Received: 2 January 2025 | Accepted: 25 February 2025

DOI: 10.1097/HC9.0000000000000691

REVIEW

OPEN

Sexual health and function in liver disease

Alberto Ferrarese[1] | **Ivonne Hurtado Díaz de León**[2] | **Elliot B. Tapper**[3] | **Patrizia Burra**[1]

[1]Multivisceral Transplant Unit, Gastroenterology, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy

[2]Department of Gastroenterology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

[3]Division of Gastroenterology and Hepatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA

Correspondence
Patrizia Burra, Multivisceral Transplant Unit, Gastroenterology, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, via Giustiniani 2, Padua 35122, Italy.
Email: burra@unipd.it

Abstract

Sex is a central aspect of human life and is significantly impacted by chronic illness. Cirrhosis, due to its unique pathophysiology and the side effects of common therapies, serves as a paradigmatic example, being associated with very high rates of sexual dysfunction in both men and women. Liver transplantation can modify certain hormonal and pathophysiological aspects related to sexual dysfunction, but complete recovery occurs in only a relatively small percentage of patients. This review examines the pathophysiology, epidemiology, and management of sexual and reproductive dysfunction in patients with cirrhosis and those undergoing liver transplantation. It provides a framework for understanding the sources of dysfunction, tools for identifying it in clinical settings, and interventions to improve sexual health and functioning in these patients.

Keywords: alcohol, cirrhosis, depression, liver transplantation, portal hypertension

INTRODUCTION

Sexual health is a complex state of well-being that is influenced by multiple body systems. Sex is also a central aspect of human life that is negatively impacted by chronic illnesses, such as cirrhosis. In such diseases, rates of sexual dysfunction are as high as 79% in men and 64% in women.[1,2] Herein, we review the pathophysiology, epidemiology, and management of sexual dysfunction among patients with cirrhosis and liver transplantation (LT).

SHARED PATHOPHYSIOLOGY OF SEXUAL DYSFUNCTION

Overview

The pathogenesis of sexual dysfunction is multifactorial, with all contributing factors being more prevalent in individuals with cirrhosis (Figure 2). As disease severity increases, liver dysfunction and portal hypertension lead to altered metabolism and trafficking of sex hormones, along with symptoms such as ascites and

Abbreviations: ART, artificial reproductive technology; CLD, chronic liver disease; ED, erectile dysfunction; FSD, female sexual dysfunction; FSFI, Female Sexual Function Index; IIEF, International Index of Erectile Function; LT, liver transplantation; PDE5, phosphodiesterase type 5.

Elliot B. Tapper and Patrizia Burra share joint senior authorship.

HE that further impact sexual function. In addition, many patients with cirrhosis have comorbid conditions, including anxiety, depression, and chronic pain, which can contribute to poor sexual function. These conditions are often managed with therapies (eg, antidepressants, sedatives, opioids) that have well-documented side effects related to sexual dysfunction.

Endocrinology

Cirrhosis causes hypogonadism,[3] inducing changes in body hair distribution, gynecomastia, testicular atrophy, muscle wasting, decreased sexual function, and fatigue.[4] It has been demonstrated that a decrease in serum testosterone is a common occurrence in men diagnosed with cirrhosis, with the prevalence of this phenomenon reaching 90%, commensurate with disease severity.[5] Testosterone deficiency in cirrhosis can stem from multiple disruptions along the hypothalamus-pituitary-testicular axis.[4] First, patients with cirrhosis experience an increased peripheral conversion of androgens to estrogens, regardless of the underlying cause of liver disease.[6] Furthermore, liver disease has been demonstrated to elevate levels of sex hormone–binding globulin, a protein that facilitates the binding of sex hormones within the bloodstream.[7] Given that sex hormone–binding globulin has a greater affinity for testosterone than for estradiol, a larger portion of testosterone becomes bound, thereby reducing the levels of free, bioactive testosterone. This results in unbound estradiol being relatively higher, which in turn shifts the hormonal balance toward estrogen dominance.[4] Furthermore, approximately half of the patients with cirrhosis exhibit decreased spermatogenesis and an increased presence of peritubular fibrosis.[3]

Etiology of liver disease

Alcohol misuse causes poor sexual function and desire, in both males and females.[8,9] In women, it inhibits progesterone secretion and estrogen levels,[10] resulting in an increased likelihood of developing sexual dysfunction, which can manifest as reduced sexual arousal, decreased vaginal lubrication, dyspareunia, difficulties with sexual arousal, and an inability to achieve orgasm.[8] In men, heavy or chronic alcohol use has been associated with reduced libido, hormonal imbalances, such as lowered testosterone levels, and an increased risk of erectile dysfunction (ED).[11,12] Alcohol directly injures the testes and may also impair the secretion of gonadotropins, leading to testicular shrinkage and a consequent decrease in testosterone levels.[4,13] Abstinence is associated with spontaneous recovery of hormonal function and balance in both men and women.[10,14] One in 4 men with ED who remained abstinent for a minimum of 6 months reported restoration of normal sexual function.[14] Beyond alcohol, other etiologies of chronic liver disease (CLD) have implications for sexual function. For instance, many with metabolic-associated steatotic liver disease have a history of diabetes. At least 1 in 2 people with diabetes (both men and women) report sexual dysfunction; erectile, arousal, and lubrication are neurovascular processes that are impaired by microvascular disease.[15]

Pharmacology

The management of cirrhosis complications often requires therapeutic interventions with deleterious influences on sexual function. β-blockers may increase the risk of depressive symptoms and may cause vasodilation, which is another contributing factor to ED.[16] Spironolactone, a first-line therapy for ascites, has antiandrogenic effects which are linked to reduced libido and ED.[9,16] It directly inhibits the enzyme 17α-hydroxylase, which is essential for testosterone biosynthesis. Furthermore, spironolactone blocks 5-alpha reductase, the enzyme responsible for converting testosterone into dihydrotestosterone, a more potent androgen. These changes can reduce testosterone's effects and slightly raise estradiol levels, leading to determining gynecomastia[17] and, although evidence is limited, ED.[2,18] In addition, the inhibitory effect of spironolactone on the androgen receptor may disrupt the anabolic actions of androgens on vulvar tissue, potentially leading to vestibular gland dysfunction and atrophy of the vulvar vestibule. This disruption may contribute to the development of conditions such as vestibulodynia and female sexual arousal disorder.[19]

Psychology

The prevalence of mental health disorders in patients with CLD may significantly contribute to the development of sexual dysfunction. Several studies have highlighted the high prevalence of mental health disorders among patients with CLD. For example, one study examined the prevalence of depression and anxiety in patients with cirrhosis using a telephone survey across 3 US health care systems. The findings revealed that 15.6% of patients experienced moderately severe to severe depression, and 42.6% exhibited high levels of anxiety.[20] Sexual dysfunction is common among individuals with psychiatric conditions. Contributing factors include psychotropic medication use, age, and somatic illnesses. This relationship is found to be bidirectional, as shown in a meta-analysis of 49 studies where ED was associated with a higher risk of

depression, and depression was linked to an increased risk of ED.[21] The most affected phase of the sexual response cycle was *sexual desire* in patients with depressive disorders, posttraumatic stress disorders, and schizophrenia. In patients with obsessive-compulsive disorder and anxiety disorders, the most frequent dysfunction occurred during the *orgasm phase*, affecting between 24% and 48% of patients.[22]

MALE SEXUAL DYSFUNCTION IN LIVER DISEASE

The term "male sexual dysfunction" encompasses a range of conditions, including ED, ejaculatory dysfunction, orgasmic dysfunction, and a reduction in sexual interest or desire.[23] ED is defined as the persistent or recurrent inability to achieve or maintain an erection that is sufficient for satisfactory sexual performance.[24] It is the most prevalent sexual dysfunction among adult males, with reported prevalence rates reaching as high as 90% in individuals over the age of 70, particularly among those with chronic conditions such as cirrhosis.[2,25–27] In a meta-analysis designed to assess the prevalence of ED and its associated risk factors in male patients with liver cirrhosis, 14 studies using the International Index of Erectile Function (IIEF) to assess ED were included. A total of 770 patients with cirrhosis were analyzed, with an overall ED prevalence of 79%. The prevalence was significantly higher in decompensated patients (88.4% vs. 53.6%).[2] Based on the IIEF severity score, the prevalence of severe, moderate, mild to moderate, and mild ED was 33%, 10%, 13%, and 11%, respectively.[2] Hypoactive sexual desire disorder or low libido is defined as a persistent or recurrent lack of sexual or erotic thoughts, fantasies, or desire to engage in sexual activities.[24] This condition is increasingly common in older age groups, with reported prevalence rates ranging from 13% to 27% in adult males.[28,29] Many studies have shown the impact of psychological disturbances on ED, particularly in men aged 30–50. The development of varying degrees of ED can, in turn, further worsen psychological and overall health and contribute to self-stigma. As a result, ED may not be adequately reported, remaining underdiagnosed and undertreated.[30,31] Stigma related to sexual dysfunction may also be associated with other forms of stigma, such as those linked to cirrhosis, obesity, and alcohol abuse, creating a multiplying effect. Therefore, stigma remains a barrier that needs to be addressed.

Assessment tools

The IIEF is a widely used, reliable tool consisting of 15 questions to assess the presence and severity of ED. It has proven sensitivity and specificity in detecting treatment-related changes in patients with ED, making it a valuable and objective measure in both clinical and research settings.[32] A shortened version of the IIEF, known as the IIEF-5, consists of 5 questions.[33] The scoring ranges from a minimum of 5 to a maximum of 25 points, with classifications as follows: 5–7 indicating severe ED, 8–11 for moderate ED, 12–16 for mild to moderate ED, 17–21 for mild ED, and 22–25 indicating no ED.[33]

Therapy

The goal of therapy for men with sexual dysfunction is to address the key aspects of sexual health affected, with treatment tailored to the underlying causes (Figure 1).

Phosphodiesterase type 5 inhibitors

Phosphodiesterase type 5 inhibitors (PDE5 inhibitors) are widely considered the first-line treatment for ED in patients both with and without cirrhosis due to their efficacy and favorable safety profile. PDE5 inhibitors work by preventing the breakdown of cyclic GMP, a compound that promotes smooth muscle relaxation and vasodilation.[34] In general, PDE5 inhibitors, including sildenafil, vardenafil, tadalafil, and avanafil, are considered to have similar efficacy for the treatment of ED. The adverse effects of PDE5 inhibitors are primarily attributable to their vasodilatory properties, which frequently manifest as symptoms such as headache, flushing, dizziness, and nasal congestion.[35] The use of PDE5 inhibitors is contraindicated in patients who utilize nitrates or nitric oxide donors for the treatment of angina, as the combination of these agents can precipitate severe hypotension and potentially life-threatening outcomes.[36]

Sildenafil has the most established safety profile among the 4 drugs, with a longer history of use and research across different populations. However, there is still limited evidence evaluating the differences between formulations and dosages, especially in patients with cirrhosis.[37] In a clinical trial evaluating the efficacy and safety of tadalafil for ED in patients with cirrhosis, 140 men with ED and cirrhosis were randomized to receive either tadalafil 10 mg daily or a placebo over a 12-week period. ED was defined as an IIEF score below 25, with the primary outcome being an increase of more than 5 points in the erectile function domain of the IIEF. Secondary outcomes included measures of anxiety, depression, and quality of life. The study found that patients treated with tadalafil experienced significantly greater improvements in erectile function, along with reductions in anxiety and depression and improvements in quality of life, compared to those receiving placebo. No significant differences in side effects or changes in HVPG were noted between the 2 groups.[38]

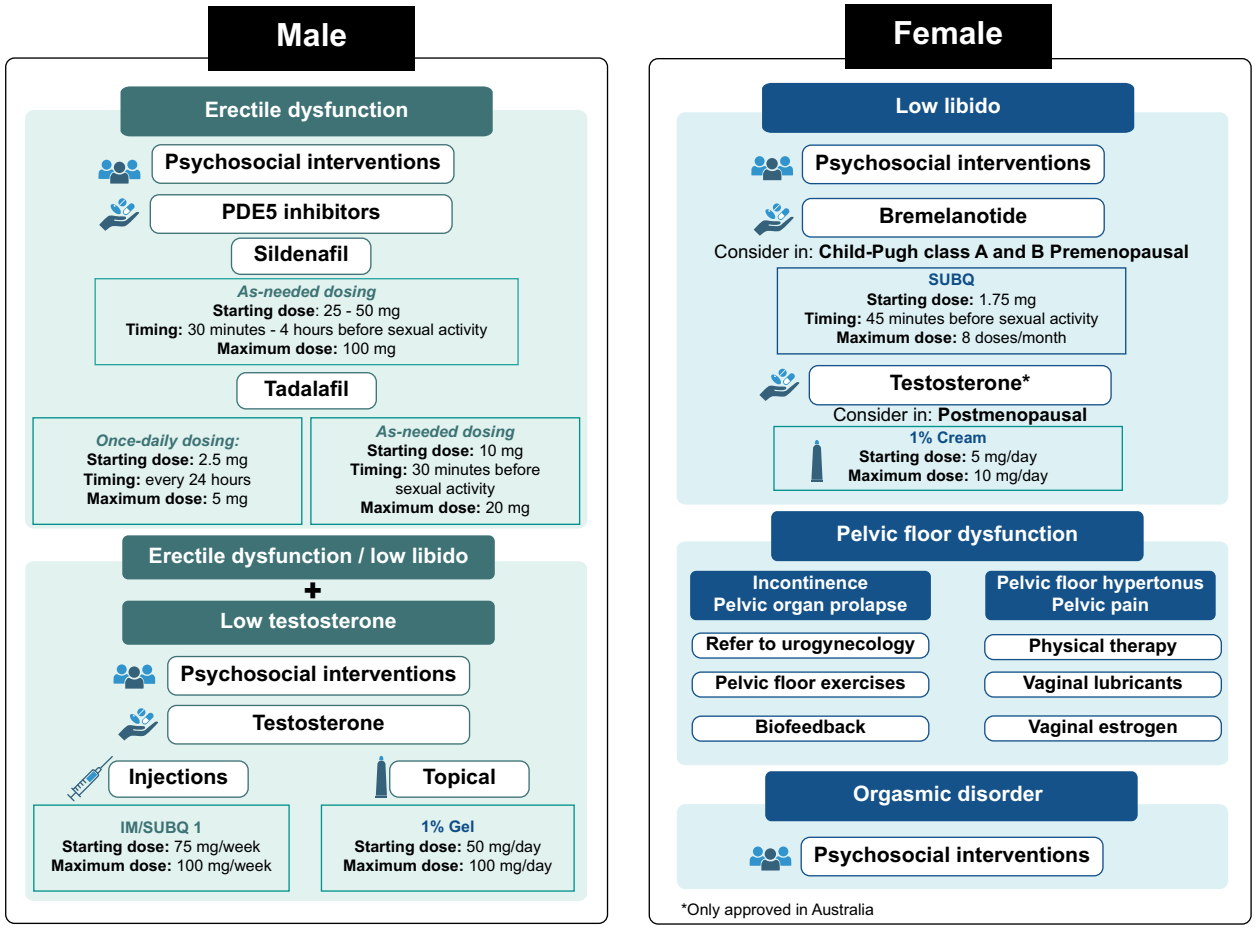

FIGURE 1 Treatment options for sexual dysfunction in men and women with liver disease. Abbreviation: PDE5, phosphodiesterase 5.

Testosterone

In patients presenting with ED and/or low libido, testosterone levels are frequently diminished, particularly in those with cirrhosis. Given this close correlation, it is prudent to assess testosterone levels in individuals exhibiting decreased libido or ED, as this evaluation can provide invaluable insights for more targeted treatment options.[39] Research on the effects of testosterone treatment for ED and low libido has yielded mixed results. However, recent findings suggest that combination therapy may be beneficial for patients with hypogonadism. A meta-analysis was conducted to evaluate the effects of testosterone therapy on sexual function in hypogonadal men, using the IIEF as the primary assessment tool. Reviewing 14 randomized controlled trials with 2298 participants, the study found significant improvements in erectile function (mean difference = 2.31 IIEF-EFD score) and in other areas of sexual function, such as libido, satisfaction, and orgasm, compared to placebo. The greatest benefits were observed in men with severe testosterone deficiency (lower than 8 nmol/L).[40]

Testosterone therapy is not recommended in patients with certain conditions due to the risk of adverse events. These include metastatic prostate cancer, breast cancer, unevaluated prostate nodules, elevated prostate-specific antigen levels (>4 ng/mL, or >3 ng/mL in high-risk individuals), hematocrit levels above 48% (or 50% at high altitudes), severe lower urinary tract symptoms from benign prostatic hypertrophy, poorly controlled congestive heart failure, and in men seeking fertility in the near future.[39]

There is very limited evidence regarding the use of testosterone in patients with cirrhosis. However, a randomized controlled trial—a 12-month, double-blinded, placebo-controlled study—aimed to investigate whether testosterone therapy could improve muscle mass in men with cirrhosis. The trial involved 101 men with established cirrhosis and low serum testosterone (total testosterone <12 nmol/L), who received intramuscular testosterone undecanoate. The results showed an improvement in muscle mass in testosterone-treated subjects, with no increase in adverse events compared to the placebo group.[41]

FEMALE SEXUAL DYSFUNCTION IN LIVER DISEASE

Female sexual dysfunction (FSD) is a broad term that encompasses various conditions related to sexual

activity. It can affect women of all ages and may stem from both physiological and psychological factors. Key components of FSD include low sexual desire or libido (a persistent lack of interest in sexual activity); arousal disorders (difficulty achieving or maintaining sexual arousal despite a desire for sexual activity); orgasmic issues (the inability to achieve orgasm despite adequate stimulation or a significant delay in reaching orgasm); and pain during intercourse (such as dyspareunia and vaginismus).

Epidemiology

Obtaining a clear picture of FSD prevalence is challenging, as available studies often examine patients with varying etiologies, ages, stages of liver disease, and diagnostic methods. Furthermore, there is a significant discrepancy between the volume of research on sexual dysfunction in males versus females, highlighting the need for increased focus on this issue among women. Few studies indicate a high prevalence of FSD among patients with CLD compared to the general population,[1,42,43] attributing this increase to both the direct effects of pathophysiological agents and a psychological component.[9,44] In a cohort with CLD of mixed etiologies (excluding alcohol-associated liver disease), 33% of female patients reported reduced sexual desire, 18% reduced arousal, 25% difficulty achieving orgasm, and 25% coital dysfunction.[45] A study of non-cirrhotic, pre-menopausal women with metabolic-associated steatotic liver disease demonstrated a prevalence of sexual dysfunction, as measured by the Female Sexual Function Index (FSFI) questionnaire, of up to 64%—significantly higher than the control population.[1] Comorbidities such as diabetes and hypertension may contribute.[42] Considering viral hepatitis, both HCV and HBV infections seem to increase the prevalence of such a condition (25%–70% of screened patients), even if comparison between cohorts is difficult to obtain according to different screening tools and inclusion criteria.[43,46] In our previous experience, FSD was reported in 65% of patients awaiting LT, with 43% experiencing severe dysfunction.[47] Other studies have confirmed that nearly half of female patients experience varying degrees of sexual dysfunction while awaiting LT, showing a direct correlation between the severity of liver disease and the increasing prevalence.[48,49]

Pathophysiology of FSD

There are multiple potential causes underlying FSD, including psychological and organic factors (Figure 2). The organic factors are detailed above. Psychological causes are often related to changes in body perception following illness, reactive responses after diagnosis, and the onset of psychiatric issues such as depression, which frequently accompanies the later stages of liver disease.[20] It is also important to consider the burden of stigma, which is often associated with cirrhosis (regardless of its etiology). The influence of stigma (whether public, self-, or structural stigma) contributes to the development of negative beliefs, refusal of treatment, and depression, which in turn can negatively impact sexual health.[50,51]

Assessment tools

The use of disease-specific questionnaires represents a reasonable first step for screening and diagnosing FSD. An ideal questionnaire should be easy to administer and reproduce, comprehensible regardless of the respondent's level of education, translatable into multiple languages, and capable of evaluating the full spectrum of FSD. The FSFI is a self-reported questionnaire of 6 domains (desire, lubrication, arousal, orgasm, satisfaction, and pain) for a total of 19 questions, producing a scale ranging from a minimum score of 2 to a maximum of 36.[52] Some pitfalls are that the fulfillment is time-consuming and is difficult to administer to patients with cognitive deficits or those with HE; therefore, shorter and easier forms have been proposed.[53] The ASEX is a 5-item rating scale that quantifies sex drive, arousal, vaginal lubrication or penile erection, the ability to reach orgasm, and satisfaction from orgasm, with scores ranging from 5 to 30 (higher scores indicate more sexual dysfunction). It offers an easy-to-use, rapid screening tool and could be applicable to both genders, even if is less detailed than the FSFI.[54] Therefore, given its ease of use and ability to provide comparable and objective data, ASEX could be considered an appropriate screening tool for the target population.

Referral to a psychologist may be recommended to evaluate the presence of psychological or psychiatric comorbidities and their impact on FSD. If there are signs of reproductive dysfunction (such as amenorrhea) alongside FSD, further investigation is necessary to exclude other chronic conditions that may be responsible for or associated with these symptoms. The strengths and limitations of the questionnaires currently available in the literature have been well-described elsewhere.[55]

Management of FSD in liver disease

Diagnosis of FSD requires appropriate therapy (Figure 1). Patients with non-advanced liver disease can be treated according to recommendations for the general population. These include both pharma and nonpharmacological treatments, such as behavioral modification

(lifestyle changes, cessation of potentially harmful factors such as smoking and alcohol, daily physical activity) and consultation with mental health specialists experienced in treating FSD (eg, sex therapists, psychologists, psychiatrists)[56,57] Another nonpharmacological strategy involves stopping or reducing chronically used medications (eg, antidepressants) that may be associated with some FSD symptoms (especially dyspareunia and vaginal dryness). Regarding pharmacological therapy, it must be prescribed under supervision by a gynecologist, taking into account the patient's age, menopausal stage, potential side effects, liver disease stage, and after proper assessment of hormone status.[9] Moreover, therapy should be tailored according to the specific domains of sexual dysfunction. For instance, the use of the PDE5 inhibitor sildenafil, commonly prescribed for ED, has been proposed for patients experiencing arousal disorders.[58] Topical treatments (eg, lubricants and vaginal moisturizers), tailored to the patient's symptoms, appear to be effective for those experiencing pain during intercourse or vaginal dryness. Considering oral estrogenic therapy for the treatment of FSD, there has been some concern regarding their use, even at low doses, in advanced liver disease, due to the hepatic first-pass metabolism and cholestatic, but this concern has not been widely confirmed in larger studies.[59] Finally, there is no solid data on the use of hormone therapy in post-liver transplant patients for this specific indication. It is worth noting, however, that this therapy should be prescribed with caution, taking into account the risk of venous thromboembolism, ischemic stroke, and breast cancer, and also that there are some reports of interactions between estrogen and calcineurin inhibitors.

REPRODUCTIVE DYSFUNCTION IN LIVER DISEASE

Reproductive dysfunction in men

Men with CLD may experience alterations in reproductive health due to various pathophysiological mechanisms that can arise at different stages of the disease. Considering patients without cirrhosis, heavy alcohol use can impair spermatogenesis,[60] while HCV may lead to a higher incidence of aneuploidies, diploidy, and alterations in sperm density, motility, and morphology.[61,62] Metabolic-associated steatotic liver disease may impact sperm concentration, sperm count, and total motility compared to control groups, too.[63] Finally, certain storage disorders, such as hemochromatosis or Wilson's disease, may cause testicular damage, with a potential impact on reproductive function. Cirrhosis per se determines further hormonal dysfunctions that lead to hypogonadism and hyperestrogenism.[64] Furthermore, the development of portosystemic shunts (both during disease progression or artificially created through TIPS placement) increases the peripheral conversion of androgens to estrogens.[65] ED, whose pathophysiology has already been discussed above, is not the only aspect of reproductive dysfunction to consider, as spermatogenesis may also be affected. Studies on mice with CCL4-induced cirrhosis showed an alteration in the spermatogenesis process, though without a generalized degeneration of the seminiferous epithelium.[66,67] Clinical studies on semen characteristics in patients with

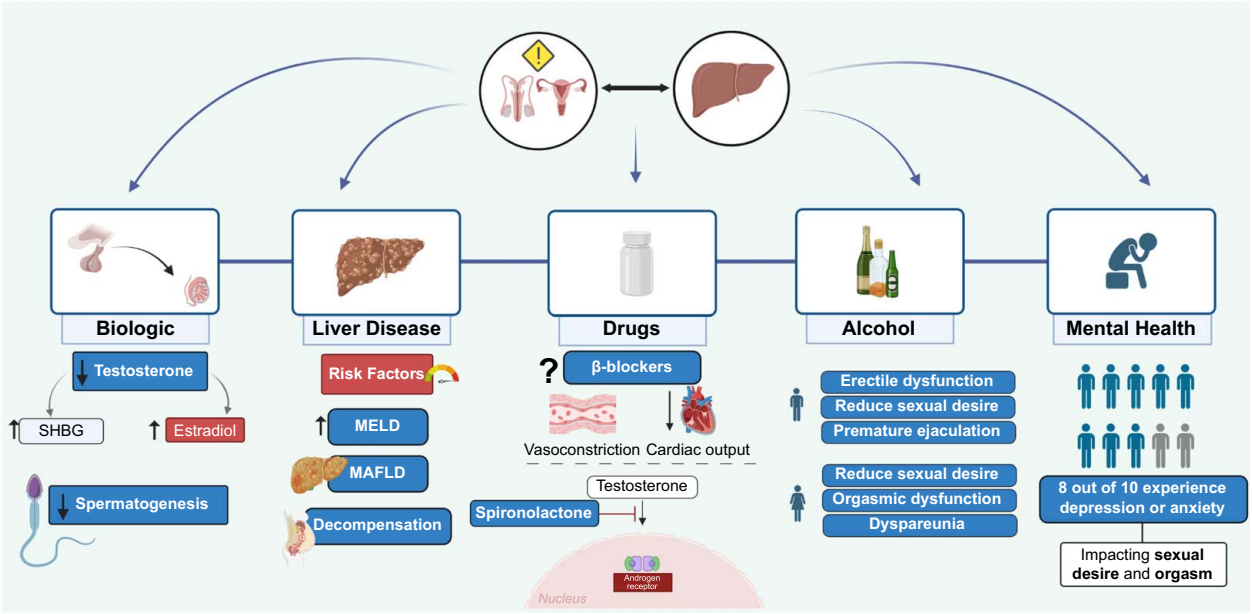

FIGURE 2 Pathophysiology of sexual dysfunction in patients with liver disease. Hormonal imbalances, progression of liver disease, medications, alcohol consumption, and mental health conditions, as significant contributors to sexual dysfunction in such patients. Abbreviations: MAFLD, metabolic-associated fatty liver disease; SHBG, sex hormone binding globulin.

cirrhosis are limited, mostly due to the high rate of ED in patients with CLD.

Reproductive dysfunction in women

Amenorrhea/oligomenorrhea (absence or irregular/infrequent menstrual periods), infecundity (biological incapability to conceive after 1 year of regular, unprotected intercourse, or 6 months if the woman is over 35), and infertility (incapability to having offspring) are observed in patients with CLD, especially at later disease stages. The disruption of the hypothalamic-pituitary-gonadal axis (ie, hepatic hypogonadism, where both ovarian function and hormonal signaling pathways are affected) usually increases the serum concentration of estrogens, thus impairing the production and function of gonadal hormones. This can cause amenorrhea and, consequently, infecundity. As in men, there is a strong correlation between the severity of liver disease and the degree of reproductive dysfunction.[68] Conversely, the role of portosystemic shunt in worsening reproductive function in women remains controversial, as the results previously reported in males (in terms of changes in serum hormone levels) have not been confirmed in females.[65] Superimposed factors such as malnutrition, sarcopenia, portal hypertension, and certain medications can also further impair reproductive function. Regarding etiology of liver disease, alcohol seems to reduce ovarian volume and the number of oocytes, thereby lowering the chances of becoming pregnant.[69] Uncontrolled or poorly controlled autoimmune hepatitis may reduce fertility, which can be restored following better disease management.[70] It is important to note, however, that chronic steroid use can lead to reproductive dysfunction by causing secondary hypogonadism. Primary sclerosing cholangitis, on the other hand, does not appear to affect fertility, especially at early disease stages.[71] From a clinical point of view, amenorrhea has been frequently encountered in patients with CLD, especially in cases with advanced diseases like cirrhosis, where prevalence rates can range between 30% and 80% depending on disease severity.[72,73] As a consequence, fertility is reduced in patients with cirrhosis, being up to 40% lower in those with decompensated disease.[74]

Barriers to conception in CLD

Despite the multiple factors that can reduce fertility in both genders among patients with CLD, especially those with cirrhosis, there are encouraging data regarding recent trends. In a landmark study by Flemming et al, the incidence of childbirth in women with cirrhosis increased more than 7-fold from 2000 to 2016, with an average annual increase of 8% per year. Moreover, the overall rate of childbirth in women with compensated cirrhosis was slightly higher compared to the general population.[74] These data suggest that pregnancy is not a rare event in patients with cirrhosis, as was once thought. Improved management of the underlying disease, active surveillance for some expected complications (eg, portal hypertensive complications), and more thorough counseling that enables pregnancy planning have likely led health care providers to be more open to not prohibiting pregnancy outright in women with liver cirrhosis.[72]

Many barriers still need to be addressed to further increase the number of childbirths.

Some of these should be addressed by improving knowledge at a patient-level, increasing the awareness that the risk of vertical transmission of certain conditions (such as viral infections) could easily and effectively minimized.[75,76]

Another barrier is the tendency not to prescribe pharmacological and nonpharmacological therapies to couples with CLD in the same way as for the general population. A landmark study by Karampatou et al[77] demonstrated that HCV-positive patients had a 2-fold increased risk of infertility, but the achievement of sustained virologic response after antiviral treatment reduced the risk of miscarriage by 2-fold. Two recent studies have explored the role of artificial reproductive technology (ART) in the context of CLD and LT. There are still some concerns about recommending this procedure for such patients, given the risk of ovarian hyperstimulation syndrome and estrogen-induced liver dysfunction. One study described the outcomes of 42 women (25 with CLD, 6 with cirrhosis, and 11 recipients of LT) who underwent in vitro fertilization. Clinical pregnancy occurred in 75% of cases, with live births occurring in 32 out of 57 cycles (56%). Liver enzyme alteration occurred in 9 out of 57 (16%) cycles, without long-term sequelae. Two out of 6 patients with cirrhosis experienced decompensation during treatment or pregnancy, and 1 died 12 months postpartum.[78] A second study considered 295 women with CLD, including 6 with cirrhosis and 8 recipients of LT who underwent ART, mostly using in vitro fertilization. When comparing clinical outcomes between patients with CLD and control patients, there were no significant differences in rates of clinical pregnancy (70.3% vs. 65.5%), clinical pregnancy loss (7.1% vs. 8.8%), or live birth (64.9% vs. 58.6%).[79] Although these studies are not enough to present a valid scenario for ART in the setting of CLD (even advanced) and LT, and while we await prospective studies in more carefully selected patient groups, these 2 experiences shed light on this therapeutic possibility that had previously not been adequately studied. Finally, a persistent barrier is the concern over adverse maternal and child perinatal outcomes compared to the general population. While this topic should be considered and thoroughly addressed during

preconception counseling, it is beyond the scope of this review.[74,80]

LT as a cure for sexual and reproductive dysfunction?

LT can theoretically correct hormone imbalances caused by cirrhosis, enhance psychological well-being, and improve overall quality of life, positively influencing various aspects of sexual health. However, the literature on sexual health following LT is mixed, with conflicting results. A study of 28 females (70% of them being sexually active) reported a satisfied sexual health after LT (75% had weekly intercourse associated with orgasm in 70% of cases).[81] A meta-analysis showed that patients reported statistically significant improvements in sexual function after transplantation when this was considered in the setting of health-related quality of life.[82] In our experience, however, female patients with liver cirrhosis showed equal prevalence of FSD before and after transplantation, with a correlation with depression and reduced quality of life in the posttransplant phase.[83] Similarly, 233 LT women and 291 on a waiting list showed no significant differences in availability of a sexual partner, sexual activity, orgasm experience, dyspareunia, and satisfaction with sex life before and after LT.[84] Similar data have been already published in a cohort of 34 women from the United States, in another group of 45 women from Switzerland, and more recently, in a small cohort of LT women from Turkey.[85–87] According to other experiences, there can be a worsening of FSD prevalence after transplant, usually due to de novo onset of dysfunctional symptoms. A study from Canada on 62 women who underwent LT reported that 15 of them had pre-LT FSD, who persisted after surgery in 50%. De novo FSD occurred in 18 patients, with a significant increase after transplantation. Notably, the prevalence of FSD was well distributed between reduced libido, dyspareunia, and anorgasmia. Despite the reported sex-related problems, 59% of patients were moderately to very satisfied with their sex life since transplantation, and only 23% found their sexual relationship very to moderately dissatisfactory.[88] The aforementioned studies employed different designs and used various tools for screening FSD, assessed at different time points. Therefore, the clinical message derived from the literature can be summarized as follows: a significant improvement in certain domains of FSD may occur after LT, although this does not always translate into a return to normal sexual health. This improvement appears to be associated with better postoperative quality of life, highlighting the psychological impact on this condition. Conversely, a variable degree of FSD-related symptoms may arise after surgery, both in females who had or who did not have such conditions

TABLE 1 Open issues in the diagnosis and management of sexual dysfunction and potential strategies to address them

Open issues in sexual dysfunction	Potential strategies
• *Underestimation* of the prevalence of sexual dysfunction and its impact on quality of life by health care providers	• Systematic screening of this condition. • Routine screening during outpatient evaluation. • Use of validated tools. • Multiplied delivery formats: In-person evaluations and digital options, such as online forms through patient portals.
• *Limited awareness in special populations*, including adolescents and young adults, who often require simultaneous information about sexual health, reproductive health, and fertility.	• Development of accessible educational materials: creation of brochures, websites, and videos to ensure information is easy to understand and widely available. • Educational campaigns, social media initiatives, and public debates. • Engagement with scientific societies and patient organizations. • Collaborations between health care professionals • Raising awareness at multiple levels:
• *Uncomfortable feelings* associated with sexual dysfunction act as barriers to both diagnosis and therapy.	• Practicing and training nonjudgmental, open communication. • Inclusion of other professionals such as nurses and psychologists. • Making educational information readily available in print form in the clinic or on the clinic website/portal.
• Lack of a *holistic approach* to sexual dysfunction.	• Embrace multidisciplinary management with early and accessible referral to professionals such as endocrinologists, gynecologists, urologists, and andrologists; psychologists and therapists; active involvement of the general practitioner particularly for follow-up care after the initial assessment.
• Lack of *robust data* on the pathophysiology of the disease, and the effectiveness of therapies, both pharmacological and nonpharmacological.	• Research through collaborative studies, to explore and improve sexual dysfunction, both in cirrhosis and after liver transplantation. • Dissemination of knowledge: Share data at national and international conferences to increase awareness of daily clinical practices.

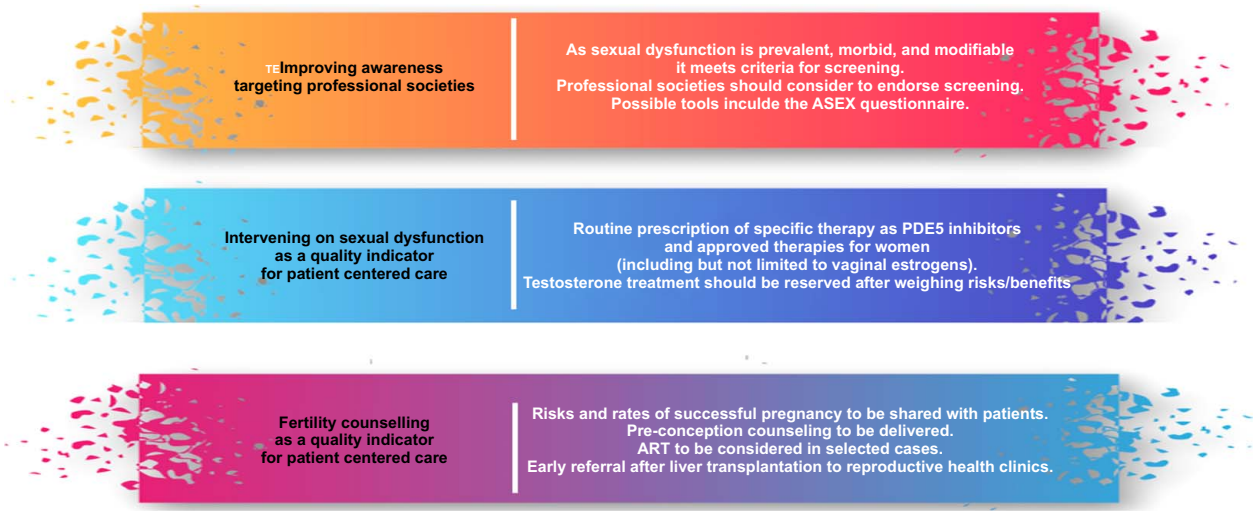

FIGURE 3 A call to action for a better management of sexual dysfunction in liver disease and transplantation. Abbreviations: ART, artificial reproductive technology; ASEX, Arizona Sexual Experience Scale; PDE5, phosphodiesterase 5.

before LT. This may be caused by a temporal correlation between the posttransplant phase and the onset of menopause, an under/misdiagnosis before surgery, the onset of psychological disturbances that can arise after transplantation, and the potential role of medications such as antidepressants.

Among females, the restoration of the hypothalamic-pituitary-gonadal axis can lead to the return of the menstrual cycle for most women who undergo LT during reproductive age. In the aforementioned study by Mass, 95% of women younger than 46 years experienced a return of menstrual bleeding within the first year after transplantation.[73] The return to regular menses was observed at 3 and 12 months in 35% and 70% of patients, respectively, after transplantation in a cohort from Poland.[89] Both studies showed a high prevalence of menstrual irregularities, partly attributable to the perimenopausal age.

The role of LT on menopausal symptoms, as well as its influence on post-liver transplant quality of life, remains questionable. A small study from Brazil highlighted that the peri/postmenopausal stage did not influence the quality of life in recipients of liver transplants and that these recipients did not experience more intense climacteric symptoms than healthy women.[90] However, factors such as the age at transplantation, the pretransplant hormonal disturbances made by cirrhosis, and the non-universal postoperative return to menses are challenging aspects to be considered in this setting.

Preliminary experiences with ART in recipients of LT have shown that these patients had a significantly higher number of oocytes retrieved, mature oocytes, and fertilized embryos compared to patients with CLD, suggesting that fertility and response to ART treatments may be restored after liver transplantation.[79] However, this finding needs validation in larger cohorts. In males, the impact of LT in ED has been previously described. Few data are available on patients having preoperative azoospermia. In small groups of recipients of kidney transplants, there was a certain increase in the number of sperm precursor cells at the testicular level after transplant, but most patients continued to have signs of late-stage maturational arrest.[91] A study on 9 patients evaluated pre-liver transplant and post-liver transplant showed normal seminal parameters in 5 of them postoperatively, even if 2 suffered from oligo-astheno-teratospermia. Notably, 4 were unable to produce an ejaculate for semen analyses.[92] Data on the possibility of de novo infertility after transplantation are still unavailable. One possible reason for this could be related to the use of immunosuppressive therapy, as preclinical studies have shown that calcineurin is strongly expressed in the testis and plays a role in cellular mechanisms essential for the normal function of sperm,[93] whereas clinical studies have demonstrated a correlation between sirolimus and suppression of gonadal function.[94] Finally, given the potentially teratogenic role of mycophenolic acid in women, it has also been studied in men, without showing a significant increase in the risk of malformations in children exposed in a cohort of kidney transplant patients.[95]

CONCLUSIONS

Sexual dysfunction is common, morbid, and modifiable. It is underdiagnosed and undertreated in cirrhosis and LT. In Table 1, we summarize our review, enumerating the barriers to optimal care and their solutions. We crystalize the key action items needed to tackle the problem of underdiagnosis and treatment (Figure 3). We believe this is a problem that meets the criteria for screening with proven, readily available interventions for those with unmet needs. It is imperative that we

overcome our discomfort with this issue to better serve our patients.

AUTHOR CONTRIBUTIONS

Concept: Patrizia Burra and Elliot B. Tapper. Writing: Alberto Ferrarese and Ivonne Hurtado Díaz de León. Editing: Elliot B. Tapper and Patrizia Burra.

CONFLICTS OF INTEREST

Patrizia Burra consults for Biotest, Chiesi Farmaceuticals, Alpha Wasserman, Novartis, Kedrion, Astellas Pharma, and Sandoz. The remaining authors have no conflicts to report.

ORCID

Alberto Ferrarese https://orcid.org/0000–0002–3248–2038
Patrizia Burra https://orcid.org/0000–0002–8791–191X

REFERENCES

1. Lee JY, Shin DW, Oh JW, Kim W, Joo SK, Jeon MJ, et al. Non-alcoholic fatty liver disease as a risk factor for female sexual dysfunction in premenopausal women. PLoS One. 2017;12: e0182708.
2. Yoo HJ, Lee B, Jung EA, Kim SG, Kim YS, Yoo JJ. Prevalence and risk factors of erectile dysfunction in patients with liver cirrhosis: A systematic review and meta-analysis. Hepatol Int. 2023;17:452–62.
3. Karagiannis A, Harsoulis F. Gonadal dysfunction in systemic diseases. Eur J Endocrinol. 2005;152:501–13.
4. Sinclair M, Grossmann M, Gow PJ, Angus PW. Testosterone in men with advanced liver disease: Abnormalities and implications. J Gastroenterol Hepatol. 2015;30:244–51.
5. Grossmann M, Hoermann R, Gani L, Chan I, Cheung A, Gow PJ, et al. Low testosterone levels as an independent predictor of mortality in men with chronic liver disease. Clin Endocrinol (Oxf). 2012;77:323–8.
6. Gordon GG, Olivo J, Rafil F, Southren AL. Conversion of androgens to estrogens in cirrhosis of the liver. J Clin Endocrinol Metab. 1975;40:1018–26.
7. Handelsman DJ, Strasser S, McDonald JA, Conway AJ, McCaughan GW. Hypothalamic-pituitary-testicular function in end-stage non-alcoholic liver disease before and after liver transplantation. Clin Endocrinol (Oxf). 1995;43:331–7.
8. Salari N, Hasheminezhad R, Almasi A, Hemmati M, Shohaimi S, Akbari H, et al. The risk of sexual dysfunction associated with alcohol consumption in women: A systematic review and meta-analysis. BMC Womens Health. 2023;23:213.
9. Neong SF, Billington EO, Congly SE. Sexual dysfunction and sex hormone abnormalities in patients with cirrhosis: Review of pathogenesis and management. Hepatology. 2019;69:2683–95.
10. Hill M, Popov P, Havlíková H, Kancheva L, Vrbíková J, Kancheva R, et al. Altered profiles of serum neuroactive steroids in premenopausal women treated for alcohol addiction. Steroids. 2005;70:515–24.
11. Boddi V, Corona G, Monami M, Fisher AD, Bandini E, Melani C, et al. Priapus is happier with Venus than with Bacchus. J Sex Med. 2010;7:2831–41.
12. Dachille G, Lamuraglia M, Leone M, Pagliarulo A, Palasciano G, Salerno MT, et al. Erectile dysfunction and alcohol intake. Urologia. 2008;75:170–6.
13. Lotti F, Maggi M. Sexual dysfunction and male infertility. Nat Rev Urol. 2018;15:287–307.
14. Van Thiel DH, Gavaler JS, Sanghvi A. Recovery of sexual function in abstinent alcoholic men. Gastroenterology. 1983;84: 677–82.
15. Corona G, Isidori AM, Aversa A, Bonomi M, Ferlin A, Foresta C, et al. Male and female sexual dysfunction in diabetic subjects: Focus on new antihyperglycemic drugs. Rev EndocrMetab Disord. 2020;21:57–65.
16. Nunes KP, Labazi H, Webb RC. New insights into hypertension-associated erectile dysfunction. Curr Opin Nephrol Hypertens. 2012;21:163–70.
17. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. N Engl J Med. 1999;341:709–17.
18. Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, et al. Erectile dysfunction. Nat Rev Dis Primers. 2016;2: 16003.
19. Mitchell L, Govind V, Barela K, Goldstein AT. Spironolactone may be a cause of hormonally associated vestibulodynia and female sexual arousal disorder. J Sex Med. 2019;16:1481–3.
20. Hernaez R, Kramer JR, Khan A, Phillips J, McCallister K, Chaffin K, et al. Depression and anxiety are common among patients with cirrhosis. Clin Gastroenterol Hepatol. 2022;20:194–203.e1.
21. Liu Q, Zhang Y, Wang J, Li S, Cheng Y, Guo J, et al. Erectile dysfunction and depression: A systematic review and meta-analysis. J Sex Med. 2018;15:1073–82.
22. Herder T, Spoelstra SK, Peters AWM, Knegtering H. Sexual dysfunction related to psychiatric disorders: A systematic review. J Sex Med. 2023;20:965–76.
23. Hatzimouratidis K. Epidemiology of male sexual dysfunction. Am J Mens Health. 2007;1:103–25.
24. McCabe MP, Sharlip ID, Atalla E, Balon R, Fisher AD, Laumann E, et al. Definitions of sexual dysfunctions in women and men: A consensus statement from the Fourth International Consultation on Sexual Medicine 2015. J Sex Med. 2016;13:135–43.
25. Selvin E, Burnett AL, Platz EA. Prevalence and risk factors for erectile dysfunction in the US. Am J Med. 2007;120:151–7.
26. Nguyen HMT, Gabrielson AT, Hellstrom WJG. Erectile dysfunction in young men—A review of the prevalence and risk factors. Sex Med Rev. 2017;5:508–20.
27. Allen MS, Walter EE. Erectile dysfunction: An umbrella review of meta-analyses of risk-factors, treatment, and prevalence outcomes. J Sex Med. 2019;16:531–41.
28. Laumann EO, Nicolosi A, Glasser DB, Paik A, Gingell C, Moreira E, et al. Sexual problems among women and men aged 40-80 y: Prevalence and correlates identified in the Global Study of Sexual Attitudes and Behaviors. Int J Impot Res. 2005;17:39–57.
29. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: Prevalence and predictors. JAMA. 1999;281: 537–44.
30. Dewitte M, Bettocchi C, Carvalho J, Corona G, Flink I, Limoncin E, et al. A psychosocial approach to erectile dysfunction: Position statements from the European Society of Sexual Medicine (ESSM). Sex Med. 2021;9:100434.
31. Bechoua S, Hamamah S, Scalici E. Male infertility: An obstacle to sexuality? Andrology. 2016;4:395–403.
32. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): A multidimensional scale for assessment of erectile dysfunction. Urology. 1997;49:822–30.
33. Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Pena BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res. 1999; 11:319–26.

34. Corbin JD. Mechanisms of action of PDE5 inhibition in erectile dysfunction. Int J Impot Res. 2004;16(suppl 1):S4–7.
35. Yuan J, Zhang R, Yang Z, Lee J, Liu Y, Tian J, et al. Comparative effectiveness and safety of oral phosphodiesterase type 5 inhibitors for erectile dysfunction: A systematic review and network meta-analysis. Eur Urol. 2013;63:902–12.
36. Schwartz BG, Kloner RA. Drug interactions with phosphodiesterase-5 inhibitors used for the treatment of erectile dysfunction or pulmonary hypertension. Circulation. 2010;122:88–95.
37. Pyrgidis N, Mykoniatis I, Haidich AB, Tirta M, Talimtzi P, Kalyvianakis D, et al. The effect of phosphodiesterase-type 5 inhibitors on erectile function: An overview of systematic reviews. Front Pharmacol. 2021;12:735708.
38. Jagdish RK, Kamaal A, Shasthry SM, Benjamin J, Maiwall R, Jindal A, et al. Tadalafil improves erectile dysfunction and quality of life in men with cirrhosis: A randomized double blind placebo controlled trial. Hepatol Int. 2023;17:434–51.
39. Bhasin S, Brito JP, Cunningham GR, Hayes FJ, Hodis HN, Matsumoto AM, et al. Testosterone therapy in men with hypogonadism: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2018;103:1715–44.
40. Corona G, Rastrelli G, Morgentaler A, Sforza A, Mannucci E, Maggi M. Meta-analysis of results of testosterone therapy on sexual function based on International Index of Erectile Function Scores. Eur Urol. 2017;72:1000–11.
41. Sinclair M, Grossmann M, Hoermann R, Angus PW, Gow PJ. Testosterone therapy increases muscle mass in men with cirrhosis and low testosterone: A randomised controlled trial. J Hepatol. 2016;65:906–13.
42. Fouad TR, Mohamad NE, Elabd M, Abd-Elwahab R, Elsary AY, Abd-Elghafar TS, et al. Nonalcoholic fatty liver disease and female sexual dysfunction in Egyptian premenopausal women: Is there a link between metabolic syndrome and sexual function? J Sex Med. 2024;21:770–6.
43. Elshimi E, Morad W, Mohamad NE, Shebl N, Waked I. Female sexual dysfunction among Egyptian patients with chronic hepatitis C. J Sex Med. 2014;11:768–75.
44. Jagdish RK. Sexual dysfunctions and their treatment in liver diseases. World J Hepatol. 2022;14:1530–40.
45. Bach N, Schaffner F, Kapelman B. Sexual behavior in women with nonalcoholic liver disease. Hepatology. 1989;9:698–703.
46. Liao X, Zhao S, Yin J, Liu L, Liang J, Jiang Y, et al. Sexual dysfunction in patients with chronic hepatitis B: Prevalence and risk factors. J Sex Med. 2022;19:207–15.
47. Burra P. Sexual dysfunction after liver transplantation. Liver Transpl. 2009;15(suppl 2):S50–6.
48. Sorrell JH, Brown JR. Sexual functioning in patients with end-stage liver disease before and after transplantation. Liver Transpl. 2006;12:1473–7.
49. Fidan C, Akdur A, Kırnap M, Selçuk H, Yıldırım S, Moray G, et al. Analysis of quality of life, depression, and sexual function in patients on the liver transplant list. Turk J Gastroenterol. 2021; 32:801–7.
50. Schomerus G, Leonhard A, Manthey J, Morris J, Neufeld M, Kilian C, et al. The stigma of alcohol-related liver disease and its impact on healthcare. J Hepatol. 2022;77:516–24.
51. Younossi ZM, AlQahtani SA, Funuyet-Salas J, Romero-Gómez M, Yilmaz Y, Keklikkiran C, et al. The impact of stigma on quality of life and liver disease burden among patients with nonalcoholic fatty liver disease. JHEP Rep. 2024;6:101066.
52. Meston CM, Derogatis LR. Validated instruments for assessing female sexual function. J Sex Marital Ther. 2002;28(suppl 1): 155–64.
53. Isidori AM, Pozza C, Esposito K, Giugliano D, Morano S, Vignozzi L, et al. Development and validation of a 6-item version of the female sexual function index (FSFI) as a diagnostic tool for female sexual dysfunction. J Sex Med. 2010;7:1139–46.
54. McGahuey CA, Gelenberg AJ, Laukes CA, Moreno FA, Delgado PL, McKnight KM, et al. The Arizona Sexual Experience Scale (ASEX): Reliability and validity. J Sex Marital Ther. 2000;26: 25–40.
55. Giraldi A, Rellini A, Pfaus JG, Bitzer J, Laan E, Jannini EA, et al. Questionnaires for assessment of female sexual dysfunction: A review and proposal for a standardized screener. J Sex Med. 2011;8:2681–706.
56. Pauls RN, Kleeman SD, Karram MM. Female sexual dysfunction: Principles of diagnosis and therapy. Obstet Gynecol Surv. 2005;60:196–205.
57. Bulletins—Gynecology ACoOaGCoP. Female sexual dysfunction: ACOG Practice Bulletin Clinical Management Guidelines for Obstetrician-Gynecologists, Number 213. Obstet Gynecol. 2019;134:e1–18.
58. Mayer M, Stief CG, Truss MC, Uckert S. Phosphodiesterase inhibitors in female sexual dysfunction. World J Urol. 2005;23: 393–7.
59. Pereira SP, O'Donohue J, Moniz C, Phillips MG, Abraha H, Buxton-Thomas M, et al. Transdermal hormone replacement therapy improves vertebral bone density in primary biliary cirrhosis: Results of a 1-year controlled trial. Aliment Pharmacol Ther. 2004;19:563–70.
60. Pajarinen JT, Karhunen PJ. Spermatogenic arrest and 'Sertoli cell-only' syndrome—Common alcohol-induced disorders of the human testis. Int J Androl. 1994;17:292–9.
61. La Vignera S, Condorelli RA, Vicari E, D'Agata R, Calogero AE. Sperm DNA damage in patients with chronic viral C hepatitis. Eur J Intern Med. 2012;23:e19–24.
62. Goldberg-Bittman L, Kitay-Cohen Y, Hadari R, Yukla M, Fejgin MD, Amiel A. Random aneuploidy in chronic hepatitis C patients. Cancer Genet Cytogenet. 2008;180:20–3.
63. Li Y, Liu L, Wang B, Chen D, Wang J. Nonalcoholic fatty liver disease and alteration in semen quality and reproductive hormones. Eur J Gastroenterol Hepatol. 2015;27:1069–73.
64. Burra P. Liver abnormalities and endocrine diseases. Best Pract Res Clin Gastroenterol. 2013;27:553–63.
65. Nolte W, Schindler CG, Figulla HR, Wuttke W, Hüfner M, Hartmann H, et al. Increase of serum estradiol in cirrhotic men treated by transjugular intrahepatic portosystemic stent shunt. J Hepatol. 2001;34:818–24.
66. Horn MM, Ramos AR, Winkelmann L, Matte US, Goldani HA, Silveira TR. Seminiferous epithelium of rats with food restriction and carbon tetrachloride-induced cirrhosis. Int Braz J Urol. 2006; 32:94–9; discussion 9.
67. Castilla-Cortazar I, Diez N, Garcia-Fernandez M, Puche JE, Diez-Caballero F, Quiroga J, et al. Hematotesticular barrier is altered from early stages of liver cirrhosis: Effect of insulin-like growth factor 1. World J Gastroenterol. 2004;10:2529–34.
68. Sarkar M, Lai JC, Sawinski D, Zeigler TE, Cedars M, Forde KA. Sex hormone levels by presence and severity of cirrhosis in women with chronic hepatitis C virus infection. J Viral Hepat. 2019;26:258–62.
69. Fan D, Liu L, Xia Q, Wang W, Wu S, Tian G, et al. Female alcohol consumption and fecundability: A systematic review and dose-response meta-analysis. Sci Rep. 2017;7:13815.
70. Westbrook RH, Yeoman AD, Kriese S, Heneghan MA. Outcomes of pregnancy in women with autoimmune hepatitis. J Autoimmun. 2012;38:J239–44.
71. Wellge BE, Sterneck M, Teufel A, Rust C, Franke A, Schreiber S, et al. Pregnancy in primary sclerosing cholangitis. Gut. 2011;60: 1117–21.
72. Sarkar M, Brady CW, Fleckenstein J, Forde KA, Khungar V, Molleston JP, et al. Reproductive health and liver disease: Practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;73:318–65.

73. Mass K, Quint EH, Punch MR, Merion RM. Gynecological and reproductive function after liver transplantation. Transplantation. 1996;62:476–9.
74. Flemming JA, Mullin M, Lu J, Sarkar MA, Djerboua M, Velez MP, et al. Outcomes of pregnant women with cirrhosis and their infants in a population-based study. Gastroenterology. 2020;159:1752–62.e10.
75. Funk AL, Lu Y, Yoshida K, Zhao T, Boucheron P, van Holten J, et al. Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: A systematic review and meta-analysis. Lancet Infect Dis. 2021;21:70–84.
76. Freriksen JJM, van Seyen M, Judd A, Gibb DM, Collins IJ, Greupink R, et al. Review article: Direct-acting antivirals for the treatment of HCV during pregnancy and lactation—Implications for maternal dosing, foetal exposure, and safety for mother and child. Aliment Pharmacol Ther. 2019;50:738–50.
77. Karampatou A, Han X, Kondili LA, Taliani G, Ciancio A, Morisco F, et al. Corrigendum to "Premature ovarian senescence and a high miscarriage rate impair fertility in women with HCV" [*J Hepatol* 68 (2018) 33-41]. J Hepatol. 2018;68:867.
78. Rahim MN, Theocharidou E, Yen Lau KG, Ahmed R, Marattukalam F, Long L, et al. Safety and efficacy of in vitro fertilisation in patients with chronic liver disease and liver transplantation recipients. J Hepatol. 2021;74:1407–15.
79. Lee JD, Gounko D, Lee JA, Mukherjee T, Kushner T. Assisted reproductive technology treatment outcomes in women with liver disease. Am J Gastroenterol. 2023;118:2184–90.
80. Sciarrone SS, Ferrarese A, Bizzaro D, Volpato S, Donato FM, Invernizzi F, et al. Safe pregnancy after liver transplantation: Evidence from a multicenter Italian collaborative study. Dig Liver Dis. 2022;54:669–75.
81. Parolin MB, Coelho JC, Urbanetz AA, Pampuch M. [Contraception and pregnancy after liver transplantation: An update overview]. Arq Gastroenterol. 2009;46:154–8.
82. Bravata DM, Olkin I, Barnato AE, Keeffe EB, Owens DK. Health-related quality of life after liver transplantation: A meta-analysis. Liver Transpl Surg. 1999;5:318–31.
83. Burra P, Germani G, Masier A, De Martin E, Gambato M, Salonia A, et al. Sexual dysfunction in chronic liver disease: Is liver transplantation an effective cure? Transplantation. 2010;89:1425–9.
84. Gomez-Lobo V, Burgansky A, Kim-Schluger L, Berkowitz R. Gynecologic symptoms and sexual function before and after liver transplantation. J Reprod Med. 2006;51:457–62.
85. Park ES, Villanueva CA, Viers BR, Siref AB, Feloney MP. Assessment of sexual dysfunction and sexually related personal distress in patients who have undergone orthotopic liver transplantation for end-stage liver disease. J Sex Med. 2011;8:2292–8.
86. Klein J, Tran SN, Mentha-Dugerdil A, Giostra E, Majno P, Morard I, et al. Assessment of sexual function and conjugal satisfaction prior to and after liver transplantation. Ann Transplant. 2013;18:136–45.
87. Karabulut N, Koraş K, Gürçayır D. Effects of liver transplantation on sexual function and quality of life. Psychol Health Med. 2022;27:1532–43.
88. Ho JK, Ko HH, Schaeffer DF, Erb SR, Wong C, Buczkowski AK, et al. Sexual health after orthotopic liver transplantation. Liver Transpl. 2006;12:1478–84.
89. Jabiry-Zieniewicz Z, Kaminski P, Bobrowska K, Pietrzak B, Wielgos M, Smoter P, et al. Menstrual function in female liver transplant recipients of reproductive age. Transplant Proc. 2009;41:1735–9.
90. Baccaro LF, Boin IeF, Costa-Paiva L, Pinto-Neto AM. Quality of life and menopausal symptoms in women with liver transplants. Rev Bras Ginecol Obstet. 2013;35:103–10.
91. Prem AR, Punekar SV, Kalpana M, Kelkar AR, Acharya VN. Male reproductive function in uraemia: Efficacy of haemodialysis and renal transplantation. Br J Urol. 1996;78:635–8.
92. Madersbacher S, Grünberger T, Maier U. Andrological status before and after liver transplantation. J Urol. 1994;151:1251–4.
93. Foresta C, Schipilliti M, Ciarleglio FA, Lenzi A, D'Amico D. Male hypogonadism in cirrhosis and after liver transplantation. J Endocrinol Invest. 2008;31:470–8.
94. Huyghe E, Zairi A, Nohra J, Kamar N, Plante P, Rostaing L. Gonadal impact of target of rapamycin inhibitors (sirolimus and everolimus) in male patients: An overview. Transpl Int. 2007;20:305–11.
95. Midtvedt K, Bergan S, Reisæter AV, Vikse BE, Åsberg A. Exposure to mycophenolate and fatherhood. Transplantation. 2017;101:e214–7.

How to cite this article: Ferrarese A, Hurtado Díaz de León I, Tapper EB, Burra P. Sexual health and function in liver disease. Hepatol Commun. 2025;9:e0691. https://doi.org/10.1097/HC9.0000000000000691