Table S1 Inclusion and Exclusion Criteria for the GRACE-IgANI cohort

Inclusion criteria	**Exclusion criteria**
Age ≥18 years	Secondary IgA nephropathy: e.g. due to lupus, liver cirrhosis, Henoch-Schonlein purpura.
Primary IgAN diagnosed by renal biopsy	Glomerular filtration rate as estimated by the CKD-EPI equation <10 ml/min/1.73 m^2.
Immunosuppression naive for three months prior to recruitment	Patients with systemic diseases that can affect the kidneys like diabetes, systemic lupus erythematosus, presence of HIV, HBsAg, HCV infections, malignancies etc.
Willing to come for follow-up visits	Patients with a history of psychological illness or condition which interferes with their ability to understand or comply with the requirements of the study.

Abbreviations: HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus.

Table S2 Impact of gender on demographic and baseline clinical characteristics of the GRACE-IgANI cohort

Baseline characteristic	Entire Cohort (n=201)	Male (n=142)	Female (n=59)	*P* value
Age (years, mean±SD)	36±10.02	36.85±10.42	33.97±8.75	0.06
BMI (kg/m^2, mean±SD)	24.7±4.05	24.52±4.0	25.44±4.1	0.15
Hypertension (Yes/Evaluable patients (%))	169/201 (84.1)	124/143 (86.7)	45/58 (77.6)	0.08
Time to renal biopsy from onset of hypertension (months, median (IQR) (n))	10 (2 to 36) (167)	9 (2 to 36) (122)	12 (5 to 28) (45)	0.93
Systolic blood pressure (Hg) (mean±SD)	138±20.33	140.56±19.1	133.49±22.4	**0.024**
Diastolic blood pressure (mmHg) (mean±SD)	86.69±12.56	87.67±12.4	84.32±12.	0.09
Mean arterial pressure (mmHg) (mean±SD)	103.95±14.34	105.3±14	100.71±14.8	**0.011**
Blood pressure ≥ 140/90mmHg (Yes/Evaluable patients (%))	110/201 (55)	85/143 (59)	25/59 (42)	**0.020**
Synpharyngitic illness prior to presentation (Yes/Evaluable patients (%))	8/200 (4)	4/142 (2.8)	4/58 (6.9)	0.18
Pedal edema prior to presentation ((Yes/Evaluable patients (%))	93/200 (46.5)	58/142 (40.8)	35/58 (60.3)	**0.012**
Time to renal biopsy from onset of pedal edema (months, median (IQR) (n))	4 (2 to 11.5) (93)	3 (1 to 8.5) (57)	6 (2 to 17.25) (36)	0.08
Visible haematuria prior to presentation (Yes/Evaluable patients (%))	149/188 (79.3)	15/142 (10.6)	5/58 (8.6)	0.68
Time to renal biopsy from onset of visible haematuria (months, median (IQR) (n))	4 (2 to 63) (19)	5 (2 to 63) (15)	3 (0.5 to 68) (4)	0.57
Renal dysfunction prior to presentation ((Yes/Evaluable patients (%))	149/188 (79.3)	113/132 (85.6)	36/56 (64.3)	**0.001**
Time to renal biopsy from onset of renal dysfunction (months, median (IQR) (n))	3 (1 to 7) (184)	2 (1 to 7) (130)	3.5 (1 to 12) (54)	0.42
Proteinuria prior to presentation (Yes/Evaluable patients (%))	157/160 (98.1)	111/112 (99.1)	46/48 (95.8)	0.16
Time to renal biopsy from onset of proteinuria (months, median (IQR) (n))	2 (1 to 8) (160)	2 (1 to 6) (112)	4 (1 to 12) (48)	0.16
Nonvisible haematuria prior to presentation (Yes/Evaluable patients (%))	90/124 (72.6)	61/86 (70.9)	29/38 (76.3)	0.54
Time to renal biopsy from onset of nonvisible haematuria (months, median (IQR) (n))	2 (1 to 7.75) (120)	1 (0 to 4.75) (84)	4.5 (2 to 12) (36)	0.22
Family history of CKD (Yes/Evaluable patients (%))	11/201 (5.5)	8/143 (5.6)	3/58 (5.2)	0.9
On RASB prior to biopsy (Yes/Evaluable patients (%))	74/201 (37)	52/143 (36.4)	22/58 (37.9)	0.86

Table S3 Impact of gender on baseline laboratory parameters in the GRACE-IgANI cohort

Baseline characteristic	Entire Cohort (n=201)	Male (n=142)	Female (n=59)	*P* value
Haemoglobin (g/dL, mean±SD (Evaluable patients))	12.12±2.06 (201)	12.57±2.05	11.03±1.65	**<0.001**
Serum total protein (g/dL, mean±SD (Evaluable patients))	6.85±0.7 (198)	6.91±0.72 (140)	6.7±0.64 (58)	0.06
Serum albumin (g/dL, mean±SD (Evaluable patients))	4±0.56 (198)	4.04±0.53 (140)	3.76±0.6 (58)	**0.001**
24-hour urine protein (g/day, median (IQR) (Evaluable patients))	1.9 (1 to 3.75) (200)	1.95 (1 to 4) (142)	1.85 (0.78 to 3.2) (58)	0.11
Serum total cholesterol (mg/dL, mean±SD (Evaluable patients))	176.88±57.12 (198)	174.01±56.07 (140)	183.81±59.495 (58)	0.27
Serum uric acid (mg/dL, mean±SD (Evaluable patients)))	7.02±1.88 (199)	7.28±1.88 (141)	6.4±1.74 (58)	**0.003**
Serum creatinine (mg/dL, mean±SD (Evaluable patients))	2.1±1.06 (201)	2.23±1.05 (142)	1.8±1.04 (59)	**0.01**
eGFR MDRD (ml/min/1.73m^2, median (IQR) (Evaluable patients))	36 (24 to 60.5) (201)	36.5 (24.8 to 57.3) (201)	36 (22 to 76) (201)	0.79
eGFR CKD-EPI (ml/min/1.73m^2, median (IQR) (Evaluable patients))	36 (26 to 67.5) (201)	39.5 (26.8 to 64) (201)	40 (23 to 88) (201)	0.19

Table S4 Impact of gender on histopathological parameters in the GRACE-IgANI cohort

MEST-C Score	**Entire Cohort (n=185)**	**Male (n=134)**	**Female (n=51)**	***P* value**
M1 / M0 (M1 %)	21/164 **(11.4)**	16/118**(11.9)**	5/46 **(9.8)**	0.68
E1 / E0 (E1 %)	81/104 (**43.8**)	56/78 (**41.8**)	25/26 (**49**)	0.38
S1 / S0 (S1 %)	148/37 (**80**)	107/27 (**79.9**)	41/10 (**80.4**)	0.93
T2 / T1 / T0 (T2 % / T1%)	76/70/39 (**41.4** / **37.8**)	54/57/23 (40.3/42.5)	22/13/16 (43.1/25.5)	**0.04**
C2 / C1 / C0 (C2 % / C1%)	4/12/169 (**2.2 / 6.4)**	4/5/125 (3/3.7)	0/7/44 (0/13.7)	**0.025**
Global glomerulosclerosis (GS)	**Entire Cohort (n=184)**	**Male (n=133)**	**Female (n=51)**	***P* value**
(GS/total glomeruli) *100 (% (median (IQR))	32.05 (12.5 to 46.66)	30 (14.8 to 46.3)	33.33 (12.5 to 50)	0.92
Immunofluorescence staining	**Entire Cohort (n=201)**	**Male (n=142)**	**Female (n=59)**	***P* value**
IgA (+++, n (%))	148 (73.6)	104 (73.2)	44 (74.6)	0.85
IgG (++ & +++, n (%))	11 (5.5)	7 (4.9)	4 (6.8)	0.6
IgM (++ & +++, n (%))	4 (2)	2 (1.4)	2 (3.4)	0.36
C3 (++ & +++, n (%))	74(36.8)	52 (36.6)	22 (37.3)	0.93

Total number of glomeruli per biopsy (median (IQR))= 9 (7-13)

Table S5 Baseline clinical characteristics of the GRACE-IgANI cohort stratified by Total Risk Score

Baseline characteristic	Entire Cohort (n=185)	Lower Risk (n=91)	Higher Risk (n=94)	*P* value
Gender (male: female; ratio)	134:51 (2.6:1)	67:24 (2.8:1)	67:27 (2.5:1)	0.72
Age (years, mean±SD)	36.1±10.2	35.1±10.6	37.1±9.8	0.19
BMI (kg/m^2, mean±SD)	24.9±4.1	25±4.1	24.7±4	0.59
Hypertension (Yes/Evaluable patients (%))	157/185 (84.9)	68/91 (74.7)	89/94 (94.7)	**<0.001**
Time to renal biopsy from onset of hypertension (months, median (IQR) (n))	11 (2 to 36) (156)	12 (2 to 48) (67)	8 (2 to 36) (89)	0.42
Systolic blood pressure (Hg) (mean±SD)	138.4±19.9	132.5±18.3	144.2±19.7	<**0.001**
Diastolic blood pressure (mmHg) (mean±SD)	86.7±12.2	84.2±10.5	89.2±13.2	**0.005**
Mean arterial pressure (mmHg) (mean±SD)	103.94±13.9	100.3±12.5	107.5±14.3	<**0.001**
Blood pressure ≥ 140/90mmHg (Yes/Evaluable patients (%))	101/185 (54.6%)	35/91 (38.4)	66/94 (70.2)	<**0.001**
Synpharyngitic presentation (Yes/Evaluable patients (%))	7/184 (3.8)	7/90 (7.8)	0/94 (0)	**0.006**
Pedal edema at presentation ((Yes/Evaluable patients (%))	84/184 (45.7)	31/90 (34.4)	53/94 (56.4)	**0.003**
Time to renal biopsy from onset of pedal edema (months, median (IQR) (n))	4 (2 to 12) (85)	4 (2 to 12) (31)	3 (1.8 to 9.8) (54)	0.54
Visible haematuria at presentation (Yes/Evaluable patients (%))	18/184 (9.8)	11/90 (12.2)	7/94 (7.4)	0.28
Time to renal biopsy from onset of visible haematuria (months, median (IQR) (n))	4 (1.5 to 49) (17)	3 (1 to 6) (10)	35 (3 to 183) (7)	0.07
Renal dysfunction prior to biopsy ((Yes/Evaluable patients (%))	138/174 (79.3)	54/84 (64.3)	84/90 (93.3)	**<0.001**
Time to renal biopsy from onset of renal dysfunction (months, median (IQR) (n))	2 (1 to 7.3) (170)	2 (1 to 10.25) (82)	2 (1 to 6) (88)	0.77
Proteinuria prior to biopsy (Yes/Evaluable patients (%))	146/147 (99.3)	71/72 (98.6)	75/75 (100)	0.31
Time to renal biopsy from onset of proteinuria (months, median (IQR) (n))	2 (1 to 8) (147)	3 (1 to 10.5) (73)	2 (1 to 6) (74)	0.85
Nonvisible haematuria prior to biopsy (Yes/Evaluable patients (%))	82/113 (72.6)	40/58 (69)	42/55 (76.4)	0.38
Time to renal biopsy from onset of nonvisible haematuria (months, median (IQR) (n))	2 (1 to 8) (109)	3 (1 to 10) (58)	2 (1 to 6) (51)	0.46
Family history of CKD (Yes/Evaluable patients (%))	11/184 (6)	5/90 (5.6)	6/94 (6.4)	0.81
On RASB prior to biopsy (Yes/Evaluable patients (%))	67/184 (36.4)	39/90 (43.3)	28/94 (29.8)	0.056

Table S6 Baseline laboratory parameters of the GRACE-IgANI cohort stratified by Total Risk Score

Baseline characteristic	Entire Cohort (n=185)	Lower Risk (n=91)	Higher Risk (n=94)	*P* value
Haemoglobin (g/dL, mean±SD (evaluable patients))	12.2±2.1 (185)	12.9±1.9 (91)	11.4±1.9 (94)	**<0.001**
Serum total protein (g/dL, mean±SD (evaluable patients))	6.85±0.7 (182)	7.09±0.71 (90)	6.61±0.63 (92)	**<0.001**
Serum albumin (g/dL, mean±SD (evaluable patients))	4±0.6 (182)	4.12±0.62 (90)	3.8±0.46 (92)	**<0.001**
24-hour urine protein (g/day, median (IQR) (evaluable patients))	1.9 (1 to 3.8) (184)	1.1 (0.7 to 1.9) (90)	3.6 (1.8 to 5.1) (94)	**<0.001**
Serum total cholesterol (mg/dL, mean±SD (evaluable patients))	176.3±58 (182)	175.69±63.3 (89)	176.96±52.7 (93)	0.88
Serum uric acid (mg/dL, mean±SD (evaluable patients)))	7±1.9 (183)	6.74±1.85 (90)	7.28±1.91 (93)	0.052
Serum creatinine (mg/dL, mean±SD (evaluable patients))	2.1±1.0 (185)	1.47±0.6 (91)	2.69±1 (94)	**<0.001**
eGFR MDRD (ml/min/1.73m^2, median (IQR) (evaluable patients))	37 (24.5 to 61) (185)	55 (38 to 87) (91)	25 (19 to 36.3) (94)	**<0.001**
eGFR CKD-EPI (ml/min/1.73m^2, median (IQR) (evaluable patients))	40 (26.5 to 68.5) (185)	61 (41 to 102) (91)	27 (20 to 40) (94)	**<0.001**

Table S7 Histopathological parameters in the GRACE-IgANI cohort stratified by Total Risk Score

MEST-C Score	**Entire Cohort (n=185)**	**Lower Risk (n=91)**	**Higher Risk (n=94)**	***P* value**
M1 / M0 (M1 %)	21/164 (11.4)	10/81 (11)	11/83 (11.7)	0.88
E1 / E0 (E1 %)	81/104 (43.8)	33/58 (36.3)	48/46 (51.1)	**0.043**
S1 / S0 (S1 %)	148/37 (80)	58/33 (63.7)	90/94 (95.7)	**<0.001**
T2 / T1 / T0 (T2 % / T1%)	76/70/39 (41.4 / 37.8)	3/49/39 (3.3/53.8)	73/21/0 (77.7/22.3)	**<0.001**
C2 / C1 / C0 (C2 % / C1%)	4/12/169 (2.2 / 6.5)	2/7/82 (2.2/7.7)	2/5/87 (2.1/5.3)	0.81
Global glomerulosclerosis (GS)	**Entire Cohort (n=184)**	**Lower Risk (n=91)**	**Higher Risk (n=94)**	***P* value**
(GS/total glomeruli) *100 (% (median (IQR))	32.1 (12.5 to 46.7)	16.7 (0 to 33.3)	41.7 (27.8 to 57.1)	**<0.001**
Immunofluorescence staining	**Entire Cohort (n=201)**	**Lower Risk (n=91)**	**Higher Risk (n=94)**	***P* value**
IgA (+++, n (%))	148 (73.6)	75 (82.4)	63 (67)	**0.016**
IgG (++ & +++, n (%))	11 (5.5)	6 (6.6)	4 (4.3)	0.48
IgM (++ & +++, n (%))	4 (2)	4 (4.4)	0 (0)	**0.04**
C3 (++ & +++, n (%))	74 (36.8)	32 (35.2)	37 (39.4)	0.56

Total number of glomeruli per biopsy (median (IQR))= 9 (7-13); LR 10 (7-14) and HR 9 (6-13)

Table S8 Baseline clinical characteristics of the GRACE-IgANI cohort stratified by the five-year risk of progression to the combined endpoint of 50% decline in eGFR or ESKD using the IIGANN risk calculator

Baseline characteristic	Entire Cohort (n=185)	IIGANN risk <35% (n=90)	IIGANN risk ≥35% (n=95)	*P* value
Gender (male: female; ratio)	134:51 (2.6:1)	64:26 (2.5:1)	70:25 (3:1)	0.7
Age (years, mean±SD)	36.1±10.2	35.5±10.8	36.7±9.6	0.44
BMI (kg/m^2, mean±SD)	24.9±4.1	25.3±4.3	24.5±3.8	0.18
Hypertension (Yes/Evaluable patients (%))	157/185 (84.9)	68/91 (74.7)	89/94 (94.7)	**<0.001**
Time to renal biopsy from onset of hypertension (months, median (IQR) (n))	11 (2 to 36) (156)	12 (2 to 48.5) (66)	9 (2 to 36) (90)	0.7
Systolic blood pressure (Hg) (mean±SD)	138.4±19.9	133.4±18.1	143.2±20.4	**0.001**
Diastolic blood pressure (mmHg) (mean±SD)	86.7±12.2	84.4±10.5	88.9±13.3	**0.01**
Mean arterial pressure (mmHg) (mean±SD)	103.94±13.9	100.7±12.2	107±14.7	**0.002**
Blood pressure ≥ 140/90mmHg (Yes/Evaluable patients (%))	101/185 (54.6%)	38/89 (42.7)	63/95 (66.3)	**0.001**
Synpharyngitic presentation (Yes/Evaluable patients (%))	7/184 (3.8)	7/89 (7.9)	0/95 (0)	**0.005**
Pedal edema at presentation ((Yes/Evaluable patients (%))	84/184 (45.7)	33/89 (37.1)	51/95 (53.7)	**0.024**
Time to renal biopsy from onset of pedal edema (months, median (IQR) (n))	4 (2 to 12) (85)	4 (2 to 12) (33)	4 (2 to 9) (52)	0.83
Visible haematuria at presentation (Yes/Evaluable patients (%))	18/184 (9.8)	11/89 (12.4)	7/95 (7.4)	0.26
Time to renal biopsy from onset of visible haematuria (months, median (IQR) (n))	4 (1.5 to 49) (17)	3 (1 to 6) (10)	35 (3 to 183) (7)	0.07
Renal dysfunction prior to biopsy ((Yes/Evaluable patients (%))	138/174 (79.3)	49/83(59)	89/91 (97.8)	**<0.001**
Time to renal biopsy from onset of renal dysfunction (months, median (IQR) (n))	2 (1 to 7.3) (170)	2 (1 to 10.75) (80)	2 (1 to 6) (90)	0.62
Proteinuria prior to biopsy (Yes/Evaluable patients (%))	146/147 (99.3)	71/72 (98.6)	75/75 (100)	0.31
Time to renal biopsy from onset of proteinuria (months, median (IQR) (n))	2 (1 to 8) (147)	3 (1 to 11.5) (73)	2 (1 to 5.25) (74)	0.22
Nonvisible haematuria prior to biopsy (Yes/Evaluable patients (%))	82/113 (72.6)	42/56 (75)	40/57 (70.2)	0.57
Time to renal biopsy from onset of nonvisible haematuria (months, median (IQR) (n))	2 (1 to 8) (109)	3 (1 to 10) (55)	2 (1 to 4) (54)	0.12
Family history of CKD (Yes/Evaluable patients (%))	11/184 (6)	6/89 (6.7)	5/95 (5.3)	0.67
On RASB prior to biopsy (Yes/Evaluable patients (%))	67/184 (36.4)	38/89 (42.7)	29/95 (30.5)	0.09

Table S9 Baseline laboratory parameters of the GRACE-IgANI cohort stratified by the five-year risk of progression to the combined endpoint of 50% decline in eGFR or ESKD using the IIGANN risk calculator

Baseline characteristic	Entire Cohort (n=185)	IIGANN risk <35% (n=90)	IIGANN risk ≥35% (n=95)	*P* value
Haemoglobin (g/dL, mean±SD (evaluable patients))	12.2±2.1 (185)	12.9±2 (90)	11.4±1.8 (95)	**<0.001**
Serum total protein (g/dL, mean±SD (evaluable patients))	6.85±0.7 (182)	7.06±0.8 (89)	6.66±0.6 (93)	**<0.001**
Serum albumin (g/dL, mean±SD (evaluable patients))	4±0.6 (182)	4.07±0.6 (89)	3.84±0.5 (93)	**0.007**
24-hour urine protein (g/day, median (IQR) (evaluable patients))	1.9 (1 to 3.8) (184)	1.1 (0.7 to 2.2) (89)	3.1 (1.7 to 4.9) (95)	**<0.001**
Serum total cholesterol (mg/dL, mean±SD (evaluable patients))	176.3±58 (182)	173.8±64.8 (88)	178.7±51 (94)	0.58
Serum uric acid (mg/dL, mean±SD (evaluable patients)))	7±1.9 (183)	6.7±1.9 (89)	7.3±1.9 (94)	**0.031**
Serum creatinine (mg/dL, mean±SD (evaluable patients))	2.1±1.0 (185)	1.34±0.5 (89)	2.8±0.9 (95)	**<0.001**
eGFR MDRD (ml/min/1.73m^2, median (IQR) (evaluable patients))	37 (24.5 to 61) (185)	61 (44 to 89.5) (90)	25 (19 to 33) (95)	**<0.001**
eGFR CKD-EPI (ml/min/1.73m^2, median (IQR) (evaluable patients))	40 (26.5 to 68.5) (185)	68.5 (48 to 102.3) (90)	27 (20 to 37) (95)	**<0.001**

Table S10 Histopathological parameters in the GRACE-IgANI cohort stratified by the five-year risk of progression to the combined endpoint of 50% decline in eGFR or ESKD using the IIGANN risk calculator

MEST-C Score	**Entire Cohort (n=185)**	**IIGANN risk <35% (n=90)**	**IIGANN risk ≥35% (n=95)**	***P* value**
M1 / M0 (M1 %)	21/164 (11.4)	9/81 (10)	12/83 (12.6)	0.57
E1 / E0 (E1 %)	81/104 (43.8)	36/54 (40)	45/50 (47.4)	0.31
S1 / S0 (S1 %)	148/37 (80)	59/31 (65.6)	89/95 (93.7)	**<0.001**
T2 / T1 / T0 (T2 % / T1%)	76/70/39 (41.4 / 37.8)	10/42/38 (11.1/46.7)	66/28/1 (69.5/28/1)	**<0.001**
C2 / C1 / C0 (C2 % / C1%)	4/12/169 (2.2 / 6.5)	2/7/81 (2.2/7.8)	2/5/88 (2.1/5.3)	0.78
Global glomerulosclerosis (GS)	**Entire Cohort (n=184)**	**IIGANN risk <35% (n=90)**	**IIGANN risk ≥35% (n=95)**	***P* value**
(GS/total glomeruli) *100 (% (median (IQR))	32.1 (12.5 to 46.7)	16 (0 to 28.9)	42.9 (33.3 to 60)	**<0.001**
Immunofluorescence staining	**Entire Cohort (n=185)**	**IIGANN risk <35% (n=90)**	**IIGANN risk ≥35% (n=95)**	***P* value**
IgA (+++, n (%))	148 (73.6)	72 (80)	66 (69.5)	0.1
IgG (++ & +++, n (%))	11 (5.5)	6 (6.7)	4 (4.2)	0.46
IgM (++ & +++, n (%))	4 (2)	4 (4.4)	0 (0)	**0.038**
C3 (++ & +++, n (%))	74 (36.8)	35 (38.9)	34 (35.8)	0.66

Total number of glomeruli per biopsy (median (IQR))= 9 (7-13); IIGANN risk <35%= 11 (8-14) and IIGANN risk ≥35%= 8 (6-12)