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LETTER

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The pathophysiology of abdominal surgical diseases and the therapeutic potential of mesenchymal stem cells

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Dear Editor,

Mesenchymal stem cells (MSCs) have emerged as promising tools in regenerative medicine due to their antifibrotic, pro-angiogenic, and immunomodulatory effects that address limitations in standard surgical approaches. Abdominal pathologies—characterized by inflammation, tissue injury, and fibrotic progression—are particularly suitable for MSC-based interventions (1). Whether derived from bone marrow, adipose tissue, or umbilical cord, MSCs exert their regenerative functions through paracrine signaling, extracellular vesicle release, and immune regulation (2). Their delivery route is pathology-dependent: local injection targets mucosal or fistulous areas, while portal-hepatic, intraperitoneal, or systemic routes provide organ-wide or systemic effects (3). A recent letter in this journal illustrated MSC efficacy in cytokine storm suppression during COVID-19, reinforcing their broad therapeutic potential (4). Concurrently, the comprehensive review by Azizoglu et al. on surgical diseases has also served as an inspiration for the preparation of this editorial letter (1).

Refractory peptic ulcer

Refractory ulcers, resistant to acid suppression, arise from persistent inflammation, poor angiogenesis, and stromal deficit. In a porcine NSAID-ulcer model, endoscopic submucosal injection of adipose-derived MSCs accelerated healing by over 50%, with MSC secretome achieving comparable results. Pilot studies now explore MSC-enhanced biomaterials as adjuncts to endoscopic therapy, aiming to reduce surgical resections. Endoscopic submucosal delivery appears most effective, combining localized action with low systemic exposure (3,5).

Inflammatory bowel disease

Crohn's disease (CD) and ulcerative colitis (UC) result from chronic immune dysregulation and mucosal destruction (2). In a phase III trial, a single local injection of adipose MSCs into CD-associated perianal fistulas led to combined clinical-radiologic remission in 51% of patients, sustained over four years (6). For luminal IBD, meta-analysis suggests that repeated systemic MSC infusions at $\geq 4\times10^6$ cells/kg induce steroid-free remission in approximately 40% of cases (2). Intra-arterial delivery is also being explored for diffuse mucosal inflammation (7) (Table 1).

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Table 1: Mesenchymal stem cell delivery strategies in abdominal surgical pathologies

Condition	Route of MSC administration	Main therapeutic outcome	Reference
Refractory peptic ulcer	Endoscopic submucosal injection	>50% faster ulcer closure in porcine model	(5)
Crohn's perianal fistula	Local tract injection	51% combined clinical and radiologic remission at 24 weeks	(6)
Luminal inflammatory bowel disease	Repeated intravenous infusion	~40% steroid-free remission rate	(7)
Severe acute pancreatitis	Early single intravenous administration	43% mortality reduction in animal models	(8)
Decompensated liver cirrhosis	Hepatic arterial or portal vein route	MELD score improvement by 2–3 points; increased serum albumin level	(10)

Acute pancreatitis

Severe acute pancreatitis (SAP) is associated with autodigestion, cytokine storm, and multi-organ dysfunction. Rodent models demonstrate that early intravenous MSC therapy significantly reduces pancreatic necrosis, systemic inflammation, and mortality. These effects are mediated through macrophage polarization, IL-10 upregulation, and oxidative stress modulation (8). A first-in-human trial evaluating intravenous umbilical-cord MSCs within 48 hours of SAP onset is currently recruiting (9).

Cirrhosis

Cirrhosis involves progressive fibrosis and hepatocellular dysfunction, with limited nonsurgical treatment options (1). A recent meta-analysis of 14 clinical trials (n=785) found that MSC infusion via hepatic artery or portal vein significantly improved MELD scores and serum albumin levels within six months (10). In acute-on-chronic liver failure, MSCs reduced stellate cell activation and collagen deposition while improving survival rates (11). Sequential infusions may further enhance antifibrotic signaling pathways (12).

Perspective

MSC therapy provides a biologically consistent and increasingly evidence-based approach for managing difficult gastrointestinal diseases (1). Advances such as hypoxic preconditioning, exosome formulations, and genetic modification further enhance therapeutic efficacy and safety (1,13). The experience from COVID-19 ARDS shows that MSCs can robustly counteract systemic inflammation (4). To expedite clinical translation, we support unified protocols for MSC characterization, disease-specific composite endpoints, and route-of-delivery comparison trials (14,15).

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