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In Context

IN CONTEXT

Automating kidney transplant rejection diagnosis: a simple solution for a complex problem?

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Yoo and colleagues developed the 'Banff automation system', an automated application of the Banff Classification rules for Kidney Allograft Pathology that uses simple logical operations to reach one or several diagnoses [1]. User input consists of histological information (Banff lesion scores and concomitant diagnoses), serology (presence of donor-specific antibodies) and molecular data (if available). The tool aims to avoid misclassifications due to misinterpretation or errors, and provides not only the final diagnosi(e)s, but also a visualized decision tree illustrating the steps of the Banff rules used to reach it/them. Performance of the tool is assessed by comparing the automated diagnosis to the pathologist's diagnosis, and by comparing their prognostic performance. This automated diagnosis enables an objective Banff diagnosis for clinical use, and is potentially relevant for determining endpoints in future studies.

An important output of this study is how the painstaking analysis of discrepancies between pathologist and automated diagnoses reveals potential problems in how we diagnose rejection. Indeed, the tool demonstrates how convoluted the Banff Classification has become since its inception 30 years ago, and how easily it can be misunderstood [2]. Frequent changes to the Classification were also an important source of discrepancy, especially in borderline for T cell–mediated rejection, and 'equivocal for AMR' [3]. Importantly, the automated tool is based on interpretation of the Banff Classification by skilled pathologists and transplant physicians from a single centre, and does not correct its flaws. As the authors indicate, the pathologist's experience remains crucial since the Banff Classification is based on detecting and scoring histological lesions. Application of the tool does not avoid the old adage of 'rubbish in, rubbish out' and improvements are required, such as artificial intelligence (AI) applied to digital pathology and consensus on molecular data and non–human leukocyte antigen (HLA) antibodies (Fig. 1, top and middle).

Finally, the study urges clinicians to reflect on how the rejection diagnosis is made. It is striking that pathologists in this study often provide a different diagnosis from that the Banff rules codify. Aside from misinterpretation, this could also reflect integration of clinical information and multidisciplinary discussion. This raises the question of whether strict application of the Banff diagnostic scheme or a more clinically integrated reasoning scheme—as proposed by Labriffe *et al.* [4]—and making use of AI would be more suited to the complexities of transplant diagnosis (Fig. 1, bottom). The better prognostic value of the 'Banff automation system' compared with the pathologist's reading does not necessarily make it a better diagnostic parameter. What is needed is prospective randomized analysis of the effect of using the tool on diagnosis and treatment decisions. We caution against using the Banff Classification as a prognostic tool, when it could never outperform applications that have been specifically designed for this context of use [5].

The 'Banff automation system' is an elegant attempt to solve some problems with the current application of the Banff Classification and reduce variability. The study pinpoints the

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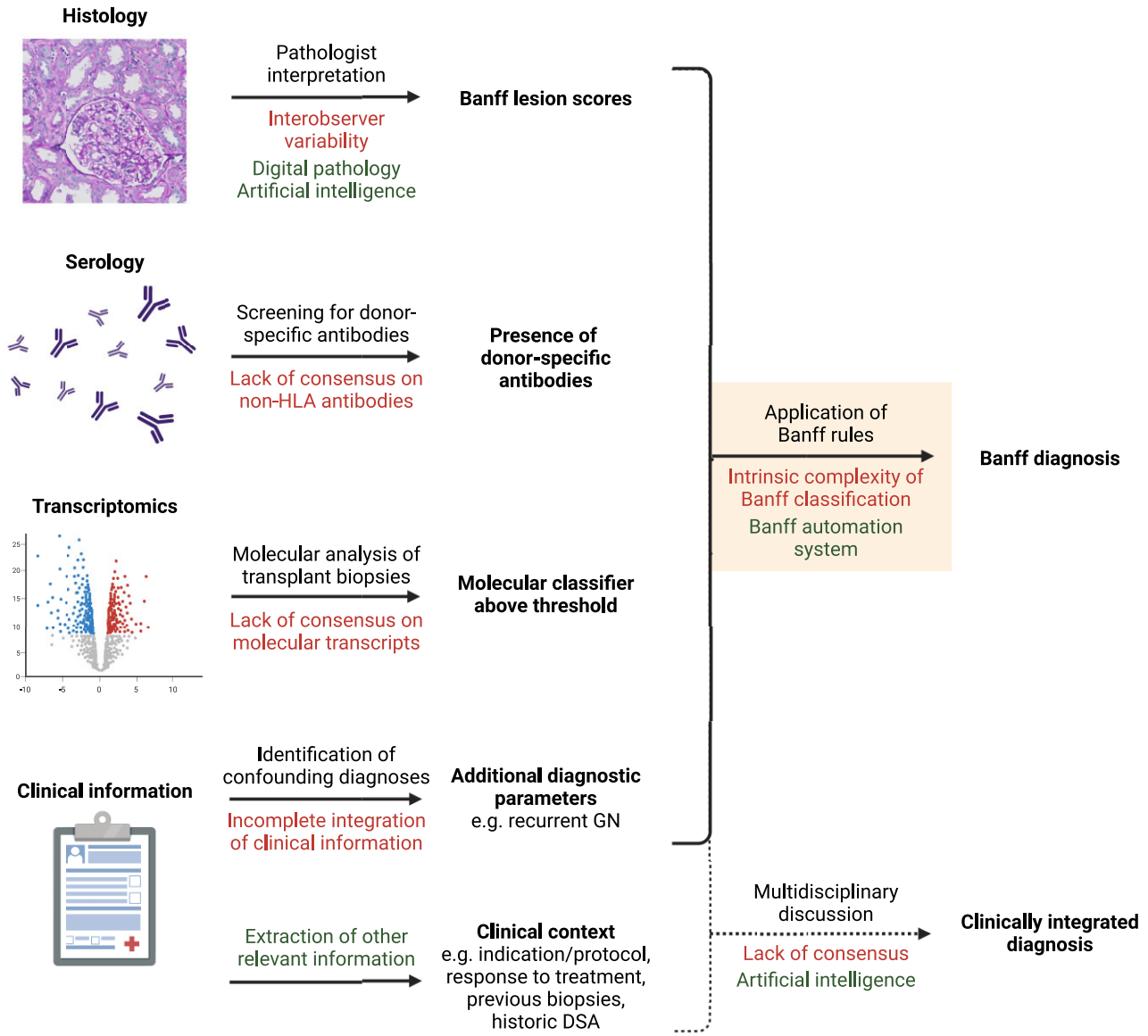

Figure 1: Pitfalls and potential solutions for the diagnosis of rejection after kidney transplantation. Diagnosis of rejection is based on integration of histological, serological, molecular and clinical information (left). The collection of this information has intrinsic flaws (red font), for which several solutions are proposed (green). These input parameters are then integrated by the Banff rules to obtain a diagnosis of rejection: the 'Banff automation system' was developed as a solution to this data integration stage. The addition of other clinical features, such as previous biopsies or response to treatment, is sometimes used in multidisciplinary discussions, and may be important for a clinically integrated diagnosis (bottom, dashed line). GN: glomerulonephritis; DSA: donor-specific antibody. Created with Biorender.com.

limitations and complexity of the Banff Classification, and invites further work evaluating simplified Banff Classification rules and/or AI-supported diagnosis reflecting real-life clinical complexity.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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