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ORIGINAL ARTICLE

Comparison of reconstruction methods used during liver transplantation in case of a graft with replaced or accessory right hepatic artery: A retrospective study

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Abstract

Variations in graft arterial anatomy can increase the risk of postoperative hepatic arterial thrombosis (HAT), especially in presence of a replaced or accessory right hepatic artery (RHA). We retrospectively analyzed 223 cases of liver transplantations with the presence of an RHA on the graft. Patient outcomes were compared according to the four different reconstruction methods used: (i) the re-implantation of the RHA into the splenic or gastroduodenal artery ($n = 106$); (ii) the interposition of the superior mesenteric artery (SMA) ($n = 83$); (iii) dual anastomosis ($n = 24$); (iv) use of an aortic patch including the origins of both the SMA and the coeliac trunk ($n = 10$). A competing risk analysis and Inverse Probability Weighting (IPW) were used. We found that the interposition of the SMA method was associated with a significantly lower incidence of HAT, at 4.8% compared to the re-implantation method at 17.9%, dual anastomosis at 12.5%, and aortic patch at 20%, $p = .03$. In the competing risk analysis with IPW, the only risk factor for RHA thrombosis was the type of reconstruction. Taking the SMA interposition group as the reference, the sub-hazard ratio (sHR) was 5.05 (CI 95 [1.72; 14.78], $p < .01$) for the re-implantation group, sHR = 2.37 (CI 95 [0.51; 11.09], $p = .27$) for the dual anastomosis group and sHR = 2.24 (CI 95 [0.35; 14.33], $p = .40$) for the aortic patch group. There were no differences for intraoperative transfusion, hospitalization duration ($p = .37$) or incidence of severe complications ($p = .1$). The long-term graft ($p = .69$) and patient ($p = .52$) survival was not different. In conclusion, the SMA interposition method was associated with a lower incidence of RHA thrombosis.

KEYWORDS

graft anatomy, hepatic artery thrombosis, liver transplantation, reconstruction method, right hepatic artery

1 | INTRODUCTION

Arterial anastomosis remains a major surgical challenge during liver transplantation (LT). Indeed, the incidence of hepatic artery thrombosis (HAT) varies from 4% to 15%[1–3] and significantly impacts graft and patient outcomes.[4,5]

Variations in graft arterial anatomy usually require complex reconstruction, resulting in a higher incidence of arterial or biliary complications.[6,7] Among these variations, the presence of a replaced or accessory right hepatic artery (RHA) arising from the superior mesenteric artery (SMA) is the most frequent and is encountered in approximately 10%–20% of cases.[8] Numerous reconstruction methods have been described, such as anastomosis of the RHA with the graft splenic artery (SA)[9,10] or gastroduodenal artery (GDA),[11] interposition of the graft SMA,[12,13] or use of a graft aorta patch including both the coeliac trunk and the SMA.[12]

In most cases, all reconstruction techniques are feasible but since there has been no comparative study, the decision usually depends on the surgeon's usual practice.

The aim of our study was to compare the four different reconstruction methods used in our experience of liver transplantation when an RHA is present on the graft.

2 | PATIENTS AND METHODS

2.1 | Patient selection

All LTs performed between January 2003 and December 2018 in two European high-volume LT centres (University Medical Center Groningen, the Netherlands, and Rennes University Hospital, France) were retrospectively analyzed ($n = 2502$).

All adult patients transplanted with a graft presenting an RHA arising from the SMA were reviewed ($n = 293$, 11.7%).

Patients transplanted with a graft from a living donor or a split liver graft ($n = 4$), without the need for reconstruction due to a total replacement of the hepatic artery supply by the RHA (i.e., Type-V of HIATT classification,[8] $n = 31$) or due to an accidental section of the RHA during the procurement without the possibility of reconstruction ($n = 7$), were excluded from the analysis. Patients with complex arterial or venous reconstruction requiring the use of a conduit or caval transposition ($n = 18$), patients who died intra-operatively ($n = 3$), and patients with no information on the reconstruction methods ($n = 7$) were also excluded (Figure 1).

Finally, our population comprised patients transplanted with a graft presenting a replaced or accessory RHA (type-III or IV of HIATT classification[8]) and the four different reconstruction methods used were compared:

1. The re-implantation group: the RHA is anastomosed on the graft splenic or gastroduodenal arterial stump, followed by anastomosis between the recipient's artery with the graft celiac trunk or common hepatic artery.
2. The SMA interposition group: the graft celiac trunk is anastomosed with the distal stump of the graft SMA, followed by anastomosis between the proximal stump of the SMA and the recipient's artery.
3. The dual anastomosis group: the graft RHA is anastomosed with the right branch of the proper hepatic artery (or the recipient's RHA when present) while the common or proper hepatic artery of the graft is anastomosed with the recipients' proper HA or its left branch.
4. The aortic patch group: an aortic patch from the donor including the origin of both the SMA and the celiac trunk is anastomosed directly with the recipient's artery.

2.2 | Perioperative management and surgical procedure

Orthotopic LT (OLT) with inferior vena cava preservation was performed in all cases. After standard

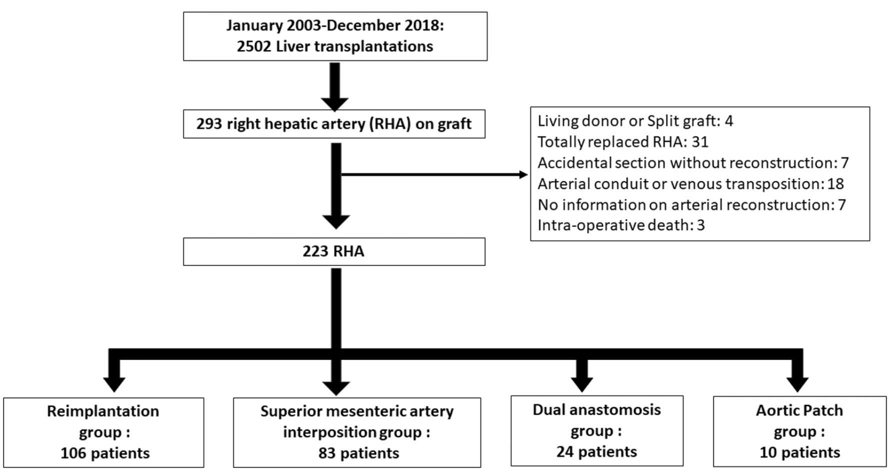

FIGURE 1 Flow chart of the study.

hepatectomy, graft implantation started with caval anastomosis, which was performed with an original or modified (i.e., side-to-side) piggy-back technique, followed by an end-to-end portal vein anastomosis. The graft was then vascularized prior to arterial anastomosis and subsequent biliary anastomosis. All RHA arterial reconstruction were performed by a senior surgeon. The choice of the reconstruction method was purely dependent on his preference.

After the procedure, patients were transferred to the intensive care unit (ICU) until graft and recipient functions were satisfactory. Routine immunosuppression was similar in the two centres and based on calcineurin inhibitors (mostly tacrolimus) combined with mycophenolate mofetil and a short course of corticosteroids. Aspirin was provided in all cases when possible.

Systematic Doppler ultrasound was routinely performed at POD 1 and 7 and repeated or completed by a contrast-enhanced CT-scan according to the clinical course.

After discharge, patients were followed up according to center policies. Systematic imagery (i.e., Doppler ultrasound or CT-scan) was performed at least every 6 months in the first year, and yearly thereafter.

2.3 | Data collection

The following variables were collected from a prospective database and analyzed:

1. Recipient characteristics: age, gender, body mass index (BMI), underlying liver disease, Child–Pugh score, and Model for End-stage Liver Disease (MELD) score.
2. Donor characteristics: age, gender, BMI, type of donor: brain death (DBD) or circulatory death (DCD), cold ischemia duration.
3. Arterial reconstruction: all operative notes were systematically reviewed in order to identify the reconstruction method as well as the arterial anatomy of the graft.
4. Outcomes: intraoperative and postoperative outcomes, especially the occurrence of arterial complications, and patient and graft survival. The severity of complications during initial hospitalization was graded using the Clavien–Dindo classification.

2.4 | Ethics

For University Medical Center Groningen, patient data was derived from a post-hoc analysis of an observational cohort study (www.trialregister.nl—Trial NL6334), which was approved by the Medical Ethics Committee (METc 2014/77).

For Rennes university hospital, patient data were mostly retrieved from the database of the national agency of regulation of the procurements and transplantations ("Agence de la Biomédecine"). A formal approval from the local ethics committees was also obtained (avis n°22.81).

Data was retrieved from each center and made anonymous prior to analysis.

The study adhered to the Declaration of Helsinki and the Declaration of Istanbul.

2.5 | Statistical analysis

Quantitative variables were expressed as medians with extreme values (ranges) and compared using the Kruskal–Wallis test.

Qualitative variables were expressed as numbers and percentages and compared using chi-square or Fisher's exact tests, as appropriate.

2.5.1 | Competing risk analysis

Patients undergoing OLT are at risk of presenting mutually exclusive events. Since the occurrence of death can prevent occurrence of HAT, the usual Kaplan–Meier model is inappropriate to correctly estimate the incidence of HAT. Therefore, a competitive risk analysis using a Fine and Gray model[14] was used in order to specifically evaluate the risk factors for HAT and estimate the cause-specific hazard also called sub-hazard ratio (sHR).

The two competing events were therefore the occurrence of HAT or death (without HAT). Patients were "right-censored" at the latest update or the re-transplantation date.

2.5.2 | Inverse probability weighting (IPW) ponderation

In order to carry out efficient analyses and to correct for bias due to population heterogeneity, stabilized Inverse Probability Weighting (IPW)[15] was performed. Comparisons were made using an adjusted log-rank test.[16]

Only the impacting variables (i.e., variables significantly different across groups in the bivariate analysis) were selected and used in the propensity score calculation.

A *p*-value $<.05$ was considered significant. All statistical analyses were performed on R software version

3.1.3 using the "survival" v3.1–12, "ipw" v0.1.0–11 and "Weightit" v0.12.0 packages.

3 | RESULTS

3.1 | Population characteristics

During the study period, 2502 OLTs were analyzed. An RHA was present in 293 cases (11.7%). After the selection process (Figure 1), 223 cases were analyzed. The reconstruction methods used were (i) re-implantation of the RHA for 106 (47.5%) (into the GDA for 62 and into the splenic artery for 44), (ii) interposition of the SMA for 83 (37.2%), (iii) dual anastomosis for 24 (10.8%), and (iv) the use of an aortic patch for 10 (4.5%).

The main characteristics of the grafts and recipients are summarized in Table 1.

The main differences between groups were the MELD score at transplantation (p = .01), the involvement of a DCD donor (p < .01), the donor's age (p < .01), and cold ischemia duration (p < .01). All these variables were used for the IPW ponderation.

The median follow-up was 65.7 months without significant differences between groups (p = .08).

3.2 | Arterial complications

During the study period, 28 patients (12.6%) presented thrombosis of the RHA at a median time-lapse of 9.5 days [1; 3020]. The incidence was significantly different across groups, with an incidence of 17.9% (n = 19) in the re-implantation group, 4.8% (n = 4) in the SMA interposition group, 12.5% (n = 3) in the double anastomosis group, and 20% (n = 2) in the aortic patch group (p = .03).

Thrombosis of the RHA was responsible for a complete hepatic arterial thrombosis in 22 cases (9.9%) and was also significantly different across groups (p = .04).

3.2.1 | Details and outcomes of the RHA thrombosis

Among the four (4.8%) thrombosis occurring in the SMA interposition group, two (2.4%) occurred during the first month and two (2.4%) during the second month. The RHA thrombosis was associated with a complete arterial thrombosis in all four cases and resulted in a re-transplantation in three (3.6%) cases (at month 7–11 and 63 after initial LT). The last patients died at month 16 due to HCC recurrence without biliary or other consequences of the arterial thrombosis.

In the reimplantation group, among the 19 (17.9%) RHA thrombosis, a complete arterial thrombosis was present in 16 (15.1%) cases and occurred during the first months in 16 (15.1%) cases and after in three (2.8%) cases (at month 4–5 and 99). Among the 16 early thrombosis, six (5.6%) were directly retransplanted (at month 1–2 and 3), two (1.8%) had surgical repermeabilization but were also retransplanted later (at month 3 and 48) due to biliary necrosis, one (0.9%) had a radiological revascularization that failed and was retransplanted (at month 2), two (1.8%) patients were not transplantable and died of septic complication related to the arterial thrombosis, one (0.9%) patient died of septic complication not related to the arterial thrombosis (pneumonia), four (3.7%) patients were treated medically or by endoscopic treatment and keep a functional grafts. The three patients presenting a late thrombosis were treated conservatively (i.e., no surgical procedure or retransplantation) due to minor symptoms in two cases and advanced aged in one patient (presenting biliary necrosis with biliary cast syndrome).

In the dual anastomosis group, all three (12.5%) thrombosis occurred during the first week after LT. A complete arterial thrombosis was present in two (8.3%) cases and needed retransplantation while the last one was treated conservatively.

In the aortic patch group, one (10%) thrombosis occurred within the first month and needed retransplantation while the other one occurred at month 8 and was treated conservatively due to minor symptoms.

There was no difference for arterial stenosis across groups (p = .47).

3.3 | Risk factors for right hepatic artery thrombosis

Using a competing risk model, the only risk factor for RHA thrombosis was the type of reconstruction (Table 2). When taking the SMA interposition method as the reference, the sHR was significantly higher in the re-implantation group (sHR = 4.09 [1.41; 11.84], p < .01) while it was not significant for the dual anastomosis group (sHR = 2.84 [0.63; 12.89], p = .18) or the aortic patch group (sHR = 4.26 [0.84; 21.63], p = .08).

After applying the IPW ponderation with the competing risk analysis, the type of reconstruction was still significantly associated with RHA thrombosis (p = .02). Taking the SMA group as the reference, the sHR was 5.05 (CI 95 [1.72; 14.78], p < .01) for the reimplantation group, sHR = 2.37 (CI 95 [0.51; 11.09], p = .27) for the dual anastomosis group, and sHR = 2.24 (CI 95 [0.35; 14.33], p = .40) for the aortic patch group.

TABLE 1 Patient and donor characteristics.

	Total (n = 223)	Reimplantation (n = 106)	SMA interposition (n = 83)	Dual anastomosis (n = 24)	Aortic patch (n = 10)	p
Recipient characteristics						
Gender (male)	164 (73.5%)	79 (74.5%)	58 (69.9%)	19 (79.2%)	8 (80%)	.82
Age (years)	59 [18; 73]	58 [22; 73]	60 [18; 70]	57 [35; 69]	60 [42; 65]	.90
BMI	26.2 [17.2; 44.1]	25.7 [18.2; 38.1]	26.5 [18.1; 44.1]	27.7 [18; 39.7]	26.3 [17.2; 33.1]	.35
MELD	16.7 [5; 40]	19.5 [5; 40]	14.07 [5.4; 40]	17 [6.4; 32]	11.43 [5; 17.1]	.01
Retransplantation procedure	16 (7.2%)	9 (8.5%)	6 (7.2%)	0 (0%)	1 (10%)	.48
Donor characteristics						
Donor Type DBD DCD	193 (86.5%) 30 (13.5%)	83 (78.3%) 23 (21.7%)	81 (97.6%) 2 (2.4%)	21 (87.5%) 3 (12.5%)	8 (80%) 2 (20%)	<.01
Gender (male)	122 (54.7%)	57 (53.8%)	48 (57.8%)	13 (54.2%)	4 (40%)	.75
Age	56 [10; 92]	61 [16; 89]	55 [16; 92]	56 [10; 80]	39 [11; 48]	<.01
BMI	25 [18.3; 44.9]	25.1 [18.3; 44.9]	24.5 [18.4; 43.1]	26.5 [19.1; 38.7]	25.9 [19.6; 35.6]	.61
Anatomical variation[a] Type III Type IV	163 (73.1%) 60 (26.9%)	80 (75.5%) 26 (24.5%)	59 (71.1%) 24 (28.9%)	16 (66.7%) 8 (33.3%)	8 (80%) 2 (20%)	.77
Cold ischemia duration (min)	545 [58; 1393]	517 [58; 1393]	607 [181; 1009]	491 [306; 808]	459 [183; 681]	<.01
Operative outcome						
Intraoperative transfusion Red blood cell Fresh Frozen Plasma Platelet count	5 [0; 32] 5 [0; 41] 0 [0; 10]	5 [0; 32] 5 [0; 25] 0 [0; 10]	4 [0; 20] 6 [0; 22] 0 [0; 2]	5 [0; 12] 4 [0; 30] 0 [0; 2]	5.5 [0; 14] 2.5 [0; 41] 0 [0; 64]	.99 .39 .48
Procedure duration (min)	420 [170; 933]	443 [175; 933]	385 [170; 689]	417 [180; 654]	465.5 [220; 680]	.01
Postoperative outcomes						
Hospitalization ICU Total	4 [1; 82] 20 [1; 127]	4 [1; 82] 21 [1; 127]	4 [1; 56] 20 [3; 74]	5 [1; 26] 21.5 [7; 38]	3.5 [1; 22] 16.5 [13; 30]	.68 .37
Clavien-Dindo grade ≥3	75 (33.6%)	43 (40.6%)	26 (31.3%)	4 (16.7%)	2 (20%)	.1
RHA thrombosi 1-Year study period	26 (11.7%) 28 (12.6%)	17 (16%) 19 (17.9%)	4 (4.8%) 4 (4.8%)	3 (12.5%) 3 (12.5%)	2 (20%) 2 (20%)	.048 .03
Complete arterial thrombosis	22 (9.9%)	16 (15.1%)	4 (4.8%)	1 (4.3%)	1 (10%)	.04
Arterial stenosis	22 (9.9%)	14 (13.2%)	6 (7.2%)	2 (8.3%)	0 (0%)	.47
Graft survival 1 Year	171 (76.7%)	80 (75.5%)	65 (78.3%)	17 (70.8%)	9 (90%)	.69
Patient survival 1 Year	186 (83.4%)	87 (82.1%)	70 (84.3%)	19 (79.2%)	10 (100%)	.52
Median follow up (months)	65.7 [0; 232]	61 [0; 232]	65.8 [0.1; 217.6]	75.2 [0.1; 166.2]	167 [0.5; 193.1]	.08

Abbreviations: DBD, donor from brain death; DCD, donor from circulatory death; ICU, intensive care unit; RHA, right hepatic artery; SMA, superior mesenteric artery.

[a]according to the HIATT classification.

TABLE 2 Risk factors for right hepatic artery thrombosis using a competing risk model.

	Competing risk analysis	
Variables	***p***	**sHR [CI 95%]**
Recipient characteristics		
Gender (male)	.28	1.71 [0.65; 4.49]
Age (years)	.61	1.01 [0.98; 1.04]
BMI	.52	1.02 [0.95; 1.1]
MELD	.92	1 [0.96; 1.04]
Retransplantation procedure	.44	0.46 [0.06; 3.31]
Donor characteristics		
Donor Type (DCD)	.51	1.38 [0.54; 3.56]
DBD		
DCD		
Gender (male)	.18	0.6 [0.28; 1.26]
Age	.68	1 [0.97; 1.02]
BMI	.81	0.99 [0.92; 1.06]
Anatomical variation	.51	0.74 [0.3; 1.82]
Cold ischemia duration	.148	1 [1; 1]
Reconstruction method:	ref = 1	4.09 [1.41; 11.84]
SMA interposition	<.01	2.84 [0.63; 12.89]
Reimplantation	.18	4.26 [0.84; 21.63]
Dual anastomosis	.08	
Aortic patch		

Abbreviations: DCD, donor from circulatory death; SMA, superior mesenteric artery.

3.4 | Postoperative outcomes

The use of intraoperative transfusions was not significantly different across groups (Table 1). The duration of the procedure was significantly shorter when SMA interposition was implemented ($p < .01$).

There was no difference in hospitalization duration ($p = .37$) nor in the incidence of severe postoperative complications (i.e., Clavien–Dindo grade >3) ($p = .1$) across groups.

One-year graft ($p = .69$) and patient survival ($p = .52$) did not differ across groups, nor did long-term graft ($p = .5$) (Figure 2) and patient survival ($p = .6$) (Figure 3).

4 | DISCUSSION

To our knowledge, this is the first study to compare the four most common reconstruction methods used in case of a right hepatic artery in the graft.

Our results showed that RHA patency was significantly better when an SMA interposition method was used rather than the other methods. This difference was observed in HAT incidence at 1 year ($p = .048$) over the whole study period ($p = .03$), and it was confirmed after application of a competing risk model with IPW ponderation ($p = .02$). However, this difference was observed only when comparing the SMA interposition group with the re-implantation group and not with the two other groups (probably because of the very small population size). RHA thrombosis was associated with complete arterial thrombosis (i.e., affecting the RHA and the other arteries on the graft) in a large majority of cases. It can be thought that the thrombosis initially occurred in anastomoses with the highest risk (i.e., RHA reconstruction) and then extended to the other arteries.

Our results can be explained by the fact that the SMA interposition method resulted in two anastomoses with a large diameter (i.e., between the graft celiac trunk and the graft SMA, followed by the graft SMA and the recipient artery), while anastomosis between the graft RHA with the splenic or GDA artery involved smaller caliber anastomoses, with a high risk of malrotation of the re-implanted RHA. On the other hand, the SMA interposition method resulted in a longer arterial length compared to the re-implantation method, which is sometimes described as a risk factor for thrombosis.[17] Regarding the other two groups, no conclusions could be drawn because of the limited number of cases.

Complex arterial reconstruction including the use of a conduit,[18,19] the use of an alternative arterial site on the recipient,[20] or variations in the graft arterial anatomy[7] are well-known risk factors for HAT. The presence of an RHA on the graft is frequent in liver transplantation[8,21] and several reconstruction methods have been described. The most common technique is to anastomose the RHA with the graft splenic artery or GDA[21–23] since ensuring that the arterial length is as short as possible is considered to be better. However, the results of this reconstruction technique are not always reported[21,23] and no comparisons have been made to date, in particular using a competing risk model. In their study, Tsaroucha et al.[24] reported 25 cases of reconstructed RHA and described seven different methods of reconstruction. The authors reported that SMA interposition was their preferred method since it had been used 12 times with a HAT incidence of 8.3% and graft survival reaching 83%. They also reported seven cases of anastomosis with the splenic stump with a HAT incidence of 14% and graft survival at 72%. These results are in line with our findings. In another study, Melada et al.[22] reported 52 cases of arterial reconstructions for RHA. The most frequent reconstruction methods were anastomoses with the splenic artery in 26 cases (50%) or with the GDA in six cases (11.5%), interposition of the SMA in 17 cases (32.7%), and dual anastomosis in two cases (3.8%). They reported an overall 5.4% incidence of HAT, without providing details on the reconstruction methods, and also a 26.8% incidence

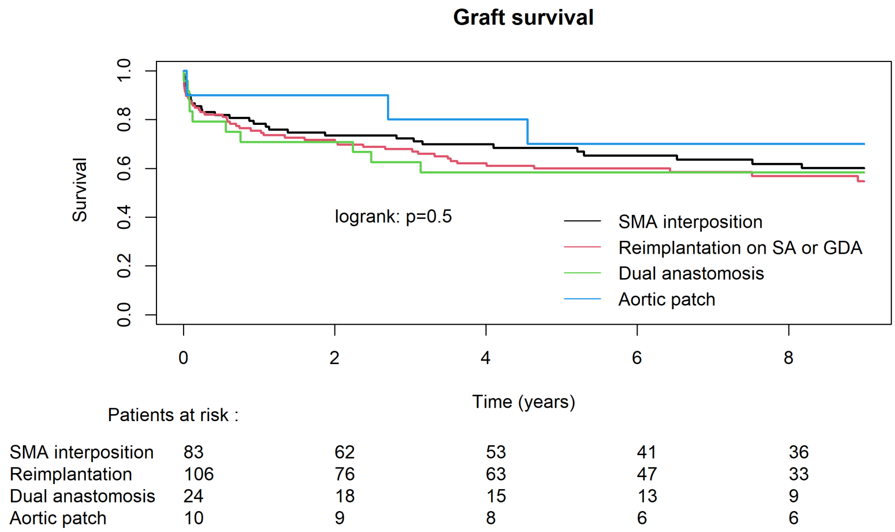

FIGURE 2 Graft survival.

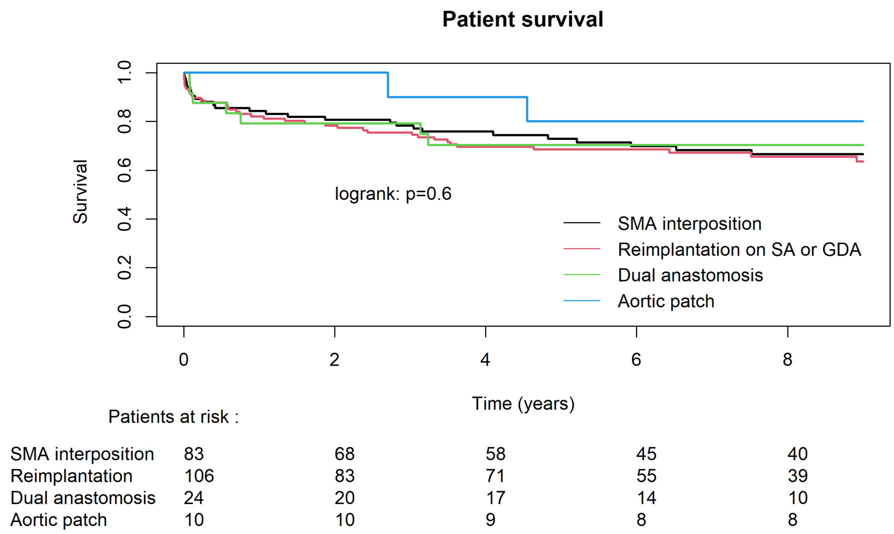

FIGURE 3 Patient survival.

of graft loss at 1 year. Their results highlight the need to use a competing risk model in order to accurately evaluate the incidence of HAT. Recently, Karakoyun et al.[6] reported a series of 117 cases of hepatic variations including 42 RHAs arising from the SMA and 15 triple arteries (type-IV of Hiatt). The reconstruction method was anastomosis with the graft GDA in 26 cases (38.8%) cases, with the splenic artery in 10 (14.9%), dual anastomosis in 11 (16.4%), and interposition of the SMA in three (4.5%). The authors reported only one case of arterial complications.

With 223 cases of RHA analyzed, our study is the largest to date, and after systematically analyzing the outcomes of all cases, we provide new data in favor of SMA interposition, despite the fact that the re-implantation method (using the GDA or the splenic artery) was also the most popular method in our study.

However, our results should be interpreted with caution. First, the retrospective nature and the absence of randomization in the choice of the reconstruction method led to significant differences across groups for demographic data and could have induced a selection bias. However, using advanced statistical methods (i.e., IPW ponderation) we believe that this bias was partly compensated. Second, the small numbers of patients, especially in the dual anastomosis and the aortic patch groups, reduced the power of our results. However, the two most frequently used methods (i.e., the re-implantation and SMA interposition methods) concerned 106 and 83 patients, providing sufficient strength for our results. We recognize that no conclusions can be drawn regarding the other two groups, but we believe that it was important to include them in the analysis.

In all events, our results need to be confirmed in a larger multicenter study, since a prospective randomized study could be difficult to set up.

In conclusion, when a right hepatic artery was present, we found that reconstruction with interposition of the SMA was associated with lesser incidence of arterial thrombosis.

AUTHOR CONTRIBUTIONS

MR, RP, VdM designed the study. MR, IB, DW, MB, WvdP, LN, CC collected the data. MR, IB, DW drafted the manuscript. All authors reviewed and approved the manuscript.

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This study received no financial support.

CONFLICT OF INTEREST

The authors declare no conflict of interest regarding this study.

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