ORIGINAL ARTICLE

Short- and long-term outcomes of arterial reconstruction on recipient splenic artery in adult liver transplantation. Single-center prospective study 25 years after first description

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SUMMARY

Several techniques have been proposed for liver transplantation with inadequate hepatic artery (HA) anastomosis. We aimed to analyze outcomes of arterial reconstruction with the splenic artery (SA). This was a prospective study of our experience with recipients who underwent arterial anastomosis on the SA compared with patients who underwent standard HA. We included 54 patients in the SA group and 1405 in the HA group. Patients in SA group were more frequently retransplantation (31% vs. 8%; $P = 0.001$), required more transfusion (11 ± 12 vs. 6 ± 9.9 PRC; $P = 0.001$), had longer surgeries (424 ± 95 vs. 394 ± 102 min; $P = 0.03$), and longer hospital stays (28 ± 29 vs. 20 ± 18 days; $P = 0.002$). There were no differences in vascular and biliary complications (15% and 7%; $P = 0.18$; and 32% and 23%; $P = 0.32$), primary dysfunction (11% and 9%; $P = 0.74$), reoperation (12% and 10%; $P = 0.61$), postoperative mortality (13% and 7%; $P = 0.12$) and 5 years survival (66% vs. 63%; $P = 0.71$). Following primary transplantation, there were no differences. The outcomes of arterial reconstruction using the recipients' SA in adult liver transplantation are comparable to those for standard HA reconstruction after a first transplant.

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Introduction

Avoiding vascular complications in liver transplantation (LT) is essential to preventing graft loss, especially with the current lack of donors. Key to this is maintaining an adequate arterial supply, with arterial thrombosis or stenosis both capable of inducing graft loss through nonfunctional and/or ischemic biliary complications [1–3]. Standard hepatic artery (HA) reconstructions are performed between the donor celiac trunk and the recipient HA, though the latter may be inadequate because of intimal dissection, preoperative or intraoperative thrombosis, or severe atherosclerosis. In such cases, a donor arterial interposition graft to the aorta is typically used [4–6]. However, extra-anatomic aortohepatic conduits have been associated with long-term HA thrombosis (HAT) and impaired graft and patient survival [7,8].

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In 1992, our group first described the option of using the recipient's splenic artery (SA) for arterial reconstruction [9]. Shortly after, we then described the short-term outcomes in a series of 23 patients who underwent SA reconstruction [10]. However, although a few others studies have described short-term outcomes in cases series [11–13], there has been no comprehensive long-term report on the outcomes of this technique. Otherwise it has been published recent evidence for an alternative technique using arterial anastomosis directly to the recipient's celiac trunk [14]. The authors report good short-term outcomes in a short series of seven patients performed with this arterial reconstruction technique.

In the present study, we aimed to analyze the short- and long-term outcomes in patients after LT using SA reconstruction.

Materials and methods

This was a single-center study of all adult patients undergoing LT at our institution between 1984 and May 2016, based on an analysis of the prospectively maintained database of our unit. The database included patient and donor demographics, indications for transplantation, donor and transplantation related data, post-transplantation complications, and graft and patient survival data. Follow-up data were included until May 2017, ensuring that all patients had data for at least 1 year of follow-up. Most liver grafts were whole organ grafts from deceased donors, though we included 41 domino LTs. During the study period, 1500 LTs were performed in our center. Among these, 1405 arterial reconstructions were to the recipient's HA, of which 113 were during retransplantations. By contrast, 54 arterial reconstructions were to the recipient's SA and 17 were for retransplantations.

For the analysis, we compared HA group (n = 1405) and the SA group (n = 54). We excluded 41 LTs; 27 of them had an arterial conduit, and the other 14 patients had some other type of anastomosis or even no arterial reconstruction because of intraoperative death (Fig. 1).

Surgical technique

Despite the long study period, the surgical technique remained largely unchanged. Most LTs (n = 1327; 89%) were performed using a piggy-back technique in the standard sequence, as previously described [15]. Since 2002, portocaval shunts were used depending on the initial portal flow [16]. In most cases, the graft was first perfused via the portal vein and then via the HA. Standard arterial reconstruction was between the donor celiac trunk and the recipient's common HA or proper HA. SA was used in case of no adequate arterial flow was based on surgeon′s judgment and/or in case of flow lower than 100 ml/min measured by intraoperative transit-time ultrasound [9].

Briefly, after graft revascularization through the portal vein, the SA was exposed by reflecting the stomach downward through the lesser omentum and incising the retroperitoneum at the upper edge of the pancreas. The SA was then encircled and clamped, and the distal end was ligated and divide 2–3 cm from the celiac trunk. Finally, the proximal end of the SA was turned to the right and an end-to-end anastomosis performed with the celiac trunk of the donor (Fig. 2). In some cases, the SA may not be dilated or may not be tortuous, making it difficult to encircle, while in other cases, there may be a discrepancy between the donor celiac trunk and the recipient SA. In both cases, the SA can be clamped laterally and an end-to-side anastomosis can be used. Since 1999, final arterial and portal flow patency has been confirmed by transit-time ultrasound (Transonic Flowmeter, HT311, Ithaca, NY, USA).

Follow-up

Postoperative arterial and venous patency was routinely evaluated by Doppler ultrasound at 24 h, 1 week, and at 1 and 3 months. Ultrasound was repeated every 6 months for 2 years and yearly thereafter. Computed tomography was performed if there was clinical or

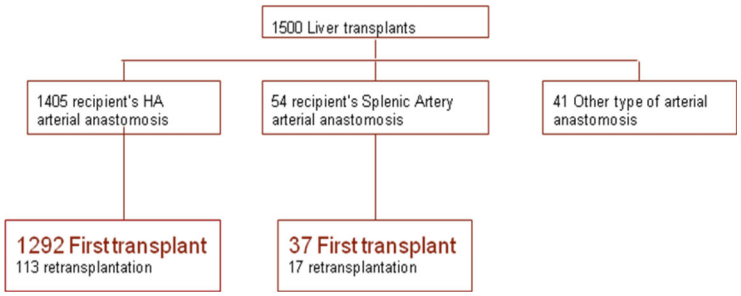

Figure 1 Patients flow diagram.

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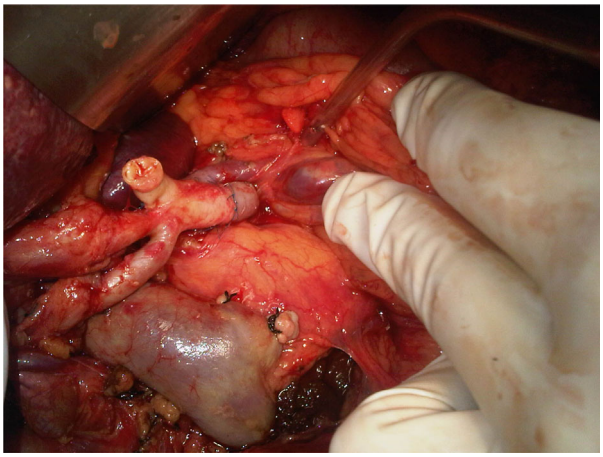

Figure 2 Liver transplantation with arterial reconstruction between the donor's celiac trunk and the recipient's splenic artery.

radiological suspicion of compromised arterial flow, and we opted for angiography, surgical exploration, or control based on the patient's condition and time since LT.

Acetylsalicylic acid was used prophylactically in all patients considered at risk of HAT (i.e., arterial donor reconstruction). A diagnosis of HAT was determined by the absence of hepatic artery flow by Doppler ultrasound at any time, confirmed either by computed tomography and/or angiography. A diagnosis of HAT within 1 month after transplantation was considered early onset, while a diagnosis after that time was considered late onset. HA stenosis was defined as vessel narrowing of >50% by computed tomography.

Statistical analysis

Differences between groups were evaluated using parametric or nonparametric tests, as appropriate. Qualitative variables were analyzed using the chi-square or Fisher test, while quantitative variables were analyzed using the student *t*-test, or in the case of nonnormal distributions, the Mann–Whitney *U* test. The 5 years actuarial survival was analyzed by the Kaplan–Meier method. All statistical analyses were performed using IBM SPSS for Windows, Version 22 (IBM Corp., Armonk, NY, USA), and statistical significance was set at a *P*-value of <0.05.

Results

We compared 1405 patients in the HA group with 54 patients in the SA group. Only 7 of the 54 SA reconstructions (13%) required an end-to-side anastomosis. Sixty-eight percent of the SA reconstructions (37 out from 54) were performed during the early experience period of the study (1990–2002), and the other 17 (32%), during the later period (2002–2016). As shown in Table 1, patients in the SA group were slightly younger and in more cases they were cases of retransplantation. There were no significant differences in severity of disease (MELD score) or previous transarterial chemoembolization. Indeed, surgical duration and arterial ischemic time was longer in the SA group. Patients in SA group required significantly more red blood units transfusion. Final flows, both arterial and portal, were similar between two groups.

Both intensive care stay and hospital stay were longer in patients in the SA group (Table 2). Referring to main complications directly related to the arterial reconstruction technique, there were two cases (3.7%) of acute pancreatitis in the SA group, compared to nine cases (0.6%) in the HA group, being the difference statistically significant. The only case of severe acute pancreatitis (not infected) was seen in the HA group. All the other cases were mild acute pancreatitis (according to revised Atlanta classification).

There was only one case of splenic ischemia in the SA group, without clinically significant relevance. There were no differences in the incidence of vascular or biliary complications, primary graft dysfunction, reoperation, or postoperative mortality. Equally, there were no differences in any type of arterial complication, early onset thrombosis, late-onset thrombosis, or stenosis. Indeed, the 5-year actuarial patient and graft survival were comparable between groups (Fig. 3).

We noted that there was a significantly higher proportion of retransplantations in the SA group ($n = 17$; 32%) compared with the HA group ($n = 113$; 8%; $P = 0.001$). Given that retransplanted patients are a specific subgroup, we performed a secondary comparative analysis excluding all cases of retransplantation. For this, we analyzed only patients who underwent a first LT in the SA group ($n = 37$) and the HA group ($n = 1292$). The patient and surgical characteristics are shown in Table 3, with the only differences being that patients in SA group were younger and had longer arterial ischemia times. As shown in Table 4, there were also no differences in the postoperative outcomes. Moreover, the incidence rates of long-term arterial and biliary complications, as well as the 5 years patient and graft actuarial survival, were similar between groups.

Discussion

Surgical complications after LT have improved significantly over recent years, but HAT remains a dreaded

Table 1. Patients demographics and surgical characteristics.

	HA group (n = 1405)	SA group (n = 54)	P
Age (years old), mean (SD)	53 (11)	49 (13)	**0.05**
Sex M/F, n (%)	959 (69)/419 (31)	32 (57)/23 (43)	0.06
MELD, mean (SD)	17 (6)	15 (5)	0.74
PreoLT TACE, n (%)	164 (11.6)	2 (3.7)	0.07
Emergent, n (%)	8 (5.7)	2 (3.7)	**<0.001**
Indication, n (%)			
HCC	434 (31)	12 (22)	**<0.001**
HCV	248 (18)	6 (11)	
ALCI	307 (22)	8 (15)	
HBV	41 (3)	2 (4)	
Others	375 (27)	26 (48)	
Retransplantation, n (%)	113 (8)	17 (31)	**0.001**
Surgical characteristics			
Donor age >70 years old, n (%)	161 (12)	4 (7)	0.38
Operation time (min), mean (SD)	394 (102)	424 (95)	0.03
Cold ischemia time (min), mean (SD)	444 (163)	470 (168)	0.27
Warm ischemia time (min), mean (SD)	57 (37)	60 (22)	0.65
Arterial ischemia time (min, mean (SD)	36 (28)	69 (55)	**0.005**
Final arterial flow (ml/min), mean (SD)	334 (374)	191 (120)	0.14
Final portal flow (ml/min), mean (SD)	1854 (934)	1630 (981)	0.39
PRBC transfusion (units), mean (SD)	6 (9.9)	11 (12)	**0.001**

ALCI, alcoholic cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LT, liver transplantation; MELD, only available since 2004; M/F, male/female; PRBC, packed red blood cells; TACE, transarterial chemoembolization. Bold indicates statistical significant value.

Table 2. Postoperative and long-term outcomes.

	HA group (n = 1405)	SA group (n = 54)	P
ICU stay (days), mean (SD)	6 (9)	10 (13)	**0.003**
Hospital stay (days), mean (SD)	18 (20)	28 (29)	**0.002**
Acute pancreatitis, n (%)	9 (0.6)	2 (3.7)	**0.007**
Severe acute pancreatitis, n (%)	1 (0.07)	0	–
Splenic ischemia, n (%)	0	1 (1.8)	–
Total vascular complications, n (%)	96 (7)	8 (15)	0.18
Early HAT, n (%)	32 (2.3)	2 (3.7)	0.31
Late HAT, n (%)	26 (1.8)	3 (5.5)	0.06
Arterial stenosis, n (%)	27 (1.9)	2 (3.7)	0.37
Bile duct complications, n (%)	319 (23)	17 (31)	0.32
Primary dysfunction, n (%)	122 (8.7)	6 (11)	0.74
Reoperation, n (%)	151 (10.7)	7 (13)	0.61
Postoperative mortality, n (%)	98 (7)	7 (13)	0.12

HAT, hepatic artery thrombosis; ICU, intensive care unit. Bold indicates statistical significant value.

complication. Despite technical improvements, 5–10% of cases tend to develop HAT, which may lead to the need for early retransplantation, or late biliary complications. In either case, both patient and graft survival rates may decrease [1–3].

Many factors can influence the development of HAT, but the quality of the donor celiac trunk and the recipient hepatic artery are key [3,17,18]. In some cases, the recipient HA may be unsuitable for anastomosis and achieving good revascularization. In our experience from 1984 to 2016, including 1500 LTs, we found that inadequate flow of the recipient HA occurred in 95 patients (6%). This is comparable to reports in other large published series. No adequate arterial flow was

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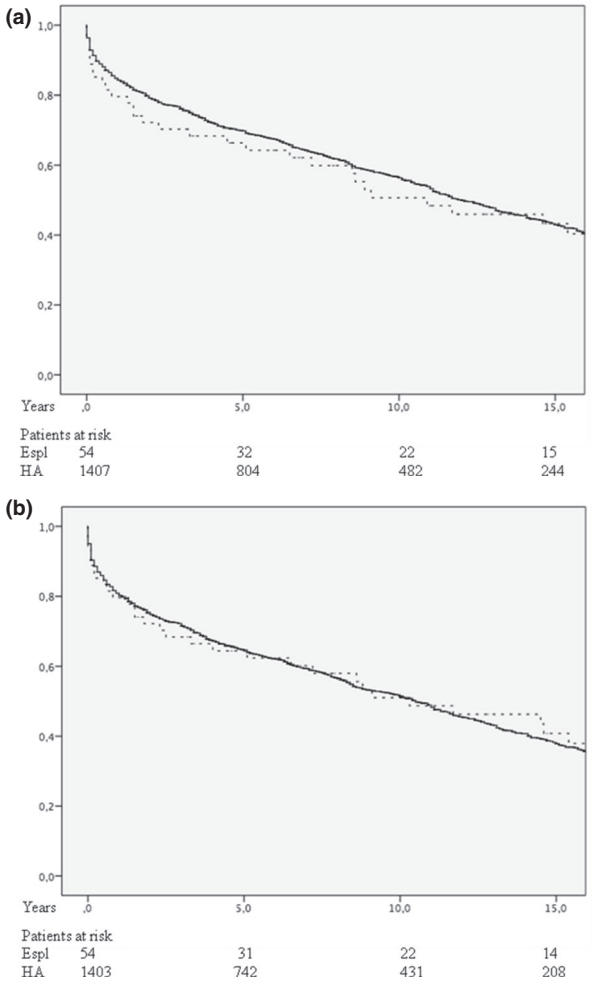

Figure 3 (a) Actuarial patient survival by type of arterial anastomosis ($P = 0.71$). ____ HA group ($n = 1407$) ----- SA group ($n = 54$). (b) Actuarial graft survival by type of arterial anastomosis ($P = 0.56$) ____ HA group ($n = 1407$) ----- SA group ($n = 54$). HA, hepatic artery; SA, splenic artery.

based on surgeon's judgment and/or in the case of flow lower than 100 ml/min measured by intraoperative transit-time ultrasound. Alternative approaches to arterialize the graft are needed in these cases [2,19,20], with aortohepatic conduits being the most commonly reported option [19,20].

We excluded patients with arterial conduits from our study. As said, since our group described the SA reconstruction, we use arterial conduits as the last option. We used this alternative approach in 27 cases. Most of the arterial conduits cases were performed during the early experience period of the study [23 (85%) before 2000] and/or as a salvage option. It is a different group of patients, as shown by analyzing its characteristics. Twenty-six percent were urgent transplantations, 44% were retransplantations, and 33% died during the postoperative period (data not shown). Thus, data on performance of arterial conduits was not comparable with the series included in our study.

Numerous studies have evaluated the results of using aortohepatic conduits [19]. In most of these studies, the use of arterial conduits has been demonstrated to be and independent risk factor for both early and late HAT as well as for biliary complications [19,20]. Indeed, some studies have shown lower patient and graft survival rates when using arterial conduits [7,21], leading authors, such as Hibi *et al.* [7], to recommend strictly limiting their use. Indeed, a recent meta-analysis [21] has concluded that the use of arterial conduits is a rescue option, and transplant surgeons should be alert of the potential risk of inferior outcome. Arterial conduits should always be reserved for salvage situations, and considering their risks, we always consider them the last alternative. In our study, we excluded the 27 conduit cases, because as we use them only as a salvage situation (SA reconstruction has been considered not feasible or has failed), we consider it a quite different group of patients. To provide a safer alternative in these settings, in 1992 our group first described using the recipient's SA [9]. The initially favorable short-term outcomes published in 1994 led us to consider it as our first alternative when routine HA anastomosis failed [10].

Thus, our decision algorithm is as follows. In case of preoperative or intraoperative consideration of and inadequate recipient HA, or failure of achieving adequate arterial flow after HA anastomosis, we evaluate the CT scan and intraoperative field to consider the use of splenic artery. If considered inadequate we consider the RCT reconstruction or suprarenal aortic anastomosis. It is important to note that in some cases of HA inadequacy because of arterial dissection, SA may also be involved. In such cases neither SA anastomosis nor RCT reconstruction is advisable, and primary aortic anastomosis would be the best choice.

A few other studies in the literature have analyzed the results of using the SA in cases of HA inadequacy [11–13,22]. Most of these have been short-term case reports of fewer than 10 cases [11–13]. Apart from our initial description of 23 cases, the largest report included 17 cases and was published in 2017, reporting incidence rates of 6% and 17% for HAT and vascular complications, respectively, with the use of SA reconstruction [22]. With the inclusion of 54 cases and a median follow-up of 11.6 years, the present study not only is the largest to have evaluated SA reconstruction but also has the longest follow-up.

Table 3. Primary liver transplantation: patients demographics and surgical characteristics.

	HA group (n = 1292)	SA group (n = 37)	P
Age (years old), mean (SD)	52 (10)	46 (13)	**0.01**
Sex M/F, n (%)	526 (67)/253 (23)	18 (56)/14 (44)	0.12
MELD, mean (SD)	16.7 (6.5)	14.5 (5.7)	0.51
PreoLT TACE, n (%)	41 (3)	0	–
Emergent, n (%)	162 (12)	2 (5.4)	0.19
Indication, n (%) Afegir			
HCC	434 (33)	12 (32)	0.46
HCV	248 (19)	6 (16)	
ALCI	307 (23)	8 (21)	
HBV	41 (3)	2 (5)	
Others	375 (29)	26 (70)	
Surgical characteristics			
Donor age >70 years old, n (%)	156 (12)	3 (8)	0.31
Operation time (min), mean (SD)	395 (99)	437 (95)	0.69
Cold ischemia time (min), mean (SD)	461 (176)	468 (146)	0.14
Warm ischemia time (min), mean (SD)	59 (27)	61 (46)	0.11
Arterial ischemia time (min), mean (SD)	36 (28)	69 (55)	**0.005**
Final arterial flow (ml/min), mean (SD)	203 (164)	336 (334)	0.54
Final portal flow (ml/min), mean (SD)	1850 (934)	1650 (981)	0.39
PRBC transfusion (units), mean (SD)	6 (8)	9 (8)	0.87

ALCI, alcoholic cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LT, liver transplantation; MELD, only available since 2004; M/F, male/female; PRBC, packed red blood cells; TACE, transarterial chemoembolization. Bold indicates statistical significant value.

Table 4. Primary liver transplantation: postoperative and long-term outcomes.

	HA group (n = 1292)	SA group (n = 37)	P
ICU stay (days), mean (SD)	6 (7)	6 (5)	0.61
Hospital stay (days), mean (SD)	20 (16)	22 (15)	0.58
Acute pancreatitis, n (%)	3 (0.2)	1 (2.7)	0.14
Severe acute pancreatitis, n (%)	0	0	–
Splenic ischemia, n (%)	0	1 (2)	–
Total vascular complications, n (%)	165 (13)	8 (22)	0.25
Early HAT, n (%)	30 (2)	2 (5)	0.17
Late HAT, n (%)	25 (2)	2 (5)	0.17
Arterial stenosis, n (%)	23 (2)	1 (2)	0.17
Bile duct complications, n (%)	290 (22)	11 (30)	0.61
Primary dysfunction, n (%)	110 (9)	6 (16)	0.25
Reoperation, n (%)	126 (10)	4 (11)	0.61
Postoperative mortality, n (%)	98 (7)	7 (13)	0.12
5-year actuarial patients survival (%)	69	67	0.95
5-year actuarial graft survival (%)	70	64	0.95

HAT, hepatic artery thrombosis; ICU, intensive care unit.

Kazemi *et al.* [22] concluded that SA reconstruction was at least as good as arterial conduits, and that the method could be used safely. However, we consider that SA reconstruction should be the first alternative after standard HA reconstruction. Previous studies of SA reconstruction, including our previous report of 23 cases [10], have showed good short-term results with no complications [11–13]. In the study by Vanderlan *et al.* [12], three of seven patients who underwent SA reconstruction developed either thrombosis or stenosis, but it is

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important to note that each of these arterial complications occurred in patients with end-to-side anastomosis.

In our experience, all arterial complications, early HAT, late HAT, and stenosis, were similar between the SA and HA groups, and were comparable to the rates reported in most series [1,2]. Patients in both the SA and HA groups were also comparable for the most part in this study, though the SA group were somewhat younger and tended to require retransplantation. The high retransplantation rate explains the findings of longer surgical durations, intensive care stays, and hospital stays, as well as the greater volumes of blood transfused, which reflect the higher surgical complexities and poor patient statuses in this group. Even with the more complicated surgery and postoperative evolution, the arterial and biliary complications, postoperative mortality, and long-term patient and graft survival were similar between the groups. However, to eliminate the bias of retransplantation in the SA group, we performed a secondary analysis of only first LTs to keep the groups more comparable. This removed all the differences identified in the full cohorts. Although the SA group remained slightly younger, all operative and postoperative data were otherwise similar between the groups.

Recently, Dokmak *et al.* [14] proposed the recipient celiac trunk (RCT) as the best alternative to the HA for arterial reconstruction. The main drawbacks they attributed to the SA reconstruction were the risks of bleeding and pancreatitis. However, despite being possible risks, their incidence with the technique is low; for example, we only encountered two cases of mild pancreatitis and only one case of asymptomatic splenic ischemia, with a similar reoperation rate to the HA group. Moreover, the spleen is supplied from the short gastrosplenic vessels and the left gastric artery, so the SA approach should rarely be associated with splenic complications. Indeed, experimental data have shown that the immunological function of the spleen is preserved after ligation of the SA [23,24].

We agree with the assessment by Dokmak *et al.* [14] that it is important to review computed tomography scans preoperatively. When deciding on the best option in the case of an inadequate recipient HA, the characteristics of the recipient SA need to be considered carefully (i.e., its size, relationship with the pancreas, and tortuosity). In our experience, the SA is usually feasible for use because it is typically large and superficial in cirrhotic patients. An end-to-side anastomosis may be also be employed to encircle the SA when the direct end-to-end anastomosis is not possible, though it should be considered that this option is indirect and may be related with higher complication rates [12]. Nevertheless, only one of our seven cases using this option had arterial complications.

Recipient celiac trunk reconstruction has been described in another short report of nine cases with only four adult cases [14]. That study described no complications of the technique after a short follow-up period of 23 months. Therefore, the RCT option should remain as an alternative technique in our armamentarium, though in our opinion, there is a lack of data to support its use as the first choice alternative. We consider its use best reserved for cases of HA inadequacy in which the SA is also inadequate because of its small size.

Our study has some drawbacks that should be addressed. Firstly, the study was performed based on the prospectively maintained database of our unit, during a long period of time. Thus, the groups are quite hard to compare. However, as shown in Tables 1 and 3, main demographics and surgical characteristics were comparable.

And secondly, some interesting data were not available in the prospective database (i.e., indication of splenic artery anastomosis as a primary anastomosis, number of patients on prophylactic use of aspirin, time of occlusion of HA).

Another relevant data not available are the site of anastomosis at the donor celiac trunk in cases of standard reconstruction. Anastomosis was performed at the best site of the donor celiac trunk considered by surgeon′s judgment. In fact, this has changed through the evolution of our series, trying to shorten it as much as possible, to reduce the risk of HAT [19].

Although there were not statistically significant differences on the rate of arterial complications, SA group had slightly higher rate of late HAT. We could speculate that the use of aspirin could be recommended to improve long-term arterial patency in the case of SA reconstruction.

In conclusion, the short- and long-term outcomes of arterial reconstruction using the recipient's SA are comparable to those of standard reconstruction using the HA in first-time adult LT. In the setting of retransplantation, the perioperative evolution is more complex, but this does not affect vascular complications or survival. In our experience, SA reconstruction should be considered the first alternative to standard HA reconstruction whenever possible.

Finally, the experienced surgical team should have all options available for inadequacy of native hepatic

arteries, from conduits to SA reconstruction, depending on several factors including the vascular anatomy, ease of access to aorta or splenic artery and the presence of atherosclerotic disease of aorta and splanchnic vessels.

Authorship

LL: designed the study, analyzed data, and writted the manuscript. ER and JF: designed the study and reviewed the draft; AB and AC: analyzed the data; CB, KM, JB, LS, NP, and EFV: collected data and reviewed the manuscript.

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Conflict of interest

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