ORIGINAL ARTICLE

A 2020 Banff Antibody-mediated Injury Working Group examination of international practices for diagnosing antibody-mediated rejection in kidney transplantation – a cohort study

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SUMMARY

The Banff antibody-mediated rejection (ABMR) classification is vulnerable to misinterpretation, but the reasons are unclear. To better understand this vulnerability, we evaluated how ABMR is diagnosed in practice. To do this, the Banff Antibody-Mediated Injury Workgroup electronically surveyed an international cohort of nephrologists/surgeons (n = 133) and renal pathologists (n = 99). Most providers (97%) responded that they use the Banff ABMR classification at least sometimes, but DSA information is often not readily available. Only 41.1% (55/133) of nephrologists/surgeons and 19.2% (19/99) of pathologists reported that they always have DSA results when the biopsy is available. Additionally, only 19.6% (26/133) of nephrologists/surgeons responded that non-HLA antibody or molecular transcripts are obtained when ABMR histologic features are present but DSA is undetected. Several respondents agreed that histologic features concerning for ABMR in the absence of DSA and/or C4d are not well accounted for in the current classification [31.3% (31/99) pathologists and 37.6% (50/133) nephrologist/surgeons]. The Banff ABMR classification appears widely accepted, but efforts to improve the accessibility of DSA information for the multidisciplinary care team are needed. Further clarity is also needed in Banff ABMR nomenclature to account for the spectrum of ABMR and for histologic features suspicious for ABMR when DSA is absent.

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Key words
histocompatibility and immunogenetics, HLA-antibody post-transplantation, kidney clinical, pre-sensitisation, rejection

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Introduction

Antibody-mediated rejection (ABMR) is a major contributor to kidney allograft loss and having uniform diagnostic and management practices is critical for improving long-term kidney allograft survival. The Banff pathology-based classification system for ABMR has been a major contributor to standardizing diagnostic practices [1–3]. Prior work by the Banff Antibody-Mediated Injury Working group (Banff AMI-WG, also previously known as "Clinical and Laboratory Assessment of Highly Sensitized Patients Working Group") has shown that a discrepancy exists in how the Banff foundation intended its ABMR classification to be used and how it is actually used in practice [4]. With the use of a case-based survey, we found that pathologists and clinicians would assign a diagnosis different than intended by Banff when presented with the same case approximately 30% of the time. Furthermore, the respondents' treatment approaches were associated with the assigned diagnoses, suggesting that the inconsistent use of the Banff classification in practice likely has implications for patient management [4].

The factors associated with the observed discrepant diagnoses among practicing providers and the actual Banff classification remains unclear. Understanding the issues underlying the inconsistencies in how the Banff ABMR classification system is used is essential to improve the classification system. Factors that may have contributed to the observed findings from our initial survey include the use of outdated classifications, a deliberate decision not to use the Banff system, or inappropriately incorporating patient characteristics (e.g., allograft dysfunction) into the pathologic diagnosis. It is also unknown whether the Banff system should be refined or the focus should be on improved education of the current system to minimize inconsistency in the future [5]. In an attempt to further our understanding of the aforementioned gaps, we have chosen to send a follow-up survey to an international group of kidney transplant providers (nephrologists, surgeons, and pathologists) to obtain a clearer understanding of why the Banff ABMR classification is vulnerable to misinterpretation. The aims of this follow-up project were (i) to evaluate the current practice patterns for obtaining the relevant information needed to diagnose ABMR, (ii) to determine the perceived role of the Banff classification for practicing providers and (iii) to determine opportunities to improve the classification and/or better educate providers on the appropriate use of the Banff ABMR classification.

Materials and methods

We conducted an international survey of transplant clinicians (nephrologists/transplant surgeons) and renal pathologists to determine how the Banff ABMR classification is used in practice [2]. The study was approved by the Mayo Clinic Research Ethics Board (Rochester, MN, USA).

The survey was distributed by E-mail to members of the American Society of Transplantation—Kidney/Pancreas Community of Practice and Transplant Diagnostic groups, The Canadian Society of Transplantation, The Canadian Society of Nephrology, The Canadian National Transplantation Research Network, the Chilean Society of Transplantation, the European Kidney Transplant Association (section of the European Society for Organ Transplantation), the Renal Pathology Society, Japanese Society of Nephrology, Middle East Society of

Organ Transplantation, Dutch Transplant Society, African Society of Transplantation, the Latin American Congress and Caribbean Transplant Society, Egyptian Transplant Society, and the Transplantation Society of Australia and New Zealand. The survey was also distributed as an announcement in the Weekly Tribune of The Transplantation Society. The survey was administered from April through September 2019. The authors of the manuscript also sent emails to 498 personal contacts (pathologists, nephrologists, surgeons) and advertised a link to the survey at the 2019 Banff meeting.

To maximize the response rate, a follow-up E-mail/announcement by each of the societies was sent at least once after a 2-week interval. We asked the respondents to provide their name and contact information to exclude duplicate responses, but this was not an absolute requirement. We estimated a response rate of 11.6% [232 separate responses from individuals who identified themselves as a nephrologist, surgeon, or pathologist/2000]. The total number of surveys used to for this calculation (2000) was an estimate based on our 498 personal email contacts and society memberships.

We provide descriptive statistics on the distribution of diagnoses assigned by the survey participants. Chi-square tests were used to compare categorical data among survey participants. All analyses were performed with JMP software version 13 (Cary, NC, USA).

Results

Demographics of survey respondents

We received results from 245 respondents. Of these, nine duplicate surveys and four surveys from individuals who did not identify themselves as a pathologist or nephrologist/surgeon were excluded. Therefore, a total of 232 surveys were analyzed. Nephrologists and surgeons completed 57.3% (133/232) of these surveys and pathologists completed 42.7% (99/232) of surveys. We received responses from providers representing six of the seven continents, small and large transplant centers, and academic and private practices Table 1.

The largest proportion of responders practiced in North America [30.8% (41/133) of nephrologist/surgeons and 49.5%(49/99) of pathologists], but a substantial proportion was from Europe, and Central/South America. The largest proportion of respondents also was from large transplant centers with transplant volumes greater than 200 per year. Approximately 30% of nephrologist/surgeons and 45.5% of pathologists were affiliated with centers that performed more than 200 kidney transplants per year. The majority of respondents were affiliated with an academic center. Only 5.4% (7/133) of nephrologists/surgeons and 11.1% (11/99) of pathologists were from a nonacademic private practice. The majority of nephrologists/surgeons responded that they practiced at centers that performed transplants in the context of known donor-specific HLA (Human leukocyte antigen) antibody [referred to as donor-specific antibody (DSA) throughout the rest of the manuscript]. Specifically, 66.2% (88/133) practiced at centers that at least performed transplants with known DSA. However, only 36.4% (36/99) of pathologists responded that they are affiliated with centers that perform transplants in individuals with known DSA. Approximately 60% of respondents also practice at centers that perform surveillance biopsies at least sometimes [57.9% (77/133) of nephrologists/surgeons and 58.5% (58/99) of pathologists]. Follow-up biopsies after ABMR diagnosis and/or treatment are not consistently performed. Only 29.3% (39/133) of nephrologist/surgeons and 29.3% (29/99) of pathologists responded that follow-up biopsies are always performed at their center.

We did not find that the respondents' location was associated with the performance of DSA positive transplants or routine use of surveillance biopsy. We also did not find an association between performing DSA positive transplants and routine surveillance biopsy Tables S1–S4.

Tools for antibody-mediated rejection diagnosis

The overwhelming majority of nephrologists/surgeons and pathologists responded that they use the Banff classification in the context of the ABMR diagnosis Table 2. Only 3.0% of the nephrologist/surgeon group and 3.0% of pathologists responded that they *never* use the Banff classification. The majority of respondents also report that the actual Banff scores are incorporated in their pathology report. Among the pathologists who responded, 75.8% (75/99) always incorporate the Banff scores in the pathology report, and only 12.1% (12/99) never incorporate the Banff scores in their report.

Although there appears to be widespread adoption of the Banff classification among survey respondents, providers do not always have the information that is necessary for diagnosis readily available. Only 41.1% (55/133) of nephrologists/surgeons and 19.2% (19/99) of pathologists report that they always have DSA testing available at the time of the biopsy. A substantial proportion [18.2% (18/99)] of pathologists never have DSA information at the time of the biopsy.

Adjunctive testing for additional diagnostic criteria such as non-HLA antibody testing and/or molecular

Table 1. Demographics of survey respondents.

	Nephrologists/surgeons *n* (%) 133 (57.3)	Pathologist *n* (%) 99 (42.7)	*P*-value
Practice location			
North America	41 (30.8)	49 (49.5)	<0.0001
Europe	34 (25.6)	23 (23.2)	
Central/South America	35 (26.3)	5 (5.1)	
Asia	3 (2.3)	17 (17.2)	
Africa	11 (8.3)	2 (2.0)	
Australia/Oceania	9 (6.8)	2 (2.0)	
Unanswered	0 (0)	1 (0)	
Size of transplant center (number of kidney transplants/year)			
<50	19 (14.3)	10 (10.1)	0.27
51–100	29 (21.8)	15 (15.2)	
101–150	27 (20.3)	15 (15.2)	
151–200	14 (10.5)	12 (12.1)	
>200	41 (30.8)	45 (45.5)	
Unanswered	3 (2.3)	2 (2.0)	
Practice affiliation			
Academic center only	89 (66.9)	65 (65.7)	0.38
Academic and private practice	36 (27.1)	22 (22.2)	
Nonacademic private practice only	7 (5.4)	11 (11.1)	
Unanswered	1 (0.8)	1 (1.0)	
Performance of DSA positive transplants			
DSA positive with negative crossmatch	88 (66.2)	36 (36.4)	<0.0001
Flow cytometric crossmatch positive transplants performed	41 (30.8)	19 (19.2)	0.05
CDC positive crossmatch transplants performed	10 (7.5)	5 (5.1)	0.57
Surveillance biopsies performed			
Always	43 (32.3)	24 (24.2)	0.41
Sometimes	34 (25.6)	34 (34.3)	
Never	55 (41.4)	40 (40.4)	
Unanswered	1 (0.8)	1 (1.0)	
Follow-up biopsies performed after ABMR diagnosis and/or treatment			
Always	39 (29.3)	29 (29.3)	0.13
Sometimes	79 (59.4)	67 (67.7)	
Never	14 (10.5)	3 (3.0)	
Unanswered	1 (0.8)	0 (0.0)	

transcripts to support the diagnosis of ABMR are also rarely pursued Table 2. Nearly 90% of both nephrologists/surgeons and pathologists responded that they never incorporate molecular transcripts into the ABMR diagnosis. Even when DSA is absent and the biopsy shows features suggestive of ABMR (e.g., microvascular inflammation without C4d deposition), only 19.6% (26/133) of nephrologists/surgeons always order additional non-HLA antibody testing or molecular transcripts. Nearly half [44.4% (59/133)] of nephrologists/surgeons never order these tests. Eighty-two percent [82.0% (109/133)] of respondents believe that these tests will not change management and 48.1% (64/133) of respondents do not have non-HLA or molecular transcript tests readily available Fig. 1.

Availability of DSA testing

Because DSA testing is central to the diagnosis of ABMR, further analysis was done to understand why DSA information is not readily available for pathologists or nephrologists/surgeons. Among pathologists who report that they always use the Banff classification, 16.5% (15/91) also report that they never have DSA results available at the time the biopsy is interpreted Fig. 2. The proportion of nephrologists/surgeons who report that they always use the Banff classification, yet never have DSA results available at the time of diagnosis is lower at 4.6% (5/110). The responses from participants were similar when stratified by size of transplant center ($P = 0.83$), location of transplant center

Table 2. Information available to make an antibody-mediated rejection diagnosis.

	Always *n* (%)	Sometimes *n* (%)	Never *n* (%)	Unanswered *n* (%)	*P**
I use the Banff classification in the context of ABMR diagnosis					
Nephrologist/surgeon	110 (82.7)	18 (13.5)	4 (3.0)	1 (0.8)	0.11
Pathologist	91 (91.9)	4 (4.0)	3 (3.0)	1 (1.0)	
Banff scores are incorporated in the pathology reports					
Nephrologist/surgeon	118 (88.7)	9 (6.8)	6 (4.5)	0 (0)	0.03
Pathologist	75 (75.8)	10 (10.1)	12 (12.1)	2 (2.0)	
DSA information is available at the time of biopsy interpretation					
Nephrologist/surgeon	55 (41.4)	67 (50.4)	9 (6.8)	2 (1.5)	<0.0009
Pathologist	19 (19.2)	61 (61.6)	18 (18.2)	1 (1.0)	
Our center incorporates molecular transcripts in the ABMR diagnosis					
Nephrologist/surgeon	3 (2.3)	9 (6.8)	119 (89.5)	2 (1.5)	0.21
Pathologist	0 (0)	10 (10.1)	89 (89.9)	0 (0)	
When a biopsy is consistent with ABMR but no anti-HLA antibody is identified, I routinely order follow-up testing (e.g., non-HLA antibody or molecular transcripts					
Nephrologist/surgeon question only	26 (19.6)	47 (35.3)	59 (44.4)	1 (0.8)	NA

*Difference in responses among nephrologist/surgeon group and pathologists. Surveys from 133 nephrologists/surgeons and 99 pathologists were analyzed.

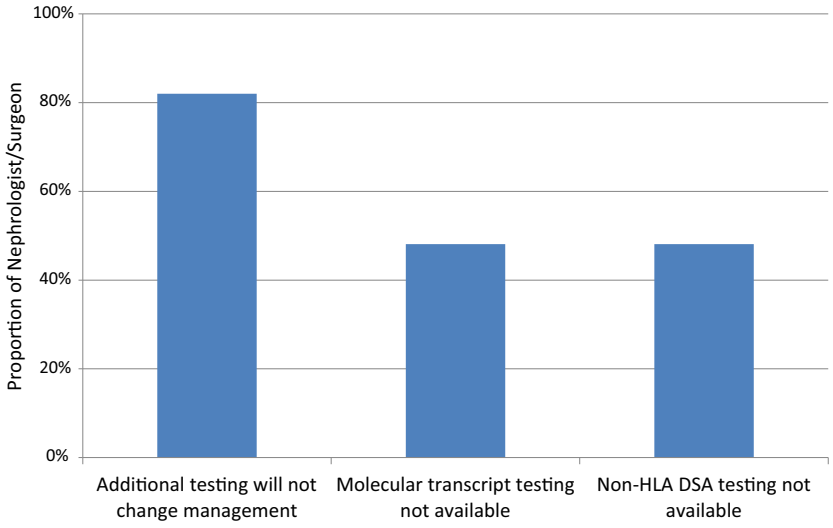

Figure 1 Reasons non-HLA DSA testing and molecular transcripts not ordered by nephrologists/surgeons.

($P = 0.17$), and transplant center practice affiliation (academic, academic and private practice, or private practice; $P = 0.9$; data not shown). Similar responses were also obtained regardless of whether their transplant center performs DSA positive only or positive cross-match (flow cytometric or positive CDC) kidney transplants.

Several comments were made to explain the absence or delay in DSA test results. The themes included the unavailability of HLA information needed to interrogate for DSA presence, DSA testing only performed on certain days of the week, delay in getting results from days to weeks, DSA testing not always ordered, and limited communication with HLA laboratories.

ABMR diagnosis from the pathologist's perspective

Pathologists were asked several questions about the factors used in making an ABMR diagnosis Fig. 3. The majority of [75.8% (75/99)] respondents from the pathologist group agreed that their final pathologic diagnosis depended upon both Banff lesion scores and DSA test results. A large proportion of pathologists also allowed factors not part of the Banff classification to influence their final ABMR diagnosis including the time post-transplant and allograft dysfunction. Specifically, 40.4% (40/99) of pathologists agreed that the timing post-transplant influences their ABMR diagnosis and 57.6% (57/99) of pathologists agreed that they consider

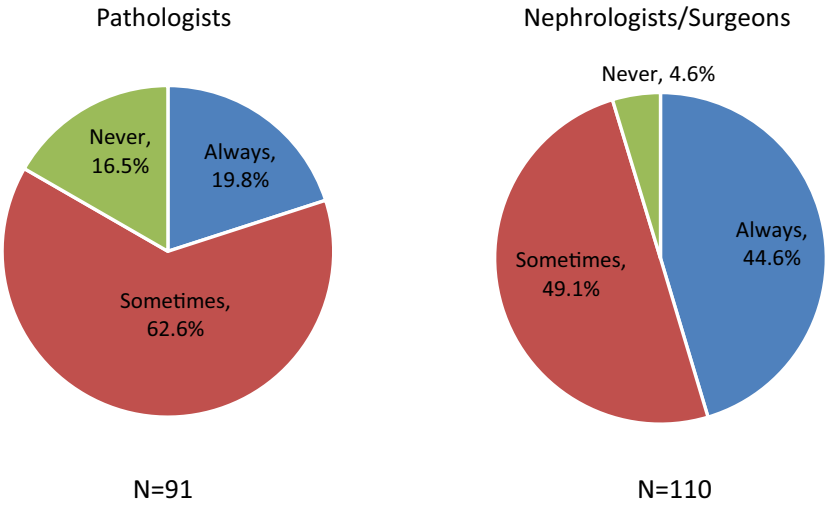

Figure 2 How often are DSA results available at the time of ABMR diagnosis among respondents who *always* use the Banff classification?

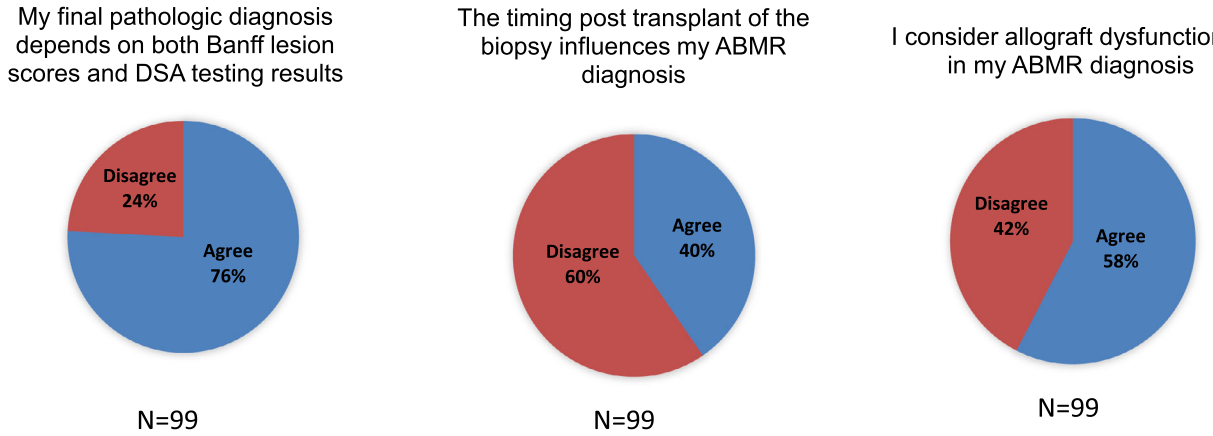

Figure 3 ABMR diagnosis from the pathologists' perspective. Pathologists were asked whether specific clinical features (not currently part of the Banff ABMR classification) were incorporated into their ABMR diagnosis.

allograft dysfunction (e.g. elevated serum creatinine and/or proteinuria) when making the ABMR diagnosis. How the pathologist ultimately makes final ABMR diagnosis is important because 81.7% (107/131) of the nephrologist/surgeon group agreed with concept that in the context of ABMR, the management plan was based on the final pathologic diagnosis rather than individual Banff scores.

Opportunities to improve the Banff ABMR classification system

Few survey participants responders [7.1% (7/99) of pathologists and 9.0% (12/133) of nephrologists/transplant surgeons] felt that there were no problems with the current ABMR Banff classification system Fig. 4. One of the main issues identified was the dichotomous nature (active and chronic active ABMR) of the ABMR categories: 57.6% (57/99) of pathologists and 65.4% (87/133) of the nephrologist/surgeon group felt that these dichotomous Banff categories of ABMR did not fully reflect the disease spectrum. Several respondents also felt that inflammatory changes concerning ABMR in the absence of DSA and/or C4d are not well accounted for [31.3% (31/99) pathologists and 37.6% (50/133) nephrologist/surgeons]. Additionally, over 20% of both groups responded that Banff was not easy to use. The minority of respondents felt that the current classification was difficult to understand, unlikely to change management, more appropriate for research than clinical use, or changes too frequently.

Discussion

While there appears to be widespread adoption of the Banff ABMR classification system among pathologists and practicing nephrologists/surgeons throughout the international community, the tools needed for optimal

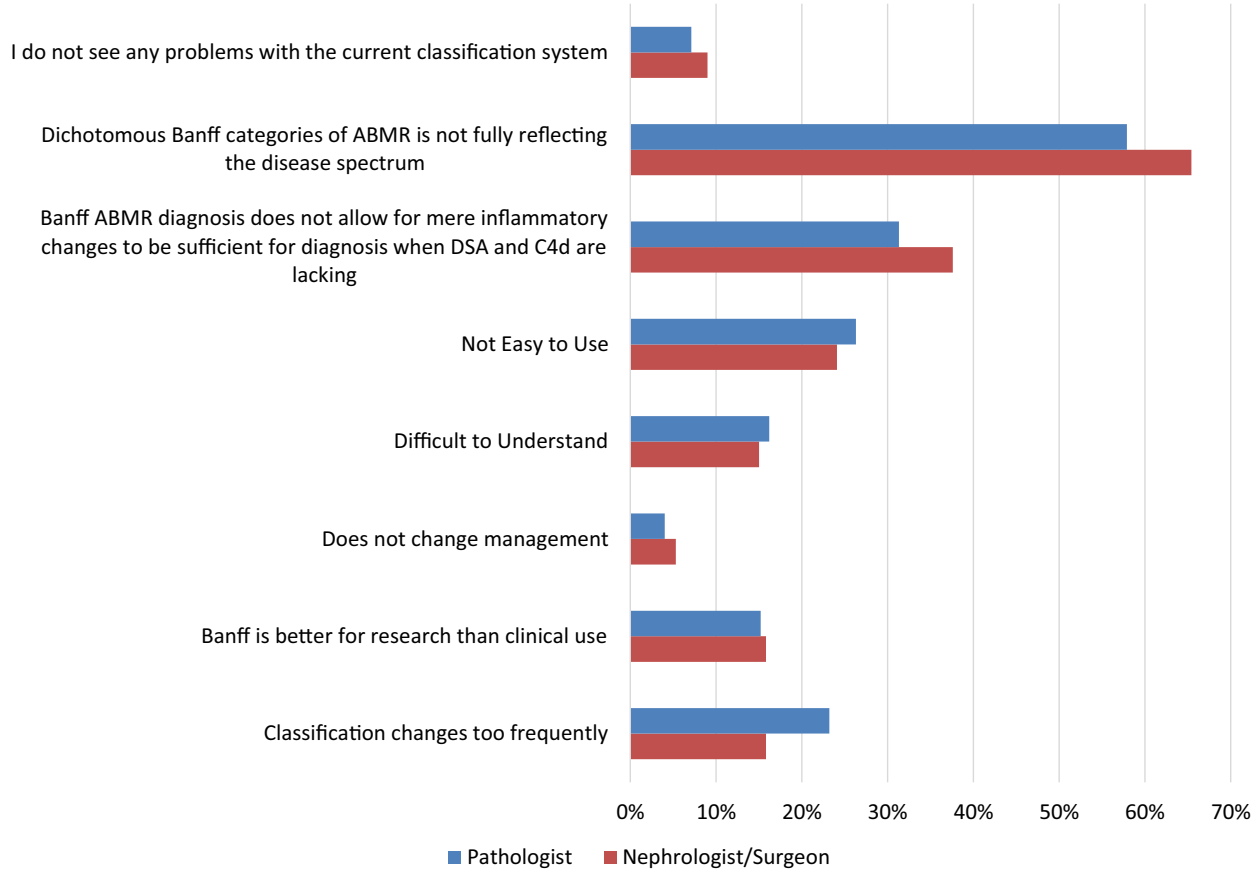

Figure 4 Limitations of the current ABMR Banff classification. Both pathologists and nephrologists/surgeons were asked yes/no questions about the various potential limitations of the Banff classification.

use of this classification system are not readily available or utilized. It is alarming that one of the cornerstones of ABMR diagnosis—DSA [6]—is often not readily available, especially because chronic ABMR is a leading cause of late graft loss [7]. Some would argue that this is irrelevant because of the lack of proven effective ABMR therapy [8], but without a clear diagnosis, it is difficult to adequately study treatment efficacy or the natural history of disease and its underlying mechanisms. Another key finding from our survey was that many pathologists incorporate features not part of the Banff classification into their diagnosis such as the time post-transplant or allograft dysfunction. These findings aid in our understanding why the Banff ABMR classification is vulnerable to misclassification as described in our previous manuscript [4].

Our survey results also suggest that tools such as non-HLA antibody testing and molecular diagnostic testing have not been fully embraced by practicing providers despite data suggesting their potential utility in practice [9–14]. This may contribute to confusion about what to do when the light microscopic features from the biopsy are consistent with ABMR, but DSA is absent. Part of the reason why these tests are not fully embraced is due to inherent issues with the antibody tests themselves (both DSA and non-HLA antibody tests) [15,16] and the lack of clarity about the clinical relevance of positive non-HLA antibody results [12,17–19]. The incidence of non-HLA antibodies is largely unknown, and the relevance of these antibodies independent of DSA is unclear due to the wide diversity of such targets and lack of testing methods that are robust and reproducible enough for wide adoption as a routine standard of care. This highlights the ongoing need for researchers, histocompatibility experts, and pathologists to better understand the role of different non-HLA and HLA antibodies in kidney transplant.

It is notable that nearly 30% of respondents felt that the Banff classification does not account for mere inflammatory changes concerning for ABMR without DSA or C4d positivity. This presents an opportunity for adding clarity in the nomenclature, particularly because there remain many unanswered questions regarding the mechanisms underlying these histologic findings [20].

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The current Banff classification attempts to incorporate complex patterns of surrogate markers (e.g., endothelial transcripts or non-HLA antibody) when DSA are absent in order to make the ABMR diagnosis. This creates confusion in the ABMR diagnosis and subsequent treatment—especially when most providers do not use non-HLA or molecular transcript information when formulating a diagnosis. One solution could be to clearly point out ABMR by HLA antibodies (called HLA-ABMR in analogy to MPO- and PR3-ANCA vasculitis or PLA2R positive membranous nephropathy), which can only be diagnosed when HLA antibodies are now or previously present and confirmed by HLA laboratory. In the presence of non-HLA antibodies, ABMR could be specifically defined as such and named non-HLA antibody ABMR (e.g., AT1R-ABMR). If neither DSA nor non-HLA antibodies are detected, the diagnosis should reflect this has well (e.g., microvascular inflammation suspicious for ABMR or ABMR-like disease) in order to make this very clear. Only by consistency in measurement of Banff lesions scores, use of diagnostic criteria appropriately, and clarity in the nomenclature will misclassification be reduced.

The original goal of this current survey was to obtain information to better understand the reasons for the discrepancies in diagnoses made by providers (nephrologists, surgeons, and pathologists) and those diagnoses intended by Banff [4]. Indeed, we found that pathologists often incorporate characteristics that are not explicitly part of the Banff classification such as the timing of the biopsy post-transplant or allograft dysfunction into the final diagnosis. A likely explanation of these survey results is that the Banff classification in its current form does not account for the full clinicopathologic spectrum of ABMR. Furthermore, pathologists often do not have access to required elements for ABMR diagnosis (in particular, DSA testing results). This is important because we found that nephrologists and surgeons rely on the pathologist's final diagnosis or interpretation of the histological features as provided in the biopsy report rather than the individual Banff scores themselves.

Over half of the participants also felt that the dichotomous (active or chronic active) categories of ABMR in the Banff classification was a limitation and not truly reflective of the spectrum of the disease. This issue was addressed at the Banff meeting in 2019 and acknowledged in the meeting report [3]. A "simple" diagnosis of active ABMR can include patients with a wide range of clinicopathologic features [8] including (i) a patient two weeks post-transplant with acute graft dysfunction, high serum levels of DSA, and a biopsy that shows acute tubular injury, minimal microvascular inflammation and diffuse C4d deposition in peritubular capillaries or (ii) a patient with stable graft function who has a history of DSA and undergoes a 2-year post-transplant protocol biopsy that shows moderate microvascular inflammation and negative peritubular capillary staining for C4d. A minority of participants felt that the complexity and frequent changes in the classification were significant barriers. Other strategies to improve the utility of Banff classification such as the use of morphometry to develop a continuous rather than ordinal scoring system are currently under consideration, but are not ready for widespread adoption [21,22].

How can we use the findings of this survey to improve ABMR diagnosis and treatment practices internationally? We recognize that many unanswered questions remain (e.g. relevance of non-HLA antibody and microvascular inflammation when no antibody is detected), but at this time we can focus on at least expanding the accessibility of DSA test results. This issue must be recognized by international transplant societies and extends beyond the scope of our Banff working group. It is also important to appreciate that this is not an isolated issue and the solutions are not isolated to the HLA laboratory. It appears to be as problematic for large academic centers in resource rich countries as it is for small private practice groups. Our survey was not designed to discern why DSA testing is often unavailable, but we assume that the reasons are varied and differ depending on the practice environment Table 3.

One of the main problems are delays in receiving results. These delays often depend on laboratory resources and the priority to test samples for DSA when the test is ordered as part of ABMR workup. Sometimes DSA testing is just not ordered because ABMR is not a consideration at the time of the biopsy. Occasionally, donor and/or recipient HLA genotyping is not available, incomplete, or of low resolution thereby making the solid phase single antigen bead assays difficult to interpret unless no HLA antibodies are detected. The lack of HLA typing can be a problem when patients move or get care from a facility other than their transplant center. These problems are only exacerbated when the HLA laboratory is located far from the practicing providers and incompatible medical record systems and/or paper charts are used. Communication barriers among HLA laboratory directors, pathologists, and the treating clinicians also underlie the unavailability of important DSA test results and highlight the need for standardized exchange formats.

Table 3. Availability of DSA results: barriers and strategies for improvement.

	Barriers	Strategies for improvement
Delay in DSA test results	Laboratory not aware of test priority	Establish tiered STAT (<8 h), urgent (24–72), and routine orders to communicate and prioritize testing within HLA laboratory
	Delays in DSA samples drawing or receipt in the laboratory	Expedite blood draws by developing protocols with outpatient laboratories or dialysis centers that allow electronic orders, availability of blood tubes, and shipping labels
DSA not ordered	Low suspicion of ABMR by ordering provider	Develop serum archive protocol with HLA laboratory or send blood kits home with patients. DSA testing can then be ordered and performed only if needed by pathologists (prior to final sign out) or provider
	DSA is not ordered with surveillance biopsies	Determine clinical features (degree of dysfunction, HLA mismatch, immunosuppression lowering) that would trigger DSA order with surveillance or "for cause" biopsies
HLA typing information not available or incomplete	Incomplete donor HLA typing (low resolution, not all classical HLA loci)	Original antigen level HLA typing (donor only) can be accessed via transplant agencies (for example UNOS)
		Contact the original recipient and donor HLA laboratory to obtain detailed HLA typing results which may rule in/out particular HLA alleles or request access to archived DNA for additional testing
		Storage of DNA samples on donors and recipient for future additional HLA typing
		HLA typing can be performed at time of biopsy from DNA extracted from serum clot tube (recipient), frozen biopsy tissue (donor), and possibly from fixed biopsy tissue
Communication breakdown	Multidisciplinary team practicing at different locations and/or institutions	Establish effective consistent channels of communication among Histocompatibility lab directors, pathologists and transplant clinicians
		Develop standard report criteria and time-to-report for routine, urgent, and de novo DSA results using electronic medical record and secure email
		Encourage pathologists to make recommendations about need for DSA testing if not otherwise ordered
	Medical records not accessible to all those involved in patient care	Hold regular multidisciplinary meetings to discuss routine and complex cases and assess clarity and timeliness of DSA reporting
	HLA typing and DSA information not included in medical records	Work with electronic medical record systems to incorporate readily accessible HLA and DSA information to the provider
	Lack of digital records of HLA typing and DSA information	
	Lack of understanding of new tests by providers	Hold ongoing educational seminars for new staff and trainees and at time of new test development or new clinical protocol implementation to facilitate clear communication

Fortunately, there are many systematic changes that can be made to improve the access to reliable DSA information Table 3. These improvements range from obtaining complete donor HLA typing that includes DQ and DP, developing processes to store serum for future testing, and customizing the appropriate timing for test results to be reported based on medical need. Incorporating both new and archived HLA information into the electronic medical record are of great importance and having regular multidisciplinary meetings and education sessions can overcome communication barriers.

We recognize the limitations of our study given that we relied on survey data. Like other surveys, it was prone to response bias related to the voluntary nature of study participation. The response rate was also relatively low, but larger and more comprehensive than similar surveys [23]. The respondents were largely from academic centers and most likely interested in the topic of ABMR, and thus the perceived availability of

important ABMR diagnostic tools may be overestimated. We acknowledge that the views elicited by this survey may not representative of the transplant providers who practice in the community. Some participants may have been approached more than once because of membership in multiple associations, but known duplicate responses were excluded. A perceived lack of anonymity may have influenced the responses. Additionally, the survey results were also largely descriptive.

In conclusion, the Banff ABMR classification system appears to be widely accepted and almost always used by transplant nephrologists, surgeons, and pathologists. However, DSA information is often not readily available, which is remarkable given that DSA is central to the ABMR diagnosis. We call to action major transplant histocompatibility societies to support efforts that will improve the accessibility of DSA information. Certain features such as the timing post-transplant and degree of allograft dysfunction also influence the final ABMR diagnosis despite not being part of the classification. This information illuminates an opportunity to further educate providers on how to standardize the application of use the Banff classification and for the Banff system to evolve to more accurately reflect the spectrum of antibody-mediated injury in the allograft.

Authorship

CAS: designed and performed research study, collected and analyzed data, and wrote paper. MA, LDC, EC, DD, FD, DAH, AMJ, ZK, FL, MN, JJR, FL, MN, JJR, RS-P, ESK and IB: designed and performed research study, analyzed data and wrote paper. SMB and LB: designed and performed research study, and wrote paper. KB, PC, MC and RC: designed and performed research study, and wrote paper. MCC-vG: designed and performed research study, collected data, and wrote paper.

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Conflicts of interest

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Surveillance biopsy stratified by location.

Table S2. Proportion of respondents whose center performs transplants with DSA, stratified by continent.

Table S3. Proportion of respondents whose center performs transplants with positive flow cytometric crossmatch, stratified by continent.

Table S4. Correlation between Surveillance biopsies and DSA + transplants.

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