Outcomes of patients with chest tube insertion for hepatic hydrothorax

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Abstract

Purpose Case reports and small case series have reported a high rate of complications associated with chest tube placement for hepatic hydrothorax. We describe the in-hospital and 3-month outcomes of patients who have had this procedure.

Methods A retrospective medical record review was performed of all patients admitted to a tertiary care center over a 10-year period with a chest tube placed for hepatic hydrothorax. Demographic data and outcomes were collected and analyzed.

Results Seventeen patients were identified; 12 were taking diuretics and 8 were taking multiple diuretics at the time of admission. MELD score was 14 (range = 7–34). During hospitalization, 16 had at least 1 and 12 had more than 1 complications. The most common complications were acute kidney injury ($n = 11$), pneumothorax ($n = 7$), and empyema ($n = 5$). Two patients died during the index admission and four others within 3 months of that admission. Six of seven patients who received TIPS survived.

Conclusions Chest tube insertion for hepatic hydrothorax carries significant morbidity and mortality, with questionable benefit.

Keywords Hepatic hydrothorax · Chest tube · Cirrhosis · Ascites · Acute kidney injury

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ICD	International classification of diseases
INR	International normalized ratio
MELD	Model for end-stage liver disease
TIPS	Transjugular intrahepatic portosystemic shunt

Introduction

Hepatic hydrothorax is an uncommon complication of chronic liver disease, occurring in 5–10% of patients with cirrhosis [1]. It is defined as a transudative effusion in patients with liver disease without a primary cardiopulmonary cause. Although its pathogenesis is not entirely clear, hepatic hydrothorax is believed to be a consequence of ascitic fluid translocation through congenital diaphragmatic defects into the pleural cavity. These defects, which occur most often in the right hemidiaphragm, are usually smaller than 1 cm and are covered with pleuroperitoneum. When ascites accumulate and intraperitoneal pressure increases, the pleuroperitoneal membrane ruptures and ascitic fluid can move into the low-pressure pleural space [2–4]. This explanation for the appearance of hepatic hydrothorax is supported by studies showing intraperitoneal-injected radiotracer activity in the pleural fluid of such patients [1].

Compared with ascites, the volume of pleural fluid required to cause symptoms is relatively small, given the relatively low compliance of the thoracic cavity. Thus, patients can become markedly dyspneic with as little as 500 mL of intrapleural fluid, compared with many liters of

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ascites. In addition, like ascites, hepatic hydrothorax can become spontaneously infected, a condition known as spontaneous bacterial empyema, which carries a mortality of up to 20%. The morbidity, then, of hepatic hydrothorax is significant, and its management is important in patients with end-stage liver disease.

The only definitive treatment of hepatic hydrothorax is liver transplantation [5]. The role of other therapies is to alleviate symptoms and prevent the complications of hepatic hydrothorax in patients awaiting transplant, or to palliate in those who are not transplant candidates. Treatments of hepatic hydrothorax are similar to those of ascites, as the pathogenesis of both conditions is related. Sodium restriction and diuresis are currently the mainstay of therapy [3, 4, 6, 7]. In patients with refractory hydrothorax, recommended therapies include therapeutic thoracentesis, TIPS [8, 9], and pleurodesis [10–12].

Chest tube insertion in patients with cirrhosis is fraught with complications including pneumothorax, hemothorax, empyema, electrolyte abnormalities, and renal failure [7, 13, 14]. Although various authors have cautioned against chest tube insertion in patients with cirrhosis [14], this procedure is still performed. We describe the in-hospital and 3-month outcomes of patients who have had chest tube placement for hepatic hydrothorax.

Materials and methods

All adult patients admitted to the University of Michigan Hospitals from 1997 to 2006 for the treatment of hepatic hydrothorax were identified by matching ICD-9 codes for both liver disease (570, 571, 572, 573, 789.1, 789.5, 794.8, V42.7) and pleural disease (510, 511, 512, 517.8, 518.89, 793.1, 860, 861.2, 861.3). The study protocol was approved by our institutional review board. For inclusion, patients had either biopsy-proven cirrhosis or cirrhosis based on radiologic studies (computed tomography or ultrasound) with radiographically confirmed pleural effusion. Subjects were excluded if they previously underwent liver transplantation, if they had underlying pulmonary disease at the time of chest tube placement, or if the effusion was likely due to another cardiopulmonary condition.

Data were extracted from the electronic and hard copy medical records by one of the authors (E.S.O.). The following baseline patient variables were collected either at the time of chest tube insertion or at the time of admission for those in whom chest tube was placed in an outside hospital: age, gender, race/ethnicity, etiology of liver disease, diuretic regimen, complete blood cell count, serum sodium, creatinine, albumin, AST, ALT, alkaline phosphatase, total bilirubin, and INR.

The following in-hospital complications were identified: infection (including empyema, cellulitis, pneumonia, bacteremia, and bacterial peritonitis), pneumothorax, encephalopathy, acute kidney injury, and clinically significant bleeding from any site. *Empyema* was defined as pleural fluid with grossly purulent appearance, positive culture result, or pH below 7.20 [15]. The diagnosis of cellulitis at the chest tube site was based on clinical assessment. *Pneumonia* was defined as a new infiltrate on chest radiography. Bacteremia was determined by positive blood culture results. *Bacterial peritonitis* was defined as ascitic fluid with at least 250 neutrophils/mm³ or positive culture result. *Hepatic encephalopathy* was defined as altered mental status without other identifiable cause that was responsive to lactulose. *Acute kidney injury* was defined as either a new hemodialysis requirement or an increase in serum creatinine level of at least 0.5 mg/dL compared with the patient's baseline creatinine level. *Clinically significant bleeding* was defined as bleeding at any site requiring transfusion of red blood cells or medical intervention to achieve hemostasis.

Repeat interventions including thoracentesis, chest tube placement, and TIPS placement during the index hospitalization and in the subsequent 3 months were identified. In-hospital and 3-month mortality and outcomes were also recorded.

Results

Seventeen patients met the eligibility criteria. The baseline clinical and laboratory features are noted in Table 1. Seven (41%) patients were men, 12 were Caucasians, and the mean age was 55 years. Etiology of the underlying cirrhosis was hepatitis C and/or alcohol in 13 (76%) patients. None of the patients had hepatocellular carcinoma. Twelve patients were taking diuretics at the time of admission. Of these, 8 were receiving a combination of furosemide and spironolactone. MELD score was 14 (range = 7–34). Nine (53%) patients had a baseline leukocytosis ($>10^4/\text{mm}^3$) and 9 were anemic (hemoglobin <12 g/dL). Fifteen (88%) patients were hyponatremic (serum sodium <135 mmol/L), 8 (47%) had serum sodium level of less than 130 mmol/L, and 7 of those 8 patients had a sodium level less than 125 mmol/L. Seven patients had renal insufficiency (creatinine >1.2 mg/dL).

During the index admission, 16 (94%) patients had at least 1 prespecified complication and 12 (70%) patients had more than one complication (Table 2). The most common complications were acute kidney injury (in 11 patients, with 1 requiring hemodialysis), pneumothorax ($n = 7$), and empyema ($n = 5$). Two patients died during the index admission: one patient from pneumonia 5 days

Table 1 Baseline characteristics of the study patients ($N = 17$)^a

Age, years	55 (9.4)
Gender: men	7 (41.2)
Race/ethnicity: Caucasian	12 (70.6)
Etiology of cirrhosis	
Hepatitis C	8 (47.0)
Alcohol	5 (29.4)
Taking diuretics	12 (70.6)
Multiple diuretics	8 (47.0)
Diuretic dose	
Furosemide, mg	64 (37.1)
Spironolactone, mg	103 (54.2)
Hemoglobin, g/dL	12.2 (1.75)
Leukocytes, $10^3/\text{mm}^3$	12.3 (6.37)
Platelets, $10^3/\text{mm}^3$	133 (66.8)
INR	1.4 (0.25)
Albumin, g/dL	2.2 (0.49)
AST, IU/L	77 (31.4)
ALT, IU/L	58 (33.3)
Bilirubin, mg/dL	2.8 (2.11)
Alkaline phosphatase, IU/L	213 (127.9)
Sodium, mmol/L	127 (7.7)
Creatinine, mg/dL	1.4 (0.92)
MELD score	16 (7.1)

^a Gender, race/ethnicity, etiology of cirrhosis, taking diuretics, and multiple diuretics were presented as number (%) and the others as mean (SD)

after the admission and one from acute respiratory distress syndrome 10 days after the admission. Five patients had TIPS placement during the index admission and all survived to discharge; two of these five patients required repeat thoracentesis after discharge, and one patient later died from worsening liver failure. Two patients had repeat chest tube placement during the index admission: one for palliation of dyspnea and one for empyema; both survived to discharge but died within 3 months of worsening liver failure and septic shock, respectively. Of the remaining eight patients who survived to discharge, two had TIPS placement at a later date and both survived (one had repeat chest tube placement prior to TIPS placement for recurrent hydrothorax). Among the six patients who did not have TIPS placement, one died from worsening liver failure.

In total, six (35%) patients died: two during and four within 3 months of the index admission. The primary cause of death was sepsis in three patients and worsening liver failure in three patients. Seven patients had TIPS placement; of these, six (86%) survived. Three patients had repeat chest tube placement; only one (33%) survived.

Table 2 Complications during index admission and outcomes within 3 months of the index admission^a

	Index admission	Cumulative 3-month outcomes
Number of patients with complications		
None	1 (5.9)	
1	4 (23.5)	
>1	12 (70.6)	
Type of complications		
AKI	11 (64.7)	
Hemodialysis, % of AKI	1 (9.1)	
Pneumothorax	7 (41.2)	
Empyema	5 (29.4)	
Encephalopathy	3 (17.6)	
Pneumonia	3 (17.6)	
Bacteremia	2 (11.8)	
Peritonitis	1 (5.9)	
Cellulitis	1 (5.9)	
Bleeding	1 (5.9)	
Additional interventions and mortality		
Repeat thoracentesis	2 (11.8)	6 (35.3)
Mortality	0	1 (5.9)
TIPS placement	5 (29.4)	7 (41.2)
Mortality	0	1 (5.9)
Repeat chest tube	2 (11.8)	3 (17.6)
Mortality	0	2 (11.8)
No intervention	9 (52.9)	6 (35.3)
Mortality	2 (11.8)	2 (11.8)
Overall mortality	2 (11.8)	6 (35.3)

AKI acute kidney injury

^a Values expressed as number (%)

Discussion

All except one patient in this series of 17 patients suffered a complication related to chest tube placement for hepatic hydrothorax, and overall 3-month mortality was 35%. Although numerous case reports have been published on the topic [13, 14, 16–18], only the study by Liu et al. [7] examined the outcomes of a sizeable group of cirrhotic patients with chest tubes. Their findings were similar to ours, with an 80% complication rate and 27% mortality. The study of Liu et al., however, included patients who had a chest tube placed for multiple reasons, including empyema and pneumothorax, indications that require chest tube drainage. This study, then, is the largest to examine outcomes of chest tubes specifically placed for hepatic hydrothorax, and it is consistent with previous reports showing significant morbidity and mortality.

Table 3 Reports of chest tubes placed for hepatic hydrothorax

	<i>N</i>	Successful removal	TIPS	Complications	Mortality
Andrade et al. [25]	1	Yes	Yes	Renal failure Pneumothorax Hemothorax	5 months
Borchardt et al. [13]	1	No	No	Renal failure Hyponatremia Empyema	~20 days
Chen et al. [18]	1	No	No	Renal failure Hypotension	25 days
Conklin et al. [26]	1	Yes	Yes	Infection	Avoided with TIPS; 8-month follow-up
Dumortier et al. [27]	1	Yes	No	Renal failure	Avoided with octreotide; 5-month follow-up
Haskal and Zuckerman [28]	1	Yes	Yes	Variceal hemorrhage Volume depletion	Avoided with TIPS; 10-month follow-up
Ibrisim et al. [16]	1	Yes	No	Renal failure Hyponatremia Empyema Encephalopathy	Avoided with terlipressin and albumin; short-term follow-up
Liu et al. [7]	56 ^a	36 (64%) ^a	1 (2%) ^a	Renal failure Electrolyte imbalances Infection ^a	15 (27%) after 1–39 days ^a
Pfammatter et al. [17]	1	Yes	No	Encephalopathy Electrolyte loss Protein loss	Avoided with octreotide; unclear follow-up
Runyon et al. [14]	2	No	No	Hyponatremia Hypoalbuminemia Peritonitis Renal failure	2 days, few weeks

^a Refers to chest tubes placed in patients with cirrhosis for multiple indications

The existing literature on the outcomes of patients who had chest tubes placed for hepatic hydrothorax is summarized in Table 3. In these case reports and case series, mortality was high and most deaths occurred within 1 month. In a few patients, death was avoided only with intensive measures such as terlipressin and somatostatin analogues that have been shown to facilitate mesenteric vasoconstriction and thereby reduce portal pressure [19, 20]. Furthermore, as in our series, renal failure and infection were common complications, and in most of the series, the chest tubes could not be successfully removed. The authors of these series generally attributed the complications of renal failure and electrolyte disturbances to the drainage of large volumes of protein-rich pleural fluid. They also indicated that failure to remove the chest tubes was related to respiratory instability due to rapid reaccumulation of the effusion upon clamping of the chest drain. These findings are consistent with our experience. Notably, the literature contains few cases in which TIPS was placed after a chest tube.

In our series, TIPS was subsequently performed in 7 (41%) patients, 6 of whom survived compared with 5 of 10 patients who did not have the procedure. These data suggest that when possible, TIPS should be attempted in patients who have had chest tube for hepatic hydrothorax to facilitate tube removal and to prevent recurrent hepatic hydrothorax. Another reason for pursuing TIPS, a more definitive management of hepatic hydrothorax, is that of the three patients who had repeat chest tube placement, two died within 3 months.

Data on the efficacy of other interventions for hepatic hydrothorax are sparse. Sodium restriction and diuresis are recommended as initial therapy based on their efficacy in the management of ascites [4, 21]. TIPS has been shown to be effective in preventing reaccumulation of pleural effusion in patients who are refractory to diuretics and in decreasing mortality. Clinical and radiographic improvement in hydrothorax has been documented in up to 68% of patients undergoing TIPS [8, 22–24]. Jeffries et al. [9] reported one response lasting greater than 2 years. In

addition, short-term mortality in the series in which therapeutic TIPS was performed is <30% [23, 24].

This study is limited by its design. As a retrospective case series, there is no control group to compare outcomes. Patients with symptomatic hepatic hydrothorax typically have advanced liver disease, which carries high morbidity and mortality independent of chest tube placement. However, studies examining other treatments of hepatic hydrothorax have shown lower mortality [8]. Our conclusions are also limited by the relatively small sample size, which reflects the rarity of this clinical situation. This rarity seems appropriate given the documented poor outcomes, but the fact that physicians continue to perform this procedure reinforces the importance of physician education and awareness of these complications and outcomes. On the basis of our findings, chest tubes should not be placed to relieve hepatic hydrothorax because of the significant morbidity and mortality associated with the procedure. In those who have had this procedure, TIPS should be considered to facilitate chest tube removal and to prevent recurrence of hepatic hydrothorax.

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