Benefits and Consequences of an Increased Threshold to Listed Unacceptable Antigens for Renal Transplant Waitlist Candidates

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INTRODUCTION

Preformed DSA are a known contraindication to transplant, and ideally all DSAs would be avoided in selecting a prospective donor. Unfortunately, such an approach is impractical given the scarcity of transplantable organs and an estimated 45% of renal waitlist patients who have some degree of sensitization against HLA antigens. To date there is no consensus MFI threshold for positivity in the SAB assay, and as such, interpretation of HLA specificities, their exclusion as unacceptable antigens, and use for pre-transplant risk assessment are left to individual transplant programs.

METHODS/DEMOGRAPHICS

We reanalyzed a cohort of actively listed kidney patients (n=171) at a proposed cutoff of 4000 MFI from our previous 2000 MFI cutoff in our single antigen bead assay (One Lambda Inc,) to examine the corresponding effect on CPRAKAS scoring, and virtual/flow XM rates.

Age (mean ± std)		
	56.8	± 8.6
Sex (n,%)		
Male	155	(90.6)
Female	16	(9.4)
Previous Transplant (n,%)		
No	166	(97.1)
Yes	5	(2.9)
Race (n,%)		
White	57	(33.5)
Black	94	(55.3)
Asian	6	(3.5)
Unreported	13	(7.6)

RESULTS

Our assessment showed that the proposed shift in MFI cutoff would result in a significant decrease to CPRA for our kidney cohort (**Fig 1A**). When stratified by ΔCPRA, 77/96 patients positive for HLA ab would see a decrease, however in 42 of those 77 cases the resultant change in CPRA was <10 (**Fig 1B**). Thus only 35/96 of HLA ab+ may be significantly affected.

RESULTS

Fig 1A. CPRA change

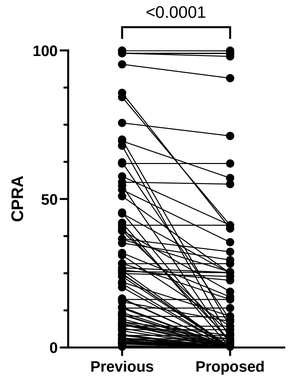


Fig 1B. ΔCPRA stratified

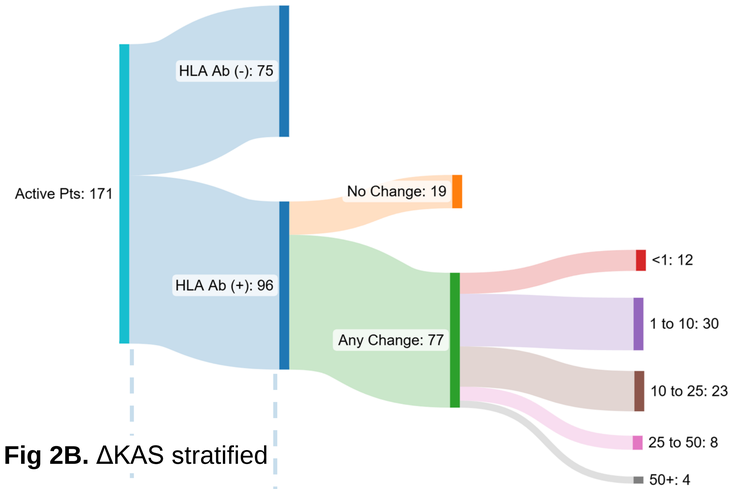


Fig 2A. KAS change

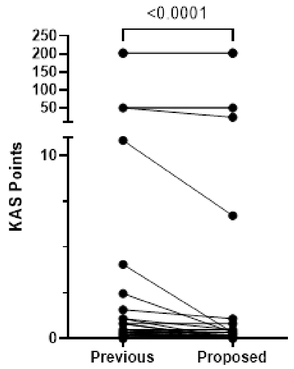


Fig 2B. ΔKAS stratified

We next calculated how the resultant changes in CPRA would in turn modify allocation of KAS points. KAS points scale exponentially with CPRA to provide more equitable access to highly sensitized patients. Therefore the potential benefits of increasing the available donor pool by means of CPRA reduction can result in an offsetting loss in KAS prioritization. As expected, there would be a significant reduction in the KAS scores of our patient cohort accompanying the proposed switch in MFI cutoff (**Fig 2A**). 31/96 of HLA ab+ would experience a loss in KAS points (**Fig 2B**), and of those, 5 of whom where ΔKAS was >1. Altogether an MFI cutoff increase, 80% of our patient population would stand to gain increased access to donors, whereas 5% would lose a considerable level of KAS-based prioritization on the waitlist.

Patients for which the proposed cutoff increase would be most disadvantageous (highlighted red in **Fig 3**), fell into two categories: 1) large shifts in CPRA moving them below the highly sensitized threshold of CPRA>80 and associated preferential scoring, or 2) small shifts in patients who had CPRA>95, where incremental decreases in CPRA reduce KAS points on an exponential scale. Interestingly, the proposed shift may benefit some of our most highly sensitized patients. Two 100% CPRA patients had the largest antigen dropout (highlighted purple in **Fig 3**) thus reducing unacceptable burden, but as the fractional ΔCPRA did not shift them out of the 100% CPRA category they maintained maximum KAS scoring.

RESULTS

Fig 3.

Δ CPRA	Δ # of UA	Δ KAS
65.0169	7	0.81
62.9830	7	1.09
53.2770	8	0.48
52.9994	9	0.81
45.6581	8	3.71
43.9016	3	0.34
43.1037	6	2.12
42.0044	2	0.34
37.8815	4	0.34
34.6228	4	0.21
26.0513	3	0.08
25.9541	4	0.4
24.9047	2	0.08
24.7922	3	0.08
23.9618	1	0.08
23.9482	7	0.21
21.5466	3	0.08
20.6251	4	0.21
20.2984	2	0.08
20.1241	5	0.26
17.6674	7	0.27
16.5609	2	0
16.5083	3	0
16.4259	5	0.14
16.3964	2	0
14.8047	2	0.21
13.6642	2	0
13.2331	1	0
12.4776	7	0.61
12.1535	2	0.08
11.5099	2	0
11.4379	1	0.08

Δ CPRA	Δ # of UA	Δ KAS
11.206	3	0
11.0096	4	0.13
10.9887	3	0
9.5322	2	0
8.3343	1	0
8.1497	2	0
7.7227	3	0
6.6351	2	0
6.5604	2	0
5.7549	2	0.13
5.4765	1	0
4.8009	4	0
4.6751	10	4.11
4.5936	2	0
4.4266	1	0
4.421	5	0
4.3805	7	0.49
4.0869	1	0
3.4228	1	0
3.0936	1	0
3.0936	1	0
2.9782	1	0
2.9782	1	0
2.9589	1	0
2.9306	1	0
2.413	2	0
1.8149	2	0
1.7182	2	0
1.6249	3	0
1.4241	2	0
1.259	2	0
1.1927	1	0

Δ CPRA	Δ # of UA	Δ KAS
1.0468	10	25.69
0.9429	1	0
0.6697	1	0
0.6473	2	0
0.4163	1	0
0.2525	19	0
0.2382	1	0
0.1805	1	0
0.0314	18	0
0.0198	1	0
0.0198	1	0
0.0187	1	0
0.0123	2	0
0	0	0
0	1	0
0	0	0
0	0	0
0	0	0
0	0	0
0	0	0
0	0	0
0	0	0
0	0	0
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0	0	0
0	0	0
0	0	0
0	0	0
0	0	0
0	0	0
0	0	0
0	0	0
0	1	0

Fig 4. XM and Txp 8mo previous- and post-swtich

	Previous	Post
Virtual XM (% pos)	221 (5.4%)	152 (8.5%)
Flow XM (% pos)	92 (11.0%)	52 (5.8%)
Transplants	17	26

Despite a theoretically expanded donor pool, there was no increase in virtual or flow XMs performed. Effect on XM positivity is negligible.

CONCLUSIONS

Each transplant center must make its own determination of acceptable risk that best serves their respective patient populations. Our preliminary assessment into raising the MFI cutoff for listing of unacceptable antigens was interpreted as overall beneficial by our transplant program. Balancing accessibility versus risk tolerance is a conundrum for all in the transplant community, and our findings provide insights into the potential advantages and drawbacks that accompany adjusting the criteria for listing unacceptable antigens.