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Current Hypothesis of Preservation Injury of Hepatic Grafts (Mini Review)

The liver comprises of several cell types. Hepatocytes, nonparenchymal cells - endothelial cells, Kupffer cells, and hepatic stellate cells).

Earlier studies (from 1997 up to 2001) showed that Kupffer cell activation and endothelial cell damage plays key roles of hepatic graft injury after cold ischemia-reperfusion of rat livers (1-6). This fact was further supported by a finding that endothelial cell damage can be prevented by anti-angionetic agents (7).

However, our study (from 1997) in isolated, a blood-free reperfused rat liver model, showed that Kupffer cells played a minor role in cold ischemia-reperfusion injury, because liver function was not altered by Kupffer cell depletion (8). This led us to review the role of hepatocytes (liver parenchymal cells) in reperfusion of hepatic grafts (9). We clearly analyzed that energy stores, which are derived chiefly from hepatocytes plays a major role in hepatic graft function (9).

Further, we found that stores of energy (ATP, ADP, AMP) can be repleted by short-term warm reperfusion even after 18 hours of cold storage of rat livers (10).

ATP synthesis prior to liver transplantation can be also done by hypothermic oscillating liver perfusion. (11, 12). In addition, protective effect of energy repletion into hepatic grafts was also found in a blood-reperfused model of cold ischemia-reperfusion injury of rat livers (13).

Finally, ATP stores can be repleted by machine perfusion of hepatic grafts (see for review (14)). Repletion of tissue energy by machine perfusion was also confirmed in multicentric study in human liver transplantation model (15).

Thus, current hypothesis of preservation hepatic graft injury indicates that Kupffer cells and endothelial liver cells have minimal effects, while repletion of energy stores, (which are mainly derived from hepatocytes) have a pivotal role in primary graft function in the recipient. There is also a strong hypothesis that hepatic stellate cells can contribute to preservation-reperfusion injury (16), especially during several (hours/days) post transplantation surgery.

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