World J Surg (2010) 34:868–869
DOI 10.1007/s00268-009-0327-5

World Journal of Surgery

A Clinical Perspective on the Criteria for Liver Resection and the Use of Liver Function Tests

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Published online: 10 December 2009

To the Editor,

In a recently published survey of 100 liver centers, Breitenstein et al. [1] reported that on a global scale, (1) the average minimal remnant liver volume for resection is 25% (range = 15-40%) for normal liver parenchyma and 50% (range = 25–90%) for cirrhotic livers, (2) portal vein occlusion is employed in 89% of the centers for purposes of augmenting liver volume before surgery, and that (3) 38% of the centers employed liver function tests as part of their clinical routine, of which 76% used the ICG clearance test.

The interesting survey provoked a few issues that we feel obliged to address. The authors contend that "below a certain volume, a remnant liver cannot sustain metabolic, synthetic, and detoxifying functions" [1]—a statement that is unequivocal and uncontested. However, it should be born in mind that liver volume is not a directly proportional measure of liver function. We have demonstrated a few fundamental aspects of the volume-function relationship that support this notion: (i) Whereas liver function correlates with volume in uncompromised livers [2], there is significantly less correlation between liver volume and function in patients with coexisting parenchymal liver disease [3, 4]. (ii) This discrepancy also applies to the regenerating liver [3]. (iii) The liver often exhibits functional heterogeneity [3]. These findings have been corroborated to some extent by others [5]. Consequently, a marginal remnant liver volume (e.g., 25% for cirrhotic livers [1]) may translate to functional deficiencies following resection and hence predisposes the organ to the "small-for-size" or, rather, the "small-for-function" syndrome. Likewise, allowing the organ to regenerate to a predetermined volume before resection bears comparable implications and strongly pleads for the use of *dynamic* liver function tests rather than CT volumetry as the gold standard, particularly for borderline surgical decisions.

We emphasize specifically the use of quantitative dynamic liver function tests [i.e., ICG clearance, ^{99m}Tc-mebrofenin hepatobiliary scintigraphy (HBS) [2–4], galactose elimination capacity (GEC) [5], and ^{99m}Tc-labeled galactosyl human serum albumin scintigraphy (GSAS)] inasmuch as conventional liver function tests such as prothrombin time, serum bilirubin, and the Child-Pugh score are relatively insensitive and are thus lagging indicators for determining whether a liver resection can be safely performed. It is well known that there are notable discrepancies between the above-mentioned dynamic liver function tests in the assessment of liver function. In our patient population, ICG and ^{99m}Tc-mebrofenin uptake exhibited similar pharmacokinetics in regenerating rat livers (that also corresponded well to the extent of hepatic damage), whereas the GSAS and GEC tests displayed an underestimation and an overestimation, respectively, of liver function in comparison to ICG and ^{99m}Tc-mebrofenin uptake (unpublished). This is because liver function encompasses a broad spectrum of processes, ranging from uptake, synthesis, biotransformation, and systemic and canalicular

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secretion, whereby each test measures a different component of that spectrum.

In summary, criteria on the basis of which extended liver resections are performed should preferably be dictated by functional parameters rather than volume alone, especially when livers are resected to a minimally accepted remnant volume. Furthermore, we advocate the use of dynamic liver function tests such as ICG or ^{99m}Tc-mebrofenin uptake for testing liver function due to their sensitivity and prognostic strength. We acknowledge that each of these tests reflects a limited aspect of liver function only. However, currently no better, clinically viable alternatives are available.

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