

Appendix 1

The Chinese IgG4-RD Consortium IgG4-RD Damage Index (CIC IgG4-RD DI)

Item	Score
1. Nervous system	
Persistent/residual meningeal thickening (imaging)	1
Cranial or peripheral nerve damage (not including optic nerve)	1
2. Pituitary gland	
Anterior pituitary dysfunction	1
Central diabetes insipidus	1
3. Orbit	
Visual impairment (if blindness, rate 2)	1(2)
Diplopia or exophthalmos	1
4. Lacrimal/salivary gland²³	
Dry mouth with objective evidence of xerostomia	1
Dry eyes with objective evidence of xerophthalmia	1
5. Mastoid/auris media	
Persistent mastoiditis (imaging)	1
Hearing loss	1
6. Nose/nasal sinus	
Persistent nasal sinus/turbinal lesions (imaging) with relevant clinical symptoms	1
7. Thyroid gland	
Hypothyroidism (exclusion of other causes)	1
Persistent enlargement of thyroid gland compressing bronchia	1
8. Lung	
Persistent lung fibrosis/pleural thickening/masses/bronchial lesions (imaging)	1
Pulmonary hypertension	1
Impaired lung function (FVC<80% or FEV ₁ <80% or DLCO <70% predicted values)	1
9. Cardiovascular system	
Luminal stenosis, formation of aneurysms (imaging), or need for interventional procedure or surgery	1
Constrictive pericarditis	1
10. Retroperitoneum/mediastinum	
Persistent retroperitoneal or mediastinal masses	1
Hydronephrosis/long-term D-J tube placement (more than 6 months) ¹⁰	1
11. Pancreas	
Pancreatic atrophy, persistent enlargement, or pseudocyst (imaging)	1
Long-term pancreatic enzyme replacement due to exocrine insufficiency	1
12. Liver/biliary tree	
Intra- and/or extrahepatic biliary duct stricture (imaging)	1
Persistent elevation of liver enzyme/bile duct enzyme/bilirubin over two times the normal upper limit	1
Compensated cirrhosis (Child-Pugh grade A) or regional portal hypertension	1
Decompensated cirrhosis (Child-Pugh grade B/C)	2
13. Kidney	
Persistent renal parenchyma/pelvis masses (imaging)	1
24-hour urinary protein > 0.5 g	1
eGFR 30-60 ml/(min·1.73m ²) (calculated by CKD-EPI)	2
eGFR 15-30 ml/(min·1.73m ²) or need for renal replacement therapy	3
14. Others	
Irreversible damage to other organs not listed above (cumulative if > one site)	1
New-onset malignancy (cumulative in case of more than one kind of malignancy)	1
Disease-related or treatment-related cerebrovascular/cardiovascular event (if more than once, rate 2)	1(2)
Persistent drug-related myelosuppression (more than six months)	1
Glucocorticoid-related ischaemic osteonecrosis	1
Glucocorticoid-related osteoporosis with fractures or vertebral collapse	1
Cataracts caused by glucocorticoids	1
Disease-related or treatment-related diabetes mellitus	1
Partial or total resection of organs due to IgG4-RD (cumulative if > one site), including but not limited to orbitotomy, pulmonary wedge resection, Whipple procedure, nephrectomy, pituitary surgery, and thyroidectomy.	1

Supplementary Table S1. Baseline characteristics of all patients included in the study.

	n=334
Sex, male (n, %)	213 (63.8%)
Age (years, median [IQR])	55.0 [46.0, 61.8]
Baseline laboratory test results	
Eos %	3.30 [1.50, 6.30]
ESR (mm/h, median [IQR])	22.0 [9.00, 51.0]
CRP (mg/L, median [IQR])	1.96 [0.78, 6.38]
C3 (mg/L, mean $\pm$ SD)	0.93 $\pm$ 0.30
C4 (mg/L, median [IQR])	0.16 [0.11, 0.22]
IgG (mg/L, median [IQR])	18600 [14200, 25800]
IgA (mg/L, median [IQR])	1920 [1330, 2500]
IgM (mg/L, median [IQR])	770 [550, 1170]
IgG1 (mg/L, median [IQR])	8740 [6965, 10600]
IgG2 (mg/L, median [IQR])	5500 [4250, 7230]
IgG3 (mg/L, median [IQR])	422 [244, 810]
IgG4 (mg/L, median [IQR])	8780 [3250, 18100]
T-IgE (KU/L, median [IQR])	278 [115, 657]
Baseline involved organs	
Pancreas (n, %)	125 (37.4%)
Bile duct (n, %)	72 (21.6%)
Submandibular gland (n, %)	173 (51.8%)
Lacrimal gland (n, %)	172 (51.5%)
Parotid gland (n, %)	64 (19.2%)
Retroperitoneum (n, %)	52 (15.6%)
Lung (n, %)	85 (25.4%)
Kidney (n, %)	42 (12.6%)
Aorta (n, %)	34 (10.2%)
Mediastinum (n, %)	8 (2.4%)
Prostate (n, %)	35 (10.5%)
Lymph node (n, %)	154 (46.1%)
Inflammatory pseudotumour (n, %)	5 (1.5%)
Nasal sinus (n, %)	111 (33.2%)
Thyroid gland (n, %)	10 (3.0%)
Liver (n, %)	10 (3.0%)
Pituitary gland (n, %)	8 (2.4%)
Meninges (n, %)	2 (0.6%)
Orbit (n, %)	12 (3.6%)
Other (n, %)	12 (3.6%)
Total organs (median [IQR])	3.0 [2.0, 5.0]
RI (median [IQR])	8.0 [6.0, 10.0]
Remission induction treatment	
GCs* (mg/d, median [IQR])	40.0 [30.0, 50.0]
IM intensity	
GC-sparing	2 (0.6%)
Mild	87 (26.0%)
Moderate	59 (17.7%)
Strong	88 (26.3%)
None	98 (29.3%)

*Prednisone or equivalent dose.

IQR: interquartile range; GC: glucocorticoid; IM: immunosuppressant; RI: responder index.

Supplementary Table S2. Comparison of baseline characteristics and treatments between different damage subgroups of patients with IgG4-RD by the 10-year assessment.

	Damage increase (n=42)	Damage stable (n=22)	No damage (n=35)	p-value
Sex, male (n, %)	27 (64.3%)	16 (72.7%)	24 (68.6%)	0.783
Age (yrs, median [IQR])	55.5 [51.0, 60.5]	56.0 [42.8, 58.8]	53.0 [45.5, 60.0]	0.488
Baseline laboratory test				
Eos % (median [IQR])	3.3 [1.5, 6.1]	4.4 [1.4, 6.5]	3.4 [2.6, 7.2]	0.858
ESR (mm/h, median [IQR])	24.0 [13.0, 67.8]	41.0 [28.0, 64.2]	23.5 [10.0, 57.8]	0.470
CRP (mg/L, median [IQR])	1.6 [0.6, 6.8]	2.5 [1.6, 6.4]	3.7 [1.2, 7.8]	0.406
C3 (mg/L, mean $\pm$ SD)	0.97 $\pm$ 0.32	0.84 $\pm$ 0.25	1.08 $\pm$ 0.38	0.245
C4 (mg/L, mean $\pm$ SD)	0.18 $\pm$ 0.10	0.14 $\pm$ 0.09	0.17 $\pm$ 0.07	0.540
IgG (mg/L, median [IQR])	19500 [15500, 26600]	23000 [17800, 32300]	21800 [16900, 26600]	0.447
IgA (mg/L, median [IQR])	1900 [1400, 2300]	1800 [1400, 2600]	1900 [1400, 2300]	0.939
IgM (mg/L, median [IQR])	800 [500, 1000]	700 [600, 1000]	800 [600, 1000]	0.818
IgG1 (mg/L, median [IQR])	8720 [6885, 10650]	8750 [7095, 10850]	8555 [6845, 9840]	0.599
IgG2 (mg/L, median [IQR])	5070 [3878, 7335]	6395 [5485, 7532]	5295 [3875, 6612]	0.240
IgG3 (mg/L, median [IQR])	442 [278, 881]	583 [316, 1129]	408 [259, 848]	0.428
IgG4 (mg/L, median [IQR])	8610 [4020, 16300]	12200 [3098, 20100]	12700 [8350, 23250]	0.308
T-IgE (KU/L, median [IQR])	350 [131, 922]	180 [115, 672]	511 [203, 980]	0.419
Baseline involved organs				
Pancreas (n, %)	22 (52.4%)	5 (22.7%)	12 (34.3%)	0.052
Bile duct (n, %)	14 (33.3%)	3 (13.6%)	7 (20.0%)	0.167
Submandibular gland (n, %)	25 (59.5%)	9 (40.9%)	23 (65.7%)	0.172
Lacrimal gland (n, %)	23 (54.8%)	12 (54.5%)	21 (60.0%)	0.878
Parotid gland (n, %)	11 (26.2%)	8 (36.4%)	10 (28.6%)	0.692
Retroperitoneum (n, %)	9 (21.4%)	7 (31.8%)	5 (14.3%)	0.290
Lung (n, %)	12 (28.6%)	7 (31.8%)	11 (31.4%)	0.949
Kidney (n, %)	8 (19.0%)	4 (18.2%)	7 (20.0%)	1.000
Aorta (n, %)	8 (19.0%)	3 (13.6%)	1 (2.9%)	0.091
Mediastinum (n, %)	2 (4.8%)	1 (4.6%)	1 (2.9%)	1.000
Prostate (n, %)	3 (7.1%)	4 (18.2%)	6 (17.1%)	0.303
Lymph node (n, %)	23 (54.8%)	14 (63.6%)	24 (68.6%)	0.452
Inflammatory pseudotumour (n, %)	1 (2.4%)	0 (0.0%)	2 (5.7%)	0.602
Nasal sinus (n, %)	9 (21.4%)	6 (27.3%)	11 (31.4%)	0.606
Thyroid gland (n, %)	2 (4.8%)	0 (0.0%)	0 (0.0%)	0.506
Liver (n, %)	1 (2.4%)	0 (0.0%)	3 (8.6%)	0.345
Pituitary gland (n, %)	0 (0.0%)	1 (4.6%)	1 (2.9%)	0.329
Orbit (n, %)	3 (7.1%)	0 (0.0%)	0 (0.0%)	0.238
Other (n, %)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0.576
Total organs (median [IQR])	4.0 [3.0, 5.0]	4.0 [3.0, 5.0]	4.0 [3.0, 5.5]	0.792
RI (median [IQR])	8.0 [6.0, 11.5]	8.0 [6.0, 11.5]	8.0 [7.0, 12.0]	0.758
Remission induction treatment				
GCs (mg/d, median [IQR])	40.0 [30.0, 40.0]	45.0 [40.0, 50.0]	40.0 [30.0, 50.0]	0.266
IM intensity (n, %)				0.459
Mild	8 (19.0%)	2 (9.1%)	7 (20.0%)	
Moderate	7 (16.7%)	2 (9.1%)	3 (8.6%)	
Strong	11 (26.2%)	12 (54.5%)	12 (34.3%)	
None	16 (38.1%)	6 (27.3%)	13 (37.1%)	
Relapse frequency in 10 yrs (median [IQR])	1.0 [0.0, 1.0]	0.5 [0.0, 1.0]	0.0 [0.0, 1.0]	0.391
Duration of GC treatment in 10 yrs (mths, median [IQR])	109 [92.0, 125]	110 [103, 122]	111 [100, 124]	0.911

*Prednisone or equivalent dose.

IQR: interquartile range; GC: glucocorticoid; IM: immunosuppressant; yrs: years; mths: months; RI: Responder Index.

Supplementary Table S3. Univariate and multivariate logistic regression analyses of risk factors for damage accrual in patients with IgG4-RD by the 10-year assessment.

Variable	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Sex, male (n, %)	0.72	(0.30, 1.70)	0.448			
Age (yrs, median [IQR])	1.03	(0.99, 1.05)	0.128	1.02	(0.98, 1.06)	0.192
Baseline laboratory test results						
Eos % (median [IQR])	0.99	(0.94, 1.04)	0.768			
C3 (mg/L, median [IQR])	0.81	(0.09, 6.99)	0.847			
IgG1 (mg/L, median [IQR])	1.00	(0.99, 1.00)	0.934			
IgG4 (mg/L, median [IQR])	1.00	(0.99, 1.00)	0.375			
Baseline involved organs (n, %)						
Pancreas	2.79	(1.19, 6.50)	0.018	2.89	(1.02, 8.16)	0.045
Bile duct	2.49	(0.96, 6.43)	0.060	1.28	(0.39, 4.11)	0.681
Submandibular gland	1.27	(0.55, 2.89)	0.567			
Lacrimal gland	0.82	(0.36, 1.84)	0.625			
Retroperitoneum	1.08	(0.40, 2.89)	0.880			
Lung	0.75	(0.30, 1.83)	0.529			
Kidney	1.04	(0.37, 2.89)	0.946			
Aorta	3.27	(0.89, 11.9)	0.072	2.45	(0.62, 9.62)	0.198
Lymph node	0.56	(0.24, 1.30)	0.176	0.58	(0.23, 1.44)	0.239
Mediastinum	1.44	(0.18, 10.9)	0.724			
Total organs (median [IQR])	1.01	(0.80, 1.26)	0.921			
Baseline RI (median [IQR])	1.01	(0.91, 1.12)	0.778			
Remission induction therapy						
GCs* (mg/d, median [IQR])	0.99	(0.96, 1.01)	0.366			
IM intensity†						
Strong	0.54	(0.20, 1.46)	0.225			
Moderate	1.66	(0.43, 6.37)	0.454			
Mild	0.83	(0.25, 2.72)	0.758			
Relapse frequency in 10 yrs (median [IQR])	1.48	(0.88, 2.47)	0.135	1.35	(0.78, 2.34)	0.272
Duration of GC treatment in 10 yrs (mths, median [IQR])	1.00	(0.98, 1.01)	0.991			

*Prednisone or equivalent dose.

IQR: interquartile range; GC: glucocorticoid; IM: immunosuppressant; yrs: years; mths: months; RI: Responder Index.

Supplementary Table S4. Patients who died during follow-up.

	Patient 1	Patient 2	Patient 3
Sex	Female	Male	Male
Age at diagnosis (yrs)	69	60	63
IgG (mg/L)	15300	19400	10990
IgG4 (mg/L)	13400	9000	3520
Involved organs	Pancreas, kidney, submandibular gland, lymph node	Submandibular gland, lacrimal gland, parotid gland, retroperitoneum, lung, kidney, aorta, mediastinum, prostate, lymph node	Pancreas, bile duct
Baseline RI	8	14	6
Remission induction treatment			
GCs* (mg/d)	30	40	40
IMs	CsA	CTX	None
DI			
Baseline	0	0	0
5 years	1	1	1
10 years	1	N/A	N/A
Damage items	Pancreatic imaging abnormality	Diabetes	Malignancy
Relapse frequency within 5 years	1	0	0
Maintenance treatment			
AZA	Prednisone 10 mg/d		
TwHF	Prednisone 15 mg qd		
AZA	Prednisone 15 mg/d		
Cause of death	Complications of Alzheimer's disease	Unknown	Colorectal cancer
Time from initial diagnosis to death (mths)	141	66	69

*Prednisone or equivalent dose.

AZA: azathioprine; TwHF: Tripterygium wilfordii Hook F.