



Analysis and Validation of Damage Parameters for Peri- and Postoperative Assessment of Transplant Liver Organs

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Short Communication

Success in standardized liver transplantation is based on immense advances in surgical techniques & an optimized, patient-adapted immunosuppressive therapy. The use of cadaver organs is influenced by i) (possibly short) organ transfer, ii) (minimized) ischemia consequences of the tissue with lowered organ temperature including effective solutions for conservation such as HTK / UW media & iii) reperfusion effects (by oxidative stress). From a clinical point of view, an objective & immediate assessment of the quality of function of the transplanted organ in the recipient is extraordinarily important, which has great impact onto the final outcome of the patient.

The aim of the study was to assess the quality of the donor organ by objective parameters, which can be simply analyzed already during the ongoing transplantation based on the postulate that the severity of the organ damage is associated with the duration of ischemia.

Over a defined investigation period, from all consecutive liver transplant recipients blood samples (representing systemic compartment; at -1 h; 0; +1/+6 h; +1/+3/+7 d) and fractionated samples from the liver rinsing process during the phase of liver reperfusion after accomplishment of vascular anastomoses (at -1 h; 0; +1 h) were obtained and analyzed for factors, which were released from the cells due to ischemia-/reperfusion-induced damage: 1) enzyme activity of AST, ALT & GLDH (established parameters in liver diagnostics characterizing liver damage) & 2) parameters of oxidative stress such as MDA & protein carbonyl each in correlation with parenchymatous damage as well as cold & warm ischemia time (CIT/WIT); 3) postoperative factor V & ATIII (synthesis of coagulation factors as representative correlate for postoperative transplant at function).

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1) Overview: In total, over a 14-years time period 75 patients (49 males, sex ratio [m/f]: 1.88:1; mean age: 61.1 [49-68] years) were registered out of them, 60 patients with complete spectrum of analyzed parameters were finally evaluated.

2) Summary: The peri-operatively obtained rinsing blood of the transplanted liver is suitable to determine parameters of parenchymatous damage & oxidative stress.

- For liver transplantations included in this study, CIT & WIT were within a restricted time frame by the standardized transplant management & surgical technique. Significant correlations of damage parameters & ischemia time periods were not found & therefore, this does not allow to derive causal associations; the nearest association could be seen in CIT with AST.

- Parameters of oxidative stress showed only moderate amplitudes & low correlations to other parameters. Again, a causal association via the axis ischemia/reperfusion – oxidative stress – cell damage cannot be easily derived. Obviously, the conservation media used provides an effective anti-oxidative protection.

- With regard to the possible impact of ischemia onto transplant function during the postoperative phase, it was found that ischemia time influences serum level of GLDH supporting GLDH as suitable parameter related to postoperative course and outcome as known.

The results show that explanation-induced stop of blood supply induces a potential damage of the liver parenchyma, which can become relevant by the more or less long time period of ischemia during organ transfer. During reperfusion phase, additional events of cell/organ damage occur leading to the final (summative) damage of liver parenchyma. The re-established metabolism and organ function has then substantial impact onto the outcome of the organ recipient.

From the pathophysiological point of view, cell/parenchymatous damage is caused by oxidative stress due to ischemia and reperfusion. The extend of the parenchymatous damage can be

quantified by analysis of suitable parameters within the rinsing blood. However, the advanced standardization of the pathway in managing liver transplantation in a clinical setting did not reveal important (significant) associations or courses of damage in the investigated group of patients. If there will be novel sensitive parameters becoming

relevant for liver transplant management to better assess or predict the quality of the transplanted organ, rinsing blood can be considered a suitable material and the demonstrated procedures of analysis and analyzed parameters are relevant for further investigations.