Experimental evaluation of liver regeneration patterns in small-for-size livers

Ji-Hua Shi[1,2] ,Wen-Zhi Guo[1], Shui-Jun Zhang[1], Pål-Dag Line[2*]

[1]Department of HPB Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou University, China;

[2]Department of Transplantation Medicine, Institute of Surgical Research, Oslo University Hospital, Rikshospitalet, Oslo, Norway

**Correspondence to:* p.d.line@medisin.uio.no

Background

Liver surgery including liver resection and liver transplantation is the principle potential curative treatment option for patients with primary and secondary liver tumors. Unfortunately, only about 20-30% of the patients will be resectable. The main limiting factor is the size of the **future liver remnant (FLR)**. The FLR needs to be of adequate size and quality to avoid postoperative liver failure and **small-for-size liver syndrome (SFSS)** with associated high morbidity and mortality. Previous studies have indicated that the size of the FLR should be at least 25 per cent of total liver volume[1] or a ratio greater than 0.5 between FLR and bodyweight[2, 3]. The altered hemodynamic factors and sinusoidal injury after inflammatory response following liver surgery are assumed to be key factors initiating rapid hypertrophy *through* systemic release of cytokines and growth factors[4, 5]. Protective efforts against of SFSS are still limited, and the underlying mechanism of liver regeneration in the small-for-size liver is still unclear.

Objective

The aim of this study was to evaluate liver regeneration characteristics of future liver remnant (FLR) and restoration of function in the small-for-size livers.

Methods

Rat models of 80 per cent hepatectomy (Group Hepatectomy), associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) with 20 per cent FLR size (Group ALPPS), and 20 per cent partial liver transplantation (Group Transplantation) were employed to mimic the operative small-for-size status and to investigate the liver regeneration characteristics of small-for-size liver (Table 1).

Three different surgical groups with the same FLR size of 20 per cent of total liver volume were compared with control, 70 per cent hepatectomy (Group Control) with respect to liver regeneration response. The magnitude of liver regeneration following the surgical interventions was evaluated by assessment of kinetic growth rate (KGR) and the ratio of the remnant liver weight relative to body weight (LBW), proliferation markers (Ki-67, PCNA), and HPC activation.

Table 1. Experimental design

Group	N	Surgery	FLR	
		Resected lobe	Volume	Remnant/transplanted lobe
Hepatectomy	15	LLL, ML, CL	20%	RL
ALPPS	15	LLL, ML, CL	20%	RL
Transplantation	15+15	ML, RL, CL,	20%	LLL
Control	15	LLL, ML	30%	RL+CL

FLR, future liver remnant; LLL, left lateral lobe; ML, median lobe; RL, right lobe; CL, caudate lobe; ALPPS, Associating Liver Partition and Portal vein ligation for Staged hepatectomy.

Results

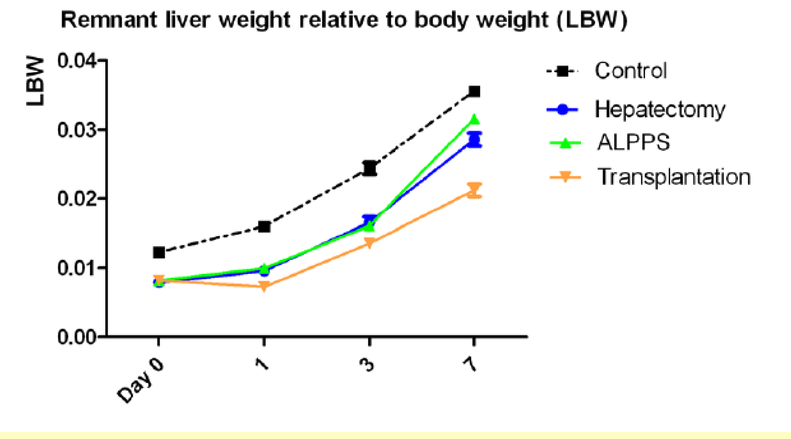

Figure 1

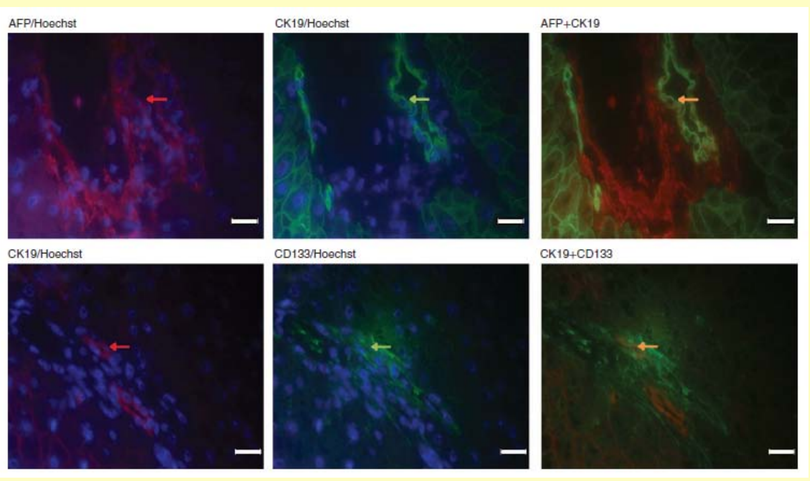

Figure 2[6]

Regenerative parameters, KGR, LBW, Ki-67 and PCNA in Group Hepatectomy, ALPPS and Transplantation were showed a similar pattern compared with Group Control.

The activation of HPC was associated with a sustained increase in levels of serum aminotransferases and bilirubin, and severe morphological sinusoidal injury on Day 1 and 3 after Group Hepatectomy, ALPPS and Transplantation (Figure 1 and 2[6]).

Conclusion

HPCs repopulating in the small-for-size livers seems to correlate with the extent of sinusoidal injury after the surgical interventions, which may provide a new strategy for maintenance of homeostasis and tissue repair during liver regeneration.

Reference

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DOI: 10.3252/pso.eu.ILTS2018.2018
Poster presented at: ILTS ANNUAL CONGRESS 2018 LISBON | PORTUGAL MAY 23 -26, 2018