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Research Article

Incidence, Location, and Natural History of Perihepatic Fluid Collections after Orthotopic Liver Transplantation

Sumail Bhogal [1], Matthew Minn [2], Pranay Krishnan [3], Reena C. Jha [3,*]

1. University of Pittsburgh School of Medicine 3550 Terrace St, Pittsburgh, PA 15213, USA; E-Mail: sumailbhogal@gmail.com
2. Musculoskeletal Imaging Scripps Clinic Medical Group Scripps Green Hospital 10666 N Torrey Pines Rd La Jolla, CA 92037, USA; E-Mail: matthewjminn@gmail.com
3. Medstar Georgetown University Hospital Department of Radiology 3800 Reservoir Road, NW Lombardi, G-184 Washington, DC 20007, USA; E-Mails: pranay.krishnan@medstar.net; jhar@gunet.georgetown.edu

* **Correspondence:** Reena C. Jha; E-Mail: jhar@gunet.georgetown.edu

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Abstract

Objective: The purpose of this study was to evaluate the common locations of perihepatic fluid collections after liver transplantation, assess their complexity, and understand their natural history and clinical significance.

Materials and Methods: A retrospective analysis of 189 postoperative orthotopic liver transplant patients with a mean age 49.6 years was performed using serial CT or MRI to characterize perihepatic fluid collections. Location, size, complexity of the collections, and clinical course were evaluated.

Results: 76 patients (40%) presented with perihepatic fluid collections with a total of 116 collections. 45 pts (59%) had a one collection, 23 pts (30%) had two, 7 pts (9%) had three and one patient (1%) had four. Collections were seen in commonly seen in certain locations, with 38 (33%) in segment 5/6, 37 (32%) in the ligamentum venosum/pericaval region, 12 (10%) in the porta hepatis, 11 (9%) the pericapsular/subdiaphragmatic location, 10 (9%) along the fissure for ligamentum teres, and the remaining 8 (7%) collections in 'other' less frequent perihepatic locations. The vast majority, 100/116 (86%) of all collections were simple and 95/105 (90%) of all collections resolved, decreased or stable on follow up. Collections located in pericapsular /subdiaphragmatic region were significantly more likely to be complex. Sixteen of the 116 collections (14%) were complex, and 4 of these required intervention.

Conclusions: Perihepatic fluid collections are seen in 40 % of patients after liver transplant. Fluid collections were commonly seen in certain locations, most commonly seen in a cleft between segment 5/6, the ligamentum venosum/ pericaval region, the porta hepatis, and the fissure for ligamentum teres. Collections in these locations tend to be simple by imaging criteria and rarely require follow up. Further evaluation may be warranted if collections are symptomatic, enlarging, have complex imaging features, or located in an atypical location.

Keywords

Incidence; location; natural history; perihepatic fluid collections; orthotopic liver transplantation

1. Introduction

The definitive treatment for end-stage chronic liver disease and acute liver failure is orthotopic liver transplantation since the first liver transplant in 1963 [1], and now is considered standard therapy [2]. Hepatic transplant complications manifest in various ways including biliary strictures, stones, and leakage, arterial and venous stenoses and thrombi, and fluid collections, both simple and complex [3, 4].

Although ultrasound is commonly used in the immediate post-operative period, liver transplant patients often have follow-up imaging with CT or MRI for post-transplant complication, or as part of routine surveillance in patients with a history of hepatocellular carcinoma of the explanted liver. These modalities are not only able to assess for disease recurrence, but also provide a reproducible method of assessing of the exact size, number and locations of perihepatic fluid collections. Furthermore, CT and MRI are able to distinguish simple from complex fluid, which may represent purulent material, gas, or hemorrhagic products [5-11].

The radiologist interpreting CT or MR images in the post liver transplant patients often detects perihepatic fluid collections, which may be misinterpreted as potentially pathologic. As such, it is important for the radiologist to know the common locations, appearance, and natural history of these collections. These collections may represent infection or bile leaks, and thus, based on the clinical presentation of the patient, there may be a need for intervention for diagnosis, as well as treatment [12, 13].

Perihepatic fluid collections are often seen in post-operative transplant patients and have been described in the perihepatic spaces as well as near the vascular and biliary anastomoses [14]. Collections are often seen on routine early postoperative ultrasound (US) performed to assess hepatic vasculature patency. Seromas and hematomas may be found during the first few days after transplantation and often disappear on follow-up imaging. There is rarely a need for intervention of these collections unless there is respiratory compromise or significant mass effect on the portal vein or inferior vena cava [14-16].

The purpose of this study was to describe the common locations of post liver transplant perihepatic fluid collections on CT and MRI in an effort to learn which collections may be considered as incidental. We also tried to understand the natural evolution of these fluid collections on follow-up CT/MRI, and any associations between location, appearance and clinical significance.

2. Materials and Methods

This study was presented to, reviewed by, and approved by this institution's affiliated institutional review board. Given the retrospective nature, a waiver was obtained.

The patients were gathered by a search of the radiology report data system inquiry over a 10-year period. In our study, 189 post liver transplantation patients were imaged with MRI (115 patients) and CT (74 patients), performed overwhelmingly as part of routine surveillance. There were 138 male and 51 female patients. The average age at time of transplantation was 49.6 yrs (range 0.5 – 75.1 years). There were 3 pediatric patients, with a mean age 1.6 years. All post-operative imaging was performed at our institution.

All 115 MR examinations after transplantation were performed during suspended respiration with a 1.5-T system and a phased-array coil (Symphony/Avanto; Siemens). The sequence specifics varied minimally over time and scanner, but the vast majority of the patients were imaged with the following protocol: two-dimensional coronal and transverse single-shot fast spin-echo T2-weighted MR imaging (TE: 60-100 msec), transverse inversion recovery T2-weighted MR imaging (TR/TE: 4000 – 6000/90 –100; TI: 150), fat-saturation spoiled gradient echo T1-weighted imaging (TR/TE: 175-200/4.4, 70° flip angle), spoiled dual gradient-echo T1-weighted in- and out-of-phase MR imaging (TR/TE: 125 –200/2.1 and 4.6, 70° flip angle). Parameters for two-dimensional images included 5– 8 mm-thick sections with a 1-mm intersection gap, 256x 115 –192 matrix, 32 by 24 cm field of view. Three-dimensional (3D) interpolated dynamic contrast-enhanced spoiled dual gradient-echo dynamic fat- suppressed MR images were obtained with a slice thickness of 1.5- 2.0 mm (TR/TE: 3.8– 4.3/1.2-1.4, 12° flip angle) pre and dynamic post infusion of gadolinium. Gadopentetate dimeglumine–enhanced images (Magnevist, Berlex Laboratories, Monteville, NJ) were acquired with a dose of 0.1 mmol/kg of body weight.

CT was performed with two separate (16 and 128 slice) CT scanners (Siemens Medical System, Iselin, NJ) in 74 examinations following the standard liver transplantation protocol, which includes a portal-venous phase (70 sec delay) and a delayed phase (120 sec delay). Iohexal 350 enhanced images (Omnipaque, GE Healthcare Co, Princeton, NJ) were acquired at a dose of 2ml/kg of body weight.

Two radiologists with 2 and 5 years of experience independently read available MRI and CT for each patient. The reviewer evaluated the presence or absence of perihepatic fluid collections, their number, size and location.

Fluid collections were measured in transverse and anterior-posterior dimensions on axial slices (length by width in cm) using Philips PACS software. As some collections were long and thin, while others were round, rather than use the longest dimension to describe its size, we multiplied the two measurements in the axial plane to create an 'area-equivalent metric' (recognizing that this is the equation for area of a square). Given the odd shapes and on occasion, intra-fissural location, performing volume assessments were difficult, and are not routinely performed in clinical practice, we used this metric to compare the size of collections.

After initial measurement, the location of all fluid collections was categorized using standard liver segmental anatomy and descriptions. Each fluid collection was categorized as simple or complex. The criteria used are as follows: On MRI, simple fluid collections demonstrated signal that paralleled simple fluid: hyperintense signal on T2 weighted images, hypointense signal on T1 weighted images, and no enhancement, using cerebral spinal fluid as visual internal reference. On CT, simple collections were homogenous, hypoattenuating with Hounsfield units of simple fluid (HU<10) and without enhancing components. If these criteria were not met, these were defined as complex fluid collections. Presence of gas within a fluid collection was categorized as a complex fluid collection.

The natural evolution of the fluid collections was evaluated. All collections were followed on all available subsequent cross sectional studies to identify the persistence of fluid collections, and if present, to assess for changes in size, whether these were simple verses complex, and if there was any intervention performed for the collections, and if so, the patient's clinical status and outcome.

All data collected was submitted for statistical analysis, using frequencies and percentages for categorical variables and means and standard deviations for continuous variables. Bivariate associations were examined using Fisher's exact test for categorical variables and Analysis of Variance (ANOVA) with Bonferroni adjusted post-hoc tests for continuous variables. Significance was assessed in all cases at the 0.05 or 0.01 for p-value.

3. Results

Of the 189 patients, 76 patients (40%) presented with a total 116 fluid collections (Table 1). Patients with no fluid collections were imaged at a mean of 374.8 days (1-3903 days) after transplant, while patients with a fluid collection were imaged earlier, with a mean of 92.3 days (1 - 2031 days).

Of the 76 patients, 45/76 (59%) had a single fluid collection while smaller subset 23/76 (30%) had two collections, with, 7/76 (9%) with three collections, with 1/76 (1%) had four collections. The majority (33%) of the collections were found in the cleft between segment 5 and segment 6 (Figure 1A) followed by 31% in the pericaval / ligamentum venosum regions (Figure 1B) 10% in the porta hepatis (Figure 1C), 10% in the right subcapsular/subdiaphragmatic regions (Figure 1D), 9% along the course of the fissure for ligamentum teres, (Figure 1E), and 7% in other locations, such as along the left hepatic lobe or Morrison's pouch.

Table 1 Summary of all fluid collections.

Total Fluid Collection Locations	**Total Number of Fluid Collections**	**# of Simple/Complex Fluid Collections**	**Mean # of days from transplant to first imaging (Range)**	**Mean LxW* in cm^2 (Range)**	**# of Fluid Collections Drained**
Segment 5/6	38	35/3	98.5 (4-626)	3.9 (0.21-24.2)	1
Pericaval/Ligamentum Venosum	37	37/0	124.8 (3-2031)	5.4 (1.7-15.1)	1
Porta Hepatis	12	9/3	34.5 (4-107)	18.2 (1.8-53.8)	2
Pericapsular/subdiaphragmatic	11	7/4	55.1 (1-153)	42.6 (3.3-172.5)	1
Fissure for ligamentum teres	10	10/0	92.8 (29-228)	5.0 (1.4-9.4)	0
Other	8	2/6	49.1 (10-93)	50.9 (4.6-210.0)	2

*L=length; W=width

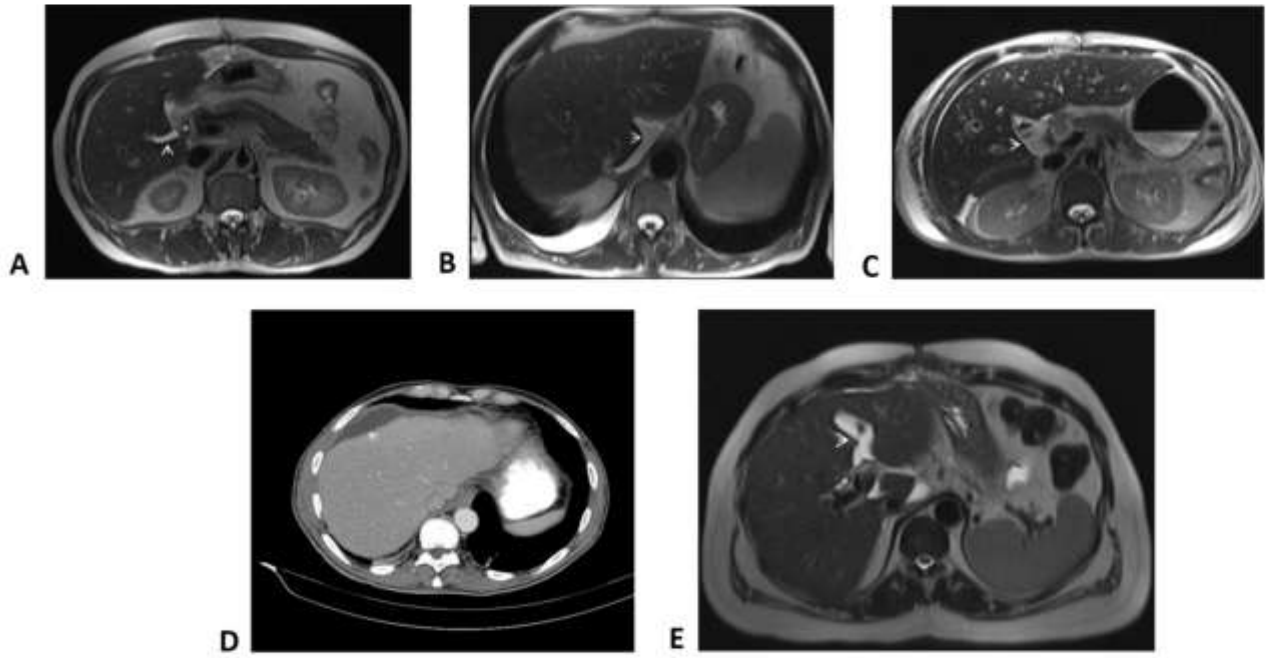

Figure 1 Common locations of post-transplant fluid collections (A-E) demonstrating simple fluid collections. **A.** Axial T2 WI -Cleft between segment 5/6(*arrowheads):* most common. **B.** Axial T2 WI -Pericaval region/ ligamentum venosum (*arrowhead);* second most common site. **C.** Axial T2 WI - Porta Hepatis (*arrowhead*); third most common site. **D.** Axial iv contrast enhanced CT-Pericapsular/subdiaphragmatic (*arrowhead*); fourth most common site. **E.** Axial T2 WI-Fissure for ligamentum teres, (arrowhead); fifth most common site.

Of the patients with fluid collections, the overall mean size by 'area-equivalent metric' was 13 cm^2 with a standard deviation of 29 cm^2 (13 ± 29 cm^2). The smallest size of collections by 'area-equivalent metric' was 0.21 cm^2 and the largest was 210 cm^2. The collections in the right subcapsular/subdiaphragmatic region and 'other' regions than commonly described sites are significantly larger than the other locations ($p < 0.001$).

Of the 116 perihepatic fluid collections, 100 simple fluid collections were seen, with an average time to imaging of 103.6 days. The locations of the simple collections were most often seen in the cleft between segment 5 and segment 6 and in the pericaval / ligamentum venosum regions in 72/100 (72%). No further follow-up imaging was available at the time of data collection in 10/100 (10 %) of simple fluid collections. Of these simple collections with follow-up, 87/90 (97%) resolved, decreased or was stable in size on follow-up imaging. However, 3 'simple' fluid collections were sampled percutaneously because of a clinical concern for bilomas in 2 patients and due to an increase in size in one patient. All of the 'simple' fluid collections requiring percutaneous sampling resolved on available follow up imaging.

There were 16 complex fluid collections seen, with an average time to imaging of 21.6 days (Table 1). Based on imaging and clinical presentation, 13 (81%) of these were felt to represent hematomas (Figure 2 and Figure 3) based on symptoms and imaging, while the remaining 3 (19%) collections were concerning for abscesses (Figure 4). Of these complex collections, 4 (25%) required therapeutic intervention, with a drain placed for a hematoma in 2 patients and for abscess in two patients, with a fine needle aspiration performed for infection in one patient with a small collection that was subsequently treated with antibiotics.

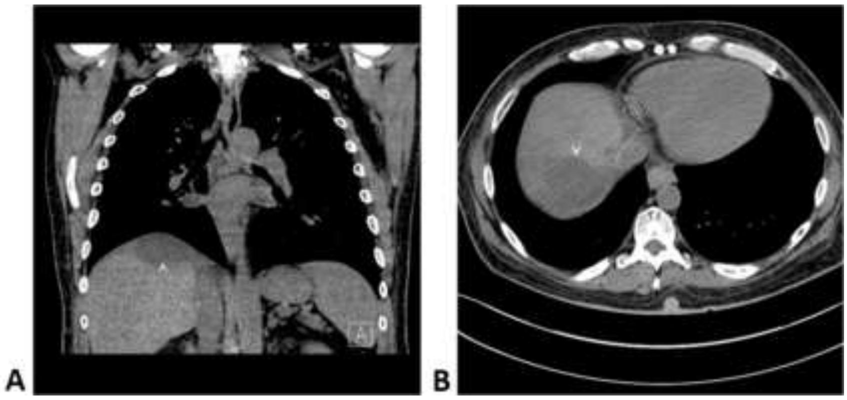

Figure 2 A and B. Coronal and axial non-contrast CT images demonstrate a heterogeneous complex subdiaphragmatic fluid collection (*arrowheads*) thought to be a hematoma.

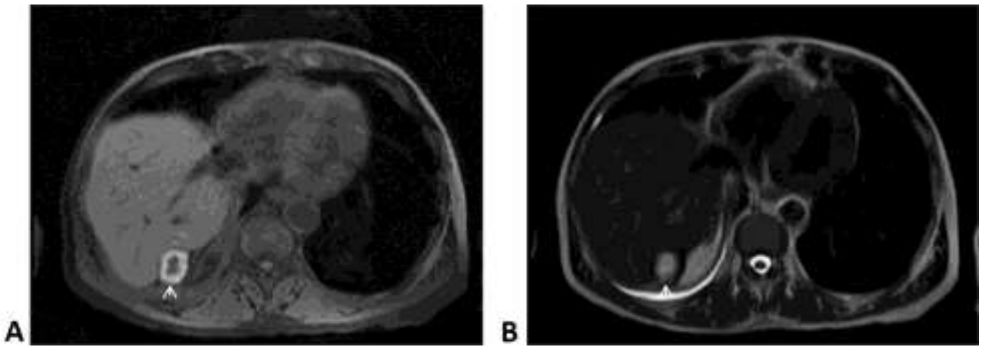

Figure 3 A and B. Axial T1 fat-saturated and T2-weighted images demonstrate a complex fluid collection (*arrowheads*) within Morrison's pouch. Note the rim of increased signal intensity on T1-WI with decreased signal intensity on T2-WI, most consistent with a hematoma.

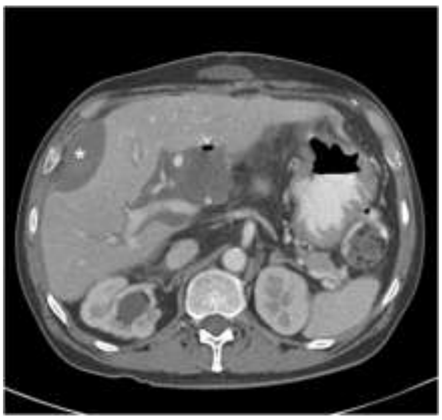

Figure 4 Axial iv contrast-enhanced CT image in a febrile patient demonstrates a complex porta hepatis fluid collection (arrowhead) that contains a single focus of gas consistent with an abscess. An additional pericapsular/subdiaphragmatic fluid collection is seen (asterisk).

When fluid collections were seen within the common location (95%-100% in the top 5 common locations), these were overwhelmingly simple. However, when fluid collections were located in pericapsular / subdiaphragmatic region and the 'other' regions, these were more likely to be complex ($p < 0.001$). Furthermore, these collections were significantly larger (Table 1) than the other locations ($p < 0.001$). Complex fluid collections tended to be drained (not statistically significant p = 0.195).

4. Discussion

In this study, using data predominantly from routine post-transplant surveillance imaging perihepatic fluid collections are seen in 40% of patients post liver transplant, and are commonly located in certain anatomic locations. In the present study, this was most commonly seen in a cleft between segment 5 and 6, followed by the ligamentum venosum/pericaval regions, and porta hepatis, the pericapsular/subdiaphragmatic regions, and the fissure for ligamentum teres.

When simple perihepatic fluid collections were seen in these typical expected locations, the vast majority remained stable, decreased or resolved on follow up, and if asymptomatic, no intervention was performed. The incidence of complex fluid collection was considerably lower, with 16 collections seen. Of the complex collections, 4(25%) of these were drained. The pericapsular /subdiaphragmatic locations and 'other' nonspecific locations showed significant association with complexity, as well a larger size of the collection.

The commonly seen locations of fluid collections are likely due to the surgical dissection of normal peritoneal reflections in these spaces [14] at the time of transplantation. Thus, fluid accumulates in these predictable sites, as seen in this study. Disruption of the lymphatics along the surgical reflections is thought to be another etiology for the development of perihepatic collections [17].

This study suggests that if a simple fluid collection is seen in the common locations described, without an increase in size and or clinical symptoms in a patient seen on routine surveillance imaging, the collection is likely to be clinically irrelevant, and in this study, 97% of these simple collections resolved or decreased in size on follow up images. On the other hand, if a collection occurs in an unusual location, is increasing, or symptomatic, this may warrant further evaluation.

Although prior authors have described locations of post liver transplant collections [18-22], these studies have not looked at their frequency and associations with clinical outcome, nor evaluated them on follow up imaging.

There are limitations to this study. First, it is a retrospective study. Second, as the imaging interval of these studies was based on clinical need, and as there was no consistent time frame for imaging in the peri- and post-operative period, true prevalence cannot be assessed. At our institution, routine abdominal ultrasound examinations with duplex Doppler are performed on post-operative days 1 and 2 to evaluate for transplant vascular patency. Accurate localization and reproducible measurement of all postoperative fluid collections via ultrasound in ICU patients is challenging, given patient state and limited field of view of the entire liver. For these reasons, we decided not to include fluid collections identified on routine postoperative abdominal ultrasound examinations in our analysis. The goal of our study was not to identify the perioperative incidence of post-transplant fluid collections, but to describe the history and progression of fluid collections identified throughout the postoperative period and predominantly during routine follow up, and help radiologists and transplant surgeons learn of their common expected locations. Thirdly, the number of cases with complex collections were small and therefore we recognize that the association between complexity and the pericapsular /subdiaphragmatic locations and 'other' nonspecific locations should be evaluated somewhat cautiously. The clinical utility of this study is to recognize the common locations of perihepatic fluid collections post liver transplant, and evaluate for simple versus complex fluid and correlate with patient symptoms in order to best guide patient management and need for intervention.

5. Conclusions

Perihepatic fluid collections in the transplant liver are seen in about 40% of patients, most often single, and are typically located in a cleft between segment 5 and 6, the pericaval/ligamentum venosum region, and within the porta hepatis, as well as along the pericapsular region and, and the fissure for ligamentum teres.

The majority of the collections are clinically insignificant. They predominantly have simple imaging characteristics, and resolve or decrease in size on follow-up.

There may be an association between collections that are complex or large and identified in atypical locations such as the pericapsular/subdiaphragmatic area and 'other nonspecific' location. These may require further evaluation, based on patient clinical presentation.

Author Contributions

R.J. conceived of the presented idea. S.B. and M.M. gathered imaging and clinical outcomes data. M.M. and P.K. performed the measurements. R.J. was involved in planning and supervised the work. M.M. and R.J. designed the figures, aided in interpreting the results and worked on the manuscript. All authors discussed the results and contributed to the final manuscript.

Competing Interests

The authors have declared that no competing interests exist.

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