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Assessing Liver Volume and Anatomy in Living Donor Liver Transplantation: Exploring Contemporary Imaging Techniques and Artificial Intelligence Integration

Imaging in liver transplantation

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Abstract

Background: The shortage of deceased donor organs has prompted the development of alternative liver grafts for transplantation. Living-donor liver transplantation (LDLT) has emerged as a viable option for expanding the donor pool and enabling timely transplantation with favorable graft function and improved long-term outcomes. Accurate evaluation of donor liver volumetry (LV) and anatomical study is crucial to ensure adequate future liver remnant (FLR), graft volume, and precise liver resection, thus ensuring donor safety and an appropriate graft-to-recipient weight ratio. Manual LV (MLV) measurement using computed tomography (CT) has traditionally been considered the gold standard for assessing liver volume. However, this method is limited by its cost, subjectivity, and variability. Automated LV techniques employing advanced segmentation algorithms offer improved reproducibility, reduced variability, and enhanced efficiency compared with manual measurements. However, the accuracy of automated LV requires further investigation. This paper provides a comprehensive review of traditional and emerging LV methods, including semi-automated image processing, automated LV techniques, and machine learning-based approaches. Additionally, this study discusses the strengths and weaknesses of each technique. **Future directions:** Artificial intelligence (AI) technologies, including machine and deep learning, are expected to become routine parts of surgical planning in the near future. The implementation of AI is expected to enable faster and more accurate image study interpretations, improve workflow efficiency, and enhance the safety, speed, and cost-effectiveness of procedures. **Conclusion:** Accurate preoperative liver assessment plays a crucial role in ensuring safe donor selection and improving LDLT outcomes. MLV has inherent limitations that have led to the adoption of semi-automated and automated software solutions. Moreover, AI has tremendous potential for LV and segmentation; however, its widespread use is hindered by costs and availability. Therefore, the integration of multiple specialties is necessary to embrace technology and explore its possibilities, ranging from patient counseling to intraoperative decision-making through automation and AI.

Key Words: Liver Transplantation; Living Donor; Diagnostic Imaging; Artificial Intelligence; Machine Learning; Deep Learning.

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Core Tip: Accurate LV is imperative for successful LDLT to ensure adequate FLR and graft volumes. Manual CT scan delineation conventionally serves as the standard approach; however, it is constrained by factors such as cost, subjectivity, and variability. In contrast, automated LV techniques using advanced segmentation algorithms present superior reproducibility, reduced variability, and enhanced efficiency compared with manual measurements. However, the accuracy of automated LV requires further investigation. This study comprehensively reviewed both traditional and emerging LV methods, including semi-automated image processing, automated LV techniques, and machine learning-based approaches, while analyzing their respective strengths and weaknesses.

INTRODUCTION

Liver transplantation is the first-line treatment for patients with terminal liver disease. Deceased donor organ shortage and cultural barriers have led to the development of alternative graft types. Living-donor liver transplantation (LDLT) has emerged as an extension of the *ex-situ* graft transection concept, encompassing reduced-size and split-liver techniques. By enabling the expansion of the donor pool, LDLT offers the advantage of timely transplantation and holds the potential for excellent graft function and improved long-term outcomes [1-6], Moreover, LDLT reduces waiting list mortality.

Adequate preoperative evaluation of the donor is essential for successful LDLT. Sufficient future liver remnants (FLR) and graft volume must be ensured through liver volumetry (LV) studies [7, 8]. An FLR of 30–35% of the original liver volume is required for donor safety, whereas at least 4% of the standard liver volume (SLV) or more than 0.8 and less than 3–3.5 of the graft recipient weight ratio (estimated before the surgery through imaging and confirmed after the graft is weighed) is required to meet the recipient's needs [9, 10]. Small grafts are associated with cellular damage due to excessive portal flow, leading to "small-for-size syndrome," whereas large grafts may receive inadequate portal flow, resulting in "large-for-size syndrome" [11-17].

Manual liver volumetry (MLV) conducted on portal venous phase multidetector computed tomography (CT) scans with intravenous contrast is conventionally considered the standard method for measuring the LV [7, 18, 19]. However, it can be costly, time-consuming, subjective, and prone to inter- and intra-observer variability. This process entails manual tracing of the liver borders using specialized software, necessitating the expertise of an experienced radiologist, often without the surgeon's input. The percentage of error (PE) may vary significantly, ranging from 2 to 20%, which can have a dramatic effect on the final graft volume and transplantation outcomes [20-24].

Advancements in medical imaging, computational algorithms, and artificial intelligence (AI) have set the stage for the development and application of automated LV techniques. Automated LV holds significant promise in the evaluation of LDLT because it utilizes sophisticated segmentation algorithms to delineate liver boundaries from CT or magnetic resonance imaging (MRI) scans. Therefore, volumetric calculations and comprehensive volumetric analyses can be used to assess lobe-specific volumes, segmental volumes, and the overall liver volume. Such automated approaches offer advantages over manual measurements, including enhanced reproducibility, reduced intra- and inter-observer variability, and improved efficiency. However, the accuracy of automated LV techniques is yet to be conclusively determined [25-28].

This study aimed to provide a comprehensive review of the literature, presenting both traditional and emerging methods of LV and anatomical liver assessment, while discussing their respective strengths and weaknesses. By examining the current state of LV techniques, this review aimed to contribute to the advancement and optimization of liver transplantation outcomes.

MANUAL LIVER VOLUMETRY

The introduction of multiphasic CT and MRI techniques has led to the widespread adoption of MLV as a standard practice in liver transplant centers to estimate liver volume before accepting a living donor as a suitable candidate. During donor evaluation, a complete anatomical analysis of the hepatic veins, portal vein, and hepatic arteries is performed using multiphasic CT and MRI. Bile duct anatomy is evaluated in cholangio-MRI studies, especially in left and right lobe donors.

If the donor´s anatomy is suitable for the planned procedure, the LV is performed. The procedure involves manual delineation of the liver borders using sequential image slices to determine the overall liver volume. Subsequently, a transection plane is selected based on the specific type of liver graft and inclusion of the middle hepatic vein (MHV) [25, 29-31] (Figure 1).

The limitations include reliance on operator expertise and medical specialty, leading to discrepancies between the analyses performed by radiologists and surgeons, potentially related to the transection line. Furthermore, the inclusion of blood vessels and bile ducts in the final volume calculation can lead to overestimations [32]. Additionally, the LV procedure itself is time-consuming, typically requiring approximately 20–40 minutes to complete, which significantly affects the daily workflow of both radiologists and surgeons [19, 33]. In terms of accuracy, the PE ranges from 5% to 36% when comparing the estimated volume with the actual graft weight (AGW) [34]. It is important to note that errors can occur in both directions, resulting in over- and underestimations [8].

The density of the liver is routinely considered equivalent to the density of water; therefore, AGW is representative of graft volume [35]. However, studies measuring AGW have identified the necessity of correction factors when estimating graft volume, as highlighted in Table 1. Recently, Lehmke *et al* [36] measured the mean physical density of 16 transplanted liver lobes to be 1.1157 g/mL, asserting that the conversion factor was, on average, 12% higher than expected. Tongyoo *et al* [32] demonstrated that the AGW of a right lobe donor liver graft (RLDG) was approximately 91% of the estimated right lobe liver volume. The 9% volume reduction was attributed to intrahepatic blood flushed out of the liver by the preservation solution during back-table preparation [9, 31, 37]. Other inaccuracies may have been due to the inclusion of the MHV and/or caudate lobe [38].

SEMI-AUTOMATED IMAGE PROCESSING (SAIP)

Semi-automated methods have been developed to address observer-related issues associated with manual measurements and enhance the efficiency of LV and hepatic segmentation. An example of such a method is the MeVis Liver Analyzer (MeVis Medical Solutions AG, Bremen, Germany), which is a computer-assisted software that operates on CT images. Moreover, the software employs a modified live-wire algorithm to automatically determine the contours between user-defined boundary points based on CT values and gradients. The algorithm parameters were tailored for each CT phase, including the venous (V), arterial (HA), and native (N) phases. To ensure accurate liver segmentation, the automatically delineated contours are manually corrected and the contour parts are manually drawn. Live-wire contours are interactively determined on 3 mm axial two-dimensional (2-D) CT slices. The software automatically interpolates and optimizes the contours of the intermediate slices, with final adjustments made by the operator through manual corrections, if necessary.

Volumetric calculations, expressed in milliliters (mL), are performed by adding the areas of all the segmented regions. Surrounding structures, such as major extrahepatic vessels (portal vein, hepatic artery, and inferior vena cava) and the gallbladder fossa, are excluded from the volume calculations (Figure 2).

Goja *et al* [39] discovered that semiautomated software tools exhibited the highest correlation (*r* = 0.82) for measuring right lobe grafts. However, left lobe grafts tend to be overestimated, whereas left lateral segment (LLS) grafts are underestimated in approximately 66% of cases. One possible explanation for the underestimation of LLS grafts is that CT scans typically underestimate the volume, because the actual surgical plane of transection is approximately 1 cm to the right of the falciform ligament, whereas the radiological plane of transection is exactly at the falciform ligament. Other studies have addressed the accuracy of the SAIP, and the results are presented in Table 2.

AUTOMATED LIVER VOLUMETRY TECHNIQUES

Automated LV relies on advanced image processing techniques and algorithms to accurately segment the liver from CT or MRI scans. The principles and algorithms used vary depending on the approach employed. However, some common techniques and concepts are involved.

Image Preprocessing

Before liver segmentation, image preprocessing techniques may be applied to enhance the image quality, reduce noise, and improve the contrast between the liver and surrounding structures. These techniques include filtering, intensity normalization, and image enhancement methods (Figure 3).

Segmentation Algorithms:

Segmentation algorithms are used to delineate the liver region of interest from the remaining images. Additionally, such algorithms aim to accurately identify liver boundaries. Commonly used algorithms include threshold-based methods, region growing, active contours (or snakes), level sets, graph cuts, and machine learning-based techniques.

Threshold-based Methods:

Threshold-based methods involve setting intensity thresholds to separate the liver from background or other organs. The liver is segmented based on predefined intensity ranges or statistical measures such as mean intensity or intensity distribution.

Region Growing:

Region-growing algorithms start from a seed point within the liver and iteratively develop the region by including pixels with similar characteristics (e.g., intensity, texture, or gradient) until a stopping criterion is met. This method is particularly useful when the liver has a distinct intensity pattern compared with the surrounding tissues.

Active Contours (Snakes):

Active contour models, also known as snakes, use an energy-optimization approach to iteratively deform a contour to fit the liver boundary. The contours are attracted to the image edges or intensity gradients to ensure accurate delineation of the liver boundaries.

Level Sets:

Level-set methods are mathematical techniques used to evolve a curve or surface over time to delineate liver boundaries. These methods use the concept of level sets, which represent an evolving contour as a zero-level set of a higher-dimensional function.

Graph Cuts:

Graph cut algorithms model the liver segmentation problem as an optimization task in a graph framework. The graph is constructed using image features, and the segmentation is achieved by identifying the minimum energy cut that separates the liver from the background.

Machine Learning-based Techniques and Deep Learning

Machine learning algorithms, such as random forests, support vector machines, and deep learning models, can be trained on annotated liver images to automatically segment the liver. Such algorithms learn the patterns and features that distinguish the liver from other structures and can provide accurate and robust segmentation results [40].

Most software tools employ a combination of techniques or advanced algorithms that are specific to their methodology. The choice of algorithm depends on factors such as image quality, complexity of the liver structures, computational efficiency, and specific requirements of the application. Each algorithm has its advantages, limitations, and parameter settings, which must be carefully considered and optimized for an accurate LV. A combination of techniques can be used to improve the accuracy and robustness [41].

For example, initial segmentation can be obtained using thresholding or region growth, followed by refinement using active contours or graph cuts. Hybrid approaches that combine multiple algorithms can leverage the strengths of each technique to achieve a more accurate LV. Additionally, the validation and evaluation of automated LV results against ground truth or manual segmentations are critical for assessing the performance and reliability of the algorithm [42].

Most computer-aided diagnostics used in clinical practice use conventional machine learning approaches, the effectiveness of which depends on the domain expertise of the developers. Therefore, the limitations of conventional learning are linked to those of human developers. Manual and semiautomated volumetry depend on conventional machine learning. Deep learning has emerged as a state-of-the-art machine-learning method for many applications. Deep learning is a representation-learning method in which a complex multilayer neural network architecture learns representations of data automatically by transforming input information into multiple levels of abstraction [43].

Deep convolutional neural networks (DCNN) are widely used for image-pattern recognition. They automatically extract relevant features from training samples by adjusting their weights through backpropagation (Figure 5). In contrast to manual feature design, a DCNN learns feature representations during training. When trained with a large and representative dataset, DCNN features outperformed the handengineered features because they were highly selective and invariant. Automated deep learning enables the analysis of numerous cases, surpassing human capabilities. Deep learning is robust in handling variations across different classes as long as the training set is diverse and extensive [40-43].

ACCURACY AND RELIABILITY

Automated LV and deep machine learning for LDLT have gained attention in recent years. There has been an increase in the number and quality of artificial intelligence (AI) and machine learning studies in the medical field, mainly those focused on automating the interpretation of 2D image tests (MRI, CT, and radiographs), assembling three-dimensional models of organs and tissues, and volumetric calculations, including virtual segmentation of the liver. In liver resection and transplantation, most studies had a small number of cases and focused on adult liver transplantation and RLDG, with very few studies on LLDG and LLSDG [26, 27, 42-45]. The higher risk of small-for-size syndrome in adult liver transplantation justifies intense volumetric and anatomical studies on RLDG. Usually, for pediatric recipients (< 10 kg), an inaccurate volumetric assessment rarely leads to insufficient liver volume; in contrast, the risk of large-for-size syndrome is higher than that of small-for-size syndrome. In such cases, the surgeon usually reduces the graft on the backtable or converts it into a monosegmental graft before implantation [46].

Automated software allows the surgeon to choose the transection plane, and some studies have compared the correlation of these measurements for RLDG performed by the surgeon using automated software with manual measurements performed by radiologists. Moreover, both measurements had a good correlation with AGW ($r > 0.80$), and there was no significant difference between the measurements by the surgeon and the radiologist [29].

As it is of paramount importance that the surgeon who is going to perform the procedure also perform the anatomical assessment and choose the adequate liver segmentation plane, new software focusing on the surgeon's interaction are being developed. A more user-friendly automated platform was developed by a group from the Republic of Korea [47], which they referred to as Dr. Liver (Figure 4). They validated the method in 50 RLDG and compared it with the MLV. The correlation with AGW was better for the automated Dr. Liver ($r = 0.98$) than for MLV ($r = 0.92$), although both had good correlations. However, the percentage of absolute difference (%AD) from AGW of Dr. Liver (3.1% ± 2.8%) was significantly smaller than that of the MLV (10.2% ± 7.5%). None of the Dr. Liver measurements of %AD were > 10%, whereas they were 46% for MLV measurements. Evaluation of %AD is very important in clinical practice, because an error percentage of more than 10% can result in a small-for-size boundary graft volume. Additionally, the total time for task completion was shorter for Dr. Liver than for MLV (7.3 ± 1.4 min *vs* 37.9 ± 7.0 min).

CONCLUSION

Accurate preoperative liver assessment is critical in ensuring the selection of suitable donors and improving recipient outcomes after LDLT. MLV initially emerged as the gold standard for accurate assessment. However, the time-consuming nature of manual analysis, reliance on operator expertise, and high variability in PE have prompted the adoption of SAIP software tools and, more recently, automated software solutions. AI represents the future of LV segmentation and offers immense potential in the field, leading to fully automated liver segmentation and volumetry based on deep learning. However, the widespread adoption and daily application of AI have been hindered by cost and accessibility. We are responsible for embracing technology and fostering interdisciplinary collaborations in radiology, engineering, informatics, and surgery. The possibilities afforded by AI are limitless, ranging from patient counseling and education to intraoperative decision-making facilitated by automation and AI assistance.

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