What's the Risk? A Multicenter Comparative Study of Virtual Crossmatch Risk Assessments

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STUDY AIMS

The degree of acceptable immunologic risk varies among transplant centers and directors, but this variability is not well characterized. Utilization of physical crossmatch (XM) , interpretation and reporting of antibodies have been evolving in recent years. A key pivot point to the acceptance of a donor organ stems from the comment provided by the HLA laboratory director at the time of consult. A director's consult recommendation incorporates the results of the recipient's antibody analysis and specific recipient and donor properties. We undertook a multicenter study that examined 20 cases with unclear or Positive virtual and/or flow XM results to examine the range of variability in director's consults.

STUDY DESIGN

- 4 Directors evaluated a total of 20 cases
- 4-6 cases were submitted by each director
- Cases were rated on a scale from 0-5 (Table 1)
- Scores of individual directors were compared
- Average score based on type of case were compared.

Table 1. Director Consult Decision Score description

Consult Decision Score	Interpretation
0	No concerns. Proceed as standard DSA monitoring protocol.
1	Minimal Risk. Standard DSA monitoring recommended.
2	Low Risk. Enhanced DSA monitoring recommended.
3	Moderate-High Risk. Enhanced DSA monitoring recommended.
4	High Risk. Close DSA monitoring through desensitization recommended.
5	Advise against proceeding.

RESULTS

- General agreement for 14/20 cases (70%)
- Key Factors for variability:
  - Transplant type (heart/lung vs kidney)
  - Center established pre-transplant desensitization protocols
  - General risk tolerance of the transplant center DSA targets (C, DP)
  - DSA strength
  - Current vs. historic DSA
  - Sensitization status

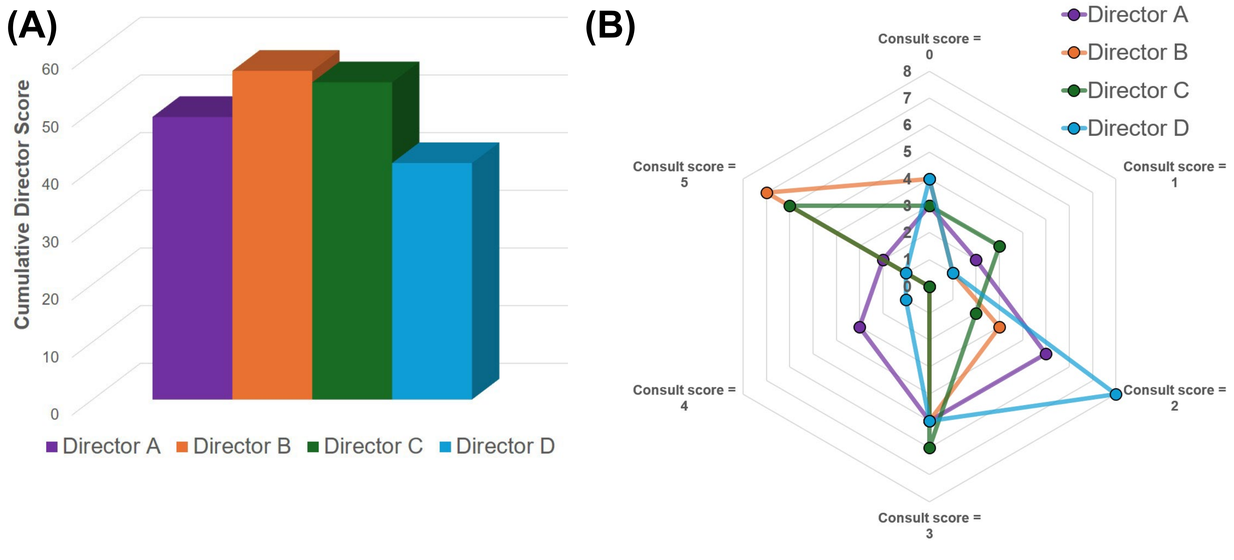


Figure 1. Director's consult scores. Cumulative Director scores were summed up and are shown **(A)**. Individual variances among the director scores are demonstrated on the radar plot on the right **(B)**.

DETAILED CONSULT COMPARISON

Case No.	vXM Result	# of DSAs	Primary DSA Targets MFI	FCXM Result (T -, B -)	Recip. cPRA	Recip. Age	Recip. Sex	Recip. Dialysis time (Years, Kidney)	Recip. Status (Heart)	Donor Age	Donor KDPI (%)	Prev. Tx. (Y/N)	Repeat MM(s) to Prev Tx	Director A Consult Score	Director B Consult Score	Director C Consult Score	Director D Consult Score
1	Neg	0	N/A	T Pos B Neg	18%	64	M	5.7	N/A	52	47	N	N/A	0	0	0	0
2	Neg	0	Nonspecific binding	T Neg B Pos	97%	46	M	1.3	N/A	50	29	Y	A2	1	1	0	1
3	Neg	1	Hx of DQ6, 2000 MFI	T Pos B Pos	75%	71	F	4.3	N/A	53	49	N	N/A	2	2	1	2
4	Neg	9	Many - nonspecific binding	T Neg B Neg	0%	60	M	30	N/A	5	51	N	N/A	0	0	0	0
5	Pos	1	B4005, 3119 MFI	T Pos B Pos	59%	60	F	6	N/A	23	63	N	N/A	2	3	3	2
6	Pos	1	DR8, 2061 MFI	T Neg B Pos	0%	32	F	N/A	2	23	13	N	N/A	2	3	5	3
7	Pos	1	DPA01, 5976 MFI	T Neg B Pos	99.76%	38	M	9.8	N/A	31	12	Y	DPA1/3 (?)	3	5	3	3
8	Pos	1	A1, 5759 MFI	T Pos B Pos	99.58%	48	F	17.0	N/A	18	20	Y	A1	3	5	5	2
9	Pos	2	Allelic DQ6, 19K MFI DR52, 18K MFI	N/A	100%	23	M	3	N/A	41	42	Y	N/A	5	5	5	5
10	Pos	1	DPB1*02:01, 23K MFI	T Neg B Neg	100%	32	F	N/A	2	26	36%	N	N/A	3	3	3	2
11	Neg	1	C*07:01 2000 MFI	T Neg B Neg	0%	45	M	11.3	N/A	49	24%	N	N/A	0	0	1	0
12	Neg	2	DR52 3000 MFI DQ6 1000 MFI	T Neg B Neg	0%	57	M	3.6	N/A	38	6%	N	N/A	1	0	1	0
13	Neg	3	A3, ~1200 MFI DRB3*03, ~1000 MFI all 3 DSAs hx up to 3000 MFI	T Neg B Pos	98	72	F	0.6	N/A	28	20%	N	N/A	3	3	2	2
14	Pos	3	A1, 1520 MFI DQ2 1081 MFI DQA1*05 5388 MFI 2 DSAs hx>10000 MFI	T Pos B Pos	84.89%	54	M	N/A	1	20	?	N	N/A	4	5	3	3
15	Pos	3	Cw6, 2001 MFI DP17, 16424 MFI	N/A	0%	63	F	N/A	1	25	14%	N	N/A	4	5	5	2
16	Pos	1	DQ4, 1376-1854 MFI	T Neg B Neg	0%	15	M	N/A	1B	12	12%	N	N/A	3	3	3	2
17	Pos	5	A1, 8889 MFI DQ0602, 5695 MFI	T Pos B Pos	50.79%	38	M	N/A	1	?	?	N	N/A	5	5	5	3
18	Pos	2	A23, 1656 MFI A34, 1005 MFI	T Neg B Neg	100%	52	F	5	N/A	48	38%	Y	N/A	2	2	3	3
19	Pos	2	B63, 2446 MFI Cw5, 1057 MFI	T Neg B Neg	98%	69	F	1.5	N/A	29	26%	Y	N/A	2	2	2	2
20	Pos	3	DQA02, 12987 DPA03, 2057 DP04:02, 2592	T Neg B Pos	99.87%	32	F	1.3	N/A	33	21	Y	DQA02, DPA03, DP04:02	4	5	5	4

CONCLUSIONS

Our data suggests that consultation on unclear or high immunologic risk cases is complicated, leading to variable director consultations that largely depend on the transplant center's standard practices including experience with pre-transplant desensitization. Additionally, the target DSA or in cases of multiple DSAs, consults may greatly differ. Further studies of this type are encouraged in order to gain a better understanding of director's approaches cases where a clear answer is not defined.

FUTURE AIMS

1. **Information was bare minimum**
   - Raw data was preferred by most directors
   - Information regarding epitope reactivity was requested; in some cases, it may influence the risk score
   - Separate evaluation of heart/lung vs kidney transplant consultation
2. **More directors surveyed**
3. **More cases!**
   1. Additional nonspecific binding scenarios
   2. Historic DSA
   3. Shared epitope cases