

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2021 July 27; 13(7): 620-733



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Editorial Board Member of *World Journal of Gastrointestinal Surgery*, Kun-Ming Chan, MD, Professor, Department of General Surgery and Chang Gung Transplantation Institute, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Taoyun 33305, Taiwan. chankunming@cgmh.org.tw

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INDEXING/ABSTRACTING

The *WJGS* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, and PubMed Central. The 2021 edition of Journal Citation Reports® cites the 2020 impact factor (IF) for *WJGS* as 2.582; IF without journal self cites: 2.564; 5-year IF: 3.378; Journal Citation Indicator: 0.53; Ranking: 97 among 212 journals in surgery; Quartile category: Q2; Ranking: 73 among 92 journals in gastroenterology and hepatology; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Jia-Hui Li*; Production Department Director: *Xiang Li*; Editorial Office Director: *Ya-Juan Ma*.

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Shu-You Peng, Varut Lohsirivat, Jin Gu

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

PUBLICATION DATE

July 27, 2021

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

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<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Robotic donor hepatectomy: Are we there yet?

Ashwin Rammohan, Mohamed Rela

ORCID number: Ashwin Rammohan 0000-0001-9528-8892; Mohamed Rela 0000-0003-4282-4676.

Author contributions: Rammohan A and Rela M contributed to conception and design, acquisition, analysis and interpretation of data, drafted the article, revised it critically for important intellectual content; Rela M gave the final approval of the version to be published.

Conflict-of-interest statement: The authors declare no conflicts of interest.

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Manuscript source: Invited manuscript

Specialty type: Transplantation

Country/Territory of origin: India

Ashwin Rammohan, Mohamed Rela, Institute of Liver Disease & Transplantation, Dr. Rela Institute & Medical Centre, Bharath Institute of Higher Education & Research, Chennai 600044, India

Corresponding author: Ashwin Rammohan, FACS, FRCS, MCh, Surgeon, Institute of Liver Disease & Transplantation, Dr. Rela Institute & Medical Centre, Bharath Institute of Higher Education & Research, CLC Works Road Chromepet, Chennai 600044, India. ashwinrammohan@gmail.com

Abstract

In living donor liver transplantation (LDLT) the safety of the live donor (LD) is of paramount importance. Despite all efforts, the morbidity rates approach 25%-40% with conventional open donor hepatectomy (DH) operations. However, most of these complications are related to the operative wound and despite increased self-esteem and satisfaction in various quality of life analyses on LD, the most common grievance is that of the scar. Performing safe and precise DH through a conventional laparoscopic approach is a formidable task with a precipitous learning curve for the whole team. Due to the ramifications the donor operation carries for the donor, the recipient, the transplant team and for the LDLT program in general, the development and acceptance of minimally invasive DH (MIDH) has been slow. The robotic surgical system overcomes the reduced visualization, restricted range of motion and physiological tremor associated with laparoscopic surgery and allows for a comparatively easier transition from technical feasibility to reproducibility. However, many questions especially with regards to standardization of surgical technique, comparison of outcomes, understanding of the learning curve, *etc.* remain unanswered. The aim of this review is to provide insights into the evolution of MIDH and highlight the current status of robotic DH, appreciating the existing challenges and its future role.

Key Words: Liver transplantation; Donor hepatectomy; Minimal invasive surgery; Robotic surgery; Outcomes

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Core Tip: While pioneering attempts are necessary in surgery to allow the development of expertise, the use of technologies in progressively sophisticated procedures must be carefully monitored and gradually implemented to ensure patient safety. The robotic

Peer-review report's scientific quality classification

Grade A (Excellent): 0
 Grade B (Very good): B, B
 Grade C (Good): 0
 Grade D (Fair): 0
 Grade E (Poor): 0

Received: February 8, 2021**Peer-review started:** February 8, 2021**First decision:** March 30, 2021**Revised:** April 9, 2021**Accepted:** June 16, 2021**Article in press:** June 16, 2021**Published online:** July 27, 2021**P-Reviewer:** Ferrarese A**S-Editor:** Zhang H**L-Editor:** Filipodia**P-Editor:** Wang LL

surgical system overcomes reduced visualization, restricted range of motion and physiological tremor associated with conventional laparoscopic surgery. However, robotic donor hepatectomy needs to be evaluated carefully in experienced hands and a cautious approach is crucial, as even one untoward event in the donor surgery may significantly set back progress.

Citation: Rammohan A, Rela M. Robotic donor hepatectomy: Are we there yet? *World J Gastrointest Surg* 2021; 13(7): 668-677**URL:** <https://www.wjgnet.com/1948-9366/full/v13/i7/668.htm>**DOI:** <https://dx.doi.org/10.4240/wjgs.v13.i7.668>

INTRODUCTION

Surgical innovations help facilitate the continuous refinement of the art of surgery. One such remarkable advancement has been the advent of minimally invasive surgery (MIS). It has dramatically improved outcomes with regards to pain, morbidity and recovery. The undeniable benefits of MIS have led to its acceptance across various surgical specialties, making it an integral component of a surgeon's armamentarium[1-4]. As expected, even in the field of hepatobiliary surgery, the benefits of minimally invasive hepatectomy (MIH) have been unequivocally demonstrated by meta-analyses, consensus guidelines and recommendations, and the procedure is becoming a standard practice[5,6].

In living donor liver transplantation (LDLT), the safety of the live donor is of paramount importance. Despite all efforts, the morbidity rates approach 25%-40% with conventional open donor hepatectomy (ODH) operations[7-10]. However, most of these complications are related to the operative wound (hernia, obstruction, wound infection, chronic pain, *etc.*) and despite increased self-esteem and satisfaction in various quality of life analyses on live donor (LD), the most common grievance is that of the scar[6-10]. Considering the advantages of MIH, it is but intuitive to try and transfer these benefits to the LD operation. Apart from its other purported benefits, adaptation of MIH to the donor hepatectomy (DH) operations extends beyond the realms of the operation itself. Improved patient satisfaction helps reduce the barriers to donation, thereby improving donation rates in general. To this end, minimally invasive DH (MIDH) using conventional laparoscopy was introduced. Nonetheless, performing a safe and precise DH operation through a conventional laparoscopic approach remains a formidable task with a precipitous learning curve for the whole team[5,6,11]. Due to the ramifications the donor operation carries for the donor, the recipient, the transplant team and for the LDLT program in general, the development and acceptance of MIDH has been slow.

The robotic platform along with its purported advantages has helped overcome many of the disadvantages inherent to conventional laparoscopic surgery[12-16]. These systems are now gaining traction and are replacing the conventional laparoscopic operation. However, many questions especially with regards to standardization of surgical technique, comparison of outcomes, understanding of the learning curve, *etc.*, remain unanswered[6,11-14]. The aim of this review is to provide insights into the evolution of MIDH and highlight the current status of robotic DH (RDH), appreciating the existing challenges and its future role.

EVOLUTION OF MIDH

The concept of minimal invasive donor operation was first introduced in the live donor renal transplantation by Ratner *et al*[17] in 1995. Buoyed by the unequivocal success and safety of the renal donor operation, the team from France (Cherqui and Soubrane) performed the first MIDH as a conventional laparoscopic DH (CLDH) operation in 2002[18]. Notwithstanding the proponents of hybrid (laparoscopy assisted, hand assisted or small incision) techniques, for close to a decade MIDH was limited to paediatric liver transplantation (LT)[10,19,20]. It was in 2012 that a Korean team and almost simultaneously a French team independently performed a purely laparoscopic MIDH for right lobe donation[21,22]. The same year a Belgian team of

surgeons presented their series of purely laparoscopic left lobe MIDH[23]. Despite the initial successes, the operation remained confined to highly specialised centres, and MIDH accounted for less than 2% of all LD operations[12,24-26]. The robotic platform was introduced to aid and flatten the learning curve of MIS. Surgeons from the University of Illinois-Chicago pioneered the robotic LD nephrectomy operation and demonstrated excellent results[21,27,28]. With a proficiency of over 70 robotic hepatectomy for various indications, Giulianotti *et al*[29] from Chicago successfully performed the first right lobe RDH. Several other units, including those from Taiwan and Saudi Arabia have successfully replicated the results and safety of RDH since that first report[6,14-16,21,27,28,30].

EVIDENCE FOR MIDH

To date over 500 MIDH left lateral segment have been performed[6]. Case-control studies comparing it with ODH and 5 meta-analyses observed a significantly reduced intraoperative blood loss, similar or lower donor morbidity and shortened hospital stay in the MIDH (CLDH and RDH) cohort[1,31-34]. A lower blood loss was explained by the magnified view in MIDH which allowed for a better dissection and bleeding control. The presence of pneumoperitoneum, with its higher intraabdominal pressure reduced low pressure venous bleed and allowed for an easier control. While literature has been mixed with regards to superiority of the MIDH, none of the meta-analyses showed MIDH to have higher complication rates. A study from Korea suggested that there could be a higher risk of operative morbidity including traction injuries, hematomas and a higher post-operative liver enzyme levels at the beginning of the learning curve[2,35]. There is no report of a donor mortality with MIDH. One patient had a cardiac arrest during a hybrid procedure[3]. However, this incident was not contributed to by the size of the incision.

Post-operative pain score and morphine requirements were significantly less with MIDH, so were rates of early wound related complications[1,6,31-34]. Interestingly liver-specific morbidity (bile leak, *etc.*) was also not significant between the two groups (ODH *vs* MIDH). Cosmesis, body image and reduced absenteeism from work was significantly better with MIDH. Long term outcomes especially with regards to the incision (keloid, *etc.*) and quality of life analyses have significantly favored the MIDH [1,6,31-34]. However, no major difference was noted between a limited midline incision based hybrid MIDH and a CLDH[6,10,32-34] (Table 1).

An interesting study showed that the complication profile of left lateral segment (LLS) MIDH was comparable to a standard minimal invasive donor nephrectomy, suggesting a decisive shift in mindset towards accepting LLS MIDH as a similarly standard procedure[36]. Most studies looking at recipient outcomes have shown similar overall recipient morbidity and 90 d mortality with both MIDH and ODH[1,6,32-34]. Despite concerns of a longer warm ischemia time related to retrieving the graft in MIDH, comparative studies including those with propensity score matching did not show a higher incidence of primary non-function or differences in liver function tests in the early post-operative period[6,36-38].

When comparing right lobe liver grafts, a series showed a higher incidence of hepatic vein stenosis in the MIDH[2,35,37]. Another large case-control study from Korea with propensity score matched analysis showed a higher incidence of Clavien-Dindo complication 3b-5 in the right lobe MIDH group[6,37]. The mortality and graft failure rates at 1 year were however not different from ODH. These complications were attributed to the use of a vascular stapler in the division of hepatic veins. A recent large case-control study from Korea with propensity matched groups of 198 cases each observed a higher incidence of early and late biliary complication in the right lobe MIDH group as compared to the ODH group (early 10% *vs* 4% and late 39% *vs* 21%, $P < 0.05$)[2,6,35,37]. One reason cited for this was difference was the site of duct division leading to a higher number of ducts in a right lobe graft from MIDH. These points were highlighted in a recent consensus to stress the importance of structured and proctored training in MIDH.

It must however be conceded that anecdotal negative experiences especially during the initial stages of an innovative technology may not get reported. This bias often leads to an overtly optimistic opinion of the novel technique. Another fallacy is with regards to selecting the cases for MIDH. More often the “ideal” donor is chosen to enable a relatively facile operation. Extrapolating data from these experiences may not reflect the real-world scenario. Idiosyncrasies and expertise available in the unit are also likely to influence outcomes and would need to be taken into consideration before

Table 1 Evidence based comparison between open, conventional laparoscopic and robotic donor hepatectomy

	ODH	CLDH	RDH
Pre-operative aspects			
Selection	Favourable anatomy during the learning curve	Favourable anatomy & body habitus during the learning curve[6,11,39,40,42]	Favourable anatomy during the learning curve[13-15,29,44]
Intra-operative aspects			
Operative time	Comparable	Comparable[1,31-34]	Comparable[17,18,33,47,48]
Blood loss	Higher	Lower than ODH[1,31-34]	Lower than ODH[1,31-34]
Warm ischemia time	Shorter	Longer[1,31-34]	Longer[1,31-34]
Post-operative aspects			
Pain scores	Higher	Lower[1,6,31-34]	Lower (similar to CLDH) [1, 31-34]
Analgesic use	Higher	Lower[1,6,31-34]	Lower (similar to CLDH) [1,6, 31-34]
Peak AST	Higher	Lower[1,6,31-34]	Lower (similar to CLDH) [17, 18,33,47,48]
Donor morbidity			
Overall donor complication rates	Standard[3,7-9]	Lower[1,6,31-34]	Lower (similar to CLDH)[17, 18,33,47,48]
Biliary complications	Higher	Lower[6,10,32-34]	Lower[17,18,33,48]
Wound complications	Higher	Lower[1,6,31-34]	Lower (similar to CLDH)[17, 18,33,47,48]
Return to work	Later	Earlier[1,6,31-34]	Earlier (similar to CLDH)[17, 18,33,47,48]
Analgesic use	Higher	Lower[1,6,31-34]	Lower (similar to CLDH)[17, 18,33,47,48]
Hospital stay	Longer	Shorter[1,6,31-34]	Shorter (similar to CLDH)[17, 18,33,47,48]
QOL scores	Lower[7-10]	Higher[1,6,31-34]	Higher (similar to CLDH)[17, 18,33,47,48]
Donor mortality	Reported[7-10]	None reported[1,6,31-34]	None reported
Recipient morbidity			
Outcomes (overall Clavien-Dindo 3b-5 complication rates)	Standard	Higher in right lobe CLDH[6,37], higher early and late biliary complications[2,6,35,37], higher incidence of hepatic vein stenosis[2,35,37]	Lower (Similar to ODH)[15, 16,30,44]
Primary-non function	Similar	Similar[6,36-38]	Similar[17,18,33,47,48]
90 d mortality	Similar	Similar[1,6,32-34]	Similar[15,16,30,44]
Surgical expertise			
Learning curve	Gold Standard	Longer[6,11,39,40,42]	Shorter (comparable to ODH) [13-15,29,44]
Surgeon ergonomics & operative ease (vision, ease of suturing etc.)	Gold standard	Poorer[6,11,39,40,42]	Better (comparable to ODH) [13-15,29,44]
Haptic feedback	Present	Present	Absent[17,18,33]
Surgical adjuncts	Available	Available	Limited availability[13-15,29, 44]
Surgical expertise required	Open donor surgery	Open and laparoscopic liver surgery[6,11,39,40,42]	Open liver surgery[33,47,48]
Logistics & infrastructure			
Economics	Standard	Comparable to ODH	Expensive[15,16,30,44]
Availability	Every LDLT unit	Centres with expertise in liver and laparoscopic surgery[6, 11,39,40,42]	Limited to centres with a robotic platform[17,18,33,47]

ODH: Open donor hepatectomy; CLDH: Conventional laparoscopic donor hepatectomy; RDH: Robotic donor hepatectomy; AST: Aspartate transaminase; LDLT: Living donor liver transplantation; QOL: Quality of life.

interpreting the evidence. Ideally large multicenter randomized trial would help even the playing field. However, given the poor permeation of the technique, this may not be realistic or ethical. Instead, establishing an international donor registry might help elucidate the granularity of international experience.

CHALLENGES IN MIDH

The LD operation is unique in that it has the potential to cause serious complications to the donor and the recipient. This caveat has led to a slower acceptance of MIDH. Operative challenges in the MIDH include tackling complex and myriad anatomical variations, transecting highly vascular liver parenchyma to minimize congestion/ischemia, the need for precise transection of the bile duct to avoid biliary issues to both donor and recipient and securing hemostasis in the presence of bleeding. Hence, the level of technical expertise required for a safe CLDH include amalgamating an in-depth knowledge of liver anatomy and liver surgery along with a mastery of advanced laparoscopic surgery. This is a rare combination, restricting the propagation of CLDH beyond a handful of highly specialized units across the globe.

A learning curve is defined as the improvement in performance over time or the change in the ability to complete a task until failure is decreased to a constantly acceptable rate. The learning curve for CLDH is sharp and precipitous. As a part of the learning curve, LLS CLDH requires approximately 20 procedures by an experienced transplant-laparoscopic surgeon, the same increases to between 45 and 60 for right lobe CLDH[39-42]. Moreover, the learning curve is not limited to the surgeon. MIDH imposes immense demands on the transplant program with regards to equipment, trained allied health personnel in both laparoscopic surgery and DH. An institution wide competence is a sine qua non for the successful implementation of MI LDLT program[6,11,39,40,42].

The benefits of MIDH can only be realized when done safely, and it must be remembered that safety is the primary tenet of LDLT. Therefore, the use of MIDH can only be rationalized if outcomes for the transplant pair are equal if not better than the ODH. In this regard it is important to recognize that irrespective of the type of DH, the donor assessment process remains the same. A donor evaluation is aimed at revealing conditions that could increase the risk perioperative complications in the healthy donor. This systematic evaluation excludes an unfit prospective donor at an early stage, while allowing for suitable candidates to proceed towards donation. Every LDLT program is required to have its own well-defined criteria and algorithmic process of selecting the transplant pair; remarkably these protocols published by teams across the globe are very similar.

Donor selection on the other hand varies depending on the expertise available and type of access chosen, more so in the early phases of evolution of a unit's LDLT program. Centers embarking on MIDH have invariably chosen patients with a relatively lax abdominal wall and without previous surgeries to facilitate the laparoscopic view of the abdomen. It is but natural to err on the side of caution and select out donors with a favorable body habitus and anatomy during this learning curve. These are more pertinent when MIDH is performed for a right lobe graft. The unanimously used albeit ill-defined criteria include one with a standard anatomy ideally with a single and longer right hepatic artery, right portal vein and right hepatic duct along with a large future liver remnant (35%-40%). Recipient characteristics also play an important role in selecting the access for DH. A stable and low MELD recipient (LT for hepatocellular carcinoma, *etc.*) is intuitively preferred over one with acute or acute on chronic liver failure. The importance of selecting out the donors during the learning phase of the operation allows for the acquisition of experience and standardization of techniques before more challenging anatomy can be safely handled[2,35,43]. With accruing experience and surgical expertise, most centers expand their selection criteria with no increase in surgical morbidity for MIDH.

ADVANTAGES OF RDH

The primary advantage of robot assisted surgery lies in the fact that it mirrors open surgery rather than conventional laparoscopic surgery, handing the reins back into the hands of the “open surgeon”. The robotic platform also has the added benefits of overcoming restrictions in range of motion, physiological tremor and a limited field of vision. The high resolution amplified 3D image, tremor filtration and additional degrees of freedom of instruments allow for meticulous tissue handling, precise dissection and easier suturing capabilities[13-15,29,44]. All of which are important prerequisites of a safe LD operation. As compared to the CLDH, RDH allows for a suture closure of hepatic duct stump following the donor operation. Obviating the need for clipping, this suture ligation provides an additional few millimeters of duct length on both the donor and graft sides; potentially reducing the probability of multiple bile ducts in the graft and biliary morbidity in the donor[15,16,30]. Integration of image guidance has aided crucial intraoperative steps like bile duct division. Real-time fluoroscopic guidance using indocyanine green enhances precision and safety of bile duct division. Indocyanine green injection after temporary inflow control enhances visualization of ischemic line of demarcation, allowing for a precise dissection to minimize blood loss and ischemic parenchyma in the graft and donor[15,16,30,44].

Surgeons performing RDH claim to recognize an amplified sense of donor safety due to aforementioned dexterity and optics. Teams have also maintained that the recognition of vascular structures during hilar dissection and parenchymal transection is superior to that of CLDH. All of these advantages converge to ensure that the learning curve for RDH is a fraction of the CLDH. A series from Taiwan proposed that the learning curve for RDH was 15 cases, which is just a third of what is required for CLDH[15,16,30]. More importantly, a prior knowledge of laparoscopic surgery was not an absolute prerequisite to initiate a RDH program. This has enormous implications in the dissemination of MIDH across LT units worldwide. Given the niche area of expertise, most established LDLT centers are likely to have surgeons who are only acquainted with basic laparoscopic skills. For these senior surgeons to learn advanced laparoscopic skills would be akin to reinventing the wheel. Robotic surgery appears to circumvent this issue of a steep learning curve and facilitates the laparoscopic approach for surgeons entering the world of MIS at an already mature stage.

Literature comparing RDH with ODH shows comparable blood loss, complication rates and donor recovery times. A series from Taiwan consisting of 13 RDH showed a reduced analgesic requirement and earlier return to work in the RDH group[30]. Series from Saudi Arabia consisting of 150 RDH also showed a significantly lower pain score, blood loss and in-hospital stay than ODH patients[15,16]. There were no differences in recipient’s biliary and vascular complications rates. A recent study by Troisi *et al*[45] comparing CLDH with RDH in 75 MIDH cases showed that both MIDH techniques were equally safe and efficacious in terms of donor outcomes. The RDH procedure however, had a shorter learning curve. Hence, while literature does not demonstrate an inherent superiority of one technique over the other, it must be borne in mind that these studies are from highly specialized units with competence in open, laparoscopic and robotic surgery, leading to an inherent bias. Two international consensus guidelines from 2018 and 2021 have suggested that the true benefits of RDH need further elucidation, however the dramatically shorter learning curve to master the procedure cannot be ignored[5,6].

LIMITATIONS AND FUTURE OF RDH

It is important to realize that CLDH has been performed for many more years than its robotic counterpart and as proposed by the Morioka and Southampton Consensus is standard practice especially for minor hepatectomy. Another aspect is that regardless of its complexity, the consumables in RDH costs an average 2000 USD per procedure more than ODH[15,16,30]. Adding to this the high cost of acquiring a robot makes the broader adoption of RDH more restrictive than CLDH. A series from Taiwan showed an almost three-fold increase in cost (\$13436 *vs* \$5019, $P < 0.001$) between RDH and ODH[30]. This combination of escalated cost and novelty has hindered its widespread application.

Both the robotic system and its instruments are relatively in their infancy. Specific tools dedicated to liver surgery are lacking and at present cannot be compared to those used in ODH. Though seemingly trivial, lack of appropriate instruments can be quite vexing for a novice robotic surgeon. Rigid energy devices used for liver parenchymal

transection are one such example, where RDH needs advancements in technical solutions. The robot itself is cumbersome and takes time to dock and undock at the bedside. In MIDH, this potentially extra time to gain access to the patients during an emergency situation raises concerns of safety. Unlike CLDH, the robotic arms work the instruments, causing a lack of haptic feedback to the surgeon. In inexperienced hands, dissection of fragile tissue and traction on suture material along with use of excessive force while tying knots may be fraught with danger due to this uncontrolled pressure applied by the robotic instruments. There also remains the need for two experienced surgeons. One of them at the bedside to handle the non-robotic energy device like cavitron ultrasonic suction aspirator. In RDH, should there be an intraoperative adverse event, the role of the second surgeon becomes crucial in a rapid conversion to open surgery.

Most of the surgical experience in robotic surgery is with the da Vinci platform (Intuitive Surgical Inc., Milford, CT, United States), leading to a natural polarization of resources and demands by the parent company. Nevertheless, other robotic systems are entering the surgical arena and will help reduce the financial burden and dependence on one platform[46-51]. Experience with regards to RDH is limited to a few centers and are primarily retrospective case control studies or case series from specialized units. Inherent selection bias and center experience limits the generalizability of this data. A prospective international registry for RDH remains a viable alternative to performing large trials[5,6].

CONCLUSION

While pioneering attempts are necessary in surgery to allow the development of new technologies, the use of such technologies in progressively sophisticated procedures must be carefully monitored and gradually implemented to ensure patient safety. Existing reports were derived from centers with tremendous experience in both laparoscopic hepatectomy and DH. The technical complexity associated with these procedures indicates an arduous transition from technical feasibility to reproducibility and disseminated application. The application of MIS to DH is fraught with difficulty due to anatomic variations and need for parenchymal transection. The robotic surgical system overcomes the reduced visualization, restricted range of motion and physiological tremor associated with conventional laparoscopic surgery. However, RDH need to be evaluated carefully in experienced hands and a cautious approach is crucial, as even one untoward event in donor surgery may significantly set back progress.

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