Insight on ALPPS - Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy - mechanisms: activation of mTOR pathway

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Abstract

Background: ALPPS procedure has been introduced to increase the volume of future liver remnant. The mechanisms underlying the accelerated regeneration observed with ALPPS are unknown. It was hypothesized that AMPK/mTOR is activated as an integrating pathway for metabolic signals leading to proliferation and cell growth. Our aim was to analyze increase in liver volume, proliferation parameters and expression of AMPK/mTOR pathway-related molecules in patients undergoing ALPPS.

Methods: A single center prospective study of patients undergoing ALPPS was performed from 2013 to 2015. Liver and serum samples, clinical laboratory results and CT-scan data were obtained. ELISA, Ki-67 immunostaining and qRT-PCR were performed in deportalized and remnant liver tissue in both stages of the procedure.

Results: 11 patients were enrolled. Remnant liver volume increased 112 +/- 63% (p < 0.05) in 9.1 +/- 1.6 days. Proliferation-related cytokines IL-6, TNF-alpha, HGF and EGF significantly increased, while higher Ki67 immunostaining and cyclin D expression were observed in remnant livers after ALPPS. mTOR, S6K1, 4E-BP1, TSC1 and TSC2 expression were significantly increased in remnant livers at second stage, while AMPK and Akt increased only in deportalized liver samples.

Conclusion: Rapid liver regeneration with ALPPS might be associated with hepatocyte proliferation induced by mTOR pathway activation.