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The incidence and natural history of ascites after liver transplantation

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Abstract

Background: Ascites is common in cirrhosis but uncommon after liver transplant. We aimed to characterize the incidence, natural history, and current management strategies of post-transplant ascites.

Methods: We performed a retrospective cohort study of patients who underwent liver transplantation at 2 centers. We included patients who underwent deceased donor whole graft liver transplants between 2002 and 2019. Chart review identified patients with post-transplant ascites, requiring a paracentesis between 1 and 6-month post-transplants. Detailed chart review identified clinical and transplant characteristics, evaluation of ascites etiology, and treatments.

Results: Of 1591 patients who successfully underwent a first-time orthotopic liver transplant for chronic liver disease, 101 (6.3%) developed post-transplant ascites. Only 62% of these patients required large volume paracentesis for ascites before transplant. 36% of patients with post-transplant ascites had early allograft dysfunction. Most patients with post-transplant ascites (73%) required a paracentesis within 2 months of transplant, but 27% had delayed ascites onset. From 2002 to 2019, ascites studies were obtained less often, and hepatic vein pressure measurement was performed more often. Diuretics were the mainstay of treatment (58%). The use of albumin infusion and splenic artery embolization to treat post-transplant ascites increased over time. Larger pre-transplant spleen size was associated with a greater number of post-transplant paracenteses ($r = 0.32$ and $p = 0.003$). For patients who underwent splenic intervention, paracentesis frequency was significantly reduced (1.6–0.4 paracenteses/month,

Abbreviations: HCV Ab, HCV antibody; HV, hepatic vein; HVPG, hepatic venous pressure gradient; LVP, large volume paracentesis; MELD, model for end-stage liver disease; MGH, Massachusetts General Hospital; OLT, orthotopic liver transplant; RRT, renal replacement therapy; SAAG, serum-ascites albumin gradient; UM, University of Michigan.

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$p = 0.0001$). The majority (72%) of patients had clinical resolution of their ascites at 6-month post-transplant.

Conclusions: Persistent or recurrent ascites continues to be a clinical issue in the modern era of liver transplantation. Most had clinical resolution within 6 months, some requiring intervention.

INTRODUCTION

Ascites is a common complication of chronic liver disease. Less commonly, ascites persists or develops after orthotopic liver transplant (OLT). The incidence and natural history of post-transplant ascites in the modern era of liver transplantation are largely unknown.

Single-center data from over 20 years ago suggested that 5%–7% of liver transplant recipients experience substantial post-transplant ascites.[1–3] Three contemporaneous single-center studies of that time period drew 3 different conclusions about the main etiology of post-transplant ascites: (1) impaired graft blood outflow (post-sinusoidal portal hypertension), (2) recurrent (HCV) infection in the allograft and resulting perisinusoidal fibrosis, and (3) bacterial or fungal peritonitis.[1–3] In the last 20 years, there has been ongoing evolution and improvement in surgical techniques, HCV cure with direct-acting antivirals, and antimicrobial prophylaxis.

The incidence and natural history of post-transplant ascites in modern deceased donor liver transplantation is relatively unstudied. It is also unclear how post-transplant ascites is currently being evaluated and treated. Case reports have suggested some efficacy of splenic artery embolization in treating this condition, but it remains unknown how often and successfully this treatment is being applied.[4–6] In this retrospective cohort study of 2 transplant centers, we aim to characterize the incidence, natural history, and current management strategies of post-transplant ascites.

METHODS

We performed a retrospective cohort study of patients who underwent liver transplantation at 2 transplant centers in the US: the Massachusetts General Hospital and the University of Michigan. We aimed to investigate the modern era in terms of surgical techniques and the model for end-stage liver disease (MELD) score–based organ allocation. We included patients who underwent their first deceased donor whole graft liver transplant between February 2002 and April 2019. Patients were included in the study if they met the following inclusion criteria: (1) no prior solid organ transplant, (2) survived to at least 1-year post-transplant, and (3) received a deceased donor graft. Patients were excluded if: (1) they underwent a multiorgan transplant, (2) acute liver failure was the indication for transplant, or (3) a split or living donor graft was used.

Patients who met the above criteria were then interrogated through chart review for the presence of post-transplant ascites. Post-transplant ascites was defined as ascites requiring a therapeutic paracentesis of at least 500 cc between 1 and 6-month post-transplants. We chose 500 cc because that volume was used in a prior study,(1) and volumes under 500 cc were too small to be considered clinically significant. Patients who only had residual ascites in the first month post-transplant were not included. A clinical resolution was defined as no longer requiring paracentesis by 6-month post-transplant.

A detailed chart review was performed on all patients with post-transplant ascites, including clinical characteristics, and pre-, intra-, and post-transplant variables. Spleen size was obtained from a radiologist report on cross-sectional imaging, required of every transplant candidate. Pre-transplant large volume paracentesis (LVP) was defined as removing at least 5 L of ascites. Evaluation and treatment of post-transplant ascites were also documented. We also recorded the presence or absence of early allograft dysfunction, as this could be a risk factor for post-transplant ascites, defined as bilirubin $>$ or $=$ 10 mg/dL on day 7, international normalized ratio $>$ or $=$ 1.6 on day 7, and alanine or aspartate aminotransferases $>$ 2000 IU/L within the first seven days.[7] Data points to extract from chart review were clearly defined to enhance uniformity between collections at the 2 sites. Data were collected in RedCap (Research Electronic Data Capture), a secure data collection platform. The institutional review boards of Massachusetts General Hospital and University of Michigan approved this study. The study was conducted in accordance with the Declarations of Helsinki and Istanbul. Informed consent was waived by the institutional review boards.

Statistical methods

We used descriptive statistics to describe the natural history of post-transplant ascites, including the percentage of patients who underwent each diagnostic test and treatment. Continuous variables with a normal distribution

were reported as mean ± SD. Continuous variables with a skewed distribution were reported as median and interquartile range. Binary and categorical variables were reported as proportions. Comparative statistics were calculated as t-tests for normally distributed data and the Mann-Whitney U test for skewed data. Statistical significance was set at alpha = 0.05. The Pearson correlation was used to assess the correlation between 2 quantitative variables. R packages were used to analyze data and for figure creation (R Foundation for Statistical Computing, Vienna, Austria).[8]

RESULTS

Of the 622 patients at Massachusetts General Hospital and 969 patients at U-M who successfully underwent a first-time orthotopic liver transplant for chronic liver disease and survived at least one year, 101 (6.3%) developed post-transplant ascites that persisted beyond 1-month post-transplant. These patients have a median of 57 years old and had a median natural MELD of 18 at transplant (range 7–40), and 63 (62%) required LVP before transplant (Table 1). A mix of hepatic vein (HV) anastomoses was used (19% bicaval, 56% cavo-cavostomy, and 25% piggyback), 20 (20%) required post-transplant renal replacement therapy, and 36 (36%) had early allograft dysfunction.

Timing of post-transplant paracenteses

The number of paracenteses per month peaked in the second-month post-transplant, with a gradual decline thereafter (Figure 1).

Twenty-seven (27%) patients required their first post-transplant paracentesis 2 months or more after the transplant (Figure 2). Patients with early-onset post-transplant ascites (within 2 mo post-transplant) had a larger pre-transplant spleen size than those with late-onset (first post-transplant paracentesis at least 2 mo post-transplant; 16.3 cm versus 14.8 cm, $p = 0.01$). Patients with early-onset post-transplant ascites were more likely to have a cavocavostomy (62% versus 41%, $p < 0.001$).

Sixteen (16%) patients had a large number of post-transplant paracenteses (>6 paracenteses in 6 mo). Patients with a large number of post-transplant paracenteses had a larger spleen size than those with a small number (17.6 cm versus 15.3 cm, $p = 0.04$) and were more likely to have a cavocavostomy (75% versus 53%, $p = 0.0001$).

73 (72%) patients had clinical resolution of their ascites by 6-month post-transplant, and these patients exhibited similar characteristics to those patients without clinical resolution (Supplemental Table S1, http://links.lww.com/HC9/A284; Figure 3).

Evaluation of post-transplant ascites

The most common tests performed in patients with post-transplant ascites were ascites fluid studies [serum-ascites albumin gradient (SAAG), total protein, and total nucleated cells] and liver biopsy (Table 2). Over time, SAAG and triglycerides were tested less often, and hepativ vein pressure gradient (HVPG) was tested more often. There was no change in the incidence of post-transplant ascites ($p = 0.23$) or in key baseline characteristics across the 3 eras examined (Supplemental Table S2, http://links.lww.com/HC9/A285) except for a change in HV anastomosis ($p < 0.001$).

Since SAAG > 1.1 g/dL strongly suggests portal hypertension and is widely used in pre-transplant ascites evaluation, we compared subsequent evaluation and management in patients with high SAAG (> 1.1 g/dL) versus low SAAG (< 1.1 g/dL). Patients with high SAAG were no more or less likely to undergo subsequent HVPG ($p = 0.85$), HV venogram ($p = 0.79$), or liver biopsy ($p = 0.29$). Patients with high SAAG were also no more or less likely to be treated with diuretics within 30 days ($p = 0.42$), undergo splenic artery embolization ($p = 0.54$), HV intervention ($p = 0.89$), and portal vein intervention ($P = 0.95$), or have clinical remission at 6 months ($p = 0.90$).

Attempted treatments for post-transplant ascites

Diuretics were the most common treatment used to treat post-transplant ascites (58% within 30 d post-transplant). The use of albumin infusion and splenic artery embolization has increased over time (Table 3).

At one site, 12 patients underwent either splenectomy (1) or splenic artery embolization (11) to treat their post-transplant ascites. For these patients, the number of paracenteses per month decreased from 1.6 (SD 0.7) to 0.4 (SD 0.4) after splenic intervention ($p = 0.0001$; Figure 4). The mean pre-transplant spleen size for patients who underwent a splenic intervention was 18.1 cm (range 12.9–27.8 cm).

Associations with post-transplant paracentesis

Pre-transplant MELD ($r = -0.06$ and $p = 0.54$), post-transplant HVPG ($r = 0.03$ and $p = 0.85$), and SAAG ($r = -0.14$ and $p = 0.25$) did not correlate with the number of post-transplant paracenteses. The number of post-transplant paracenteses also did not differ by a history of pre-transplant LVP ($p = 0.33$), pre-transplant hemodialysis ($p = 0.76$), pre-transplant ascites ($p = 0.69$), or history of HCC ($p = 0.97$). Pre-transplant spleen size significantly correlated with the

TABLE 1 Transplant characteristics of patients with post-transplant ascites[a]

Characteristic	Overall (N = 101)	MGH (N = 26)	UM (N = 75)
Sex (M)	78 (77)	21 (81)	57 (76)
Age (y)	57 (51, 62)	62 (52, 69)	56 (50, 61)
Etiology of cirrhosis			
Alcohol	32 (32)	8 (31)	24 (32)
NAFLD	25 (25)	7 (27)	18 (24)
Viral	39 (39)	9 (35)	30 (40)
Autoimmune	5 (5)	1 (4)	4 (5)
Other	17 (17)	5 (19)	12 (16)
HCC	26 (26)	9 (35)	17 (23)
MELD	18 (15, 26)	31 (23, 38)	17 (14, 21)
Pre-transplant ascites	80 (79)	23 (88)	57 (76)
Pre-transplant RRT	7 (7)	5 (19)	2 (3)
Pre-transplant LVP	63 (62)	21 (81)	42 (56)
Pre-transplant albumin Level, g/dL	3.0 (2.4, 3.4)	3.2 (2.5, 3.6)	2.9 (2.4, 3.3)
Cold ischemia time (min)	362 (294, 445)	359 (306, 412)	372 (281, 466)
Warm ischemia time (min)	33 (26, 40)	42 (32, 48)	32 (25, 38)
HCV Ab positive donor	9 (9)	3 (12)	6 (8)
HV vein anastomosis			
Bicaval	19 (19)	15 (58)	4 (5)
Cavocavostomy	57 (56)	0	57 (76)
Piggyback	25 (25)	11 (42)	14 (19)
Post-transplant RRT	20 (20)	7 (27)	13 (17)
Early allograft dysfunction	36 (36)	18 (69)	18 (24)

[a]n (%); median (interquartile range).
Abbreviations: HCV Ab, HCV antibody; HV, hepatic vein; LVP, large volume paracentesis; MELD, model for end-stage liver disease; MGH, Massachusetts General Hospital; RRT, renal replacement therapy; UM, University of Michigan.

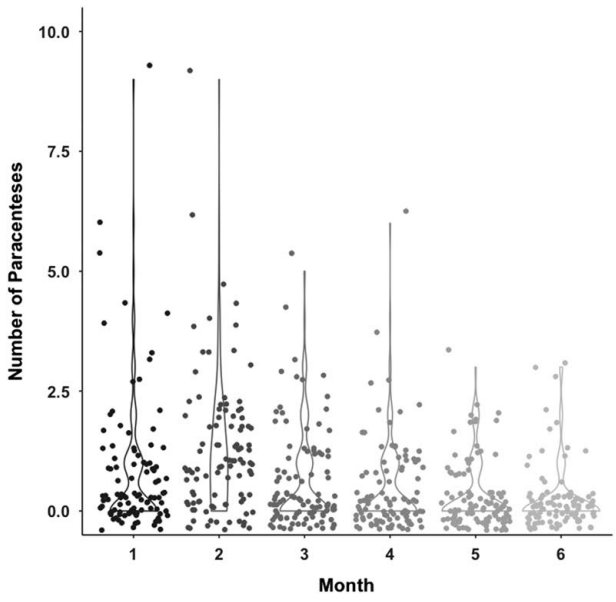

FIGURE 1 Number of therapeutic paracentesis per month post-transplant.

number of post-transplant paracenteses ($r = 0.32$ and $p = 0.003$). Patients with early allograft dysfunction had a lower total number of post-transplant paracenteses (3.2 versus 4.1 paracenteses, $p = 0.02$). The mean number of post-transplant paracenteses varied by HV anastomosis type (cavocavostomy: 4.6, bicaval: 2.7, piggyback: 2.6; and $P = 0.007$).

Patients without clinical resolution at six months

Twenty-five patients at one site did not achieve clinical resolution of refractory ascites by 6-month post-transplant. Detailed chart review of those patients by a transplant surgeon (SW) and transplant hepatologist (PPB) at 6-month post-transplant revealed 11 (44%) with recurrent HCV infection, 6 (24%) with chronic kidney disease, and 4 (16%) with complex medical comorbidities as possible causes (some had more than one cause). However, 8 (32%) did not have a clear cause despite extensive testing. Six (24%) of those patients ultimately improved with a splenic intervention and 3 (12%) with HV or IVC intervention.

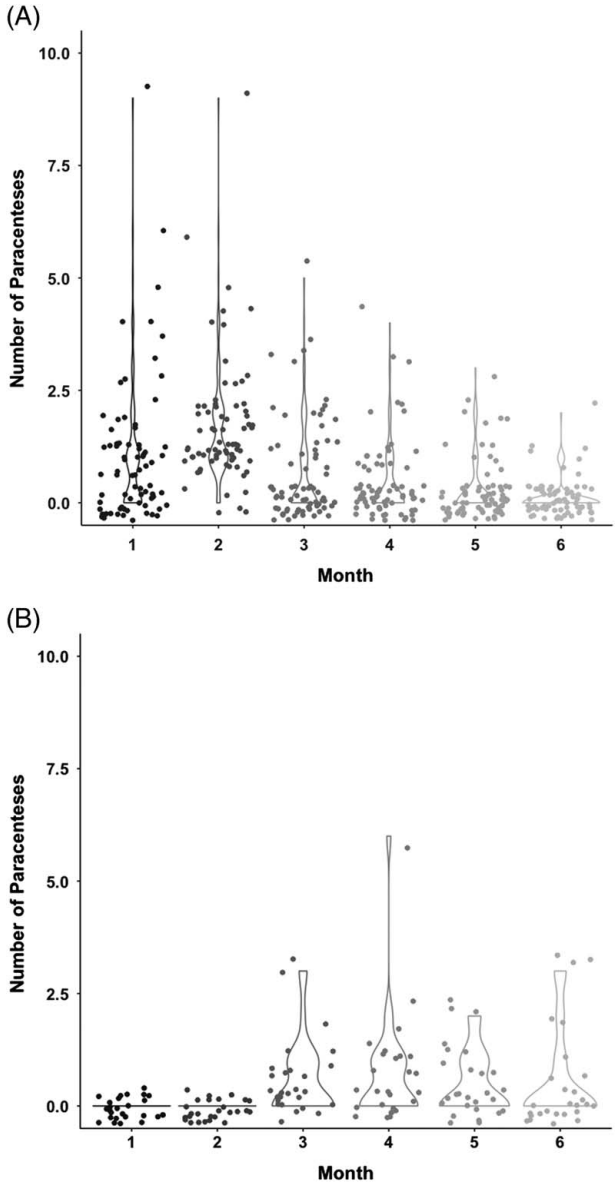

FIGURE 2 (A) Number of therapeutic paracentesis per month in early post-transplant ascites. (B) Number of therapeutic paracentesis per month in late post-transplant ascites.

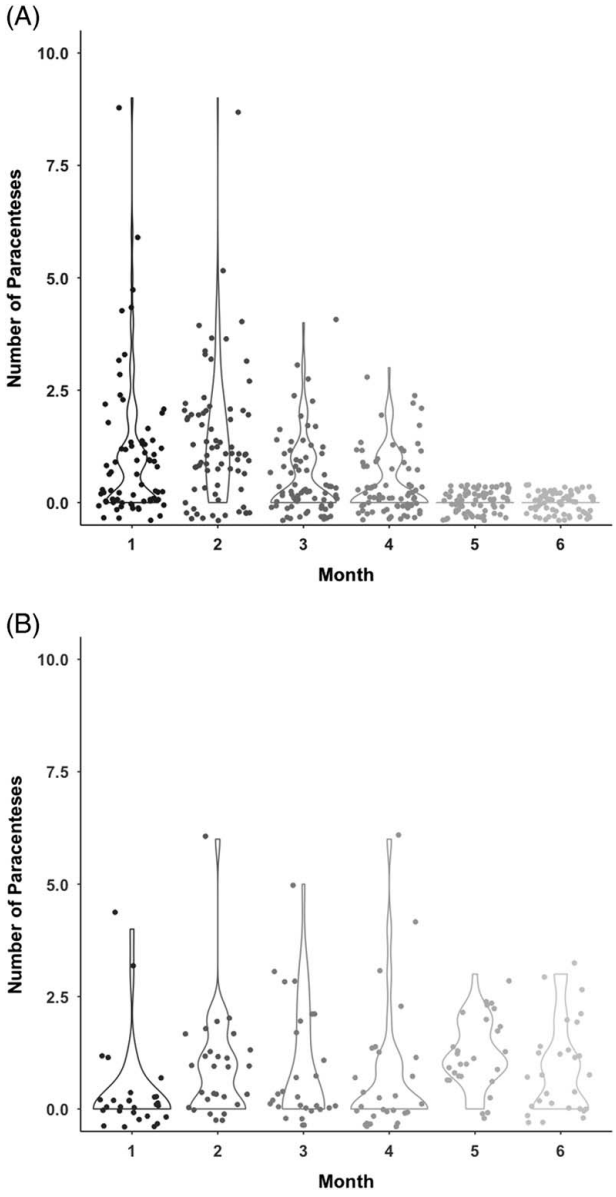

FIGURE 3 (A) Number of therapeutic paracentesis per month in the patients with clinical resolution. (B) Number of therapeutic paracentesis per month in the patients without clinical resolution.

DISCUSSION

These data on post-transplant ascites from 2 large academic transplant centers confirm and extend our understanding of the incidence and natural history of post-transplant ascites in 3 main ways. First, in our study of liver-alone transplantation during the contemporary MELD era (transplanted 2002–2019), we found that 6.3% of patients developed clinically significant post-transplant ascites. We confirm older data (last reported in 2013) estimating an incidence of ascites requiring paracentesis in 5%–7% of transplants.[1–3] Second, we show that most (72%) patients had clinical resolution within 6 months. Third, we demonstrate that a minority of the patients required splenic artery embolization, splenectomy, or HV, IVC, or portal vein intervention to achieve clinical remission.

Clinical correlates

Most patients who developed post-transplant ascites required a therapeutic paracentesis within 2 months of transplant, but 27% of patients developed late-onset ascites, 2 months or more after transplant. Most of our cohort underwent liver transplants before the advent of direct-acting antivirals for the safe and effective treatment of HCV infection. At one site in our cohort, 44% of the patients without clinical resolution of ascites at 6 months

TABLE 2 Evaluation of post-transplant ascites over time[a]

Characteristic	Overall (N = 101)	2002-2007 (N = 25)	2008-2013 (N = 31)	2014-2019 (N = 45)	*p* Value[b]
SAAG performed	74 (73)	20 (80)	23 (74)	31 (69)	0.60
SAAG result (g/dL)	1.1 (0.8, 1.5)	1.1 (0.9, 1.3)	1.3 (0.9, 1.6)	1.0 (0.8, 1.4)	0.28
SAAG ≥ 1.1 g/dL[c]	40 (54)	11 (55)	15 (65)	14 (45)	0.34
Total protein performed	71 (70)	17 (68)	24 (77)	30 (67)	0.58
Total protein result	3.1 (2.4, 3.5)	3.5 (2.9, 4.4)	2.8 (2.4, 3.2)	3.0 (2.5, 3.3)	**0.004**
Total protein > 2.5 g/dL[c]	51 (72)	14 (82)	15 (62)	22 (73)	0.37
Triglycerides performed	44 (44)	10 (40)	19 (61)	15 (33)	**< 0.05**[d]
Triglycerides result	64 (46, 89)	74 (64, 102)	62 (42, 108)	60 (47, 85)	0.43
Cell counts performed	91 (90)	23 (92)	27 (87)	41 (91)	0.79
Total nucleated cells	385 (164, 1016)	420 (184, 1080)	385 (153, 852)	339 (179, 1031)	0.45
Absolute neutrophils	14 (5, 50)	16 (4, 60)	18 (6, 54)	13 (5, 35)	0.26
HVPG performed	55 (55)	12 (48)	14 (45)	29 (66)	0.15
HVPG result	6 (3, 10)	5 (3, 8)	7 (6, 9)	4 (2, 10)	0.54
HVPG >= 10 mm Hg[c]	14 (25)	3 (25)	3 (21)	8 (28)	0.91
HV venogram performed	66 (65)	16 (64)	21 (68)	29 (64)	0.94
Liver biopsy performed	78 (77)	18 (72)	23 (74)	37 (82)	0.55

Note: The study period was arbitrarily divided into 3 eras to evaluate changes in evaluation over time.
[a]n (%); median (interquartile range)
[b]*p* value for ANOVA test if continuous variable and chi-square test if categorical, comparing 3 eras. *p* values < 0.05 are bolded.
[c]Percentage is calculated based on the number who underwent that test, not the total N for the group.
[d]Value is 0.04962.
Abbreviations: HV, hepatic vein; HVPG, hepatic venous portal gradient; SAAG, serum-ascites albumin gradient.

had untreated HCV. In the direct-acting antiviral era, this cause of post-transplant ascites should be essentially extinguished moving forward. In our cohort, 36% of patients with post-transplant ascites had early allograft dysfunction, which is much higher than typical rates in the general transplant population, suggesting that early allograft dysfunction may contribute to post-transplant ascites risk.[7] Only a minority of patients with post-transplant ascites required pre- or post-transplant renal replacement therapy. Finally, approximately 1/3 of patients with post-transplant ascites never underwent an LVP before transplant.

Investigations and etiology

Though ascitic fluid studies were not universally performed, the median SAAG was 1.1 g/dL (exact cutoff above which suggests portal hypertension), the total protein was high (median 3.1 g/dL), and ascites

TABLE 3 Interventions in patients with post-transplant ascites over time[a]

Characteristic	Overall (N = 101)	2002-2007 (N = 25)	2008-2013 (N = 31)	2014-2019 (N = 45)	*p* Value[b]
Received albumin within 30 d	21 (38)	3 (17)	4 (31)	14 (58)	**0.02**
Diuretics within 30 d					0.35
None	37 (38)	8 (38)	10 (32)	19 (42)	—
Dialysis	4 (4)	2 (10)	2 (7)	0	—
Yes	56 (58)	11 (52)	19 (61)	26 (58)	—
Peritoneal drain placement	20 (20)	5 (20)	9 (29)	6 (13)	0.24
Splenic artery embolization	13 (13)	2 (8)	3 (10)	8 (18)	0.41
Splenectomy	7 (7)	1 (4)	3 (10)	3 (7)	0.71
TIPS	1 (1)	0	1 (4)	0	0.91
HV intervention	14 (17)	5 (26)	6 (26)	3 (8)	0.08
Portal vein intervention	4 (5)	0	1 (4)	3 (8)	0.45

Note: The study period was arbitrarily divided into 3 eras to evaluate changes in evaluation over time.
[a]n (%).
[b]*p* value for the ANOVA test comparing 3 eras. *p* values < 0.05 are bolded.
Abbreviation: HV, hepatic vein.

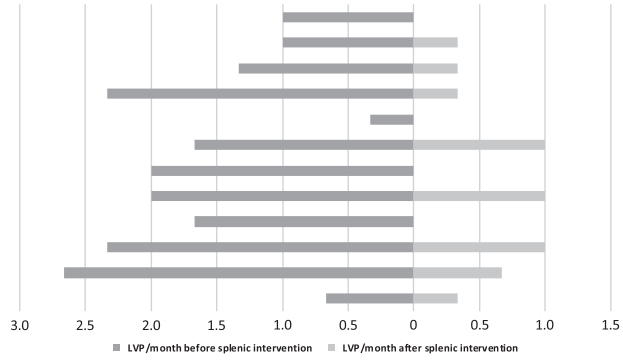

FIGURE 4 Number of therapeutic paracentesis per month before and after the splenic intervention. Each row is an individual patient. For 1 patient, "splenic intervention" was splenectomy. For 11 patients, "splenic intervention" was splenic artery embolization. Abbreviation: LVP, large volume paracentesis.

triglyceride levels were low (median 64 mg/dL). While obtaining SAAG is standard in pre-transplant ascites evaluation, this test was not universal in this post-transplant cohort (73%). Approximately half of the cohort had SAAG $\geq$ 1.1 g/dL, and this finding did not influence subsequent testing, management, or clinical remission at 6 months. Unlike one prior report,[3] bacterial peritonitis was rare in our cohort, as evidenced by low ascites neutrophil counts. HVPG was obtained in 55% of patients but was often normal or low (median 6 mmHg), suggesting that clinically significant sinusoidal portal hypertension was uncommon in our cohort.

While improvements continue in the field of transplantation, our data demonstrate a similar rate of post-transplant ascites development between historic and current cohorts: 2 single-center European and one American study report a 5%–7% incidence of post-transplant ascites, and today, we report 6.3%.[1–3] These 3 historical studies drew 3 different conclusions about the primary cause of post-transplant ascites. One group found that patients with post-transplant ascites had an elevated pressure gradient between the HV and right atrium, suggesting impaired graft blood outflow as the etiology of ascites.[1] Another center from the same time period reported no impact of HV anastomosis on the incidence of post-transplant ascites and instead found HCV infection (with resulting perisinusoidal fibrosis) or unknown reasons as the primary etiologies.[2,9] Finally, a third historical report suggested that bacterial or fungal peritonitis was the cause of persistent post-transplant ascites. In this cohort, treatments included paracentesis, diuretics, antibiotics, and albumin, but no modern treatments, such as splenic artery embolization or other vascular intervention, were pursued.[3]

As with prior retrospective reports, it is challenging to be definitive about the primary etiology of post-transplant ascites in our cohort. Similar to one historical report,[1] we found that hepatic graft outflow may contribute to post-transplant ascites for some, as 17% underwent a HV intervention. We found that cavocavostomy, in particular, was associated with early post-transplant ascites and a larger number of post-transplant paracenteses. Importantly, however, only 3 patients in the most recent era (2014–2019) required a HV intervention, suggesting that venous outflow and type of anastomosis may no longer be a major contributor to post-transplant ascites. This may be a result of evolving transplant surgical techniques. Chronic kidney disease and other complex medical comorbidities also appeared to contribute to post-transplant ascites for some patients in our cohort. While chronic kidney disease was implicated as a potential cause of ascites, none of these patients were listed for or underwent kidney transplants in the 6-month post-transplant. Splenomegaly may have contributed to the development or persistence of post-transplant ascites. Of the patients without clinical resolution at 6-month post-transplant, 24% ultimately improved with a spleen intervention. Finally, we found that 32% of patients with refractory ascites at 6 months did not have a clear etiology of ascites despite extensive diagnostic testing. Lack of clear etiology of course makes treatment more challenging. Future prospective work must explore optimal diagnostic and management strategies in these refractory cases. We wonder if aggressive nutrition intervention could have improved some medically complex refractory cases.

Interventions

Interventions to resolve ascites have evolved with contemporary interventional radiology and a better understanding of portal flow management. Diuretics remain the mainstay of treatment in our cohort, but albumin infusion and splenic artery embolization were increasingly used over time. In our cohort, larger spleens were associated with LVP early after transplant and with a larger number of post-transplant LVPs. Occluding the splenic artery decreases blood flow to the spleen and flow in the splenic vein, subsequently decreases portal vein pressure gradients, and diminishes portal hypertension.[10] Multiple case series show that splenic artery embolization for post-transplant ascites can decrease portal vein velocity, decrease diuretic requirements, and lead to weight loss and complete resolution of ascites.[4,6,11] In our dataset, splenectomy or splenic artery embolization significantly reduced LVP frequency. This tended to be done in patients with a large spleen (mean 18.1 cm). Spleen size is related to the drop in portal pressures associated with splenic artery occlusion; in other words, the larger the spleen, the greater benefit in portal pressures that can be achieved with splenic artery occlusion.[10] Given that our study was not prospective and randomized, we cannot conclude that splenic artery embolization would

be successful in all patients with post-transplant ascites. However, there is a clear benefit in select patients and worth careful consideration in those with splenomegaly and/or manometry evidence of persistent portal hypertension.

We should have caution in pursuing splenic artery embolization in all patients with post-transplant ascites. There is one documented case of worsening ascites after splenic artery embolization in a post-transplant patient, and there are additional risks, such as post-embolic syndrome (abdominal pain, nausea, and low-grade fever), spontaneous bacterial peritonitis, high-grade fever, and inferior vena cava thrombus.[5] One report of interventions for post-transplant arterial steal syndrome found a greater number of septic and thrombotic adverse events in the group that underwent splenic artery coil embolization, as opposed to those who underwent splenectomy or splenic artery banding; however, these complications have decreased considerably with adjusting location of coil placement to a more proximal location within the splenic artery.[12] Our center has previously reported on high mortality after TIPS for post-transplant ascites; however, these data are largely from >20 years ago, and recent reports are more promising, perhaps due to an evolution in TIPS procedural techniques and shunts.[13,14] There may be certain HV anastomoses that make TIPS more technically challenging and risky.[14]

Limitations

Our study was limited by sample size, though understandable as this is a relatively uncommon occurrence. We only include 2 centers; more centers would be required to evaluate how diagnostic, transplant, and therapeutic practices differing between centers may impact post-transplant ascites. Multicenter transplant consortium should pool their resources to look at this question more broadly and evaluate interventions such as splenic artery embolization. For example, we recommend a large multicenter retrospective study of patients who underwent splenic artery embolization for post-transplant ascites to better understand rates of clinical success, ideal procedure characteristics (ie, the precise location of embolization), and clinical factors that modify efficacy. Given the retrospective nature of this study, we were unable to exhaustively and uniformly search for etiologies of post-transplant ascites. There may be etiologies missed in this study. For example, there was a reported case of biopsy-proven sinusoidal obstruction syndrome induced by mycophenolate mofetil.[15] This patient developed refractory post-transplant ascites, which resolved with the cessation of mycophenolate mofetil. The hypothesized mechanism was mycophenolate mofetil–induced endothelial injury, which may occur in those with a genetic predisposition. In this retrospective cohort, we did not evaluate genes responsible for mycophenolate mofetil metabolism, though we will note that the majority of these patients were taking mycophenolate mofetil. Given the modality for data collection (ie, chart review), we were also unable to comprehensively collect data on the 1490 patients who underwent liver transplants and did not experience persistent post-transplant ascites. Therefore, this study is unable to comprehensively evaluate risk factors for developing post-transplant ascites.

CONCLUSION

In conclusion, our data suggest that persistent ascites continues to be a clinical issue in the modern era of liver transplantation. We found that 6.3% of patients who underwent first-time whole graft liver transplant experienced post-transplant ascites. In addition, we found a smaller subgroup with persistent ascites at 6-month post-transplant, who ultimately required additional intervention for ascites management.

CONFLICTS OF INTEREST

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