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Global dissemination of minimally invasive living donor hepatectomy: What are the barriers?

Kakos CD *et al*. Minimally invasive donor hepatectomy

Abstract

Minimally invasive donor hepatectomy (MIDH) is a relatively novel procedure which can potentially increase donor safety and contribute to faster rehabilitation of donors. After an initial period in which donor safety was not effectively validated, nowadays MIDH seems to provide improved results, provided that it is conducted by experienced surgeons. Appropriate selection criteria are crucial to achieve better outcomes in terms of complications, blood loss, operative time and hospital stay. Beyond a pure laparoscopic technique, various approaches have been recommended such as hand-assisted, laparoscopic-assisted and robotic donation. The latter has shown equal outcomes compared to open and laparoscopic approaches. A steep learning curve seems to exist in MIDH, mainly due to the fragility of liver parenchyma and the experience needed for adequate control of bleeding. This review investigates the challenges and the opportunities of MIDH and the barriers to its global dissemination. Surgeons need expertise in liver transplantation, hepatobiliary surgery, and minimally invasive techniques to perform the MIDH. Barriers can be categorized into surgeon-related, institutional-related and into accessibility concerns. More robust data and the creation of international registries are needed for further evaluation of the technique and the acceptance from more centers worldwide.

Key Words: Minimally invasive donor hepatectomy; Liver transplantation; Living donation; Laparoscopic donor hepatectomy; Global surgery

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Core Tip: Living donor liver transplantation provides an excellent option for expanding the donor pool. Minimally invasive donor hepatectomy can potentially minimize complications of hepatectomy to the donors and have a better cosmetic effect. This

approach demands expertise and experience in both liver surgery and minimally invasive techniques to maximize its potential.

INTRODUCTION

Living donor liver transplantation (LDLT) represents a valuable choice for end-stage liver disease, especially in regions with a limited donor pool[1]. In children with rapidly progressive liver failure, full pediatric grafts, reduced-size grafts and split grafts from cadaveric donors may not be available in time[2]. Liver grafts from living donors provide comparable or potentially better short-term graft function and long-term survival rates, especially in children, compared to whole and split cadaver liver grafts[3-5]. The occurrence of donor morbidity and mortality is the main obstacle to broad utilization of living liver donors.

Complications from the hepatectomy operation are the main contributing factors to donor morbidity. Significant complications may include biliary (*e.g.*, bile duct injury, leak), infective, or vascular (*i.e.*, bleeding). Other complications, such as bowel obstruction, incisional hernias and prolonged operative stay, can also contribute to donor morbidity[6]. Minimally invasive donor hepatectomy (MIDH) has been proposed to minimize donor complications. Potential advantages of MIDH, inherent to the minimally invasive approach, are better cosmetic results, reduced postoperative pain, faster recovery and earlier return to daily activities[7]. MIDH was first described in France, when cases of adult left lateral sectionectomy (LLS) and subsequent successful pediatric transplantation were reported[8]. The aim of this review is to describe the parameters which affect the efficiency of MIDH, as well as identify barriers to its global dissemination.

INITIAL CONCERNS

In the United States, LDLT reached a peak in 2001 accounting for 10% of the total number of liver transplants (LTs)[9]. However, a marked decrease followed reports of complications reaching up to 40%[6,10], especially for right hepatectomy (RH)[11]. As a

result, in 2019, the year with the most LTs in the United States (8896), only 5.3% of LT recipients received a graft from a living donor[12], with the majority of those being right grafts. This proportion contrasts with that of living kidney donation, which surpasses 30%[13]. In living donor nephrectomy, several meta-analyses and randomized trials have established that a laparoscopic approach is associated with decreased morbidity, less postoperative pain, shorter hospital stay and lower costs[14-16]. Living donor nephrectomy is not considered a particularly technically challenging procedure, as the kidney is removed intact with its associated pedicle and ureter, without the need for parenchymal transection. On the other hand, MIDH requires recovery of partial vascular and biliary pedicles, as well as parenchymal transection[17]. These factors along with anatomical complexity and the size of the liver itself have slowed down its progression[18]. The two main targets of minimal invasive liver procurement in living donors are donor safety and fast rehabilitation. The risk of mortality and morbidity of liver resection in a living donor depends on three parameters: Physiologic status (*e.g.*, comorbidities), proportion of liver mass removed associated with proportional risk of postoperative liver failure, and the amount of intraoperative blood loss and subsequent need for allogeneic transfusion[19]. As a result, to minimize morbidity in living donors, transplant teams must focus on the best surgical technique and leave an adequate liver remnant with the lowest blood loss. It is still unknown whether a minimal invasive technique can achieve these goals[19].

Systematic reviews of laparoscopic liver resections have confirmed growing safety of this approach when performed by experienced surgeons, suggesting that it may offer significantly fewer complications, less blood loss and shorter length of stay compared to an open technique[20,21]. It must be noted, however, that retrieving a liver graft from a living donor is not entirely equivalent to a conventional hepatectomy, since vascular pedicles of the resected part must be preserved[8].

A statement from the 2008 International Laparoscopic Liver Resection Consensus Conference in Louisville was that MIDH is the most controversial part of laparoscopic liver surgery. Donor safety has not been validated yet and the technique is limited only

to a few specialized centers as it is not easily reproducible[22]. In the Second International Consensus Conference on laparoscopic liver resections held in Morioka in 2015, it was argued that MIDH is non-inferior to the standard approach in terms of donor safety, but the procedure was not recommended due to lack of convincing data on postoperative morbidity[23]. After the first positive results of MIDH, an expert consensus was held in Seoul in order to establish clear recommendations for the safe widespread adoption of MIDH[24]. The results demonstrated that MIDH offers superior outcomes compared to an open approach, provided that the procedure is performed in high-volume centers by surgical teams with high experience in both MIDH and laparoscopy. Moreover, data from the United States suggest that donors are more willing to undergo living donation through a laparoscopic than a conventional approach[25].

LAPAROSCOPIC LIVING LLS FOR CHILDREN

Whereas MIDH has evolved into different variations (hand-assisted, laparoscopic-assisted, pure laparoscopic), LLS has been exclusively proposed as pure laparoscopic technique with mobilization and creation of the graft through 4-5 trocars and extraction *via* a remote incision. The left lateral segment is a favorable anatomic entity for pure laparoscopic resection because of its anterior position and limited number of anatomic variations[26]. Following the first achievements in France[8,27], Belgium[28] and South Korea[29], the safety and reproducibility of the procedure were confirmed by Scatton *et al*[30]. The authors noted that after a learning phase, the median hospital stay gradually decreased, median blood loss stabilized around 50 mL, and Clavien-Dindo grade II or higher complications were less frequent. However, it was emphasized that the procedure requires at least two experienced surgeons in order to follow the required learning curve[30]. Soubrane *et al*[27] stated that MIDH yields at least equal short-term outcomes compared to laparoscopic donor nephrectomy. Subsequent studies continued to report less estimated blood loss and shorter length of stay but longer operative time for pure laparoscopic LLS compared to an open approach[31-34].

RH FOR ADULTS

Adult to adult MIDH can be performed with either the right or left hemi liver, with each option having its own advantages and disadvantages. While RH provides the recipient with an adequate volume of transplanted liver parenchyma, it has raised much concern about donor safety with reported postoperative complications rates even up to 40%[6]. The laparoscopic approach was advocated in multiple centers to minimize these complications. MIDH of the right liver is more difficult than the left, due to the extensive mobilization required, as it is deeply seated below the rib cage[35].

Due to inherent difficulties of the procedure, various techniques were recommended which allowed the surgeon not only to avoid a large subcostal incision, but also to keep the familiarity of open dissection and resection. These hybrid techniques such as hand-assisted or laparoscopic-assisted[22], can represent a transitional approach for many centers before moving to pure laparoscopy. The choice of the technique depends on the surgeon's expertise and experience. It is important that if anatomic integrity is in jeopardy, conversion to open is the inevitable solution.

The first report of the hybrid technique in MIDH was from Chicago. The team used the hand-assisted technique and noted that it provides better tactile perception, crucial for the dissection of the hilum[36]. Surgeons from different centers used either midline[25,37-39] or transverse incisions[40], whereas Choi *et al*[41] presented 40 donor hepatectomies with a single port.

Pure laparoscopic right donor hepatectomy is technically more challenging. It was first reported by Soubrane *et al*[19], with the graft being removed from a suprapubic incision without any postoperative complications. After adoption of the technique from several centers worldwide, results have shown non-inferiority in terms of postoperative complications, estimated blood loss and length of stay[42-46].

LEFT HEPATECTOMY FOR ADULTS

There is evidence that left lobe hepatectomies are associated with significantly lower morbidity compared to RH. The lower morbidity is mainly due to fewer biliary and pulmonary complications, potentially due to smaller graft size[47,48]. The left lobe can be a choice when graft-to-weight ratio is > 0.8, or between 0.6 and 0.8, provided that the recipient has a model for end stage liver disease score < 15. The main risk of left lobe donation is the small-for-size syndrome which eventually leads to graft failure in the recipient. Reports from left donor hepatectomy have resulted in positive outcomes[37,49,50], whereas Soubrane *et al*[51] in a multi-national study demonstrated no difference in morbidity between right and left hepatectomy. During left lobe MIDH, the right liver is mobilized and rotated through the midline incision to allow performing hybrid surgery. Marubashi *et al*[49] noted that for a successful operation, it is the right lobe volume which has greater impact rather than abdominal depth.

SELECTION CRITERIA

Careful donor selection is considered of paramount importance for MIDH. Pretransplant evaluation includes a thorough medical assessment. Of particular importance are any cardiovascular, renal, pulmonary or coagulopathic comorbidities, as well as an infectious disease and psychiatric assessment. Several centers exclude patients with arterial hypertension and psychiatric disorders[49]. In addition, standard liver function tests, hepatitis B and C serology, chest and abdominal radiographs are always utilized. A triphasic liver computed tomography (CT) scan, with volumetric calculations and assessment of vasculature is also invariably performed.

Magnetic resonance cholangiopancreatography provides accurate and precise images of the biliary tree and can define the appropriate division point for the hepatic duct, especially in D1 biliary anomaly (right posterior duct draining into the let bile duct) (Table 1). Incorrect identification of biliary anatomy may require intraoperative cholangiography[30], yet it demands expertise, increased cost and more operative time[52]. Indocyanine green fluorescence cholangiography not only captures images but

also enables a bile leak test using methylene blue injected through the cholangiography tube[34].

Regarding liver anatomy, surgeons from different centers have defined specific criteria for a potential liver donor. Kim *et al*[43] accepted only donors who had a single and long right hepatic duct, artery and portal vein. They also excluded grafts that exceeded 650 g. Gautier considered separate drainage of segments 2 and 3 as a setback for MIDH as it can cause difficulties with stapling and lead to intraoperative bleeding[31]. Rotellar *et al*[42] agreed that single hilar elements define the best candidates, but everyone should be considered on case-by-case basis.

Portal vein variations (Table 1) used to be considered a contraindication for MIDH candidates, yet there are reports that showed encouraging results even for these donors[44,45]. After acquiring consistent, reproducible, and standardized techniques through cumulative surgical experience, it will be possible to expand these existing criteria.

CONVERSION

Any incident that might compromise donor safety or graft integrity should lead to conversion to an open approach. Conversion is not by itself a complication, but implies that some unfavorable event occurred during the procedure[51]. Most common causes for conversion to open approach are failure to recognize biliary duct or hepatic hilum anatomy, vessel injury which led to significant bleeding, and poor exposure due to extensive adipose tissue in donors with high body mass index (BMI).

Scatton *et al*[30] reported 4 conversions (6%) from 70 MIDH, of which 66 were LLS and 1 LH. Reasons for conversions were left portal vein branch injury, poor exposure, and uncertainty regarding biliary anatomy. None of the conversions were associated with acute or uncontrolled bleeding or need for transfusion and all converted donors had uneventful recovery. Choi *et al*[41] mentioned a conversion rate of 10% (2/20) in traditional hand-assisted MIDH and 5% (2/40) in single-port hand-assisted MIDH, due to right hepatic vein and adrenal gland injury. In single-port surgeries, instruments

commonly collide in tight abdominal spaces, referred to as "sword fighting" or "chopstick" effect[53]. For liver surgeries through the umbilicus, the instruments are too short to reach the entire liver surface. Soubrane *et al*[51]'s conversion rate was 4.1% with 17 conversions from 412 MIDH, due to portal vein injury, uncertainty regarding identification of important structures and difficult hilum dissection, whereas Rhu *et al*[45] found a 5% rate due to portal vein narrowing and injury, donor steatosis during intraoperative biopsy, and inferior vena cava injury.

COMPLICATIONS

It should be emphasized that a 30-d follow up underestimates morbidity after a liver resection; robust studies for a hepatectomy should cover at least 90 d follow-up after the operation[54]. The Clavien-Dindo classification, although extensively used, tends to consider only the most severe adverse events and does not consider other less severe complications[55] (Table 2). A recently proposed continuous score, the comprehensive complication index, summarizes all of the postoperative complications and represents the most sensitive tool to estimate the real overall morbidity burden of a procedure[56]. The complication rate in MIDH ranges from 0% to 40%[34,57], but in the majority of studies it lies between 10%-26%[39,45,51,58]. Most common complications are wound complications, pleural effusions, biliary leakage or stricture (Table 3). Most reports showed no statistically significant difference in the complication rate between MIDH and an open approach, but this may be attributed to the small sample size of most such studies. Rhu *et al*[45] made an interesting point, that complications were significantly higher during the first quartile of operations, which reflects potential difficulties due to surgeons' inexperience with the approach. Broering *et al*[33] also stated that the complication rate decreased from 26.7% to 9.7% after acquiring the appropriate experience in the initial period. Morbidity rates were equivalent between right and left MIDH[51] and among different portal vein variations[45].

Biliary complications are among the most serious in MIDH. Takahara *et al*[59] mentioned 3 bile leakages, although each stump had been double-clipped with hem-o-

lock clip and looked perfectly secured at the end of the operation; it was hypothesized that the clips dropped off due to ischemic changes postoperatively. Regarding incisional complications, open living donor hepatectomy requires a large, bilateral subcostal incision with major muscular transection, leading to several days of pain and multiple weeks of discomfort[8]. During that incision, sensitive nerve endings (ventral rami of intercostal nerves T8, T9) are divided which might lead to permanent abdominal wall anesthesia[8]. On the contrary, suprapubic incisions are usually well tolerated without gynecological sequelae, and incisional hernias are rare. In addition, they are almost invisible when they are made low enough in the pubic hair area[8]. Attention is needed during suture transfixion in abdominal wall closure, as bladder trauma might occur[17]. Small incisions which are made for the trocars are predisposed to local ischemia and wound infections, yet these complications are much less frequent in MIDH than the conventional approach[60].

There is a theoretical increased risk of gas embolism because of pneumoperitoneum. However, pneumoperitoneum is established by carbon dioxide insufflation, a gas with solubility greater than that of nitrogen[22]. Several experimental studies have established that carbon dioxide absorption into systemic circulation is not associated with hemodynamic instability[22].

The mortality risk of living donor lobectomy is estimated to be at 0.2% worldwide[61], with LLS having lower rates (0.05%-0.1%). It is generally accepted that adult-to-adult donation has greater morbidity - and possibly mortality - than adult-to-child donations, as right lobes are mostly used for adults, thus the tissue volume removed is larger and operative time longer.

It should be noted that the outcomes of surgical interventions in living donors should not be estimated separately from the results of recipients. In kidney transplantation, Troppmann *et al*[62] founded that laparoscopic nephrectomy is associated with delayed graft function and increased acute rejection rate. The causes about this finding were unclear, but a possible factor is the hemodynamic disturbance in kidney vasculature due to the pneumoperitoneum. On the other hand in almost all the studies comparing

laparoscopic and open living donor hepatectomy, the authors did not find any difference between MIDH and conventional approach in terms of vascular, biliary complications, graft survival and overall survival of recipients[31,33,34,42]. MIDH does not add risk to the recipient even in cases of portal vein variations[45]. Hong *et al*[44] were the only team that noted a higher rate of biliary complications to the recipients after MIDH, a finding which was attributed to the longer warm ischemia time and the increased likelihood of multiple bile duct openings.

BLOOD LOSS

A strong initial reluctance in the development of MIDH was the management of hemorrhage under laparoscopy. With technical refinements and growing expertise during the past 3 decades, multiple reports have validated decreased blood loss and lower transfusion rates during laparoscopy[63,64]. Meticulous parenchymal transection and the "cut surface effect" of pneumoperitoneum (*i.e.*, tamponade-like effect on transected surface by increased intra-abdominal pressure) have contributed to minimal blood loss during MIDH[30], as the main source of bleeding is the venous backflow. Some authors suggest to increase transiently the pneumoperitoneum pressure to 14-16 mmHg in order to minimize bleeding[30]. The greatest risk of intraoperative hemorrhage occurs during the parenchymal dissection, which in a laparoscopic approach is done very accurately and under magnification. Division of hepatic vein is also crucial as slipping of the vascular clamp may lead to massive bleeding[65].

Results from comparative studies between MIDH and conventional approach showed decreased[31,33,59,66] or similar[25,39,44,45] estimated blood loss in MIDH. However, authors emphasized that the absence of statistically significant difference was due to insufficient power related to inadequate sample size[25], so there might be an advantage of less blood loss in MIDH than an open approach.

OPERATIVE TIME AND HOSPITAL COST

MIDH tends to last longer, especially during the initial learning period of surgeons[33,44,49,59,67]. It is expected that additional experience in hilar dissection will lead eventually to reduced operative time[49]. Baker *et al*[25] found an association between increased BMI and longer operation time, whereas Rhu *et al*[66] emphasized that after the first 100 cases the operative time shortened. Although material costs were higher in MIDH, they were balanced by lower time-related operation costs, so there was no difference found by Baker *et al*[25]. In another case series, MIDH was a significantly more expensive procedure than the open procedure[39].

PAIN CONTROL AND HOSPITAL STAY

Kurosaki *et al*[37] used decreased supplemental analgesia in MIDH compared to patients who underwent open hepatectomy. Reduced amount or shorter use of analgesics was found also in multiple case-series[33,39,41,43], yet that finding was not consistently demonstrated[49,65].

Postoperative length of stay is greatly influenced by institutional and healthcare system policies. In eastern countries like Japan and South Korea, the policy is to admit donors in the hospital until they are able to return to normal daily function[49]. Additionally, some eastern national healthcare systems do not require patients to be discharged even after they have recovered from the operation[45,65,67]. In western countries there seems to be an enhanced recovery protocol, so in few reports there is no statistically significant decrease in the length of stay between MIDH and open approach[25,57]. However, the majority of centers present shorter length of stay in the MIDH group[33,45,67].

ROBOTIC DONATION

Robotic approach is much less established than laparoscopic, but it is considered safe and feasible in expert hands. The first robotic LDLT was accomplished by Giulianotti *et al*[68] in 2012 from a 53-year-old man to his 61-year-old brother, using the Da Vinci Robotic Surgical System. Compared to pure laparoscopic approach, robotic evolution is

slow and delayed. Potential advantages are the amplified and more stable view and better precision of movements: The Da Vinci surgical system can rotate in all directions with 90° articulation and 7° of freedom, which allows for a broader range of movements compared to the human hand. The latter allows manipulation and suturing in the retro hepatic space, at angles not possible with rigid instruments. On the contrary, the surgeon loses the tactile feedback and is also dependent on a trained bedside assistant who changes the robotic instruments during parenchymal transection[69].

Latest studies have shown that robotic transplantation is feasible and achieves similar short-term outcomes compared to a laparoscopic procedure[69], but with increased perioperative cost, as medical insurance plans usually do not cover it. Another barrier to dissemination of this technique is the need for high center specialization and surgical instruments; only ultrasonic scalpels, hem-o-lock clips and staplers can be used during robotic liver surgery[70].

Two studies that compared robotic with open donor hepatectomy found non-inferiority of the robotic technique in terms of complications and blood loss[70,71]. Up to date, there are no data indicating superiority of a robotic approach compared to open or laparoscopic. Troisi *et al*[72] did not find any favorable outcome to justify the higher cost of robotic approach compared to a laparoscopic one. They also emphasized that a robotic to open conversion takes longer than a laparoscopic to open conversion, so it is crucial to apply all the laparoscopic techniques to control an unexpected bleeding before converting[72]. In any case, the robotic approach is still very limited in geographic spread and requires much more experience than laparoscopy. Forthcoming introduction of new robotic systems which could support haptic feedback or cavitron ultrasonic surgical aspirator devices will contribute to further spread of robotic hepatectomy.

LEARNING CURVE

A major barrier in the global dissemination of MIDH is that it requires significant experience both in liver and laparoscopic surgery. A multinational study on global

dissemination of MIDH revealed that 65.6% of the surgeons had performed > 50 Laparoscopic hepatectomies and 43.8% had performed > 50 open donor hepatectomies before their first MIDH[24]. The steep learning curve is due to the fragility of liver parenchyma and familiarity with the control of challenging bleeding situations[71]. Several reports have emphasized that a minimum of 15-60 procedures depending on the extent of the resection are required before optimal results can be obtained[73]. Scatton *et al*[30] showed that preliminary experience with at least 20 donors is needed before achieving optimal hemostasis and postoperative course. It should be noted, however, that defining a single surgical case cutoff is unrealistic, as experience and outcomes vary amongst different surgical teams.

Rhu *et al*[66] reported no change in operative time from first to second quartile of a surgeon's operations over time, but reported significant decrease from the second to the third quartile and from the third to the fourth. His team was able to reduce the operative time after 50 laparoscopic cases[66]. In order to define the learning curve, Lee *et al*[74] used two variables: Estimated blood loss and operative time; the learning period was defined as the period before reaching a plateau in those two parameters. They showed that the experienced phase started after 15 cases, with significantly less estimated blood loss and operative time than the learning phase.

Broering *et al*[70] argued that robotic major hepatectomy could also have a short learning curve, with a mastering phase reached at 15 procedures. Chen *et al*[71] divided the learning curve of robotic hepatectomy to 3 phases: Initial (1-15), intermediate (15-25) and mature (25-52). A learning effect was demonstrated by shorter operative time and hospital stay after phase 1 and less blood loss after phase 2. The robotic approach with the double console offers a safe form of teaching, as the proctor can guide the surgeon through the dissection and take control if it is necessary[70].

BARRIERS TO GLOBAL DISSEMINATION AND FUTURE DIRECTIONS

MIDH is a promising technique to expand the liver donor pool, while ensuring the safety of both the donor and the recipient. Although evidence for the efficacy and safety

of this technique is increasing, there are several barriers currently limiting a more widespread utilization. These barriers may be categorized as those related to the transplant program institution, barriers related to the individual surgeon considering the technique, and finally accessibility concerns (Table 4). MIDH may eventually become more globally widespread, however, the technique is best utilized only at specialized LT centers around the world.

LDLT represents a highly validated choice of liver grafts; yet every effort must be made in order not to expose donors to potential risks. Any increase in morbidity would be a huge price for the sake of possibly reduced postoperative pain or hospital stay[75]. Donors are otherwise healthy people who altruistically and electively decide to donate a part of their liver, so every effort should focus on rendering their postoperative course complication-free. Every effort should be made to advocate not only for the physical, but also the psychological well-being of living liver donors. In order to recruit more living liver donors to fulfill the continuously increasing demand for liver grafts, it is necessary to optimize the postoperative course for donors[76].

So far, the benefits of MIDH are limited to retrospective or case-control studies; current literature lacks strong evidence, mainly due to ethical concerns which prevent the conduct of a randomized-control trial between MIDH and open approach[77]. Since the first report of MIDH[8], the procedure is limited to few centers worldwide. The creation of an international registry, especially, in eastern countries where the technique is more widespread, should be undertaken for further assessment of the approach.

Although preliminary reports tend to support the benefits of MIDH, future challenges must include standardization of the technique to achieve a certain degree of reproducibility among new surgeons. A multinational study from 10 LT centers from both eastern and western countries over a 10-year period showed that donor safety is not compromised under MIDH, with low transfusion and conversion rates[24]. The study revealed that right MIDH is most prevalent in South Korea, and LLS in Europe and Middle East[24]. Teams in the eastern hemisphere are not as conservative in the use of grafts with anatomical variations as they are in the West, maybe due to scarcity of

deceased donors in the Est[24]. Further studies and more robust data on short-term and long-term outcomes are needed to evaluate donor selection, learning curve, donor' quality of life and global dissemination of the technique.

CONCLUSION

Living transplant donation constitutes a promising opportunity for increasing the liver donor pool. However, LDLT has been limited in utilization. Minimally invasive approaches may offer an opportunity to increase grafts from living donors. MIDH offers to donors the advantages of minimally invasive techniques, while there is increasing evidence that it is a safe and effective approach for both the donor and the recipient at the hands of experienced surgeons. Several barriers at the institutional and individual-surgeon level limit the more widespread dissemination of MIDH to more specialized liver centers globally. International collaborative efforts can promote progress in the field of MIDH.

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