IgA NEPHROPATHY IN ELDERLY PATIENTS. Supplemental Material

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Supplemental Table 1. Number of kidney biopsies, number of them with the diagnosis of IgA nephropathy and number of IgA nephropathy diagnoses in patients > 65 in each period of time

Supplemental Table 2. CKD stages at diagnosis in the study cohort of patients >65 and in a control cohort of IgA nephropathy youger than 65.

Supplemental Table 3. Cox proportional hazard regression model for association between covariates and mortality before kidney replacement therapy, or kidney replacement therapy initiation, adjusted for competing risk of death (sub-distribution hazards model of Fine and Gray).

Supplemental Table 4. Baseline characteristics and outcome of our study cohort (>65 years old) and the 12 de Octubre cohort (<65 years old) after a propensity score matching

Supplemental Table 5. Patients presenting with asymptomatic urinary abnormalities, treated and not treated with immunosuppressive drugs.

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Supplemental Figure 1. Survival without kidney replacement therapy, death or the composite end-point (RRT or death before RRT) in the whole cohort of patients

Supplemental Figure 2. Survival without composite end-point (RRT or death before RRT) according to the period of diagnostic.

Supplementary Figure 3. Survival without composite end-point of patients of our study cohort (>65 years old) and the 12 de Octubre cohort (<65 years old) after a propensity score matching

Appendix: Statistical analysis

Supplemental Table 1. Number of kidney biopsies, number of them with the diagnosis of IgA nephropathy and number of IgA nephropathy diagnoses in patients > 65 years in each period of time[a]

	1999-1995	1996-2000	2001-2005	2006-2010	2011-2015
Total number of kidney biopsies	932	1539	1567	1918	2410
IgAN, n (%)	106(11)	171(11)	148(9)	245(12)	288(11)
IgAN≥65, n (%)	2(1.8)	4(2.3)	5(3.3)	10(4)	15(5.2)

Abbreviations: IgAN: Patients diagnosed with IgA nephropathy; IgAN≥65: Patients elderly of 65 years old diagnosed with IgA nephropathy

[a] Data from 3 hospitals with constant and regular activity in the performance of renal biopsies from the first period (1990-1995) and that performed an average number of biopsies> 100 per year

Supplemental Table 2. CKD stages at diagnosis in the study cohort of patients >65 and in a control cohort of IgA nephropathy younger than 65.

	>65 years (N=151)	<65 years (N=135)	P
Stage I, n (%)	4(2.6)	33(24.4)	0.000
Stage II, n (%)	14(9.3)	40(29.6)	0.000
Stage III, n (%)	49(32.5)	43(31.9)	0.91
Stage IV, n (%)	50(33.1)	11(8.1)	0.000
Stage V, n (%)	34(22.5)	8(5.9)	0.000

Supplemental Table 3. Cox proportional hazard regression model for association between covariates and mortality before kidney replacement therapy, or kidney replacement therapy initiation, adjusted for competing risk of death (sub-distribution hazards model of Fine and Gray).

	Kidney replacement therapy					Mortality				
		Univariable		Multivariable			Univariable		Multivariable	
Variable	**Number of events (n/N)**	**Sub-hazard ratio (95%CI SHR)**	**p**	**Sub-hazard ratio (95%CI SHR)**	**p**	**Number of events (n/N)**	**Hazard ratio (95%CI HR)**	**p**	**Hazard ratio (95%CI HR)**	**p**
Age		1.05 (0.97–1.13)	0.24				1.06 (0.97–1.17)	0.21		
Sex, male	31/116	1.34 (0.55–3.29)	0.52			22/116	1.49 (0.54–4.09)	0.44		
Smoking status (0,1)	17/65	0.80 (0.38–1.67)	0.55			15/65	1.03 (0.40–2.60)	0.96		
Diabetes mellitus (0,1)	11/39	1.30 (0.57–2.97)	0.53			6/39	1.12 (0.40–3.14)	0.83		
Oral anticoagulant therapy (0,1)	4/30	0.42 (0.13–1.43)	0.16			8/30	1.46 (0.48–4.43)	0.51		
Charlson comorbidity index		0.92 (0.72–1.18)	0.53				1.34 (0.99–1.82)	0.05	1.32 (1.09–1.60)	0.005
Systolic BP		1.00 (0.98–1.02)	0.95				0.98 (0.95–1.01)	0.19		
Diastolic BP		0.98 (0.96–1.00)	0.11				0.99 (0.94–1.03)	0.46		
Serum creatinine		1.28 (1.15–1.41)	<0.0001	1.22 (1.07–1.39)	0.002		0.99 (0.77–1.28)	0.99		
Serum albumin		0.72 (0.39–1.32)	0.29				1.10 (0.45–2.69)	0.83		
Proteinuria		1.06 (0.90–1.24)	0.48				1.04 (0.81–1.32)	0.78		
Glomerulosclerosis		1.02 (1.00-1.04)	0.05	1.02 (1.00–1.05)	0.02		1.00 (0.98–1.03)	0.88		
M1	24/100	1.12 (0.54–2.33)	0.77			19/100	0.93 (0.33–2.67)	0.89		
E1	12/42	1.07 (0.58–1.96)	0.83			10/42	4.08 (0.99–11.17)	0.56		
S1	15/56	0.96 (0.46–2.01)	0.92			11/56	1.41 (0.57–3.46)	0.46		
T1-2	24/77	2.07 (1.31–3.26)	0.002	1.68 (1.01–2.81)	0.004	14/77	0.90 (0.36–2.26)	0.82		
Crescents>25% (0,1)	9/32	1.02 (0.37–2.83)	0.98			6/32	1.90 (0.56–6.57)	0.31		
RAAS blockade (0,1)	27/127	0.15 (0.07–0.31)	<0.0001	0.20 (0.09–0.43)	<0.0001	24/127	0.43 (0.20–1.55)	0.20		
Immunosuppressive therapy (0,1)	17/70	1.75 (0.74–4.12)	0.2			15/70	0.89 (0.34–2.34)	0.81		

Abbreviations: BP: blood pressure; M1: mesangial hypercellularity; E1: endocapillary hypercellularity; S1: segmental glomerulosclerosis; T1-T2: Tubular atrophy/interstitial fibrosis >25%, RAAS: Renin-angiotensin-aldosterone system.

Supplemental Table 4. Baseline characteristics and outcome of our study cohort (>65 years old) and the 12 de Octubre cohort (<65 years old) after a propensity score matching

	All patients (n=158)	<65 years old (n=79)	>65 years old (n=79)	p
Male (%)	118 (75)	59 (75)	59 (75)	1.00
Age (years)	54±20	38±14	72±5	<0.0001
Oral anticoagulant therapy, n (%)	14 (9)	1 (1)	13 (17)	0.001
Baseline systolic BP (mmHg)	135±19	135±22	136±16	0.785
Baseline diastolic BP (mmHg)	80±12	80±14	80±10	0.933
Baseline serum creatinine (mg/dl)	2.6±2.4	2.4±2	2.8±2	0.278
M1 (%)	75 (48)	29 (37)	46 (58)	0.007
E1 (%)	22 (14)	5 (6)	17 (22)	0.006
S1 (%)	42 (27)	23 (29)	19 (24)	0.47
T1-2 (%)	42 (27)	20 (25)	22 (28)	0.86
Glomeruli with crescents (%)	22 (14)	9 (11)	13 (17)	0.36
RAAS inhibitors, n (%)	128 (81)	65 (82)	63 (80)	0.69
Immunosuppressive treatment, n (%)	67 (42)	29 (37)	38 (48)	0.147
Follow-up (months)	60 [17–159]	125 [28–262]	36 [12–73]	<0.0001
KRT, n (%)	43 (27)	20 (25)	23 (29)	0.59
KRT or death, n (%)	57 (36)	20 (25)	37 (47)	0.005

Abbreviations: BP: Blood pressure; Scr: Serum creatinine; M1: mesangial hypercellularity; E1: endocapillary hypercellularity; S1: segmental glomerulosclerosis; T1-T2: Tubular atrophy /interstitial fibrosis >25%; RAAS: Renin-angiotensin-aldosterone system; KRT: kidney replacement therapy

Supplemental Table 5. Patients presenting with asymptomatic urinary abnormalities, treated and not treated with immunosuppressive drugs

	No immunosuppressive therapy (N=55)	Immunosuppressive therapy (N=29)	P
Follow up	48(18-95)	24(12-57)	0.03
Age (years)	70±4	72±5	0.08
Males, n (%)	44(80)	24(83)	0.76
RAAS inhibitors, n (%)	44(80)	29(100)	0.01
Baseline Serum creatinine (mg/dl)	1.99±1.12	2.37±1.97	0.26
Baseline eGFR (ml/min/1.73m^2)	38.38±17.47	42.68±29.25	0.40
Baseline Proteinuria (g/d)	1.6(0.76-2.72)	3.5(1.53-6.5)	0.03
Microscopic hematuria, n (%)	41(79)	24(83)	0.67
Macroscopic hematuria, n (%)	3(5)	2(7)	0.79
Oral anticoagulant therapy, n (%)	5(9)	6(21)	0.13
KRT, n.(%)	15(27)	9(31)	0.71
Death before KRT, n. (%)	8(15)	6(21)	0.47
KRT +death, n(%)	23(42)	15(52)	0.38

Abbreviations: RAAS: Renin-angiotensin-aldosterone system; eGFR: estimated glomerular filtration rate; KRT: Kidney replacement therapy

Supplemental Table 6: **Baseline characteristics and outcomes of patients ≥72 years and <72 years.**

	All patients (N=151)	≥72 years (N=72)	<72 years (N=79)	p
Males (%)	116(77)	50(69)	88(83)	0.04
Age (year)	72±5	77±3	68±2	0,00
DM, n (%)	39(26)	19(26)	20(25)	0.00
Systolic BP (mmHg)	142±20	141±17	143±22	0.57
Diastolic BP (mmHg)	78±11	79±11	77±12	0.18
Serum creatinine (mg/dl)	3±2.3	2.81±1.44	3.24±2.24	0.26
eGFR (ml/min/1.73m^2)	32±22	37±25	27±19	0.00
Proteinuria (g/day)	2.1(1-4.1)	2.1(1-3.9)	2.1(0.9-4.2)	1
Macroscopic hematuria, n (%)	45(30)	30(42)	20(25)	0.03
Duration of macroscopic hematuria (days)	11±33	6±16	17±43	0.10
Microscopic hematuria, n (%)	130(85)	65(93)	60(82)	0.05
Oral anticoagulant therapy, n (%)	30(20)	20(28)	10(13)	0.02
KRT at presentation, n (%)	14(9)	9(13)	5(6)	0.18
M1(%)	100(66)	55(76)	45(57)	0.01
E1 (%)	42(28)	25(35)	17(21)	0.07
S1 (%)	56(37)	28(39)	28(35)	0.66
T1-T2 (%)	77(51)	29(40)	48(61)	0.01
Glomeruli with crescents (%)	0.21±0.4	4±10	5±14	0.56
Follow up	24(12-66)	38±46	56±55	0.03
Treatments				
RAS inhibitors, n (%)	127(84)	57(79)	70(89)	0.11
Immunosuppressor therapy, n (%)	70(46)	39(54)	31(39)	0.06
Death before KRT , n (%)	69(46)	17(24)	12(15)	0.18
KRT, n.(%)	40(26)	18(25)	22(28)	0.69
KRT+death, n(%)	29(20)	35(49)	34(43)	0.49

Abbreviations: DM: diabetes mellitus, BP: Blood pressure; eGFR: estimated glomerular filtration rate; KRT: kidney replacement therapy, M1: mesangial hypercellularity; E1: endocapillary hypercellularity; S1: segmental glomerulosclerosis; T1-T2: Tubular atrophy /interstitial fibrosis >25%; KRT: kidney replacement therapy

Supplemental Table 7. Patients presenting with hematuria related AKI, treated and not treated with immunosuppressive drugs

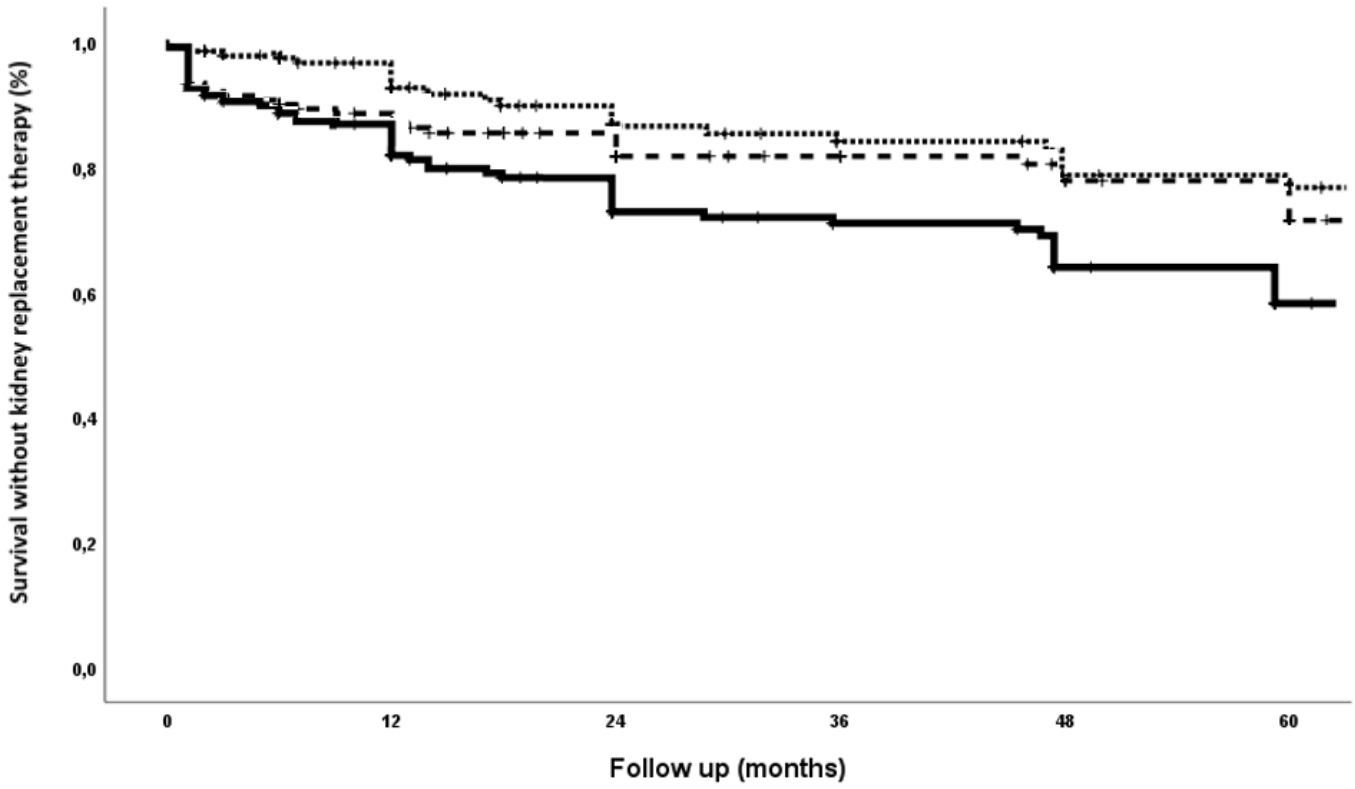
	No immunosuppressive therapy (N=21)	Immunosuppressive therapy (N=32)	P
Follow up	13(1-54)	21(12-60)	0.91
Age (years)	74±6	73±5	0.59
Males, n (%)	16(76)	21(66)	0.41
RAAS inhibitors, n (%)	16(76)	27(85)	0.45
Baseline Serum creatinine (mg/dl)	4.61±3.25	4.17±2.54	0.59
Baseline eGFR (ml/min/1.73m^2)	19.75±19.75	19.93±14.17	0.96
Baseline Proteinuria (g/d)	1.84(0.92-4.74)	1.15(0.77-2.89)	0.72
Duration of macroscopic hematuria (days)	6(1-30.75)	8(3-52)	0.74
Oral anticoagulant therapy, n (%)	3(14)	15(46)	0.01
>25% recovery serum creatinine, n(%)	8(38)	20(62)	0.08
>75% recovery serum creatinine, n(%)	2(10)	4(12)	0.73
KRT, n.(%)	8(38)	5(16)	0.06
Death before KRT, n. (%)	4(19)	6(19)	0.97
KRT+death, n(%)	12(57)	11(14)	0.10

Abbreviations: RAAS: Renin-angiotensin-aldosterone system; Scr: serum creatinine; eGFR: estimated glomerular filtration rate.

Supplemental Table 8: causes of death in patients who died before the start of kidney replacement therapy

	Death patients **(N 29)**
Infectious diseases, n (%)	9 (31)
Cardiovascular diseases, n (%)	11 (38)
Cancer, n (%)	2(7)
Pulmonary pathology, n (%)	2(7)
Unknow cause, n(%)	5(17)

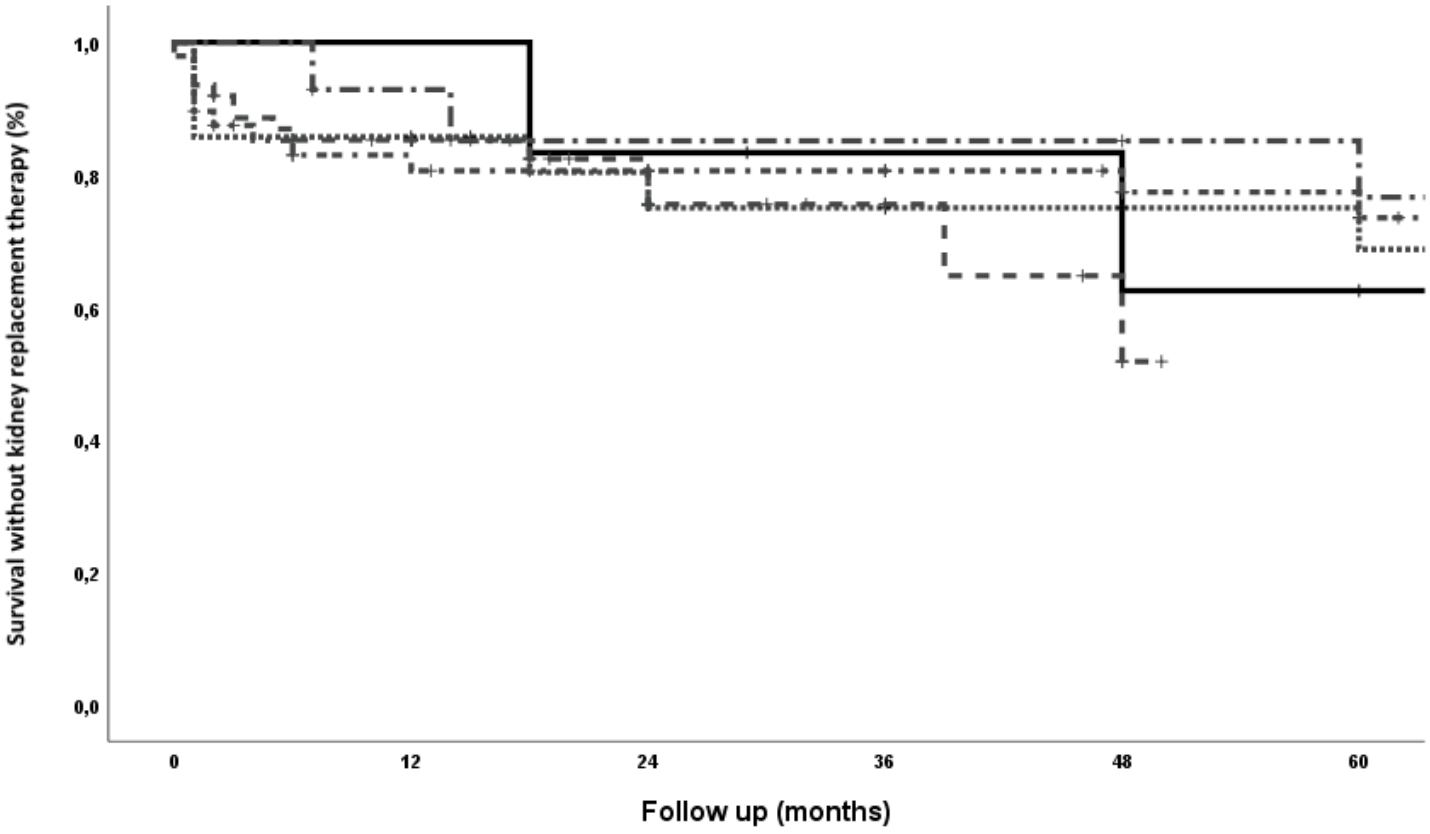
Supplemental Figure 1. Survival without kidney replacement therapy, death or the composite end-point (RRT or death before RRT) in the whole cohort of patients



C-endpoint	151	105	73	64	50	39
KRT	151	102	70	61	46	38
exitus	151	105	70	50	39	11

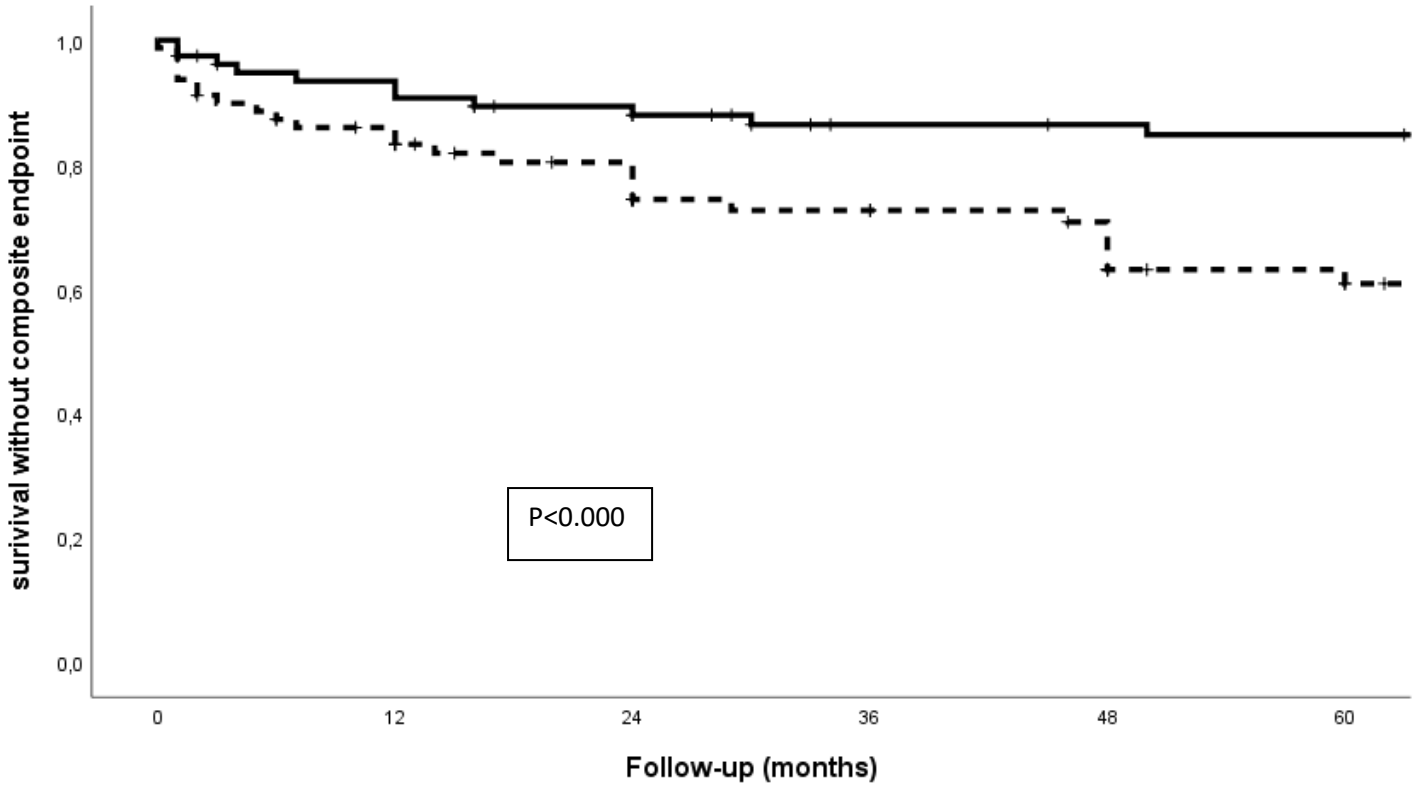
Abbreviations: KRT: kidney replacement therapy; C-endpoint: composite endpoint

Supplemental Figure 2. Survival without composite end-point (RRT or death before RRT) according to the period of diagnostic.



90-95	6	5	5	4	3	2
96-00	14	12	11	11	10	9
01-05	21	17	14	13	12	11
06-10	48	34	29	26	20	16
11-15	62	33	11	7	3	-

Supplemental Figure 3. Survival without composite end-point of patients of our study cohort (>65 years old) and the 12 de Octubre cohort (<65 years old) after a propensity score matching



<65 Y	79	68	60	54	53	52
>65 Y	79	62	42	39	29	25

Abbreviations: <65Y: <65 years old; >65Y: >65 years old

Appendix : Statistical analysis

To estimate the cumulative incidence of Kidney replacement therapy while accounting for the competing risks of dying before dialysis initiation, a competing-risk proportional hazards regression model was built using the method of Fine and Gray (supplementary material). The same covariates selected in the Cox model were also re-analyzed with the competing-risk model, and the sub-distribution hazard ratios were estimated.

A propensity score matching (PSM) analysis was applied to compare kidney outcomes of the study group with a control group of patients with IgA nephropathy under 65 years, adjusting for the following potential confounding variables: baseline serum creatinine, interstitial fibrosis and tubular atrophy, systolic and diastolic blood pressure, and treatment with RAS blockade. A 1:1 nearest neighbor matching algorithm was applied with a caliper of 0.16 without replacement.

The PSM was performed using SPSS R-Menu using in both cases the R statistical free software version R3.1.1.