In-depth Clinical, Hemodynamic, and Volumetric Assessment of the Resection and Partial Liver Transplantation With Delayed Total Hepatectomy-Type Auxiliary Liver Transplantation in Noncirrhotic Setting

Are We Simply Dealing With a Transplant Model of Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy?

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Background: The Resection And Partial Liver Transplantation with Delayed total hepatectomy (RAPID) procedure involves left hepatectomy with orthotopic implantation of a left lobe and right portal vein ligation. This technique induces volumetric graft increase, allowing for a right completion hepatectomy within 15 days. Notably, there is a lack of data on the hemodynamics of small-for-size grafts exposed to portal overflow without triggering small-for-size syndrome.

Methods: A prospective single-center protocol included 8 living donors and 8 RAPID noncirrhotic recipients. Comprehensive clinical and biological data were collected, accompanied by intraoperative arterial and portal flow and pressure measurements. Early kinetic growth rate (eKGR%) and graft function were assessed using computed tomography and 99Tc-mebrofenin scintigraphy on postoperative days 7 and 14. Findings were compared with retrospective data from 13 left living donor liver transplantation (LDLT) recipients.

Results: The median Graft-body weight ratio was 0.41% (interquartile range: 0.34–0.49), markedly lower than in LDLT. However, there was no significant difference in eKGR between RAPID and LDLT grafts. Sequential analysis revealed variable eKGR per day: 10.6% (7.8–13.2) in the first week and 7.6% (6–9.1) in the second week posttransplantation. Indexed portal flow (indexed portal vein flow) was significantly higher in RAPID compared with left LDLT ($P = 0.01$). No hemodynamic parameters were found to correlate with regeneration speed. We modulated portal flow in 2 out of 8 cases.

Conclusions: This study presents the first report of hemodynamic and volumetric data for the RAPID technique. Despite initial graft volumes falling below conventional LDLT recommendations, the study highlights acceptable clinical outcomes.

Keywords: ALPPS, living donor liver transplantation, RAPID

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Resection And Partial Liver Transplantation with Delayed total hepatectomy (RAPID) were initially described after recovery of the left lobe of cadaveric origin.[1] This 2-stage procedure begins with resection of the recipient's left liver (H1234),[2] right portal vein (PV) ligation, and orthotopic implantation of the donor left lobe (G23). Subsequent portal overflow stimulates graft growth, which allows the safe removal of the right liver remnant (RLR). The results of the index case were satisfactory and paved the way for living donations (LD-RAPID).[3] The current data underline the increased safety in the donor benefiting from a left hepatectomy as well as in the recipient retaining a right functional backup in cases of graft failure.[4,5] The RAPID auxiliary graft is currently experiencing a major craze, and a recent study demonstrated its good results in multicenter settings[6] as well as its feasibility in cirrhotic conditions.[7] RAPID allows successful adult-to-adult transplantation with very low graft-to-body weight ratio (GBWR $< 0.5\%$).

The technical difficulties encountered in this complex procedure are significant, and only a few cases have been described in the literature. The clinical and biological results of our preliminary experiments are described later. We aimed to confirm whether the RAPID procedure is associated with accelerated regeneration. Thus, we investigated the kinetics of the graft volume increment by comparing it to that observed in patients receiving a partial graft alone. We also provide the first comprehensive exploration of liver hemodynamics to address whether flow and pressure changes can support the regeneration process in this setting. The RAPID technique lies at the crossroads between living donor liver transplantation (LDLT) and

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Associating Liver Partition and Portal vein ligation for Staged hepatectomy (ALPPS), with specific flow modulation criteria that need to be defined. It also provides an incredible opportunity to study hemodynamic variations in a clinically controlled small-for-size (SFS) model.

METHODS

Resection and Partial Liver Transplantation With Delayed Total Hepatectomy

Donors and recipients undergoing RAPID transplantation were included in a prospective single-center approved by our local ethical committee (CEHF 2020/19FEC105). Indications for transplantation were validated by a multidisciplinary transplantation and oncology group. LDLT was not possible in all cases: G23 with GBWR $<0.6\%$ or G5678 with future liver remnant (FLR) lower than 30% on the donor side. Liver anatomy was thoroughly assessed using magnetic resonance imaging and computed tomography (CT). The initial RAPID surgery technique was slightly modified: the "out-of-Cantlie line technique" in cases of central metastases, the use of G234, routine hepaticojejunostomy, and systematic resection of portal convergence.[4,5] We placed a silicone sheet between the graft and the RLR to limit adhesion. The graft was subjected to daily ultrasound and biological monitoring until the second stage of the operation.

Intraoperative flow and pressure were measured in all recipients: basal values after pedicle dissection and post-transplant values before biliary anastomosis was completed; the latter limited access to pedicles. We used flowmetry probes with calibrated diameters of 4 to 20 mm (Medistim). Pressure was measured by direct puncture using a 14 g needle. The hepatic-to-portal vein gradient (HPVG) was calculated by subtracting the central vein pressure from the PV pressure. Flow rates were related to the mass of the liver, defining an indexed hepatic artery ((iQ_{HA}) and portal vein (iQ_{PV}) flow. We implemented graft inflow modulation (GIM) by ligating the splenic artery if the iQPV flow exceeded 200 mL/min/100 g.[8]

The estimated graft volume was calculated using donor magnetic resonance imaging (Vitrea, Vital Images). We subtracted 10% from this volume to define the estimated GBWR.[9] The left graft was weighed after harvesting to determine the GBWR. Volumetric growth was calculated using CT volumetry on postoperative days (PODs) 7 and 14. The daily volume increment defines the early kinetic growth rate (eKGR) volume (cm^3/d), and the relative gain, eKGR% (%/d).

^{99m}Tc labeled mebrofenin hepatobiliary scintigraphy (HBS) with SPECT was performed on POD7 and POD14. The mebrofenin uptake of the graft and the remnant right liver was related to the body surface area of the recipients.[10]

Living Donor Liver Transplantation

Data on conventional left LDLT recipients were extracted from a prospectively maintained database. In our cohort, we selected 13 left liver recipients. Six out of 13 patients had cirrhosis associated with portal hypertension (grade III or IV varices and/or splenomegaly). Patients who experienced arterial thrombosis or a biliary complication within the 15 days after the transplantation were excluded to minimize the potential impact of a complication on graft growth rate. One patient developed SFS syndrome. Supplemental Table 1 (Supplemental Digital Content Table 1 http://links.lww.com/SLA/F239) details the pre and post-operative clinical data of these patients. Graft volumetric growth was calculated for patients with available CT within 15 days of transplantation. Hemodynamic values were determined 30 minutes after arterialization.

Statistical Analyses

Continuous variables are presented as medians and interquartile ranges. The nonparametric method was chosen because of the low number and unpredictable distribution of patients. Graphical representations were obtained using GraphPad Prism version 10.

RESULTS

Clinical Results

RAPID recipients and donor data are shown in Table 1. The median GBWR was 0.42% (0.38–0.45). Blood tests and ascites are presented in Supplemental Figures 1–3 (Supplemental Digital Content Fig. 1, http://links.lww.com/SLA/F240, Supplemental Digital Content Fig. 2, http://links.lww.com/SLA/F241, and Supplemental Digital Content Fig. 3, http://links.lww.com/SLA/F242). None of the patients presented with SFS syndrome.[11] The median durations of the RAPID first step, donor retrieval, and second step were 662 minutes (643–759), 400 minutes (362–478), and 133 minutes (115–147). Intraoperative blood loss was 575 mL (425–825) in step 1 and 110 mL (65–146) in step 2. The recipient's length of hospitalization was 26.5 days (25.7–27.2). The median time interval between the two steps was 16 days (13.7–16.2).

The postoperative course of the recipients was unremarkable in 3 out of 8 patients. Patient 2 presented with graft PV thrombosis, which was conservatively treated with anticoagulation therapy. He did not present with postoperative ascites or signs of liver dysfunction. We carried out the right hepatectomy after the restoration of portal flow, 1 week later than planned. A bleed at the foot of Roux-en-Y on POD11 in patient 3 required early revision surgery combined with RLR removal. Patient 4 presented with bleeding from the right hepatic artery stump a day after the second stage. This required a reoperation for hemostasis. Patient 5 developed a collection between transection planes, requiring advanced second-stage surgery. Exploration confirmed the biliary leak in the RLR. He developed empyema, and percutaneous drainage was complicated by intercostal arterial injury, massive hemothorax, and death. The mortality at 90 days was, therefore, 12.5%. The median follow-up for the 7 living recipients was 648 days (60–1394) without associated morbidity (Eastern Cooperative Oncology Group performance status scale: 0–1). The donors' early and late courses were unremarkable (Clavien-Dindo I).

Hemodynamics

The hemodynamic findings of RAPID are presented in Table 2. The baseline iQ_{PV} was 65 mL/min/100 g (59–68). Graft iQ_{PV} was 141 mL/min/100 g (133–148) after right PV ligation and was significantly higher than baseline measurements ($P = 0.004$). There was no variation between the native liver and the graft iQ_{HA} (Fig. 1). The baseline HVPG was 5 mm Hg (3.7–5.2), which increased to 10 mm Hg (9.2–12.2; $P = 0.007$) at the end of step 1. There was a slight but statistically non-significant increase in the RLR iQ_{HA} after PV ligation. We compared these data with those obtained from conventional left LDLT (Fig. 2). The graft

TABLE 1. RAPID Donors and Recipients Demographics, Intra and Postoperative Results

			Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Clinical details	Donor	Sex/age (yr)	48/female	42/male	51/female	23/female	50/male	35/female	47/male	19/male
		Weight (kg)	67	90.5	58	70	85	60	69	71
		BMI (kg/m^2)	28	25.3	23.6	24.2	27.5	22.1	22	20.7
		PV anatomy	Type 2	Type 1	Type 1	Type 1	Type 3	Type 1	Type 1	Type 1
		HA anatomy	Modal	Modal	Modal	Modal	Modal	Modal	Modal	Modal
		Bile duct	Modal	Modal	Modal	Early SII/SIII bifurcation	Modal	Modal	Modal	Modal
		Length of stay (d)	14	8	10	8	8	11	7	7
		Complications	None	None	Intraoperative BD injury	None	None	Hyperalgesia	None	None
		Clavien-Dindo	I	I	II*	0	0	I	0	0
	Donor/recipient relationship		Sister/sister	Brother/brother	Wife/husband	Daughter/father	Brother/brother	Daughter/mother	Brother/brother	Son/father
	Recipient	Sex/age (yr)	55/female	46/male	61/male	50/male	57/male	65/female	51/male	49/male
		Weight (kg)	57	81	78	78	98.5	59	62	77
		BMI (kg/m^2)	21.4	23.7	26.4	21.8	33	22.9	21	23
		Disease	CRMets	NETMets	CRMets	CRMets	NETMets	CRMets	CRMets	CRMets
		PV anatomy	Type 1	Type 1	Type 1	Type 1	Type 3	Type 1	Type 1	Type 1
		HA anatomy	Modal	Modal	Right HA from SMA	Left HA from CT	Modal	Modal	Modal	Modal
		Bile duct	Modal	Modal	Modal	Modal	Trifurcation	Modal	Modal	Modal
		Length of stay (d)	12+6	18+8	28	10+10	25	10+8	8+10	16+13
		Complications	None	PV thrombosis	Roux-en-Y bleeding	Right HA stump bleeding	Hemothorax	None	None	Intraluminal bleeding
		Clavien-Dindo	I	II	IIIb	IIIb	V	II	I	II
Operative data	Donor	Type of surgery	G234	G234	G234	G234	G234	G234	G23	G234
		MHV harvesting	Yes	Yes	No	Yes	Yes	No	No	Yes
		Operating time (min)	310	320	642	364	395	470	453	502
		Blood loss (mL)	160	250	600	500	400	400	600	400
		Intraoperative peak lactate (mmol/L)	2.4	1.7	2.3	1.9	1.6	1.8	1	2.5
		Intraoperative urine output (mL/kg/h)	> 0.5	> 0.5	> 0.5	> 0.5	> 0.5	> 0.5	> 0.5	> 0.5
		ICU stay (h)	24	24	24	24	24	48	24	24
	Recipient first step	Type of surgery	H123458	H1234	H1234	H1234	H1234	H1234	H1234	H123
		Operating time: liver resection (min)	390	404	286	342	666	425	175	487
		Operating time: graft implantation (min)	230	300	316	328	154	222	206	364
		Blood loss (mL)	450	500	650	800	900	350	255	1100
		Hepatic vein reconstruction	CT on CT	CT on CT	Left HV on CT	CT on CT	CT on CT	Left HV on CT	Left HV on CT	CT on CT

TABLE 1. (*continued*)

			Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
		PV reconstruction	Left PV on common PV	Left PV on common PV	Left PV on common PV	Left PV on common PV	Left PV on common PV	Left PV on common PV	Left PV on common PV	Left PV on common PV
		HA reconstruction	Left HA on left HA	Left HA on Left HA	Left HA on common HA	Left HA on left HA	Left HA on left HA	Left HA on left HA	Left HA on left HA	Left HA on GDA stump
		Biliary reconstruction	Roux-en Y, 1 biliary duct	Roux-en Y, 1 biliary duct	Roux-en Y, 1 biliary duct	Roux-en Y, 2 biliary ducts	Roux-en Y, 1 biliary duct	Roux-en Y, 1 biliary duct	Roux-en Y, 1 biliary duct	Roux-en Y, 1 biliary duct
		Cold ischemia time (min)	159	63	65	31	146	40	35	30
		Warm ischemia time (min)	38	35	43	46	57	46	40	43
		Intraoperative peak lactate (mmol/L)	5.8	4.8	3.1	3.3	5.8	1.6	3.2	9.4
		Intraoperative urine output (mL/kg/h)	1.02	1.59	2.23	1.23	0.57	2.04	1.27	2.15
		ICU stay (h)	36	36	48	24	48	48	24	72
		Transfusion	No	No	No	No	No	No	No	Yes
	Time interval between two steps (d)		17	23	11	14	13	16	16	16
	Recipient second step	Type of surgery	Lap H67	Open H5678	Open H5678	Open H5678	Open H5678	Open H5678	Open H5678	Open H45678
		Operating time (min)	177	191	134	137	88	101	120	133
		Blood loss (mL)	100	120	940	145	150	50	40	70
		Intraoperative peak lactate (mmol/L)	1	1.5	1.9	1.5	1.9	0.8	1.4	1.3
		Intraoperative urine output (mL/kg/h)	1.19	1.55	2.24	0.45	6.08	2.57	0.66	1.45
		ICU stay (h)	24	24	48	48	216	24	24	120
Volumetric Data		Graft weight (g)	236	365	370	271	261	275	320	333
		Initial GRWR (%)	0.41	0.42	0.45	0.32	0.26	0.46	0.45	0.43
		Initial graft volume (mL)	287.1	401.5	405	321	287.1	302.5	352	366
		Estimated Graft volume (mL)	290	403	450.1	297	255	359	301	356
		Donor estimated FLR in case of right LDLT (%)	21	22	33.9	22.8	16	26	35	28.8

BD indicates bile duct; BMI, body mass index; CRMets, colorectal metastases; GDA, gastroduodenal artery; HA, hepatic artery; ICU, intensive care unit; MHV, median hepatic vein; NETMets, neuroendocrine metastases; SMA, superior mesenteric artery.

TABLE 2. Hemodynamic Assessment of RAPID Recipients

	Case 1	Case 2*	Case 3	Case 4	Case 5*	Case 6	Case 7	Case 8
Native recipient values (Step 1: before transsection)								
Troncular PV flow (mL/min)	1100	500	1750	1100	970	846	900	1200
Left PV flow (mL/min)	210	120	450	175	160	110	195	450
Proper HA flow (ml/min)	215	350	275	210	230	390	250	550
Left HA flow (mL/min)	105	98	150	100	120	146	95	160
PV pressure (mm Hg)	8	10	7	8	10	6	7	18
Central venous pressure (mm Hg)	3	4	2	4	6	4	4	3
Hepatic venous portal gradient (mm Hg)	5	6	5	4	4	2	3	15
Native recipient total liver weight (left + right)	1160+510	262.8 +705.5	630 +949	472+1316	430+1508	370 +950	600 +736	549+1160
Total (g)	1670	968	1579	1788	1938	1320	1336	1709
Indexed total liver PV flow (mL/min/100 g)	66	52	111	62	50	64	67	70
Indexed total liver HA flow (mL/min/100 g)	13	36	29	12	12	30	19	32
Graft and remnant values (Step 1: end of implantation)	Case 1†	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8†
Graft HA flow (mL/min)	64 (35)	100	69	60	110	130	160	100 (48)
Indexed graft HA flow (mL/min/100 g)	33 (27)	25	19	22	42	40	50	30 (14)
Right remnant HA flow (mL/min)	230	400	135	310	440	400	570	480
Right remnant weight (g)	510	706	949	1317	1508	950	736	1160
Indexed remnant HA flow (mL/min/100 g)	45	57	14	24	29	42	77	41
Graft weight (g)	236	365	370	271	261	275	320	333
GBWR (%)	0.41	0.42	0.52	0.32	0.26	0.46	0.45	0.43
Graft PV flow (mL/min)	475 (495)	480	450	450	370	420	450	380 (750)
Indexed graft PV flow (mL/min/100 g)	201 (210)	131.0	121.6	150.0	141.7	152.7	141	114 (222)
PV pressure (mm Hg)	20 (28)	12	16	15	23	23	13	16 (27)
Central venous pressure (mm Hg)	5	3	4	5	7	10	6	6
Hepatic venous portal gradient (mm Hg)	15 (23)	9	10	10	16	13	7	10 (22)
Flow modulation	Yes	No	No	No	No	No	No	Yes

*Patients who received preoperative long-term treatment with synthetic somatostatin analogs for neuroendocrine liver metastases.
†Patients who underwent GIM; values in brackets represent measurements taken before GIM. The native liver parenchyma in these cases showed grade II sinusoidal obstruction syndrome associated with nodular regenerative hyperplasia.

iQ_{PV} was significantly higher in RAPID than in LDLT (86 mL/min/100 g (72–140). However, the iQ_{HA} did not differ between the two groups.

Volumetric Results: Early Kinetic Growth Rate

Sequential analysis of RAPID graft volume showed that early growth was greater between POD0 and POD7 than between POD7 and POD14: 74% (53.7–91) versus 23% (13.2–33.7). Compared with patients with left LDLT, those with RAPID had a significantly lower GBWR (Fig. 2). Median eKGR gain was 27.5 mL/d for RAPID and 36.4 mL/d for left LDLT. No difference was found between the two groups for eKGR%: RAPID 6.7%/d (5.6–7.9) and left LDLT 8.5%/d (4.1–13). Subject to 2 cohorts of low volume, the RAPID technique does not appear to be associated with accelerated graft growth. No correlation was found between iQ_{PV}, HPVG, initial GBWR, and volumetric growth of the graft in both RAPID and LDLT patients.

Functional Assessment

The HBS findings are illustrated in Figure 3 and are compared with the GBWR increment. Initial function was not evaluated, except in patients 7 and 8. Therefore, the change in function was calculated for the graft and RLR between POD7 and POD14. graft function increase was 15% (9–94). Patient 2 presented with graft PV thrombosis with a drop in function, and step 2 was subsequently postponed. Liver function was evaluated after step 2 in patient 3; the latter was brought forward because of reoperation for bleeding. We found very high variability in the HBS results, but no lower limit was set for step 2.

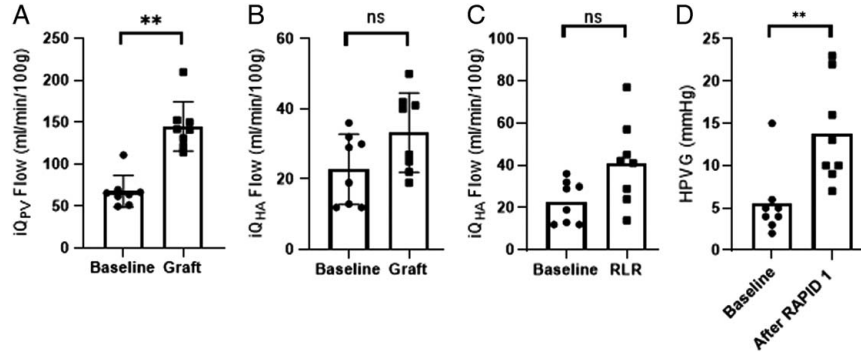

FIGURE 1. Indexed hemodynamics variations between baseline and after graft implantation regarding iQ_{PV} (A), iQ_{HA} for graft (B), iQ_{HA} for RLR (C), and HVPG (D).

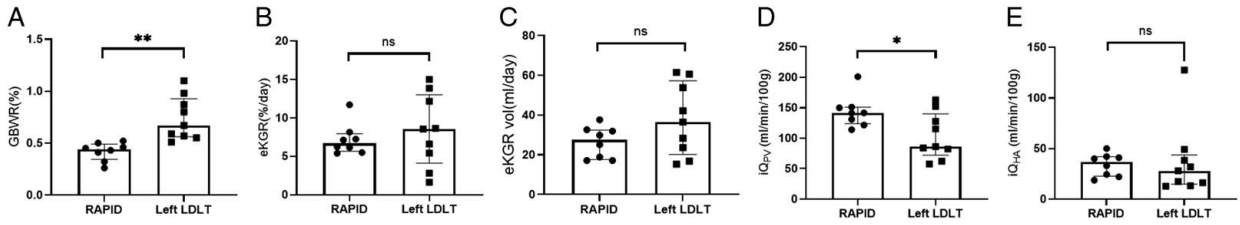

FIGURE 2. Volumetric and hemodynamic variation between RAPID and left LDLT recipients. Data for GBWR (A), eKGR in %/d (B), and mL/d (c). Graft iQ_{PV} (D), iQ_{HA} (E).

DISCUSSION

Clinical Results

Interestingly, despite the very low GBWR, no patient presented with SFS syndrome. The cytolytic disturbance (aspartate aminotransferase/alanine aminotransferase) was marked after step 1 with stability in the liver function test (bilirubin/International Normalized Ratio). The journey through our first 8 cases allowed us to confront certain clinical and technical difficulties. Metastases on the Cantlie line led us to first obtain H123458 or H123 in the recipient. The small volume of the RLR in extended left native hepatectomy allowed us to remove the RLR by laparoscopy, which was not feasible afterward in other cases. The large volume of the RLR makes dissection and laparoscopic extraction difficult despite prior preparation (loops on the residual pedicles and silicon sheet). We encountered a bile leak in the section plane of the RLR. Ex situ right

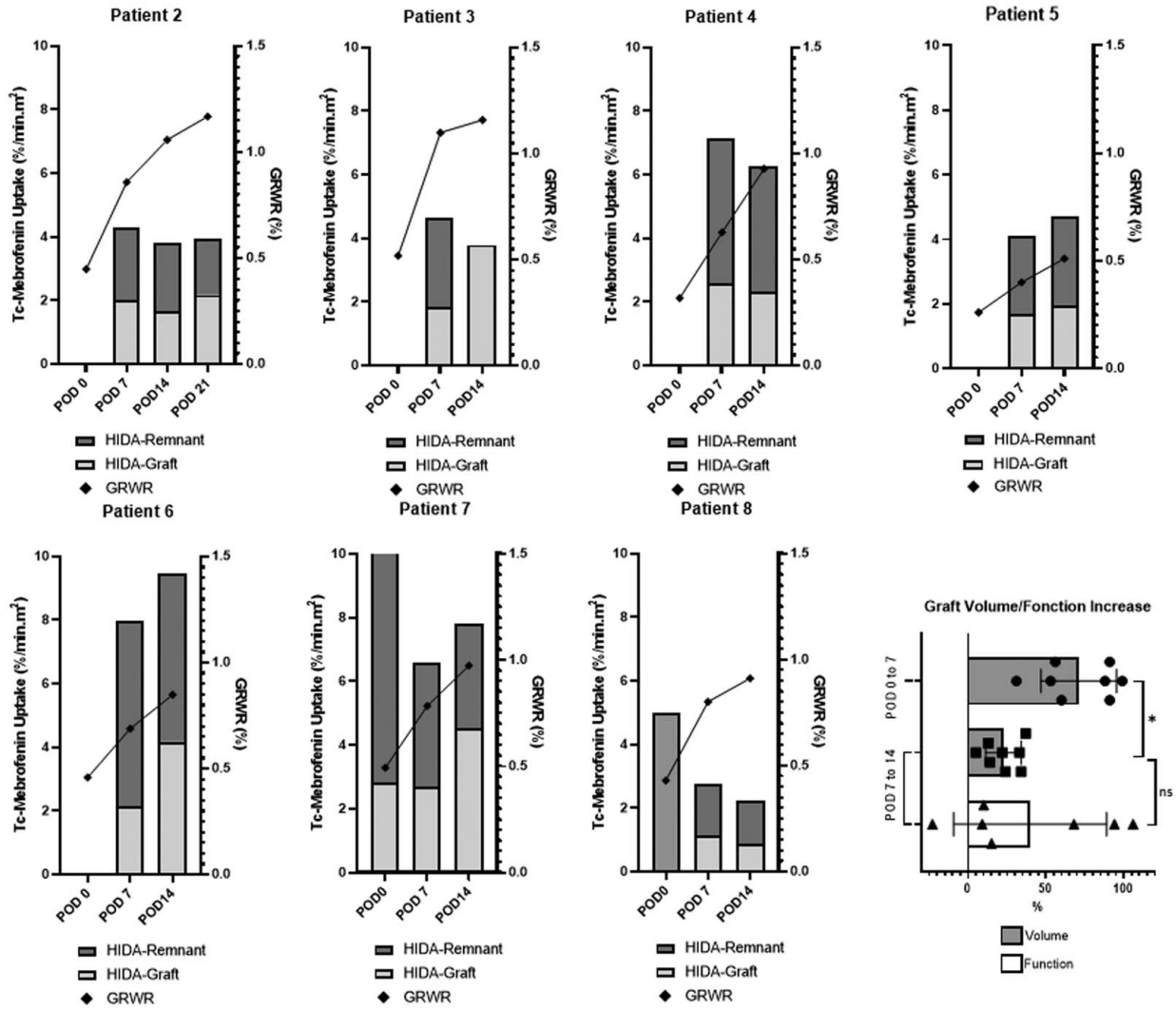

FIGURE 3. ^{99m}Tc labeled mebrofenin HBS findings. Parallel projection of the evolution of GBWR between POD0 and POD14. Patients 7 and 8 had a preoperative HBS. Second HBS was performed after stage 2 in patient 3. HIDA indicates hepatoiminodiacetic acid.

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cholangiography confirmed a leak from disconnected b8b5. This underlines the importance of preoperative biliary workup in recipients. Biliary drainage remains the Achilles heel of LDLT. We systematically performed a Roux-en-Y loop in our recipients to separate the graft structures from the right arteriobiliary pedicle. No patient developed bile leak in the early posttransplant course and no late anastomotic stenosis was observed.

Hemodynamics and Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy

The RAPID surgical model is conceptually identical to that of ALPPS, a deportalized right liver associated with right-left parenchymal separation. Techniques expose small-volume grafts or FLR to full portomesenteric flow. Portal hyperflow triggers regeneration.[12] If this increase in flow is too large, shear stress will be detrimental to this regeneration.[11,13] This phenomenon is critical in LDLT and, above certain iQPVs or HVPGs, leads to GIM.[8,14] However, the need for GIM in ALPPS is much less defined or even absent, as highlighted by the hemodynamic analysis in this procedure.[15] The increase in iQPV is also responsible for the decrease in arterial flow due to arterioportal buffering.[16]

The most clinically significant difference with ALPPS is the presence of an arterial anastomosis in RAPID. It is this anastomosis that conditions the potential need for portal modulation in RAPID, unlike in ALPPS, even though the portal hyper flow appears comparable. In other words, if we were able to create an arterial anastomosis with very low resistivity, mismatch, and roughness, then portal modulation would not be necessary for RAPID under noncirrhotic conditions. Both models exhibit arterioportal buffering, which in ALPPS does not lead to complications, but in RAPID, combined with the thrombotic risk of anastomosis, it may result in arterial occlusion. Ligation of the splenic artery should be, therefore, based more on a decrease in arterial flow rather than on intraoperative portal vein (iQPV) flow values.

Despite this complete reorientation of the portal flows towards a very small volume graft (GBWR < 0.5), we were not confronted with portal hyperflow; initial values of the recipients' native portal flow were low. Several hypotheses can explain this: on the one hand, the absence of cirrhosis in all RAPID recipients, and on the other hand, the treatment with synthetic somatostatin analogs in 2 patients with neuroendocrine metastases, and finally, a possible stabilization of the flow passing through a left PV of limited diameter. The histologic analysis of the nontumoral liver of the 6 patients with colorectal metastases shows no particularities except in the 2 patients where GIM is applied; there, a grade II sinusoidal obstruction syndrome associated with nodular regenerative hyperplasia is found.

Graft Growth Kinetics

Our findings suggest, with the caveat of small cohort size, that liver regeneration is not accelerated in RAPID compared with conventional left LDLT. These results are in line with those from the study by Croome et al,[17] who compared ALPPS, PV embolization, and LDLT, respectively, 32.7 cm^3/d, 4.4 cm^3/d, and 60.4 cm^3/d. Second, liver volume growth occurred during the first week after the RAPID transplantation. We successfully removed RLR 10 days after step 1, whereas baseline GBWR was 0.51%. As described in the ALPPS, hypertrophy decelerates after POD7.[18] This opens the way to a very short interstage, limiting inflammation and adhesion during the second stage. Third, this growth does not seem to be influenced by the baseline graft mass or iQ_{PV}, which differs from the data published in ALPPS[15,17] or LDLT.[19] We also did not find a relationship between HPVG and eKGR, as described in the hemodynamic exploration of the ALPPS. The range of iQ_{PV} was higher in RAPID than in ALPPS, which could be explained by an asymptotization of the regeneration rate and the disappearance of this portal flow/eKGR correlation above a certain threshold.

Liver Function

We assessed the graft volume before the second stage of RAPID with the aim of achieving LDLT safety values (GBWR $> 1\%$).[20] HBS is more predictive of actual liver function and allows comparative segmental mapping.[21,22] A minimum functional limit of 2.69%/min/m^2 has been set for major liver resections[10] and 2.7%/min/m^2 for ALPPS.[23] There are currently no data concerning variations in the HBS results of the graft or the RLR in the RAPID technique. These data must be interpreted with caution given the small number of patients and high variability of results, but a number of findings seem to be emerging.

We first suspected a drop in total liver function, as described in the ALPPS.[24] Five out of 7 patients had a liver function at POD7 below the norm of 7.5%/min/m^2.[22,25] As in ALPPS, this drop seems to be linked to the decrease in RLR function after deportalization, which is not compensated by the gain in graft function. However, in RAPID, we compared the function of the native left liver and that of the graft, which is different from the ALPPS data comparing the evolution of the same FLR.

Second, functions of the graft and RLR appeared stable between POD7 and POD14, with the exception of patients 6 and 7 (+94 and +68%). These 2 patients had the best clinical outcomes and shortest hospital stay (Supplemental Digital Content Table 2, http://links.lww.com/SLA/F239). The positive functional increment of the graft is, therefore, predictive of better clinical results; however, the opposite does not seem to expose patients to nonresolving SFS.

Finally, we were unable to define a graft function threshold to validate the second stage of the RAPID. Five out of 7 patients had graft function results of < 2.69%/min/m^2 the day before stage 2. The absence of postoperative liver failure in our series, therefore, suggests a lower HBS cutoff than that of ALPPS.

CONCLUSIONS

This study highlights the acceptable clinical results of the RAPID surgical technique despite the initial graft volumes being well below those recommended for conventional LDLT. RAPID solves the problem of the left graft being too small for the recipient and the right graft being too risky for the donor. The RAPID concept makes it possible to offer living donor transplantation to more donor-recipient pairs while increasing the safety of the donor (standardized left hepatectomy) and recipient (functional backup of the RLR).

The initial hypothesis of accelerated surgical liver regeneration could not be confirmed in our small series. The growth rate of grafts in RAPID corresponds to that observed in left LDLT. However, this technique allows for a

considerable decrease in the GBWR. RAPID fits well with the development of transplantation oncology without exacerbating the problem of a shortage of cadaveric organs.[26] The model also offers the opportunity to explore liver regeneration in controlled SFS grafts.

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DISCUSSANT

Hugo Pinto Marques (Lisbon, Portugal)

Thank you very much for the opportunity to discuss this paper. RAPID is a promising technique with a very interesting rationale but it has failed to be widely applied, eventually caused by the surgical expertise it requires. However, as the authors point out, encouraging results have been reported recently. The authors compared the kinetics of the graft volume increment by comparing it to that observed in patients receiving a partial graft alone. The study focuses on an innovative procedure that has the potential, with proper refinements, to increase the donor pool in selected situations. You presented one of the largest single institutional series of RAPID in the setting of a noncirrhotic liver and provided important insights into the hemodynamics of RAPID regeneration.

I have the following questions: First, this study was not able to confirm that RAPID is connected to accelerated regeneration compared with left liver LDLT. Considering that the immediate preoperative results appear to be worse compared with conventional LDLT, what do you think are the advantages of RAPID in this setting?

Second, the RAPID technique has a brilliant concept, but still faces some difficulties in its implementation, eventually due to the high technical expertise it requires. Who, in your opinion, are the best donors and patients for this approach?

Finally, what is the future of RAPID and how do you foresee its widespread implementation and in which centers?

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Response From Laurent Coubeau (Brussels, Belgium)

With regard to your first question, the main advantage of the RAPID technique is that it eliminates the volumetric constraints of the graft from the living donor equation. Our past experience and the stagnation of LDLT in Europe confirm this: we were hindered by volumetric issues – the left graft was too small for our recipient, and the right lobe graft was too risky for the donor. This is the key aspect of the technique: transplantation becomes feasible from one adult to another regardless of volumetric considerations. In addition, we have observed that RAPID is not just a means of minimizing the donor's risk; it also enhances the safety of the procedure for the recipient. We encountered a case of PV thrombosis in the graft, a dramatic complication in classic LDLT. The presence of a functional right lobe allowed us to manage the thrombosis conservatively by delaying the second stage by a week. Therefore, there is no risk transfer from the donor to the recipient, but rather an increased safety for both.

RAPID transplantation indeed represents a technical and logistical challenge. It requires a versatile surgical team proficient in both HBP and transplantation surgery. Our center already had extensive and regular experience with pediatric LD. Hence, we were already adept at handling the donor aspect.

Assessing your second point, the selection of donors follows the same standards as LDLT, with an age limit of 55 years, beyond which regenerative properties are more hypothetical. However, the anatomic selection of our donors is easier: as discussed, volumetric considerations are absent. Biliary anatomy becomes secondary: we harvest full-left lobe grafts, but a biliary anomaly, such as a right anterior sectoral branch originating from the left, can direct us toward a left lobar graft (G23). The technique offers incredible flexibility.

Finally, concerning the future of RAPID, we have now performed 11 RAPID surgeries, and the 10th one was performed with a donation after circulatory death (DCD) left lobe divided under "hypothermic oxygenated perfusion" machine perfusion. RAPID allowed us to evaluate the function of a small split DCD graft because we had the right remnant as a backup. We would never have considered reviving a split DCD program without RAPID. The future is here: this new auxiliary graft technique allows us to safely consider transplantation from partial livers with extended criteria (DCD, age, etc).

Antonio D. Pinna (Weston, United States)

I want to congratulate you. This is a great study, with very robust data. Looking for the smallest possible graft, do you think it will be possible for those small grafts to work on an adult-heavy recipient? Is it because you left a piece of the right lobe on the recipient, which acts as resistance compliance and a buffer for the artery, or do you think it is a matter to decide after portal pressure measurement on the recipient before going for a RAPID transplant?

Response From Laurent Coubeau (Brussels, Belgium)

We successfully performed a transplant with a GBWR of 0.2, which was effective without the occurrence of SFS syndrome. Initially, we were concerned that managing portal overflow with such a small graft would be challenging. However, in noncirrhotic conditions, we observed a plateau effect. The left PV is very narrow, and portal hyperflow alone does not seem to cause SFS. Thus, there appears to be no limit! Our perspective changed after encountering arterial issues in some cases. Unlike ALPPS, where hepatic artery flow is less critical, RAPID requires careful attention to the artery due to the anastomosis and the persistent risk of thrombosis. Consequently, our main objective for portal modulation is to address the artery. Regarding the extreme limit for graft volume, we are still uncertain. Some patients end up with only 1 or 2 segments after iterative hepatic surgeries. Therefore, a mono-segment graft is theoretically possible but requires correct portal flow modulation to avoid arterial thrombosis and possibly a longer interval between operative stages.

Dieter Broering (Riyadh, Saudi Arabia)

Congratulations on an outstanding presentation and for contributing such vital data to the literature. Although I acknowledge the complexity of the RAPID procedure and concur that it should be considered a last resort, there are 3 alternative approaches that warrant discussion. First, the possibility of dual transplantation using grafts from living donors. Second, a hybrid approach involving a left lateral deceased donor graft combined with a small graft from a living donor. Finally, the potential for a living donor-paired exchange. Could you please share your perspectives on these 3 alternatives?

Response From Laurent Coubeau (Brussels, Belgium)

I believe it is important to emphasize that the oncological indications for RAPID are still under discussion. In our preliminary experience, disease-free survival using the RAPID technique for colorectal metastases seems to be worse than with full liver transplantation. In such a controversial indication, it is crucial to consider the ethical aspect of LDs. There is an ethical dilemma in using the right liver donations for colorectal metastasis when there is uncertainty about providing long-term remission. Opting for 2 donors is even more controversial. Dual-living donor transplantation is parallelly more complex than RAPID. However, there are patients for whom living donor transplantation is not an option. For instance, a 65-year-old patient whose only potential donors are their children. The donation from a child to their parent is often perceived as counterintuitive and is frequently refused by many. I believe RAPID, especially without using LDs, but rather with machine perfusion and DCD grafts, is a viable perspective.

Mickaël Lesurtel (Clichy, France)

First, I would like to come back to the PV modulation. I was a little bit confused. At some point during your presentation, you said that you had to do some PV modulation, and at the end, you stated that there were no problems with that. Could you please clarify?

Second, in France, you know that we are going to start a RAPID program for HCC patients, should we anticipate any big issue with portal flow modulation?

Response From Laurent Coubeau (Brussels, Belgium)

With regard to your first question, we based our preliminary experience with RAPID on that of LDLT. There was no available data on flow management in this model. Therefore, we initially adopted the 200 mL/min/100 g portal flow cut-off described by the Troisi team. In our

first case, the flow was 205 mL, so we modulated PV flow by ligating the splenic artery, but I am not certain this was necessary.

Subsequently, we did not consistently reach this cutoff, regardless of the small size of the graft. These data fit within the context of the described "plateau" of portal flow. However, we observed in successive cases that some grafts exhibited a decrease in arterial flow despite a portal flow below 200 mL/min/100 g. The presence of arterial anastomosis, which is more prone to thrombosis and absent in ALPPS, led us to modulate the flow even when it was below the cutoff. Therefore, there is no specific flow or pressure threshold for portal flow modulation; it is the case-by-case analysis of the arterial curve and direct flow measurement that drives the decision-making process. A meticulous analysis of intraoperative Doppler arterial data will be crucial for the implementation of RAPID in cirrhotic conditions.