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Letters to the Editor

The role of proportionate kinetic growth rate fraction in future remnant liver function over volume determined by ^{99m}Tc-Mebrofenin hepatobiliary scintigraphy including SPECT and computed tomography in the risk prediction of postoperative mortality in ALPPS

We would like to propose a potential novel method for predicting posthepatectomy liver failure (PHLF) after associating liver partitioning and portal vein ligation for staged hepatectomy (ALPPS). This technique uses the combined results of future remnant liver volume (fRLV)[1,2] based on volumetric computed tomography (CT) measurements and future remnant liver function (fRLF) based on technetium-99m (^{99m}Tc)-Mebrofenin hepatobiliary scintigraphy (HBS) with a Single Photon Emission Computed Tomography (SPECT) camera.[3–6] Individually, the standard analysis of these preoperative assessments have shown shortcomings in predicting PHLF in the interstage of ALPPS.[7–10] But, by using the results in combination, we suggest a new integrated parameter: the relative proportion kinetic growth rate (KGR) fraction of functional over volume increase that might prove to be better at predicting PHLF at the interstage of ALPPS.

In 5 patients (48–57 years of age) who underwent the hybrid ALPPS procedure[11,12] for hepatic malignancy (2 intrahepatic cholangiocarcinoma, 1 colorectal liver metastasis, 1 gallbladder cancer, and 1 hepatocellular carcinoma), fRLV measurements by volumetric CT and fRLF assessment by HBS scan[5] were performed both preoperatively and during the interstage ALPPS. The decision to proceed to completion hepatectomy was performed if the predefined critical cutoff levels of both fRLV (>30%) and fRLF (>2.7%/min/m2) were met.

All patients had an insufficient fRLV (mean 22%; 10%–28.9%) preoperatively. The preoperative mean fRLF was 2.6 %/min/m^2 (range: 0.9%–3.5 %/min/m^2). At the interstage, the fRLV increased in all patients, showing a mean 98% increase after a mean interval of 10.4 days after completion of the first step (7–14 days). However, all, but 1 patient, had a fRLF growth with a mean 49% increase measured at a mean interval of 10.6 days (8–28 days; Table 1). The patient without fRLF growth did not proceed to completion hepatectomy. The remaining patients underwent completion hepatectomy. In 1 of these 4 remaining patients, completion hepatectomy had been postponed to 28 days after liver partitioning owing to an initially insufficient fRLF, but this patient developed lethal PHLF on postop day 4. The clinical course of this patient further demonstrates the drawbacks of using absolute cutoff values of fRLV or fRLF as described elsewhere[7,9,10], and the alleged importance of using KGR in clinical context as a better predictor for PHLF.[13–16]

The “disproportionate” increase of the remnant liver volume compared to fRLF might be the cause of the greater morbidity and mortality reported in ALPPS.[7] In addition, recent pathologic studies of the remnant liver showing a higher density but smaller hepatocytes in the remnant liver seem to support the dysfunctional volume theory. These hepatocytes also contain fewer organelles and are thus less metabolic active.[17] This intangible relationship has led us to recommend the increase over time of function relative to volume (proportionate KGR function over volume fraction [pKGR f/V]) as a predictor for PHLF.

$$\textbf{pKGR f/V} = \left(\frac{\frac{(fRLF\ interstage - fRLF\ preoperative)}{fRLF\ preoperative}}{Interval(days)\ fRLF}\right) \Big/ \left(\frac{\frac{(fRLV\ interstage - fRLV\ preoperative)}{fRLV\ preoperative}}{Interval\ (days)\ fRLV}\right)$$

We encourage further research to validate the ideal cutoff value of proportionate KGR function over volume fraction in larger series.

Conflict of interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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Table 1
Preoperative and interstage volumetric and HBS results with calculated fraction proportionate KGR function over volume fraction against postoperative outcome for all 5 patients.

Patient number	Preoperative fRLV (%)	Interstage fRLV (%)	Preoperative fRLF (%/min/m^2)	Interstage fRLF (%/min/m^2)	Fraction proportionate KGR function over volume fraction	Postoperative outcome
Patient 1	22.1	45.0	3.5	4.4	0.2	Alive
Patient 2	9.9	31.6	2.7	4.1	0.2	Alive
Patient 3	28.7	40.4	3.3	4.1	0.6	Alive
Patient 4	24.5	52.0	2.8	2.1	−0.2	Aborted
Patient 5	25.5	28.8 (42.1*)	0.9	2.4 (3.9*)	5.1	Deceased
Mean	**22.1**	**39.6**	**2.6**	**3.4**	2.7	

* 28 days after PVE.

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Familial nonmedullary thyroid cancer: When the data and conclusions do not match

To the Editors:

When reading the paper by El Lakis et al.[1] on familial nonmedullary thyroid cancer (FNMTC), it seems their conclusions contradict their data.

The greater number of lymph node metastases (LNMs) in FNMTC patients reported by El Lakis et al.[1] were found mostly in the central compartment; however, it is well recognized how common and clinically irrelevant these types of nodal metastases prove to be. Moreover, because total thyroidectomy was performed in FNMTC more frequently than in the Surveillance, Epidemiology, and End Results (SEER) patients (98.2% vs 84%, respectively), and because more extensive surgery could prompt more neck exploration and subsequently more central neck dissections, a greater rate of central LNMs in FNMTC patients could, in fact, represent a bias of the study. Similarly, the difference in the female-to-male ratios among groups, with more males included in the FNMTC group, could be another possible bias. Of note, the SEER group patients presented with a more aggressive histopathology, with almost twice as many tall cell and follicular thyroid cancer (TC/FTC) variants.

Separating the patients presenting with clinical disease from those discovered by screening is quite arbitrary. Most thyroid nodules today fall within the category of incidental findings, and it is unclear what definition of clinical disease the authors applied. Of interest, the 20 patients detected by screening patients with FNMTC showed more favorable features and had fewer total thyroidectomies performed than the SEER patients (84.2% vs 98.2%). However, after excluding the screening group, there was little difference regarding age, TC/FTC types, extrathyroidal extension, and number of patients with T1 stage and lateral LNMs between FNMTC and the SEER patients. Moreover, the FNMTC patients with > 2 affected relatives had a similar number of lateral LNMs and 3 times less TC/FTC variants.

Considering that recurrence-risk stratification was not applied, a recurrence rate of 12.8% in the FNMTC group falls within the widely accepted lower range for sporadic NMTC. Although patients in the SEER group were registered from 1998 to 2007, we do not know the period for the FNMTC patients. Nevertheless, the mean follow-up for the FNMTC patients was 220 ± 416 months (18 ± 35 years) compared with 70 ± 58 months (5.8 ± 4.8 years) in the SEER group. In such a timespan, the field of thyroid cancer has changed so much (American Thyroid Association risk stratification; response to initial treatment assessment; Tumor, Node, and Metastasis 8th edition, etc) that assessment and definition of recurrent disease would be very different today.