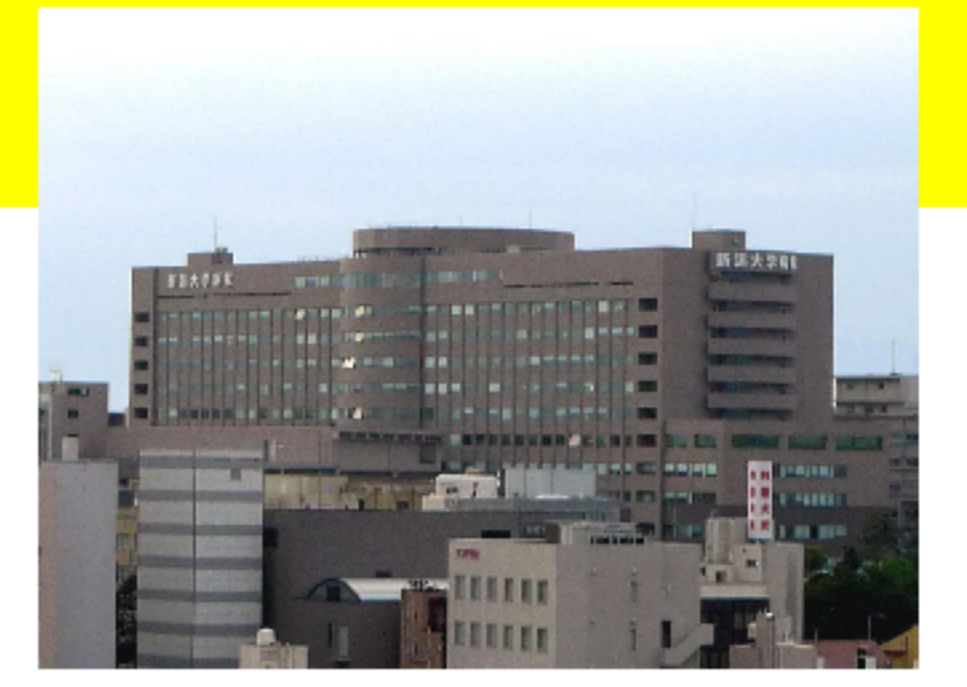


THE ROLE OF RITUXIMAB IN ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION IN JAPAN



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BACKGROUND

About three decades ago, ABO-incompatible kidney transplantation (ABOIKT) was considered immunologically contra-indication. The first planned successful case had been reported by Professor Guy Alexandre at St' Lukes Hospital in Belgium in early 1980's. In Japan, since we have reported the first success in January 1989, Over 3,000 ABOIKT have been performed to date.

Japan ABO-incompatible kidney transplantation committee had settled in 1997 and registered the cases to date.

Especially after 2001, we have introduced the desensitization therapy, started splenectomy avoiding program utilizing Rituximab since 2004 and achieved significant improvement of patient and graft survival to date.

AIM OF THE STUDY

To reveal the benefit of Rituximab for desensitization and elucidate the factors affecting the patient and graft outcome in ABOIKTx.

PATIENTS AND METHODS

Among 2,212 cases registered in Japan ABO incompatible kidney transplantation committee, we have selected 1,121 patients after 2001 era in whom the data for the use of rituximab and splenectomy status were available.

We have analyzed the patient and graft survival rate in this Group according to the Kaplan Meier's Method (Figure 2)

We have categorized the patients into 4 groups according to the splenectomy(S) and Rituximab(R) status, compared the outcome between each group, finally analyzed the factors affecting patient and graft outcome by univariate and multivariate analysis.

RESULTS

- Overall patient survival rate at 1,3,5 and 10 years were 98.5, 97.3, 95.4 and 94.8%, and graft survival rate were 97.1, 94.5, 91.3, 59 and 84.8%, respectively.
- We have categorized the patients into 4 groups according to the splenectomy(S) and Rituximab(R) status, S(-)/R(-) : N=16, S(-)/R(+) : N=738, S(+)/R(-) : N=320 and S(+)/R(+) : N=47.
- There was no statistically significant difference in patient and graft survival between 4 groups.
- The factors affecting the patient survival were postoperative antibody removal(PAR) (multivariate : p<0.004, HR 2.986, PI 1.419-6.283) and postoperative anticoagulation(PAC) (multivariate : p<0.020, HR 3.148, PI 1.199-8.261).
- The factors affecting the graft survival were PAR (multivariate: p<0.001, HR 4.238, PI 2.510-7.156) and PAC (univariate : p<0.021, HR 1.936, PI 1.107-3.385).
- There were no significant difference in patient and graft survival according to the preoperative anti-A/B IgG/IgM antibody titer.

CONCLUSION

For successful ABO-IKTx, desensitization with rituximab has become standard and the substitute of splenectomy for prevention of AMR and accommodation induction. ABOIKTx has become accepted as a therapeutic alternative treatment of choice for end-stage kidney disease. The complete elucidation of the accommodation induction mechanism in near future will open the next door to the upcoming brand-new paradigm of the field of organ transplantation.

Figure 1.

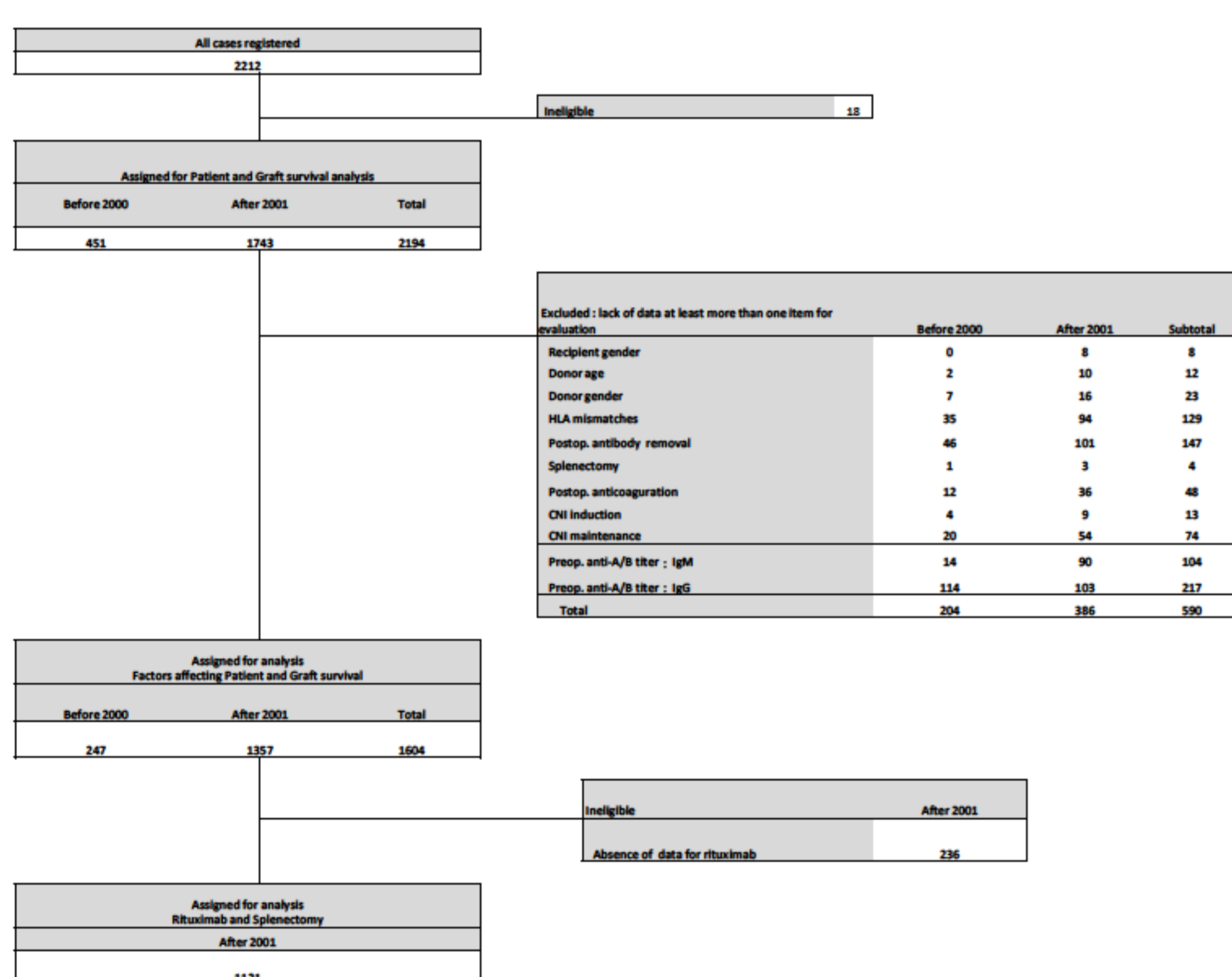


Figure 2. Overall Patient and Graft Survival

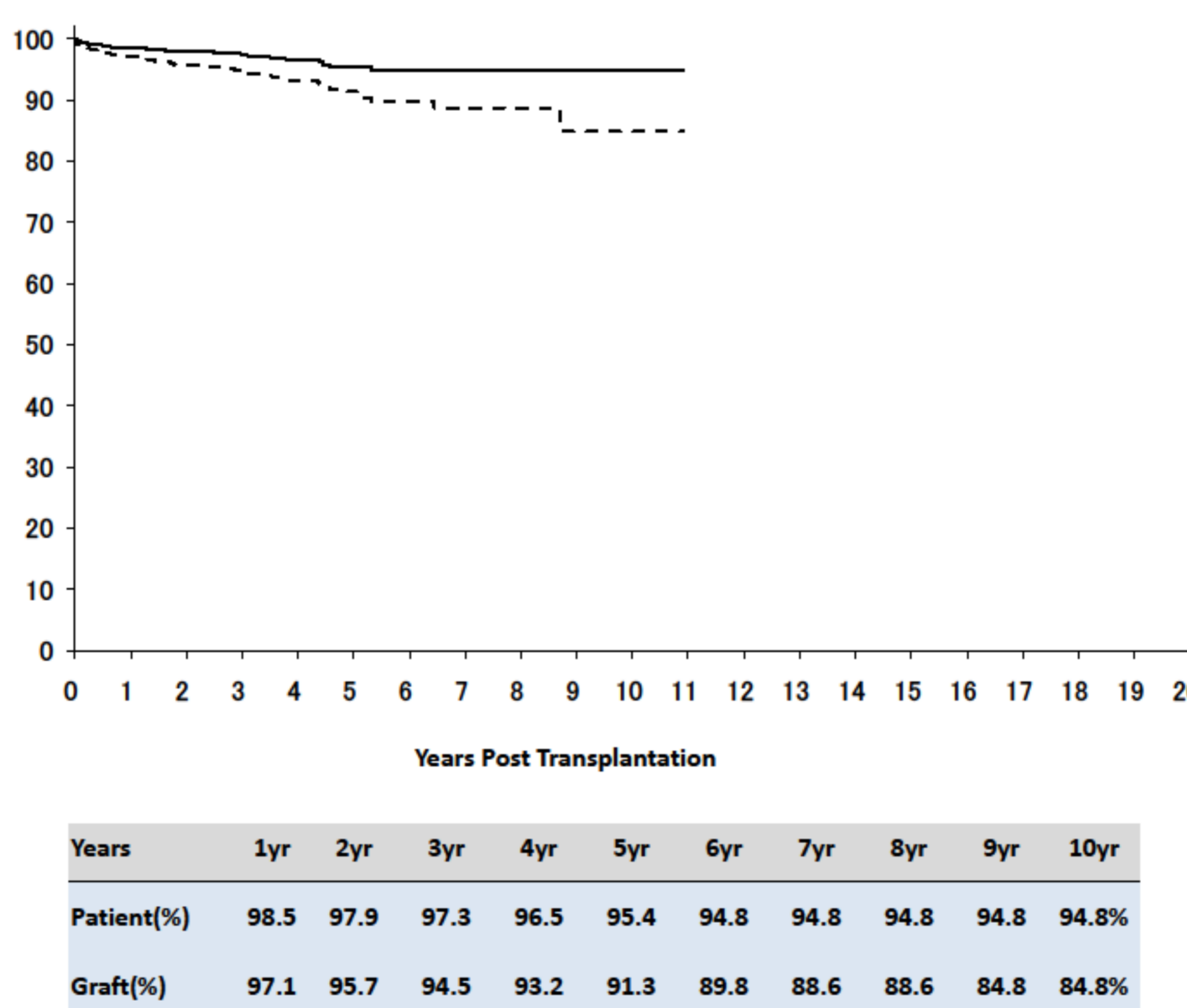


Figure 3. Graft Survival according to the Splenectomy and Rituximab status

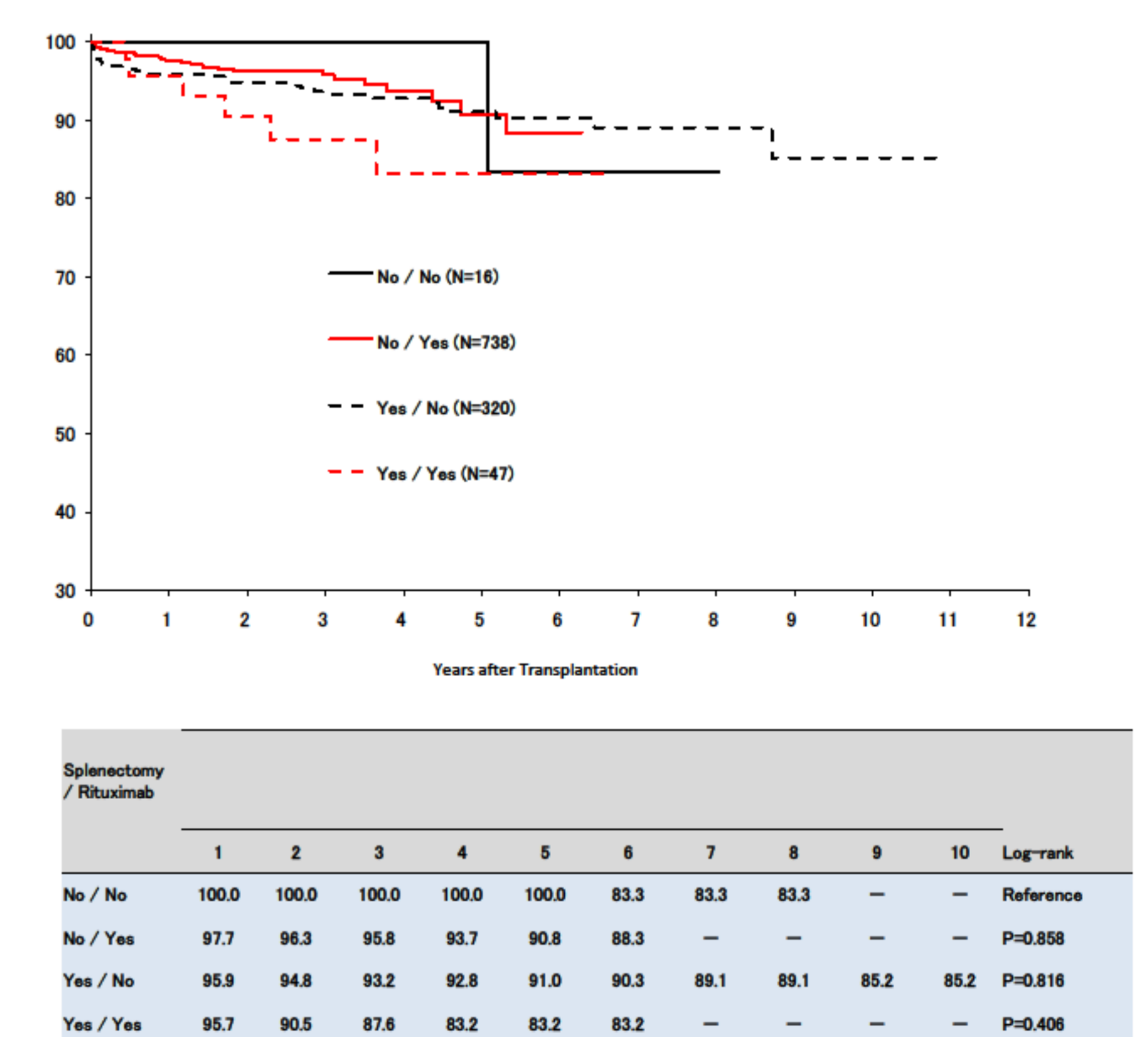


Figure 4. Patient Survival according to the Anti-A/B IgG titer

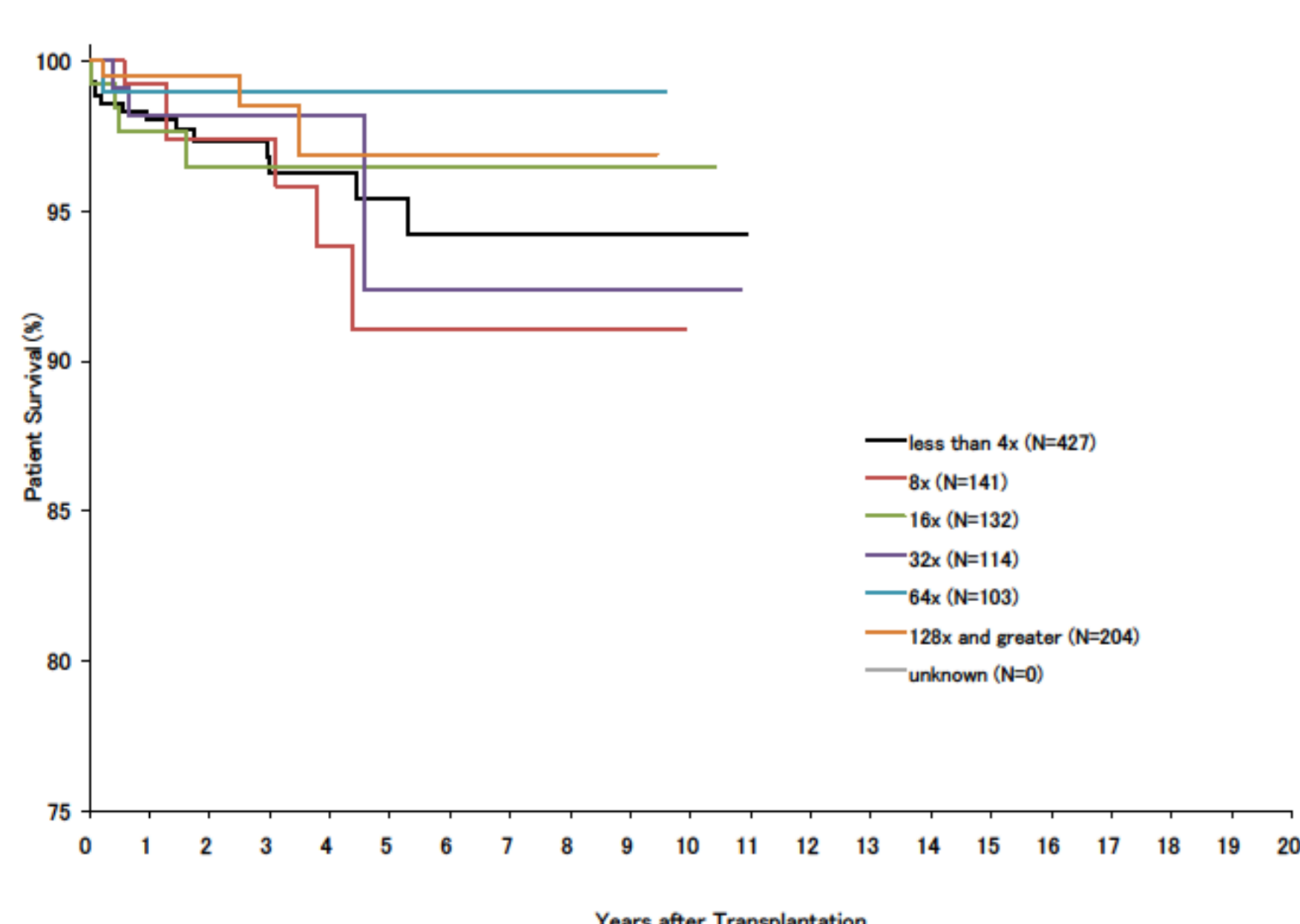


Figure 5. Graft Survival according to the Anti-A/B IgG titer

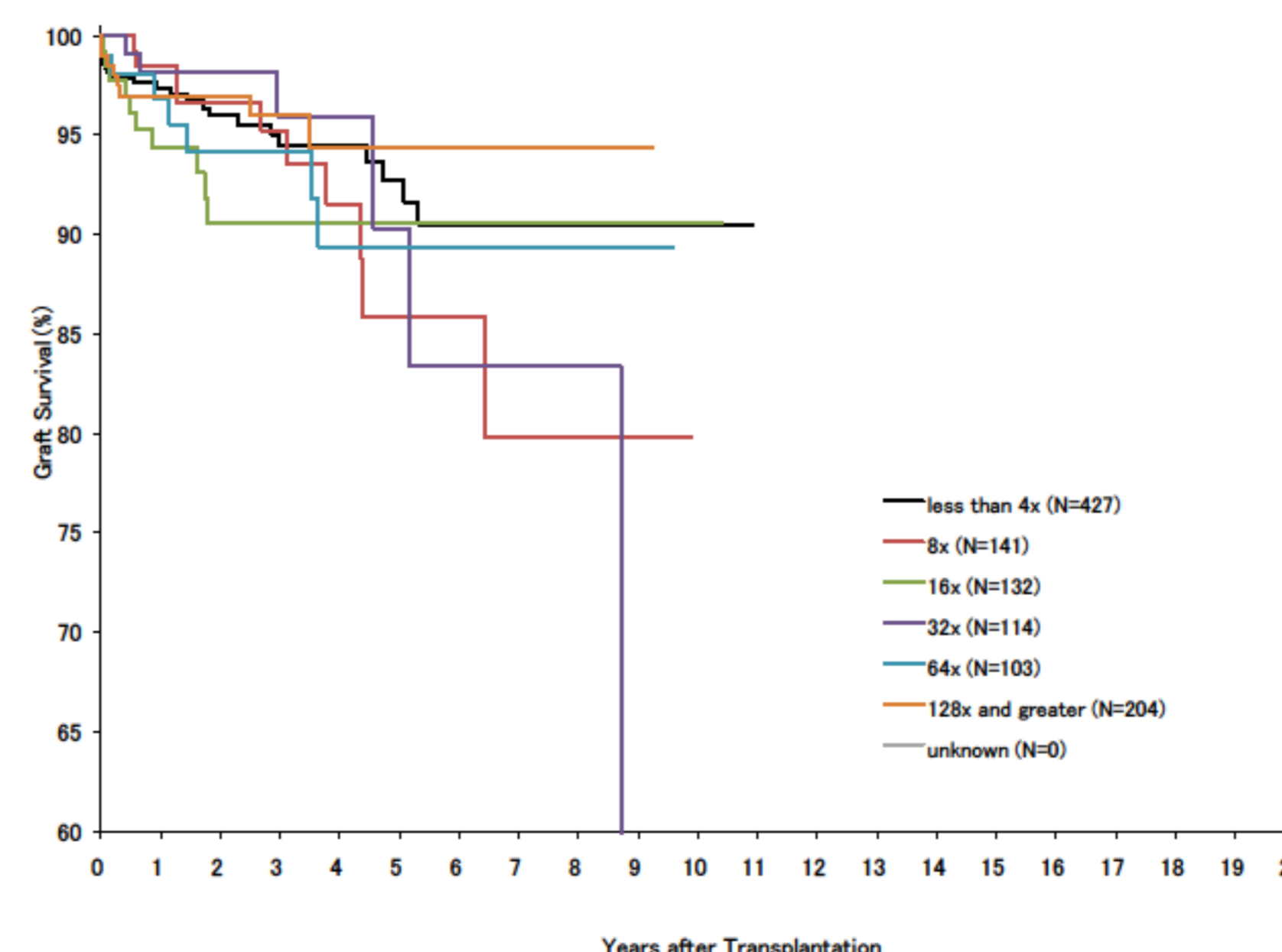


Table 1. Factors affecting the patient and graft survival

Factors affecting Patient Survival		Univariate				Multivariate		
	N	OR	95%CI	P value	OR	95%CI	P value	
PostOp Ab Removal (PAR)	No	982	20	96.2%	Reference	—	<[0.001 ***]	
	Yes	139	11	87.1%	3.492 (1.670, 7.298)	<0.001 ***	2.986 (1.419, 6.283) 0.004 **	
PostOp Anti-Coagulation (PAC)	No	456	5	98.0%	Reference	—	[0.009 **]	
	Yes	665	26	92.5%	3.666 (1.384, 9.396)	0.009 **	3.148 (1.199, 8.261) 0.020 *	

Factors affecting Graft Survival		Univariate				Multivariate		
	N	OR	95%CI	P value	OR	95%CI	P value	
PostOp Ab Removal (PAR)	No	982	38	86.2%	Reference	—	<[0.001 ***]	
	Yes	139	25	74.4%	4.439 (2.678, 7.358)	<0.001 ***	4.238 (2.510, 7.156) <0.001 ***	
Post Op Anti Coagulation (PAC)	No	456	17	93.7%	Reference	—	[0.021 *]	
	Yes	665	46	72.2%	1.936 (1.107, 3.385)	0.021 *		