

Supplementary Table 1. Organ involvements between IgG4-RD patients with positive and negative AIDs family history

Parameters	AID-pos group (n=93)	AID-neg group (n=535)	<i>P</i> value
Lymph node	24 (25.8%)	105 (19.6%)	0.221
Submandibular gland	46 (93,49.5%)	279 (533,52.3%)	0.688
Lacrimal gland	47 (93,50.5%)	248 (534,46.4%)	0.537
Parotid gland	12 (93,12.9%)	98(533,18.4%)	0.257
Nasal sinus	27 (93,29.0%)	151 (530,28.5%)	1
Pancreas	38 (92,41.3%)	198 (528,37.5%)	0.564
Bile duct	18 (93,19.4%)	107 (532,20.1%)	0.978
Lung	24 (92,26.1%)	137 (520,26.3%)	1
Kidney	7 (93,7.5%)	62 (530,11.7%)	0.316
Aorta	6 (92,6.5%)	62 (530,11.7%)	0.557
Mediastinum	1 (93,1.1%)	18 (534,3.4%)	0.336
Thyroid gland	10(92,10.9%)	13(532,2.4%)	0.001*
Liver	5 (88,5.7%)	11 (504,2.2%)	0.074
Gastrointestinal tract	2 (87,2.3%)	14 (530,2.6%)	0.729
Pituitary gland	3 (93,3.2%)	14 (530,2.6%)	0.729

Supplementary Table 2. Familial aggregation distribution of AID family history positive IgG4-RD patients in relation to demographic and clinical parameters.

Parameters	Numbers of relatives=1 (n=77)	Numbers of relatives \geq 2 (n=16)	P value
Age (years)	49.2 \pm 15.0	55.9 \pm 12.5	0.076
Male/Female	1.3:1	0.3:1	0.049*
Disease duration (Months)	18.0 (5.8, 36.0)	23.5(4.0, 78.0)	0.433
History of allergy, n (%)	39 (76, 50.0%)	10 (16, 62.5%)	0.59
ANA positivity, n (%)	19 (56, 33.9%)	8 (15, 53.3%)	0.258
RF positivity, n (%)	19 (58, 32.8%)	4 (11, 36.4%)	1
IgG4-RD RI	6 (4, 10)	6 (4, 10)	0.777
Riedel thyroiditis, n (%)	6 (76, 7.9%)	4 (16, 25.0%)	0.068
Number of organ involvement	3 (2, 4)	2 (2, 4)	0.905
First degree relatives, n (%)	63 (76, 82.9%)	13 (16, 81.2%)	1

ANA: antinuclear antibody; RF: rheumatoid factor.

Supplementary Table 3. The demographical and clinical parameters between IgG4-RD family history and other AIDs familial history.

Parameters	Family history of IgG4-RD	Family history of other AID	<i>P</i> value
	(n=16)	(n=77)	
Age (years)	48.1 ± 12.0	51.2 ± 15.2	0.354
Male/Female	1:1	1.1:1	1
Disease duration (Months)	24.0 (10.5, 39.0)	12.0 (4.0, 36.0)	0.35
History of allergy, n (%)	9 (16, 56.3%)	41 (76, 52.6%)	1
ANA positivity, n (%)	5 (12, 41.7%)	23 (61, 37.7%)	1
RF positivity, n (%)	7 (12, 58.3%)	16 (60, 28.1%)	0.088
IgG4-RD RI	7 (6, 10)	6 (4, 10)	0.465
Riedel thyroiditis, n (%)	1 (16, 6.2%)	9 (76, 11.8%)	1
Number of organ involvement	3 (3, 4)	2 (2, 4)	0.227
First degree relatives, n (%)	13 (16, 81.2%)	63 (76, 82.9%)	1

Supplementary Table 4. Univariate and multivariate cox analysis of potential factors associated with unfavorable prognosis in AID-pos group (n=87).

variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender	1.34 (0.71-2.55)	0.364		
Age (y)	0.97(0.95-0.99)	0.015*	0.97(0.94 - 0.99)	0.0384*
Allergy	0.82(0.43-1.59)	0.561		
WBC (10 ⁹ /L)	1.05(0.9-1.22)	0.533		
PLT (10 ⁹ /L)	1(1-1.01)	0.273		
Eos (10⁹/L)	1.08(1.01-1.16)	0.021*	1.1(1.02 - 1.2)	0.0199*
ESR (mm/h)	1(0.98-1.01)	0.598		
hsCRP (mg/L)	0.99(0.97-1.02)	0.494		
IgG(g/L)	0.99(0.93-1.04)	0.675		
IgA(g/L)	0.96(0.69-1.33)	0.792		
IgM(g/L)	1.25(0.66-2.37)	0.484		
C3(g/L)	0.36(0.07-1.79)	0.213		
C4(g/L)	0.09(0-13.78)	0.346		
ANA positivity	0.87(0.42-1.83)	0.722		
RF positivity (>20IU/ml)	1.12(0.5-2.5)	0.783		
IgG4-RD RI	0.99(0.92-1.07)	0.879		
Treatment (GC)	1	1		
Treatment (GC+IM)	0.42(0.19-0.95)	0.037*	0.43(0.13 - 1.36)	0.1488
Treatment (IM)	1.07(0.46-2.49)	0.879	1.74(0.6 - 5.1)	0.3095
Treatment (watchful waiting)	0.74(0.27-2.06)	0.564	1.9(0.53 - 6.86)	0.3257
Combine with other AIDs	1.07(0.44-2.59)	0.877		
Number of organs involvement	0.96(0.77-1.18)	0.679		
Salivary gland	0.58(0.29-1.14)	0.113		
Lacrimal gland	1.33(0.7-2.54)	0.385		
Parotid gland	0.67(0.25-1.82)	0.434		
Nasal sinus	0.94(0.47-1.89)	0.866		
Number of superficial organs	0.93(0.71-1.21)	0.568		
Pancreas	1.76(0.93-3.34)	0.085		
Biliary tract	1.17(0.56-2.42)	0.677		
Lung	1.49(0.76-2.9)	0.244		
Kidney	0.23(0.03-1.68)	0.147		
Aorta	0.22(0.03-1.63)	0.139		
Mediastinum	0(0-Inf)	0.997		
Thyroid gland	0.89(0.31-2.51)	0.823		
Pituitary	1.01(0.14-7.38)	0.994		
Gastrointestinal tract	0.71(0.1-5.2)	0.733		
Number of internal organs	1.01(0.79-1.29)	0.953		
Nonsmoker	1	1		
Former smoker	0.95(0.43-2.11)	0.897		
Current smoker	0.93(0.35-2.52)	0.892		

Non-alcohol drinker	1	1		
Moderate alcohol drinker	0.96(0.44-2.12)	0.927	0.92(0.35-2.45)	0.8687
Former alcohol drinker	0.66(0.15-2.88)	0.581	0.29(0.04-2.26)	0.2374
Continuous alcohol intake	4.64(1.33-16.2)	0.016*	5.74(1.44 - 22.88)	0.0133*
Number of relatives	0.87(0.57-1.33)	0.511		
First-degree relatives	0.79(0.44-1.41)	0.425		
Second-degree relatives	0.67(0.3-1.49)	0.326		
Third-degree relatives	1.32(0.32-5.56)	0.701		

P-values<0.05 shown in bold are statistically significant.

Supplementary Table 5. Univariate and multivariate cox analysis of potential factors associated with unfavorable prognosis in AID-neg group (n=484).

variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender	0.85(0.66-1.1)	0.222		
Age (years)	0.99(0.98-1)	0.213		
Allergy	1.46(1.13-1.89)	0.003*	1.33(1.02- 1.74)	0.0332*
WBC (10 ⁹ /L)	0.98(0.93-1.02)	0.278		
PLT (10 ⁹ /L)	1(1-1)	0.634		
EOS (10 ⁹ /L)	1.01(0.99-1.03)	0.384		
ESR (mm/h)	0.99(0.99-1)	0.03		
hsCRP (mg/L)	1(0.99-1.01)	0.87		
IgG (g/L)	1(0.99-1.01)	0.965		
IgA (g/L)	1(0.88-1.12)	0.943		
C3 (g/L)	1(0.99-1.01)	0.603		
C4 (g/L)	1.05(0.98-1.14)	0.178		
ANA positivity	1.17(0.84-1.63)	0.346		
RF positivity(>20IU/ml)	1.07(0.76-1.5)	0.71		
IgG4-RD RI	0.97(0.94-1)	0.037		
Treatment (GC)	1	1		
Treatment (GC+IM)	1.07(0.78-1.46)	0.693	1.04(0.75 - 1.42)	0.823
Treatment (IM)	2.99(2-4.49)	<0.001*	2.77(1.83 - 4.19)	<0.001*
Treatment (watchful waiting)	1.86(1.14-3.05)	0.013*	1.76(1.05 - 2.95)	0.0329*
Combine with other AIDs	1.25(0.77-2.03)	0.36		
Number of organs involvement	1.04(0.95-1.13)	0.386		
Salivary gland	1.24(0.96-1.59)	0.094		
Lacrimal gland	1.39(1.08-1.78)	0.01*	1.04(0.7 - 1.54)	0.862
Parotid gland	1.13(0.83-1.52)	0.436		
Nasal sinus	1.38(1.06-1.8)	0.017*	1.1(0.78 - 1.55)	0.5976
Number of superficial organs	1.16(1.05-1.28)	0.004*	1.09(0.9 - 1.32)	0.3879
Pancreas	0.88(0.68-1.14)	0.322		
Biliary tract	0.74(0.54-1.02)	0.064		
Lung	1.01(0.76-1.35)	0.923		
Kidney	0.84(0.57-1.25)	0.394		
Aorta	0.9(0.6-1.37)	0.634		
Mediastinum	1.02(0.52-1.98)	0.957		
Thyroid gland	0.32(0.08-1.29)	0.108		
Pituitary	1.47(0.69-3.12)	0.315		
Gastrointestinal tract	1.53(0.78-2.97)	0.215		
Number of internal organs	0.89(0.8-1)	0.049		
Nonsmoker	1	1		
Former smoker	0.93(0.68-1.28)	0.661		
Current smoker	0.87(0.59-1.28)	0.474		

Non-alcohol drinker	1	1
Moderate alcohol drinker	0.92(0.67-1.27)	0.625
Former alcohol drinker	1.29(0.82-2.04)	0.27
Continuous alcohol intake	0.85(0.41-1.74)	0.656

P-values shown in bold are statistically significant.

Supplementary Table 6. Univariate and multivariate cox analysis of potential risk factors associated with unfavorable prognosis in all IgG4-RD patients (n=571).

variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender	0.93(0.74-1.18)	0.57		
Age (y)	0.99(0.98-0.99)	0.048*	1(0.98 - 1.01)	0.3734
Allergy	1.31(1.04-1.66)	0.022*	1.14(0.86 - 1.51)	0.3537
WBC (10 ⁹ /L)	0.98(0.94-1.02)	0.316		
EOS (10 ⁹ /L)	1.01(1-1.03)	0.088*		
ESR (mm/h)	1(0.99-1)	0.04*		
hsCRP (mg/L)	1(0.99-1.01)	0.936		
IgG (g/L)	1(0.99-1.01)	0.828		
IgA (g/L)	1(0.89-1.12)	0.974		
C3 (g/L)	1(0.99-1.01)	0.643		
C4 (g/L)	1.06(0.98-1.14)	0.167		
ANA positivity	1.1(0.82-1.48)	0.535		
RF positivity(>20IU/ml)	1.07(0.78-1.47)	0.663		
IgG4-RD RI	0.97(0.95-1)	0.08		
Treatment (GC)	1	1		
Treatment (GC+IM)	0.94(0.71-1.26)	0.682	0.99(0.71 - 1.37)	0.9412
Treatment (IM)	2.38(1.66-3.42)	<0.001*	2.12(1.36 - 3.31)	<0.001*
Treatment (watchful waiting)	1.49(0.96-2.32)	0.074	1.56(0.89 - 2.72)	0.1195
Combine with other AIDs	1.16(0.76-1.77)	0.481		
Number of organs involvement	1.03(0.95-1.11)	0.532		
Salivary gland	1.13(0.9-1.43)	0.298		
Lacrimal gland	1.37(1.09-1.72)	0.008*	1.04(0.67 - 1.62)	0.8465
Parotid gland	1.08(0.81-1.43)	0.619		
Nasal sinus	1.31(1.02-1.680)	0.031*	1.28(0.88 - 1.86)	0.1913
Number of superficial organs	1.12(1.02-1.23)	0.014*	1(0.8 - 1.26)	0.9812
Pancreas	0.97(0.77-1.23)	0.829		
Biliary tract	0.78(0.59-1.04)	0.096		
Lung	1.08(0.83-1.4)	0.575		
Kidney	0.77(0.53-1.13)	0.179		
Aorta	0.81(0.54-1.21)	0.305		
Mediastinum	1.01(0.52-1.95)	0.988		
Thyroid gland	0.54(0.24-1.21)	0.135		
Pituitary	1.34(0.66-2.71)	0.415		
Gastrointestinal tract	1.34(0.71-2.53)	0.36		
Number of internal organs	0.91(0.82-1.01)	0.073		
Current smoker	0.93(0.72-1.2)	0.581		
Continuous alcohol intake	1.1(0.6-2.04)	0.756		

P-values shown in bold are statistically significant.

Supplementary Table 7. Univariate and multivariate cox analysis of AID family history associated with unfavorable prognosis in pos-IgG4-RD patients (n=87).

variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
The number of AID relatives	0(0-Inf)	0.996		
The degree of AID relatives	0.99(0.52-1.89)	0.976		
RA	0.69(0.42-1.13)	0.137		
IgG4-RD	1.33(0.72-2.44)	0.36		
SLE	1.15(0.49-2.68)	0.755		
Psoriasis	0.67(0.29-1.55)	0.349		
Grave's disease	0.44(0.14-1.4)	0.164		
Hashimoto's thyroiditis	0.69(0.25-1.89)	0.464		
SS	0.65(0.16-2.66)	0.546		
Spondyloarthritis	0.81(0.29-2.23)	0.685		
Vitiligo	2.39(0.58-9.95)	0.23		
PBC	1.67(0.23-12.21)	0.611		
Dermatomyositis	1.23(0.17-9.03)	0.836		
Autoimmune nephritis	0.29(0.04-2.11)	0.222		
ITP	2.15(0.29-16.05)	0.454		
UCTD	2.23(0.3-16.33)	0.431		
Type1 diabetes	2.13(0.29-15.63)	0.456		
Autoimmune hepatitis	0(0-Inf)	0.995		
Takayasu arteritis	11.49(1.43-92.49)	0.022*	12.66(1.56 - 103.02)	0.0176*
Autoimmune hemolytic anemia	8.36(1.07-65.47)	0.043*	9.24(1.17 - 73.12)	0.0351*

The number of AID relatives: A large proportion of patients had only one relative with AID, a median number at 1 (IQR:1-5); The degree of AID relatives: pos-IgG4-RD patients was divided two groups by the involvement condition of first degree relative: first degree relative group and non-first-degree relative group, respectively.