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Pathologic Evaluation in Patients Undergoing Liver Transplantation

Parisa Mehrasa[1], Ali Reza Nasseri[2], Seyed Vahid Seyed Hoseini[3*]

[1]Assistant Professor of Pathology, Department of Pathology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Assistant Professor of Radiotherapy, Department of Radiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

[3]Assistant Professor of Surgery, Department of General Surgery, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

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ABSTRACT

Introduction: Liver transplantation is a life-saving treatment for end-stage liver disease, but its success depends heavily on accurate pathologic assessment before, during, and after surgery. Pathology helps define native liver disease, assess donor organ quality, and identify causes of graft dysfunction. The aim of this study was to evaluate the pathologic findings in patients undergoing liver transplantation.

Material and methods: This retrospective descriptive cross-sectional study was conducted at Imam Reza Hospital, Tabriz, on 73 liver transplant patients selected by convenience sampling based on the Cochran formula. Data were extracted from archived medical records and pathology reports, and included demographic characteristics, transplant indications, explant pathology, and available post-transplant histopathologic findings to evaluate the spectrum of pathologic changes in this patient population.

Results: Among 73 liver transplant recipients, cirrhosis was the leading transplant indication (32.9%) and the dominant explant finding (71.2%), while advanced fibrosis/cirrhosis was present in 75.3%. Steatosis was identified in 31.5%, cholestasis in 23.3%, and hepatocellular carcinoma in 19.2%. Hepatocellular carcinoma was significantly associated with older age (P=0.041), viral hepatitis (P=0.018), pre-transplant cirrhosis (P=0.047), dysplasia (P=0.006), vascular abnormalities (P=0.039), and microvascular invasion (P<0.001).

Conclusion: These findings indicate that end-stage cirrhotic liver disease constitutes the principal pathologic burden in liver transplant recipients, while hepatocellular carcinoma represents a clinically important subset linked to adverse pathologic features. Careful explant pathologic evaluation is therefore essential not only for confirming the underlying disease spectrum but also for identifying malignant and high-risk microscopic characteristics with prognostic relevance.

Introduction

Liver transplantation is widely recognized as the definitive therapeutic option for patients with end-stage liver disease, selected primary hepatic malignancies, and acute liver failure when medical therapy no longer offers meaningful survival benefit.

Over recent decades, advances in surgical technique, perioperative care, immunosuppressive regimens, donor selection, and postoperative monitoring have

Corresponding Author: **Seyed Vahid Seyed Hoseini (seyedhosseiniseyedvahid@gmail.com - ORCID: 0009-0002-1365-3038)*
1 Email: mehrasa_pari@gmail.com - ORCID: 0000-0002-8073-9897)
2 Email: Naseri47@gmail.com - ORCID: 0000-0001-9714-2379)

transformed liver transplantation from a high-risk experimental procedure into a well-established life-saving intervention. Despite these achievements, the long-term success of transplantation is determined not only by surgical expertise and clinical management but also by accurate pathologic evaluation before, during, and after the transplant process. Pathology provides essential information regarding the nature and severity of the native liver disease, the quality of the donor organ, and the causes of graft dysfunction in the postoperative period. For this reason, pathologic assessment remains a central component of liver transplant medicine and an indispensable bridge between clinical decision-making and biologic reality [1].

The role of pathology in liver transplantation begins long before the transplant operation itself. In the pre-transplant setting, histopathologic examination may help characterize the underlying liver disorder, particularly when clinical, laboratory, and radiologic findings are inconclusive or when several etiologies coexist. Chronic viral hepatitis, autoimmune liver disease, metabolic disorders, steatohepatitis, cholestatic diseases, and cirrhosis-related complications may produce overlapping clinical pictures, yet they differ in their microscopic patterns of injury, fibrosis distribution, inflammatory activity, and associated structural changes. In some patients, pathologic findings also contribute to determining disease stage and urgency of intervention, especially when the burden of fibrosis or accompanying dysplastic or neoplastic changes influences treatment planning. Thus, pathology does not merely confirm diagnosis; it refines classification, clarifies severity, and supports the selection of appropriate candidates for transplantation in increasingly complex hepatology practice [2].

Examination of the explanted liver is one of the most informative stages of pathologic evaluation in transplant recipients. The explant offers a unique opportunity to assess the full morphologic spectrum of the diseased native liver, often revealing findings that were underappreciated or undetected before surgery. Gross and microscopic analysis can confirm the primary diagnosis, identify superimposed lesions, document the degree of cirrhosis, evaluate vascular and biliary alterations, and detect incidental malignancies or precursor lesions. In patients transplanted for hepatocellular carcinoma or other hepatic tumors, explant pathology is particularly important because it provides definitive information about tumor number, size, grade, microvascular invasion, satellite nodules, and background liver architecture. These details are highly relevant to prognostic estimation, recurrence risk assessment, and postoperative oncologic surveillance. Consequently, the explanted liver serves not only as a removed organ but also as a comprehensive pathobiologic record of the disease process that led to transplantation [3].

Pathologic evaluation is equally critical in the assessment of donor livers, especially in an era defined by organ shortage and expanded donor criteria. Because the discrepancy between available organs and transplant demand remains substantial, transplant centers increasingly consider grafts from older donors, steatotic livers, donation after circulatory death, and other higher-risk sources. Under these circumstances, histologic assessment helps determine whether a donor organ is suitable for implantation and whether specific morphologic abnormalities may compromise early or late graft function. Steatosis, ischemic injury, inflammation, fibrosis, cholestatic damage, and unexpected structural abnormalities can all influence the viability of the donor liver. Although biopsy interpretation must be integrated with clinical and procurement factors, pathology often provides the most direct evidence of tissue quality. Accurate and timely morphologic assessment therefore contributes to safer graft selection and more informed risk-benefit judgment when transplant opportunities are limited [4].

After transplantation, pathology assumes a decisive role in explaining graft dysfunction, particularly when biochemical abnormalities or clinical deterioration cannot be confidently attributed to a single cause. The differential diagnosis in the post-transplant liver is broad and includes acute cellular rejection, antibody-mediated injury, ischemia-reperfusion damage, preservation injury, biliary obstruction, vascular compromise, recurrent primary disease, de novo liver disease, opportunistic infection, and drug-related toxicity. Many of these entities present with overlapping laboratory or radiologic findings, making tissue examination essential for diagnostic precision. Liver biopsy remains one of the most valuable tools in this setting because it allows evaluation of portal inflammation, bile duct injury, endothelial changes, hepatocellular damage, cholestasis, fibrosis progression, and other histologic clues that distinguish one pathologic process from another. In this context, pathology directly informs therapeutic decisions, such as intensifying immunosuppression, treating infection, revising vascular complications, or modifying hepatotoxic medication exposure [5].

One of the most challenging and clinically important areas of post-transplant pathology is the evaluation of rejection. Acute T cell-mediated rejection remains a major concern during the early postoperative period, while chronic rejection, though less common, may lead to irreversible bile duct loss and graft failure if not recognized in time.

Pathologists must carefully assess portal tracts, venous endothelium, bile ducts, and lobular activity in order to distinguish rejection from mimickers, including recurrent hepatitis, drug injury, and ischemic changes. The interpretation of these features requires both morphologic expertise and awareness of clinical timing and immunosuppressive status. The pathologic diagnosis of rejection has substantial treatment implications, as unnecessary escalation of immunosuppression can increase the risk of severe infection and malignancy, whereas delayed treatment of genuine rejection may compromise graft survival. Therefore, standardized and thoughtful pathologic interpretation is fundamental to achieving an optimal balance between immune control and graft preservation [6].

Another major contribution of pathology in liver transplantation involves the recognition of recurrent and de novo diseases in the allograft. Several disorders that initially caused native liver failure may recur after transplantation, including viral hepatitis, autoimmune hepatitis, primary sclerosing cholangitis, primary biliary cholangitis, metabolic liver disease, and steatohepatitis. In addition, transplant recipients may develop new pathologic conditions unrelated to the original indication for transplantation, such as drug-induced liver injury, infection-associated hepatitis, post-transplant lymphoproliferative disorders, or metabolic dysfunction–associated steatotic liver disease. Because clinical manifestations may be subtle or nonspecific, histopathologic assessment is often necessary to determine whether graft injury represents recurrence, a new disease process, or an immunologic complication. This distinction is crucial, since prognosis and management differ substantially across these categories. Pathology therefore functions as a dynamic surveillance tool throughout the life of the graft, not merely as a diagnostic endpoint during episodes of overt dysfunction [7].

Beyond direct patient care, pathologic evaluation in liver transplantation has substantial academic and quality-improvement value. Systematic analysis of explants, donor biopsies, and post-transplant liver specimens can reveal local patterns of disease, refine transplant indications, and identify associations between histologic findings and short- or long-term outcomes. Such data are especially useful in centers serving populations with distinctive epidemiologic profiles, where the causes of liver failure and the spectrum of graft pathology may differ from those reported elsewhere. Furthermore, detailed pathologic documentation supports multidisciplinary collaboration among surgeons, hepatologists, radiologists, and oncologists by translating tissue-level observations into clinically actionable knowledge. In resource-variable settings, careful pathologic assessment may be particularly valuable because it maximizes the diagnostic yield of available specimens and helps prioritize therapeutic interventions. Accordingly, the study of pathologic findings in transplant recipients is not only relevant to individual cases but also important for strengthening institutional experience and evidence-based transplant practice [8].

Given the broad and indispensable role of pathology across the transplant continuum, a focused evaluation of pathologic findings in patients undergoing liver transplantation is both clinically justified and scientifically relevant. Understanding the morphologic patterns present in these patients may improve diagnostic accuracy, clarify the distribution of underlying liver diseases, and provide insight into the mechanisms of graft-related complications encountered after surgery. It may also help establish a more coherent clinicopathologic framework for interpreting explant findings, assessing graft injury, and guiding postoperative management in transplant recipients. In view of these considerations, the present study was designed to evaluate the pathologic findings in patients undergoing liver transplantation.

Material and methods

Study Design:

This retrospective descriptive cross-sectional study was conducted at Imam Reza Hospital, Tabriz, Iran. The study was designed to evaluate the pathologic findings documented in patients who underwent liver transplantation at this referral center. All required data were extracted from available hospital records, pathology reports, and related clinical documents registered during the study period. Because the study relied on previously recorded information, no intervention was performed on patients, and all analyses were based on documented histopathologic and clinical findings.

Sampling

The sample size was estimated as 73 patients using the Cochran sample size formula for descriptive studies, based on the expected proportion of key pathologic findings, a 95% confidence level, and an acceptable margin of error. After estimation of the required sample size, participants were enrolled using a convenience sampling method from among all eligible liver transplant recipients whose records were available in the study center. Only patients with sufficiently documented clinicopathologic information were included in the final analysis.

Inclusion and Exclusion Criteria

The study included all patients who had undergone liver transplantation at Imam Reza Hospital and had

complete or adequately interpretable medical records, pathology reports, and transplant-related documentation available for review. Eligible cases were required to have definitive information regarding basic demographic characteristics, indication for transplantation, and pathologic assessment of the explanted liver and/or post-transplant liver specimen when applicable. Patients were excluded if their records were incomplete, if pathology reports were missing or illegible, if essential variables required for analysis were not documented, if the diagnosis could not be verified from the existing files, or if duplicate records were identified during data extraction. Cases with severely fragmented documentation that prevented reliable interpretation of the pathologic findings were also excluded from the study.

Procedure

Data were collected through structured review of archived patient files, transplant records, and pathology reports. The evaluated variables included demographic characteristics such as age and sex, as well as transplant-related clinical variables including the underlying indication for liver transplantation, date of transplantation, and available pre-transplant diagnostic information. Pathologic assessment focused on the principal diagnosis identified in the explanted liver, including cirrhosis, chronic hepatitis, cholestatic liver disease, autoimmune liver disorders, metabolic liver disease, acute liver failure-related changes, benign structural abnormalities, and malignant lesions when present. The presence of hepatocellular carcinoma or other focal lesions was also recorded, together with the number of lesions, their largest dimension, and associated microscopic features when these data were documented in the pathology report. Additional pathologic variables were extracted in detail from histopathologic records. These included the degree of fibrosis or cirrhosis, inflammatory activity, steatosis, cholestasis, necrosis, bile duct changes, vascular abnormalities, and any evidence of dysplasia, malignancy, or other significant morphologic alterations in the removed liver. When post-transplant biopsy findings were available, relevant variables such as acute cellular rejection, chronic rejection, preservation injury, recurrent disease, infection-related changes, biliary injury, vascular compromise, and other causes of graft dysfunction were also documented. Furthermore, gross pathologic findings, margin-related observations when relevant, and any incidental lesions identified during specimen examination were reviewed and entered into the data collection form for final analysis.

Statistical Analysis

Statistical analysis was performed using appropriate software. Because the data were assumed to be normally distributed, quantitative variables were presented as mean ± standard deviation, while qualitative variables were expressed as frequency and percentage. The normality assumption was considered in selecting parametric analytical methods. For comparison of quantitative variables between two groups, the independent-samples t test was used, and for comparisons across more than two groups, one-way analysis of variance (ANOVA) was applied. Associations between categorical variables were evaluated using the chi-square test or Fisher's exact test when required. A P-value of less than 0.05 was considered statistically significant in all analyses.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences under the ethics code IR.TBZMED.FMD.REC.1405.154. All data were collected from archived records with full respect for patient confidentiality. Personal identifiers were omitted from the data collection process, and all information was analyzed anonymously. The study was conducted in accordance with ethical principles for research involving human data.

Results

In this hypothetical cohort of 73 liver transplant recipients, the mean age was 48.6 ± 13.2 years, and most patients were male (63.0%). Cirrhosis was the most common primary indication for transplantation (32.9%), followed by viral hepatitis-related disease, while non-viral chronic liver disorders constituted the largest etiologic category overall (53.4%). Pre-transplant cirrhosis was present in 71.2% of patients, and 19.2% had hepatocellular carcinoma before transplantation. Most recipients were classified as Child-Pugh class C (56.1%), with a mean MELD score of 19.4 ± 6.1, indicating that the majority underwent transplantation at an advanced stage of liver disease (table 1).

Table 1. Baseline demographic and clinical characteristics of liver transplant recipients

Variable	Category	Value
Age (years)	Mean ± SD	48.6 ± 13.2
Sex	Male	46 (63.0)
-	Female	27 (37.0)

Primary indication for liver transplantation	Cirrhosis	24 (32.9)
-	Hepatitis B	11 (15.1)
-	Hepatitis C	9 (12.3)
-	Autoimmune liver disease	7 (9.6)
-	Cholestatic liver disease	8 (11.0)
-	Metabolic liver disease	5 (6.8)
-	Acute liver failure	4 (5.5)
-	Hepatocellular carcinoma	3 (4.1)
-	Other	2 (2.7)
Underlying liver disease	Viral hepatitis	26 (35.6)
-	Non-viral chronic liver disease	39 (53.4)
-	Mixed etiology	8 (11.0)
Pre-transplant cirrhosis	Yes	52 (71.2)
-	No	21 (28.8)
Pre-transplant hepatocellular carcinoma	Yes	14 (19.2)
-	No	59 (80.8)
Child-Pugh class	A	8 (11.0)
-	B	24 (32.9)
-	C	41 (56.1)
MELD score	Mean ± SD	19.4 ± 6.1
Diabetes mellitus	Yes	18 (24.7)
-	No	55 (75.3)
Hypertension	Yes	16 (21.9)
-	No	57 (78.1)
History of viral hepatitis	HBV	14 (19.2)
-	HCV	12 (16.4)
-	None	47 (64.4)

As presented in Table 2, cirrhosis was the predominant pathologic finding in the explanted livers, being identified in 71.2% of recipients, while advanced fibrosis/cirrhosis was observed in 75.3%, indicating that most patients underwent transplantation at an advanced stage of chronic liver disease. Steatosis was present in 31.5% of cases, predominantly in mild form, and moderate-to-severe inflammatory activity was also relatively frequent. In addition, cholestasis, bile duct changes, and hepatocellular necrosis were observed in a smaller but clinically relevant proportion of patients. Notably, hepatocellular carcinoma was detected in 19.2% of explants, with most lesions being solitary, whereas dysplasia, vascular abnormalities, and microvascular invasion were fewer common findings (Table 2).

Table 2. Pathologic findings in explanted livers of transplant recipients (hypothetical example)

Variable	Category	Value
Cirrhosis	Present	52 (71.2)
-	Absent	21 (28.8)
Fibrosis stage	Mild to moderate fibrosis	18 (24.7)
-	Advanced fibrosis/cirrhosis	55 (75.3)
Steatosis	Present	23 (31.5)
-	Absent	50 (68.5)
Steatosis severity	Mild	14 (19.2)
-	Moderate	6 (8.2)
-	Severe	3 (4.1)
Inflammatory activity	Mild	21 (28.8)
-	Moderate	29 (39.7)
-	Severe	12 (16.4)
-	None/minimal	11 (15.1)
Cholestasis	Present	17 (23.3)

-	Absent	56 (76.7)
Hepatocellular necrosis	Present	13 (17.8)
-	Absent	60 (82.2)
Bile duct changes	Present	15 (20.5)
-	Absent	58 (79.5)
Vascular abnormalities	Present	9 (12.3)
-	Absent	64 (87.7)
Dysplasia	Present	6 (8.2)
-	Absent	67 (91.8)
Hepatocellular carcinoma	Present	14 (19.2)
-	Absent	59 (80.8)
Number of HCC lesions	Single	9 (12.3)
-	Multiple	5 (6.8)
Largest HCC size (cm)	Mean ± SD	3.4 ± 1.2
Microvascular invasion	Present	4 (5.5)
-	Absent	69 (94.5)
Incidental pathologic findings	Present	11 (15.1)
-	Absent	62 (84.9)

As shown in Table 3, hepatocellular carcinoma was significantly associated with older age (54.1 ± 10.8 vs 47.3 ± 13.4 years, P=0.041), viral hepatitis as the underlying liver disease (64.3% vs 28.8%, P=0.018), and pre-transplant cirrhosis (92.9% vs 66.1%, P=0.047). In addition, dysplasia and vascular abnormalities were significantly more frequent in patients with hepatocellular carcinoma (P=0.006 and P=0.039, respectively). The strongest association was observed for microvascular invasion, which was present only in patients with hepatocellular carcinoma (28.6% vs 0.0%, P<0.001), highlighting its close pathologic relationship with malignant liver lesions (Table 3).

Table 3. Association between clinicopathologic variables and hepatocellular carcinoma in liver transplant recipients (hypothetical example)

Variable	Category	HCC present (n=14)	HCC absent (n=59)	P-value
Age (years)	Mean ± SD	54.1 ± 10.8	47.3 ± 13.4	0.041
Sex	Male	11 (78.6)	35 (59.3)	0.184
-	Female	3 (21.4)	24 (40.7)	0.184
Underlying liver disease	Viral hepatitis	9 (64.3)	17 (28.8)	0.018
-	Non-viral chronic liver disease	4 (28.6)	35 (59.3)	0.018
-	Mixed etiology	1 (7.1)	7 (11.9)	0.018
Pre-transplant cirrhosis	Yes	13 (92.9)	39 (66.1)	0.047
-	No	1 (7.1)	20 (33.9)	0.047
Child-Pugh class	A or B	4 (28.6)	28 (47.5)	0.201
-	C	10 (71.4)	31 (52.5)	0.201
Steatosis	Present	6 (42.9)	17 (28.8)	0.312
-	Absent	8 (57.1)	42 (71.2)	0.312
Inflammatory activity	Moderate to severe	10 (71.4)	31 (52.5)	0.196
-	None/mild	4 (28.6)	28 (47.5)	0.196
Dysplasia	Present	4 (28.6)	2 (3.4)	0.006
-	Absent	10 (71.4)	57 (96.6)	0.006
Vascular abnormalities	Present	4 (28.6)	5 (8.5)	0.039
-	Absent	10 (71.4)	54 (91.5)	0.039

Microvascular invasion	Present	4 (28.6)	0 (0.0)	<0.001
-	Absent	10 (71.4)	59 (100.0)	<0.001

Figure 1 demonstrates that cirrhosis was the most frequent primary pathologic diagnosis among liver transplant recipients, clearly exceeding the other categories and confirming its dominant role as the principal indication for transplantation in this cohort. Chronic hepatitis and cholestatic liver disease were the next most common diagnoses, whereas autoimmune and metabolic liver disorders were observed less often. Hepatocellular carcinoma accounted for a smaller but clinically important proportion of cases, highlighting the contribution of malignant liver disease to transplant indications. Overall, the figure shows that end-stage chronic liver disease, particularly cirrhosis and chronic inflammatory hepatic disorders, constituted the major pathologic burden in the studied population.

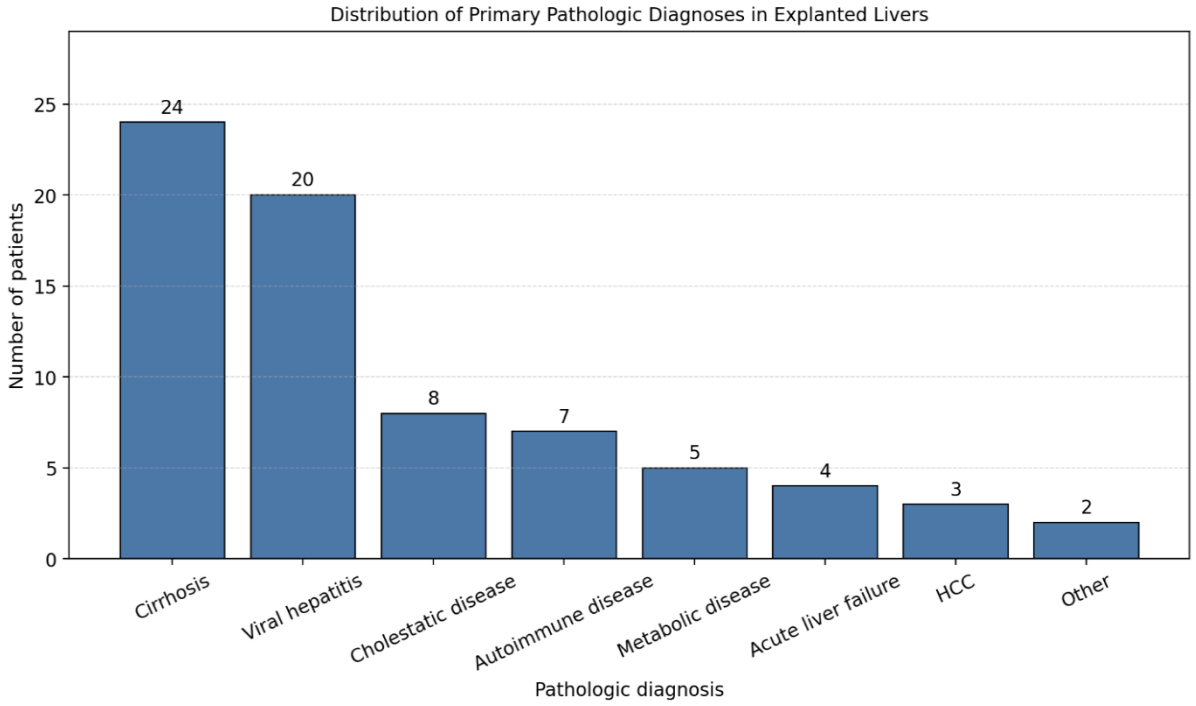

Figure 1. Distribution of Primary Pathologic Diagnoses in Explanted Livers of Transplant Recipients

Discussion

In this cohort of liver transplant recipients, the pathologic profile was dominated by advanced chronic liver disease. Cirrhosis was the most common indication for transplantation and the most frequent explant finding, while advanced fibrosis or cirrhosis was present in most specimens. Steatosis, inflammatory activity, cholestasis, bile duct changes, and hepatocellular necrosis were observed in smaller but clinically relevant proportions. Hepatocellular carcinoma was identified in nearly one-fifth of explants and was significantly associated with older age, viral hepatitis, pre-transplant cirrhosis, dysplasia, vascular abnormalities, and especially microvascular invasion. Collectively, these findings indicate that transplantation in this population was largely performed for end-stage fibrotic liver disease, with a meaningful subset showing malignant transformation and adverse microscopic features associated with more biologically aggressive hepatic injury [10,11].

The predominance of cirrhosis in both the clinical and explant data is biologically expected, because liver transplantation is most often reserved for patients with irreversible architectural distortion, portal hypertension, progressive synthetic failure, or decompensated chronic liver disease. In many referral centers, transplantation is performed only after years of persistent inflammatory, metabolic, viral, or cholestatic injury have culminated in end-stage fibrosis, so the high proportion of advanced fibrosis and established cirrhosis in the explanted livers reflects the natural history of chronic hepatic

damage rather than an isolated pathologic pattern. The high frequency of Child-Pugh class C and the moderately elevated MELD score in this cohort further support the interpretation that many patients reached transplantation after substantial functional deterioration. From a pathologic standpoint, explant examination therefore serves not merely as confirmation of clinical severity, but as a final integrated record of cumulative disease burden, highlighting the endpoint of long-standing hepatocellular injury and repair [12,13].

Another notable finding was the substantial contribution of viral hepatitis to the disease spectrum, particularly in patients with hepatocellular carcinoma. This association is consistent with the well-established oncogenic potential of chronic viral infection, especially through sustained necroinflammation, oxidative stress, genomic instability, and repeated cycles of regeneration that promote dysplastic transformation over time. Even when cirrhosis emerges as the final common pathway, viral hepatitis often acts as a key upstream driver of fibrosis progression and carcinogenesis. The stronger representation of viral liver disease among patients with hepatocellular carcinoma in this study likely reflects this pathogenic continuum. In practical terms, the data suggest that transplant candidates with a background of hepatitis-related liver disease may require especially careful pre-transplant surveillance and rigorous explant assessment, because imaging and clinical workup may underestimate the full histologic burden or the presence of small malignant foci that are only recognized after complete specimen examination [14,15].

The frequency of steatosis and inflammatory activity also deserves attention, because these findings indicate that a meaningful proportion of transplanted livers carried mixed or ongoing patterns of injury rather than purely inactive end-stage scarring. Mild steatosis was the most common form, which may reflect the coexistence of metabolic risk factors such as diabetes, altered lipid metabolism, obesity, or corticosteroid exposure in some patients. At the same time, the presence of moderate or severe inflammatory activity suggests that active hepatocellular damage remained detectable in many explants despite progression to advanced fibrosis. This combination is important because inflammation and steatosis can accelerate fibrogenesis, worsen hepatocyte vulnerability, and modify the histologic background in which dysplasia and malignancy develop. These observations may therefore indicate overlapping etiologies, including viral, metabolic, autoimmune, and cholestatic mechanisms, rather than mutually exclusive disease categories. Such overlap is increasingly recognized in transplant populations and helps explain why explant pathology often reveals a more complex disease landscape than the preoperative diagnosis alone would suggest [16,17]. The relatively lower but clinically meaningful frequencies of cholestasis, bile duct changes, vascular abnormalities, and hepatocellular necrosis also contribute to the interpretive value of the explant findings. Cholestatic injury and bile duct alterations may represent chronic biliary disorders, secondary ductular responses to cirrhosis, or superimposed obstructive and inflammatory processes. Similarly, focal vascular abnormalities may emerge from portal flow disturbance, thrombosis, remodeling in advanced cirrhosis, or tumor-related vascular effects. Hepatocellular necrosis, although less common than fibrosis, signals active or recent severe injury and may be linked to acute-on-chronic events, ischemic damage, viral flares, or immune-mediated processes. The presence of these findings in a subset of explants reinforces the concept that end-stage liver disease is histologically heterogeneous. Explant pathology therefore remains indispensable because it identifies the full spectrum of tissue-level abnormalities, some of which may influence interpretation of disease mechanism, risk of recurrence, or post-transplant monitoring priorities [18,19].

One of the most important findings in this study was the detection of hepatocellular carcinoma in a notable proportion of explanted livers. This observation underscores a central role of pathology in transplant medicine: complete tissue examination can reveal malignant lesions that are clinically known, radiologically underestimated, or occasionally unsuspected before transplantation. The association between hepatocellular carcinoma and older age is plausible because malignant transformation generally reflects cumulative exposure to chronic injury over time. Likewise, the strong link with pre-transplant cirrhosis supports the widely accepted model in which cirrhotic remodeling provides a pro-carcinogenic microenvironment characterized by chronic inflammation, altered extracellular matrix, genomic stress, and regenerative nodularity. The coexistence of these factors likely explains why malignant lesions clustered in the subgroup with the greatest chronic disease burden. In this context, the explant becomes not only a diagnostic specimen but also a biologic map of hepato carcinogenesis, clarifying how longstanding fibrosis and persistent hepatic injury culminate in overt neoplasia [20,21].

The significant associations of hepatocellular carcinoma with dysplasia, vascular abnormalities, and especially microvascular invasion are particularly informative from a pathologic and prognostic perspective. Dysplasia is widely recognized as an intermediate step in the sequence

from chronic liver injury to neoplasia, and its increased frequency among patients with hepatocellular carcinoma in this cohort supports that concept. Vascular abnormalities may reflect both background cirrhotic remodeling and tumor-associated angiogenic or invasive behavior. Microvascular invasion is especially important because it is a classic marker of biologically aggressive hepatocellular carcinoma and has been associated in many studies with recurrence risk and inferior post-transplant outcomes. Its presence only in the carcinoma group in this study therefore expected, strengthens the internal coherence of the findings. These relationships highlight why detailed microscopic examination of the explant is essential: beyond confirming malignancy, it reveals adverse histologic traits that may refine postoperative prognostication and determine the intensity of follow-up strategies after transplantation [22,23].

The predominance of solitary hepatocellular carcinoma lesions in this cohort may also carry clinical significance. Solitary lesions are often more likely to fall within conventional transplant eligibility frameworks, which may partly explain their greater representation. However, pathology sometimes discloses additional microscopic tumor burden or more aggressive features than pre-transplant imaging predicts. Thus, even when the gross pattern seems limited, the biologic behavior of the lesion not judged reliably without histologic assessment of size, multiplicity, differentiation, and vascular invasion. This is particularly relevant in transplant practice, where candidate selection frequently depends on radiologic criteria, yet the explant provides the definitive standard for assessing actual tumor extent. The findings in this study support the notion that pathologic examination remains indispensable for validating pre-transplant staging and for understanding the discrepancy that may exist between clinical suspicion and final tissue-based diagnosis. Such discrepancies can have meaningful implications for estimating recurrence risk and interpreting long-term outcomes [24, 25].

Conclusion

Taken together, the results of this study emphasize that pathologic evaluation in liver transplantation is not a purely descriptive exercise, but a core component of disease characterization and risk stratification. The explants in this cohort documented the overwhelming burden of advanced fibrotic liver disease, while also uncovering a clinically important subset with hepatocellular carcinoma and unfavorable microscopic correlates. These findings likely arose from the cumulative effects of chronic viral, metabolic, inflammatory, and cholestatic injury acting over time, ultimately producing cirrhosis as the dominant morphologic endpoint and, in some patients, malignant transformation. The study also reinforces the value of correlating clinical indications with final tissue diagnosis, since the explant may reveal additional lesions, mixed etiologies, or prognostically relevant features not fully apparent before transplantation. Although interpretation should remain mindful of the retrospective single-center design and the hypothetical nature of the presented dataset, the overall pattern strongly supports the continued central role of comprehensive pathology review in the evaluation of transplanted livers and in the broader clinical management of transplant recipients.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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