Hepatic hydrothorax

Hannah Wilkins[1], Ellie Britt[2], Malvika Bhatnagar[3], Benjamin Pippard[3]

[1]Department of Gastroenterology, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; [2]Department of Respiratory Medicine, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; [3]Department of Respiratory Medicine, South Tyneside and Sunderland NHS Foundation Trust, South Tyneside, UK

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Correspondence to: Benjamin Pippard, PhD, MRCP. Department of Respiratory Medicine, South Tyneside and Sunderland NHS Foundation Trust, Harton Lane, South Shields, NE34 0PL, UK. Email: benjamin.pippard@nhs.net.

Abstract: Hepatic hydrothorax (HH) refers to the presence of a pleural effusion that develops in the context of underlying liver cirrhosis and portal hypertension. It carries a high risk of morbidity and mortality, with a median survival of 8–12 months. Diagnosis is usually confirmed by pleural aspiration, demonstrating typical features of a transudative effusion in the absence of co-existent cardio-pulmonary or renal pathology. The clinical presentation is quite variable, with some patients remaining relatively asymptomatic in the presence of small or incidental effusions, while others present with frank respiratory failure requiring pleural intervention. The development of spontaneous bacterial empyema (SBEM) is a significant and not infrequent complication, requiring prompt recognition and treatment. While the mainstay of management is focused on optimising fluid balance through dietary salt restriction and diuretic therapy, liver transplantation remains the definitive treatment option. As such, it is crucial to adopt a multi-disciplinary approach—involving pulmonologists, hepatologists, dieticians, and palliative care physicians—in order to optimise care for this often complex group of patients. This review will discuss the basic pathophysiology of HH, its clinical presentation and diagnosis, as well as the approach to management of HH in clinical practice, focussing on both interventional and non-interventional treatment modalities.

Keywords: Hepatic hydrothorax (HH); pleural effusion; liver failure

Introduction

Pleural effusions—the accumulation of fluid within a pleural cavity—represent a major contributor towards global healthcare burden. The estimated annual incidence of pleural disease is 360 per 100,000 individuals and continues to rise, largely as a result of longer life expectancy in patients with cancer and other chronic illnesses (1). A recent analysis conducted in the United States (US) revealed that 43,000 emergency room visits, including 361,270 hospitalisations, were related to pleural disease alone (2). Of these, non-malignant pleural effusions (the most common type of pleural effusion encountered) accounted for 85% of attendances (2).

Hepatic hydrothorax (HH) refers to a pleural effusion in a patient with liver disease and associated portal hypertension, in the absence of underlying cardio-pulmonary, renal, or malignant disease (3). The size of pleural effusion is typically in excess of 500 mL, and frequently occurs in the presence of significant ascites (4); however, HH can occasionally present without definite evidence of ascites (5,6) and, rarely, secondary to non-cirrhotic portal hypertension (7), which may lead to delays in diagnosis if not specifically considered.

HH is thought to account for around 2% of all pleural effusions, regardless of aetiology (8). Nonetheless, in
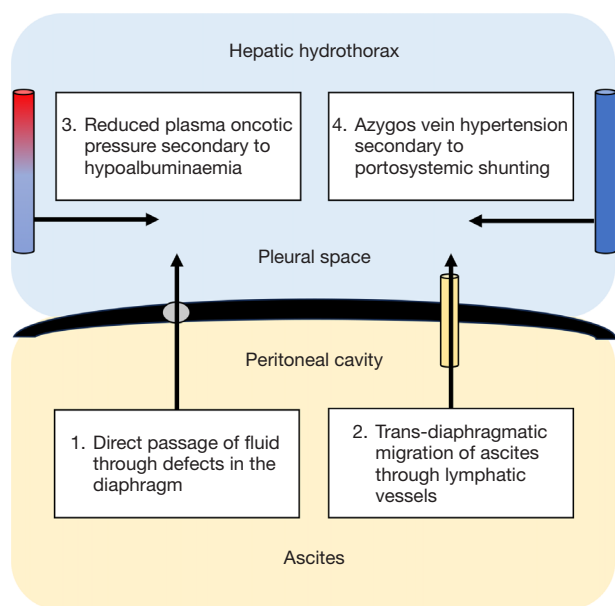
Figure 1 Proposed mechanisms leading to the development of hepatic hydrothorax. The most widely accepted mechanism relates to the direct passage of fluid from the peritoneal cavity into the pleural space, via defects in the diaphragm (box 1). Other potential mechanisms include: trans-diaphragmatic migration of ascitic fluid into the pleural space via the lymphatic system (box 2); fluid accumulation within the pleural space secondary to reduced plasma oncotic pressure associated with hypoalbuminaemia (box 3); and azygos vein hypertension stemming from porto-systemic shunting (box 4). Each of these mechanisms is based upon the flow of fluid into the pleural space by a pressure gradient difference between the pleuro-peritoneal cavities and/or systemic vasculature. Adapted from Pippard *et al.* (16). Creative Commons Attribution 4.0 International License.

patients with cirrhosis, the prevalence of HH is estimated to be between 5% and 16%, rising substantially (up to 90%) in those with Child Pugh B or C decompensated liver disease (9-12). The associated mortality in patients with cirrhosis and HH is high, with a reported median survival of 8–12 months (13). Notably, in one retrospective cohort study by Badillo and Rockey (12), mortality rates in 77 patients with HH were reported as 10%, 26% and 57% at 30 days, 90 days and 1 year, respectively. Overall survival was considerably improved in those patients who had undergone TIPSS procedure (transjugular intrahepatic portosystemic shunt) or liver transplantation (12). Additionally, it is recognised that patients with HH have reduced 5-year survival rates (15.4% versus 30.9%) compared to patients without HH

who have similar degrees of liver dysfunction (14). As such, this represents an important clinical entity to consider as part of the broader differential of non-malignant pleural effusions.

The purpose of this article is to provide an overview of the pathophysiology, clinical characteristics, diagnosis, and management of HH, highlighting the various interventional and non-interventional therapeutic strategies that may be considered.

Pathophysiology

The development of a pleural effusion fundamentally stems from the rate of fluid accumulation in the pleural space exceeding the natural rate of fluid absorption from the pleural membrane. In the case of HH, this is directly linked to the presence of portal hypertension secondary to underlying liver disease, accounting for the frequent co-existence of ascites in this group of patients (12,15). While the exact pathophysiology of HH formation remains uncertain, several mechanisms have been proposed, as outlined in *Figure 1*.

Of these, it is thought that the direct passage of fluid from the peritoneal cavity into the pleural space via small diaphragmatic defects represents the principal mechanism underpinning development of HH (17,18). Huang *et al.* (19) have previously proposed four different classifications of diaphragmatic defect leading to HH formation (see *Table 1*), based on direct video thoracoscopic assessment, which may occur independently or concurrently.

Such pleuro-peritoneal communications are typically less than 1cm in diameter, and reflect points of anatomical weakness within the tendinous structure of the diaphragm. This mechanism may help to explain the right-sided predominance of HH (see clinical presentation, below): specifically, during embryological development, the right hemi-diaphragm assumes a more collagenous structure compared to the more muscular left hemi-diaphragm, which consequently appears less prone to bleb formation and rupture (20). Additionally, it has been proposed that the close apposition of the liver to the right hemi-diaphragm acts in a piston-like manner to facilitate fluid migration preferentially into the right hemithorax (8).

The unidirectional flow of fluid across these diaphragmatic defects (i.e., from the peritoneal cavity into the pleural space) is governed by the intrinsic negative intrathoracic pressure gradient that exists, and may be further exacerbated by raised intra-abdominal pressure

Table 1 Classification of diaphragmatic defects proposed in the development of HH [after Huang et al. (19)]

Type 1: no visibly observed defects
Type 2: diaphragmatic blebs
Type 3: fenestrations of the diaphragm (arising secondary to ruptured blebs)
Type 4: multiple gaps within the diaphragm

HH, hepatic hydrothorax.

Table 2 Summary of typical symptoms experienced by patients with HH

General
• Asymptomatic (e.g., in the presence of small/incidental effusions)
• Fatigue
Respiratory
• Dyspnoea
• Cough
• Pleuritic chest pain
• Orthopnoea
• Respiratory failure (rarely, secondary to tension hydrothorax)
Gastrointestinal
• Nausea
• Abdominal pain
• Abdominal swelling and ascites (not always present)
• Associated manifestations of decompensated cirrhosis (e.g., encephalopathy)

HH, hepatic hydrothorax.

in the presence of significant ascites (21). This one-way migration of ascitic fluid into the pleural space has been confirmed using various imaging-based techniques, such as the tracking of injected technecium-labelled colloids (22) and peritoneal scintigraphy (23). Notably, however, it is possible for HH to develop even without demonstrable ascites (5,6); this most likely occurs when fluid migration into the pleural cavity either matches or exceeds the accumulation of fluid in the peritoneum, through a combination of the natural pleuro-peritoneal pressure gradient and the higher absorptive capacity of the peritoneum compared to pleura (6). Nevertheless, why this phenomenon occurs in some patients and not in others remains unclear.

Clinical presentation

The clinical presentation of HH can vary substantially between individual patients (summarised in *Table 2*), with symptoms typically dependent on the size and rapidity of pleural fluid accumulation and whether this coexists with significant ascites.

In a previous retrospective cohort study of 77 patients with HH, dyspnoea (34%), cough (22%), nausea (11%) and pleuritic chest pain (8%) were identified as the most frequently reported symptoms, respectively (12). However, it is important to recognise that some patients remain relatively asymptomatic in the presence of small effusions (which may be identified incidentally on chest radiography), whereas others present with more substantial respiratory symptoms and, occasionally, with frank respiratory failure in the context of tension hydrothorax (24). Of note, patients are often able to tolerate large volumes of fluid within the peritoneal cavity without clinical compromise, whereas even relatively modest fluid accumulation within the pleural space (e.g., 1–2 L) can lead to significant hypoxia and associated breathlessness (25). In rare cases, cardiac tamponade and haemodynamic instability may complicate HH in the context of large volume pleural effusion (26,27).

As highlighted above, HH has a right-sided predominance which reflects the underlying mechanisms of fluid accumulation characterising this condition. Badillo and Rockey identified effusions localised to the right hemi-thorax in 73% of their cohort of patients with HH, with only 17% having left-sided effusions, and 10% having bilateral effusions (12). This finding has been consistently borne out in the literature, with right-sided effusions reported in up to 85% of cases (8); the majority of these patients have co-existent ascites. Nonetheless, as indicated previously, patients can sometimes present with HH even in the absence of demonstrable ascites (28), which may be as high as 10% of cases (8). Rarely, HH may represent the first manifestation of underlying liver disease (5), which can present challenges to accurate and timely diagnosis.

Diagnosis

HH should be considered in any patient presenting with a unilateral effusion (particularly if this is right-sided) in the context of known or suspected underlying liver disease, regardless of the presence of ascites. It is important to exclude alternative causes for the effusion, such as co-existent cardiac, renal, or pulmonary pathology (including infection

Table 3 Classification and common causes of transudative and exudative effusions

	Transudates	Exudates
Classification based on Light's criteria (29)	(I) Pleural fluid to serum total protein ratio <0.5	(I) Pleural fluid to serum total protein ratio >0.5
	(II) Pleural fluid LDH <200 U/litre (<2/3 of normal serum limit)	(II) Pleural fluid LDH >200 U/litre (>2/3 of normal serum limit)
	(III) Pleural fluid to serum LDH ratio <0.6	(III) Pleural fluid to serum LDH ratio >0.6
Common causes	(I) Congestive heart failure	(I) Malignancy
	(II) Nephrotic syndrome	(II) Parapneumonic effusion
	(III) Cirrhosis—hepatic hydrothorax	(III) Empyema
		(IV) Tuberculosis
		(V) Pancreatitis
		(VI) Pulmonary infarction
		(VII) Post-myocardial infarction
		(VIII) Trauma (haemothorax)

LDH, lactate dehydrogenase.

and malignancy). The diagnosis is confirmed by analysis of pleural fluid obtained during aspiration, which classically demonstrates a transudative process (see *Table 3*) (29).

Of note, it has been proposed that a serum-albumin gradient greater than 1.2 g/dL, or a pleural-serum albumin ratio less than 0.6 g/dL, may provide a more accurate assessment of transudative effusions in HH (29,30), particularly in the context of diuretic therapy. Nonetheless, Light's criteria remain the most widely adopted clinical method for distinguishing transudative and exudative effusions (29). Where there remains diagnostic uncertainty, the use of non-invasive imaging modalities—such as doppler ultrasound, peritoneal scintigraphy, or magnetic resonance imaging (MRI)—may be employed to clarify trans-diaphragmatic fluid migration (22,23), but is rarely required in routine practice.

Occasionally, a chylothorax can occur in the context of liver cirrhosis (31), and is an important differential to consider; nevertheless, this is usually easy to distinguish from uncomplicated HH, based on its high triglyceride composition and milky appearance, often with co-existent chylous ascites (32). A more concerning differential and potential complication of HH is spontaneous bacterial empyema (SBEM). This has been reported in up to 16% of patients with HH (33), and is often viewed in a similar manner to the development of spontaneous bacterial peritonitis (SBP) as a complication of ascites. However, importantly, SBEM may be present even in the absence of ascites or SBP (34,35). Factors associated

with the development of SBEM include low levels of C3 (complement factor 3) and total protein in the pleural fluid, and a high Child-Pugh classification score (36). Patients are often unwell, and there may be features of pyrexia, worsening chest pain and encephalopathy (35). The condition requires a high index of suspicion, since the mortality rate has been estimated as high as 20–38% (37), even in those receiving treatment (typically, intravenous antibiotics); the role of pleural drainage in these patients remains uncertain. *Table 4* summarises the pleural fluid composition of uncomplicated HH and SBEM, respectively.

Management

The management of HH can be broadly classified according to: medical management options (principally, dietary modification and diuretic therapy); pleural interventions for symptomatic benefit (e.g., thoracocentesis); and definitive surgical procedures, which include TIPSS and liver transplantation in suitable patients. A suggested approach to the management of HH is summarised in *Figure 2*. Decisions are often extremely challenging, owing to the complex nature of patients presenting with multiple co-morbidities, as well as the potential for developing significant complications (38). In a recent multi-centre survey of over 500 French-speaking hepatologists and pulmonologists (39), substantial differences in the approach to refractory HH (including use of pleural intervention,

Table 4 Typical pleural fluid characteristics of uncomplicated HH and SBEM

HH	SBEM
• Total cell count <1,000 cells/mm^3	• ANC >500 cells/mm^3 with negative pleural fluid culture
• ANC <250 cells/mm^3	• ANC >250 cells/mm^3 with positive pleural fluid culture
• Protein concentration <2.5 g/dL	Fluid analysis can indicate both transudative and exudative effusions in the context of SBEM [see Xiol *et al.* (34)]
• Pleural fluid/serum total protein ratio <0.5	
• Pleural fluid/serum LDH ratio >0.6	
• Pleural fluid/serum albumin gradient >1.1	
• pH >7.4	
• Pleural glucose concentration similar to serum	

HH, hepatic hydrothorax; SBEM, spontaneous bacterial empyema; ANC, absolute neutrophil count; LDH, lactate dehydrogenase.

TIPSS and liver transplantation) were revealed, reflecting a lack of standardised guidelines. As such, it is crucial that care is guided by involvement of a multi-disciplinary team, including pulmonologists, hepatologists, transplant physicians, and palliative care colleagues where relevant.
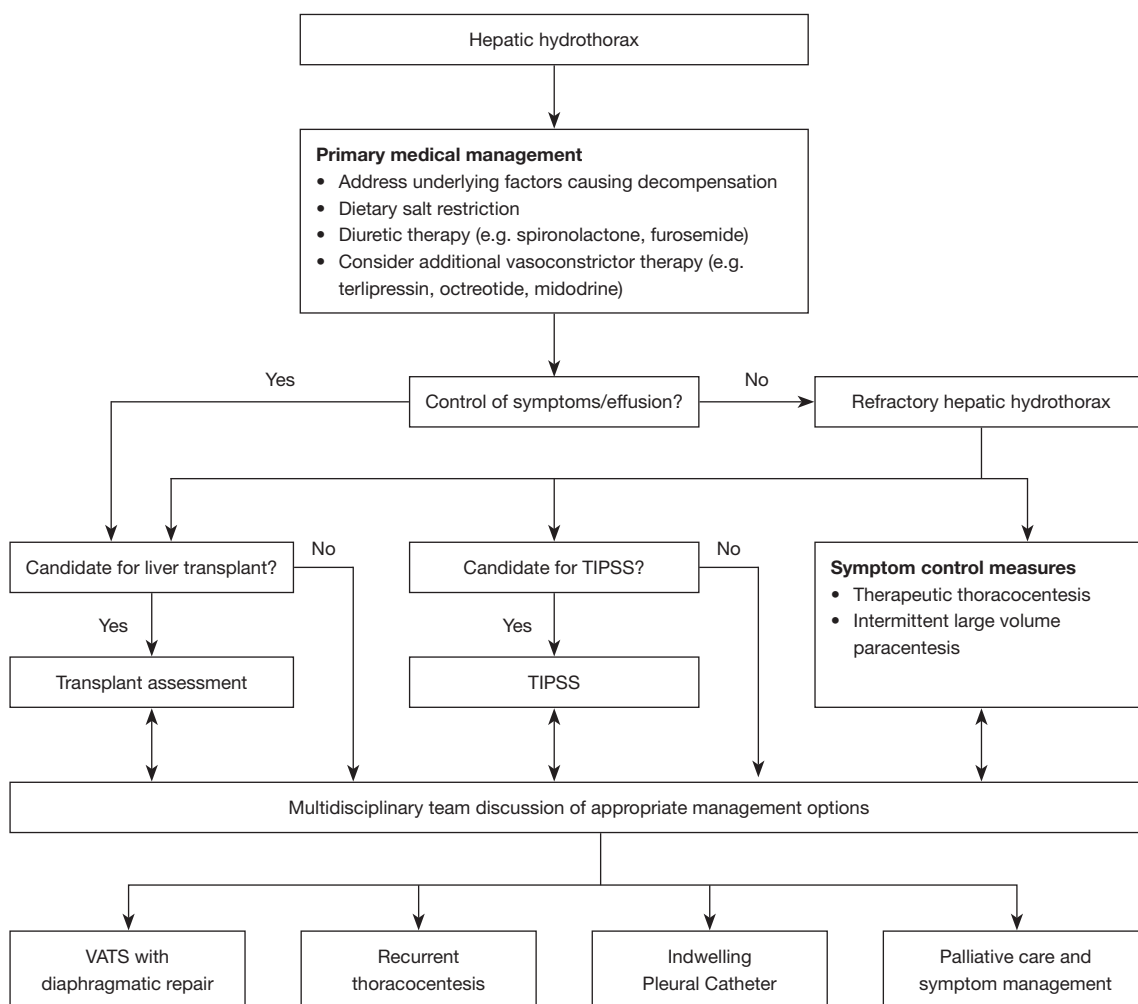
Medical management

Given the fundamental relationship to underlying liver disease and cirrhosis, management of HH must inherently focus on ensuring any drivers of decompensation are appropriately addressed. This may include, for example, the identification and treatment of viral hepatitis, or achieving abstinence from alcohol in relevant patients (16). Beyond this, the initial medical management of HH is largely centred on the elimination and subsequent prevention of ascites which, in turn, reduces the volume of fluid accumulation within the pleural cavity. A low sodium diet is often implemented—with a recommended maximum daily salt intake of approximately 5 g (~90 mmol sodium)—although this has relatively low success when used as monotherapy (4,40). The optimisation of nutritional support in patients with HH is especially important to improving outcomes. Notably, in a study by Yoon *et al.* (41), it was found that the strongest links to poor survival were low body mass index (BMI) (<19) and cachexia; it has been suggested that the combination of cachexia and muscle atrophy increases the risk of thinning and separation of fibrous tissues comprising the tendinous portion of the diaphragm (42), influencing the primary mechanism of HH formation outlined above. Consequently, engagement with dietetic teams regarding the adoption of nutritionally-rich, low-salt diets is a key component of the initial conservative management of HH.

The use of diuretic therapy is usually required to aid management of HH, alongside dietary modifications and adoption of low sodium diets. Typically, aldosterone receptor antagonists (such as spironolactone) are implemented as first-line agents, preventing sodium reabsorption in the distal renal tubules (43). Second line agents, such as the Loop of Henle diuretic furosemide, are frequently utilised in conjunction with aldosterone antagonists in patients who have failed to respond appropriately to diuretic monotherapy. The dose of diuretic is typically increased, if tolerated, in a step-wise fashion until appropriate fluid balance is achieved (aiming for a reduction in body weight of 0.5–1 kg/day, depending on the presence of peripheral oedema) (44), or until maximal doses are reached (e.g., 400 mg/day for spironolactone; 160 mg/day for furosemide) (45,46). Patients must have their renal function monitored carefully following initiation of diuretic therapy to ensure they do not develop diuretic-induced renal impairment, which can usually be reversed on cessation of treatment (43).

It is feasible that the use of splanchnic and peripheral vasoconstrictors, such as octreotide, terlipressin and midodrine, could offer a viable approach to the management of HH by increasing sodium (and, subsequently, fluid) excretion in the kidneys (16). Notably, a study by Singh *et al.* (44) found that midodrine was superior to conventional medical therapy in reducing ascites formation after 3 months of treatment. Both terlipressin and octreotide have been utilised in the context of gastrointestinal bleeding and hepatorenal syndrome, serving to reduce portal venous pressure in these conditions (47,48). However, none of these medications are used regularly in practice and there is little evidence to support their widespread application in HH.

Despite optimisation of dietary salt intake and medical

Figure 2 Proposed approach to the management of hepatic hydrothorax, illustrating the various invasive and non-invasive treatment options available. Initial management is usually focused on dietary modification with a low salt diet, in combination with diuretic therapy. Patients frequently require pleural intervention for symptom control in the presence of refractory effusions. Definitive treatment options include TIPSS and liver transplantation, but many patients will not be suitable for these procedures. Involvement of the multidisciplinary team is central to guiding appropriate treatment decisions to optimise patient care. Adapted from Pippard *et al.* (16). Creative Commons Attribution 4.0 International License. TIPSS, transjugular intrahepatic portosystemic shunt; VATS, video-assisted thoracoscopic surgery.

therapy, some patients will unfortunately experience ongoing debilitating symptoms relating to persistent HH, even with successful management of ascites. The term 'refractory HH' may be applied in this circumstance, necessitating consideration of additional interventional procedures, as well as assessment of suitability for TIPSS and liver transplantation.

Pleural interventions

As highlighted above, the diagnosis of HH is confirmed by performing a diagnostic pleural aspiration (i.e., by removing approximately 50–100 mL of pleural fluid for analysis), demonstrating the classic findings of a transudative effusion. When initial management with dietary modification and diuretic therapy has failed to achieve an adequate response, removal of larger volumes of fluid (e.g., up to 1.5 L at a time) is often necessary, particularly in the presence of ongoing symptoms, like breathlessness.

Therapeutic thoracocentesis, as with any pleural procedure, does carry a risk of complication, including bleeding and infection (49,50). However, in general these

risks are relatively low when performed by an experienced operator, even in the context of potential coagulopathy and thrombocytopenia (51,52). Abnormal clotting or platelet function (which often characterise liver disease) is therefore not a contraindication to thoracocentesis per se, though should be appreciated and, in the presence of disseminated intravascular coagulation (DIC), invasive intervention avoided (20). Notably, the effects of therapeutic pleural aspiration for HH are often short lived, since persistent underlying liver pathology can lead to rapid fluid re-accumulation within the pleural space. Consequently, it is not unusual—and, indeed, may be advocated—to perform repeated thoracocenteses in patients with HH for symptomatic purposes (53,54). In some patients with large volume ascites, abdominal paracentesis (drainage of ascitic fluid) may also benefit management of HH and its associated symptoms (4). However, unlike large volume paracentesis, there is currently no evidence to support the use of intravenous albumin infusions following thoracocentesis (which involves comparatively smaller drainage volumes) (38,55) and this is therefore not routinely recommended.

It is important to recognise that repeated thoracocentesis is not without risk, and this risk appears to be more prominent in patients with HH compared to other aetiologies of pleural effusion. Specifically, in one retrospective case control study, Shojaee et al. (56) reported an approximate 8% increased risk of complications (including haemothorax, pneumothorax and infection) in patients with HH. The risk of re-expansion pulmonary oedema does, however, appear to be relatively low in this group of patients (57). Importantly, it is thought that the largest predictor of complications relates to prior pleural intervention (56), supporting the notion that repeated thoracocentesis must be carefully considered before performing this procedure.

The use of intercostal chest drains in the management of HH should generally be avoided, since this procedure is associated with high risks of protein loss, infection, haemothorax, and electrolyte abnormalities (58-60). Moreover, given the high rates of ongoing fluid production and accumulation within the pleural space, removal of the chest drain once inserted is often challenging (61). This also influences the chances of achieving successful chemical pleurodesis following chest drain insertion (through failure to sustain apposition of the visceral and parietal pleura), with variable results reported in the literature (59). Of note, the reported outcomes for patients undergoing chest drain insertion for HH are consistently poor: Yoon et al. (41) highlight 12-month mortality rates of up to 90% in patients undergoing pig-tail drain insertion, compared to 18.2% for those undergoing therapeutic thoracocentesis. Similarly, in a large Taiwanese study of 1,278 patients undergoing chest drain insertion for HH, the 30-day mortality rate was reported as 23.5% (compared to 18.6% in a matched group undergoing thoracocentesis) (62). Previous retrospective cohort studies examining 3-month mortality rates in patients with HH report these as between 27% and 40%, respectively (59,60). Given the high rates of complication and death associated with pleural intervention in this group of patients, it is paramount that clinicians remain cautious in relation to performing repeated thoracocentesis and, in particular, intercostal chest drain insertion.

Indwelling pleural catheters (IPCs) have been utilised widely in the management of symptomatic malignant pleural effusions (63,64); however, their use in the long-term management of non-malignant pleural effusions is less certain. Recent case series have indicated the potential to achieve successful pleurodesis in 11–51% of patients with non-malignant or transudative effusions (65-70) and, more specifically, have highlighted the possible use of IPCs in refractory HH as a bridge to transplantation (66-68). Nonetheless, the risk of infection remains high in this patient population, occurring in approximately 5–35% of cases (65-70). Notably, the only randomised trial involving IPCs in refractory transudative effusions (including 16 patients with HH) suggests that, while there may be no symptomatic difference between IPC and repeated thoracocentesis for management of breathlessness, there is an increased risk of developing complications, primarily infection (71). As such, the use of IPCs—as with intercostal chest drains—must be carefully considered in this setting.

Definitive surgical interventions

Attempts to repair the underlying diaphragmatic defects contributing to HH formation through video-assisted thoracoscopic surgery (VATS), with or without chemical (talc) pleurodesis, have been reported in the literature. Specifically, Hou et al. (13) conducted the largest review of this technique in 180 patients with refractory HH, citing successful pleurodesis in up to 72% across all patients, with combined diaphragmatic repair and chemical pleurodesis more successful than pleurodesis alone. Similar findings were observed in a study of 63 patients led by Huang and colleagues (72), with successful resolution of HH reported

in over 90% of patients following combined diaphragmatic mesh repair and chemical pleurodesis. However, the authors report high overall complication rates associated with these procedures (82% and 32%, respectively); importantly, Huang *et al.* observed that approximately one quarter of patients (25.4%) died following surgical intervention, with 37.5% of these deaths attributable to septic shock (72). While these studies represent single-centre experience and may not be fully generalisable, the role of diaphragmatic repair in the management of refractory HH remains controversial.

For patients with refractory HH, TIPSS has been shown to improve symptoms in approximately 70–80% of patients (11) and represents an important intervention to consider, either as a definitive treatment strategy or with a view to future liver transplantation (73) (see *Figure 2*, above). The technique is based on creating an artificial channel ('shunt') between the higher-pressure portal vein and lower-pressure hepatic vein, permitting blood to bypass the diseased liver and reduce the overall porto-systemic pressure gradient. In one study involving patients with refractory HH, an improvement in the size of effusion was observed in 82% of cases following TIPSS, with a reported 1-year survival rate of 64% (74). Moreover, in a systematic review of 198 patients with HH, approximately 55% demonstrated a complete response to TIPSS procedure; however, the mortality at 45 days was not insubstantial, at 17.7% (75). Notably, a previous retrospective analysis of patients receiving TIPSS for HH or refractory ascites revealed no significant difference in outcomes between groups at 1, 3 and 6 months, though there was a larger proportion of non-responders in the HH group at all time points (76). 90-day mortality rates (HH: 12.5%; ascites: 6%) and overall survival (HH: 672 days; ascites: 1,224 days) were not statistically different, but did suggest a trend towards worse outcomes in the HH group (76). The number of patients in this retrospective study was small, however, and therefore must be treated with caution.

Additional complications relating to TIPSS procedure largely stem from metabolic derangement, most commonly hepatic encephalopathy. This is thought to occur in around 20–50% of patients post-procedure (77), but usually responds well to medical therapy (e.g., laxatives and rifaximin). Other complications include haemorrhage, acute kidney injury, acute respiratory distress syndrome, congestive cardiac failure, and acute liver failure (78,79). General contraindications to TIPSS procedure include: significant heart failure or pulmonary hypertension; severe hepatic encephalopathy; severe systemic infection;

untreated biliary obstruction; polycystic liver disease; or diffuse hepatic malignancy (74,80). The highest predictors of poor outcome following TIPSS relate to advancing age, the presence of severe underlying liver disease—determined by Child-Pugh or MELD (Model for End stage Liver Disease) scoring systems—and co-existent renal impairment (74,81). As such, appropriate patient selection is crucial in optimising the likelihood of successful response to intervention.

Liver transplantation represents the most definitive treatment option for patients with refractory HH and, in view of the high rates of mortality associated with this condition, patient suitability for transplantation should be assessed at the earliest opportunity. In general, potential candidates for liver transplant are determined by their UKELD score (United Kingdom model for End stage Liver Disease), which is based on measures of international normalised ratio (INR), creatinine, bilirubin and sodium levels. A score of 49 or more indicates a 1-year mortality of 9% and is an indication to consider listing for transplantation (82). Internationally agreed criteria for liver transplant in the context of HH include: patients with refractory HH; patients with HH and poor synthetic liver function (determined by a MELD score of less than 15); or patients with HH and development of SBEM (4). Notably, in a study of 28 patients with HH conducted by Xiol *et al.* (83), post-transplant outcomes (including length of stay, need for mechanical ventilation, mortality, and long-term survival) were no different in this cohort compared to patients undergoing liver transplantation for other conditions. Additionally, in their small case series, Serste and colleagues concluded that HH had no demonstrable impact on survival outcomes following liver transplant, with none of the eleven patients included requiring subsequent thoracocentesis (84). Nonetheless, it is important to appreciate that many patients with refractory HH will not be suitable for either liver transplantation, or TIPSS procedures; in these circumstances, the focus of care should prioritise effective symptom control, with involvement of palliative care colleagues a central component of this process (16).

Conclusions

HH is an important and challenging clinical entity associated with end-stage liver disease, which carries a high risk of mortality and symptomatic burden for patients. In this article, the underlying pathophysiological mechanisms

of HH formation, as well as its clinical manifestations, diagnosis and management, have been addressed. Notably, clinicians must maintain a high index of suspicion for HH in any patient with an effusion in the context of known or suspected liver disease, regardless of the presence ascites. While the mainstay of treatment is conservative, based on dietary modification and diuretic therapy, patients often require pleural interventions for symptomatic purposes. Nonetheless, the insertion of intercostal chest drains is not routinely recommended, owing to the high risk of complications, including infection. In cases of refractory HH, early consideration of suitability for TIPSS and/or liver transplantation—as well as identifying the individual palliative care needs of patients—is paramount, given the high mortality rates characteristic of this particular population.

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Footnote

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