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Liver Disease Predicts 30-Day Postoperative Complications in Head and Neck Microvascular Surgery

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ABSTRACT

Objective: To investigate the association between liver disease and postoperative outcomes of head and neck microvascular free tissue transfer (MFTT) surgeries.

Methods: This retrospective cohort study queried the 2005 to 2021 American College of Surgeons National Surgical Quality Improvement Program databases. Reconstructive cases performed by otolaryngologists (CPT: 15756, 15757, 15758, 15842, 20955, 20956, 20957, 20962, 20969, 20970, 20972, 20973, 43116, 43496, 49006, and 49906) with available age values and preoperative laboratory data were included. Liver disease severity was assessed using the AST-to-platelet ratio index (APRI), a marker of liver fibrosis, and the Model for End-Stage Liver Disease-Sodium (MELD-Na), which predicts mortality. Mild liver disease (MLD) was classified as an APRI score ≥ 0.7 and a MELD-Na score < 10 . Advanced liver disease (ALD) was defined as an APRI score ≥ 0.7 and a MELD-Na score ≥ 10 . Univariate and multivariable logistic regression were performed.

Results: A total of 5459 cases met the inclusion criteria, of which 93 (1.7%) had mild liver disease, and 105 (1.9%) had advanced liver disease. Adjusted multivariable logistic regression showed that ALD was associated with a significantly higher risk of postoperative complications (OR = 1.62, $p = 0.03$), medical complications (OR = 2.05, $p < 0.01$), and return to the operating room within 30 days (OR = 1.87, $p = 0.01$). ALD patients also experienced prolonged hospital stays and a higher incidence of pneumonia, unplanned intubation, and acute renal failure.

Conclusion: ALD is correlated with increased postoperative complication risks in MFTT surgeries. This study suggests that preoperative liver function assessment and optimization may mitigate surgical risks.

Level of Evidence: 3.

1 | Introduction

Liver disease causes two million deaths annually, comprising 4% of global mortality. The leading causes of mortality from liver disease include complications from cirrhosis and hepatocellular carcinoma. Cirrhosis is primarily caused by viral hepatitis, alcohol abuse, and non-alcoholic fatty liver disease [1].

Advanced liver disease (ALD) severely impacts postoperative outcomes by impairing the synthesis of clotting factors and albumin, increasing the risk of bleeding and poor wound healing [2, 3]. Studies have demonstrated that liver disease increases morbidity and mortality in cardiac and open abdominal surgeries [4, 5]. However, the risks associated with liver disease in head and neck microvascular surgery are not well

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documented. Complications in head and neck microvascular surgery for liver disease patients are uncharacterized, partly due to the asymptomatic nature of cirrhosis, with only 60% exhibiting symptoms [6]. Given the complexity of microvascular free tissue transfer (MFTT) and the critical role of liver function in coagulation and wound healing, understanding these risks is essential for patient counseling and improving surgical outcomes.

Although liver biopsy is the gold standard for diagnosing liver disease, its invasiveness necessitates alternative methods. Thus, multiple metrics have been developed to noninvasively assess liver disease severity and surgical risk. The AST-to-platelet ratio index (APRI) noninvasively measures liver fibrosis, with a threshold of ≥ 0.7 showing 77% sensitivity and 72% specificity [7, 8]. The Model for End-stage Liver Disease (MELD) score, used since 2002 for transplant prioritization, incorporates total serum bilirubin, serum creatinine, and the international normalized ratio (INR) to estimate mortality [9]. Furthermore, the MELD-sodium (Na) score is a better predictor of mortality, with scores < 10 indicating mild liver disease (MLD) and ≥ 10 indicating ALD [7, 9].

This study aims to investigate the relationship between liver disease, as determined by APRI and MELD-Na scores, and the outcomes of head and neck MFTT surgeries. Elucidating these relationships may provide evidence-based guidance for the preoperative assessment and management of patients with liver disease undergoing these surgeries.

2 | Methods

The National Surgical Quality Improvement Program (NSQIP) database was queried for head and neck free flap patients from 2005 to 2021. This national database includes over 150 variables from more than 650 hospitals, maintained by certified surgical clinical reviewers of the American College of Surgeons (ACS) [10]. Literature has defined free flaps with Current Procedural Terminology codes: 15756, 15757, 15758, 15842, 20955, 20956, 20957, 20962, 20969, 20970, 20972, 20973, 43116, 43496, 49006, and 49906 [11, 12]. Patients not treated by an otolaryngologist, with missing BMI, age < 18 , or without laboratory information necessary to calculate an APRI and MELD-Na score were excluded.

The ACS-NSQIP Data Dictionary provides definitions for all preoperative and postoperative variables [11]. The readmission variable was only available for cases documented beginning in 2011. APRI was calculated using the formula: $APRI = [(AST \text{ level IU/L}/40)/\text{platelet count } 10^9/\text{L}] \times 100$ [7]. MELD scores were calculated using the formula: $MELD = 3.8 \times (\ln[\text{bilirubin mg/dL}]) + 11.2 \times (\ln[\text{INR}]) + 9.6 \times (\ln[\text{creatinine mg/dL}]) + 6.43$, using a minimum value of 1 for all variables and a maximum creatinine value of 4. Creatinine was set at 4 if a patient was receiving dialysis [7]. Next, MELD-Na scores were calculated using the formula: $MELD-Na = MELD - \text{sodium} - (0.025 \times MELD \times [140 - \text{sodium}]) + 140$, using a sodium value with a minimum of 125 and a maximum of 140 [9]. MLD was defined as $APRI \geq 0.7$ with $MELD-Na < 10$. ALD was defined as $APRI \geq 0.7$ with $MELD-Na \geq 10$.

Differences between the cohorts with no liver disease (NLD), MLD, and ALD were assessed using Analysis of variance (ANOVA) for all continuous variables. Pearson's chi-square test was used to assess the association between liver disease severity and categorical variables, with Fisher's exact test applied when cell counts were less than five. Primary outcomes included 30-day postoperative variables: return to the operating room (OR), readmission, and complication rates. Multivariable logistic regression models were used to identify variables associated with liver disease severity. All analyses were performed using R version 4.0.2, and a p value < 0.05 was considered statistically significant.

3 | Results

3.1 | Preoperative Analysis

A total of 5459 patient records met the inclusion criteria and were analyzed from the NSQIP database. Of these, 93 (1.7%) patients had MLD and 105 (1.9%) had ALD, while 5261 (96.4%) patients had NLD. The MLD cohort was younger (60.8, 56.5, and 60.9 years for NLD, MLD, and ALD, respectively; $p < 0.01$). ALD patients more frequently had severe American Society of Anesthesiologists (ASA) classifications, with 73.3% in ASA class 3 (severe disturbance) and 15.2% in ASA classes 4–5 (life-threatening or moribund), compared to 67.2% and 8.8%, respectively, in NLD patients ($p = 0.015$). MLD patients had higher partially or totally dependent preoperative status (8.6%) compared to those with NLD (3.5%) and ALD (3.8%) ($p = 0.042$). ALD patients were more likely to be smokers (26.8%, 40.9%, and 43.8% for NLD, MLD, and ALD, respectively; $p < 0.0001$), have bleeding disorders (3.2%, 7.5%, and 14.3% for NLD, MLD, and ALD, respectively; $p < 0.0001$), have experienced $> 10\%$ weight loss in 6 months prior to surgery (8.2%, 10.5%, and 16.3% for NLD, MLD, and ALD, respectively; $p = 0.019$), and hypertension requiring medication (48.2%, 37.6%, and 58.1% for NLD, MLD, and ALD, respectively; $p = 0.016$). All preoperative patient characteristics are detailed in Table 1.

3.2 | Postoperative Analysis

Postoperative outcomes are presented in Table 2. ALD patients had a longer median time from operation to discharge (8.0, 9.0, and 11.0 days for NLD, MLD, and ALD, respectively; $p < 0.0001$). The median length of total hospital stay was longer for ALD patients (9.0, 9.0, and 12.0 days for NLD, MLD, and ALD, respectively; $p < 0.0001$). Although readmission rates were comparable across groups (10.0%, 10.8%, and 13.3% for NLD, MLD, and ALD, respectively; $p > 0.05$), ALD patients had a higher rate of OR returns within 30 days post-surgery (31.4%) compared to those with NLD (18.2%) and MLD (19.4%) ($p < 0.01$). Complication rates were notably higher in ALD patients (46.3%, 43.0%, and 61.9% for NLD, MLD, and ALD, respectively; $p < 0.01$). Although the difference in the overall rate of surgical complications was nonsignificant ($p = 0.115$), ALD patients had higher rates of superficial surgical site infection (7.1%, 5.4%, and 13.3% for NLD, MLD, and ALD, respectively; $p = 0.041$) and bleeding transfusions (29.8%, 32.3%, and 42.9% for NLD, MLD, and ALD, respectively; $p = 0.041$).

TABLE 1 | Comparing patient characteristics for those with no, mild, and advanced liver disease.

Factor	Total (N= 5459)	No liver disease (N= 5261)		Mild liver disease (N= 93)		Advanced liver disease (N= 105)		p
		N	Statistics	N	Statistics	N	Statistics	
Age (years)	60.8 ± 13.6	5261	60.8 ± 11.8	93	56.5 ± 11.9	105	60.9 ± 13.7	< 0.01 ^a
BMI	25.7 [22.2,30.1]	5261	25.7 [22.3,30.1]	93	25.4 [21.2,29.4]	105	24.9 [21.1,29.5]	0.157 ^a
ASA Classification		5261		93		105		0.015 ^c
1. No Disturb	73 (1.3)		72 (1.4)		1 (1.1)		0 (0.0)	
2. Mild Disturb	1220 (22.3)		1194 (22.7)		14 (15.1)		12 (11.4)	
3. Severe Disturb	3680 (67.4)		3533 (67.2)		70 (75.3)		77 (73.3)	
4. Life Threat + 5. Moribund	486 (8.9)		462 (8.8)		8 (8.6)		16 (15.2)	
Race		5261		93		105		0.59 ^c
Unknown	711 (13.0)		686 (13.0)		13 (14.0)		12 (11.4)	
Native Hawaiian or Pacific Islander	36 (0.7)		36 (0.7)		0 (0.0)		0 (0.0)	
American Indian or Alaska Native	24 (0.4)		22 (0.4)		2 (2.2)		0 (0.0)	
Asian	197 (3.6)		192 (3.6)		3 (3.2)		2 (1.9)	
White	4036 (73.9)		3887 (73.9)		65 (69.9)		84 (80.0)	
Black or African American	455 (8.3)		438 (8.3)		10 (10.8)		7 (6.7)	
Functional health status Prior to Surgery		5261		93		105		0.042 ^c
Independent	5262 (96.4)		5076 (96.5)		85 (91.4)		101 (96.2)	
Partially/totally Dependent	197 (3.6)		185 (3.5)		8 (8.6)		4 (3.8)	
Comorbidities								
Diabetes		5261		93		105		0.297 ^b
None/diet controlled	4627 (84.8)		4449 (84.6)		85 (91.4)		93 (88.6)	
Non-insulin dependent	500 (9.2)		489 (9.3)		5 (5.4)		6 (5.7)	
Insulin dependent	332 (6.1)		323 (6.1)		3 (3.2)		6 (5.7)	
Current smoker within 1 year	1492 (27.3%)	5261	1408 (26.8)	93	38 (40.9)	105	46 (43.8)	< 0.0001 ^b
Bleeding Disorder(s)	190 (3.5)	5261	168 (3.2)	93	7 (7.5)	105	15 (14.3)	< 0.0001 ^c
Ventilator Dependent	31 (0.57)	5261	28 (0.53)	93	1 (1.1)	105	2 (1.9)	0.1 ^c
Preop Dialysis	30 (0.55)	5261	28 (0.53)		0 (0.0)		2 (1.9)	0.195 ^c
Heart failure (CHF) in 30 days before surgery	49 (0.90)	5261	48 (0.91)	93	0 (0.0)	105	1 (0.95)	0.838 ^c
History of severe COPD	374 (6.9)	5261	360 (6.8)	93	6 (6.5)	105	8 (7.6)	0.941 ^b

(Continues)

TABLE 1 | (Continued)

Factor	Total (N=5459)	No liver disease (N=5261)		Mild liver disease (N=93)		Advanced liver disease (N=105)		p
		N	Statistics	N	Statistics	N	Statistics	
Chronic Steroids (Immunosuppressive Therapy)	280 (5.1)	5261	269 (5.1)	93	3 (3.2)	105	8 (7.6)	0.382 ^c
Wound Infection	629 (11.5)	4593	610 (13.3)	84	8 (9.5)	92	11 (12.0)	0.565 ^b
> 10% weight loss	399 (7.3)	4593	376 (8.2)	84	8 (10.5)	92	15 (16.3)	0.019^b
Ascites	4 (0.07)	5261	4 (0.08)	93	0 (0.0)	105	0 (0.0)	1.0 ^c
Hypertension requiring medication	2630 (48.2)	5261	2534 (48.2)	93	35 (37.6)	105	61 (58.1)	0.016^b
Disseminated cancer	385 (7.1)	5261	373 (7.1)	93	5 (5.4)	105	7 (6.7)	0.81 ^b

Note: Statistics presented as Mean $\pm$ SD, Median [P25, P75], N (column %). Bold values denote statistical significance at the $p < 0.05$ level.

^aAnalysis of Variance.

^bPearson's chi-square test.

^cFisher's Exact test.

Furthermore, medical complications were higher among the ALD cohort (16.9%, 15.1%, and 29.5% for NLD, MLD, and ALD, respectively; $p < 0.01$). These complications include pneumonia (5.8%, 1.1%, and 13.3% for NLD, MLD, and ALD, respectively; $p < 0.001$), unplanned intubation (2.5%, 2.2%, and 9.5% for NLD, MLD, and ALD, respectively; $p < 0.01$), and acute renal failure (0.2%, 0.0%, and 2.9% for NLD, MLD, and ALD, respectively; $p < 0.01$). Despite increased complications, the mortality rate within 30 days of the procedure was comparable across all groups (0.3%, 0.0%, and 0.0% for NLD, MLD, and ALD, respectively; $p > 0.05$).

In a multivariable analysis, ALD in free flap patients was associated with an increased likelihood of a postoperative complication (aOR=1.62 [95% CI 1.04–2.57], $p=0.03$) and medical complications (aOR=2.05 [95% CI 1.28–3.20], $p < 0.01$) (Table 3). ALD was associated with an elevated likelihood of returning to the OR within 30 days (aOR=1.87 [95% CI 1.17–2.92], $p=0.01$) and undergoing any reoperation (aOR=1.68 [95% CI 1.03–2.66], $p=0.03$). However, ALD was not linked to higher 30-day readmission rates (aOR=1.31 [95% CI 0.68–2.32], $p > 0.05$) (Table 4). The covariates used in the multivariable models were age, BMI, ASA classification, race, functional status, history of diabetes, smoking status, history of bleeding disorder, heart failure within 30 days before surgery, history of severe COPD, presence of open wound or wound infection, >10% weight loss within the last 6 months, ascites within 30 days prior to surgery, hypertension requiring medication, currently requiring dialysis, and disseminated cancer.

4 | Discussion

This study examines the relationship between liver disease, specifically as determined by APRI and MELD-Na scores, and the postoperative outcomes of head and neck MFTT surgeries.

Callander et al. studied the impact of hepatitis C virus (HCV) infection on free tissue transfer outcomes, finding no significant association between HCV status and postoperative complications

or length of stay [13]. Additionally, Cramer et al. found that ALD patients had significantly higher 30-day mortality rates compared to those with NLD or MLD in head and neck surgeries [7]. Kao et al. evaluated the association between postoperative complications and the severity of liver cirrhosis as assessed by Child-Pugh classification in head and neck cancer patients who underwent tumor ablation followed by microsurgical free tissue transfer, finding higher morbidity and mortality in patients with severe cirrhosis [14]. Our study aimed to provide a more nuanced understanding of how liver disease severity, as quantified by APRI and MELD-Na scores, correlates with the outcomes of MFTT surgeries. This focus is crucial, as microvascular reconstructions, distinct from other types of cancer surgeries like head and neck surgical resections without reconstruction or surgical ablations, may follow a different postoperative course.

4.1 | Return to OR and Readmission

In an adjusted model, ALD was significantly associated with a higher risk of unplanned return to the OR and reoperation for head and neck MFTT patients. This finding is consistent with a previous study which found a significant association between ALD and reoperation in head and neck surgeries [7]. This likely can be attributed to complications such as coagulopathies, poor wound healing, and increased infection risk. While this does not establish a direct causal relationship between ALD and OR returns and reoperations, it underscores the association and highlights the need for focused perioperative management.

Interestingly, our study observed no significant relationship between ALD and 30-day postoperative readmission. Previous studies have not specifically characterized the relationship between liver disease and readmission of head and neck reconstruction patients. This is unexpected given that patients with severe comorbidities typically have higher readmission rates. For example, surgical site infections (SSI) have been found to predict readmission [15]. Furthermore, cirrhotic patients are known to be immunocompromised [16]. Although our

TABLE 2 | Postoperative outcomes comparing patients with no, mild, and advanced liver disease.

Factor	Total (N=5459)	No liver disease (N= 5261)		Mild liver disease (N=93)		Advanced liver disease (N=105)		p
		N	Statistics	N	Statistics	N	Statistics	
Days from Operation to Discharge	8.0 [6.0,13.0]	4387	8.0 [6.0,13.0]	74	9.0 [7.0,14.0]	92	11.0 [8.0,21.0]	< 0.0001^a
Total Operation Time (minutes)	516.3 ± 216.5	5256	515.3 ± 216.0	93	558.3 ± 234.6	105	529.1 ± 221.8	0.136 ^a
Length of total hospital stay	9.0 [6.0,14.0]	5145	9.0 [6.0,14.0]	89	9.0 [7.0,14.0]	104	12.0 [8.0,21.0]	< 0.0001^a
Still in Hospital > 30 Days	179 (3.5)	5000	171 (3.4)	85	3 (3.5)	100	5 (5.0)	0.556 ^c
Return to OR	1006 (18.4)	5261	955 (18.2)	93	18 (19.4)	105	33 (31.4)	< 0.01^b
Death within 30 days of procedure	15 (0.3)	5261	15 (0.3)	93	0 (0.0)	105	0 (0.0)	1.0 ^c
Any Readmission	551 (10.1)	5261	527 (10.0)	93	10 (10.8)	105	14 (13.3)	0.524 ^b
Any Unplanned Readmission	530 (9.7)	5261	506 (9.6)	93	10 (10.8)	105	14 (13.3)	0.419 ^b
Any Reoperation	948 (17.4)	5261	902 (17.1)	93	16 (17.2)	105	30 (28.6)	< 0.01^b
Any Complication	2542 (46.6)	5261	2437 (46.3)	93	40 (43.0)	105	65 (61.9)	< 0.01^b
Surgical Complication	2218 (40.6)	5261	2128 (40.4)	93	37 (39.8)	105	53 (50.5)	0.115 ^b
Occurrence of Superficial surgical site infection	394 (7.2)	5261	375 (7.1)	93	5 (5.4)	105	14 (13.3)	0.041^b
Occurrence of Deep Incisional SSI	201 (3.7)	5261	194 (3.7)	93	4 (4.3)	105	3 (2.9)	0.910 ^c
Occurrence of Organ Space SSI	201 (3.7)	5261	196 (3.7)	93	2 (2.2)	105	3 (2.9)	0.870 ^c
Wound dehiscence/ disruption	295 (5.4)	5261	279 (5.3)	93	8 (8.6)	105	8 (7.6)	0.226 ^b
Preop Transfusion of ≥ 1 unit of whole/packed RBCs in 72h prior to surgery	66 (1.2)	5261	63 (1.2)	93	2 (2.2)	105	1 (1.0)	0.479 ^c
Occurrence of Bleeding Transfusions (Transfusions/ Intraop/Postop)	1644 (30.1)	5261	1569 (29.8)	93	30 (32.3)	105	45 (42.9)	0.014^b
Medical Complication	934 (17.1)	5261	889 (16.9)	93	14 (15.1)	105	31 (29.5)	< 0.01^b

(Continues)

TABLE 2 | (Continued)

Factor	Total (N=5459)	No liver disease (N= 5261)		Mild liver disease (N=93)		Advanced liver disease (N=105)		p
		N	Statistics	N	Statistics	N	Statistics	
Occurrence of Pneumonia	322 (5.9)	5261	307 (5.8)	93	1 (1.1)	105	14 (13.3)	<0.001 ^b
Occurrence of Unplanned Intubation	146 (2.7)	5261	134 (2.5)	93	2 (2.2)	105	10 (9.5)	<0.01 ^c
Occurrence of Urinary Tract Infection	72 (1.3)	5261	68 (1.3)	93	1 (1.1)	105	3 (2.9)	0.266 ^c
Occurrence of DVT/Thrombophlebitis	88 (1.6)	5261	84 (1.6)	93	3 (3.2)	105	1 (1.0)	0.371 ^c
Occurrence of Pulmonary Embolism	47 (0.9)	5261	47 (0.9)	93	0 (0.0)	105	0 (0.0)	1.0 ^c
Occurrence of Ventilator > 48 h	325 (6.0)	5261	303 (5.8)	93	6 (6.5)	105	16 (15.2)	<0.001 ^b
Dyspnea	362 (7.6)	4593	342 (7.4)	84	7 (8.3)	92	13 (14.1)	0.0547 ^b
CVA/Stroke with Neurological Deficit	28 (0.5)	5261	28 (0.5)	93	0 (0.0)	105	0 (0.0)	1.0 ^c
Cardiac arrest requiring CPR	47 (0.9)	5261	46 (0.9)	93	0 (0.0)	105	1 (1.0)	0.83 ^c
Occurrence of Myocardial Infarction	50 (0.9)	5261	48 (0.9)	93	0 (0.0)	105	2 (1.9)	0.41 ^c
Systemic Sepsis	130 (2.4)	5261	120 (2.3)	93	1 (1.1)	105	9 (8.6)	<0.01 ^c
Occurrence of Progressive Renal Insufficiency	18 (0.4)	4593	17 (0.4)	84	0 (0.0)	92	1 (1.1)	0.49 ^c
Occurrence of Acute Renal Failure	13 (0.2)	5261	10 (0.2)	93	0 (0.0)	105	3 (2.9)	<0.01 ^c
Occurrence of <i>Clostridium difficile</i> (C. diff) Colitis	53 (1.4)	3764	52 (1.4)	67	0 (0.0)	70	1 (1.4)	0.85 ^c

Note: Statistics presented as Mean ± SD, Median [P25, P75], N (column %). Bold values denote statistical significance at the $p < 0.05$ level.

^aAnalysis of Variance.

^bPearson's chi-square test.

^cFisher's Exact test.

findings indicated higher rates of superficial SSI among ALD patients, this was not associated with increased readmissions. This could be because superficial SSIs, unlike deep incisional SSI and organ space SSI which were not statistically significant, are often managed on an outpatient basis and do not necessarily require hospital readmission. Additionally, our data indicate that ALD patients have a significantly longer hospitalization, which likely contributes to fewer readmissions,

as complications may have been managed during the initial hospitalization.

4.2 | Complications

Our study demonstrated that ALD patients experienced significantly more medical complications, such as pneumonia,

TABLE 3 | Multivariable logistic regression analysis of factors associated with complications.

Factor	Any complication		Surgical complication		Medical complication	
	OR (95% L, U)	<i>p</i> .	OR (95% L, U)	<i>p</i>	OR (95% L, U)	<i>p</i>
Liver Disease (Advanced) (Ref: None)	1.62 (1.04–2.57)	0.03	1.25 (0.81–1.94)	0.31	2.05 (1.28–3.20)	<0.01
Liver Disease (Mild) (Ref: Non)	0.72 (0.45–1.13)	0.16	0.78 (0.48–1.23)	0.28	0.97 (0.51–1.70)	0.91
Age	1.00 (1.00–1.01)	0.43	1.00 (0.99–1.00)	0.96	1.00 (1.00–1.01)	0.24
BMI	0.96 (0.96–0.97)	<0.0001	0.96 (0.95–0.97)	<0.0001	0.99 (0.98–1.01)	0.26
ASA Classification 2 (Ref: Class 1)	1.61 (0.90–3.08)	0.13	1.53 (0.84–2.98)	0.18	3.31 (1.01–20.44)	0.10
ASA Classification 3 (Ref: Class 1)	3.13 (1.76–5.96)	<0.001	2.92 (1.62–5.68)	<0.001	5.54 (1.70–34.02)	0.02
ASA Classification 4 (Ref: Class 1)	6.02 (3.25–11.84)	<0.0001	5.45 (2.91–10.89)	<0.0001	7.60 (2.28–47.17)	0.01
American Indian or Alaska Native (Ref: White)	1.21 (0.50–2.89)	0.66	1.51 (0.63–3.57)	0.35	0.79 (0.18–2.41)	0.72
Asian (Ref: White)	1.22 (0.89–1.68)	0.22	1.17 (0.85–1.61)	0.33	1.02 (0.65–1.55)	0.92
Black or African American (Ref: White)	1.38 (1.11–1.73)	<0.01	1.52 (1.22–1.90)	<0.001	1.21 (0.92–1.57)	0.17
Native Hawaiian or Pacific Islander (Ref: White)	2.88 (1.35–6.57)	0.01	2.31 (1.12–4.94)	0.03	3.60 (1.70–7.39)	<0.001
Unknown (Ref: White)	1.00 (0.84–1.21)	0.96	0.95 (0.79–1.15)	0.60	1.02 (0.80–1.30)	0.85
Partially Dependent (Ref: Independent)	1.19 (0.83–1.69)	0.34	1.22 (0.86–1.73)	0.27	1.44 (0.97–2.11)	0.06
Totally Dependent (Ref: Independent)	1.80 (0.71–5.18)	0.24	2.02 (0.82–5.47)	0.14	0.78 (0.24–2.12)	0.65
Insulin Use Diabetes (Ref: No)	1.58 (1.22–2.07)	<0.01	1.42 (1.09–1.84)	0.01	1.73 (1.29–2.30)	<0.001
Non-Insulin Use Diabetes (Ref: No)	0.81 (0.65–1.00)	0.06	0.86 (0.69–1.07)	0.17	0.71 (0.53–0.95)	0.02
Smoke (Ref: No)	1.17 (1.02–1.35)	0.03	1.11 (0.96–1.28)	0.15	1.11 (0.93–1.33)	0.25
Bleeding Disorder (Ref: No)	1.23 (0.89–1.70)	0.22	1.29 (0.94–1.78)	0.12	0.89 (0.59–1.30)	0.56
Congestive Heart Failure (Ref: No)	1.33 (0.61–3.08)	0.48	1.41 (0.66–3.10)	0.39	2.36 (1.07–5.08)	0.03
COPD (Ref: No)	1.32 (1.03–1.70)	0.03	1.08 (0.84–1.38)	0.55	1.57 (1.19–2.05)	<0.01
Existing Open Wound/Infection (Ref: No)	1.15 (0.96–1.37)	0.13	1.09 (0.91–1.30)	0.36	1.27 (1.01–1.57)	0.04
> 10% loss body weight in last 6 months (Ref: No)	1.84 (1.46–2.32)	<0.0001	1.80 (1.44–2.26)	<0.0001	1.35 (1.04–1.73)	0.02
Ascites (Ref: No)	2.03 (0.20–51.71)	0.59	2.99 (0.30–76.44)	0.40	2.55 (0.29–22.57)	0.36
Hypertension Requiring Medication (Ref: No)	1.17 (1.02–1.34)	0.02	1.05 (0.92–1.21)	0.44	1.30 (1.09–1.54)	<0.01
On Dialysis (Ref: No)	1.79 (0.77–4.69)	0.20	1.72 (0.77–4.13)	0.20	1.22 (0.51–2.72)	0.64
Disseminated Cancer (Ref: No)	1.12 (0.89–1.42)	0.33	1.18 (0.94–1.49)	0.16	0.98 (0.73–1.31)	0.90

Note: Bold values denote statistical significance at the $p < 0.05$ level. A separate multivariable logistic regression model was created for each post-operative outcome. The covariates used in the multivariable models were age, BMI, ASA classification, race, functional status, history of diabetes, smoking status, history of bleeding disorder, heart failure within 30 days before surgery, history of severe COPD, presence of open wound or wound infection, > 10% weight loss within the last 6 months, ascites within 30 days prior to surgery, hypertension requiring medication, currently requiring dialysis, and disseminated cancer. Abbreviation: aOR, adjusted odds ratio.

TABLE 4 | Multivariable logistic regression analysis of factors associated with readmission, reoperation, and return to the operating room in head and neck free flap patients.

Factor	Any readmission		Any reoperation		Return to OR within 30 days	
	OR (95% L, U)	<i>p</i>	OR (95% L, U)	<i>p</i>	OR (95% L, U)	<i>p</i>
Liver Disease (Advanced) (Ref: None)	1.31 (0.68–2.32)	0.38	1.68 (1.03–2.66)	0.03	1.87 (1.17–2.92)	0.01
Liver Disease (Mild) (Ref: Non)	1.10 (0.53–2.07)	0.78	0.99 (0.54–1.71)	0.97	1.09 (0.61–1.84)	0.76
Age	1.00 (0.99–1.01)	0.61	1.00 (0.99–1.00)	0.40	1.00 (0.99–1.00)	0.24
BMI	1.00 (0.98–1.01)	0.86	0.99 (0.98–1.01)	0.28	0.99 (0.98–1.00)	0.21
ASA Classification 2 (Ref: Class 1)	1.11 (0.44–3.75)	0.85	1.04 (0.51–2.42)	0.92	1.21 (0.59–2.80)	0.63
ASA Classification 3 (Ref: Class 1)	1.65 (0.66–5.53)	0.34	1.38 (0.68–3.19)	0.40	1.52 (0.75–3.51)	0.28
ASA Classification 4 (Ref: Class 1)	1.81 (0.69–6.26)	0.28	1.59 (0.75–3.76)	0.26	1.78 (0.85–4.22)	0.15
American Indian or Alaska Native (Ref: White)	0.35 (0.02–1.71)	0.31	0.91 (0.26–2.50)	0.87	0.86 (0.24–2.34)	0.78
Asian (Ref: White)	1.11 (0.66–1.76)	0.68	1.05 (0.68–1.56)	0.83	0.98 (0.63–1.46)	0.91
Black or African American (Ref: White)	0.74 (0.50–1.05)	0.10	1.17 (0.89–1.51)	0.25	1.22 (0.94–1.56)	0.13
Native Hawaiian or Pacific Islander (Ref: White)	1.25 (0.37–3.25)	0.68	1.12 (0.41–2.56)	0.81	1.02 (0.38–2.35)	0.96
Unknown (Ref: White)	0.47 (0.32–0.68)	<0.001	0.91 (0.71–1.16)	0.45	0.98 (0.78–1.24)	0.88
Partially Dependent (Ref: Independent)	1.59 (0.99–2.48)	0.05	1.17 (0.76–1.74)	0.46	1.27 (0.85–1.87)	0.23
Totally Dependent (Ref: Independent)	NA	0.96	0.93 (0.26–2.56)	0.90	1.41 (0.49–3.53)	0.48
Insulin Use Diabetes (Ref: No)	1.43 (0.98–2.03)	0.06	0.90 (0.64–1.24)	0.53	0.90 (0.64–1.23)	0.51
Non-Insulin Use Diabetes (Ref: No)	0.87 (0.61–1.23)	0.45	0.88 (0.66–1.15)	0.35	0.85 (0.64–1.11)	0.24
Smoke (Ref: No)	1.11 (0.89–1.39)	0.34	1.21 (1.02–1.44)	0.03	1.15 (0.97–1.36)	0.11
Bleeding Disorder (Ref: No)	1.05 (0.64–1.65)	0.83	0.86 (0.56–1.27)	0.46	0.81 (0.53–1.21)	0.32
Congestive Heart Failure (Ref: No)	1.03 (0.29–2.77)	0.96	1.55 (0.63–3.47)	0.31	1.47 (0.59–3.29)	0.38
COPD (Ref: No)	1.40 (0.99–1.95)	0.05	1.11 (0.83–1.48)	0.47	1.09 (0.81–1.45)	0.55
Existing Open Wound/Infection (Ref: No)	1.03 (0.77–1.35)	0.84	1.05 (0.84–1.32)	0.65	1.15 (0.92–1.42)	0.22
> 10% loss body weight in last 6 months (Ref: No)	1.26 (0.90–1.72)	0.16	1.49 (1.15–1.91)	<0.01	1.48 (1.16–1.89)	<0.01
Ascites (Ref: No)	2.34 (0.11–25.44)	0.50	1.71 (0.08–18.83)	0.67	2.58 (0.28–23.41)	0.37
Hypertension Requiring Medication (Ref: No)	1.17 (0.94–1.44)	0.16	1.36 (1.15–1.61)	<0.001	1.37 (1.16–1.62)	<0.001
On Dialysis (Ref: No)	1.17 (0.34–3.15)	0.78	1.29 (0.50–3.00)	0.57	1.26 (0.51–2.86)	0.60
Disseminated Cancer (Ref: No)	0.93 (0.63–1.33)	0.71	1.25 (0.94–1.64)	0.11	1.28 (0.97–1.66)	0.07

Note: Bold values denote statistical significance at the $p < 0.05$ level. A separate multivariable logistic regression model was created for each post-operative outcome. The covariates used in the multivariable models were age, BMI, ASA classification, race, functional status, history of diabetes, smoking status, history of bleeding disorder, heart failure within 30 days before surgery, history of severe COPD, presence of open wound or wound infection, > 10% weight loss within the last 6 months, ascites within 30 days prior to surgery, hypertension requiring medication, currently requiring dialysis, and disseminated cancer. Abbreviation: aOR, adjusted odds ratio.

unplanned intubation, prolonged use of ventilator (> 48 h), systemic sepsis, and acute renal failure. Although the difference in the occurrence of surgical complications overall

was nonsignificant, the occurrence of a superficial SSI and bleeding requiring transfusions was both significantly elevated.

The increased incidence of medical complications can be attributed to the immunocompromised state of patients with liver disease. Cirrhosis impairs the immune response due to defects in the innate immune system, including neutrophil burst, phagocytosis, and opsonization, and the presence of a systemic inflammatory response syndrome-like state. Bacterial translocation from the gut to systemic circulation, due to increased intestinal permeability and bacterial overgrowth, further exacerbates the risk of systemic infections. Pneumonia and sepsis, which were significantly higher in ALD patients, likely, contribute to the higher rates of intubation and ventilation, as these conditions can lead to respiratory failure. This aligns with the findings of Bajaj et al., who reported that infections in end-stage liver disease are associated with high mortality and often require intensive care due to severe sepsis and septic shock [17]. As a result, head and neck surgeons may consider lowering the threshold for ICU admission in the early postoperative period for ALD patients to ensure closer monitoring and timely intervention in case of respiratory failure or other complications.

Our study demonstrated that ALD patients had a 3.8× greater risk of unplanned intubation compared to NLD patients. This underscores the consideration for one to lower the threshold for elective temporary tracheostomy in patients with liver disease who are undergoing complex head and neck surgeries, particularly in reconstructions such as oral cavity where the airway risk is greater at baseline. Previous research has shown that elective tracheostomy can significantly reduce postoperative ventilation time and the incidence of hospital-acquired pneumonia, highlighting its potential benefits for optimizing respiratory outcomes in high-risk surgical populations [18]. Although our data does not specifically evaluate the risk of tracheostomy in patients with liver disease, these findings suggest that elective tracheostomy may improve pulmonary hygiene and reduce the risk of respiratory complications in ALD patients. Utilizing tools like the Cameron and TRACHY scoring systems, which are used to predict the need for elective tracheostomy in head and neck cancer surgeries, in conjunction with liver disease status, may help guide surgical decision-making [19, 20].

Previous studies have highlighted the increased risk of postoperative complications in patients with liver disease. For instance, our findings were mostly consistent with a prior NSQIP study which characterized the increased morbidity caused by liver disease in all head and neck surgeries [7]. However, their findings that myocardial infarction/cardiac arrest, deep vein thrombosis, pulmonary embolism, UTIs, and wound dehiscence were significantly elevated in liver disease patients are inconsistent with our study [7]. This discrepancy may be due to the different surgical focuses in both studies. In addition, a single-institution study of 62 patients found that patients with more severe cirrhosis, described by Child-Pugh Class B and C, had significantly higher rates of postoperative complications compared to Class A in head and neck cancer resections followed by microsurgical free tissue transfer. Unlike our study, which compared liver disease patients to those without liver disease, this prior study did not include a comparison group of patients without liver disease, thus focusing exclusively on varying severities within cirrhotic patients [14].

The connection between ALD and complications in head and neck MFTT surgeries has not been well documented until now.

This study highlights specific complications to improve preoperative evaluation, perioperative management, and patient counseling, aiming to reduce complication rates and enhance outcomes for this high-risk population.

4.3 | Managing Liver Disease

This study highlights the association between ALD and postoperative complications in head and neck microvascular reconstruction, echoing findings from other head and neck surgical studies and from other surgical specialties. While optimizing liver function preoperatively remains challenging, evidence supports the role of comprehensive medical management of the complications of ALD, including coagulopathy, immune dysregulation, and hypoalbuminemia to improve surgical outcomes.

Correcting coagulopathies in cirrhotic patients preoperatively remains controversial. Vitamin K administration (10mg per day for 3 days) is sometimes recommended, but its efficacy in cirrhotic patients is unclear [21]. Fresh frozen plasma can transiently normalize laboratory values, but its additional volume may increase bleeding risks by raising intravascular venous pressure [22, 23]. Similarly, there is a lack of data demonstrating the efficacy of cryoprecipitate in cirrhotic patients [23]. While the role of these interventions remains uncertain preoperatively, they are recommended as part of a rescue strategy for postoperative bleeding [24].

Patients with cirrhosis also suffer from immune dysregulation, which increases the risk of infection following surgery. Those on chronic antibiotics for conditions like spontaneous bacterial peritonitis prophylaxis can continue these medications perioperatively. However, additional prophylactic antibiotics beyond routine intraoperative use are not currently supported [24].

Nutritional support plays a critical role in managing patients with liver disease. Multiple studies have demonstrated that preoperative total parenteral nutrition in patients with hypoalbuminemia can significantly reduce postoperative complications across various surgical subspecialties [25–27]. However, the use of albumin infusions to correct hypoalbuminemia has not been shown to significantly impact postoperative outcomes and is not recommended as a primary treatment strategy [28, 29].

A multidisciplinary approach involving hepatologists, surgeons, medicine physicians, and nutritionists to manage liver dysfunction is imperative to optimize patient outcomes in head and neck reconstruction surgeries. Furthermore, shared decision-making and patient discussions about surgical risks, benefits, and liver function optimization ensure a personalized and effective treatment plan. This patient-centered approach fosters better understanding and cooperation, ultimately contributing to improved surgical outcomes and patient satisfaction.

4.4 | Limitations and Future Directions

This study has several limitations that should be acknowledged. First, the retrospective nature of the study design inherently limits the ability to establish causality between liver disease

severity and postoperative complications in head and neck MFTT surgeries. Additionally, the reliance on the NSQIP database, while extensive, may be subject to data entry errors, missing data, and coding inconsistencies, which could impact the accuracy of our findings. The exclusion of cases with unknown lab values necessary to calculate the MELD-Na and APRI scores may have skewed the cohort, potentially affecting the representativeness of our sample. Lastly, the NSQIP database does not provide detailed information on long-term outcomes beyond the 30-day postoperative period, limiting our understanding of the longer-term implications of liver disease on surgical outcomes. Despite these limitations, this study provides valuable insights into the impact of liver disease on head and neck MFTT surgeries, underscoring the need for tailored perioperative management strategies in this high-risk patient population.

Future research should focus on prospective studies to better establish causal relationships between liver disease and surgical outcomes in head and neck MFTT surgeries. Additionally, investigations into long-term outcomes and the effectiveness of tailored perioperative management strategies for patients with liver disease are essential to further improve surgical care and patient prognosis in this high-risk population.

5 | Conclusion

This study underscores the significant association between ALD and postoperative complications in patients undergoing head and neck MFTT surgeries. ALD is correlated with an increased likelihood of OR returns and reoperation, with no significant association with readmission rates. Our findings highlight the importance of thorough preoperative assessment and the possible role for preoperative optimization of liver function to mitigate surgical risks. While liver disease is associated with poor surgical outcomes, its specific implications in head and neck MFTT surgeries have yet to be investigated. This study characterized these associations and demonstrated the need for tailored perioperative management strategies to improve patient outcomes. Future prospective studies should validate these findings and explore long-term outcomes to further enhance the care of this high-risk population.

Conflicts of Interest

The authors declare no conflicts of interest.

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