Surgery 166 (2019) 247–253

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg

# Accuracy of estimated total liver volume formulas before liver resection

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## ARTICLE INFO

*Article history:*
Accepted 6 May 2019
Available online 14 June 2019

## ABSTRACT

*Background:* Future remnant liver volume is used to predict the risk for liver failure in patients who will undergo major liver resection. Formulas to estimate total liver volume based on biometric data are widely used to calculate future remnant liver volume; however, it remains unclear which formula is most accurate. This study evaluated published estimate total liver volume formulas to determine which formula best predicts the actual future remnant liver volume based on measurements in a large number of patients who underwent associating liver partition and portal vein ligation for staged hepatectomy surgery.
*Methods:* All patients with complete liver volume data in the associating liver partition and portal vein ligation for staged hepatectomy registry were included in this study. Estimate total liver volume and estimated future remnant liver volume were calculated for 16 published formulas. The median over- or underestimation compared with actual measured volumes were determined for estimate total liver volume and future remnant liver volume. The proportion of patients with an under- or overestimated future remnant liver volume for each formula were compared with each other using a 25% cut-off for each formula.
*Results:* Among 529 studied patients, the formulas ranged from a 19% underestimation to a 63% overestimation of estimate total liver volume. Estimation of future remnant liver volume lead to a 10% underestimation to a 5% overestimation among the formulas. Of all studied formulas, the Vauthey1 formula was the most accurate, generating underestimation of future remnant liver volume in 20% and overestimation of future remnant liver volume in 6% of patients.
*Conclusion:* Validation of 16 published total liver volume formulas in a multicenter international cohort of 529 patients that underwent staged hepatectomy revealed that the Vauthey formula (estimate total liver volume = 18.51 × body weight + 191.8) provides the most accurate prediction of the actual future remnant liver volume.


Major liver resection should be performed only when the planned resection leaves behind sufficient remnant liver function for recovery of the patient from surgery.[1,2] Although preoperative assessment of remnant liver function using regional liver function tests like mebrofenin and albumin scintigraphy is gaining interest,

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https://doi.org/10.1016/j.surg.2019.05.003

assessment of remnant liver volume remains most widely used method to assess risk of posthepatectomy liver failure and small-for-size syndrome, likely owing to the wide availability of volumetry.[1,3,4] Most clinicians calculate liver volume by volumetry programs based on 3-dimensional reconstruction on computed tomography (CT) imaging, which has been shown to correlate well with actual liver size.[4] The proportion of future remnant to total liver size (FLRV) is the most frequently used metric.

Total liver size, however, has variation among individual patients; tumor volume is a confounder and FLRV assessment is faster when total liver volume does not have to be determined volumetrically but can be calculated based on biometric data. Based on large numbers of patients, estimated total liver volumes (eTLV) based on biometrics that predict metabolic demands such as weight, height, or body surface area (BSA) have been proposed, specifically to help with size matching of grafts in liver transplantation,[5] but also before liver resection.[6] In liver resection, volume estimation based on parameters of metabolic demand has the additional advantage that nonfunctional tumor masses in the liver, dilated bile ducts or occluded vasculature have no impact.[6–20] The proportion of measured future remnant liver volume over standardized total volume could be a more reliable metrics to guide the decision to proceed to liver resection because it only takes presumably functional tissue into account.

Based on different patient cohorts in centers across the world, several different estimated liver volume formulas were generated. Considering the differences in clinical parameters, such as weight and length across continents and races, it remains debated which formula is the best.[21] It is important to consider that the estimation of liver volume could lead to over- or underestimation of liver volume and therefore an under- or overestimated of risk of liver failure after resection or transplantation. Few studies have set out to validate published formulas with existing volumetry.

This study aims to compare existing formulas with measured volumes in a large unselected cohort of patients from across the world. The database was developed in 2011 to record outcomes of the novel associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) procedure, but includes detailed assessments of biometrics and measured liver volumes. The main end point for this study is the difference between calculated and measured actual liver volumes.

## Methods

All patients with complete data on calculated total liver volume and future remnant liver volume using CT-volumetry and body weight and height in the ALPPS registry were included, using an export from November 9, 2017. The ALPPS registry is described in detail elsewhere.[22] Ethical approval for the data registry was obtained from the Cantonal Ethical Committee Zurich and project was registered at ClinicalTrials.gov (NCT01924741).

Variables were calculated from biometric data and included body mass index and BSA. To calculate BSA, either the Mosteller[23] (BSA $(m^2) = (\text{height (cm)} \times \text{weight (kg)}/3600)^{½}$) or the BuBois[24] formula (BSA $(m^2) = 0.20247 \times \text{height(m)}^{0.725} \times \text{weight(kg)}^{0.425}$) was used, depending on the respective original publication (Supplemental Table I). Estimated TLV formulas were applied to individual patients based on the formula presented in respective original publication (Supplemental Table I). Measured FLRV was calculated using the formula: FLRV = (measured FLR volume/measured TLV) × 100%. Estimated FLRV was calculated using the same formula, but using the respective estimated TLV value. All measured liver volumes were clean liver volumes with the tumor volumes subtracted. Estimated volumes were generated using the software available in each individual center according to local protocols on preoperative CT or magnetic resonance scans with all tumor volumes excluded.

Correlations of measured TLV and estimated TLVs and measured FLRV with estimated FLRVs were tested using Spearman's correlation coefficient. The proportion of patients with an estimated TLV within 10% of the measured TLV was determined for each formula. In addition, the proportion of patients with an estimated FLRV within 5% above or below the measured FLRV was determined for each formula as well. The 5% cut-off was chosen because 20%, 25%, and 30% are reported most in literature as cut-off to proceed to resection and a 5% difference in a patients' FLRV is likely to affect clinical practice. The proportion of patients with an estimated FLRV above 25% and a calculated FLRV below 25% was determined for each formula because this could result in the lack of a possibly indicated preoperative regenerative liver surgery maneuver like portal vein embolization (PVE). Alternatively, the proportion of patients with an estimated FLRV below 25% and a calculated FLRV above 25% was determined, which may result in the unnecessary performance of a regenerative liver surgery maneuver. Because an incorrectly not applied regenerative procedure (estimated FLRV above 25% and measures below 25%) is considered more dangerous compared to an underestimated FLRV, this was reflected in a formula score to evaluate the best formula. The overestimation of FLRV with the 25% cut-off provides 3 points and the overestimation 1 point, correct estimation provides 0 points. This score was calculated for all formulas to determine the best formula.

For parametric data, mean and standard deviation are reported, for nonparametric data median and interquartile range are reported. Kolmogoroff-Smirnov tests were used to evaluate distribution. Correlations were testes using Spearman's correlation coefficient. Differences between categorical variables were analyzed using $\chi^2$ tests. Statistical analyses were performed using SPSS (IBM, Chicago, IL) and figures were generated using Graphpad Prism (Graphpad Inc., La Jolla, CA).

## Results

Among 1047 patients in the ALPPS registry collected from 2011 to 2017, 529 had sufficient biometric and volumetry data for inclusion in the study. Baseline characteristics of the patients are shown in Table I.

**Table I**
Patient characteristics

| Cohort | N = 529 |
|---|---|
| Age, median (IQR) | 59 (51–67) |
| Male, *n* (%) | 308 (58) |
| Race, *n* (%) | (*n* = 527) |
| Caucasian | 450 (85) |
| Asian | 43 (8) |
| Black | 8 (2) |
| Other | 26 (5) |
| Continent of inclusion, *n* (%) | (*n* = 527) |
| Europe | 410 (78) |
| North America | 18 (3) |
| South America | 46 (9) |
| Asia | 46 (9) |
| Africa | 7 (1) |
| Length, cm, median (IQR) | 169 (162–176) |
| Weight, cm, median (IQR) | 72 (63–83) |
| BMI, kg/m$^2$, median (IQR) | 24.9 (22.7–27.8) |
| BSA, m$^2$, median (IQR) | |
| Mosteller | 1.84 (1.69–2.00) |
| Du Bois | 1.83 (1.68–1.99) |
| Measured clean TLV, mL, median (IQR) | 1396 (1131–1661) |

*IQR*, interquartile range.

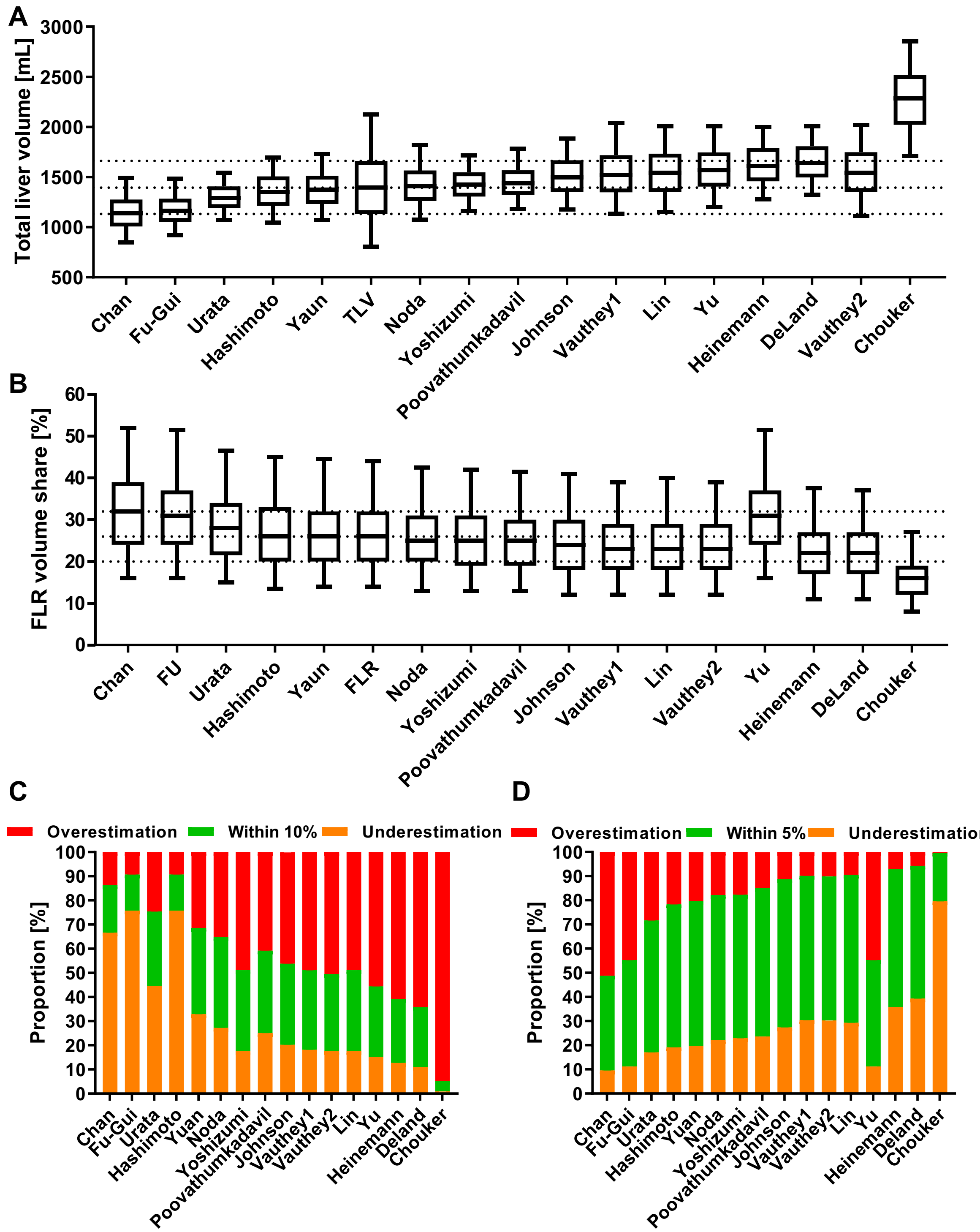


**Fig 1.** (*A*) For all eTLV formulas, medians, IQRs and 95% confidence intervals are plotted. The dotted line corresponds to the median and IQRs of the measured total liver volume. (*B*) For all eFLR formulas, medians, IQRs, and 95% confidence intervals are plotted. The dotted line corresponds to the median and IQRs of the measured future remnant liver volume share. (*C*) Proportion of cases in which each formula either over- or underestimates by a relative 10% or correctly estimates the measured TLV. (*D*) Proportion of cases in which each formula either over- or underestimates by an absolute 5% or correctly estimates the measured FLR.

For TLV formulas, medians, IQRs, and 95% confidence intervals are plotted in Fig 1, *A*. All formulas correlated well with the measured TLV with only marginal differences in Spearman's correlation coefficients (Table II). However, there were considerable median differences between estimated and measured TLV for individual formulas (−19% to 63%; Table II). The majority of formulas overestimate TLV which is demonstrated in Fig 1, *C*. The overall proportion of patients with a predicted TLV within 10% of the measured liver volume was only modest for all formulas, with the best result (38%) achieved by the Noda formula (Table II).

Figure 1 and Table III display estimated and measured FLRV and TLV. The formulas are more accurate for estimation of FLR than TLV,

**Table II**
Correlation between estimated and measured TLV and proportion of eTLV within 10% of measured TLV for each formula

| TLV | Spearman correlation | | Median difference | Proportion of eTLV within 10% of measured TLV |
|---|---|---|---|---|
| | Coefficient | *P* value | Relative % | |
| Chan et al[8] | 0.470 | < .001 | −19 (−28–4) | 19% |
| Fu-Gui et al[9] | 0.472 | < .001 | −16 (−27–1) | 22% |
| Urata et al[10] | 0.476 | < .001 | −7 (−20–9) | 31%* |
| Hashimoto et al[11] | 0.476 | < .001 | −3 (−16–13) | 37%* |
| Yuan et al[12] | 0.464 | < .001 | −1 (−15–15) | 36%* |
| Noda et al[13] | 0.472 | < .001 | 1 (−12–19) | 38%* |
| Yoshizumi et al[14] | 0.479 | < .001 | 3 (−12–20) | 34% |
| Poovathumkadavil[15] | 0.472 | < .001 | 4 (−10–23) | 34%* |
| Johnson et al[7] | 0.486 | < .001 | 7 (−7–25) | 34%* |
| Vauthey1[6] | 0.472 | < .001 | 9 (−4–30) | 33%* |
| Vauthey2[6] | 0.479 | < .001 | 9 (−3–30) | 34%* |
| Lin[16] | 0.472 | < .001 | 10 (−4–31) | 32%* |
| Yu et al[17] | 0.476 | < .001 | 13 (−1–33) | 29% |
| Heinemann et al[18] | 0.476 | < .001 | 15 (0–35) | 27% |
| Deland et al[19] | 0.476 | < .001 | 18 (2–39) | 25% |
| Chouker et al[20] | 0.401 | < .001 | 63 (39–93) | 4% |

* Best performance.

as expected, because FLR is generally tumor-free, whereas TLV may include tumors and diseased liver. The correlation coefficients are higher (0.652–0.693), and the median differences between estimated and measured are smaller (−10% to −5%) for estimation of FLRV than for TLV.

Several formulas predict the FLRV within 5% of the measured FLRV in the majority (>50%) of patients (Table III, the best performances are denoted with asterisks), but under- and overestimation persists (Fig 1, *D*). The formulas with the highest accuracy to predict FLRV (Poovathumkadavil and Lin) were plotted against the measured FLRV in Fig 2, *A*, which illustrated the estimation in both formulas is more accurate when FLRV is low, compared with when FLRV is higher. When using 25% FLRV as a cut-off, the prediction of estimated FLR was more accurate in the lower volumes for all formulas (Table III).

Table III also shows that the Vauthey2 formula is the most accurate to predict estimated FLRV with 73% prediction within 5% of measured volume for FLRs <30%.

To quantify the potential impact of incorrect estimation of FLRV in the range that most authors recommend PVE or ALPPS (preoperative estimate of <25%–30% FLRV), we examined the effect of a 25% FLRV cut-off (Table IV). The table illustrates that most formulas will lead to considerable over- or underuse of regenerative liver volume augmentation. Given that a volume measurement that overestimates FLRV would lead to surgery with a higher risk of the significant complication(s) associated with posthepatectomy liver failure, whereas underestimation of the volume cut-off would lead to an unnecessary but a less dangerous overapplication of PVE, the formulas were compared using a formula score. The formula score weights incorrect volumetry leading to surgery with an inadequate volume 3 points, whereas volume underestimation leading to unnecessary PVE was weighted 1 point. The formula score demonstrates that the Vauthey formulas are the safest TLV estimation formulas, that is, lead to the fewest operations in patients with actually inadequate liver remnants, and to the fewest unnecessary PVEs. Although the Vauthey formulas both performed well, the Vauthey1 formula was slightly more accurate.

## Discussion

The present study shows that using formulas to estimate TLV will predict the FLRV within 5% of the measured FLRV in ≤61% of patients and that the accuracy is ≤78% in the range where regenerative liver surgery is usually needed (ie, the patients with <25%

**Table III**
Correlation between estimated and measured FLR and proportion of eFLR within 5% of measured FLR, also stratified for measured FLRs <25% and measured FLRs >25%

| FLR | Spearman correlation | | Median difference | Proportion within 5% | Estimated FLR within 5% | | *P* value |
|---|---|---|---|---|---|---|---|
| | Coefficient | *P* value | Absolute % | | Measured FLR < 25% | Measured FLR > 25% | |
| Chan et al[8] | 0.685 | < .001 | 5 (1–10) | 39% | 45% | 34% | < .001 |
| Fu-Gui et al[8] | 0.689 | < .001 | 4 (0–9) | 44% | 51% | 39% | < .001 |
| Urata et al[10] | 0.691 | < .001 | 2 (−2 to 6) | 55%* | 64%* | 47% | < .001 |
| Hashimoto et al[11] | 0.693 | < .001 | 1 (−3 to 5) | 59%* | 71%* | 50% | < .001 |
| Yuan et al[12] | 0.689 | < .001 | 0 (−3 to 4) | 60%* | 73%* | 50% | < .001 |
| Noda et al[13] | 0.688 | < .001 | 0 (−4 to 3) | 60%* | 74%* | 49% | < .001 |
| Yoshizumi et al[14] | 0.691 | < .001 | −1 (−4 to 3) | 59%* | 76%* | 46% | < .001 |
| Poovathumkadavil[15] | 0.690 | < .001 | −1 (−5 to 3) | 61%* | 77%* | 50% | < .001 |
| Johnson et al[7] | 0.652 | < .001 | −2 (−6 to 2) | 61%* | 76%* | 48% | < .001 |
| Vauthey1[6] | 0.686 | < .001 | −2 (−6 to 1) | 60%* | 78%* | 45% | < .001 |
| Vauthey2[6] | 0.689 | < .001 | −2 (−6 to 1) | 50%* | 78%* | 48% | < .001 |
| Lin[16] | 0.690 | < .001 | −2 (−6 to 1) | 61%* | 77%* | 46% | < .001 |
| Yu et al[17] | 0.689 | < .001 | 4 (0–9) | 44% | 51% | 39% | < .001 |
| Heinemann et al[18] | 0.693 | < .001 | 3 (−7 to 0) | 57%* | 78%* | 40% | < .001 |
| Deland et al[19] | 0.692 | < .001 | −4 (−8 to 1) | 55%* | 77%* | 37% | < .001 |
| Chouker et al[20] | 0.668 | < .001 | −10 (−14 to 6) | 20% | 34% | 9% | < .001 |

* Best performance.

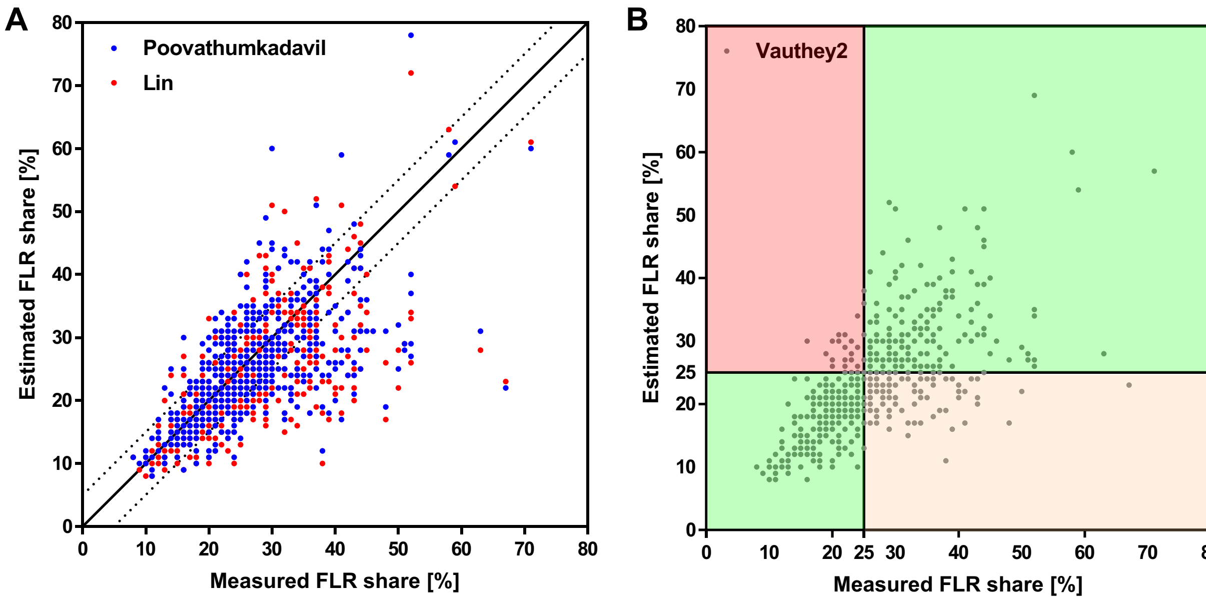


**Fig 2.** (*A*) Correlation of eFLR with measured FLR for the (blue) Poovathumkadavil and (red) Lin formulas. The dotted lines indicate the 5% under and overestimation barriers. (*B*) Correlation of eFLR with measured FLR for the (blue) Vauthey2 formula. Dots in the green square represent accurate predictions. Dots in de red square indicate incorrectly overestimated eFLR which would lead to incorrectly not performing a regenerative procedure. The dots in the orange square are incorrectly overestimation and would lead to an unnecessary regenerative procedure.

FLR). In contrast, under- and overestimation of estimated TLV is quite common. Using a score that emphasizes a minimal number of overestimations for patient safety, the standardized FLR formula by Vauthey et al (formula Vauthey1) performs best among 16 formulas and provides the most accurate volumetric information to surgeons planning major resection with or without PVE, PLV, or ALPPS.

It has been shown that assessment of liver volume using volume assessment on CT or magnetic resonance images correlates well with actual liver volume.[25,26] Several imaging software packages with manual operation or even semiautomatic or automatic volume calculations have been published[25,27,28] and are commercially available. A variety of factors contribute to the accuracy of functional volume assessment in imaging, for instance the in- or exclusion of hepatic blood vessels in the measurements.[29] Differences in CT scan slice thickness may lead to under- or overestimation of total liver volume.[30] Interobserver and intraobserver variability can lead to significant differences in manual volume assessment.[31] In patients undergoing resections, liver volume assessment has to exclude nonfunctional masses or dilated bile ducts. The exclusion of the masses volume or liver disease or dilated bile ducts from the liver volume assessment is cumbersome and laborious.[6]

Patient size and liver size are related, and liver volume is linked to liver function.[32] Thus, the principle of TLV volume estimation is

**Table IV**
Under and overestimation of future remnant liver volume using a 25% cut-off

| | Regenerative maneuver performed incorrectly | Incorrectly no regenerative maneuver performed | Formula score* |
|---|---|---|---|
| | Estimated <25% Measured ≥25% | Estimated ≥25% Measured <25% | |
| Chan et al[8] | 21 (4) | 111 (21) | 354 |
| Fu-Gui et al[9] | 22 (4) | 103 (19) | 331 |
| Urata et al[10] | 42 (8) | 70 (13) | 252 |
| Hashimoto et al[11] | 52 (10) | 58 (11) | 226 |
| Yuan et al[12] | 57 (11) | 54 (10) | 219 |
| Noda et al[13] | 69 (13) | 48 (9) | 213 |
| Yoshizumi et al[14] | 74 (14) | 49 (9) | 221 |
| Poovathumkadavil[15] | 86 (16) | 44 (8) | 218 |
| Johnson et al[7] | 100 (19) | 35 (7) | 205 |
| Vauthey1[6] | 106 (20) | 30 (6) | 196† |
| Vauthey2[6] | 108 (20) | 32 (6) | 204† |
| Lin[16] | 111 (21) | 32 (6) | 207 |
| Yu et al[17] | 22 (4) | 103 (19) | 331 |
| Heinemann et al[18] | 134 (25) | 24 (5) | 206 |
| Deland et al[19] | 146 (28) | 22 (4) | 212 |
| Chouker et al[20] | 254 (48) | 0 (0) | 254 |

* The formula score was generated by adding the amount of patient who incorrectly received a regenerative procedure based on the respective formula with a 25% cut-off to the patients who incorrectly did not underwent a regenerative procedure multiplied by 3.
† The lowest score indicates the best formula.

to provide a means to standardize the FLR volume to the patient to provide a consistent method of understanding the global functional reserve that will remain after major liver resection. This method overcomes limitations of measuring the intrinsic TLV in a patient that will undergo liver resection, measurement of a TLV containing tumors, underling liver disease or in some cases dilated bile ducts, which may alter the true or necessary TLV.[6] Using this method, only the FLR is directly measured; the FLR generally has no or few lesions and frequently no dilated bile ducts to contribute to measurement error. Indeed, many TLV formulas found in the literature were developed for estimation of liver volume before liver transplantation, where their utility is established to determine the safe volume needed to avoid small-for-size syndrome after liver transplantation. For at least 20 years, however, these formulas are used before major hepatectomy for a similar purpose: to preoperatively plan to assure an adequate liver volume postoperatively.[6,22,33,34] Pursuit of minimal risk for liver insufficiency and minimum risk for liver failure brought focus on the potential inaccuracies related to liver function prediction using estimated TLV. The present report shows that in at least 1 out of 4 patients, the predicted FLRV may be at least 5% too low or too high in the most reliable formula. This leads to overuse of FLR volume augmentation in patients with adequate volumes and underuse of preoperative portal diversion in patients with marginal volumes. In the example of the 25% cut-off for preoperative PVE as in the series studied herein, the use of the Vauthey2 formula would lead to the possibly unnecessary use of PVE in 108 out of 529 patients, although 32 may not undergo any regenerative preparation even though they should. In contrast, using the Johnson formula is unacceptable, and 133 out of 529 patients would incorrectly not undergo PVE. Whether these errors have clinical relevance, depends on how much weight is given to liver volumetry to start with and how relevant statistical cut-offs are in daily clinical practice.

Another alternative to measured FLRV or estimated FLRV is the liver remnant volume to body weight ratio (RLV:BWR), in which the remnant liver weight calculated as percentage of body weight. A ratio below 0.5% has been shown to correlate with adverse outcomes in an evaluation of a cohort of patients who underwent right trisectionectomy and all had relatively low remnant livers.[35] This metric also avoids the problem of nonfunctinonal masses and can be used in repeat hepatectomy, when total liver volume usually does not completely reach original liver volume.[35] How RLV-BWR relates to estimated and measured FLRV in a larger heterogeneous cohort remains to be established in future studies.

Although this report identified the Vauthey formula as most accurate for the use before major liver resection, a previous report that focused on the field of liver transplantation identified the Johnson and Poovathumkadavil as most useful. This discrepancy is likely caused by the relation to the remnant liver volume in the present report and strictly total liver volume analyses only in the previous report. Also, in this report an absolute proportion of estimated patients within 5% was chosen for the FLRV as opposed to the proportion of patient within a relative estimated TLV within 10% of measured TLV.

In recent years, the need for functional assessment of the remnant liver has gained interest and several centers have included quantitative assessment of liver function into daily practice.[36–43] This increased interest might be partly due to the initial enthusiasm over the rapid liver volume growth seen with the ALPPS technique, which has later been demonstrated to lack proportional functional gain.[44] Considering the liver volume is only a surrogate for liver function, and given that liver function may not be homogenous throughout the liver and can be compromised in case of parenchymal liver disease, quantitative functional assessment has been proposed as a complimentary and possibly a superior methodologic approach to prediction of postoperative liver failure.[1,37,44–46] Better methods of liver functional assessment, and methods that link volumetry and functional studies, will be of great interest in the future. However, liver volume assessment is still the clinical standard, and structural implementation of functional assessment requires additional validation studies and has several financial hurdles.

This study was not designed to correlate liver volume and posthepatectomy outcomes because it is based on a database of ALPPS, a complex regenerative procedure with an impact on liver function that is not well understood. Rather, these data assess and validate the accuracy of TLV formulas using measured FLRV as a reference. The clinical implications of volume estimations are an important next stage and future studies in extended hepatectomies should simultaneously correlate measured FLRV, estimated FLRVs, and remnant liver-to-body weight ratio to liver failure incidence in large cohorts. A limitation of the present study is that the ALPPS registry cohort overrepresents whites, which may well have favored formulas derived from Western cohorts. Although this global multicenter cohort of 529 patients is most likely more diverse compared with most formulas and the sample size is adequate compared with the derivation cohorts (Supplemental Table I), the bulk of patients are Caucasian Europeans. Previous reports illustrated the Vauthey formulas are less accurate in an Asian population.[47] Therefore, the present conclusions are most applicable to Western populations. For institutions in other regions, it might be vital to consider the accuracy of the used formula in their practice before implementation in order to avoid misinterpretations. An additional limitation is that there is no information about the volumetry program or the volumetrist in the ALPPS database. This is an inherent limitation of the database, but it is also known that contributing centers have significant expertise in liver imaging and volumetry. Differences between techniques are a systemic bias because intra- and interobserver variability apply to all formulas equally, and the broad sample and large patient number reflect the reality of liver volumetry across many institutions. A third potential limitation of the present study is the relatively small FLR range; the studied patients come from a cohort that would undergo ALPSS for FLR hypertrophy. However, this is not a strict limitation because there is a range of very small to larger volumes spanning the 25% to 30% FLR volume range, at which FLR volume augmentation is indeed indicated.

In conclusion, most formulas to estimate TLV lead to a reasonable proportion of estimated FLRVs within 5% of the measured FLRV. Of all tested formulas, the Vauthey formulas seem to result in the lowest overestimation at the expense of the lowest underestimation of the remnant liver. Future studies should correlate different FLR volume estimations to the functional assessment and clinical outcome to have solid ground to guide clinical decision making.

## Conflicts of interest

The authors report no conflicts of interest.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.surg.2019.05.003.

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