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Metabolic bariatric surgery, alcohol misuse and liver cirrhosis: a narrative review

Matthew L. Basa[1,2], Danielle S. Cha[2,3,4,5], David P. Mitchell[1,2], Daniel L. Chan[1,2,6]

[1]Department of General Surgery, Royal Brisbane and Women's Hospital, Herston 4029, Queensland, Australia.
[2]School of Clinical Medicine - Royal Brisbane Clinical Unit, University of Queensland, Herston 4006, Queensland, Australia.
[3]Department of Psychiatry, Royal Brisbane and Women's Hospital, Queensland Health, Herston 4006, Queensland, Australia.
[4]Brain and Cognition Foundation, Toronto, ON M5S 1M2, Canada.
[5]Mood Disorders Psychopharmacology Department, Toronto Western Hospital, University Health Network, Toronto, ON M5T 2S8, Canada.
[6]St George and Sutherland Clinical School, Faculty of Medicine and Health, Kogarah 2217, New South Wales, Australia.

Correspondence to: Dr. Daniel L. Chan, Department of General Surgery, Level 4, James Mayne Building, Royal Brisbane and Women's Hospital, Herston 4029, Queensland, Australia. E-mail: daniel.l.chan@unsw.edu.au

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Abstract

Bariatric surgery and liver cirrhosis have considerable overlap. Bariatric procedures intend to reduce metabolic dysfunction-associated steatotic liver disease (MASLD); however, these procedures are thought to increase the propensity for alcohol misuse. This may predispose the bariatric surgical patient to a new form of liver insult in the postoperative period. This review explores the complex relationship between obesity and alcohol misuse in the context of the bariatric surgical patient. There is evidence to support the safety of bariatric procedures in compensated cirrhotic patients, with an improvement of liver function and architecture. However, data suggest that after a two-year period, these patients exhibit an increased propensity for alcohol misuse postoperatively, particularly after sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) procedures. A paucity of evidence exists with respect to alcohol-induced liver dysfunction, or MASLD and increased alcohol intake (MetALD) in the post-bariatric surgery patient. This review aims to provide an overview of the current evidence and offer recommendations for further robust studies.

Keywords: Bariatric surgery, metabolic surgery, steatohepatitis, MASH, MetALD, cirrhosis, alcohol, obesity

INTRODUCTION

Metabolic bariatric surgery (MBS) has emerged as a significant tool to counteract the growing epidemic of obesity and its accompanying multisystem organ pathologies, typically defined as metabolic syndrome. A commonly impacted organ in metabolic syndrome is the liver, with a spectrum of steatotic liver disease (SLD). Metabolic dysfunction-associated steatotic liver disease (MASLD) may progress to metabolic dysfunction-associated steatohepatitis (MASH), which can result in fibrosis with varying degrees of cirrhosis.

This review recognises the recent nomenclature changes from the multinational liver society statement (2023) on new fatty liver disease[1]. In accordance with the new nomenclature, SLD is the overarching term encompassing various aetiologies of steatosis. Non-alcoholic fatty liver disease (NAFLD) is replaced with MASLD, and additionally, non-alcoholic steatohepatitis (NASH) is replaced with MASH. Outside of pure MASLD are the new term MSALD and increased alcoholic intake (MetALD) (140 g/week for females and 210 g/week for males) [Figure 1]. The non-metabolic dysfunctions associated with SLD are not within the scope of this review.

MBS aims to reduce this hepatic injury; however, the post-surgical patient is predicted to have an increased risk of alcohol misuse, and hence, surgery may predispose them to an alternative form of liver insult[2]. Parallel to obesity, alcohol misuse has remained prevalent in society and difficult to manage and treat. Obesity and alcohol misuse share demographic and behavioural similarities, compounding on the hypothesised increased alcohol sensitivity in the post-bariatric patient.

With an array of weight loss surgery methods, the psychosocial complexity of obesity, and the potential risks of bariatric procedures, a concise review of the existing literature is required from a holistic viewpoint to assess the overall impact on liver function. Given the significant overlap between bariatric surgery and liver disease, this narrative review aims to inform clinicians, particularly bariatric surgeons and physicians, of the current literature on this topic, to better inform patient selection, interventions, and follow-up when considering MBS.

METHODS

We prepared a narrative review article by searching multiple electronic databases (PubMed, MEDLINE, Google Scholar, Ovid, Scopus, and Web of Science). The following search words were used: “cirrhosis”, “obesity”, “alcohol”, “alcohol use disorder”, “liver”, “addiction”, alone and in combination with “Roux-en-Y”, “bariatric”, “sleeve-gastrectomy”, “metabolic surgery”, “obesity surgery”, and “gastric bypass”. An example of the PubMed search strategy is in Supplementary Figure 1. All papers retrieved via the search terms were scanned by title and abstract for applicability to the study. Those deemed relevant had their full texts evaluated. Articles were selected at the author’s discretion based on robust methodology and resistance to bias. Articles were excluded if the full text was unavailable, if they were not in the English language, or if they were published before 2010 (exclusion criteria). Additionally, supplementary references among articles considered in the first search were selectively analysed.

DISCUSSION

Prevalence and cost of obesity, alcohol and cirrhosis

Obesity

Obesity implies a stressed physiological state that is detrimental to normal health, primarily based on body mass index (BMI), despite some limitations of this measure[3]. Although obesity has garnered significant social and financial attention, its prevalence continues to rise, demonstrating the complexity of this health

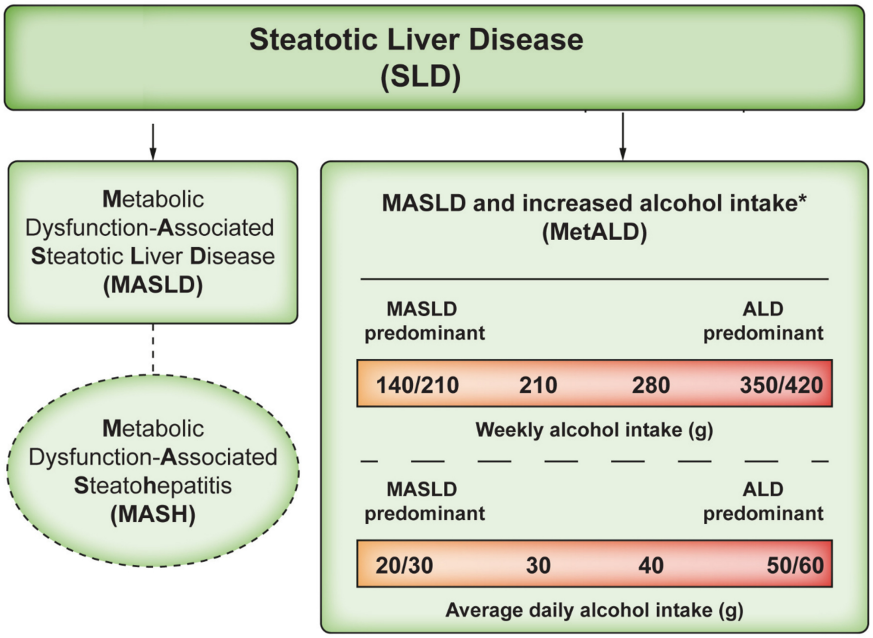

Figure 1. SLD and the sub-categories associated with metabolic dysfunction. Adapted from Rinella *et al.*[1]. SLD: Steatotic liver disease.

issue[4,5]. The World Health Organisation (WHO) has declared obesity an epidemic of our generation, with very few countries being spared[6].

Obesity is the second most preventable cause of death worldwide, following smoking[7,8]. The direct costs of treating obesity can be 70%-230% higher per patient compared to other conditions, with costs increasing as the severity of obesity rises[9,10]. Additionally, indirect costs such as early retirement, sickness absence, premature death due to comorbidities, and loss of productivity have been shown through meta-analysis to contribute to over 50% of the total costs of obesity[9,10].

Metabolic syndrome, resulting from obesity, is a diagnosed state based on waist circumference, triglyceride levels, high-density lipoprotein (HDL) levels, fasting glucose levels, and blood pressure targets, specified in Table 1[11]. While these measures are seemingly innocuous, they translate to a significant impact on numerous organ systems, primarily the cardiovascular system, the liver and kidneys, as well as predisposing to Type 2 diabetes mellitus (T2DM)[12,13]. Although there is a significant association between obesity and metabolic syndrome, the relationship is complex, exemplified by the presence of metabolically healthy obesity[14]. Furthermore, the metabolic syndrome criteria have limitations compared to other cardiometabolic risk stratification methods and BMI variability may be more important than standalone BMI[14,15].

Alcohol misuse

Alcohol misuse, like obesity, is extremely prevalent in most cultures and is estimated to account for five percent of the world's burden of disease[16,17]. On average, two percent of a country's population will have misuse of alcohol, and this figure doubles when excluding those that abstain[18]. Worldwide, the average yearly consumption of alcohol was 19.4 litres of pure alcohol for males and 7.0 litres for females, corresponding with 4.2 and 1.5 standard drinks per day, and has remained unchanged over several decades[17]. Mirroring obesity, the classification of alcohol use disorder (AUD) is graded into mild,

Table 1. Diagnostic criteria of metabolic syndrome (Adapted from the WHO)

Parameter	Measure
Waist circumference	> 89 cm in females, > 102 cm in males
Triglyceride level	> 150 mg/dL or 1.7 mmol/L
HDL cholesterol level	< 50 mg/dL or 1.3 mmol/L in females < 40 mg/dL or 1.04 mmol/L in males
Blood pressure	> 130/85 mmHg
Fasting blood sugar	> 100 mg/dL or 5.6 mmol/L

WHO: World Health Organisation; HDL: high-density lipoprotein.

moderate, and severe classes in the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5th edition, with increasing class corresponding to increased cost and burden of disease[19].

The direct cost of AUD to the health care system represents approximately 12% of the total costs, proportionally less than those of obesity[20]. The majority of expenses are indirect[20]. Although variation between nations and studies was noted, 20% of the costs are attributed to criminal justice-related expenditures, 40% are due to loss of productivity, and 25% are related solely to road vehicle accidents[21-25]. These figures do not account for the collateral damage to those closely associated with someone who has AUD, severely underestimating costs and overall impact.

With respect to mortality, the WHO attributes alcohol misuse to approximately five percent of deaths worldwide, due to both behavioural and direct health consequences[26]. Specifically, alcohol misuse was associated with 39% of road accident fatalities worldwide, with males being heavily over-represented[27]. Seven percent of cancer deaths were attributed to alcohol, and alcohol misuse was deemed to reduce lifespan on average by 3 years[28,29]. Additionally, alcohol misuse is responsible for an estimated 48.4% of liver cirrhosis-related deaths worldwide[30].

Cirrhosis

The prevalence of cirrhosis worldwide was 1.4% in 2017 and accounted for 2.4% of deaths globally[31]. MASLD and alcoholic cirrhosis were the main aetiologies in developed nations, which are the primary consumers of MBS, accounting for approximately 30% of all cirrhosis cases[31-33]. Research on cirrhosis aetiology highlights an increasing incidence of alcoholic and MASLD-induced cirrhosis, with a corresponding decrease in hepatitis-related cirrhosis over the past several decades. If current trends continue, alcoholic cirrhosis and MASLD-associated cirrhosis will become even more prominent global health issues. This trend has been recognised by the recent addition of MetALD in the international literature to recognise the combination of these effects.

The economic impact of cirrhosis in the hospital setting is increasing, with the cost of a cirrhotic patient being 30% more than 8 years prior[34]. Most of the direct healthcare-associated costs are related to compensated cirrhotic patients, due to the higher prevalence, ranging from 1.08 to 1.3 times the cost of an average admission[34,35]. Although less frequent, decompensated cirrhotic patients cost exceptionally more (1.2-1.7 times) than the standard hospital patient, attributed to mechanical ventilation, procedures, length of stay, renal pathologies, and infectious complications[34,36].

In patients with alcohol-induced liver cirrhosis, liver-related mortality is responsible for most fatalities, with the 5-year risk of death being 25.8%[37-40]. Beyond 5 years, extrahepatic causes such as cancer and cardiovascular disease were more common[37,39]. Similar trends are followed with MASLD, with liver-related

mortality accounting for close to 50% of deaths in this patient population, with cardiovascular and extrahepatic cancer impacting later in the disease process[38,40].

Addiction model of obesity and alcohol dependence

The role of addiction in obesity warrants consideration when evaluating the risks and benefits of surgical intervention for patients. More specifically, it is plausible that clinical subpopulations of individuals with obesity have a propensity for addiction based on underlying neural substrates and/or circuits that reinforce the reward network. In this clinical subpopulation, identifying behavioural traits that exist in both individuals with obesity and individuals with AUD would support a more standardised approach to preoperative screening and postoperative care[41-44]. Available evidence suggests that the prevalence of metabolic disorders (e.g., obesity, metabolic syndrome, insulin resistance, *etc.*) is associated with an aging population in an obesogenic environment, with data indicating that higher levels of education correlated to significantly better metabolic health compared to lower levels of education[45]. Moreover, it is increasingly being recognised that the relationship between depressive symptomatology and metabolic disturbance is intricately linked, with reports indicating that older adults identified as being "metabolically unhealthy" are at increased risk of experiencing moderate-to-severe depressive symptoms, affecting females disproportionately more than males[46,47]. Taken together, it should be recognized that metabolic syndrome exhibits significant heterogeneity, and that sex and depressive disorders are major risk modifiers that can also affect the risk of progressive liver disease owing to variable co-factors[48-50].

At present, excessive oral intake - as it relates to obesity - is not recognised as an addiction in the DSM-5 or the WHO; however, many similarities have been drawn between excessive oral intake in individuals with obesity and substance use disorder (SUD)[51]. The criteria for diagnosing SUD include impaired control, social impairment, risky use, and physiological criteria [Table 2]. Given the data suggesting these similarities, this review considers these factors when exploring the relationship between excessive oral intake and the possibility that obesity may be linked to neural substrates that increase susceptibility to addiction[52].

A barrier surrounding the concept of food addiction resulting in obesity is that eating is an unavoidable behaviour, unlike that of drug addiction, and hence, from some aspects, it may not be appropriately assessed. For example, craving food when hungry - a natural response evolutionally developed - does not constitute an addiction alone. Another common example is spending time in restaurants, which could be considered spending excessive time getting and using a substance, but is a common part of healthy social culture. With consideration of these aspects, food addiction caused by over-eating still deserves consideration, as physiological changes primarily induced by altered hormone levels resulting in increased hunger, do not account entirely for obesity levels[53-57]. These factors include mirroring others, automatic responses to stimuli (such as watching sports games), lack of education on portion size and sound nutritional advice, priming (use of marketing to enhance the purchasing of unhealthy foods), and emotional situations emotions (when low moods are experienced or to serve as an outlet during stressful situations)[56]. Simply labelling a meal as a "snack" can impact the amount of caloric intake, as can environmental and situational cues such as utensils and plating[54,55]. Furthermore, when individuals lose weight, hormones implicated in appetence such as leptin, ghrelin, peptide YY, GLP-1, and many others revert to a normal level, with an associated reset of hunger and appetite, yet despite this, many return to obese levels, demonstrating that satiety hormones only make up part of the equation[58].

Impaired ability to control caloric intake is common in individuals with obesity[59]. Eating for longer (or more than intended) is universally reported, as well as failed attempts to eat in moderation[52,60]. Individuals

Table 2. SUD diagnostic criteria (adapted from DSM - 5th Ed.)

Symptom (one point each)	Parameter
1. Taking the substance in larger amounts or for longer than intended	Impaired control
2. Wanting to cut down or stop using the substance but unable to	
3. Spending excessive time getting, using, or recovering from substance use	
4. Subjective cravings	
5. Failure to fulfill duties (such as work or school) because of substance use	Social impairment
6. Relationship problems due to continued substance use	
7. Giving up important activities due to substance use	
8. Repeated substance use despite the risk or dangers to oneself or others	Risky use
9. Continued substance use despite associated physical and psychological problems it causes	
10. Needing more of the substance to get the same effect	Physiological criteria
11. Development of withdrawal symptoms, alleviated by taking more of the substance	

Generic criteria applied to any substance, such as alcohol. SUD: Substance use disorder; DSM: Diagnostic and Statistical Manual of Mental Disorders.

with obesity tend to reflect and think about food more often than those with a lower BMI, and experience physical or emotional distress after over-eating based on feelings of guilt and regret[61,62]. Those with overeating tendencies have higher measures of impulsivity and highly palatable foods have been shown to be addictive with a heightened sense of reward sensation, like the effect of alcohol[52,63].

Dopamine release is paramount in AUD and, with respect to food, is higher in meals containing substantial amounts of sugar and fat, although released at a substantially lower rate than that of substances of abuse[41,64,65]. Individuals with obesity have a reported decreased sense of self-worth and hence may consume food to induce a dopamine release to mitigate negative emotions[66]. An alternate hypothesis is that individuals with obesity have lower levels of dopamine receptors, leading them to eat more in an attempt to restore dopamine signalling to a normal level[65]. Food cravings and excessive oral intake, like craving alcohol, support the notion that these behaviours share underlying pathophysiological and psychological processes[67]. Moreover, food cravings have been associated with higher BMI, emphasising the powerful effect they have on individuals and their food-related behaviour (i.e., excessive oral intake despite increasing BMI)[68].

With respect to social impairment, patients with obesity have significantly lower social functioning, inversely correlating with BMI. This has been attributed to poor self-worth, self-consciousness, bullying and weight stigmatisation impacting relationships[69,70].

Body image has increasingly become a topic of discussion with disparate perspectives and opinions on what is considered socially acceptable. The biopsychosocial impact of this on individuals with obesity is complex and multifactorial, with data suggesting that individuals with obesity recognise their condition is causing them harm and reducing their life expectancy, but usually to an underestimated level[71,72]. Weight misconception can account for a lack of awareness in some individuals; however, more people overestimated their weight and BMI, and their perception was correlated with their perceived lifestyle rather than actual weight[73].

Tolerance is a feature of a substance's misuse risk, and in obesity, it is primarily extrapolated from the increased consumption of similar foods over time in the same individual for the same sense of pleasure[52,74]. Withdrawal symptoms upon abstinence from sugar have been found in animal models and qualitative

studies in humans, with symptoms of fatigue, anxiety, and agitation being reported[75,76].

The foregoing observations suggest that the similarities between the experience of food cravings and activation of the reward pathway in individuals with obesity are similar to those with addiction to other substances (e.g., alcohol) and may contribute to what is termed "addiction transfer" - when an individual suffering from one addiction shifts to another[77]. In keeping with this hypothesis, available evidence indicates that patients with AUD have a higher propensity for consuming sweet foods, suggesting a common pathway[77]. Many individuals in early recovery from SUD have increased cravings for "addictive" foods high in sugar, fat, and salt[78,79]. Moreover, individuals with disordered eating tendencies have reported higher rates of AUD. However, it should be noted that these participants were formally diagnosed with binge-purge disordered eating, which limits the generalisability of the findings to individuals with obesity alone[80].

While excessive oral intake resulting in obesity is not formally identified as an addiction, a significant overlap exists between the patient with obesity and the patient with alcohol misuse from a biopsychosocial viewpoint. Therefore, it warrants awareness and is paramount in identifying those with an increased proclivity towards alcohol use post MBS, with the goal of prevention.

MBS types and indications

Sleeve gastrectomy (SG) is the most common metabolic bariatric procedure worldwide, representing about 60.4% of bariatric operations, followed by Roux-en-Y gastric bypass (RYGB) (28.8%) and one-anastomosis gastric bypass (OAGB) (4.1%) according to the international bariatric registry[81]. This study will primarily focus on RYGB and SG patients, although it is acknowledged that there is a greater emphasis on RYGB studies given the procedural trends mentioned and temporal lag of liver cirrhosis development.

An exhaustive list of benefits and supporting research for MBS is outside the scope of this review. Long-term durability of weight loss, more than ten years after surgery, has been consistently demonstrated[82-84]. The resulting improvement in obesity-related comorbidities such as cardiovascular disease, stroke, insulin insensitivity, and some specific cancers are repeatably demonstrated with tangible morbidity and mortality benefits[85-90]. The benefits and detriments of bariatric surgery on the liver in both an acute and chronic setting will be discussed in depth below, with the indications for bariatric surgery in adult patients being summarised in Table 3[91].

As with any procedure, perioperative risk must be assessed in the context of the patient's physiological state[91]. In patients with liver cirrhosis, the risk is assessed using a combination of Child-Pugh and Model for End-Stage Liver Disease (MELD) scores[92]. These scores do not capture the long-term benefits of performing bariatric surgery on the patient with metabolic syndrome, nor factor in the propensity for AUD in years post-procedure. Specific contraindications universally accepted by bariatric surgical societies worldwide are untreated psychiatric conditions, inability to lose weight even temporarily without surgical intervention, excessive alcohol use, and illicit drug use[91,93]. With a specific focus on alcohol misuse, there is a propensity of the population to underreport problematic drinking and therefore the postoperative risks may not fully be accounted for[94,95].

Alcohol misuse and MBS

With the global burden of obesity, unwavering levels of alcohol consumption and the increasing accessibility of metabolic bariatric procedures, the propensity for alcohol misuse in patients undergoing such surgery requires further evaluation.

Table 3. A summary of the current indications for MBS relating to BMI and secondary requirements, which may include metabolic diseases such as SLD

BMI	Secondary requirements
> 27.5 kg/m^2	Asian populations
30-34.9 kg/m^2	Presence of T2DM OR Presence of metabolic disease and unable to achieve sustainable or durable weight loss or comorbidity improvement with non-surgical methods
> 35 kg/m^2	Regardless of the presence or absence of metabolic-related disease

MBS: Metabolic bariatric surgery; BMI: body mass index; SLD: steatotic liver disease; T2DM: Type 2 diabetes mellitus; OR: odds ratio.

RYGB

The correlation between the RYGB procedure and AUD has been well explored, reflecting the popularity of the procedure in previous decades. Cohort studies have shown that AUD prevalence did not change significantly in the early postoperative period but was significantly increased at 2 years[2]. Multiple other large-scale, statistically significant studies support the viewpoint that the RYGB procedure is correlated with AUD[96-100]. There was no significant association between gastric banding (GB) and AUD, but these higher-powered studies similarly lacked an SG cohort. Multiple smaller studies with a focus on RYGB demonstrated a strong correlation in a wide range of population subsets, with up to a 2.2-fold to 7-fold increase in risk of AUD[101-104]. Interestingly, some cohort studies examined this relationship within the initial 2-year postoperative period and did not find any correlation[105,106]. When examined from an alternate perspective, in a cohort of AUD patients, close to five percent had previously undergone a RYGB procedure[107].

The physiological effect that alcohol has on patients undergoing MBS has been explored primarily through the administration of alcohol and analysis of blood alcohol levels at different time periods. In a comparison of 12 RYGB patients versus 12 controls, the RYGB group demonstrated an increased max blood alcohol concentration and a lower median time to peak concentration[108]. This finding has been confirmed by additional findings of a doubling of blood alcohol concentration and an increased time for the blood alcohol level to return to zero[109]. Moreover, the correlation became more pronounced the longer the duration since surgery in RYGB patients[110-112]. A recent study that reproduced the increase in blood alcohol concentration in RYGB patients found the median time to peak concentration was 6 *vs.* 42 min in non-surgical patients[113]. This indicates a hazardous combination of a more rapid increase in blood alcohol concentration, prolonged elevated levels, and increased overall alcohol absorption, with the effect becoming more pronounced the longer it has been since RYGB.

SG

In an examination of over 5,000 patients (4,718 SG and 1,006 RYGB), these trends were reproduced with a decrease in AUD 1 year postoperatively and a rebound increase of 4.3% for both SG and RYGB at 2 years following surgery. This indicates that SG and RYGB may have a similar correlation to AUD[114]. A large database study also demonstrated this association with AUD and RYGB [hazard ratio (HR) 1.86], and following SG (HR 1.35)[115]. No association was reported for GB. This finding supports the notion that the most common metabolic bariatric procedures worldwide are predisposing patients to AUD risk.

The concerning blood alcohol concentration trends in RYGB may be mirrored with SG, with an increased concentration and a longer time of elevation, correlating to an increased propensity for alcohol misuse[116]. In a mixed group of RYGB patients, SG patients, and non-surgical controls, blood alcohol concentration increased two-fold in both SG and RYGB procedures[117]. This group performed a similar study with a mixed

cohort of patients undergoing RYGB, SG, and GB, with results showing increased blood alcohol concentrations in RYGB and SG but not in GB[118].

Certainly, it can be postulated that the differences in the anatomy of a SG compared to a RYGB, such as the preservation of the gastric pylorus sphincter mechanism in SG, may be somewhat protective. Consistent with this hypothesis, there are trials that demonstrate no increase in blood alcohol concentration or time to sober levels following SG[119,120]. When considering the heterogeneity and limitations of the available literature, SG likely has an association with AUD that is less pronounced than RYGB.

Qualitative reasons for misuse

Given the complex behavioural element of overeating and the propensity for alcohol misuse in the postoperative patient following MBS, understanding why alcohol consumption increases may highlight a specific screening method or follow-up intervention to reduce harm. The perioperative examination of psychological factors in patients undergoing MBS has reported higher rates of depression, anxiety, food addiction symptoms, and lower self-worth[121]. In a qualitative cohort study of RYGB patients who had developed AUD, reasons for increased postoperative alcohol use included replacement of food as a coping mechanism, increased socialisation due to their new weight loss, replacement of the soothing mechanism of food, and having an increased subjective sensitivity to alcohol[122]. Another study on post-RYGB patients also found that unresolved psychological issues were managed through eating. However, as eating was physically more difficult, alcohol was used to fill the void[123].

Perhaps this is reflected in the notion of postoperative bariatric surgery patients being at increased risk of psychological harm, reporting substantially increased rates of self-harm and even suicide[124]. Unfortunately, patient education concerning alcohol consumption has also been insufficient and although the patients may recall alcohol use information, they are often unaware of the increased risk of dependence and misuse postoperatively[125]. This highlights that alcohol use education well into the postoperative follow-up period is an area for improvement.

Anatomical factors related to alcohol absorption

Anatomical and hormonal factors affecting the absorption of medications in patients following MBS are well-documented in the literature. With respect to alcohol, gastric emptying has a significant influence on its absorption, and hence, extrapolation can be made when this specific parameter is augmented, as in RYGB and SG patients[126]. The effect of gastric emptying and its effect on alcohol absorption has been well supported for many decades[127]. It is known that SG accelerates gastric emptying and small bowel transit with a concurrent delay of caecal filling due to ileocecal competency, resulting in a potential early and prolonged contact with ingested alcohol, which may explain elevated alcohol concentration peaks and prolonged blood levels of alcohol in the previously listed experimental studies[128]. A more pronounced process is thought to occur in RYGB given the lack of sphincter mechanism associated with the gastroenterostomy, and theoretically, this rapid gastric emptying should also translate to OAGB, notwithstanding the differences in gastric pouch formation[129]. A complex set of hormonal changes occur in patients post MBS, through the mechanism of weight loss via "resetting" of the homeostatic thermostat and through anatomical changes unrelated to weight loss[130]. However, those found to have lower weight loss post-bariatric procedures have been found to have a reduction in satiety-associated hormones[131]. The confounding factor is that those with higher weight loss and lower BMIs tend to have higher levels of circulating hormones, and hence, simply attributing weight loss to one element is erogenous[58].

Sex differences

Sex differences are recognised in AUD, obesity, and uptake in MBS[132,133]. Females are both more likely to suffer from obesity and MetALD, despite lower levels of alcohol exposure compared to male counterparts[133]. These differences have been attributed to several sex differences, including reduced total body weight and body water leading to reduced volume of alcohol distribution; reduced alcohol dehydrogenase and delayed gastric emptying in first-pass metabolism leading to increased bioavailability; and increased estrogen levels and estrogen-sensitized Kupffer cells increasing proinflammatory cytokines[133].

Although the extent of the sex differences varies between cultures, females are more likely than males to seek various treatment interventions, including MBS, for both AUD and obesity[132,134]. Concerningly, females are not only at higher risk of MetALD, but also at higher risk of AUD and liver cirrhosis following MBS. A retrospective study compared 41 patients with a previous RYGB to 122 non-surgical controls who were seeking treatment for AUD; females were over-represented in the RYGB group (n = 29, 70.7%), and more likely to meet the AUD criteria at an earlier age (19.1 *vs.* 25.0 years old, $P < 0.05$)[107]. Another retrospective study found female patients following MBS had an increased risk of both AUD [HR 1.98 (95%CI 1.93-2.04)] and liver cirrhosis [HR 2.1 (95%CI: 1.79-2.41)] compared to those without surgery[115].

Alcohol use risk levels

The difficulties surrounding which patients are more prone to AUD post-surgery can be attributed to the widespread use of alcohol in most societies. The threshold for detecting which post-MBS patients were more at risk was determined to be a frequency of ≥ 2 drinking sessions per month and ≥ 30 g/drinking day, providing the highest combined sensitivity and specificity cut-off[135]. This is markedly lower compared to the 100 g/week low-risk bracket of all-cause mortality demonstrated in the general population[136].

Furthermore, a recent 1:1 propensity-score matched cross-sectional study of 537,757 patients compared those who underwent MBS with those who had other abdominal surgeries, to examine the association between bariatric surgery, AUD, liver cirrhosis, and psychiatric disorders associated with AUD. The bariatric surgery group had an increased risk of AUD [odds ratio (OR): 1.9; 95%CI: 1.85-1.95], cirrhosis (OR 1.39; 95%CI: 1.37-1.42), and psychiatric disorders associated with AUD (OR 3.59; 95%CI: 3.37-3.84)[137].

The available evidence supports that RYGB and SG procedures correlate with an increased risk of AUD postoperatively. The variability in patients, surgical approach, sampling methods and timings compound the heterogeneity across the current literature.

MBS, the pre-cirrhotic and cirrhotic liver

With the presence of obesity and alcohol use prominent in most societies, evaluation of MBS on the cirrhotic liver is paramount, due to the anticipated increased risk of adverse outcomes. The Global Burden of Disease Collaborators showed a significant increase in MASH-related liver disease deaths and an increase in the progression from MASH to cirrhosis in the past decade, while other causes of death from cirrhosis are mostly decreasing[31,33]. Alcohol-related cirrhosis mortality increased in European and Asian countries, and it is important to consider this as a future element of potential liver insult in this patient cohort[138].

Risk and prevalence

The risk of major adverse liver outcomes following SG and RYGB was lower, with an adjusted absolute 10-year risk difference of 12.4% compared to non-surgical control[139]. This supports that, overall, bariatric surgery results in gross risk reduction in liver mortality. If alcohol use were mitigated, this benefit would be

more pronounced.

With respect to patients with pre-cirrhotic and cirrhotic liver disease, detection is paramount to mitigate or prepare for increased risk of complications. Routine intraoperative liver biopsies during SG and RYGB have shown that 66% of patients had MASLD, 34% MASH, and 31% liver fibrosis, with 14% of these being advanced fibrosis at the time of surgery[140]. This proportion increased to 83% MASLD and 4% cirrhosis in a population with a macroscopically abnormal liver[141].

Risk of MBS in the cirrhotic and pre-cirrhotic patient

As cirrhotic patients, by definition, have irreversible liver damage, we hypothesise that very few bariatric surgeons would be willing to undertake the risk of an operation to preserve liver function, unless there is strong supporting evidence[142]. The following studies represent a heterogeneous population sample with respect to procedure type, and hence are discussed together.

A US nationwide database study examined outcomes of MBS in decompensated cirrhotic, compensated cirrhotic and non-cirrhotic patients and demonstrated significantly increased mortality rates (16.3% *vs.* 0.9% *vs.* 0.3%, $P = 0.002$)[143]. Another US database study of 558,017 patient admissions again demonstrated similar mortality rates between compensated liver cirrhosis patients and non-cirrhotic patients; however, decompensated cirrhosis patients had a significantly higher risk of mortality (adjusted OR of 85.8)[144]. These larger studies suggest that compensated cirrhotic patients can undergo MBS without a significant increase in perioperative mortality. A further study of SG patients in a small pre-liver transplant patient group also demonstrated no increase in adverse events[145].

Multiple other studies have stratified patients based on the severity of their liver cirrhosis. When evaluating patients with Child-Pugh A cirrhosis undergoing either SG or RYGB, there appears to be an increased risk of complications compared to non-cirrhotic patients[146-148]. Perhaps of greatest concern is the risk of inducing decompensated cirrhosis and liver failure, which has been reported to occur between 6 months to 17 years following surgery[149-151].

When evaluating longer-term outcomes of cirrhotic patients, the results are mixed. Studies with a median follow-up of 4-5 years following bariatric surgery (either SG or RYGB) demonstrated an increase in overall complications but significantly improved MELD scores, which exemplifies the balance of risk and reward in these patients[152,153].

When specifically evaluating cirrhotic patients with or without portal hypertension who underwent a SG, there have been few reported complications but an overall dramatic improvement in liver structure when re-evaluated on ultrasound[154,155].

This evidence is consistent with the meta-analysis on the safety of bariatric procedures in liver cirrhosis patients, reporting an overall mortality rate of 1.3%, with the rate of mortality in compensated cirrhosis being 0.9% and decompensated cirrhosis reported as 18.2%[156]. Certainly, it is recognised that the available evidence in patients with cirrhosis is limited in scope, often a single-centre experience or lacking control cohorts.

The outcome of metabolic bariatric procedures on the liver

The improvement of MASLD, MASH, fibrosis, and cirrhosis have been well targeted in the literature across a wide range of geographical centres, surgical techniques, and research methodologies. The effectiveness of

weight loss, regardless of the method in which it is achieved, reduces MASLD and results in the restoration of hepatic function[157]. Objective histological regression of liver fibrosis after RYGB has been demonstrated[158].

At 30-month follow-up, the degree of fibrosis was also noted to improve following SG, with 54% of patients with borderline MASH having complete resolution[159]. These results have been validated by other studies through improvements in histology, ultrasound findings, and liver function tests[160-162].

The persistence of MASH was associated with less weight loss (BMI reduction ranging between 2.2 and 10.4). Among those who experienced substantial BMI loss, fibrosis began to decrease one year after surgery and continued to decline for up to 5 years, highlighting the importance of sustained weight loss[163,164]. Multiple studies examining RYGB, OAGB, and SG have shown significant improvements in histology evaluation of liver biopsies, supporting the positive impact of MBS on liver architecture and function[165-167]. These benefits have also been confirmed more recently through liver elastography. Notably, SG had a greater improvement in fibroscan scores for MASH compared to RYGB[168].

Of significant concern, however, is the evidence of lower survival and higher rates of cirrhosis in patients hospitalised with alcohol-associated hepatitis. A single-centre study of 2,634 patients found the presence of previous RYGB surgery increased the risk of 30-day readmission (20.3% *vs.* 11.7%, $P < 0.01$), the development of cirrhosis (37.5% *vs.* 20.9%, $P < 0.01$), and overall 3-year mortality (31.4% *vs.* 24%, $P = 0.03$)[169]. Another database study demonstrated RYGB was at increased hazard of any *de novo* alcohol-related diagnosis (alcoholic hepatitis, abuse, and poisoning) [adjusted hazard ratio (AHR) 1.51, 95%CI: 1.40-1.62), while this was reduced with SG (AHR 0.77, 95%CI: 0.64-0.91). As these patients are generally admitted under the medical or hepatology teams, consultation with an appropriate bariatric surgical service is recommended[170].

A major concern surrounding bariatric surgery is the propensity to develop a higher likelihood of liver failure after an episode of alcohol-related liver hepatitis, with rates of mortality during the episodes of liver failure being ~3.8 times higher[171]. Furthermore, post-bariatric surgical patients have higher rates of alcohol-related cirrhosis after acute episodes of alcoholic hepatitis (approximately 1.8 times) and higher rates of readmission in the first 30 days after the episode (20.3% *vs.* 11.7%)[169]. Patients with previous obesity surgery also tend to present at a younger age for acute alcoholic hepatitis, correlating with a reduced life expectancy when factoring in the increased mortality risk[172].

The foregoing evidence underscores the importance of identifying bariatric patients who are at greatest risk of alcohol misuse in the postoperative setting, particularly two years or more post-operation. Despite the available evidence indicating the risk of developing AUD in postoperative bariatric patients, particularly in the longer term, only one study has considered this at a correlation level. Mellinger *et al.*, when analysing the prevalence of bariatric surgery and alcohol misuse, examined the correlation between bariatric surgery and alcoholic cirrhosis[115]. They found no significant correlation despite the predilection for AUD. No other notable studies have investigated this topic. Taken together, further research is warranted as these patients may be at risk of an alternative form of liver insult in the future.

GLP-1 analogue therapy and alcohol misuse

GLP-1 analogues are a rapidly expanding field for targeting subjects of obesity and metabolic syndrome, with significant weight loss demonstrated in meta-analysis[173]. Emerging research has suggested that GLP-1 agonists may have utility in the treatment of SUDs, further emphasising its use for those with AUD

propensity; however, robust clinical evidence on this concept is lacking[174,175]. Clearly, the advantage of medical therapy is that it does not anatomically alter the pathways of alcohol absorption and that if any ill effects are experienced, treatment can be ceased. This suggests that patients identified at moderate to high risk of alcohol misuse should be treated with a GLP-1, or trialled, prior to any consideration of MBS. However, more long-term research is required.

Risk factor control and precision medicine approaches

Patients with liver disease in the context of MBS are influenced by a broader complex interplay of social, cultural, environmental, economic and even commercial factors and co-factors that are determinants of health. Age, genetic predisposition, and environmental exposure (factors of diet, sedentary lifestyle, patterns of alcohol consumption) can lead to more advanced liver disease[176]. Management strategies to control or mitigate these risk factors should be considered at a broad societal level with promotion of political support, prioritization of healthcare policy and research funding intended to raise awareness, improving screening practices, and advocating for early diagnosis and treatment[176].

Constant advances in our understanding of the pathophysiology and genetics of obesity and AUD are expected to lead to a shift from traditional treatments towards tailored management options for individual patients. Our understanding of the pathogenic heterogeneity and the complex interplay of factors impacting an individual patient's progression to MASLD, MetALD, and end-organ damage is continually evolving[177]. The exact role of gut microbiome, concurrent viral infections, and hormonal profiles, as well as future therapeutic possibilities in these areas, is still unclear[177]. This establishes a foundation for further research into personalised medicine approaches which may include a tailored combination of screening, lifestyle and dietary modification, psychosocial interventions, pharmacological therapy, MBS, and long-term care[176,177].

Decompensation of liver failure and liver transplantation

MASLD is currently the fastest-growing indication of liver transplantation in Western countries, both in the context of end-stage liver disease and associated hepatocellular carcinoma[178]. In addition to the existing multidisciplinary management of liver transplantation, these patients have the additional consideration of the systemic implications of metabolic syndrome, which is associated with higher risks of post-transplant cardiovascular events, renal impairment, and recurrent MASH[178]. AUD is likely the main cause of liver disease in these patients, given the resolution of MASH post MBS previously mentioned.

Given that many transplant programs still consider BMI ≥ 40 kg/m^2 a surgical contraindication to liver transplantation, MBS may help patients suffering from obesity and end-stage liver disease gain access to waiting lists[179]. The overlap of these conditions will likely result in an increase in transplant candidate patients with a history of previous MBS. In a small case series, patients following MBS had a median time to liver cirrhosis diagnosis of 7.2 years[180]. There were also more severe signs of severe hepatic decompensation and a shorter delay between diagnosis, listing, and liver transplantation, denoting a more rapid progression of cirrhosis and decompensation[180].

Several studies addressing the perioperative and long-term outcomes of this clinical scenario report a similar intensive care unit and total hospital length of stay (5.3 *vs.* 4.1 days, $P = 0.16$), a similar 30-day complication rate (76% *vs.* 85%, $P = 0.43$), and similar survival outcomes in patients with or without prior MBS[181,182]. Even in synchronous liver transplantation and SG, there were similar perioperative outcomes and reduced postoperative metabolic issues in a case series[183]. However, it is recognised that current series are limited by sample size and there are no guidelines on the use of MBS in patients with cirrhosis, or consensus on the preferred procedure.

Summary of evidence

The current literature supports that individuals with previous AUD are at an increased risk of problematic alcohol use following bariatric procedures. Those with regular alcohol use that is non-problematic also have an increased potential to develop AUD postoperatively. Patients identified as at risk should be assessed in a multidisciplinary setting, including patient education, psychology support, and long-term follow-up.

However, problematic alcohol use can develop at any time after a bariatric procedure, with evidence indicating a marked increase in prevalence beyond 2 years postoperatively. Long-term follow-up and ongoing education on alcohol use are therefore required.

The RYGB and SG procedures have the strongest evidence for the restoration of liver function induced by obesity-related metabolic factors. The evaluated evidence supports the predisposition of alcohol misuse in both RYGB and SG patients, with RYGB patients being at a higher risk. On this basis, it is suggested that if a patient is identified as being at a higher (but acceptable) risk of alcohol use and is to have a weight loss procedure, SG would be preferred in terms of minimising potential alcohol-related harms postoperatively with concurrent metabolic benefits.

Bariatric surgery may be considered in selected patients with compensated liver cirrhosis, but potential candidates warrant intensive assessment for AUD. Perioperative mortality rates are many times higher in patients with decompensated liver cirrhosis. Patients with compensated liver cirrhosis are still at increased risk of perioperative adverse events compared to non-cirrhotic patients. The American Gastroenterological Association guidelines suggest that SG is likely the optimal procedure for patients with cirrhosis, but that these patients should be managed by a multidisciplinary bariatric surgical team that includes specialists in anaesthesia and hepatology, who are experienced in managing patients with portal hypertension and cirrhosis[184].

Strengths

This review provides a broad and filtered overview of the current landscape of bariatric surgery, cirrhosis, and the influence of alcohol. It raises awareness of the complex interactions between physiology, anatomical, and psychological elements. In an area in which robust quantitative studies are lacking from a wholistic viewpoint, this review helps to draw conclusions between isolated studies, so the available information can be applied. No other paper at present provides an extensive overview with specific recommendations as this review does.

Limitations

Robust quantitative studies, specifically randomised controlled trials, are lacking from each of the domains investigated in this review. Although the evidence is compelling, heterogeneity in study design and results exists. The inherent nature of a narrative review is to provide a personalised scoping review of the literature, which we acknowledge may result in subconscious bias based on study selection. It is also acknowledged that the scope of this review does allow for the exploration of other complementary and alternative interventions including psychological intervention, lifestyle changes, and emerging medical treatments.

CONCLUSION

A complex interplay exists between obesity and AUD with innumerable environmental, psychosocial, and genetic factors. Current evidence suggests SG may be the preferred metabolic bariatric procedure in patients at higher risk of MetALD. Post-surgical follow-up should include assessment of alcohol use and should continue beyond the 2-year mark, to detect and treat any potential misuse disorder.

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Authors' contributions

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