol-related cirrhosis, liver transplant, steatohepatitis, substance use disorder (sud)

Introduction And Background

Alcohol-related liver disease (ALD) encompasses a spectrum of alcohol-related liver injury, ranging from steatosis to fibrosis and cirrhosis. In a US analysis of 436,814 ALD-related deaths between 1999 and 2022, Pan et al. [1] found that the age-adjusted mortality rate increased from 6.71 to 12.53 per 100,000 population, with particularly concerning increases among women and younger adults. Although men continue to account for more ALD-related deaths in absolute terms, these changing epidemiologic patterns indicate that women should be considered a priority population for prevention, early recognition, and treatment rather than a smaller subgroup to whom evidence derived predominantly from men is automatically applied.

Women may develop clinically important alcohol-related liver injury at lower levels of exposure than men, although susceptibility is influenced by drinking patterns and other clinical factors. In a systematic review and meta-analysis of 2,629,272 participants and 5,505 cases of cirrhosis, Roerecke et al. [2] identified a dose-dependent association between alcohol consumption and cirrhosis, with consistently higher relative risks among women than men at comparable levels of intake. In a population-based cohort of 3,340 adolescents and young adults with alcohol-associated hepatitis, Flemming et al. [3] reported that female sex was associated with a 47% higher risk of subsequent cirrhosis or hepatic decompensation among patients who were alive and without cirrhosis six months after the index episode. Ten-year liver-related mortality was 11.0% among women compared with 6.9% among men [2,3].

These findings highlight the need to determine how sex-related susceptibility and disparities in treatment access should inform clinical care. Although these differences are increasingly recognized, the extent to which available management strategies address the needs of women remains uncertain. This narrative review critically examines the evidence supporting strategies to improve outcomes in women with ALD and identifies areas requiring further investigation.

Review

Methods

A literature search was conducted in PubMed/MEDLINE, Embase, and the Cochrane Library with no publication-date restrictions. Different combinations of the keywords “alcohol-associated liver disease”, “alcohol-related liver disease”, “alcoholic liver disease”, “alcohol-associated hepatitis”, “alcohol use disorder”, “women”, “female”, “sex differences”, and “gender differences” were used with the Boolean operators “AND” and “OR.”

Eligible publications addressed biological susceptibility, pathogenesis, clinical management, treatment access, or outcomes relevant to women with ALD. Studies involving both sexes were included when they reported sex-related differences or informed management approaches applicable to women. Priority was given to clinical guidelines, systematic reviews, meta-analyses, randomized controlled trials, and large observational studies. Experimental studies were included when clinical evidence regarding biological mechanisms was limited.

Duplicate records, conference abstracts, commentaries, publications outside the review’s scope, and articles providing insufficient relevant information were excluded. Findings were synthesized narratively by clinical theme without new quantitative pooling. No formal risk-of-bias assessment was performed, but study limitations were considered in the narrative discussion.

Pathogenesis of ALD in women

The greater susceptibility of women to ALD likely reflects the combined effects of higher systemic alcohol exposure, oxidative hepatocellular injury, enhanced inflammatory signaling, gut-barrier dysfunction, and individual genetic susceptibility. In a prospective population study, women had a greater risk of ALD than men at comparable levels of alcohol consumption [4]. However, direct mechanistic studies in women remain limited, and much of the evidence explaining sex-related differences is derived from experimental models.

Ethanol Metabolism and Systemic Exposure

Ethanol is metabolized primarily by cytosolic alcohol dehydrogenase (ADH), with additional contributions from the microsomal ethanol-oxidizing system, principally cytochrome P450 2E1 (CYP2E1), and catalase. Acetaldehyde produced through these pathways is subsequently oxidized by mitochondrial aldehyde dehydrogenase, particularly ALDH2, to acetate [5]. Chronic alcohol exposure induces CYP2E1, increasing reactive oxygen species production and oxidative cellular injury (Figure *1*) [6].

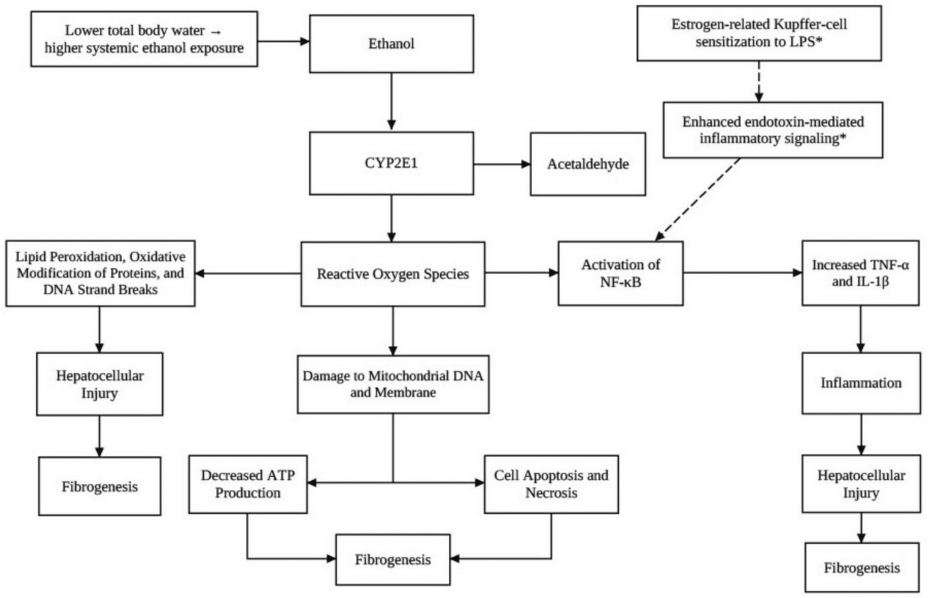


FIGURE 1: Cytochrome P450 2E1-mediated oxidative stress in alcohol-associated liver disease

*Predominantly experimental evidence; contribution to disease progression in women remains incompletely established

CYP2E1: cytochrome P450 2E1; NF-κB: nuclear factor kappa B; TNF-α: tumor necrosis factor α; IL-1β: interleukin 1β; LPS: lipopolysaccharide; ATP: adenosine triphosphate

Image credit: This is an original image created by the authors using yEd Graph Editor (yWorks GmbH, Tübingen, Germany)

Genetic variants in ADH and ALDH2 alter ethanol and acetaldehyde clearance and may modify susceptibility to liver injury [7]. Acetaldehyde also forms protein and DNA adducts, impairs mitochondrial function, and activates inflammatory and profibrotic pathways (Figure *2*).

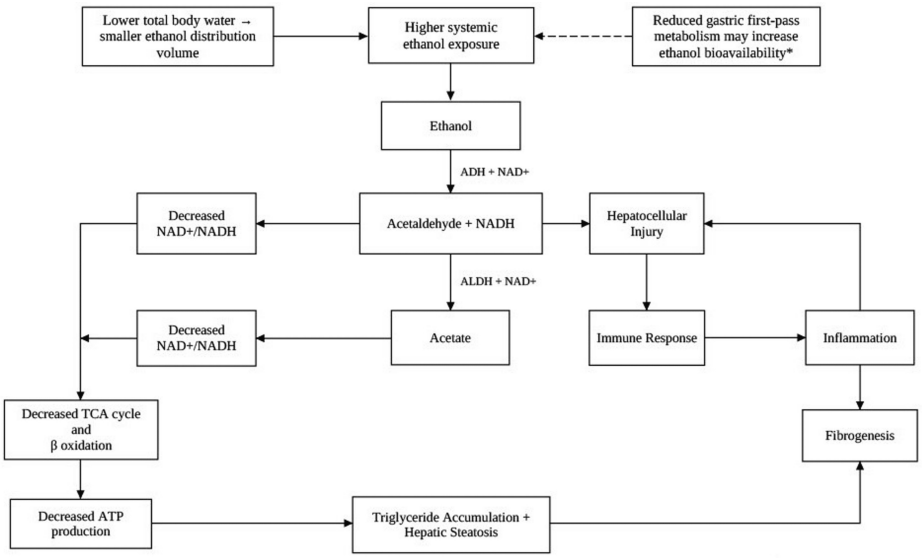


FIGURE 2: Acetaldehyde-induced hepatocellular injury in alcohol-associated liver disease

*Proposed contributor; evidence for sex differences in first-pass metabolism is inconsistent

ADH: alcohol dehydrogenase; ALDH: aldehyde dehydrogenase; NAD+: nicotinamide adenine dinucleotide; ATP: adenosine triphosphate; NADH: nicotinamide adenine dinucleotide plus hydrogen

Image credit: This is an original image created by the authors using yEd Graph Editor (yWorks GmbH, Tübingen, Germany)

Women generally have lower total body water than men, allowing an equivalent dose of alcohol to produce a higher blood alcohol concentration. Early pharmacokinetic studies also suggested that lower gastric ADH activity and reduced first-pass metabolism may increase ethanol bioavailability in women [8]. However, subsequent studies did not consistently confirm a clinically important sex difference in first-pass metabolism, suggesting that differences in body composition and alcohol distribution provide a more established explanation for greater systemic alcohol exposure among women [9]. Experimental models have also demonstrated more severe steatosis, inflammation, and hepatocellular injury in female animals than in males despite comparable ethanol exposure, indicating that pharmacokinetic differences alone do not fully explain female susceptibility [10].

Inflammation and the Gut-Liver Axis

Alcohol-induced hepatocyte injury promotes progression from steatosis to steatohepatitis through activation of inflammatory pathways. Injured hepatocytes activate Kupffer cells and recruit circulating immune cells, which release tumor necrosis factor α, interleukin 1β, interleukin 6, and interleukin 8, thereby promoting neutrophil recruitment and further hepatocellular injury [11]. Experimental evidence suggests that endotoxin-mediated inflammation may be more pronounced in females. Ethanol-fed female rats developed greater endotoxemia, Kupffer-cell activation, nuclear factor κB signaling, and tumor necrosis factor α expression than similarly exposed males [12]. Estrogen may contribute by increasing Kupffer-cell sensitivity to lipopolysaccharide. Experimental studies have shown that estrogen increases Kupffer-cell inflammatory responses, whereas ovariectomy attenuates alcohol-induced steatosis, endotoxemia, and hepatocyte necrosis [13,14]. These findings suggest that estrogen may amplify early endotoxin-mediated injury, although its contribution to disease progression in women has not been adequately established in human studies.

Disruption of the gut-liver axis further contributes to hepatic inflammation. Chronic alcohol exposure alters the intestinal microbiome, disrupts epithelial tight junctions, and increases intestinal permeability, allowing lipopolysaccharide and other microbial products to enter the portal circulation and activate hepatic inflammatory signaling [15].

Genetic Susceptibility and Fibrogenesis

Genetic factors also modify disease susceptibility. Variants in PNPLA3, TM6SF2, and MBOAT7 are associated with alcohol-related steatosis or cirrhosis, whereas alcohol exposure can produce persistent changes in DNA

methylation, histone modification, and microRNA expression [16,17]. Repeated hepatocyte injury ultimately activates hepatic stellate cells, resulting in pericellular fibrosis, bridging fibrosis, vascular remodeling, and cirrhosis [18].

The greater risk of advanced ALD among women therefore likely reflects the cumulative effects of higher systemic alcohol exposure, amplified inflammatory responses, metabolic and nutritional factors, and genetic susceptibility rather than a single female-specific pathway. These biological mechanisms provide a rationale for earlier recognition and intervention, although psychosocial and structural factors also substantially influence treatment access and clinical outcomes.

Sex-related susceptibility and barriers to treatment

In a prospective UK Biobank cohort of 365,966 participants, Fang et al. [19] found that each additional 70 g/week of alcohol intake was associated with a greater increase in ALD risk among women (hazard ratio (HR), 1.21; 95% CI, 1.19-1.23) than men (HR, 1.06; 95% CI, 1.06-1.06).

The need for a women-focused approach is not explained by biological susceptibility alone. Access to evidence-based AUD treatment remains low throughout the ALD population and may be particularly limited among women. Mellinger et al. [20] examined privately insured adults with alcohol-associated cirrhosis and found that only 10% received a face-to-face mental health or substance-use treatment visit and 0.8% received an approved relapse-prevention medication during the first year after cirrhosis diagnosis. Women were less likely than men to receive several forms of AUD treatment. Because all patients had private insurance, the observed disparity could not be attributed solely to lack of insurance coverage and may have reflected differences in referral, stigma, psychiatric comorbidity, caregiving responsibilities, or the organization of addiction services.

Assessment should identify factors that may interfere with treatment participation, including stigma, childcare and caregiving responsibilities, transportation difficulties, financial instability, depression, anxiety, trauma, and interpersonal violence. These barriers should inform coordination of liver, addiction, psychiatric, and reproductive care. Women-specific intervention studies in ALD remain limited; consequently, service adaptations such as childcare assistance, telehealth, flexible scheduling, and trauma-informed treatment should be considered important targets for prospective evaluation rather than interventions with definitively established survival benefits [20].

Focused identification and risk stratification

The diagnostic component of care should remain focused on decisions that influence treatment and prognosis. The 2024 American College of Gastroenterology (ACG) guideline recommends validated instruments such as the Alcohol Use Disorders Identification Test-Consumption or the full Alcohol Use Disorders Identification Test to identify unhealthy alcohol use [21]. Alcohol biomarkers, including phosphatidylethanol, may complement self-report when the results will influence clinical management, but they should not replace a nonjudgmental history addressing the quantity and frequency of alcohol use, binge-drinking patterns, recent escalation, previous withdrawal, prior treatment, and periods of abstinence [6].

Risk stratification should determine whether the patient has compensated cirrhosis, a history of decompensation, or any associated complications. For patients with severe alcohol-associated hepatitis, the Model for End-stage Liver Disease (MELD) score is recommended for initial prognostication, while the Lille score should be used to assess treatment response after corticosteroid initiation [21]. Pregnancy status and reproductive plans should also be established before medications with limited pregnancy safety data are prescribed. This focused evaluation allows clinicians to initiate AUD treatment, determine the urgency of transplant referral, and identify modifiable factors associated with poor outcomes without turning the review into an extensive discussion of differential diagnosis.

Alcohol abstinence and long-term treatment of alcohol use disorder

Sustained alcohol abstinence is the most important modifiable prognostic factor in established ALD. In a cohort of 100 patients with biopsy-confirmed alcohol-related cirrhosis, Verrill et al. [22] reported a seven-year survival of 72% among patients who were abstinent one month after diagnosis compared with 44% among those who continued drinking. More recently, Hofer et al. [23] evaluated patients with alcohol-related cirrhosis and clinically significant portal hypertension and found that abstinence was associated with lower risks of hepatic decompensation and mortality across all evaluated stages of portal hypertension, including high-risk disease. Although these studies were observational and residual confounding cannot be excluded, their consistent findings support abstinence as the central long-term therapeutic target. Abstinence should not, however, be used as a prerequisite for receiving treatment. AUD is a chronic relapsing disorder, and recurrence of alcohol use should prompt reassessment of craving, psychiatric symptoms, treatment adherence, medication effectiveness, and social stressors rather than termination of hepatology or transplant care.

Behavioral treatment may include motivational interviewing, cognitive behavioral therapy, relapse-prevention counseling, contingency management, and mutual-help programs [24]. The evidence for individual behavioral interventions in patients with advanced ALD is less extensive than in the general AUD population, making it reasonable to individualize the behavioral approach and combine it with pharmacotherapy whenever clinically appropriate.

A structured plan for responding to recurrent alcohol use should be established before hospital discharge. Such a plan should specify how the patient can rapidly contact the treatment team, how medications will be reassessed, and how the patient can re-enter behavioral treatment. This approach is consistent with management of AUD as a chronic disease and is more clinically informative than classifying patients permanently as either “abstinent” or “relapsed.”

Pharmacotherapy for alcohol use disorder

Evidence for Pharmacotherapy

Pharmacotherapy remains markedly underused despite increasing evidence that it may improve both alcohol-related and liver-related outcomes. Baclofen has the most direct randomized evidence in patients with cirrhosis. In a double-blind trial of 84 alcohol-dependent patients with cirrhosis, Addolorato et al. [25] found that 71% of patients assigned to baclofen achieved and maintained abstinence compared with 29% assigned to placebo. No excess hepatic toxicity was identified. The study was small and conducted at a single center, but it demonstrated that pharmacologic treatment of AUD can be feasible in cirrhosis. Sedation, dizziness, renal impairment, falls, and confusion that may resemble hepatic encephalopathy nevertheless require careful monitoring. Observational evidence also supports systematic consideration of acamprosate or naltrexone in appropriately selected patients. Rabiee et al. [26] analyzed 9,131 patients with alcohol-associated cirrhosis and high-risk alcohol use in the Veterans Outcomes and Costs Associated With Liver Disease cohort. Only 886 patients received medication for AUD, but medication exposure was associated with improved survival after adjustment for liver disease severity, age, and engagement with the health care system. Because treatment allocation was not randomized, patients who received medication may have differed from untreated patients in ways that were not fully captured. Nevertheless, the low treatment rate and adjusted survival association argue against relying on counseling alone without assessing pharmacologic options.

Medication Selection and Safety

Medication selection should account for hepatic and renal function, current or anticipated opioid use, encephalopathy risk, psychiatric comorbidity, and reproductive considerations. Acamprosate undergoes minimal hepatic metabolism but requires renal dose adjustment and a three-times-daily schedule. Naltrexone may reduce heavy drinking but should not be used in patients taking opioids and is generally avoided during acute hepatitis or marked clinical instability. Gabapentin and topiramate may be considered when preferred agents are unsuitable, although evidence in advanced ALD is less robust. Disulfiram is generally avoided because of its potential hepatotoxicity [21].

Reproductive Considerations

For women, pregnancy potential, contraception, and breastfeeding should be reviewed before medication initiation. The American Association for the Study of Liver Diseases reproductive health guidance recommends multidisciplinary management of pregnancy in women with cirrhosis and emphasizes preconception counseling [27]. Because pregnancy-specific data for most AUD medications remain limited, decisions should be individualized through collaboration among hepatology, addiction medicine, psychiatry, and maternal-fetal medicine.

Integrated hepatology and addiction care

The available evidence favors concurrent treatment of AUD and liver disease rather than sequential or disconnected care, although much of this evidence remains observational. Elfeki et al. [28] conducted a systematic review and meta-analysis of 20 studies involving 38,329 patients with liver disease, including 7,072 who received an AUD intervention. Compared with standard care, AUD intervention was associated with 44% lower odds of hepatic decompensation, 59% lower odds of 30-day readmission, and 58% lower odds of mortality. However, each pooled clinical outcome was informed by only a small number of studies, limiting the precision and generalizability of the estimates. The analysis therefore supports simultaneous AUD and liver disease management while also demonstrating the need for larger controlled studies.

Prospective and contemporary cohort studies provide additional evidence for specific integrated-care models. Mahle et al. [29] compared an inpatient service combining hepatology and addiction consultation with a historical addiction-only control. Integrated care increased the uptake of AUD medication, hepatic fibrosis screening, and viral hepatitis vaccination, although early alcohol remission did not differ significantly between the groups. George et al. [30] subsequently compared integrated hepatology-addiction care with addiction care alone at two academic centers and found fewer incident liver-related

decompensating events, greater uptake of AUD pharmacotherapy, and fewer alcohol-associated readmissions in the integrated-care group. Because neither study was randomized, the results cannot prove that care integration alone caused the observed benefits. Their consistent findings nevertheless provide stronger evidence for a coordinated pathway than for passive referral after discharge.

Another narrative review comprehensively discussed the integration of AUD management among females as a concurrent component of ALD treatment and identified the barriers to achieving such integrated care [31]. For women, this pathway should include screening and treatment for depression, anxiety, trauma, and interpersonal violence, with reproductive counseling when relevant. Practical modifications such as telehealth, consolidated appointments, transportation support, and childcare resources are rational responses to documented treatment barriers [32]. However, their direct effects on abstinence, decompensation, and survival among women with ALD have not been established and should be tested as part of future implementation studies.

Nutrition, frailty, and women's health

Malnutrition and sarcopenia are important outcome determinants because they are not fully represented by conventional liver severity scores. The ACG guideline recommends nutritional support for patients with alcohol-associated hepatitis, generally targeting approximately 35 kcal/kg per day and 1.2-1.5 g/kg per day of protein [21]. Enteral nutrition should be considered when oral intake is inadequate, while routine protein restriction should be avoided because it may aggravate muscle loss. Thiamine should be administered promptly when deficiency or alcohol withdrawal is suspected, and other micronutrient deficiencies should be corrected according to clinical and laboratory findings [21].

The prognostic evidence for sarcopenia is substantial. In a meta-analysis of 22 studies involving 6,965 patients with cirrhosis, Tantai et al. [33] found a pooled sarcopenia prevalence of 37.5%. Sarcopenia was associated with an adjusted HR for mortality of 2.3, and the association persisted across subgroups defined by sex, liver disease etiology, and severity of hepatic dysfunction. These findings support assessment of muscle mass and function, particularly because ascites or obesity may conceal clinically important loss of lean tissue. Nutrition combined with individualized resistance and aerobic activity is a reasonable management strategy, although trials demonstrating that reversal of sarcopenia specifically improves survival among women with ALD remain limited.

Women may additionally experience amenorrhea, infertility, osteoporosis, and pregnancy-related complications [27]. Bone health should be evaluated in women with cirrhosis, prolonged amenorrhea, early menopause, previous fractures, or other established osteoporosis risks. These outcomes are clinically important because they influence physical function and quality of life, but women-specific studies examining their contribution to ALD-related mortality or decompensation remain sparse.

Alcohol-associated hepatitis and advanced liver disease

Treatment of Severe Alcohol-Associated Hepatitis

Management of severe alcohol-associated hepatitis requires evidence-based selection and reassessment of corticosteroid therapy. In the Steroids or Pentoxifylline for Alcoholic Hepatitis trial of 1,103 patients, Thursz et al. [34] found no benefit from pentoxifylline and no sustained 90-day or one-year survival benefit from prednisolone. Prednisolone produced only a short-term survival signal and was associated with an increased risk of serious infection. A subsequent worldwide study by Arab et al. [35] found that the greatest 28-day survival benefit from corticosteroid treatment occurred among patients with MELD scores between approximately 25 and 39, whereas benefit diminished at very high MELD scores.

These findings support the guideline recommendation to reserve corticosteroids for appropriately selected patients with severe disease, evaluate for contraindications before treatment, and reassess response with the Lille score at day 4 or 7 [21]. Corticosteroids should be discontinued in nonresponders because continued exposure is unlikely to improve survival and may increase infectious complications.

Management of Cirrhosis and Transplant Referral

Patients with compensated cirrhosis require surveillance and prevention of portal hypertensive complications in parallel with treatment of AUD. The first occurrence of ascites, hepatic encephalopathy, variceal bleeding, or another decompensating event should prompt transplant referral rather than repeated short-term stabilization without long-term planning. For women, early referral may be particularly important because smaller body size and psychosocial barriers may prolong or complicate the progression from transplant evaluation to transplantation.

Liver transplantation and sex-specific disparities

Early Transplantation

Early liver transplantation can provide a substantial survival benefit for carefully selected patients with severe alcohol-associated hepatitis who do not respond to medical therapy. In the landmark study by Mathurin et al. [36], six-month survival was 77% among 26 patients who underwent early transplantation compared with 23% among matched patients who did not receive transplantation. In the 12-center American Consortium for Early Liver Transplantation for Alcoholic Hepatitis cohort of 147 early transplant recipients, Lee et al. [37] reported survival of 94% at one year and 84% at three years. Sustained alcohol use occurred in 10% and 17% of recipients at one and three years, respectively, and was associated with higher mortality. These results do not support unrestricted early transplantation but demonstrate that a fixed abstinence interval should not be the sole selection criterion when predicted short-term mortality is high.

Disparities in Evaluation and Listing

Potential sex disparities should be evaluated before listing decisions are finalized. McElroy et al. [38] studied 949 patients with alcohol-associated liver disease referred for transplantation and found that women and men had similar MELD scores, yet women were less likely to be listed. After adjustment, men were 95% more likely to be listed and 105% more likely to undergo transplantation. Similarly, in a six-center cohort of 617 patients with ALD evaluated for transplantation with less than six months of abstinence, Cooper et al. [39] found that women had lower adjusted odds of listing than men (OR, 0.64; 95% CI, 0.42-0.91). Mediation analyses identified mood disorders and unemployment as contributors to this disparity. Differences in psychiatric and substance-use characteristics contributed to some listing decisions.

MELD Scoring and Donor-Size Barriers

Beyond these listing considerations, earlier MELD models could disadvantage women through their reliance on serum creatinine. Women generally have lower muscle mass and may therefore have lower creatinine concentrations despite comparable renal impairment, resulting in underestimation of mortality risk and lower transplant priority. MELD 3.0 was developed partly to address this disadvantage by incorporating female sex, with a coefficient of 1.33, and serum albumin, lowering the creatinine ceiling from 4.0 to 3.0 mg/dL, and updating model coefficients and interaction terms [40]. However, scoring revisions alone do not address all barriers, particularly for candidates whose priority is determined by exception scores rather than calculated MELD. In a cohort of 31,725 candidates receiving hepatocellular carcinoma exception scores, Cron et al. [41] found that women were less likely to undergo transplantation. This disparity was largely explained by differences in candidate size, although shorter women remained disadvantaged compared with shorter men, highlighting barriers beyond creatinine-related scoring bias. These findings support early referral, standardized psychosocial assessment, and active treatment of potentially modifiable barriers rather than reliance on subjective judgments concerning social support or relapse risk.

Post-transplant Addiction Care

AUD treatment should continue after transplantation because transplantation treats liver failure rather than the underlying addiction. Daniel et al. [42] studied 611 liver transplant recipients with ALD, including 190 managed by an integrated addiction team, and found that integrated addiction follow-up was associated with a lower risk of severe alcohol relapse. Although treatment assignment was not randomized and greater patient engagement may have contributed to the results, the study supports incorporating longitudinal addiction care into routine post-transplant management.

Evidence-based priorities for improving outcomes

Clinical priorities include earlier identification of liver injury, sustained AUD treatment, and timely recognition of advanced disease (Table *1*).

Clinical area	Assessment or management	Considerations for women	References
Alcohol-use assessment	AUDIT-C or AUDIT; history of drinking patterns, withdrawal, previous treatment, and abstinence. Biomarkers supplement self-report	Liver injury may develop at lower alcohol exposure than in men	[2,19,21]
Disease severity	Assess cirrhosis, decompensation, and complications; use MELD for prognosis in severe alcohol-associated hepatitis	Lower muscle mass and creatinine may underestimate risk with earlier MELD models; MELD 3.0 partly addresses this disadvantage	[21,40]
Abstinence and behavioral treatment	Motivational interviewing, cognitive behavioral therapy, relapse-prevention counseling, contingency management, and mutual-help programs. Reassess treatment after recurrent alcohol use	Tailor treatment to psychiatric symptoms and social stressors	[22,24,32]
Baclofen	Randomized evidence supports abstinence in cirrhosis. Monitor sedation, dizziness, renal impairment, falls, and confusion	-	[25]
Acamprosate	Minimal hepatic metabolism; requires renal dose adjustment and three-times-daily administration	Available analyses suggest similar efficacy and tolerability in women and men	[21,26]
Naltrexone	May reduce heavy drinking; avoid with opioids and generally during acute hepatitis or marked clinical instability	Several studies suggest similar efficacy between sexes; nausea-related discontinuation may be more frequent in women	[21,26]
Other AUD medications	Consider gabapentin or topiramate when preferred agents are unsuitable; evidence in advanced ALD is limited. Avoid disulfiram because of hepatotoxicity	Sex-specific evidence for gabapentin and topiramate remains limited	[21]
Integrated and psychosocial care	Coordinate hepatology, addiction, and psychiatric care; assess depression, anxiety, trauma, and interpersonal violence	Address stigma, caregiving, transportation, and financial barriers	[20,28-32]
Nutrition and sarcopenia	Assess intake, muscle mass, and function; correct deficiencies and individualize exercise. In alcohol-associated hepatitis: approximately 35 kcal/kg/day and 1.2-1.5 g protein/kg/day	Survival benefits from reversing sarcopenia specifically in women remain uncertain; obesity and ascites may obscure muscle loss	[21,33]
Reproductive and bone health	Review pregnancy intentions, contraception, and breastfeeding; assess bone health according to risk	Address menstrual disturbances, infertility, early menopause, fractures, and pregnancy complications; provide preconception and multidisciplinary pregnancy care	[27]
Severe alcohol-associated hepatitis	Assess corticosteroid eligibility and contraindications; calculate Lille score at day 4 or 7 and discontinue corticosteroids in nonresponders	-	[21,34,35]
Transplant evaluation	Refer with decompensation; consider early transplantation in selected medical nonresponders. Abstinence duration should not be the sole selection criterion	Address psychosocial barriers, MELD-related disadvantage, and access to size-compatible donor organs	[21,36-42]
Post-transplant care	Continue AUD treatment and longitudinal addiction follow-up	Address ongoing psychiatric and practical barriers to care	[3,29,30,32,42]

TABLE 1: Assessment and management of alcohol-associated liver disease in women

AUDIT-C: Alcohol Use Disorders Identification Test-Consumption; AUDIT: Alcohol Use Disorders Identification Test; MELD: Model for End-Stage Liver Disease; AUD: alcohol use disorder; ALD: alcohol-related liver disease

Abstinence and appropriate pharmacotherapy should be pursued alongside liver disease management [21,22,24,25]. Coordinated hepatology and addiction care can facilitate treatment engagement [27-29]. Nutritional assessment, evaluation of muscle mass and function, and attention to psychiatric and

reproductive needs should inform the care plan [20,26,32]. Timely transplant referral permits assessment of candidacy and identification of potentially modifiable barriers [20,37].

Limitations and evidence gaps

Evidence specific to women remains limited across several aspects of ALD management. Many mechanistic findings derive from experimental models, while several treatment strategies are supported by observational studies involving both women and men. These limitations restrict conclusions about causality and treatment effectiveness specifically in women. Further research should evaluate sex-specific treatment outcomes, reproductive safety, and the effects of interventions addressing barriers to care.

Conclusions

Sex-related differences in susceptibility and disparities in treatment access should inform the assessment and management of women with ALD. Clinical care should connect treatment of AUD with hepatology services and address individual barriers to sustained engagement. Future studies should enroll sufficient numbers of women, report sex-stratified outcomes, and directly evaluate whether women-responsive service adaptations reduce alcohol recurrence, hepatic decompensation, hospital readmission, and mortality. Adaptations reduce alcohol recurrence, hepatic decompensation, hospital readmission, and mortality.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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References

1. Pan CW, Abboud Y, Chitnis A, Zhang W, Singal AK, Wong RJ: Alcohol-associated liver disease mortality . JAMA Netw Open. 2025, 8:e2514857. 10.1001/jamanetworkopen.2025.14857
2. Roerecke M, Vafaei A, Hasan OS, et al.: Alcohol consumption and risk of liver cirrhosis: a systematic review and meta-analysis. Am J Gastroenterol. 2019, 114:1574-86. 10.14309/ajg.0000000000000340
3. Flemming JA, Djerboua M, Chapman O, Ayonrinde O, Terrault NA: Epidemiology and outcomes of alcohol-associated hepatitis in adolescents and young adults. JAMA Netw Open. 2024, 7:e2452459. 10.1001/jamanetworkopen.2024.52459
4. Becker U, Deis A, Sørensen TI, et al.: Prediction of risk of liver disease by alcohol intake, sex, and age: a prospective population study. Hepatology. 1996, 23:1025-9. 10.1002/hep.510230513
5. Cederbaum AI: Alcohol metabolism. Clin Liver Dis. 2012, 16:667-85. 10.1016/j.cld.2012.08.002
6. Peter Guengerich F, Avadhani NG: Roles of cytochrome P450 in metabolism of ethanol and carcinogens . Alcohol and Cancer. Springer, Cham; 2018. 1032:10.1007/978-3-319-98788-0_2
7. Bosron WF, Lumeng L, Li TK: Genetic polymorphism of enzymes of alcohol metabolism and susceptibility to alcoholic liver disease. Mol Aspects Med. 1988, 10:147-58. 10.1016/0098-2997(88)90019-2
8. Frezza M, di Padova C, Pozzato G, Terpin M, Baraona E, Lieber CS: High blood alcohol levels in women. The role of decreased gastric alcohol dehydrogenase activity and first-pass metabolism. N Engl J Med. 1990, 322:95-9. 10.1056/NEJM199001113220205
9. Ammon E, Schäfer C, Hofmann U, Klotz U: Disposition and first-pass metabolism of ethanol in humans: is it gastric or hepatic and does it depend on gender?. Clin Pharmacol Ther. 1996, 59:503-13. 10.1016/S0009-9236(96)90178-2

10. Iimuro Y, Frankenberg MV, Arteel GE, Bradford BU, Wall CA, Thurman RG: Female rats exhibit greater susceptibility to early alcohol-induced liver injury than males. Am J Physiol. 1997, 272(5 Pt 1):G1186-94. 10.1152/ajpgi.1997.272.5.G1186
11. Yan C, Hu W, Tu J, Li J, Liang Q, Han S: Pathogenic mechanisms and regulatory factors involved in alcoholic liver disease. J Transl Med. 2023, 21:300. 10.1186/s12967-023-04166-8
12. Kono H, Wheeler MD, Rusyn I, et al.: Gender differences in early alcohol-induced liver injury: role of CD14, NF-kappaB, and TNF-alpha. Am J Physiol Gastrointest Liver Physiol. 2000, 278:G652-61. 10.1152/ajpgi.2000.278.4.G652
13. Ikejima K, Enomoto N, Iimuro Y, et al.: Estrogen increases sensitivity of hepatic Kupffer cells to endotoxin . Am J Physiol. 1998, 274:G669-76. 10.1152/ajpgi.1998.274.4.G669
14. Yin M, Ikejima K, Wheeler MD, et al.: Estrogen is involved in early alcohol-induced liver injury in a rat enteral feeding model. Hepatology. 2000, 31:117-23. 10.1002/hep.510310119
15. Szabo G: Gut-liver axis in alcoholic liver disease . Gastroenterology. 2015, 148:30-6. 10.1053/j.gastro.2014.10.042
16. Buch S, Stickel F, Trépo E, et al.: A genome-wide association study confirms PNPLA3 and identifies TM6SF2 and MBOAT7 as risk loci for alcohol-related cirrhosis. Nat Genet. 2015, 47:1443-8. 10.1038/ng.3417
17. Habash NW, Sehrawat TS, Shah VH, Cao S: Epigenetics of alcohol-related liver diseases . JHEP Rep. 2022, 4:100466. 10.1016/j.jhepr.2022.100466
18. Fujii H, Kawada N: Fibrogenesis in alcoholic liver disease . World J Gastroenterol. 2014, 20:8048-54. 10.3748/wjg.v20.i25.8048
19. Fang L, Zhao J, Liu G, et al.: Sex-specific disparities in alcohol-associated liver disease and cancers: insights from a large prospective cohort and plasma proteomics. Cancer Epidemiol. 2026, 103:103129. 10.1016/j.canep.2026.103129
20. Mellinger JL, Fernandez A, Shedden K, et al.: Gender disparities in alcohol use disorder treatment among privately insured patients with alcohol-associated cirrhosis. Alcohol Clin Exp Res. 2019, 43:334-341. 10.1111/acer.13944
21. Jophlin LL, Singal AK, Bataller R, Wong RJ, Sauer BG, Terrault NA, Shah VH: ACG clinical guideline: alcohol-associated liver disease. Am J Gastroenterol. 2024, 119:30-54. 10.14309/ajg.0000000000002572
22. Verrill C, Markham H, Templeton A, Carr NJ, Sheron N: Alcohol-related cirrhosis--early abstinence is a key factor in prognosis, even in the most severe cases. Addiction. 2009, 104:768-74. 10.1111/j.1360-0443.2009.02521.x
23. Hofer BS, Simbrunner B, Hartl L, et al.: Alcohol abstinence improves prognosis across all stages of portal hypertension in alcohol-related cirrhosis. Clin Gastroenterol Hepatol. 2023, 21:2308-17.e7. 10.1016/j.cgh.2022.11.033
24. Patel AK, Balasanova AA: Treatment of alcohol use disorder . JAMA. 2021, 325:596. 10.1001/jama.2020.2012
25. Addolorato G, Leggio L, Ferrulli A, et al.: Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: randomised, double-blind controlled study. Lancet. 2007, 370:1915-22. 10.1016/S0140-6736(07)61814-5
26. Rabiee A, Mahmud N, Falker C, Garcia-Tsao G, Taddei T, Kaplan DE: Medications for alcohol use disorder improve survival in patients with hazardous drinking and alcohol-associated cirrhosis. Hepatol Commun. 2023, 7:e0093. 10.1097/HC9.0000000000000093
27. Sarkar M, Brady CW, Fleckenstein J, et al.: Reproductive health and liver disease: practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021, 73:318-65. 10.1002/hep.31559
28. Elfeki MA, Abdallah MA, Leggio L, Singal AK: Simultaneous management of alcohol use disorder and liver disease: a systematic review and meta-analysis. J Addict Med. 2023, 17:e119-28. 10.1097/ADM.0000000000001084
29. Mahle R, McLean Diaz P, Marshall C, Goodman RP, Schaefer E, Luther J: Integrated hepatology and addiction care for inpatients with alcohol use disorder improves outcomes: a prospective study. Hepatol Commun. 2023, 7:e0119. 10.1097/HC9.0000000000000119
30. George P, Marshall C, Zhang W, et al.: Integrating hepatology with addiction care for inpatients with alcohol use disorder reduces future liver-related events. Hepatol Commun. 2025, 9:e0780. 10.1097/HC9.0000000000000780
31. Carlini LE, Fernandez AC, Mellinger JL: Sex and gender in alcohol use disorder and alcohol-associated liver disease in the United States: a narrative review. Hepatology. 2026, 83:178-94. 10.1097/HEP.0000000000000905
32. McCrady BS, Epstein EE, Fokas KF: Treatment interventions for women with alcohol use disorder . Alcohol Res. 2020, 40:08. 10.35946/arcr.v40.2.08
33. Tantai X, Liu Y, Yeo YH, et al.: Effect of sarcopenia on survival in patients with cirrhosis: a meta-analysis . J Hepatol. 2022, 76:588-99. 10.1016/j.jhep.2021.11.006
34. Thursz MR, Richardson P, Allison M, et al.: Prednisolone or pentoxifylline for alcoholic hepatitis. N Engl J Med. 2015, 372:1619-28. 10.1056/NEJMoa1412278
35. Arab JP, Díaz LA, Baeza N, et al.: Identification of optimal therapeutic window for steroid use in severe alcohol-associated hepatitis: a worldwide study. J Hepatol. 2021, 75:1026-33. 10.1016/j.jhep.2021.06.019
36. Mathurin P, Moreno C, Samuel D, et al.: Early liver transplantation for severe alcoholic hepatitis. N Engl J Med. 2011, 365:1790-800. 10.1056/NEJMoa1105703
37. Lee BP, Mehta N, Platt L, et al.: Outcomes of early liver transplantation for patients with severe alcoholic hepatitis. Gastroenterology. 2018, 155:422-30.e1. 10.1053/j.gastro.2018.04.009
38. McElroy LM, Likhitsup A, Scott Winder G, et al.: Gender disparities in patients with alcoholic liver disease evaluated for liver transplantation. Transplantation. 2020, 104:293-8. 10.1097/TP.0000000000002843
39. Cooper KM, Patel AK, Colletta A, et al.: Gender disparity in access to early liver transplant among patients with alcohol associated liver disease and limited sobriety is mediated by psychosocial factors. Liver Transpl. 2026, 32:388-99. 10.1097/LVT.0000000000000722
40. Kim WR, Mannalithara A, Heimbach JK, et al.: MELD 3.0: the model for end-stage liver disease updated for the modern era. Gastroenterology. 2021, 161:1887-95.e4. 10.1053/j.gastro.2021.08.050

41. Cron DC, Mazur RD, Bhan I, Adler JT, Yeh H: Sex and size disparities in access to liver transplant for patients with hepatocellular carcinoma. JAMA Surg. 2024, 159:1291-8. 10.1001/jamasurg.2024.3498
42. Daniel J, Dumortier J, Del Bello A, et al.: Integrating an addiction team into the management of patients transplanted for alcohol-associated liver disease reduces the risk of severe relapse. JHEP Rep. 2023, 5:100832. 10.1016/j.jhepr.2023.100832