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Aggressive management of the arterial complications of liver transplantation. Impact upon survival and biliary complications

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A B S T R A C T

A study was made of the arterial complications documented in 400 transplants performed between 1997 and 2006. The patients were divided into two groups according to the type of treatment provided. Group I: invasive management (arterial treatment or re-transplant), and Group II: conservative or symptomatic management. The impact of management on survival and biliary complications was analysed.

Results: There were 18 arterial complications (4.5%): 10 early (7 thromboses and 3 stenoses) and 8 late (5 thromboses and 3 stenoses). Ninety percent of the early complications were subjected to invasive management (4 emergency thrombectomies, one re-transplant and 3 angioplasties), while 25% of the late complications were treated with re-transplant and the remaining 75% were subjected to symptomatic treatment. Survival after 12 and 60 months was lower in Group II (57% and 42%) than in Group I (90% and 68%), although without reaching statistical significance. The overall biliary complications rate among the patients with arterial thrombosis was 50%. The rate was significantly lower in Group I than in Group II (10% versus 71%) (P<.04).

Conclusions: Invasive management of the arterial complications of liver transplantation is associated with longer short-term survival and significantly fewer biliary complications. In our experience, patients benefit from an early diagnosis and aggressive management of complications of this kind.

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Tratamiento agresivo de las complicaciones arteriales del trasplante hepático. Impacto sobre la supervivencia y las complicaciones biliares

Palabras clave:
Complicaciones de la arteria hepática
Estenosis arterial
Trombosis arterial
Trasplante hepático

RESUMEN

Se estudian las complicaciones arteriales (CA) ocurridas en 400 trasplantes realizados entre 1997 y 2006. Se dividen en 2 grupos según el tipo de tratamiento realizado: grupo I: tratamiento invasivo (tratamiento sobre la arteria o retrasplante), y grupo II: tratamiento conservador o sintomático. Se analizan el impacto del tratamiento sobre la supervivencia y las complicaciones biliares (CB).

Resultados: Se han presentado 18 CA (4,5%), 10 complicaciones precoces (7 trombosis y 3 estenosis) y 8 complicaciones tardías (5 trombosis y 3 estenosis). El 90% de las complicaciones precoces se trató de forma invasiva (4 trombectomías urgentes, un retrasplante, 3 angioplastias y una ligadura de arteria hepática), y el 25% de las complicaciones tardías se trató con retrasplante (3); el 75% restante recibió tratamiento sintomático.

La supervivencia a 12 y 60 meses fue inferior en el grupo II (el 57 y el 42%) que en el grupo I (el 90 y el 68%), aunque sin alcanzar significación estadística. La tasa global de CB de enfermos con trombosis arterial fue del 50%. La tasa fue significativamente menor en el grupo I que en el grupo II (10% versus 71%) ($p<0,04$).

Conclusiones: El tratamiento invasivo de las CA en el trasplante hepático se asocia a una mayor supervivencia a corto plazo y reduce de forma significativa la aparición de CB. En nuestra experiencia, los pacientes se benefician de un diagnóstico precoz y un tratamiento intensivo en este tipo de complicaciones.

Arterial complications (AC) in liver transplantation are the most frequent cause of vascular complications and are present in 3% to 9% of all transplants.[1] Early complications tend to present in the form of acute liver failure, and frequently lead to loss of the graft and patient death if they are not treated properly and immediately. Retransplantation is frequently necessary to resolve the problem[2]; however, in the case of early diagnosis, this can be avoided through revascularisation surgery or percutaneous treatment with interventional radiology.[3]

Patients and method

This retrospective observational study of data collected prospectively was carried out between March 1997 and July 2006. It included 400 liver transplants in 387 patients, all of which were performed in our centre. The patient group was 69% male and 31% female, with an average age of 51 years. The most common indications were hepatitis C cirrhosis (31%) and alcohol (28%). Of the transplants, 3.5% were performed on an emergency basis. Arterial anastomosis was done using the donor celiac trunk in 80% of the cases. In the rest, depending on anatomical findings, it was done avoiding long arterial segments. The bifurcation of the hepatic artery or the right hepatic artery was used in the recipient to construct a continuous termino-terminal anastomosis with 6-0 polypropylene. There were arterial anomalies in 30% of the grafts. The most common were right hepatic artery of the mesenteric artery (9%) and left hepatic artery of the coronary artery (10%). Vascular reconstruction on the surgical bench was required for 13% of the grafts. Routine echo-Doppler screening was performed on the first day after surgery and after first week of the postoperative period. Diagnoses of AC were performed based on clinical and biological findings, the echo-Doppler test and the arteriography when the Doppler showed pathological findings or when the clinical profile suggested thrombosis.

We studied the AC incidence rate and type, as well as the impact of treatment on survival and the appearance of biliary complications (BC). To this end, patients were divided into two groups according to type of treatment received. Group I: patients who underwent radical treatment involving revascularisation surgery, angioplasty or retransplantation. Group II: patients treated conservatively or symptomatically. The statistics software used for the analysis was SPSS 12.0.

Results

There were 18 ACs (4.5%), consisting of 10 early complications (7 thromboses and 3 stenoses) and 8 late complications (5 thromboses and 3 stenoses) (Table 1). Early complications were those that occurred within the 30 days after the surgery and late complications were those occurring after 30 days. The two most common ways they presented were as BC (38%) and as a casual finding in the routine echo-Doppler screening (38%). The rest were classified as collections (5%), hepatic infarction (11%), and haemoperitoneum caused by a ruptured pseudoaneurysm (5%).

Table 1 – Manner and time of presentation, diagnosis, treatment and results for biliary complications after liver transplantation

		Day presented	Manner presented	Treatment	Biliary complication		Cause of death
1	Stenosis	7	Doppler	Angioplasty	No	Died at 19 m	Refractory ascites
2	Stenosis	2	Doppler	Angioplasty	No	Alive after 14 m	
3	Stenosis	1	Enzymes	Angioplasty	No	Alive after 20 m	
4	Thrombosis	1	Enzymes	Thrombectomy	No	Alive after 36 m	
5	Thrombosis	1	Enzymes	Thrombectomy	No	Alive after 25 m	
6	Thrombosis	6	Doppler	Thrombectomy	Yes	Died at 24 m	Chronic rejection
7	Thrombosis	1	Doppler	Thrombectomy	No	Alive after 28 m	
8	Thrombosis	15	Fistula	Re-transplant	No	Alive after 100 m	
9	Pseudoaneurysm	24	Haemoperitoneum	Hepatic artery ligation	No	Died at 1 m	Haemorrhage and liver failure
10	Thrombosis	25	Infarction	Symptomatic	No	Died at 8 m	Biliary sepsis
11	Stenosis	180	Biliary stenosis	Re-transplant	No	Alive after 121 m	
12	Stenosis	120	Biliary stenosis	Symptomatic	Yes	Alive after 76 m	
13	Stenosis	250	Biliary stenosis	Symptomatic	Yes	Alive after 81 m	
14	Thrombosis	180	Biliary stenosis	Symptomatic	Yes	Died at 8 m	Biliary sepsis
15	Thrombosis	75	Infarction	Symptomatic	No	Died at 51 m	Chronic rejection
16	Thrombosis	45	Infarction	Symptomatic	Yes	Died at 11 m	UGIB, 2ary to portal vein thrombosis
17	Thrombosis	180	Biliary stenosis	Re-transplant	No	Alive after 38 m	
18	Thrombosis	1,460	Biliary stenosis	Symptomatic	Yes	Alive after 40 m	

UGIB: upper gastrointestinal bleeding.

Routine echo-Doppler screening was the means by which 70% of the early complications were diagnosed (positive predictive value: 100%). Of this group, only 30% presented enzyme abnormalities or a graft dysfunction that led us to suspect the diagnosis. All of these patients were diagnosed in the first seven days following the transplant. The remaining 30% presented as early biliary fistula, hepatic infarction and haemoperitoneum, and all arose more than 15 days after the transplant. The late-onset complications presented as biliary stenosis in 75% of that patient group and as hepatic infarctions in the other 25%. The time of presentation was at about 180 days, with infarctions arising earlier and biliary problems occurring later.

Invasive treatment was used for 61% of the cases and conservative treatment for 39%. Treatments carried out consisted of 3 angioplasties, 5 surgical reinterventions (4 thrombectomies and a hepatic artery ligation due to a ruptured pseudoaneurysm) and 3 retransplantations, none of which was urgent. Postoperative anticoagulation therapy was not applied in any of the cases. The patient group that underwent symptomatic treatment was subjected to procedures which included draining fluid collections, biliary drainage and antibiotic treatment. Immediate mortality was 5.5% and the yearly mortality due to causes attributed to AC was 22%. In all of the cases, the artery remained permeable during the follow-up period.

Some form of BC occurred in 50% of the patients with AC. In Group I, this occurred in 10% of patients, significantly less than in Group II with 71% ($P<.04$). The rate of BC in Group I can be compared to the BC rate for the entire series (15%). BC was treated with percutaneous or endoscopic dilatations in 50% of the cases, and with hepaticojejunostomy in the other 50%. Only one patient received a subsequent retransplant.

Survival rates at 12 and 60 months were higher in Group I (90% and 68%) than in Group II (57% and 42%), although without reaching statistical significance (log rank: 0.3). Furthermore, there were no survival differences at 12 and 60 months between Group I and the patient group without AC.

Discussion

ACs in liver transplantation are the most frequent cause of vascular complications and are present in 3% to 9% of all transplants. In our case, 4.5% of the transplant patients presented AC; 2.5% were early complications and 2% were late complications. The clinical profile and laboratory tests were not much use for diagnosing early ACs, since only 30% of the patients presented enzymatic abnormalities. The routine echo-Doppler screening was what determined the diagnosis in 40% of patients with unsuspected early ACs. Echo-Doppler screening has a sensitivity of 91% and a specificity of 99% for diagnosing arterial stenosis or thrombosis.[4]

In general, revascularisation surgery presents poor results; however, four patients subjected to this treatment in our series were able to avoid losing the graft and only one

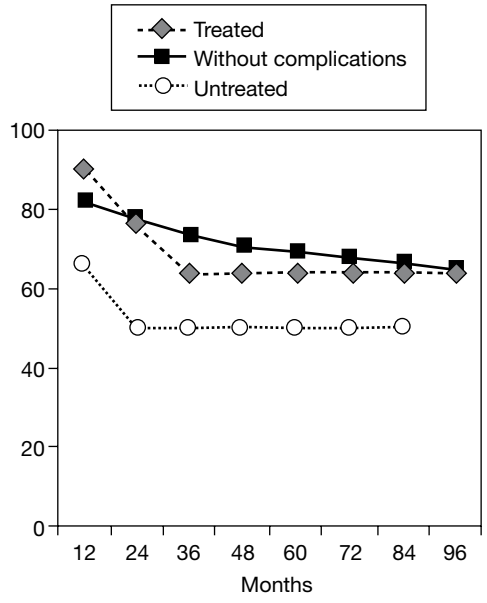

Figure – Actuarial survival rates for treated and untreated patients and those without complications.

presented long-term BC. This was also the case for percutaneous treatment; the three patients receiving it managed to keep the graft with no BCs.[5] Since the bile duct has a very poor tolerance to arterial ischaemia, early diagnosis and treatment are fundamental to obtaining good results. All patients treated with surgery or angioplasty resolved their conditions in the first week after transplant, and the best results were seen in cases treated in the first 24 to 48 hours.

Retransplantation is the most common treatment for arterial thrombosis, with a rate between 25% and 60% depending on the series, and it is burdened with a high mortality rate. In our series, only 16% of the patients with AC underwent a retransplant: 10% of those with early ACs and 25% of those with late AC. There were no mortalities following a retransplant.[6,7] This low retransplantation rate for late thrombosis is due in part to the poor clinical state of some of the patients since their symptoms began, and also to the good response to treatment of BCs with intact liver function.

Immediate mortality and mortality at one year was 9% in the patient group receiving invasive treatment, and the BC rate was 9%, which was lower than the overall mean for the series (15%).[8]

Survival rates at 12 and 60 months were higher in Group I (90% and 68%) than in Group II (57% and 42%), although without reaching statistical significance (log rank: 0.3). Conservative treatment of ACs has a clear impact on survival, but it does not reach statistical significance in our series, which is probably due to the small sample size. On the other hand, patients who received intensive treatment present a survival curve similar to that of patients who did not have AC (Figure).

A large percentage of patients (39%) received symptomatic treatment and presented a BC rate of 71% and a mortality rate of 43% at one year. For late thromboses, direct treatment of the artery provides no benefits whatsoever since the biliary lesion tends to be established. Therefore, the only alternative is retransplantation.[9] Given the low number of retransplantations in our series, results from this subgroup could probably have been improved through proper selection of patients for liver retransplantation after late ACs appeared.

In conclusion, routine echo-Doppler screening is highly sensitive and specific for providing an early diagnosis of AC. In our experience, early diagnosis and immediate treatment of patients with AC by means of surgery or angioplasty can prevent retransplantation in most cases and are not associated with a higher number of late BCs.

Conflict of interest

The authors affirm that they have no conflicts of interest.

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