IMPLEMENTING REGENERATIVE MEDECINE ACROSS SURGICAL PATHWAYS IN LIVER CIRRHOSIS

Negari Nadejda[2,3], Minchevici Delia[2], Cazacov Vladimir[1], Nacu Viorel[3,4]
[1]Department Surgery nr. 2 *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
[2]Department of Surgery nr. 5, *Nicolae Testemițanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
[3]Department of Anatomy and Clinical Anatomy, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
[4]Laboratory of Tissue Engineering and Cellular Cultures, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Republic of Moldova

Introduction: Liver cirrhotic patients often face surgical and interventional procedures, such as hepatectomy with modulation of future liver remnant, portoenterostomy in cases of biliary atresia, transjugular intrahepatic portosystemic shunt, and liver transplant. Regenerative medicine is progressively tested for the improvement of liver regeneration, prevention of progression of liver fibrosis, and reduction of liver failure.
Materials and methods: A systematic review (2020-2026) was performed in PubMed/Medline, Scopus, and ClinicalTrials.gov using "cirrhosis", "mesenchymal stem cells/MSC/umbilical cord", "liver-derived progenitor/HALPC/HepaStem", "organoid/iPSC/hepatocyte-like cells", and procedural terms like "Kasai", "transplantation", "hepatectomy", "portal vein embolization", "ALPPS", "future liver remnant". The information was collected regarding population, time frame, delivery method, evaluation criteria, and safety. The selection was made using descriptive statistics due to heterogeneity in results.
Results: Allogeneic infusion of umbilical cord-derived mesenchymal stem cells has been performed in postoperative cirrhotic patients after Kasai portoenterostomy, allowing the short-term monitoring of liver function. The perioperative administration of MSC has been tested in a controlled form in transplant patients to modulate alloimmune responses, reduce inflammatory damage, and boost graft recovery of function. Liver-derived progenitor products: the development of human allogeneic liver-derived progenitor cells (HALPC/HepaStem) in severe cirrhosis-related syndromes such as ACLF gave a regulated development platform that could be potentially applied to surgical mitigation. Regenerative liver surgery, including portal vein embolization, liver venous deprivation, and ALPPS-based procedures, represents the most established strategy to enhance the growth of the future liver remnant in selected patients with compromised liver parenchyma to reduce the risk of post-hepatectomy liver failure. In contrast, the iPSC-based graft strategies have been in the field of translation, thus limiting the perioperative use of such methods.
Conclusions: Regenerative strategies for operative cirrhosis remain advanced for surgical interventions that stimulate pre-hepatectomy hypertrophy, while MSC and liver-derived progenitor cell-based regenerative therapies remain in early-phase, safety-focused trials for the post-Kasai and peri-transplant context. Future research should focus on standard product, procedure-specific timing, endpoints such as MELD/Child-Pugh, portal hypertension, post-hepatectomy liver failure, and properly powered randomized trials within surgical pathways.
Keywords: liver cirrhosis; regenerative medicine; mesenchymal stem cells; umbilical cord MSC; future liver remnant