## ORIGINAL ARTICLE

# Predicting the available space for liver transplantation in cirrhotic patients: a computed tomography-based volumetric study

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## Abstract

**Background** Anthropometric parameters (weight, height) are usually used for quick matching between two individuals (donor and recipient) in liver transplantation (LT). This study aimed to evaluate clinical factors influencing the overall available space for implanting a liver graft in cirrhotic patients.

**Methods** In a cohort of 275 cirrhotic patients undergoing LT, we calculated the liver volume (LV), cavity volume (CV), which is considered the additional space between the liver and the right hypocondrium, and the overall volume (OV = LV + CV) using a computed tomography (CT)-based volumetric system. We then chose the formula based on anthropometric parameters that showed the best predictive value for LV. This formula was used to predict the OV in the same population. Factors influencing OV variations were identified by multivariable logistic analysis.

**Results** The Hashimoto formula (961.3 × BSA_D-404.8) yielded the lowest median absolute percentage error (21.7%) in predicting the LV. The median LV was 1531 ml. One-hundred eighty-five patients (67.2%) had a median CV of 1156 ml (range: 70–7006), and the median OV was 2240 ml (range: 592–8537). Forty-nine patients (17%) had an OV lower than that predicted by the Hashimoto formula. Independent factors influencing the OV included the number of portosystemic shunts, right anteroposterior abdominal diameter, model for end-stage liver disease (MELD) score > 25, high albumin value, and BMI > 30.

**Conclusions** Additional anthropometric characteristics (right anteroposterior diameter, body mass index) clinical (number of portosystemic shunts), and biological (MELD, albumin) factors might influence the overall volume available for liver graft implantation. Knowledge of these factors might be helpful during the donor–recipient matching.

**Keywords** Anthropometrics · Body mass index · Liver weight · Liver transplantation · Donor · Recipient matching · Liver volume · Ascites · Portosystemic shunts · Portal hypertension · Right anteroposterior diameter

## Abbreviations

| | |
|---|---|
| BMI | Body mass index |
| BSA | Body surface area |
| BW | Body weight |
| BH | Body height |
| LT | Liver transplantation |
| LW | Liver weight |
| MAPE | Median absolute percentage error |
| LV | Liver volume |
| CV | Cavity volume |
| OV | Overall volume |

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## Introduction

Donor-to-recipient matching in liver transplantation is a multifactorial process in which several parameters are combined to make a clinical decision. Biological and clinical factors are prevalently used in this process [1, 2], but

anthropometric characteristics (weight, height, and BMI) are usually used for a "first fast" virtual matching between a given donor and a recipient. Discrepancies between the large volume of a liver graft and a small volume of the right hypochondria can lead to the occurrence of a "large-for-size" syndrome that has been associated with up to 40% postoperative mortality and decreased graft and patients survival in liver transplantation [3–8].

In the preoperative setting, several formulas have been described in the literature to estimate the liver volume and/ or liver weight based on anthropometrics data [9, 10]. The accuracy of these formulas in predicting total LW and/or LV in healthy subjects remains variable, and a recent study reported that LW cannot be predicted with a $\leq 20\%$ margin of error in about 30% of subjects [11]. These predictive formulas are even less accurate when predicting the LV/LW in cirrhotic patients, who can present with variable degrees of hypertrophy and atrophy during the natural course of disease [12]. In clinical practice, the space for implanting a liver graft in cirrhotic patients is not only determined by the volume of the recipient's liver but also by that of the right hypochondrium. This space can be greatly influenced either by variations in LV, such as seen in atrophy/hypertrophy and/or of the right hypochondrium and/or massive ascites/ adherences [5]. Virtual donor–recipient matching based exclusively on anthropometric parameters might therefore not always be accurate in cirrhotic patients because of these variations. In the current study, we aimed to determine clinical, anthropometric, and biological factors influencing the available space for liver graft implantation in a large cohort of cirrhotic patients using computer tomography (CT)-based volumetric evaluation of the liver and right abdominal cavity.

## Materials and methods

### Data collection

#### Clinical data

This study was conducted as a retrospective cohort study in which data from consecutive cirrhotic patients undergoing orthotopic LT from June 1, 2014 to December 31, 2019 at the Hepato-Pancreato-Biliary Surgery and Liver Transplantation Centre, University of Strasbourg, France were selected. Exclusion criteria included patients undergoing LT after liver resection, LT for fulminant hepatic failure and/ or in presence of healthy liver, early and late liver re-transplantation, and patients with missing biological and radiological data. Clinical characteristics of patients included basic anthropometric characteristics (age, sex, and body weight and height [BW and BH, respectively]), and body mass index [BMI]), comorbidities (arterial hypertension,

diabetes, and hyperlipidemia), history of previous digestive hemorrhage, encephalopathy, ascites, and indications for liver transplantation (type of cirrhosis and presence of hepatocellular carcinoma). Biological parameters included serum liver function tests, electrolytes, and model for end-stage liver disease (MELD) scores. Body surface area (BSA) was determined according to Dubois and Dubois as BSA-d or Motseller as BSA-m [13]. Final LW was considered the weight of the explanted liver during LT as measured on a balance.

### Radiologic data

All pre-operative CT scans of the patients were retrospectively reviewed. We estimated LV from pre-operative CT images using a semi-automated method provided on a dedicated interactive workstation console by the Philips Intellispace portal console (Koninklijke Philips NV, Amsterdam, The Netherlands). The resulting contours were inspected and corrected manually if necessary. Total liver volume (LV) and volumes of the right and left (RL and LL, respectively) livers were calculated in addition to the ratio between the LL/RL. Using a manual segmentation method, the presence and the volume of additional available space between the liver and the right hypochondriac cavity (cavity volume) was traced in patients. The ratio between the cavity volume and the total liver volume (CV/LV) was also calculated. Finally, the overall volume available (CV + LV) was calculated (Fig. 1). The longest cranio-caudal measurement in the coronal images of the spleen was used to define the presence of splenomegaly (> 13 cm). Massive splenomegaly was defined when the longitudinal diameter was > 18 cm. The caliber of the main portal trunk was also measured just before the portal vein bifurcation at the hepatic hilum was reached. Morphological distances were measured in all patients: (1) the anteroposterior (AP) distance in cm (lower extremity of the xiphoid process to the anterior wall of vertebra), (2) the side-to-side (SS) distance in cm (the largest intra-peritoneal and horizontal distance), and (3) the longest right anteroposterior (RAP) vertical distance between anterior and posterior parts of ribs [3] as shown in Fig. 1. The presence, type, and number of spontaneous portosystemic shunts (SPSS), including umbilical, gastric, splenorenal, mesocaval, and mesoiliac, and the presence of transjugular intrahepatic portosystemic (TIPS) were recorded. Large shunts were defined as those measuring > 8 mm [14]. The presence of ascites was recorded. Extensive and/or refractory ascites were defined as ascites that recur on at least three occasions within a 12-month period despite dietary sodium restriction and adequate diuretic doses [15]. To define the presence of sarcopenia in all cases the psoas muscle area (PMA, taken as the sum of the areas of the two psoas at the level of the third or fourth lumbar vertebra) was calculated based on a CT scan.
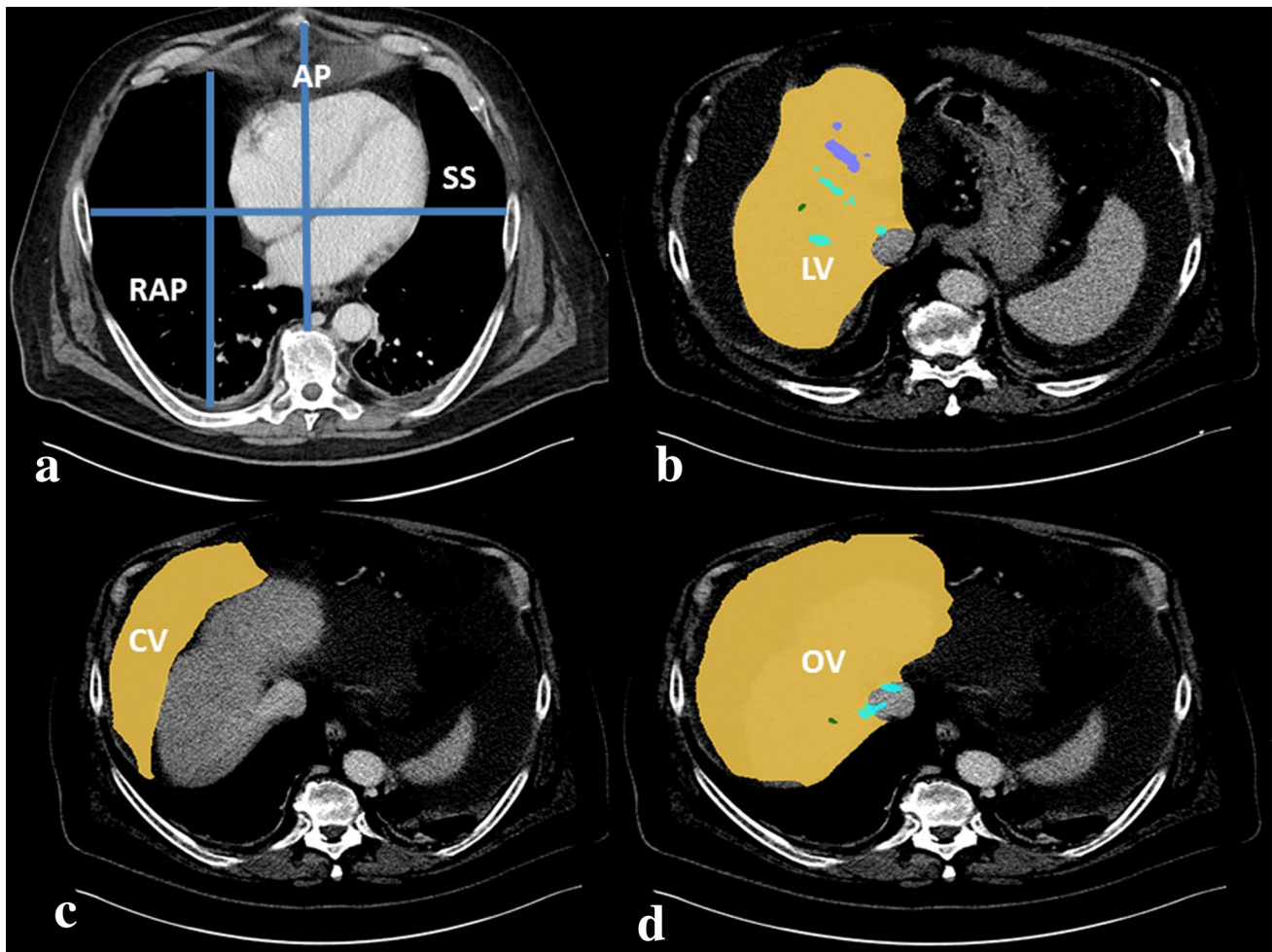
**Fig. 1** Anthropometric and volumetric data studied on computed tomography: Anteroposterior (AP), side-to-side (SS) distance, and the longest right anteroposterior (RAP) vertical distance (Panel **a**). Total liver volume (LV) (Panel **b**). Volume of right hypochondria cavity (cavity volume [CV]) (Panel **c**). Available overall volume (OV) (Panel **d**)

Sarcopenia was then defined as PMA $\leq$ 1561 and 1464 mm in male and female, respectively, as reported by Golse et al. [16]. Clinically evident portal hypertension was defined as the presence of esophageal varices, ascites, or an association of thrombopenia ($< 100,000/mm^3$) and splenomegaly. Severe portal hypertension was defined by the presence of varices/spontaneous shunts, splenomegaly, thrombopenia, and ascites [17].

### Statistical analysis

Results for continuous data were expressed as means $\pm$ standard deviations or median when appropriate, whereas categorical variables were presented as numbers and percentages. A total of 17 different formulas predicting the liver volume based on anthropometric measurements were selected and tested [9, 10, 18–31]. In order to compare different formulas (Table 1) for estimating liver volume, the median absolute percentage error (MAPE) with respect to the observed liver volume was used. We selected the formula associated with the lowest MAPE [11]. A second analysis was conducted using this formula for predicting the overall volume (OV) for a virtual matching based on anthropometric characteristics. Univariate and multivariate analyses were used for identifying factors associated with LV, CV, and OV variations. A backward Wald method was used to select the most relevant variables for the definitive multivariate model. Only the variables with a $p < 0.20$ were included in multivariate analysis. All analyses were conducted using statsmodel 0.11.0 (https://www.statsmodels.org/) and the SAS 9.4 version system (SAS Cary, NC).

**Table 1** State of art formulas predictive of liver weight or liver volume based on anthropometrics

| Author | Year | Population | Formula |
|---|---|---|---|
| Deland | 1968 | North American | $1020 \times BSA\_D - 220$ |
| Urata | 1995 | Japanese | $706.2 \times BSA\_D + 2.4$ |
| Noda | 1997 | Japanese | $50.12\ weight^{0.78}$ |
| Lin | 1998 | China | $13 \times height + 12 \times weight - 1530$ |
| Heinemann | 1999 | German | $1072.8 \times BSA\_D - 354.7$ |
| Vauthey—formula 1 | 2002 | North-American European | $18.51 \times weight + 191.8$ |
| Vauthey—formula 2 | 2002 | North-American European | $1267.28 \times BSA\_M - 793.41$ |
| Yoshizumi | 2003 | North American | $772 \times BSA\_M$ |
| Yu | 2004 | Korean | $21.585 \times (weight^{0.732}) \times (height^{0.225})$ |
| Chouker | 2004 | German | $16.434 \times weight + 11.85 \times age - 166 \times gender + 452$ |
| Johnson | 2005 | United Kingdom | $0.722 x BSA^{1.176}$ |
| Hashimoto | 2006 | Japanese | $961.3 \times BSA\_D - 404.8$ |
| Chan | 2006 | China | $12.29 \times weight + 50.74 \times gender$ |
| Yuan | 2008 | China | $949.7 \times BSA\_D - 48.3 \times age\ factor - 247.4$ |
| Fu-Gui | 2009 | China | $11.508 \times weight + 334.024$ |
| Poovathumkadavil | 2010 | Middle Eastern Arabic adults | $12.26 \times weight + 555.65$ |
| Um | 2015 | Korea | $893.485 \times BSA - 439.169$ |

# Results

## Patient population

### Patient characteristics

According to our inclusion criteria, 275 consecutive cirrhotic patients who underwent liver transplantation at our center constituted the final study population. The median age was 58 years (range: 18–70) with a majority of male study patients (72%). Alcoholic cirrhosis constituted the main indication for LT in about half of the population (51.6%), and previous digestive hemorrhage (30.9%), encephalopathy (50.5%), ascites (82.1%), and hepatocellular carcinoma (31.6%) had complicated the clinical course of cirrhosis in this population. The median MELD score was 25 (range: 6–40) as shown in Table 2, and the median delay between the CT scan and LT was 66 days (mean 140 days). Anthropometric characteristics included a median weight of 80 kg, a median height of 172 cm, and a median BMI of 26 kg/$m^2$ with a median BSA-d of 1.9 $m^2$. Eighty patients (30%) had BMI values > 30. The median LW was 1320 g and the median liver volume was 1531 ml with a linear correlation ($r = 0.80$) between both liver volume and weight. As in healthy subjects, the volume of the right liver was significantly higher than that of the left liver with a mean left/right ratio volume of 0.67 as shown in Table 3. However, 36 patients (14%) showed a ratio left/right volume > 1 indicating right lobe atrophy. Additional space was found in 185

**Table 2** Demographics of patients population ($n = 275$)

| | |
|---|---|
| Age, median (range) | 58 (18–70) |
| Male/female | 198/77 |
| Arterial hypertension | 115 (41.8%) |
| Diabetes | 83 (30.1%) |
| Dyslipidemia | 48 (17.4%) |
| Indications for liver transplnatations | |
|   Alcoholic | 142 (51.6%) |
|   Viral | 54 (19.6%) |
|   Cirrhosi other | 79 (28.8%) |
|   + Hepatocellular carcinoma | 87 (31,6%) |
| Previous digestive haemorrage | 85 (30.9%) |
| Encephalopathy | 139 (50.5%) |
| Ascites | 226 (82.1%) |
| Esophageal varices | 197 (71.6%) |
| Serum blood test | |
|   Albumine | 29 (14–39) |
|   Prothrombine time | 42 (10–100) |
|   Bilirubin | 84 (2.7–1300) |
|   Platelet | 78.000 (4000–375.000) |
| MELD score | 25 (6–40) |
| Weigth | 80 (48–156) |
| Heigth | 172 (150–196) |
| BMI | 26 (16–53) |
| BSA-d | 1.9 (1.4–2.5) |

*BMI* body mass index, *BSA-d* body surface area according Dubois

**Table 3** Radiological data ($n = 275$)

| | |
|---|---|
| Liver weight | 1320 (464–5600) |
| Liver volume (LV) | 1531 (558–6174) |
| Right liver | 860 (250–4213) |
| Left liver | 580 (181–2442) |
| *L/R* ratio | 0.67 (0.16–3.81) |
| *L/R* > 1 | 36 (13,9%) |
| Cavity volume | 1156 (70–7006) |
| Overall volume | 2240 (592–8537) |
| Cavity volume/liver volume ratio > 1 | 173 (62.91%) |
| Anteroposterior (AP) distance | 14 (7.6–24.3) |
| Side-to-side (SS) distance | 26.8 (19.2–32.3) |
| Right anteroposteriorior (RAP) vertical distance | 19.3 (10–28.5) |
| Portal vein diameter | 15.8 (7.0–49.0) |
| Splenic diameter | 14.1 (7.7–24.7) |
| Splenomegaly | 175 |
| Massive splenomegaly | 125 |
| Portosystemic shunts | 171 (62.1%) |
| Ombilical | 53 |
| Splenoparietal | 11 |
| Splenosystemic direct (splenorenal, mesneterico-caval, mesentericoilaic) | 44 |
| Gastric and/or oesophageal varices | 64 |
| TIPS | 18 |
| More than 1 shunt | 56 (32,7%) |
| Severe portal hypertension | 55 (20.1%) |
| Psoas muscle area | 1553 (445–3472) |
| Female | 1277 ± 409.0 |
| Male | 1768 ± 620.0 |
| Sarcopenia | 131 (47.6%) |

patients (67.2%) with a median CV of 1156 ml, and the space segment around the liver was ≥ 1000 ml in 116/185 patients (62.7%). The median OV was therefore 2240 ml on an average. The ratio between the cavity and the total liver volumes (CV/LV) was ≥ 1 in 173 patients (62, 91%) and < 0.5 in 74 patients (26.9%). No differences in median overall volume and liver weight among patients with alcoholic cirrhosis or other cirrhosis etiologies were found.

## Correlation between liver and cavity volumes with clinical and anthropometric data

Linear regression analysis showed that LV increased linearly with body weight ($r = 0.30$; $p < 0.00001$), height ($r = 0.20$; $p = 0.0005$), BMI ($r = 0.13$; $p = 0.03$), BSAd ($r = 0.31$; $p < 0.00001$), right anteroposterior diameter ($r = 0.14$; $p = 0.01$), side-to-side distance ($r = 0.17$; $p = 0.003$), portal vein and splenic diameters ($r = 0.11$; $p = 0.04$ and $r = 0.15$; $p = 0.01$, respectively). Liver volume decreased linearly with age and number of portosystemic shunts ($r = -0.14$; $p = 0.01$). Liver volume was also greater in subjects with

BMI > 30. (1826.0 ± 846.9 vs 1608 ± 687.5; $p = 0.02$). Cavity volume linearly increased with body weight ($r = 0.53$; $p = 0.04$), height ($r = 0.21$; $p = 0.003$), BMI ($r = 0.12$; $p = 0.09$), RAP ($r = 0.23$; $p = 0.001$), ascites ($p = 0.44$; $p < 0.00001$). Overall volume then linearly increased with body weight ($r = 0.16$; $p = 0.007$), height($r = 0.26$; $p = 0.00001$), BSA-d ($r = 0.22$; $p = 0.0001$), right anteroposterior diameter ($r = 0.29$; $p = 0.000001$), side-to-side diameter ($r = 0.17$; $p = 0.003$), ascites ($r = 0.30$; $p < 0.00001$), MELD score ($r = 0.15$; $p = 0.008$) and decreased with number of portosystemic shunts ($r = -0.17$; $p = 0.003$).

## Differences in volumetric and anthropometric data according to gender

Comparison of the different liver and anthropometric data showed that female patients ($n = 77$) compared with males ($n = 198$) had statistically significant lower body weight (74 ± 16 versus 83 ± 17; $p < 0.00001$), lower body height (161.4 ± 6.7 versus 175.5 ± 7.1; $p < 0.00001$), lower RAP (17 ± 2.3 vs 19 ± 2.3; $p < 0.0001$), lower AP distance (12.7 ± 2.4 vs 14.7 ± 2.4; $p < 0.0001$), lower SS distance (24.6 ± 2.0 vs 27.5 ± 2.1; $p < 0.0001$) and lower BSA-d (1.7 ± 0.18 vs 1.9 ± 0.20; $p < 0.0001$).

Female and male have however similar BMI (28.3 ± 6.0 vs 27.2 ± 6.2; $p = 0.19$).

Female patients had also statistically significant lower LW (1267 ± 449 vs 1487 ± 601; $p = 0.003$), and volume of the right liver (1006.0 ± 467 vs 875 ± 484; $p = 0.03$) but the overall liver volume (1550 ± 784 vs 1719 ± 721; $p = 0.09$) and volume of the left liver (614 ± 331 vs 669 ± 345; $p = 0.23$) were comparable. Overall the median cavity volume was larger in male (1593 ± 1412 vs 860 ± 767; $p < 0.0001$) such as the overall volume (2732 ± 1411 vs 2090 ± 963; $p = 0.0003$) despite lower median MELD score in males (24 ± 11 vs 28 ± 10.8; $p = 0.01$) and similar rate of ascites, severe portal hypertension, splenomegaly. Female patients had lower main portal vein diameter (14.9 ± 3.7 vs 16.2 ± 4.1; $p = 0.01$), lower longitudinal spleen diameter (13.8 ± 3.6 vs 14.6 ± 3.1; $p = 0.07$), lower PMA (1277 ± 409 vs 1768 ± 620; $p < 0.001$) and were more frequently sarcopenic (68% vs 39.3%; $p < 0.0001$).

## Differences in volumetric and anthropometric data according to MELD scores

Comparison of the different liver and anthropometric data showed that patients with MELD scores ≥ 25 ($n = 135$) compared with patients < 25 ($n = 140$) were more frequently female showed comparable BH, BW, and BMI but lower RAP, AP, and SS distances with similar BSA-d (1.9 ± 0.21 vs 1.9 ± 0.2; $p = 0.25$). Patients with MELD scores ≥ 25 also had similar LW, LV, and volumes of right and left liver

compared with those with MELD scores < 25. Overall, the median CV was similar in patients with MELD scores ≥ 25 and < 25 but the OV was larger in patients with MELD scores > 25 (2770 ± 1315 vs 2327 ± 1315; $p = 0.005$) because of larger proportion of patients having CV > 1 L (53% vs 30%; $p = 0.0001$) due to ascites (68.5 vs 36%; $p < 0.0001$). Patients with MELD scores ≥ 25 were more frequently sarcopenic.

## Differences according to BMI in volumetric and anthropometric data

Comparison of the different liver and anthropometric data showed that patients with BMI values > 30 ($n = 80$) compared with BMI < 30 ($n = 195$) had greater LV and higher volume of the right liver (1103.4 ± 566 vs 915 ± 421; $p = 0.001$) but comparable volume of the left liver (687.4 ± 352 vs 640.5 ± 337.9; $p = 0.63$). Patients with BMI > 30 ($n = 80$) had similar cavity volume (1212 ± 1058 vs 1461 ± 1391; $p = 0.24$) and overall volume (2506 ± 1141 vs 2572 ± 1404; $p = 0.70$) but greater RAP (20 ± 2.6 vs 18.9 ± 2.4; $p = 0.001$), AP distance (14.3 ± 2.6 vs 13.9 ± 2.5; $p = 0.01$), similar SS distance (27.1 ± 2.5 vs 26.6 ± 2.3; $p = 010$) but higher BSA-d (2.1 ± 0.2 vs 1.8 ± 0.1; $p < 0.0001$) and albumin level (28.1 ± 5.6 vs 29.07 ± 77) There were no differences in age,

gender, platelet, bilirubin, ascites, sarcopenia, and porto-systemic shunts.

## Prediction of the liver volume in cirrhotic patients using formula based on anthropometrics

We compared the expected and observed liver volumes in cirrhotic patients using the 17 anthropometric-based formulas. The Hashimoto formula (961.3 × BSA_d-404.8) had the lowest median percentage error (21.7%) as shown in Fig. 2. Using this formula, the LV of cirrhotic patients was underestimated with a margin of error ≥ 20% in 29.4% (81/275) and overestimated with a margin of error ≥ 20% in 22.5% (62/275) of individuals. Multivariate analysis found that BSA-d, (OR = 1.27, CI95% = 1.10–1.46; $p = 0.0007$), age (OR = 0.85, CI95% = 0.74–0.98; $p = 0.02$), portosystemic shunts (OR = 0.68, CI95% = 0.51–0.91; $p = 0.009$) and massive splenomegaly (OR = 1.43, CI95% = 1.08–1.89; $p = 0.01$) were independent factors associated with LV variations.

## Analysis of factors influencing cavity and \overall volumes for implanting a liver graft in cirrhotic patients

In multivariate analysis, predictive factors influencing a cavity volume ≥ 1 L were ascites large direct portosystemic
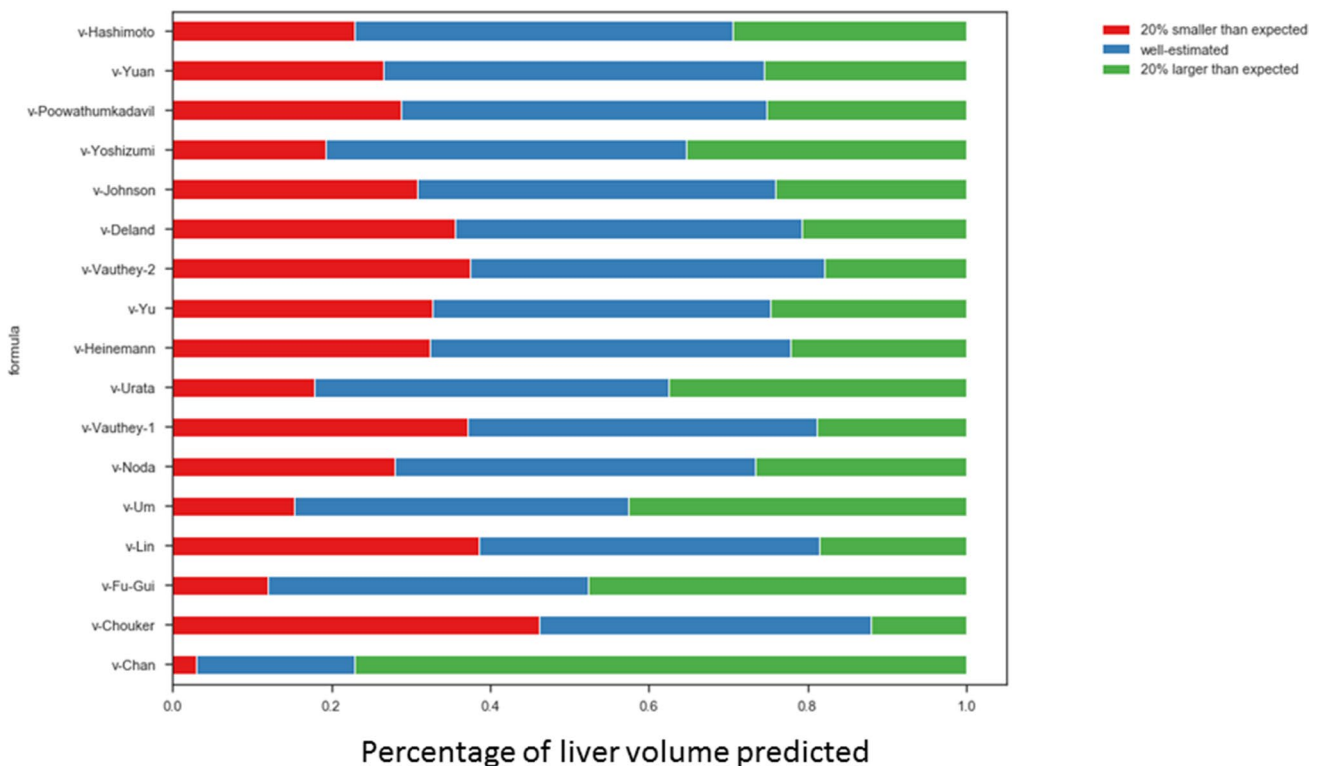


Fig. 2 Predictive value of different formulas in terms of percentage of predicted LV

shunt, right anteroposterior diameter values, and MELD scores. A cavity volume ≥ 1 L was found in patients having statistically significant higher MELD scores and higher ascites rates but lower prothrombin levels and platelet counts. Those patients having cavity volume > 1L also had statistically significant lower liver weight, liver volume, right liver volume, and psoas muscle area but higher RAP distances (Table 4). When using the Hashimoto formula alone for predicting the overall volume in the entire population for a virtual matching compared to the observed overall volume, 49 (17%) patients had an OV inferior to the predicted volume. Independent factors influencing the OV were the number of portosystemic shunts, the right anteroposterior diameter values, MELD > 25, albumin values, and BMI > 30 as shown in Table 5. The 49 identified patients had comparable RAP, SS, AP, and BH values but higher BMI (29.3 vs 27.1; $p = 0.03$) and BW (86.2 vs 80.0; $p = 0.02$) compared with the rest of the population. They also had higher values of Albumin and platelet counts but showed lower bilirubin levels

and MELD scores (21.0 vs 26.1; $p = 0.01$). Those patients had more portosystemic shunt (81.6% vs 57.9; $p = 0001$), more frequently more than one shunt, and more direct portosystemic shunt of large caliber. (30 vs 12%; $p = 0.004$). They also had less ascites (30% vs 57%; $p = 0.0008$).

## Discussion

Matching of anthropometric parameters is routinely used in LT-based on brain-dead donors. In contrast to living donors, a pre-operative volumetric liver assessment is rarely needed since a whole liver is thought to be always sufficient in terms of function and volume for an adult individual. LT surgeons usually base their selection of a given donor on a first "rapid" matching based on anthropometrics. This virtual matching is sometimes not reliable because of variations in LV or abdominal cavity leading to the "large-for-size syndrome" [3, 5]. The current study is the first to examine

**Table 4** Comparison of patients according to the presence of cavity ≥ 1 L

| | Cavity volume ≥ 1L (n = 116) | Cavity volume < 1L (n = 159) | p |
|---|---|---|---|
| Age | 57.2 ± 9.1 | 55.6 ± 10.5 | 0.15 |
| Male gender | 89 (79%) | 109 (68%) | 0.17 |
| Albumin | 29.06 ± 6.1 | 29.4 ± 7.1 | 0.67 |
| Prothrombin time | 37.8 ± 17.3 | 52.57 ± 23.4 | < 0.0001 |
| Creatinin | 96.2 ± 58 | 86.2 ± 48.7 | 0.12 |
| Bilirubin | 187 ± 215 | 157 ± 197 | 0.23 |
| Platelet | 84.672 ± 54,122 | 100,242 ± 63,353 | 0.03 |
| MELD score | 29 ± 10 | 22 ± 11 | < 0.0001 |
| Weigth | 81 ± 16 | 80 ± 18 | 0.60 |
| Heigth | 172.1 ± 8.9 | 171 ± 9.8 | 0.42 |
| BMI | 28.0 ± 7.2 | 27 ± 5.4 | 0.26 |
| BSA-d | 1.94 ± 0.19 | 1.92 ± 0.24 | 0.47 |
| Liver weight | 1288 ± 420 | 1527 ± 642 | 0.0005 |
| Liver volume (LV) | 1477 ± 493.6 | 1813 ± 854 | 0.0002 |
| Right liver | 813.7 ± 323 | 1070 ± 539 | < 0.0001 |
| Left liver | 601.7 ± 269.7 | 692.4 ± 383 | 0.02 |
| *L/R* ratio | 0.79 ± 0.46 | 0.69 ± 0.29 | 0.02 |
| Anteroposterior (AP) distance | 14.5 ± 2.3 | 14.02 ± 2.7 | 0.12 |
| Side-to-side (SS) distance | 26.96 ± 2.5 | 26.6 ± 2.35 | 0.48 |
| Right anteroposterior (RAP) distance | 19.80 ± 2.28 | 18.8 ± 2.68 | 0.001 |
| Portal vein diameter | 15.6 ± 3.5 | 16.0 ± 4.4 | 0.39 |
| Splenic diameter | 14.18 ± 3.2 | 14.5 ± 3.4 | 0.37 |
| Splenomegaly | 75 (65%) | 100 (63%) | 0.79 |
| Spontaneous Portosystemic shunts | 68 (58,6%) | 103 (64,5%) | 0.38 |
| > 1 Shunt portosystemic shunts | 21 (18%) | 35 (22%) | 0.45 |
| Ascites | 95 (81.9%) | 50 (31.4%) | < 0.0001 |
| Severe portal hypertension | 37 (32.1%) | 18 (11.3%) | < 0.0001 |
| Psoas muscle area | 1530 ± 523 | 1703 ± 652 | 0.02 |
| Sarcopenia | 60 (51%) | 71 (44%) | 0.27 |

**Table 5** Univariate and multivariate analyses of factors predicting the overall volume for implanting a graft in cirrhotic patients

| Variables | Univariate | | | | | | Multivariate | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Beta | SE | Wald | OR | CI95% | p | Beta | SE | Wald | OR | CI95% | p |
| Age | 0.004 | 0.01 | 0.30 | 1.00 | (0.97–1.03) | 0.75 | | | | | | |
| Ascites | − 1.12 | 0.33 | − 3.32 | 0.33 | (0.16–0.63) | 0.0008 | | | | | | |
| Portosystemic shunts | 1.14 | 0.39 | 2.92 | 3.15 | (1.46–6.81) | 0.003 | | | | | | |
| RAP | − 0.10 | 0.06 | − 1.73 | 0.89 | (0.79–1.01) | 0.08 | − 0.26 | 0.07 | − 3.58 | 0.76 | (0.66–0.88) | 0.0003 |
| SS | − 0.08 | 0.06 | − 1.28 | 0.92 | (0.81–1.04) | 0.19 | | | | | | |
| BH | − 0.007 | 0.01 | − 0.45 | 0.99 | (0.96–1.02) | 0.64 | | | | | | |
| BW | 0.01 | 0.008 | 2.17 | 1.01 | (1.00–1.03) | 0.02 | | | | | | |
| Albumin | − 0.06 | 0.02 | − 2.64 | 0.93 | (0.88–0.98) | 0.008 | − 0.07 | 0.03 | − 2.33 | 0.93 | (0.87–0.98) | 0.01 |
| Portal vein diameter | − 0.03 | 0.04 | − 0.80 | 0.96 | (0.89–1.05) | 0.42 | | | | | | |
| Spleen diameter | − 0.005 | 0.04 | − 0.12 | 0.99 | (0.90–1.90) | 0.90 | | | | | | |
| BMI > 30 | 1.25 | 0.32 | 3.82 | 3.51 | (1.84–6.70) | 0.0001 | 1.76 | 0.39 | 4.49 | 5.86 | (2.71–12.68) | 0.00007 |
| MELD > 25 | − 0.03 | 0.01 | − 2.33 | 0.96 | (0.94–0.99) | 0.01 | − 1.57 | 0.40 | − 3.91 | 0.20 | (0.09–0.45) | 0.00009 |
| Gender | − 0.48 | 0.33 | − 1.45 | 0.61 | (0.32–1.18) | 0.14 | | | | | | |
| Sarcopenia | − 0.15 | 0.31 | − 0.47 | 0.85 | (0.46–1.60) | 0.63 | | | | | | |
| Number of portosystemic shunt | 0.64 | 0.20 | 3.21 | 1.90 | (1.28–2.82) | 0.001 | 0.65 | 0.23 | 2.80 | 1.92 | (1.12–3.04) | 0.005 |
| Diabetes | − 0.03 | 0.04 | − 0.80 | 0.96 | (0.89–1.05) | 0.42 | | | | | | |
| BSA-d | 1.10 | 0.70 | 1.56 | 3.01 | (0.75–1.96) | 0.11 | | | | | | |
| Age > 65 | 0.05 | 0.32 | 0.15 | 1.05 | (0.55–1.99) | 0.87 | | | | | | |

factors influencing the overall space using a CT volumetric-based approach. It was demonstrated that in up to 17% of potential cirrhotic recipients, simple anthropometric characteristics might not be enough to predict the final place available for implanting a liver graft, which is actually smaller than expected. We identified several additional anthropometric characteristics (right anteroposterior diameter), clinical (presence and number of large portosystemic shunts), and biological (MELD, albumin) factors that could be helpful in the process of matching to avoid potential mismatching.

Differences in anthropometric and liver characteristics between genders exist [3, 19, 32]. The current study confirmed that female cirrhotic patients showed consistent reductions in weight, height, and abdominal diameters compared with male. Consequently, and despite similar rates of final ascites, the overall volume available for liver implantation was inferior in female because of these reductions (described above). Interestingly, the liver volumes between the two genders were comparable. This finding was probably related to the greater volume of left liver in female, indicating a more pronounced development in the side-to-side rather than the anteroposterior. The combination of a male donor in a female recipient has been associated with an increased rate of extreme large-for-size syndrome [3, 5], most probably because of these differences in abdominal cavity measurements (RAP, SS) and LV (left and right lobes) as observed in our study.

We have chosen to consider the final available place as the sum of liver and cavity volumes since both parameters determine the overall available volume. Those two measures showed variations that were dependent on different factors. The variation in LV in our cohort was mostly dependent on age and portal hypertension severity. In fact, a linear correlation between reduced volume and increased age as seen in healthy liver was found [19]. The decrease in LV was also linearly and independently correlated with the severity of portal hypertension in term of presence and number of portosystemic shunts. Large spontaneous portosystemic shunts develop because of a progressive increase in portal pressure; in our series (excluding 18 TIPS) 55.6% (153/275) of our patients had spontaneous portosystemic shunts, and 56 presented with more than one shunt. The presence of SPSS, their caliber, and the number has been correlated to an increase in complications in cirrhotic patients and a decrease in survival independent of the MELD score values [14, 33]. In animal models, different types of portocaval shunts lead to various degrees of liver atrophy directly related to reduced portal blood flow and consequent cellular apoptosis [34, 35]. Indeed, the presence, type, and number of portosystemic shunts were identified as independent prognostic factors that influenced LV, CV, and OV in our study. The presence of multiple portosystemic and large direct portosystemic shunts (splenorenal, splenoiliac, TIPS) in direct communication with the portal and caval system led to major liver atrophy

thus explaining the less than expected OV using formulas based on anthropometric characteristics.

CV was dependent on both the severity of liver disease and anthropometric characteristics. Greater CV was present in patients with ascites and larger right anteroposterior volume. Although female and male patients had a similar rate of ascites, male patients had greater CV probably because of differences in anthropometric characteristics. The right anteroposterior distance was in fact identified as an independent factor related to both CV and OV. Allard et al. recently described a graft weight/RAP ratio as a simple model for predicting the occurrence of extreme large-for-size syndrome highlighting that the presence of ascites is not always protective to the occurrence of mismatches [3]. Even though female and male patients had similar rates of ascites and similar LVs, CVs were significantly higher in male patients, most probably because of increased RAP values.

BMI can be unreliable alone for matching based on anthropometric characteristics. In our study, males and females had similar BMI values but different anthropometric and OV values. However, BMI > 30 was associated with increased OVs. This phenomenon was mostly due to two factors: (1) the variable effect of edema and ascites on patients with BMI < 30 and (2) increased right liver volume and RAP values in patients with BMI > 30. The linear relationship in healthy subjects between liver volume and BMI should be considered when selecting obese donors or recipients [32].

In our study, a MELD score > 25 was identified as a factor associated with increased available OV. Goumard et al. reported a decrease in LV in patients with MELD score > 15 [12]. In the current study, the MELD score was not associated with inferior LV or with increased CV but rather with increased OV. This finding was probably because of the greater quantity of ascites in patients with higher MELD scores and increased rates of sarcopenia. Both sarcopenia and extensive ascites seldom coexist and usually are expressions of more advanced liver disease associated with poor nutritional state and hypoalbuminemia, which could predict an increase in compliance of the abdominal cavity [36]. In fact, high albumin levels were less likely associated with an increase in OV in our study.

Donor-recipient matching is a complex multi-factorial process in which anthropometric represents only one of the possible levels of matching. The present study showed that variability in volume of the cirrhotic liver is even more important than that found in healthy donors [11, 37]. Moreover, anthropometric characteristics vary highly between the two genders even in presence of comparable BMI. The knowledge of factors identified by our study should always be combined with donor information which finally can determine the acceptance of a given donor for a given recipient. In this regard, one could imagine that liver and cavity volumetric assessment of the recipient could be helpful in some patients (i.e. low BMI female cirrhotic high meld) in which the fear of anthropometric-mismatch seems more a frequent [38].

The current study presents several limitations which deserve comments. First, its retrospective nature with only patients undergoing LT constituting the study population presented a noteworthy selection bias toward high MELD scores. However, the chosen setting, heterogeneity of cases treated, and the high number of patients formed the strengths of the current study.

Second, the lapse of time from CT scan performance and LT (mean of two months with a median of four) could have introduced additional limitations to our finding. This finding could be true for biological values that could have changed over time, but in no way could such an interval of time modified anthropometric characteristics of the abdominal cavity (RAP, AP, and SS) and presence of portosystemic shunts. Third, we could not develop a clinical tool able to predict the donor-recipient mismatch. We however highlighted factors associated with an increased chance of lower than expected liver volume while using simple matching based on anthropometric parameters. A prospective study comparing the prediction of the overall volume based on anthropometric only with prediction integrating factors identified could add more value to our results.

## Conclusions

Donor-to-recipient matching based on anthropometric characteristics using predictive formula could lead to unexpected mismatching. Based on CT-based volumetric assessment of the abdominal cavity and liver we identified additional anthropometric (right anteroposterior diameter, BMI > 30), clinical (presence of portosystemic shunts), and biological (MELD, albumin) factors influencing the final space available for liver graft implantation which might be useful during the donor-recipient matching. These factors will need a prospective validation in a larger setting.

## Declarations

**Conflict of interest** Pietro Addeo, Benoit Naegel, Pierre De Mathelin, Chloe Paul, François Faitot, Caroline Schaaf, Alfonso Terrone, Lawrence Serfaty, Philippe Bachellier, Vincent Noblet declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical.

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