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ORIGINAL ARTICLE

Liver transplantation in patients with hepatic hydrothorax

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Summary

Hepatic hydrothorax is a uncommon complication of cirrhotic patients and the results of liver transplantation (OLT) in patients with this complication are not well defined. We studied postoperative complications and survival of 28 patients with hepatic hydrothorax transplanted at our center during a period of 12 years, comparing them with a control group of 56 patients transplanted immediately before and after each case. There were no differences between hydrothorax group and control group in days of mechanical ventilation after surgery, transfusion requirements, postoperative mortality and long-term survival (70% vs. 55% at 8 years, $P = 0.11$). Long-term evolution was similar between patients with refractory hepatic hydrothorax or spontaneous bacterial empyema and those with noncomplicated hepatic hydrothorax. Hepatic transplantation is an excellent therapeutic option for patients with hepatic hydrothorax. Presence of hepatic hydrothorax does not imply more postoperative complications, and long-term survival is similar to other indications of hepatic cirrhosis.

Introduction

Hepatic hydrothorax (HH) is the pleural effusion of patients with hepatic cirrhosis and portal hypertension without a primary cardiac, pulmonary or pleural disease [1]. HH is not a common complication in cirrhotic patients, as it only appears in 6% of cirrhotic patients with ascites [2]. Long-term management is difficult for several reasons: impaired liver function, concomitant complications of cirrhosis, and lack of clinical trials showing a satisfactory therapy. Liver transplantation (OLT) is the best treatment for decompensated hepatic cirrhosis [3], and therefore is also considered the best treatment for patients with HH [4]. Nevertheless, there are no broad series studying survival and evolution of these patients after OLT. In fact, the only reported series of OLT in patients with HH includes only four subjects [5]. Our aims were to identify the evolution of a large series of cirrhotic patients with HH who underwent an OLT, and to compare this series with a cohort of transplanted patients without hydrothorax.

Materials and methods

From January 1990 to October 2002, 575 OLT were performed at our center, a tertiary teaching hospital, excluding re-transplantations. Twenty-eight of these 575 OLT were performed in patients with HH. Mean age of patients transplanted for HH was 51 years (30–68), with 19 men. The etiology was alcoholic in 14, viral in 10, cholestatic in two and criptogenetic in two. The cause of hepatic transplantation was: refractory hydrothorax [2] in five patients, a previous episode of spontaneous bacterial empyema (SBEM) [6] in four, both refractory hydrothorax and SBEM in seven, and noncomplicated hydrothorax with bad hepatic function (Child-Pugh ≥8 points) in 12. Nine patients were Child B (8 or 9 points) and 19 were Child C (10–12 points). In addition to decompensated hepatic cirrhosis, seven had hepatocarcinoma, five discovered in the evaluation of OLT and two in the explanted liver. Most patients had both ascites and hydrothorax and two patients had only HH without ascites. Six of the 11 patients who had an episode of SBEM, had also sponta-

neous bacterial peritonitis. All the episodes of SBEM were treated with antibiotics and a tube thoracic was not inserted in any case.

A prospective historic analysis was performed reviewing the charts of the 28 patients transplanted with HH. As a control group we chose a cohort of 56 patients transplanted immediately before and after each patient with hydrothorax, i.e. two controls for each case. We studied short and long-term survival, length of surgery, intensive unit stay, days of mechanical ventilation, transfusion requirements, and evolution of the hydrothorax after transplantation. We also studied whether hydrothorax-related complications (refractory hydrothorax, SBEM) influence post-OLT evolution and long-term survival.

The results were analyzed using the *t*-test and the Fisher exact test when appropriate. Survival was calculated by the actuarial method of Kaplan–Meier and compared with log-rank test. A $P < 0.05$ was considered significant.

Results

Patients with hydrothorax and their controls were similar in terms of age, sex, etiology, presence of hepatocarcinoma, preoperative renal function and initial immunosupression (Table 1); although hepatic function measured by Child-Pugh index was significantly worse in patients with HH. There were no differences between hydrothorax group and control in length of surgery, days of mechanical ventilation, intensive unit admission days after surgery, transfusion requirements or postoperative mortality (Table 2). There were no differences, either, in long-term survival (70% vs. 55% at 8 years, $P = 0.11$ log-rank) or in graft survival (57% vs. 47% at 8 years, $P = 0.40$; Fig. 1). Mean survival of patients transplanted because of HH was 114 months (95% CI, 91–136).

Table 1. Basal characteristics of patients with hepatic hydrothorax and controls.

	Hydrothorax ($n = 28$)	Controls ($n = 56$)	*P*-value
Age	51.3 ± 11.6	53.6 ± 9.6	NS
Male sex	19 (67%)	33 (59%)	NS
Etiology			
Alcohol	14 (50%)	21 (37.5%)	NS
Virus	10 (35.7%)	25 (44.6%)	NS
Other	4 (14.3%)	10 (17.9%)	NS
Hepatocarcinoma	7 (25%)	19 (33%)	NS
Preoperative creatinine	92.3 ± 40.7	92.3 ± 25.1	NS
Preoperative Child-Pugh	9.9 ± 1.4	8.4 ± 2.1	0.001
Initial immunosuppression			
Ciclosporine	93%	93%	NS
Tracolimus	7%	7%	

Table 2. Postoperative evolution of patients with hepatic hydrothorax and controls.

	Hydrothorax ($n = 28$)	Controls ($n = 56$)	*P*-value
Length surgery (min)	435 ± 144	420 ± 98	>0.2
Machine ventilation (days)	5 ± 11	3.8 ± 8.6	>0.2
Days in intensive care unit	10.7 ± 12	7.56 ± 8.3	>0.2
Days in hospital	33 ± 24	28 ± 19	>0.2
Units of red cells transfused	13 ± 11	8.7 ± 6.4	0.06
Postoperative mortality	1 (3.67%)	2 (3.67%)	>0.2

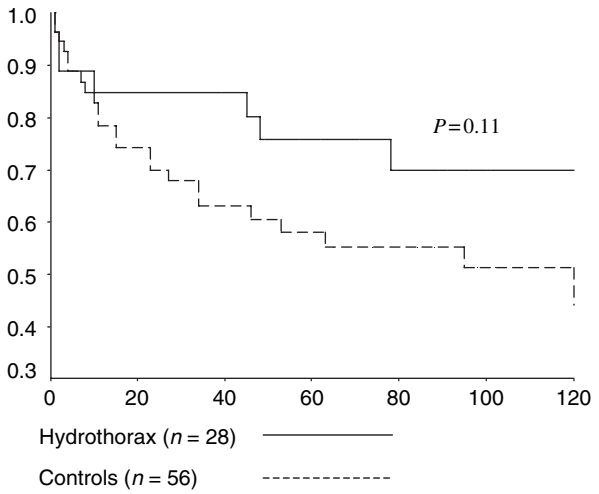

Figure 1 Survival of hydrothorax and controls after OLT.

There were no differences in survival between patients transplanted with refractory hydrothorax and those with nonrefractory hydrothorax (53% vs. 79% at 8 years, $P = 0.24$), and between patients with SBEM and those without SBEM (50% vs. 81% at 8 years, $P = 0.29$; Fig. 2).

During surgery 14 paracenteses and 14 thoracenteses were performed on 18 patients: 10 needed both thoracentesis and paracentesis, four only thoracentesis and four only paracentesis. Thoracentesis was performed transdiaphragmatically with an abocath of 14 G. Mean volume of the thoracentesis (14 patients) was 2351 ± 971 cc (500–4000 cc). Mean volume of paracentesis (14 patients) was 2625 ± 1849 (1000–7000 cc). In addition, six patients needed a thoracic tube after surgery for between 2 and 7 days, and two other patients needed therapeutic thoracentesis in the postoperative period.

One month after OLT, pleural effusion persisted in nine patients, although after 3 months the effusion persisted in only one patient and this was attributed to cardiac failure. One patient developed a new hydrothorax 5 years after OLT, because of relapse of the cirrhosis. During follow-up seven patients died, between 2 and 78 months

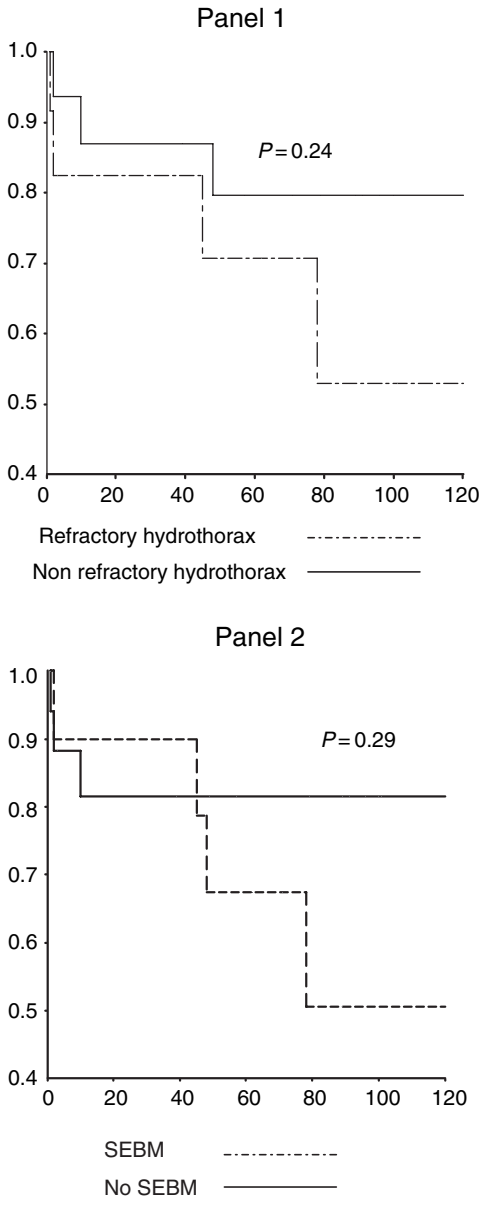

Figure 2 Comparison of survival after OLT of patients with noncomplicated hydrothorax or with refractory hydrothorax (panel 1) and previous spontaneous bacterial empyema (panel 2).

after OLT; its medical antecedents and causes of death are reported in Table 3.

Discussion

Patients with hydrothorax have the same survival rate as controls and similar postoperative evolution, indicating that the fact of having hydrothorax does not alter evolution and prognosis. Probably thoracentesis during surgery contributes to postoperative evolution being similar to controls. There were no complications relating to this practice and only six patients needed a thoracic tube transitorily. Pleural effusion persisted at 1 month in nine (36%) of the 25 living transplanted patients. However at 3 months pleural effusion disappeared in all patients except one.

There are no prospective series that specifically studied survival of patients with complicated hydrothorax, but we can extrapolate them from previous reported studies. In the case of SBEM, the spontaneous infection of a hydrothorax, the two reported series [6,7] included 24 patients, but seven died during admission. Mean survival of the 17 who survived an episode of SBEM was 13 months (95% CI, 8–18). Mean survival of transplanted patients with hydrothorax and SBEM after OLT was 98 months (95% CI, 62–134). Thus SBEM should be considered an indication for OLT.

Hepatic hydrothorax is secondary to pass of ascites through a diaphragmatic defect, and ascites is secondary to portal hypertension and salt retention by the kidney. Thus, treatment can be directed to improve salt retention (diuretics) to reduce portal hypertension (TIPS) or to close the diaphragmatic defects (through video-assisted thoracoscopy with concomitant talc pleurodesis). Refractory hydrothorax is the HH that not respond to diuretics. The reported survival of patients with refractory hydrothorax treated with TIPS or videothoracoscopy and pleurodesis is 7–13 months of mean survival [8,9], or 40–60% at 1 year [5,10–13]. Our patients with refractory hydrothorax treated with OLT had a mean survival of 97 months, with 82% survival at 1 year and 70% at

Table 3. Medical antecedents and causes a of death of the seven patients who died after liver transplantation.

	Child-Pugh	Previous SBEM	Refractory hydrothorax	Hepatocarcinoma	Cause of death	Months after OLT
1	8	No	Yes	Yes	Respiratory insufficiency	1
2	12	Yes	Yes	No	Hepatic artery thrombosis	2
3	11	No	No	Yes	Cerebral hemorrhage	2
4	10	No	No	No	*De novo* B virus cirrhosis	10
5	10	Yes	Yes	No	Acute leukemia	45
6	9	Yes	No	No	Ischemic cholangitis	48
7	12	Yes	Yes	No	Relapsed C virus cirrhosis	78

5 years after OLT. Therefore, OLT is also the best treatment for refractory hydrothorax in terms of survival.

There are no series that studied the survival of patients with noncomplicated hydrothorax, but we can assume it would be similar to that of the cirrhotic patients with ascites. Survival after OLT of these patients with noncomplicated hydrothorax is 90% at 1 year and 80% at 5 years, clearly better than the survival of nontransplanted cirrhotic patients with ascites [14]. As happens with SBEM and refractory HH, OLT is in terms of survival the best treatment for patients with noncomplicated hydrothorax, so any patient with cirrhosis who develops HH should be considered a candidate for OLT, like patients who develop ascites [15].

Management of refractory HH on the waiting list for OLT is controversial. Therapeutic thoracentesis is a useful procedure to control hepatic hydrothorax, but pneumothorax is the main complication [16]. A prospective study of thoracentesis in cirrhotic patients with hepatic hydrothorax showed 8% incidence of pneumothorax post-thoracentesis. The risk increased after ongoing taps. Although a chest tube was needed in 50% of pneumothorax cases, there was no mortality associated with the procedure [17]. Transjugular intrahepatic portal systemic shunt (TIPS) is an alternative but implies considerable short-term mortality and should not be performed in cirrhotic patients with poor liver function. The same can be expected of other alternatives such as videothoracoscopy [12,13]. Therefore, patients with an expected short wait (<3–6 months) can be managed by therapeutic thoracentesis. Patients who need frequent thoracentesis, have good risk (calculated by MELD), and an expected long waiting list can be treated with TIPS as a bridge to transplantation.

In conclusion, hepatic transplantation is an excellent therapeutic option for patients with hepatic hydrothorax. Presence of hepatic hydrothorax does not imply more perioperative and postoperative complications, and long-term survival is similar to other indications of hepatic cirrhosis.

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