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Preliminary Experience with RAPID Auxiliary Liver Transplantation Using a Partial Graft Retrieved After Circulatory Death and Split Under Hypothermic Oxygenated Machine Perfusion.

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Background

Recent advances in transplant oncology and the identification of new indications, such as unresectable colorectal liver metastases (uCRLM), have driven the search for alternatives to standard cadaveric grafts. Initially hampered by the risk of ischaemic cholangiopathy (ITBL) associated with the unavoidable warm ischaemia period, donation after circulatory death (DCD) grafts are increasingly revisited. Machine perfusion has significantly changed this risk paradigm. Hypothermic oxygenated perfusion (HOPE) have been shown to reduce ITBL incidence and to improve DCD-graft survival[1].

However, partial DCD-grafts pose additional challenges. The split procedure is ex-situ by definition; prolonging cold ischemia time (CIT) and thereby increasing biliary risk. Muiesan et al. reported preliminary experience, demonstrating acceptable graft function and biliary outcomes[2]. More recent pilot experiences with HOPE during ex-situ bipartition suggest that it mitigates the prolonged ischaemic insult[3].

Living donor liver transplantation (LDLT) offers another alternative to DCD-grafts. LDLT elective scheduling is a major advantage in oncological setting, permitting precise coordination of neoadjuvant therapies and obviating waiting-list delays/dropout risks. In adult-to-adult LDLT, graft volume remains the principal constraint: left-lobe grafts may be insufficient to sustain recipient function, while right-lobe donation risks leaving the donor with inadequate residual liver volume.

The RAPID technique (Resection and Partial liver segment II-III transplantation with Delayed total hepatectomy) combines the principles of orthotopic auxiliary transplantation with ALPPS (Associating Liver Partition and Portal vein ligation for Staged hepatectomy) approach. Left graft growth is stimulated by portal hyperflow following right portal vein (PV) ligation. Fifteen days later, the deportalized native right liver is removed (Figure 1A). This approach effectively overcomes the volumetric limitations of adult-to-adult LDLT, minimizes donor risk, and secures recipient outcomes.

Patients and Methods

In 2020, we initiated a prospective protocol, approved by our ethics committee, to evaluate the RAPID procedure in patients with uCRLM/unresectable neuroendocrine liver metastases. Clinical outcomes, along with haemodynamic and functional assessments, have recently been published[4]. However, some candidates remain without an eligible living donor. Following an ethics-board amendment, we began listing patients for RAPID using split cadaveric grafts. We report, to our knowledge, the first RAPID transplantation employing a DCD-graft split under HOPE.

A 29-year-old donor with locked-in syndrome was referred for organ donation. Hepatic morphology and laboratory parameters were unremarkable (SGOT 16 U/L, SGPT 15 U/L, GGT 8 U/L, totat bilirubine 0.2 mg/dl). In the absence of brain death, DCD-retrieval was performed after family consent under super-fast retrieval technique (1st warm ischemia time = 12 minutes).

A 48-year-old woman was listed for a RAPID transplant because of uCRLM, indication being repeatedly discussed by a dedicated oncology board. No suitable living donor was identified. After thorough discussion of the risks, she provided informed consent to proceed with a DCD-derived graft.

The right-lobe graft was allocated to a 60-year-old patient with nodular regenerative hyperplasia under antiretroviral treatment, evolved to portal hypertension treated with TIPSS and complicated by grade IV encephalopathy.

Results

Organ procurement was conducted using standard technique with an IGL-based aortic flush. The first warm ischaemia interval lasted 12 minutes. Liver was retrieved selectively and connected to a HOPE device (VitaSmart®, BridgetoLife, UK). Ex-situ bipartition was performed under continuous HOPE without dividing PV, allowing synchronous perfusion of both grafts throughout the split. Parenchymal transection was carried out immediately to the right of the falciform ligament, with ultrasonic dissector (CUSA®) and clips, and initiated via an anterior approach; yielding 2 implantable grafts (G23 and G145678) (Figure 1B). Segment 4 portal branches were ligated along the round ligament. The infra-hepatic vena cava and main PV were preserved for implantation of the right-lobe graft. Arterial anatomy revealed a late bifurcation with separate S2 and S3 branches. The proper hepatic artery was sectioned proximally to left branches emergence. Right hepatic artery was extended with a donor splenic artery graft.

Native left hepatectomy was performed according to previously reported technique: extended to S1 and the middle hepatic vein (H1234 + MHV), terminating posteriorly at IVC right margin. Right PV remained patent even during venous outflow reconstruction and was ligated afterwards, concomitantly to portal bifurcation resection. The procedure was carried out synchronously with graft bipartition and right-lobe recipient total hepatectomy. Table 1 summarizes technical data, intraoperative timings and perioperative clinical outcomes. Completion hepatectomy (H5678) was performed on postoperative day (POD) 11.

For both recipients, no biliary anomaly was identified and one-year outcomes were satisfactory, without rejection nor liver fibrosis. RAPID-patient remains in oncological remission 15 months after transplantation.

Discussion

More than 20 years ago, principle of auxiliary transplantation as a way to secure high-risk LDLT procedures was described. The right liver played the role of functional backup in case of graft failure, and full ligation of the native right pedicle mirrors the RAPID-model. Our preliminary clinical exploration follows this same logic of evaluating marginal grafts under safety: DCD partial grafts.

Pulitano described a technique for ex-situ liver splitting under normothermic perfusion, including 7 DCD-grafts[5]. Viability was satisfactory after 24H of perfusion. The risk of implantation was not specifically evaluated. The RAPID principle offers this exploratory perspective under the protection of a functional right hepatic reserve.

We favoured full-left grafts in most RAPID-procedures performed in our centre[4]. Nevertheless, ex-situ split scenario in DCD-context requires a fast and standardised procedure, already emphasised by Muiesan[2] and more compatible with G23 retrieval.

Compared to our experience with RAPID from living donors, the cadaveric context allows the use of arterial and venous vascular grafts, enabling adaptation to particular anatomical circumstances.

We have recently investigated the arterio-portal hemodynamics in the RAPID model using left lobe grafts retrieved from living donors[4]. Our experience shows that, in an initially normotensive setting (i.e., in non-cirrhotic patients), the massive portal flow tends to plateau, with no adverse impact on graft regeneration.

The key point of vigilance remains the intraoperative assessment of arterial flow, which can be attenuated due to both the arterio-portal buffering effect and potential technical irregularities at the anastomotic site. As a result, the need for portal inflow modulation should be determined based on arterial flow measurements, rather than exceeding a predefined threshold of relative portal flow.

This approach has enabled us to safely proceed with grafts having a GRWR as low as 0.2%. Notably, we did not observe any significant hemodynamic differences when using this DCD graft compared to our series of RAPID procedures with living donors—despite the theoretically increased hemodynamic resistance associated with warm and cold ischaemia in the DCD setting.

However, logistical issues remain a major challenge limiting implementation of such projects. Performing 3 complex surgical procedures simultaneously requires 3 seniors surgeons, along with strengthened anaesthesia and specialised nursing teams.

Conclusion

We report here the first RAPID-procedure using a G23 DCD-graft, bipartition being performed under HOPE. Recipient suffered from uCRLM and is good health, without recurrence, more than one year after the procedure. These preliminary satisfactory results highlight the potential of the RAPID-approach. This confirms the path opened few months ago for establishing a global and standardized policy for referencing partial left-lobe grafts. HOPE implementation, improving graft preservation and function, and auxiliary technique offering a functional right-sided backup in case of left-graft failure, support the use DCD partial graft in adults. In a context where DCD-grafts are increasingly available, this successful first clinical experience opens the way offering safe transplantation for patients with controversial oncological indications, without depleting cadaveric transplant waiting list.

Tables and Figures

Table 1. Technical perioperative data, timing and post-operative outcome.

	Right-lobe recipient	Left-lobe RAPID recipient
Patient weight	72kg	79kg
Graft weight	1450g (G145678)	461g (G23)
GRWR at LT	2.01%	0.58%
Post-operative graft volume	2293ml (POD7)	665ml (POD7) 782ml (POD10) 1362ml (POD80)
HOPE-perfusion	4H15	4H15
Splitting procedure	2H55	2H55
CIT	7H32	8H22
WIT	40min	35min
Native H1234	///	62min
Operative time	9H20	7H59
Graft implantation Outflow reconstruction Portal vein reconstruction Arterial reconstruction Biliary reconstruction	 Side-to-side cavo-cavostomy End-to-end PV anastomosis End-to-end: graft extended splenic artery conduit - recipient right hepatic artery stump Choledo-choledocostomy	 Graft left hepatic vein – recipient common trunk Jump graft between graft left PV and recipient main PV End-to-end: graft coeliac trunk – recipient common hepatic artery Hepatico-jejunostomy
Postoperative course	Uneventful	Silicone sheet infection, right hepatectomy completion POD11
LOS	21 days	34 days

Legend: CIT: cold ischemia time; GRWR: graft-to-recipient-body-weight-ratio; HOPE: hypothermic oxygenated perfusion; LOS: length of stay; LT: liver transplantation; POD: post-operative day; PV: portal vein; WIT: warm ischemia time.

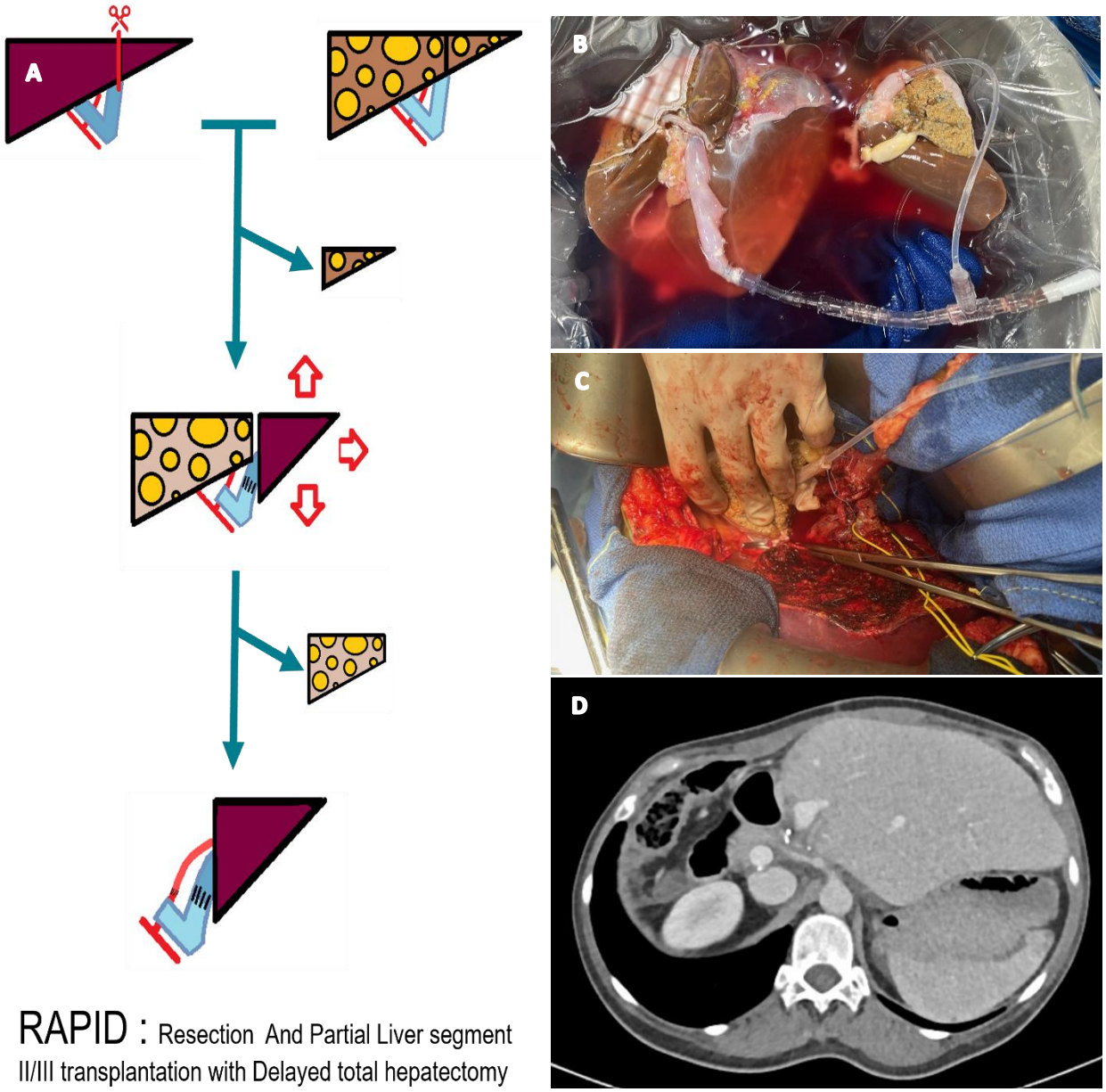

Figure 1. Scheme illustrating the RAPID procedure (A). G145678 and G23 after bipartition under HOPE (B). Peri-operative view after H1234 and start G23 implantation (C). CT-scanner of left-lobe recipient after 80 days (D).

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