Liver resection and transplantation using a novel 3D hepatectomy simulation system

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Abstract

In liver surgery, accurate assessments of liver resection volume and anatomical variation are mandatory for preoperative planning of safe curative hepatectomy. In living donor liver transplantation (LDLT), estimation of hepatic venous drainage is important to avoid liver graft and donor residual liver congestion. This paper reviews the articles on simulation-guided liver surgery and describes our novel 3D hepatectomy simulation system for liver resection and transplantation. Our 3D simulation system, based on the hepatic circulation, provided accurate volumetric and stereotactic information for preoperative planning of curative hepatectomy. In addition, our simulation program was applicable to the hepatic venous system to predict liver congestion in LDLT. Future studies include assessment of the impact of the simulation technologies on surgical education, and their exact cost-effectiveness must be also assessed objectively.

Key words: simulation, 3D CT, hepatectomy, living donor liver transplantation, liver congestion.

Introduction

Surgery demands a significant amount of cognitive analysis and integration of enormous patient data. Surgeons have always been confronted by a difficulty in understanding three-dimensional (3D) image from two-dimensional (2D) information obtained by preoperative radiological investigation. The possibility to overcome limitation of the cognitive ability was sought with the advent of high-performance computer technology. Marsh et al. [1] reported an initial experience of 3D computer simulation in the field of craniofacial surgery. Computer-aided simulation was applied for treatment planning of radiotherapy [2], neurosurgery [3], and orthopedic surgery [4] in tern.

Particularly in the field of hepatic surgery, imagination of the 3D image from the 2D computer tomography (CT) or magnetic resonance (MR) images is difficult because of the anatomical complexity and hepatic vascular variability. Intraoperative ultrasonography (IOUS) has been used to determine tumor location and to serve as a guide for hepatectomy [5]. However, there was still a difficulty in reconstructing a 3D image of the tumor and adjacent blood vessels only by the 2D information of IOUS. Despite the availability of 3D ultrasound probes for abdominal sonography, ultrasound as a means of 3D reconstruction has not proven successful because of optical distortions and low contrast behavior of the visualized lesions. The reproducibility of detected images also depends on the skill of the examiner. In contrast, innovations in CT and MR technology over the last two decades considerably improved resolution and scanning time.

In 1991, Hashimoto et al. [6] reported development of a 3D image reconstruction for hepatic anatomy. With the advent of the 3D rendering technique, improved preoperative determination of the tumor location within a liver subsegment was reported [7]. Significant anatomic variations in the segmental anatomy of the liver were also recognized using the 3D CT images [8-10]. Thus the usefulness of the 3D CT has been reported to provide detailed hepatic segmental and vascular anatomy [11-13]. In addition to the detailed topography, there are other important aspects for liver surgery.

Primary hepatocellular carcinoma (HCC) and metastatic liver cancer are the representative and refractory hepatic malignancies requiring surgical resection [14,15]. Majority of HCC have chronic liver disease and associated impaired hepatic function restricts the extent of hepatectomy. The need for living donor liver transplantation (LDLT) is also increasing because of the evolving indication including HCC cases and a shortage of

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decreased organ donation [16,17]. In LDLT, an insufficient graft may jeopardize recipient survival and an excessive liver resection may cause donor liver failure. Therefore, accurate estimations of liver resection volume and residual liver volume are mandatory for successful liver resection, donor hepatectomy, and recipient transplant operation [18,19].

Conventional planimetry has been used to estimate the resected and residual liver volumes, although considerable volumetric error has been observed [20-22]. The calculations are performed by manually tracing around the margins of the hepatic parenchyma on each 2D CT axial image using an electronic cursor. The cross-sectional area (cm^2) within the presumed liver sectors between the hepatic veins is determined, and all individual areas are summed, yielding the liver volume of the interested region (cm^3). However, this method does not account for hepatic vascular perfusion. Moreover, prediction of segmental liver volume has been impossible.

Liver resection currently offers the only potential cure for HCC and metastatic liver cancer when the resection margin is negative [23,24]. Hence, preoperative accurate assessment of the resection margin is also important to achieve curative hepatectomy [25,26]. The other important issue in LDLT includes estimation of the hepatic venous drainage to avoid liver graft and donor residual liver congestion [27]. The preoperative assessment of the hepatic vein drainage should be available to decide necessity of hepatic vein branch reconstruction.

Several studies have reported use of 3D CT as an operation planning system for liver surgery [28,29]. These pioneering studies, however, did not refer to a predictive function of the liver resection volume or resection margin. Moreover, the predicted parameters were not validated by the comparison to the actual resected specimens. Here we review the articles on simulation-guided liver surgery and describe our novel 3D hepatectomy simulation system for liver resection and transplantation.

Virtual reality and simulation

Virtual reality implies a 3D computer-generated world that mimics the real world and allows participants to interact with and navigate it. Virtual reality is created from converting a 2D image into 3D numeric data thus creating a virtual image. The term 'virtuality' was introduced by Lanier [30] in 1989, although its development dates back to the early 1960s, when the first graphic computers were built. Physicians and surgeons first encountered computer-generated images with the development of CT, US, and MR in the late 1970s. These devices dramatically changed the practice of medicine only in a decade. The word 'simulation' was first brought into the literature of plastic surgery in 1985, when Marsh et al. [1] described the term 'surgical simulation'. Simulation can be defined as a device or exercise that enables the participant to reproduce or represent, under test conditions, phenomena that are likely to occur in actual performance. During the 1990s, 3D image reconstruction became possible and the first surgical simulators appeared, starting with tendon transfer model [31] and abdominal surgery simulator [32]. The 3D visualization of images facilitates the visibility of their content and allows three new ways of perception: immersion, navigation, and interaction [33,34]. Virtual reality is particularly relevant to the analysis of the stereoscopic relationship between a tumor to be resected and the vascular anatomy of the liver for the planning of hepatic resections. The proposal for the reasonable compromise between the radicality and the hepatic damage can be optimized preoperatively.

Liver surgery simulation

There are three reasons why a hepatic surgery simulation is required. The first, is to provide the surgeon with a comprehensive visualization of the liver organ, allowing accurate presurgical localization of the pathological lesion and perception of its relation with vascular and biliary system. This step allows the surgeon to plan the best surgical approach. The second reason, is to allow planning and realistic surgical simulation, such as the detailed flight plan used by jet pilots. The surgeon will be able to practice a given procedure repeatedly and be better prepared for the intervention in the surgical conditions. The third reason, is that virtual reality is an integral part of computer-assisted surgical procedures. Augmented reality will superimpose the virtual image of the hepatic vessels and tumor onto the preplanned resection plane to create the real operating view. The surgeon will have precise knowledge about the position of crucial anatomical landmarks that were formerly unseen.

Couinaud's liver segment model

Since 1954, Couinaud's liver segment classification has become the standard basis for liver surgery [35,36]. Because the portal, arterial, biliary, and lymphatic systems are grouped together in the vasculobiliary sheaths, their intrahepatic ramification pattern corresponds in detail, and the portal branching pattern is indicative of the intrahepatic segmentation [37]. Couinaud defined avascular planes within the liver separating autonomously functioning units. Despite the reliance of surgeons on the Couinaud's classification system, increasing suspicion emerged about the segment borders, especially against the background of living-donor surgery. The position and shape of the segment borders are variable, and are hidden within the homogeneous liver mass.

Estimation of liver volume and conventional planimetry

Historically, anthropometric and radiological methods have been used for measuring liver volumes. Anthropometric data to estimate liver volume are based on height, weight, body surface area, age, and gender [38,39]. Variability due to overall body habitus, particularly the effect of obesity, gender, and racial differences, has limited their value. In addition, the anthropometric method does not allow for the differences in lobar volumes: the right liver has been shown to vary between 49% and 82% of total liver volulme [40]. Radiological methods have shown some improvement in liver volume estimation compared with anthropometric data. Early studies of liver volume measurement with CT scan traced serial 1-cm liver slices and summated them: day-to-day variability was ±6%, and interobserver variability ±5%. These calculations are performed by manually tracing around the margins of the hepatic parenchyma on each CT image using an electronic cursor. The cross-sectional area (cm^2) within the region of interest is determined, and all individual areas are summed, yielding the total liver volume (cm^3). However, considerable volumetric error has been observed by the electronic planimetry for the estimation of the resected and residual liver volumes [20-22]. In addition, the conventional method did not allow estimates of sectorial or segmental liver volume.

Development of computer-aided surgery system

Reconstruction of the liver, vessels, and tumor images using CT and MR slice data was initially reported for simulation of laser coagulation therapy of metastatic liver cancer [6]. The 3D CT assessment using arterial portography (CTAP) was useful for more accurate segmental or subsegmental location of hepatic metastases than the 2D CTAP preoperatively [11,41]. The advent of the volume rendering technique allowed simultaneous 3D display of the liver parenchyma, tumor, and vessels. By assigning a low opacity to the liver parenchyma and a high opacity to the tumor and vessels, visualization of the tumor location within the liver capsule became possible and the tumor position relative to the vascular anatomy was appreciated [42]. Zahlten et al. [43] reported a region growing technique for extraction of the 3D portal vein image from CT data. Using cadaver cross-sectional data, Marescaux et al. [33] showed potential application of 3D hepatic visualization to virtual reality concepts and surgical planning. In 2000, a pioneering concept of automatic segmentation of the hepatic vascular system were reported for liver surgery planning [12,28]. Preoperative 3D CT was used for more detailed depiction of the portal vein branch such as the caudate branch, facilitating caudate lobectomy and the selection of the interlobar plane for transection in the transhepatic anterior approach [44]. Moreover, in a clinical trial involving 27 patients scheduled for liver surgery, 3D reconstruction of CTAP image was applied to volumetric estimation of hemi-liver resections [13]. However, this method did not account for hepatic vascular perfusion and was not able to predict liver volume at Couinaud's segment level.

Operation planning system

Lamade et al. [28] evaluated the impact of 3D presentations on the operation planning. The 2D and 3D liver images of 7 virtual patients were presented to a total of 81 surgeons at different levels of training. The precision of the tumor assignment to a liver segment and resection proposal was assessed. The liver segment determination was significantly correlated to the level of training. There was a significant increase in the precision of tumor localization and resection proposal with 3D reconstruction compared with 2D reconstruction. Lang et al. [45] reported 7 cases, in whom the results of computer-associated risk analysis led to a change of operation planning with regard to the extent of resection (n=3) or the need for vascular reconstruction (n=4). In their study, resections most likely to leave devascularized segments were the extended left hepatectomy combined with wedge resection of the right lobe. This was explained by the variability of hepatic vascular system of the right and middle lobes.

Simulation for living donor liver transplantation

Living donor liver transplantation (LDLT) in the adults allows healthy adults to donate a portion of their liver to compatible recipients [46-48]. Right lobe hepatectomy should not endanger the vascular supply or metabolic function of the remaining left lobe of the healthy donor. An excessive liver resection may result in donor liver failure. Sufficient left lobe liver volume must be preserved to permit metabolic function during regeneration. Liver remnant volume of 30-40% of the total liver volume is necessary for the donor to survive, provided that the liver parenchyma is normal without evidence of fatty infiltration [49]. In contrast, a small-for-size graft may result in malfunction or may not sustain metabolic demand in the recipient. Small-for-size grafts are prone to dysfunction, not only because of the insufficient functional hepatic mass but also because of the excessive portal perfusion adversely affecting graft and sinusoidal cells [50]. The minimum graft volume required to provide sufficient functional hepatocytes to the recipient is approximately 40% of the standard liver volume, as calculated using the body surface area [51]. Total liver volume is reported to have a relatively constant relation to body weight, ranging between 2-2.7% in healthy subjects [52]. However, the right and left lobe volumes are widely variable [18]. Moreover, anatomical complexity and variability in hepatic vessels make donor hepatectomy difficult procedure. Therefore, exact preoperative information on detailed topography and precise liver graft volume should be obtained for the preoperative planning of safe donor hepatectomy and successful LDLT [18,53,54].

Application of MDCT

The use of multidetector technology has dramatically increased the speed of data acquisition, resulting in thin-slice images and decreased motion artifacts, compared with the conventional scanners. The thin-slice axial images allow accurate 3D reconstructions of the liver and depiction of the shape of the graft. The usefulness of 3D CT has been reported for the preoperative assessment in LDLT [55,56]. Selecting living adult donors has to be performed with the utmost precision, as the donor hepatectomy has to be performed with zero mortality. Exact volumetric prediction of the transplant liver lobe and residual liver lobe is important for selection of the donor. Kamel et al. [56] reported accurate and reproducible lobar volume determination by virtual right hemihepatectomy using 3D MDCT. In addition, the complex vascular anatomy of the liver and the high incidence of vascular variants reinforced the need for accurate preoperative vascular imaging. Variations in hepatic arterial anatomy, hepatic venous anatomy, and portal vein anatomy were reported in approximately 45% [57], 30% [58], and 20% [59] of patients, respectively. Portal vein variation such as absence of the right portal vein trunk is considered contraindication to living donor operation [55]. A higher spatial resolution of MDCT compared to MR angiography allowed more accurate and reliable display of the hepatic arterial system with a higher number of detected variants and a higher image quality [60]. The use of "all-in-one" MDCT technology also enabled display of biliary structures facilitating the transplant operation planning process and will be discussed later.

Venous drainage and congestion in LDLT

Adult LDLT requires a right lobe graft for adequate liver volume. However, a right lobe graft without a middle hepatic vein (MHV) potentially has problems of hepatic venous congestion, which is caused by absence of drainage via MHV tributaries (V5 and V8) or the inferior right hepatic vein (IRHV) [61,62]. Preoperative prediction of the congestion volume has been difficult. A large variability in the hepatic vein anatomy has been reported [63,64]. The inferior right hepatic vein was reported with a frequency of 6-29% [65,66]. The problem is that demarcation line of the hepatic venous congestion becomes evident only after parenchymal transection and temporary arterial clamping of the donor liver [27]. The importance of optimal venous outflow for sufficient liver function has become evident with the development of right lobe LDLT [67,68]. Venous congestion would result in functional impairment or even necrosis, predisposing to biliary and infectious complications. Generally, T2-weighted MR shows that the water component of tissue and increased signal intensity is consistent with the presence of tissue congestion in solid organs [69]. Using MR congestion score, Yamamoto et al. [70] showed that MR changes compatible with tissue congestion occurred in 80% to 90% of the grafts. There was also a correlation between the graft congestion and posttransplant ascites. In LDLT using the right lobe, IRHV with a diameter of 5 mm or more has been believed to require reconstruction. However, no quantifiable criteria for the venous reconstruction have been available to avoid liver congestion. The volumetric estimation of the hepatic venous drainage is required to avoid liver graft and donor residual liver congestion.

Novel 3D hepatectomy simulation

In order to create an operating system available for the clinical application in liver surgery, an automatic image-processing system of 3D liver reconstruction from CT images has been developed [71]. Our novel 3D image processing software (Hitachi Image Processing System, Version 0.7a) was developed by the Department of Radiology, Hyogo College of Medicine, Nishinomiya, Japan and Hitachi Medical Corporation, Tokyo, Japan. The simulation system was implemented as a plug-in in the portable PC, which is convenient to carry between the operating room and the office. The 3D images of the tumor, portal vein, hepatic vein, and liver parenchyma were reconstructed using the transferred CT image data by region growing technique. A transparent display employed in this system provides perspective views of the liver. Rotation, cross-sectioning, and enlargement functions allow detailed understanding of the anatomic structure between the hepatic vessels and the tumor preoperatively. The simulation software introduced an algorithm to define the perfusion area of individual portal vein branches according to the direction and diameter of the vessels. Computation of the perfusion area continued along the individual portal branches proximally to peripherally until the entire liver parenchyma was subdivided. Thus the vascular perfusion area was calculated by an algorithm based on the direction and diameter of hepatic vessels. The resection planning was proposed by calculation of the liver resection volume based on the vascular perfusion area, and the resection margin.

Table 1. **Clinical characteristics of patients (n=72)**

Mean of age (yr)	62
Sex	
Female	21 (29)
Male	51 (71)
Operative indication	
HCC	57 (79)
Living-related donor	3 (5)
Other malignant tumors	10 (14)
Benign tumors	2 (2)
Surgical procedure	
Trisegmentectomy or more	17 (24)
Bi- or mono-segmentectomy	26 (36)
Limited resection	29 (40)

HCC – hepatocellular carcinoma.
All number in parentheses are percentages unless indicated otherwise (from [71])

Between May 2001 and June 2004, 72 consecutive patients received preoperative hepatectomy simulation at the Hyogo College of Medicine (*Tab. 1*). Computed tomography, which was performed either angiographically or intravenously, provided fundamental information for the preoperative donor hepatectomy simulation. Multidetector CT scan (MDCT) has become routine use since 2004 with a slice thickness of 1 mm. To validate the volumetric accuracy of the simulation system, the predicted liver resection volume was compared to the actual weight of the resected specimen. A significant correlation existed between the simulation predicted liver resection volume and the actual weight of the resected specimen ($r=0.96$, $P<0.0001$) (*Fig. 1A*). The difference between the estimated volume and the actual weight was 9.3±6.0 ml. A significant correlation was also revealed between the predicted and actual resection margins ($r=0.84$, $P<0.01$) (*Fig. 1B*). The difference between the predicted and actual margins was 1.6±2.6 mm. Our simulation system enabled the accurate prediction of the liver resection volume at Couinaud's segment levels. We demonstrated systematic overestimation of liver resection volume by a mean of 9 ml, as compared to previously reported values of

Figure 1. **Validation of liver resection volume and resection margin. (A) Significant correlation existed between simulation predicted liver resection volume and actual weight of resected specimen. (B) Significant correlation also existed between predicted and actual margins (from [71])**

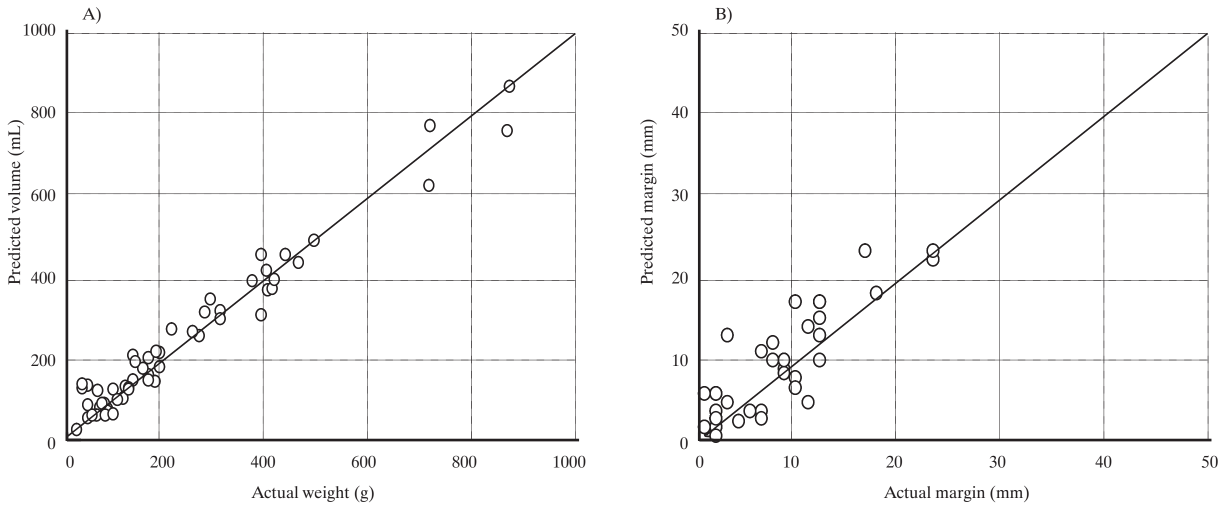
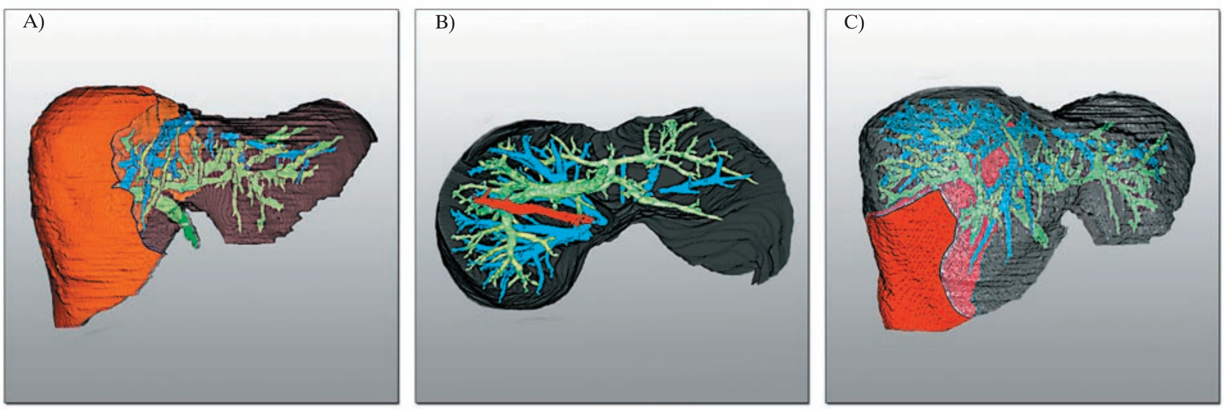


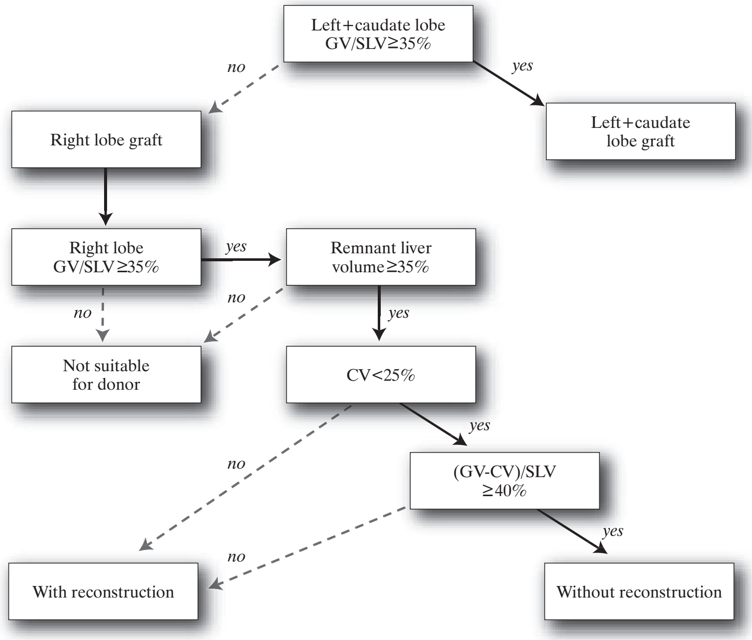
Figure 2. **Hepatectomy simulation for LDLT with right lobe graft. (A) For preoperative volumetry of the right lobe graft, the right portal pedicle was clipped. (B) Integrated 3D axial view showed IRHV. Liver was observed from caudal to cranial direction. (C) Drainage area by IRHV was shown in red color and its estimated volume was 234 mL, which accounted for 36% of proposed right lobe graft (from [73]).**



53 to 90 mL [13,22,72]. The predicted liver resection volume and margins by the simulation correlated significantly with the actual weight and margins of the surgically resected specimens. In our simulation, inclusion of the entire tumor within the predicted resection area allowed the preoperative planning of curative resection.

In cases of LDLT, the simulation algorithm was applied to the hepatic venous system to estimate the drainage area of the hepatic vein by clipping of the corresponding vein at its origin. The preoperative planning for donor hepatectomy was proposed via calculation of the liver graft volume and hepatic vein drainage area. A case of donor hepatectomy for right hemi-liver graft was presented as an example (*Fig. 2*) [73]. Clipping of the right portal pedicle at its origin prompted volumetric calculation of the corresponding portal perfusion area as a predicted graft volume. The predicted right hemi-liver graft volume was 648 mL, with a graft-to-recipient weight ratio of 0.9%. The actual liver graft weighed 640 g. In this case, an inferior right hepatic vein (IRHV) of 8 mm in diameter was identified by the preoperative simulation. Then the simulation algorithm was applied to the hepatic venous system to estimate the drainage area of the hepatic vein branch. The estimated drainage volume by the IRHV was 234 mL and accounted for 36% of the proposed graft. Based on the volumetric calculation of the hepatic vein drainage area, the reconstruction of IRHV and RHV was necessary to avoid congestion of the implanted liver graft. The recipient recovered uneventfully and the follow-up dynamic CT scan revealed patent IRHV and RHV without evidence of congestion. None of the previous studies used the volumetric assessment of the congested areas as a criterion for the venous reconstruction. Application of the simulation algorithm to the hepatic venous system provided the volumetric estimation of the hepatic vein branch drainage area, which is needed for LDLT reconstruction. Using the same simulation software as ours, Yonemura et al. [74] proposed graft selection flow chart for LDLT according to the graft volume and congestion volume (*Fig. 3*).

Figure 3. **Flow chart for the graft selection. Initially the left lobe is considered as a graft. The right lobe is selected if the estimated extended left + caudate lobe volume of the donor is less than 35% of the standard liver volume (SLV) of the recipient. If a remnant liver volume is under 35% of the total liver volume, this donor will be rejected. If congestion volume (CV) is over 25%, or the deducted CV from the graft volume (GV) is under 40% of the recipient SLV, reconstruction of venous tributaries is needed (from [74])**



3D virtual cholangiography

Although biliary variants can be depicted by means of intraoperative cholangiography, this procedure results in time delays and does not permit the surgeon to freely adjust the surgical strategy [75]. Endoscopic retrograde cholangiography represents an invasive technique and is associated with a considerable number of complications (e.g., iatrogenic pancreatitis), thus potentially subjecting the voluntary donors to a higher risk than with CT cholangiography. Standard MR cholangiopancreatography techniques based on T1-weighted MR images have been shown to be insufficient to depict the normal intrahepatic bile ducts beyond the hepatic bifurcation [76]. Yeh et al. [77] performed a comparison of contrast-enhanced CT and MR cholangiography in potential liver donors and confirmed a substantially better visualization of the biliary tract with MDCT. Schroeder et al. [66] reported that contrast-enhanced CT cholangiograms showed the biliary tree at least up to the second, and more often up to third and fourth, intrahepatic branches in 99.6% of all LDLT candidates. The substantial concordance of preoperative and intraoperative biliary anatomical findings was achieved [78]. Our simulation incorporating 3D cholangiography also facilitated preoperative identification of the variant bile duct, of which the recognition was important to avoid donor morbidity [73].

Future studies required

In the future, the impact of these new simulation technologies on surgical education and their exact cost-effectiveness must be assessed objectively [79,80]. Comparative study and even consideration for a randomized trial need taken to document advantage for the new technology over standard practice. It seems likely that future generations of surgeons will be selected, trained, credentialed, and recredentialed using simulation and virtual reality devices.

Conclusions

In conclusion, simulation will both allow training and provide expert knowledge with detailed information useful for the preoperative planning of liver resections. Our novel 3D simulation system, based on the hepatic circulation, provided accurate volumetric and stereotactic information to achieve safe and curative hepatectomy. In addition, our simulation program was applicable to the hepatic venous system to predict liver congestion in LDLT. With increasing use of ablative procedures and laparoscopic surgery, preoperative and intraoperative imaging, and navigation will hold increasing significance for the hepatobiliary pancreatic surgeon.

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