Transpl Int (2003) 16: 257–261
DOI 10.1007/s00147-003-0551-0

ORIGINAL ARTICLE

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# Hepatic-artery aneurysm in adult liver transplantation

Received: 25 January 2002
Revised: 17 June 2002
Accepted: 5 August 2002
Published online: 15 February 2003


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**Abstract** Hepatic artery aneurysm (HAA) is a rare vascular complication, but has a high mortality rate in liver transplant recipients. This study reports the precipitating factors, clinical manifestation, pre-operative diagnosis, related micro-organism, management, and outcome, in a series of HAAs that developed after adult orthotopic liver transplantation (OLT). Data on the primary disease as well as on the above were obtained from a prospective database, and all case records were reviewed. There were eight (0.5%) HAAs in 1,575 adult cadaveric OLTs between 1982 and March 2001. All were pseudo-aneurysms around the native hepatic-artery (HA) anastomosis, and all occurred in whole-organ OLTs. There were three types of clinical presentations: sudden hypotension ($n=4$), gastrointestinal (GI) bleeding ($n=2$), and abnormal liver-function tests (LFTs) ($n=2$). The majority ($n=7$) presented within the first 2 months (median: 27.5 days, range: 12–760 days) following OLT. A pre-operative diagnosis of HAA was not determined in five cases. The sensitivity of abdominal ultrasound scan (USS), computed tomography (CT) scan and angiography for detection of HAAs was 3 of 5, 1 of 2 and 3 of 4, respectively. Micro-organisms could be identified in six patients (bacteria $n=4$ and fungi $n=3$). All patients underwent urgent operations (excision of HAA in six and ligation in two cases). Immediate reconstruction of the HA was carried out, two different methods being used: repair of native arteries ($n=2$) and arterial conduit (interposition $n=3$ and aortic conduit $n=2$). Two patients died peri-operatively, two died within 2 months, and the remaining four patients are alive at between 8.6 and 12.8 years after repair. HAA following OLT is unpredictable in its presentation, and the sensitivity of clinical and radiological detection is low. A high index of suspicion is required, and urgent surgery with immediate revascularisation and use of appropriate antibiotic/anti-fungal agents is recommended.

**Keywords** Hepatic artery · Aneurysm · Liver transplant · Rupture · Infection

## Introduction

Orthotopic liver transplantation (OLT) is an accepted form of treatment for end-stage liver disease and has a proven long-term outcome [3, 5]. A hepatic artery aneurysm (HAA) is a rare vascular complication that can develop after OLT, with a reported incidence of 0.3–1.2% [2, 6, 10, 12, 15]. Although the occurrence of HAA is rare after OLT, it is associated with a high mortality rate [8, 9, 15]. The clinical manifestation of HAA is varied, and varied management strategies have been employed [1, 4, 6, 7, 8, 9, 10, 13]. This study reports precipitating factors, clinical manifestation, pre-operative diagnosis, related micro-organism, management, and outcome, in a series of HAAs that developed after adult OLTs.

## Materials and methods

Data on recipient selection, donor organs, operating factors, postoperative management, and follow-up, were collected by a data manager not involved in the clinical management of the donors or recipients, and were stored on databases developed initially with dBase (Ashton Tate) and, more recently, Chameleon Infoflex software (Chameleon Information Management Systems).

The transplant patients who developed the complication of HAA were identified from the liver unit database. Clinical information on the primary disease, clinical manifestations, pre-operative diagnosis, management, and outcome, were then obtained from the patients' records and the prospective database.

A conventional OLT with veno-venous bypass was used in the majority of cases. Hepatic artery (HA) re-vascularisation was routinely performed as an end-to-end anastomosis between the donor and the recipient native HA or a branch of the donor coeliac trunk. A cyclosporine-based (up until 1999) or tacrolimus-based (from January 2000) triple immunosuppressive protocol with azathioprine and tapering prednisolone was used in the postoperative period.

In the early postoperative period, vascular complications were suspected if the patient showed evidence of haemorrhage, bile leakage, fever, rising liver-function tests (LFTs), ascites, or abdominal pain. The primary imaging investigation was colour duplex ultrasound scan (USS). Abdominal computed tomography (CT) scan and/or hepatic angiography were used if an HAA was suspected.

## Results

Between 1982 and March 2001, 1,575 adult cadaveric OLTs were performed at the Liver Unit, Queen Elizabeth Hospital, Birmingham, UK. Of these, 1,535 were whole-organ, 35 were split, and five were cut-down OLTs. There were 1,426 primary OLTs and 149 re-transplantations. Native donor and recipient HAs were used for transplantation in 1,539 (97.7%) OLTs, and an arterial conduit was used in 36 (2.3%) OLTs.

There were eight (0.5%) cases of HAA in 1,575 patients. The median age was 36.5 (range: 32–59) years. All HAAs occurred in whole-organ OLTs. Six of the eight cases occurred after primary transplantation (five for chronic liver diseases, two for acute liver failure, and one for neoplasm), and two occurred after re-transplantation (one for previous HA thrombosis and one for chronic rejection).

All eight cases were pseudo-aneurysms of the donor and recipient HA anastomosis. A single case had two aneurysms, one at anastomosis and one proximal. No HAA occurred in OLTs where arterial conduits for hepatic re-vascularisation were used. The site of HA and biliary reconstruction in all eight cases is described in Table 1.

The onset of clinical manifestations of the patients with HAAs was a median of 27.5 (range: 12–760) days after transplantation and can be classified into three groups (Table 2):

1. Group 1: sudden hypotension from intra-abdominal bleeding due to rupture of HAAs ($n=4$). Three patients developed symptoms within the first month of transplantation and the other patient at 60 days. All required emergency re-operation.
2. Group 2: two patients presented with gastrointestinal (GI) bleeding; one presented with bright-red rectal bleeding, and the other presented with melaena stool. The bleeding in the first case was due to bleeding into the Roux loop used for biliary reconstruction, but the bleeding point in the GI tract was not identified in the second case.
3. Group 3: abnormal LFTs due to external compression of the common bile duct by the HAA ($n=2$). One patient developed cholangitis on the 25th postoperative day, and the other had an elevated serum alkaline phosphatase level, identified 760 days after transplantation.

A pre-operative diagnosis of HAA was not determined in five cases (Table 2). Three of these cases were in group 1 and therefore did not undergo pre-operative investigations. Two of the five cases were missed during

**Table 1** Site of native hepatic artery and biliary reconstruction (*CHA* common hepatic artery, *GDA* gastroduodenal artery, *RHA* right hepatic artery, *SMA* superior mesenteric artery, *CBD* common bile duct, *GB* gallbladder)

| Operating technique | HAA |
|---|---|
| Hepatic artery re-vascularisation | |
| Coeliacaxis stem – CHA | 2 |
| CHA stem – CHA | 2 |
| CHA stem – GDA | 2 |
| CHA stem – RHA from SMA | 1 |
| Splenicpatch – CHA | 1 |
| Biliary anastomosis | |
| CBD – Roux-en-Yjejunum | 4 |
| CBD – CBD with T tube | 3 |
| GB conduit | 1 |
| Total | 8 |

**Table 2** Clinical presentation, imaging and treatment of patients with HAAs (*CBD* common bile duct, *L* ligation, *NA* not available, *R* resection)

| Patient | Presentation | Onset (Days) | Imaging USS | CT | Angiography | Surgical treatment HAA | Reconstruction | Microbiological findings | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Hypotension | 12 | – | – | – | R | Native HA | Fungal hyphae[c] | Alive |
| 2 | Hypotension | 18 | – | – | – | R | Native HA | *Aspergillus* spp. | Dead |
| 3 | Hypotension | 18 | Positive | Positive | Positive | R | Interposition graft[a] | *Streptococcus* spp. + fungal hyphae[c] | Dead |
| 4 | CBD obstruction | 25 | Negative | – | – | R | Aortic conduit | *Gemella haemolysans* | Alive |
| 5 | Rectal bleeding | 30 | Negative | Negative | Negative | L | Aortic conduit | NA | Alive |
| 6 | Melaena | 55 | Positive | – | Positive | L | Aortic conduit | NA | Dead |
| 7 | Hypotension | 60 | – | – | – | R | Interposition graft | *Streptococcus faecalis* + *Enterococcus* spp. | Dead |
| 8 | Abnormal LFTs | 760 | Positive | – | Positive | R | Interposition graft[b] | *Haemophilus paraphrophilus* | Alive[d] |

[a]Portal vein interposition graft
[b]Revision of biliary-enteric anastomosis
[c]Histological examination
[d]Thrombosed aortic conduit

pre-operative investigations (USS in one case and USS, CT scan and angiography in one case). The HAAs were found during exploratory laparotomy for infected intra-abdominal collections. An HAA was diagnosed pre-operatively by USS and angiography in three cases and in five cases by USS, CT scan and angiography in three, one and three cases, respectively (Table 2).

A hepatico-jejunostomy was performed for biliary reconstruction in five of the eight patients (Table 1), one of whom had postoperative small-bowel leak. Three of the eight patients underwent a liver biopsy because their LFTs suggested acute rejection during the first week after OLT; this was confirmed by histological examination, and they were treated with high-dose steroids for 3 days. One patient had had a postoperative dental root abscess 2 weeks before the rupture of the HAA.

Six of the eight patients had microbiological material available from the wall of their aneurysm, surrounding tissue, fluid from an abdominal collection, or their blood. All six patients had organisms cultured (four bacteria and three fungi) (Table 2). The micro-organisms were identified from the wall of the HAAs in three cases, from the portal vein in one case, from an intra-abdominal collection close to the HAA in two cases, and from the blood in one case.

All eight cases of HAA were treated by one of two surgical methods (Table 2):

1. Excision of HAA: HAAs in six patients were resected, and HA re-vascularisation was performed, with either the native artery ($n=2$) being used or an arterial allograft conduit (interposition in three cases and aortic conduit in one case). One patient in whom the HAA ruptured into the Roux loop constructed for the hepatico-jejunostomy had the Roux loop re-fashioned, in addition to vascular repair, and one patient, in whom the HAA extended into the portal vein, had a portal vein resection repaired with an iliac vein allograft, in addition to HA reconstruction.
2. Ligation of HAA: in two cases the HAA was ligated and the HA re-vascularisation was performed with an aortic conduit constructed from an iliac artery allograft.

All arterial conduits were allografts from the iliac artery of donors other than the original liver donor. Treatment with broad-spectrum antibiotic and anti-fungal agents was started pre-operatively and adjusted according to the microbiological findings available after the operation.

Two patients died in the immediate postoperative period (days 1 and 3) and another two died on post-operative days 24 and 45 from sepsis and multiple organ failure. Four patients survived after surgical intervention. Three of six patients treated by excision of the HAA survived, and one of the two treated by ligation of the HAA survived.

In the four patients that died, three showed positive results to the microbiological tests, two of which were fungal infections (Table 2). Among the four surviving patients, three showed positive microbiology results (one fungal and two bacterial infections). The fourth survivor was the patient whose HAA had ruptured into the Roux loop.

Three of the four surviving patients had an arterial allograft conduit for HAA repair (two interposition and one aortic conduit), and one had the native HA used for re-vascularisation. One patient who had an arterial interposition developed a late thrombosis of the arterial conduit at 133 months, but the liver graft functioned well and re-transplantation was not required (Table 2). In the remaining three patients the reconstructed HAs were patent with normal liver function. The 30-day mortality rate after repair was 37% (1, 3 and 24 days

after repair) with an in-hospital mortality rate of 50%. The remaining four patients are alive at between 8.6 and 12.8 years.

## Discussion

The development of HAA after OLT is rare, but it increases the risk of early graft loss. In this series the incidence of HAA in adult OLTs was 0.5%, similar to other reported series [1, 9, 10, 15, 17]. All eight HAAs in this series were pseudo-aneurysms originating from the anastomosis of the native donor and recipient HAs, as found in most reports [1, 9, 10, 15, 17]. No intra-hepatic HAAs were found in our series.

Local abdominal infections [8, 9, 10, 14, 17] such as bile leakage, contamination from biliary-enteric anastomosis or iatrogenic causes [7, 11] such as needle biopsy and angioplasty have been reported as a cause of extra-hepatic HAAs following OLT. In this series biliary-enteric anastomosis was the most frequent predisposing factor, occurring in five cases. A dental root abscess in one other case was also a possible predisposing factor. Liver biopsy in three cases did not appear to be related to the extra-hepatic HAAs, but pulsed steroid therapy for the acute rejection in these cases might have aggravated the infective cause of the HAAs.

The reported clinical manifestation of HAA varies from asymptomatic [9, 15] to sudden hypovolaemic shock from rupture of the HAA [4, 8, 9, 10, 15, 17]. Most intra-hepatic HAAs are asymptomatic and are detected incidentally during ultrasound scanning [9, 15], but can cause haemobilia [13]. Intra-abdominal or GI haemorrhages from rupture are the most common presentations of extra-hepatic HAAs [7, 8, 9, 10, 15, 17]. A variety of rare presentations has been reported, such as a dropping haematocrit, back pain [17], fever [4], obstructive jaundice or abnormal LFTs [7], cardiac failure from an AV fistula [6, 13], or associated incidental finding in HA thrombosis following OLT [9, 17]. In this series all HAAs were symptomatic, and six cases presented with bleeding from rupture of the HAA (intra-abdominal in four and GI in two). Two patients with HAAs presented with obstructive jaundice ($n=1$) and elevated serum alkaline phosphatase ($n=1$) secondary to external biliary compression.

In this series most patients ($n=7$) presented in the first 2 months after OLT, similar to the most recently reported series [9, 10, 15], and six of these cases had an infective causation. Bonham et al. (1999) reported that infected HAAs presented within the first 2 months of OLT and non-infected HAAs presented later [1]. We also report a case of late presentation of HAA with abnormal LFTs at 760 days after OLT, similar to previous reports [8, 9, 13].

Because the onset and presentation of HAA are unpredictable, the diagnosis is often determined at laparotomy or autopsy [9, 10, 15]. In our series, pre-operative diagnosis of HAA was not determined in five cases because of patient instability ($n=3$) and radiological failure ($n=2$). Only one institute has reported making the diagnosis on pre-operative angiography [16, 17]. USS is the primary non-invasive imaging study for detection of HAAs; its efficacy can be increased by the addition of Doppler or colour flow, and this modality is especially good for the identification of intra-hepatic HAA [9, 16]. In this series pre-operative diagnosis was only made in three of six cases where patient stability allowed investigation. Doppler USS had a low sensitivity (3/5 cases) in our own series, but the addition of contrast might increase the sensitivity for detection of HAA [14]. The sensitivity of the CT scan in our series was lower than the Doppler USS (1/2 cases), but was performed in only two cases, and the sensitivity of angiography was 3/4 cases.

In this series six of the HAAs had microbiologically confirmed infection. Previous studies have also reported a similar pattern and frequency of documented pathogens in HAAs [9, 10, 15]. This confirms the importance of the use of appropriate antibiotic and anti-fungal agents.

HAAs often rupture without warning and should not be managed conservatively if identified [4]. Surgical repair of intra-hepatic HAAs is impossible, and re-transplantation is usually required. Super selective arterial embolisation may be used as a bridging procedure while regrafting is awaited [9]. Long-term antibiotic use is required and this should be based on microbiological findings if possible.

Re-transplantation for infected intra-hepatic and extra-hepatic HAAs is associated with high mortality [1, 9, 13]. Various management strategies have been reported for extra-hepatic HAAs, including excision of HAA without re-vascularisation [4, 8, 13], ligation or embolisation without re-vascularisation [8, 9], and ligation or excision of HAA with immediate re-vascularisation [1, 10, 13]. Ligation, embolisation or excision of the HAA without HA re-vascularisation will lead to death, liver failure, re-transplantation or an ischaemic biliary stricture in up to 70% of cases [8, 9]. In our series surgical treatment for extra-hepatic HAA was associated with 50% mortality, but attempted re-vascularisation was carried out in all cases. None of the surviving patients in our series required re-transplantation for liver failure, because of the strategy of immediate re-vascularisation. It is impossible to conclude whether ligation and re-vascularisation or excision and re-vascularisation are superior, as the numbers are small in each group. The use of arterial conduits for HA re-vascularisation in our series is promising, with a median conduit patency of 96 months.

HAA is unpredictable in its occurrence and presentation, and the sensitivity of clinical and radiological detection is relatively low. Any case of unexplained blood loss, hypovolaemia, GI bleeding or abnormal LFTs after OLT should raise suspicion. The use of multiple modalities of investigation may be necessary for the detection of an HAA, but if appropriate surgical intervention and long-term antibiotic and anti-fungal agents are employed, the outcome for patients with infected extra-hepatic HAAs is reasonable.

## References


1. Bonham CA, Kapur S, Geller D, Fung JJ, Pinna A (1999) Excision and immediate revascularization for hepatic artery pseudoaneurysm following liver transplantation. Transplant Proc 31:443
2. Cavallari A, Vivarelli M, Bellusci R, Jovine E, Mazziotti A, Rossi C (2001) Treatment of vascular complications following liver transplantation: multidisciplinary approach. Hepatogastroenterology 48:179–183
3. Goss JA, Shackleton CR, McDiarmid SV, Maggard M, Swenson K, Seu P, Vargas J, Martin M, Ament M, Brill J, Harrison R, Busuttil RW (1998) Long-term results of pediatric liver transplantation: an analysis of 569 transplants. Ann Surg 228:411–420
4. Houssin D, Ortega D, Richardson A, Ozier Y, Stephan H, Soffer M, Chapuis Y (1988) Mycotic aneurysm of the hepatic artery complicating human liver transplantation. Transplantation 46:469–472
5. Jain A, Reyes J, Kashyap R, Dodson SF, Demetris AJ, Ruppert K, Abu-Elmagd K, Marsh W, Madariaga J, Mazariegos G, Geller D, Bonham CA, Gayowski T, Cacciarelli T, Fontes P, Starzl TE, Fung JJ (2000) Long-term survival after liver transplantation in 4000 consecutive patients at a single center. Ann Surg 232:490–500
6. Karatzas T, Lykaki-Karatzas E, Webb M, Nery J, Tsaroucha A, Demirbas A, Khan F, Ciancio G, Montalvo B, Reddy R, Schiff E, Miller J, Tzakis AG (1997) Vascular complications, treatment, and outcome following orthotopic liver transplantation. Transplant Proc 29:2853–2855
7. Lowell JA, Coopersmith CM, Shenoy S, Howard TK (1999) Unusual presentations of nonmycotic hepatic artery pseudoaneurysms after liver transplantation. Liver Transpl Surg 5:200–203
8. Madariaga J, Tzakis A, Zajko AB, Tzoracoleftherakis E, Tepetes K, Gordon R, Todo S, Starzl TE (1992) Hepatic artery pseudoaneurysm ligation after orthotopic liver transplantation—a report of 7 cases. Transplantation 54:824–828
9. Marshall MM, Muiesan P, Srinivasan P, Kane PA, Rela M, Heaton ND, Karani JB, Sidhu PS (2001) Hepatic artery pseudoaneurysms following liver transplantation: incidence, presenting features and management. Clin Radiol 56:579–587
10. Marujo WC, Langnas AN, Wood RP, Stratta RJ, Li S, Shaw BW Jr (1991) Vascular complications following orthotopic liver transplantation: outcome and the role of urgent revascularization. Transplant Proc 23:1484–1486
11. Narumi S, Osorio RW, Freise CE, Stock PG, Roberts JP, Ascher NL (1998) Hepatic artery pseudoaneurysm with hemobilia following angioplasty after liver transplantation. Clin Transplant 12:508–510
12. Sanchez-Bueno F, Hernandez Q, Ramirez P, Robles R, Acosta F, Rodriguez JM, Parrilla P (1999) Vascular complications in a series of 300 orthotopic liver transplants. Transplant Proc 31:2409–2410
13. Settmacher U, Stange B, Haase R, Heise M, Steinmuller T, Bechstein WO, Neuhaus P (2000) Arterial complications after liver transplantation. Transpl Int 13:372–378
14. Sidhu PS, Marshall MM, Ryan SM, Ellis SM (2000) Clinical use of Levovist, an ultrasound contrast agent, in the imaging of liver transplantation: assessment of the pre- and post-transplant patient. Eur Radiol 10:1114–1126
15. Stange B, Settmacher U, Glanemann M, Nuessler NC, Bechstein WO, Neuhaus P (2000) Aneurysms of the hepatic artery after liver transplantation. Transplant Proc 32:533–534
16. Tobben PJ, Zajko AB, Sumkin JH, Bowen A, Fuhrman CR, Skolnick ML, Bron KM, Esquivel CO, Starzl TE (1988) Pseudoaneurysms complicating organ transplantation: roles of CT, duplex sonography, and angiography. Radiology 169:65–70
17. Zajko AB, Tobben PJ, Esquivel CO, Starzl TE (1989) Pseudoaneurysms following orthotopic liver transplantation: clinical and radiologic manifestations. Transplant Proc 21:2457–2459