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## Acute and chronic graft versus host disease of the gastrointestinal tract - Clinical symptoms and current management

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The gastrointestinal tract is a critical target organ of both acute and chronic graft versus host disease (GVHD). Clinical signs and symptoms are often non-specific and can be attributed to a variety of other medical conditions, which are frequently seen in the allogeneic HCT recipient as well. GI involvement during either acute or chronic GVHD significantly affects overall non-relapse mortality and overall survival and early identification and adequate treatment is critical. Therefore, patients should undergo a thorough work as soon as possible, including extensive infectious work up plus upper and lower GI tract endoscopy to obtain histologic proof of GVHD and/or identification/exclusion of other or concurrent underlying causes. The diagnostic role of standard imaging techniques, such as abdominal XR, CT, MRI and conventional ultrasound is rather limited, yet PET/CT and wireless video-capsule endoscopy may aid in diagnostic management and are currently under investigation. Treatment is usually initiated once the diagnosis of acute GI-GVHD is either confirmed or if clinical symptoms suggest the possibility of GVHD and other causes have been ruled out. Initial treatment of acute GI-GVHD usually consists of systemic methylprednisolone. Non-(little-) absorbable steroids, such as budesonide or beclomethasone di-propionate can be considered to augment topical steroid delivery and to potentially spare systemic steroid exposure. In chronic GI-GVHD, systemic immunosuppression with steroids plus/minus calcineurin inhibitor are commonly initiated and optimized when clinical symptoms develop or worsen. Mechanic dilation and enzyme replacement therapy are utilized for esophageal structures and pancreatic insufficiency, respectively. The role for non-absorbable steroids in chronic GI-GVHD is not well defined and in both acute and chronic GI-GVHD, switching to second/third line immunosuppressive strategies often will be required.

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## Impact of immunosuppression minimization and withdrawal in long-term hepatitis C virus liver transplant recipients

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HCV-related disease is the most common indication for liver transplantation (LT). HCV recurrence, which is almost universal, has a significant impact on patient and graft survival after LT and still represents a great unsolved issue for the liver transplant community. Since Interferon and Ribavirin have limited efficacy and can be administered only in selected transplant recipients and considering the lack of long-term results of the new direct acting antiviral agents on HCV-LT recipients, the achievement of immunosuppression minimization and when possible, the immunosuppression-free state, still play a central role in the avoidance of rapid HCV recurrence. On this regard, the antimetabolite use (namely Micophenolate) in the mid-term LT recipients seems to favorably impact the natural history of HCV recurrence. It is likely that the avoidance of IS in LT recipients should be the main purpose in order to restore the immunity and contrast the HCV disease. Literature reports 21 cases of HCV-LT recipients who successfully achieve a sustainable IS-free state but in most of them the long-term histological finding was not reported. Only our group published a long-term HCV-transplanted series on more than 300 yearly consecutive liver biopsies in which a lower fibrosis progression rate was showed in those recipients who were off any immunosuppressant agents. In conclusion, the long term LT recipients should always be considered for withdrawal. In those who require immunosuppression, the use of anti-metabolites should be considered in spite of calcineurin inhibitors.

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