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Endoscopic and Histopathological Perspectives on the Prevalence and Diagnosis of Common Digestive Disorders

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Introduction

Choosing appropriate study endpoints is a challenge faced in both animal models and patient-based research, particularly in the context of Inflammatory Bowel Disease (IBD). In animal models of IBD, the severity of the disease is often measured using semi-quantitative evaluation of intestinal histopathology, which is considered a reliable method (considered a "gold standard"). This evaluation involves using ordinal categorical scales, ranging from normal to severe, to assess various aspects such as immune cell infiltration and crypt loss. To obtain an overall severity score, different subscores measuring these histopathological features are combined.

However, it is important to note that the relevance of specific histopathological features may vary between different animal models of IBD. For example, epithelial destruction is highly relevant in the acute dextran sodium sulphate model, whereas epithelial hyperplasia is more relevant in the T-cell transfer model. Concerns exist regarding the validity of disease severity indices currently used for the Interleukin-10 knock-out [IL10 KO] mouse model of chronic intestinal inflammation. Several histopathological scoring systems have been described for this model, resembling those used for the T-cell transfer model. However, the final disease severity scores are simple combinations of item scores, lacking a methodologically rigorous scheme of index development. Consequently, there is uncertainty about the inclusion of relevant and reliable items in the final index [1,2].

Description

Intra-Endoscopy and histopathology assessments in mouse models for IBD are essential for both fundamental and translational research. Several research groups have developed ordinal classification indices, which to some extent measure overlapping features and generally have face validity [appear to be valid]. However, formal assessment of the operating properties of these indices had not been performed. In the current study, we evaluated histopathology and endoscopy scoring systems for reliability, validity and ability to discriminate differences between groups known to vary in severity in mouse models for IBD, and developed simplified prediction models from these systems. We included two widely used mouse models for chronic intestinal inflammation: the T-cell transfer and the IL10 KO models. Items within the scoring systems were chosen based on the existing indices that are currently used for these mouse models [3]. Usually an inter-rater ICC of >0.4 is used as criterion for including an item in the development of a new index. We showed that all histology items had a higher reliability than 0.4 [the lowest inter-rater ICC was 0.48, for 'ulceration']. Our observers agreed that this component was the most difficult item to score, especially on poorer quality slides. Indeed, removing the poor-quality slides from the dataset increased the inter-rater ICC of 'ulceration' to 0.53. In addition to 'ulceration', the model-building process excluded 'muscle thickness' and 'abscess', items for which the inter-rater ICCs were low. To enable a better distribution of disease severity scores, which enables better model building, the healthy control animals were excluded from the process of developing a new histological index. This process was started by investigating the bivariate relationships between the VAS score and the individual items. 'Inflammation' and 'crypt loss' exhibited non-linear relationships with the VAS and were re-categorized for the model-development process [4].

The MCHI was shown to be able to discriminate between control animals, untreated animals, and animals treated with a treatment of known efficacy. The new histological index has the potential to reduce the sample size required for detecting treatment effects, and as the readers do not have to score all initial features, to reduce the time required to read slides. The reliability coefficients of the histological components were considerably lower for the IL10 KO model than for the T-cell transfer model. As there was a lower number of slides available from the IL10 KO model for the model-development process, and the IL10 KO mice exhibited less severe disease , the MCHI may be a more efficient instrument in the T-cell transfer model. For the five items from the endoscopy scoring system introduced by Becker et al.,14 the inter-observer reliability was also assessed as 'moderate' to 'substantial'. However, as we tried to remove as much feces as possible before we performed endoscopy, no stool was visible in >20% of the endoscopy videos that were evaluated. Hence, we did not include the stool consistency item in our model development. As was the case with the histology model, control animals were excluded from the model-development process.

Consistent with the non-reasoned decision by Norwaski et al., to exclude the fibrin component from their total endoscopy score, 'fibrin' was eliminated during the model-building process. The final model, the MCEI, is comprised of 'vasculature', 'mucosal thicknesses and 'granularity', all equally weighted. Correspondingly, 'fibrin' had the weakest correlation with the VAS. This study, assessing both endoscopic and histologic semi-quantitative scoring systems in animal IBD models had several methodological strengths. We used a large number of histological slides and endoscopy videos from two different IBD models. The slides and videos were generated in a standardized manner, using mice from several different experiments that included healthy controls, diseased untreated groups, and therapeutic treatment groups. The inter- and intra-rater reliability coefficients found in this study were generally higher than those in human studies which could be due to the differences between observers, amount of tissue, pathophysiology, and/or the chosen items [5].

Conclusion

There is an absence of evidence to support platelet transfusion in a patient who is not actively bleeding and the BSG and NICE specifically recommend against this practice. Although not covered by guidelines from either NICE, the BSG, or the ACG, platelet transfusions may be encountered in two other situations: platelets are often given to patients with thrombocytopenia prior to invasive procedures such as lines or drains; secondly, patients taking antiplatelet agents such as aspirin may have normal platelet counts but have a functional platelet defect and platelet transfusion may be considered. Discussion with a haematologist may be helpful in this case.

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Conflict of Interest

None.

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