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Future Liver Remnant Augmentation Preceding Robotic Hepatectomy

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1. Abstract

1.1. Background: Incorporation of liver augmentation techniques prior to major hepatectomy allows opportunity for surgery in disease formerly considered unresectable. Additionally, as robotic surgery continues to gain momentum, studies have demonstrated outcome superiority with robotic major hepatectomies. We present our experience on the available spectrum of liver augmentation options prior to robotic major hepatectomy.

1.2. Methods: An algorithm of liver augmentation options for regeneration is employed for all patients undergoing robotic major hepatectomies with insufficient future liver remnant [FLR]. Each technique is examined in detail, outlining their unique indications, kinetic growth rates, and pitfalls.

1.3. Results: Currently, 85 patients have undergone liver augmentation prior to major hepatectomy. Of these, nine patients have undergone augmentation prior to robotic major hepatectomy, consisting of two-stage hepatectomy [n=2], portal vein embolization [n=2], liver venous deprivation [n=1], Associating Liver Partition and Portal vein ligation for Staged hepatectomy [ALPPS] [n=3], and transarterial radioembolization [n=1].

1.4. Conclusion: The progressive development of liver augmentation options facilitates a wider treatment spectrum, allowing patients with extensive tumor burden and inadequate FLR to become operative candidates. Our experience demonstrates the range of techniques along with their benefits and disadvantages, available to facilitate operative candidacy.

2. Introduction

The role of hepatectomy for malignant and benign hepatic disease is well-described and uncontested [1]. Often offering the only possibility for cure, surgeons have become adept in mastery of these operations. In the early 1990s, advancement collided with minimally invasive technique and laparoscopy for minor hepatic resections was described, issuing it to the forefront of hepatobiliary surgery [2]. Over the next two decades, laparoscopy became indisputably superior to open surgery for minor resections, demonstrating improved perioperative complications without the sacrifice of oncological outcomes [3-5]. A steeper adoption of laparoscopy for major hepatectomies attempted to slowly follow but met impediments driven by the primarily technical complexities [6-9]. In 2006, robotic hepatectomy was introduced and offered a means to overcome the limitations of laparoscopy [10]. Among its inherent advantages of three-dimensional vision, tremor suppression, instrument articulation, and improved precision, studies also demonstrated fewer postoperative complications in complex hepatic resections [11-15]. The application of robotics for major hepatectomies however has been slower than expected, remaining relatively innovative despite these published reports of success. Over the last five years, however, there has been some improvement in its progressive adoption demonstrated [16].

For all surgeons, regardless of technique, sitting hand in hand with major hepatectomy is the fear of an insufficient Future Liver Remnant (FLR). An estimated low FLR can preclude resection by leading to post-hepatectomy liver failure [17]. In an effort to avoid operative exclusion, strategies for augmentation were developed beginning with Portal Vein Embolization (PVE) in the 1980s [18]. Shortly thereafter, two-stage hepatectomy was described as an adjunct to improve rates of resectability in a case of bilateral

Colorectal Liver Metastases (CLM) [19]. The strategy began as a sequential treatment plan of a first-stage hemi-liver clearance, followed by FLR hypertrophy, often using PVE, and then a second-stage resection intended to remove all remaining disease [20]. PVE [or ligation] alone as an alternative means can also be used, although it bears a low Kinetic Growth Rate (KGR) of the FLR at <2% per week. Accordingly, the interval between the primary intervention and resection tends to be prolonged which may lead to tumor progression, reported in up to 20% of cases and of particular concern in bilobar CLM [21]. With a near quadrupling of KGR, ALPPS [Associating Liver Partition and Portal vein ligation for Staged hepatectomy] developed serendipitously by Hans Schlitt in Germany, induces rapid hepatic hypertrophy through parenchymal transection [22]. With now over 2,000 ALPPS procedures performed globally, the international ALPPs registry demonstrates feasibility with improved safety parameters, resulting in an unparalleled degree of expedited liver regeneration [23,24].

Another remodeling strategy that has gained recent popularity is Liver Venous Deprivation (LVD), consisting of radiological simultaneous embolization of both the portal vein and hepatic vein [25]. Studies have found LVD to induce faster regeneration than PVE alone, nearing similar KGRs seen after ALPPS [26,27]. A final, incidental option for hepatic augmentation is Transarterial Radioembolization (TARE). TARE can be utilized to perform radiation lobectomies which unintentionally elicit slow kinetic growth over six months while treating disease [28].

3. Methods

In 2008, the hepatobiliary group at Carolinas Medical Center (CMC), North Carolina, introduced robotic major hepatectomies into their practice, with now over 120 robotic major hepatectomies being performed. Over time, the full armamentarium of liver remolding strategies was incorporated into the robotic approach to limit resection exclusions due to inadequate FLR. The group defined inadequate FLR is defined as <25% of normal liver parenchyma, <35% of parenchyma receiving chemotherapy for ≥ three months, and <50% of cirrhotic parenchyma. All patients meeting criteria for major hepatectomy with an inadequate FLR followed an advancing algorithm for regeneration: 1 (PVE, 2) LVD, 3) ALPPS, 4) TARE. Within the last several years, the algorithm shifted to exclude PVE: 1) LVD, 2) ALPPS, 3) TARE.

4. Results

Currently, 85 patients have undergone liver augmentation prior to major hepatectomy with the following distribution: PVE (n=51), LVD (n=13), ALPPS (n=18), and TARE (n=3). Of these, nine patients have undergone augmentation prior to robotic major hepatectomy: TSH (n=2), PVE (n=2), LVD (n=1), ALPPS (n=3), and TARE (n=1). All PVE and LVD procedures were performed by the interventional radiology department and follow-up cross-sectional imaging was obtained consistently at six weeks post PVE, two weeks post LVD, and the day prior to ALPPS.

5. Discussion

The first described approach of FLR augmentation preceding robotic hepatectomy is the robotic two-stage hepatectomy. In comparison to other approaches, this is low in complexity and permits simultaneous ablation of small tumors. Difficulty is minimal and ensues from postoperative adhesions. This is exemplified in case 1; a 53-year-old male diagnosed with colorectal cancer and bi-lobar liver metastases (Table 1). As the dominant hepatic lesion was near the right main pedicle, a liver-first approach was elected. The patient underwent a robotic right hemi-hepatectomy with simultaneous ablation of a segment 4 malignant lesion. After three months, the patient underwent colonic resection of the primary tumor with excision of a segment 3 lesion to fully clear all known disease.

The second option that can be employed is PVE with robotic hepatectomy. PVE frequently targets the right-side of the liver to allow for a right trisectionectomy with adequate FLR. The challenge from this approach is found in the robotic hilar dissection due to acute reactive inflammation and potential desmoplastic reactions after embolization. Further, hilar lymphadenopathy is a frequent witnessed phenomenon.

ALPPS offers another option for molding prior to robotic hepatectomy, facilitating a more rapid and dramatic hepatic regeneration compared with the alternatives [29]. Robotic-assisted ALPPS, for both stages, was first described in Brazil in 2020 and CMC followed with the first robotic ALPPS involving transection of 50% parenchyma (Case 3) [30]. Similar to PVE, a challenge in ALPPS is found in the difficulty of the hilar dissection.

The current algorithm followed at CMC begins with LVD for augmentation as the first option prior to robotic hepatectomy. While a multidisciplinary approach is required for all interventions, it is paramount in LVD for hepatobiliary and interventional radiology teams to plan collectively. The team must determine which hepatic vein might be targeted, whether the middle hepatic vein needs embolization, and timing of neoadjuvant chemotherapy suspension. Additionally, coils cannot be placed in the middle hepatic vein within three cm of the takeover else it can cause misfiring of the stapler; interventional radiology can also elect to avoid embolization of the middle hepatic vein altogether.

TARE is a relatively new procedure that was first introduced in 2005 as a means to target and destroy Hepatocellular Carcinoma (HCC) [31]. While its intent in augmentation is purely incidental, its advantage is in the concomitant provision of radiotherapy to tumor metastases while promoting FLR growth, albeit at a very slow kinetic rate [32]. This facilitates subsequent surgical hepatectomy, although challenged by a difficult liver mobilization.

6. Conclusion

The progressive development of liver augmentation options facilitates a wider treatment spectrum, allowing patients with extensive tumor burden and inadequate FLR to become operative candidates. Our experience has demonstrated the considerable variability in liver molding techniques, ranging from two-stage hepatectomy to ALPPS. Using standardized liver volume calculations to estimate FLR prior to and after augmentation, our cases demonstrate the wide range of kinetic growth rates between techniques (Table 1). The advancement of these techniques coupled with a robotic approach to minimize physiologic burden, creates real opportunity and innovation for historically unresectable tumors.

Table 1: Augmentation techniques and kinetic growth results prior to robotic major hepatectomy procedures

Age, Gender	Diagnosis	Remolding	Robotic procedure	Standardized liver volume (cc)	Pre-FLR (cc, % of total liver volume)	Post-FLR (cc, % of total liver volume)	Time (weeks)	Kinetic growth/week
51M	MCRC	TSH	Right hemi-hepatectomy & left lateral sectionectomy	1855	631, 34%	853, 46%	11.4	1.10%
52M	MCRC	PVE	Right trisectionectomy	1938	504, 26%	659, 34%	8	1.00%
70M	MCRC	ALPPS	Right trisectionectomy	1570	346, 22%	550, 35%	1	13.00%
53F	MCRC	LVD	Right trisectionectomy	1354	420, 31%	636, 47%	2	8.00%
62F	IHC	TARE	Right trisectionectomy	1819	509, 28%	873, 48%	20.6	1.00%

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8. Declaration of Interest

There are no conflicts of interest or financial ties to disclose.

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