Brief Communication

cPRA Increases With DQA, DPA, and DPB Unacceptable Antigens in the Canadian cPRA Calculator

K. J. Tinckam[1,2,*], R. Liwski[3], D. Pochinco[4], M. Mousseau[2], A. Grattan[2], P. Nickerson[2,4,5] and P. Campbell[6]

[1]Division of Nephrology, Department of Medicine and HLA Laboratory, University Health Network, University of Toronto, Toronto, Ontario, Canada
[2]Canadian Blood Services, Organ and Tissue Donation and Transplantation, Ottawa, Ontario, Canada
[3]Department of Pathology and Laboratory Medicine, Dalhousie University, Nova Scotia, Canada
[4]Transplant Immunology Laboratory, Diagnostic Services Manitoba, Winnipeg, Manitoba, Canada
[5]Section of Nephrology, Department of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada
[6]Division of Medicine and Laboratory Medicine, University of Alberta, Edmonton, Alberta, Canada
*Corresponding author: Kathryn Tinckam, Kathryn.Tinckam@uhn.ca

A calculated panel reactive antibody (cPRA) estimates the percentage of donors with unacceptable antigens (UA) for a recipient. cPRA may be underestimated in transplant candidates with UA to DQA, DPA, and DPB if these are not included in the calculation program. To serve the National Canadian Transplant Programs, a cPRA calculator was developed with complete molecular typing for all donors at HLA-A, B, C, DRB1, DRB3/4/5, DQA1, DQB1, DPA1, and DPB1, all resolved to serologic equivalents. The prevalence of UA at DQA, DPA and DPB was evaluated in a sensitized regional population. The impact of adding these additional UA to cPRA was calculated alone and in combination, and compared to the baseline cPRA for UA at A, B, C, DR, DR51/52/53, and DQ. Of 740 sensitized transplant candidates, 18% of total and 32% with cPRA≥95% had DQA UA. Twenty-seven percent of total and 54% with cPRA≥95% had DPB UA. Of 280/740 subjects with these UA, 36/280 (13%) had cPRA increase of >20% when they were included, 7% increased cPRA to ≥80% and 6% to ≥95%. Inclusion of DQA, DPA, and DPB UA in Canadian cPRA calculations improves the accuracy of cPRA where these are relevant in allocation.

Introduction

Calculated panel reactive antibody (cPRA) is the most biologically relevant estimate of the percentage of donors to whom a recipient has HLA antibodies or declared unacceptable antigens (UA). The most commonly used cPRA calculator is provided by the Organ Procurement and Transplant Network (OPTN) (1) which initially calculated cPRA for HLA A, B, DR, DR51/52/53, and DQ UA, and in December 2013 was expanded to include antibodies to C locus UA also.

cPRA facilitates better communication with transplant candidates and clinicians as one estimate of donor access, and additionally may be utilized in allocation prioritization (2,3) as well as to provide a metric for classifying immunologic status for research, quality assessment and operational uses.

HLA antibodies and/or UA may be additionally defined for proteins encoded by DQA1, DPA1, and DPB1 genes (for simplicity, subsequently referred to herein as DQA, DPA, and DPB UA, respectively) using commonly available single antigen bead reagents; however these do not, at present, contribute to the cPRA calculation in the OPTN calculator, and cannot be defined as unacceptable in UNOS allocation.

Canadian Blood Services operates a National Kidney Paired Donation Program (4,5) facilitating transplants through donor reallocation between otherwise incompatible pairs

and a Highly Sensitized Patient Program mandating national sharing of kidneys for recipients with a cPRA $\geq 95\%$. In both of these programs, allocation is first predicated on a negative virtual crossmatch (VXM) with no HLA donor-specific antibodies to HLA A, B, C, DR, DR51/52/53, and DQB antigens (where DQB represents in this context the protein encoded specifically by the DQB1 gene, to distinguish it from DQA) but also includes DQA, DPA, and DPB in the VXM. Additional prioritization points within these programs are assigned to patients with higher cPRA and Canadian Heart and Lung transplant programs also use antibody data for DQA, DPA, and DPB in their transplant decision-making. Since UA at all HLA loci are considered in ruling out potential donors or evaluating patient immunologic risk, a cPRA calculator that includes complete donor HLA typing may more accurately describe the percentage of donors with a positive VXM (6).

A Canadian cPRA calculator (7) was launched in April of 2012, with all donors in the calculator (starting in 2008) typed by molecular methods at HLA-A, B, C, DRB1, DRB3/4/5, DQA1, DQB1, DPA1, and DPB1 in order to support the Canadian Blood Services Transplant Programs and local transplant program cPRA calculation needs.

In the present study, we examined an active sensitized waitlist population to determine the burden of antibodies to DQA, DPA, and DPB in strata defined by baseline cPRA, and the impact of including these as UA in cPRA derived using the Canadian Blood Services cPRA Calculator.

Methods

The University Health Network Research Ethics Board approved this study: REB#13-6975.

The Canadian cPRA calculator (CDNcPRA-C)

All 14 Canadian Solid Organ Transplant HLA Laboratories provided ABO blood groups and molecular HLA typing at HLA-A, B, C, DRB1, DRB3/4/5, DQA1, DQB1, DPA1, and DPB1 for all deceased donors, which were then resolved to a single serologic equivalent for each allele. The first version of the calculator used in this study, included all deceased donors in Canada from January 2008 to December 2011 (n = 1708) from whom at least one organ was recovered and transplanted. Any missing alleles were assigned centrally at the Transplant Immunology Laboratory (Diagnostic Services Manitoba). The cPRA calculation sums the total of all donors to whom a patient has at least one UA and expresses this as a percentage of the total number of donors. Race frequencies are not utilized. Typings were verified against known haplotype associations (8–11); however, no robust DPA and DPB haplotype associations are reported and typing at these loci was entered as provided by the source laboratory. The calculator further permits stratification of cPRA by ABO blood group and region within Canada (Figure S1), although these were not utilized in the present analysis.

Patient population

All active and temporarily on-hold waitlisted kidney, pancreas, heart, lung, small bowel, and multi-organ combined-liver transplant candidates on October 31, 2013 on a regional waitlist who had at least one unacceptable antigen listed in their cumulative history were considered. Cumulative (all

ever detected) UA were used for this comparative analysis. Typically UA are listed on the basis of HLA antibodies detected quarterly using Single Antigen Bead Assays (One Lambda, Canoga Park, CA) and at a minimum mean fluorescent intensity (MFI) of 1200 (if epitope reactivity patterns indicate a real antibody reaction), with MFI of UA varying widely. The allele-specific antibody (A-S-Ab) category in this instance contains UA for which there are both single A-S-Ab as well as those resulting from the unique combination of DQA-DQB proteins (12,13). Although A-S-Ab do not contribute to cPRA, they are applied in virtual crossmatching algorithms. Laboratories determine antibody presence using their own internally validated thresholds and UA once listed were not re-examined or adjudicated in this study.

DPA, DPB, and DQA unacceptable antigen and A-S-Ab prevalence

The prevalence of DPA, DBP and DQA UA, and A-S-Ab was determined in subject groups defined by Baseline CDNcPRA 0–20%, 21–50%, 50–80%, 81–95%, 96–97%, and $\geq 98\%$, with the $\geq 98\%$ group further divided to individual cPRA categories.

Comparative cPRA calculations

Antigen frequency for all unique antigens present in both the CDNcPRA-C and the OPTN cPRA Calculator (OPTNcPRA-C) were compared by the Pearson co-efficient.

Baseline CDNcPRA was defined as cPRA determined in the Canadian calculator but inclusive of only those antigens present in the OPTNcPRA-C (A, B, C, DR, DR51/52/53, DQB) and was calculated for all sensitized waitlisted patients, and compared with OPTNcPRA by the Pearson co-efficient.

For candidates with DQA, DPA, and/or DPB UA, CDNcPRA was recalculated and compared to the Baseline CDNcPRA for each locus individually and then in combination and the new CDNcPRA was compared to Baseline CDNcPRA.

Additional exploratory CDNcPRA comparisons to OPTNcPRA with the addition of DQA, DPA, and DPB UA are shown in the Supporting Information.

Statistical analysis

Stata/IC Version 13.1 for Mac was used for all calculations. Where appropriate, comparisons between cPRA estimates were made by Pearson Correlation Coefficient and expressed as R^2. Categorical variables were compared by the chi-square test. All other comparisons of newer cPRA values to baseline cPRA were expressed as a difference in cPRA from baseline.

Results

Subjects

There were 740 transplant candidates with at least one UA (or allele-specific antibody) identified in their cumulative unacceptable antigen history. The distribution of cPRA using both the CDNcPRA-C (limited to OPTN loci) and the OPTNcPRA-C is shown in Figure 1, with similar distributions at baseline. There were 49 sensitized subjects who had only very low frequency UA or A-S-Ab listed as UA (the latter of which do not contribute to cPRA), resulting in a cPRA of 0%.
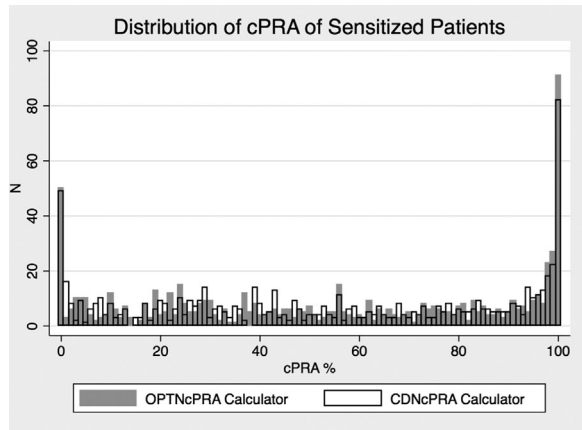
Figure 1: Distribution of cPRA of sensitized active waitlist candidates (limited to unacceptable A, B, C, DR, DRw, DQ antigens). The distribution of the cPRA of the subjects is comparable in the CDNcPRA calculator and the OPTNcPRA calculator, when the CDNcPRA calculator is limited to only those antigens present in the OPTNcPRA calculator. Sensitized subjects are present in the cohort across all cPRA quintiles. Subjects with UA of very low frequency and/or only allele-specific antibodies may still have a cPRA of 0% as allele-specific antibodies do not contribute to cPRA in either calculator. CDNcPRA, cPRA calculated from the Canadian calculator; cPRA, calculated PRA; OPTN, Organ Procurement and Transplantation Network; OPTNcPRA, cPRA calculated from the OPTN calculator; UA, unacceptable antigens.

Proportion of subjects with DQA, DPA, and DPB UA and A-S-Ab by cPRA category

There were 280 (38%) subjects with DQA and/or DPB UA listed (77 [28%] with DQA only, 142 [51%] with DPB only, and 61 [22%] with DQA and DPB UA). Only seven had DPA UA and were not included in additional detailed analyses due to this low frequency. A significant proportion of subjects with baseline cPRA>80% had DQA UA-(p < 0.001). DPA UA were listed for 37% of subjects with cPRA 80–95% and 33% with cPRA 96–97% versus 58% of those with cPRA≥98% (p < 0.001) (Table 1). For subjects with cPRA≥98%, the proportion of DQA and DPB UA was significantly greater in those with cPRA of 100% (Table 2). There were 138 (19%) of subjects with at least one A-S-Ab recorded, with a significantly higher proportion again in the ≥98% cPRA group (p < 0.001).

See Table S1 for corresponding analysis using OPTN cPRA calculator.

Baseline performance of the Canadian cPRA calculator

Antigen frequency was estimated in both calculators as cPRA for each unique antigen present in the OPTNcPRA-C (Figure 2A). Single antigen frequencies associated with known broad antigen groups that are not fully resolved to a single serologic equivalent within the OPTN calculator, are noted with arrows (DQ5,6,7,8,9). OPTN cPRA calculation methodology includes both the total broad and split serologic equivalent frequency in the estimate of each individual serologic frequency, leading to a potentially higher cPRA estimate for any single split antigen, compared to the Canadian calculator where all broad typings have been fully resolved. When only broad typings are correlated for DQB3 (DQB7/8/9) and DQB1 (DQB5/6), the two calculators yield even more highly correlated results (Figure 2B, $R^2 = 0.9992$).

cPRA for subjects are highly correlated also between the OPTN and Canadian Calculators when limited only to those loci present in the OPTN calculator (Figure 2C and D, $R^2 = 0.9980$). See Tables S1A and S1B for details regarding impact of fully resolved typing for all serologic equivalents.

Impact to cPRA with addition of C locus UA

In December 2013, the OPTN calculator was revised to include UA at C locus. Figure 3 illustrates the change in Canadian cPRA with inclusion versus exclusion of C locus UA (compared to the baseline of A, B, DR, DR51/52/53, and DQB only). Two hundred sixty-five out of seven hundred forty (36%) of subjects had C locus UA recorded. Of these, 35 (13%) had an increase in Class I cPRA of >20% when C locus specificities were included in the cPRA (data not shown). Corresponding analysis comparing the OPTNcPRA with and without C locus included is shown in Figure S2.

Impact of adding DQA, DPB UA in CDNcPRA calculation

When compared to a baseline CDNcPRA (using the Canadian Calculator for A, B, Cw, DRB, DR51/52/53, and DQB antigens), the Class II cPRA increased by >20% for

Table 1: Proportion of subjects with DQA, DPA, and DPB unacceptable antigens, and allele-specific antibodies (A-S-Ab) by cPRA category calculated with Canadian calculator

Baseline CDNcPRA	0–20% n = 165	21–50% n = 182	51–80% n = 147	81–95% n = 100	96–97% n = 24	≥98% n = 122	p-value
DQA (n = 138)	22 (13%)	13 (7%)	25 (17%)	31 (31%)	6 (25%)	41 (34%)	<0.001
DPA (n = 7)	0	0	0	0	0	7 (6%)	<0.001
DPB (n = 203)	26 (16%)	34 (19%)	27 (18%)	37 (37%)	8 (33%)	71 (58%)	<0.001
A-S-Ab (n = 189)	31 (19%)	19 (10%)	26 (18%)	18 (18%)	5 (21%)	39 (32%)	<0.001

CDNcPRA, cPRA calculated from the Canadian calculator; cPRA, calculated PRA; DPA, a protein encoded by the DPA1 gene; DPB, a protein encoded by the DPB1 gene; DQA, a protein encoded by the DQA1 gene.

Table 2: Proportion of subjects with baseline cPRA ≥ 98% with DQA, DPA, and DPB unacceptable antigens, and A-S-Ab calculated with the Canadian calculator

Baseline CDNcPRA	98% n = 18	99% n = 22	100% n = 82	p-value
DQA (n = 41)	4 (22%)	3 (14%)	34 (41%)	0.027
DPA (n = 7)	1 (5%)	0	6 (6%)	NS
DPB (n = 122)	9 (50%)	7 (32%)	55 (67%)	0.009
A-S-Ab (n = 122)	7 (39%)	3 (14%)	29 (35%)	0.121

CDNcPRA, cPRA calculated from the Canadian calculator; cPRA, calculated PRA; DPA, a protein encoded by the DPA1 gene; DPB, a protein encoded by the DPB1 gene; DQA, a protein encoded by the DQA1 gene.

43/138 (31%) of subjects with DQA UA. The Class II cPRA increased by >20% for 20/203 (10%) of subjects with DPB UA. Overall, of 280/740 subjects with DQA, DPA, and/or DPB UA, 36/280 (13%) had an increase in CDNcPRA of >20% (Table 3). See Table S4 for the corresponding analysis using OPTNcPRA as the baseline value.

For seven subjects with DPA UA, CDNcPRA increased by 20–68% when compared with baseline CDNcPRA in isolation. However, all seven subjects had DPB UA and the cPRA change due to DPA, after DPB was considered was negligible.

Figure 4 illustrates individual subjects' change in in CDNcPRA with the addition of DQA and DPB unacceptable
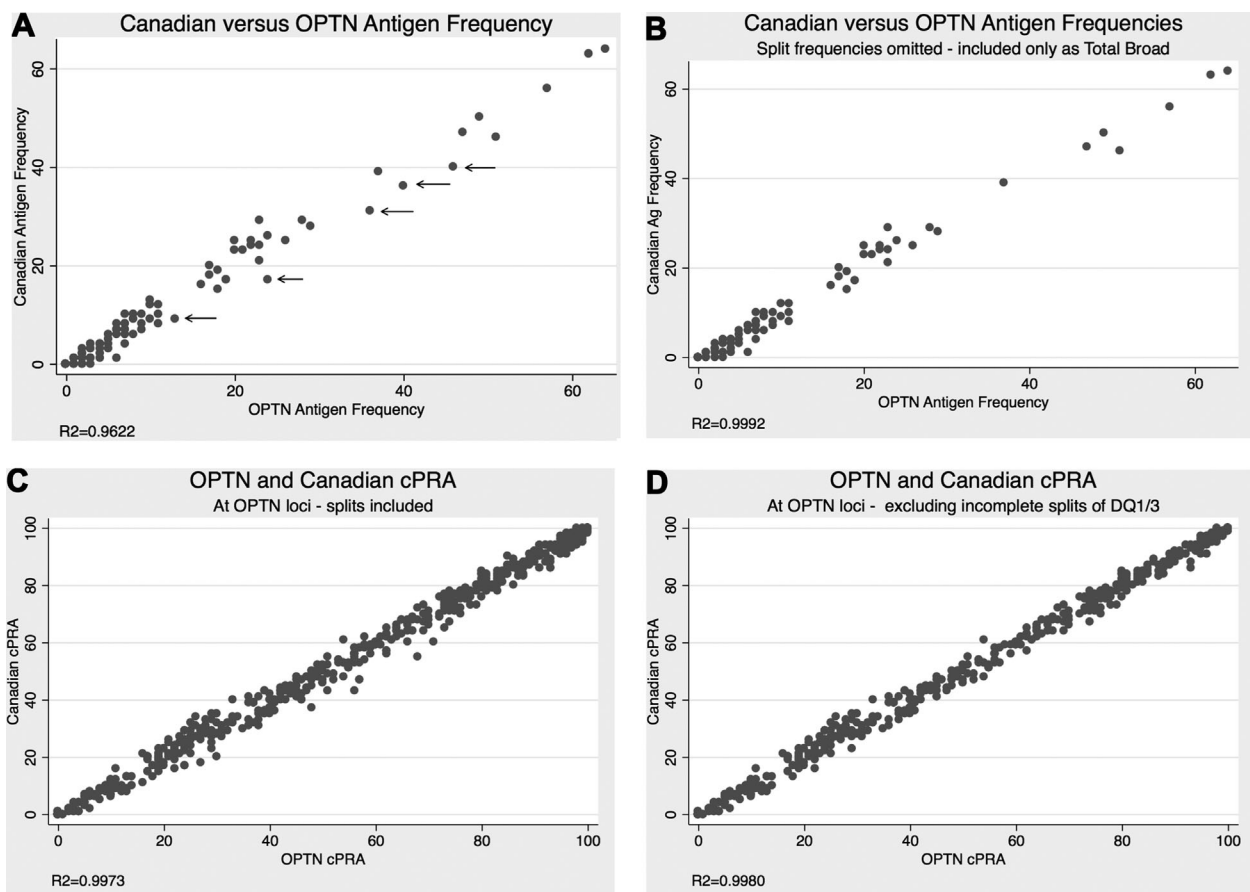

Figure 2: Canadian and OPTN cPRA calculators perform comparably for single antigen frequencies and cPRA of the study population when limited to those antigens present only in the OPTN calculator. (A) Single antigen frequencies are correlated between the Canadian and OPTN cPRA calculator. ($R^2 = 0.9622$) (outliers are notable for DQ5 and 6 (serologic equivalents from the broad DQ1) and DQ7, 8 and 9 (serologic equivalents from the broad DQ3), which are not fully resolved in the OPTN calculator. cPRA for a single antigen may be overestimated in OPTN as the broad serologic frequency is counted in its entirety when a single serologic frequency is estimated. (B) When these serologic equivalents are considered only at their broad level, the correlation of single antigen cPRA is very high ($R^2 = 0.9992$). (C) For the study population of interest, Canadian and OPTN cPRA are similarly highly correlated when limited to only those antigens included in the OPTN calculator ($R^2 = 0.9973$). (D) When those subjects with only a subset of serologic equivalents of DQ1 or DQ3 are excluded, the correlation is even higher ($R^2 = 9980$). cPRA, calculated PRA; OPTN, Organ Procurement and Transplantation Network; UA, unacceptable antigens.
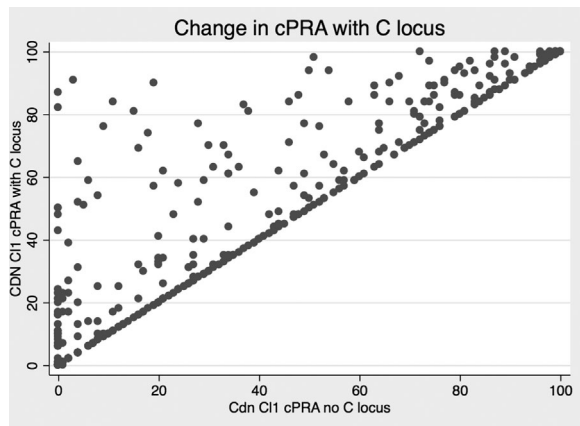
Figure 3: Change in individual subjects Class I cPRA with inclusion versus exclusion of C locus unacceptable antigens. 265/740 (36%) of subjects had C locus UA recorded. Of these, 35 (13%) had an increase in Class I cPRA of >20% when C locus specificities were included in the cPRA, with a 5–20% increase in an additional 25% of these subjects. CDNcPRA, cPRA calculated from the Canadian calculator; cPRA, calculated PRA; UA, unacceptable antigens.

over that calculated with only baseline UA. An illustration of subjects' CDNcPRA with DQA and DPB UA in comparison with OPTN cPRA is provided in Figure S3.

Figure 5 illustrates increase in total cPRA for subjects with DQA, DPA and DPB UA included. Of subjects with one or more of these UA, 7% moved from <80% to >80% cPRA and 5% moved from <98% category to ≥98% when the additional loci were included. CDNcPRA with all loci included compared to OPTNcPRA is presented in Figure S4.

Of subjects with 95% CDNcPRA and higher at baseline, 18 (12%) had a further increase in cPRA of at least 1% with inclusion of all unacceptable antigens. Of subjects with cPRA 80–95%, 14 (14%) had a further increase in cPRA of

Table 3: Difference in Canadian cPRA from baseline loci (A, B, Cw, DR, DRw, DQ) with addition of DQA, DPA, and DPB unacceptable antigens

Increase in CDNcPRA	Including DQA class II cPRA N = 138	Including DPB class II cPRA N = 203	Including all DQA, DPA, DPB total class I /II cPRA N = 280
<5%	65 (47%)	115 (57%)	174 (62%)
5–10%	5 (4%)	31 (15%)	31 (11%)
11–20%	25 (18%)	37 (18%)	39 (14%)
>20%	43 (31%)	20 (10%)	36 (13%)

CDNcPRA, cPRA calculated from the Canadian calculator; cPRA, calculated PRA; DPA, a protein encoded by the DPA1 gene; DPB, a protein encoded by the DPB1 gene; DQA, a protein encoded by the DQA1 gene.
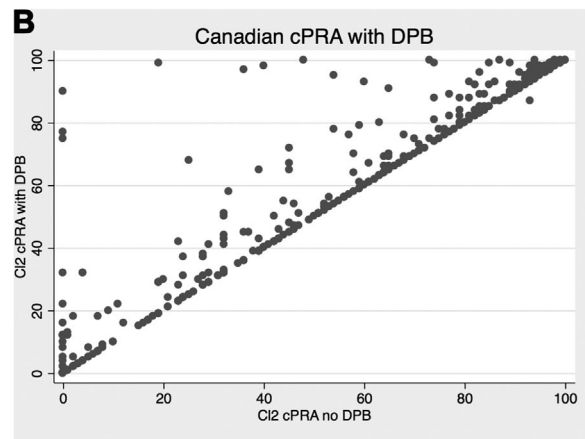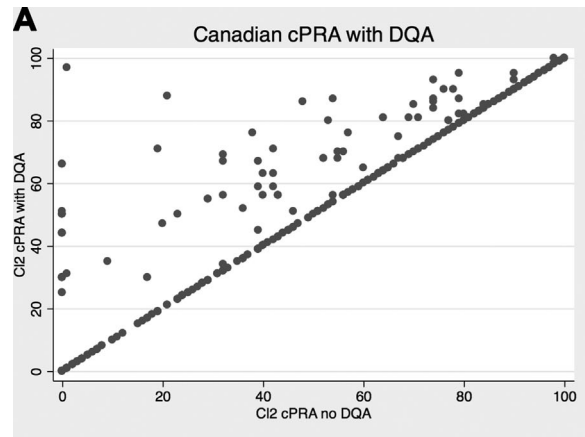

Figure 4: Increase in individual subjects' Class II CDNcPRA over baseline with the addition of DQA (Panel A) and DPB (Panel B) unacceptable antigens. (A) Class II cPRA increased by >20% in 31% of subjects with DQA UA with increase of 5–20% in an additional 22% of subjects. (B) Class II cPRA increased by >20% in 10% of subjects with DQB UA, with an increase of 5–20% in an additional 33% of subjects. CDNcPRA, cPRA calculated from the Canadian calculator; cPRA, calculated PRA; DPB, a protein encoded by the DPB1 gene; DQA, a protein encoded by the DQA1 gene; UA, unacceptable antigens.

at least 5%. At higher cPRA, even a small increase can represent an important reduction in the number of potentially acceptable donors (Table S5).

Discussion

Our study demonstrates that inclusion of DQA, DPA, and DPB UA in a cPRA calculation method increases cPRA by more than 10% in 27% of a sensitized waitlist population with any of these UA. DQA, DPA, and DPB UA are overrepresented in sensitized subjects (in particular those with 98% cPRA or greater), and the ability to define these as unacceptable may improve VXM accuracy in this population.
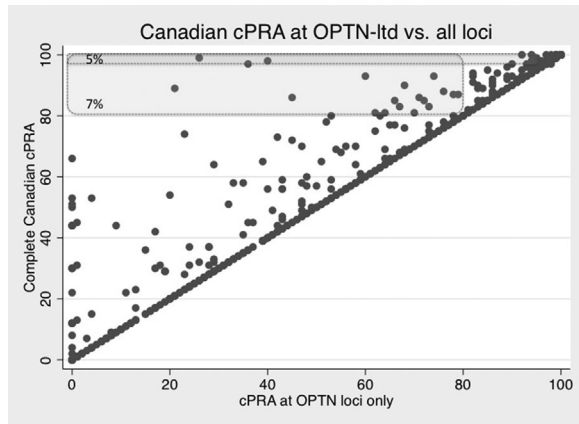
Figure 5: Overall change in individual subjects' Canadian cPRA over baseline with inclusion of all DQA, DPA, and DPB unacceptable antigens. Total cPRA increased by >20% in 13% of all subjects with any DQA, DPA, or DPB UA. Seven percent of subjects with DQA, DPA, and/or DPB unacceptable antigens moved into the cPRA>80% category. Five percent of these subjects moved into the >98% category. cPRA, calculated PRA; DPA, a protein encoded by the DPA1 gene; DPB, a protein encoded by the DPB1 gene; DQA, a protein encoded by the DQA1 gene; OPTN, Organ Procurement and Transplantation Network; UA, unacceptable antigens.

With the calculator available in 2007, the utilization of the cPRA in 2009 by the OPTN was designed to improve efficiency of allocation by reducing unexpected positive crossmatches and to ensure that cPRA was transparently reflective of the breadth of unacceptable antigens (14–16). In the development of the Canadian Blood Services Kidney Paired Donation Program and deceased donor Highly Sensitized Patient Program, the importance of cPRA to accurately prioritize patients was also recognized. Initially the OPTN cPRA calculator (1) was used in these programs, but subsequent data supported the need for a Canadian calculator reflecting our donor population and our unique national allocation priorities that evolved to include DQA, DPA, and DPB in virtual crossmatch algorithms.

A significant number of our waitlisted recipient are receiving their second or greater transplant and many have antibodies to DQA, DPA and/or DPB (17) in part due to allocation policies that have favored time on waitlist over matching except for 0ABDR (18). Additionally, from 2009 to 2011 in the Canadian KPD Program, we found that a number of proposed pairs with negative virtual cross-matches to HLA A, B C, DR, DR51/52/53, and DQB, had unexpectedly positive actual crossmatches due to anti-bodies to DQA and DPA and DPB (4), similar to other reports (19). Therefore, a decision was made to subsequently include these loci in the virtual crossmatch algorithms, and also in the CDNcPRA calculator to ensure that patients received appropriate cPRA-based allocation consideration for all UA that may exclude donors.

To ensure complete resolution to serologic equivalents, and avoid potential overestimation of cPRA that may occur with inclusion of broad antigen typings (Figure 2), it was agreed by all laboratories that 100% of donors in the calculator and subsequently all deceased donors utilized in Canada would be typed by molecular methods at all HLA loci (20), representing a substantial increase of DPA1/DPB1 typing over the 29% reported in the United States and the unknown U.S. percentage of laboratories performing DQA1 typing (21). As expected with the Canadian population, the total number of donors is small but will continue to be updated including all deceased donors in Canada from whom at least one organ is transplanted. An interval update of 1108 donors is pending in Spring 2015 and beginning in Summer 2015, the Canadian Transplant Registry will update donor data automatically on a quarterly basis.

We recognize that we have chosen a simplified and local approach to our cPRA calculator, and have not employed the rigorous population genetics methodologies, haplotype frequency analysis and race frequency analysis that were used to develop the OPTNcPRA with larger donor numbers. However, we are reassured by similar cPRA distribution to OPTN calculator when the Canadian Calculator is restricted to OPTN UA, as well as the highly correlated single antigen cPRA comparison (Figure 2). This aligns with observations by Baxter-Lowe et al (19) in a paired exchange registry analysis that the size of the donor pool is not critical in determining the percentage of donors with a positive virtual crossmatch. We would not assume that DQA, DPA and DPB frequencies in the OPTN donor population are same as the Canadian donor population without actual typing data, and more rigorous population genetic analysis; however, recent paired exchange data using a cPRA calculator from the National Kidney Registry donor pool that did include DPB typing suggest that antibodies to at least DPB affect US-based cPRA calculations comparably to the impact demonstrated in our study (19). Interpretation of DPB typing and UA may be further limited by the absence of known robust DPA/DPB haplotype associations, as well as the limited polymorphism at the DPB locus (with broad antibody specificities driven by a potentially limited number of epitope sites alone or in combination) (22) and evolution of our simplified approach to impact of DPB on cPRA requires more rigorous studies.

Ultimately the impact of including all of these additional UA in cPRA calculations depends upon whether the program regard these loci as important to avoid when proceeding with transplantation.

DQA and DPB UA and A-S-Ab have a notable prevalence in waitlisted patients in a Canadian population and are overrepresented in sensitized patients, to a similar extent as recently reported in US centers (12,19,23). Whereas the addition of these as UA may not increase cPRA (or presently in the case of A-S-Ab, not change it at all) significantly further when it is already high, the high proportion of these

additional UA/antibodies in very highly sensitized patients may result in a substantial further decrement in access to transplant. A data system, such as this one supporting the Canadian cPRA Calculator, with mandatory DQA, DPA, and DPB typing and the capability of including DQA, DPA, and DPB UA and A-S-Ab in VXM, where these are determined to be undesirable in transplant, may facilitate more efficient and equitable allocation of organs in patients with these UA with fewer unanticipated positive cell-based cross-matches (13,23). However, additional studies are needed to better understand the nature of allele-specific responses, and moreover, the nature of epitope-driven immunogenicity at the level of unique HLA proteins (24).

An accurate cPRA is important to inform patients of their likely access to transplantation, to accord points in allocation systems and to accurately characterize the clinical immunology of patient populations in research. Our study demonstrates that inclusion of DQA, DPA, and DPB as UA in Canadian cPRA calculations increases CDNcPRA in at least 13% of sensitized patients in a waitlisted population. Given the similarity in performance of the Canadian and OPTN cPRA calculators at baseline, further investigation may be warranted to determine if inclusion of DQA, DPA, and DPB UA in cPRA calculations has a similar impact in kidney paired donation programs or other jurisdictions where these UA are deemed undesirable. In the new OPTN kidney allocation scheme, inclusion of these UA in cPRA calculations (and VXM algorithms) may result in more accurate identification of highly sensitized patients to be prioritized for local, regional and national sharing and greater awareness of the full scope of their unacceptable antigens prior to organ allocation (23).

Acknowledgments

Disclosure

The authors of this manuscript have conflicts of interest to disclose as described by the *American Journal of Transplantation*. Drs. Tinckam and Nickerson are Medical Advisors (Organ and Tissue Donation and Transplantation) to Canadian Blood Services, a federal and provincial government funded Health Care Agency.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Figure S1: Canadian cPRA Calculator—Web page image. The Canadian cPRA Calculator has all donor typings by molecular methods resolved to a single serologic equivalent at HLA-A, B, C, DRB1, DRB3/4/5, DQA1, DQB1, DPA1, DPB1 loci. Additional filtering may be applied for ABO group and region within Canada.

Figure S2: Change in Class I cPRA for patients with addition of C locus unacceptable antigen to OPTN cPRA calculator. In a within OPTN calculator comparison, the addition of C locus unacceptable antigens resulted in an increase in Class I cPRA of >25% in 55/265 (21%) of subjects (data not shown).

Figure S3: Comparison of Canadian cPRA with OPTN cPRA after addition of DQA (Panel A) and DPB (Panel B) unacceptable antigens.

Figure S4: Canadian cPRA with DQA, DPA, and DPB included compared to current OPTN cPRA.

Table S1A: Proportion of subjects of DQA, DPA, and DPB unacceptable antigens, and allele-specific antibodies by cPRA Category calculated with the OPTN Calculator.

Table S1B: Proportion of subjects with Baseline cPRA≥98% with DQA, DPA, and DPB unacceptable antigens, and A-S-Ab calculated with the OPTN Calculator.

Table S2: Percent of broad typings that are unresolved to their serologic (split) equivalent in Canadian and OPTN Calculator.

Table S3: Impact of full resolution to serologic equivalents, on broad and split antigen frequency in the Canadian and OPTN Calculators.

Table S4: Increase in Canadian cPRA with addition of DQA and DPB Unacceptable antigens compared with baseline OPTN cPRA.

Table S5: Estimated frequency of acceptable HLA mismatch donors for cPRA>80%.