

SUPPLEMENTARY DATA

Supplementary Methods

To estimate GFR, we used the new Chronic Kidney Disease Epidemiology Collaboration equation expressed as a single equation, using the Scr value as follows: $eGFR_{cr} = 142 \times \min(Scr/\kappa, 1)^\alpha \times \max(Scr/\kappa, 1) - 1.200 \times 0.9938^{Age} \times 1.012$ [if female]; where Scr is standardized serum creatinine in mg/dL, κ is 0.7 for females or 0.9 for males, α is -0.241 for females or -0.302 for males, $\min(Scr/\kappa, 1)$ is the minimum of Scr/ κ or 1.0, $\max(Scr/\kappa, 1)$ is the maximum of Scr/ κ or 1.0 [23]

Supplementary Tables Legends:

Table S1: Comparison of laboratory urine test in the total cohort and between CVID patients with and without CKD.

Table S2: Comparison of laboratory data and B cells subpopulations between CVID patients with infection-only and complicated phenotype.

Table S3: Comparison of demographic characteristics, clinical, laboratory, instrumental variables and treatments between CVID patients with or without CKD, adjusted for age.

Table S4: Multivariate analysis: demographic, laboratory, clinical and therapeutic variables associated with CKD after correction for age.

Table S1

Urine test	Total cohort (n=367)	No CKD (n=344)	CKD (n=23)	p value	OR (IC95%)
Ph, median (IQR)	5.5 (5.5 - 6)	5.5 (5.5-6.2)	5.5 (5.25-5.5)	0.054	0.36 (0.13-1.02)
Urinary specific weight, median (IQR)	1019 (1013 - 1024)	1019 (1014-1025)	1015 (1011-1020)	0.685	0.99 (0.93-1.05)
Urinary Sediment, n (%)	76 (20.7)	72	4	1.000	0.874 (0.27-2.83)
Erythrocyte, cells/microL, median (IQR)	1 (0 - 8.5)	1 (0-9)	1 (0-4.5)	0.358	0.96 (0.89-1.04)
Leukocytes cells/microL, median (IQR)	2 (0 - 10)	2 (0-11)	3 (1.5-6)	0.778	0.99 (0.99-1.00)
Spot proteinuria, n (%)	28 (7.6)	28 (8.1)	0 (0)	0.382	0.246 (0.01-4.23)
Glicosuria, n (%)	3 (0.8)	3 (0.9)	0 (0)	1.000	2.39 (0.12-48.5)
Nitrites, n (%)	8 (2.2)	7 (2)	1 (4.3)	0.364	2.60 (0.30-22.8)
Bacterial flora, n (%)	34 (9.3)	32 (9.3)	2 (8.7)	1.000	1.10 (0.24-5.16)

Urinary sediment, spot proteinuria, glycosuria, nitrites and bacterial flora are reported as qualitative variables, considering either their presence or absence. We defined urinary sediment as the presence of spot proteinuria and/or urinary erythrocytes concentration above 10 mg/dl; proteinuria as the presence of urinary protein concentration above 20 mg/dl, glycosuria as the presence of urinary glucose concentration above 10 mg/dl and bacterial flora as the presence of bacterial cells above 1000 cells/microL.

Table S2

	Infection-only phenotype (n=189)	Complicated phenotype (n=178)	p value
Age, median (IQR)	53 (39-61.5)	51 (38-63)	0.407
CKD, n (%)	9 (4.8)	14 (7.9)	0.225
Creatinine (mg/dl), median (IQR)	0.77 (0.69-0.90)	0.79 (0.68-0.94)	0.715
eGFR (mL/min/1.73m2), median (IQR)	99 (84-108)	96 (84-110)	0.852
Hb (g/dl), median (IQR)	14 (13.1-15.1)	13.4 (12.2-14.6)	<0.001
Platelet-to-lymphocytes ratio, median (IQR)	121 (96-156)	114 (80-172)	0.189
Neutrophil-to- lymphocyte ratio, median (IQR)	2 (1.5-3)	2.2 (1.5-3.2)	0.513
ALC (cells/mm ³), median (IQR)	1670 (1276-2100)	1368 (880-1900)	<0.01
T cells (%), median (IQR)	76 (70-80)	79 (70-85)	0.018
B cells (%), median (IQR)	10 (6-14)	8 (3-12)	0.010
Sm B cells (%), median (IQR)	3 (1-6)	1.6 (0.7-4)	0.012
Mz B cells (%), median (IQR)	10 (4-21)	5 (1.4-15)	0.006
CD21low B cells (%), median (IQR)	5.7 (2.6-10.6)	6.6 (3-14)	0.212
Naive B Cells (%), median (IQR)	58 (31-78)	70 (40-87)	0.104
Tr B cells (%), median (IQR)	1 (0.3-2.3)	0.9 (0.2-2.6)	0.833

B cells sub-populations were identified according to EUROclass study: Sm B cells: Switched memory IgD-IgM-CD27+; CD21low B cells: Activated CD21lowCD38low; MZ B cell: Marginal zone IgD+IgM+CD27+; Tr B cells: Transitional CD38++IgMhigh; Naive B cells: Naive IgD+IgM+CD27- [22]. Statistically significant results in bold.

Table S3

	p value	OR (IC95%)
Female sex	0.522	0.74 (0.29-1.88)
Hypertension	0.357	1.55 (0.61-3.96)
Diabetes	0.126	2.56 (0.77-8.54)
Dyslipidemia	0.224	1.79 (0.70-4.56)
Complicated phenotype	0.103	2.17 (0.86-5.48)
Splenomegaly	0.154	1.99 (0.77-5.13)
AI cytopenia	0.008	3.54 (1.38-9.08)
Enteropathy	0.050	0.22 (0.05-1.00)
ILD	0.192	2.01 (0.70-5.75)
Bronchiectasis	0.960	0.98 (0.39-2.45)
COPD	0.170	1.94 (0.75-4.98)
AI systemic disease	0.422	1.94 (0.38-9.74)
Recurrent UTI	0.792	0.84 (0.22-3.15)
Antibiotic prophylaxis	0.145	2.11 (0.77-5.76)
Trimethoprim-sulfamethoxazole	0.039	6.51 (1.1-38.7)
Azithromycin	0.422	0.56 (0.13-2.31)
IVIG	0.052	2.47 (0.99-6.13)
maltose-stabilized product	0.644	0.73 (0.19-2.76)
SCIG	0.760	0.86 (0.34-2.19)
Median CVID duration	0.961	1.00 (0.96-1.03)
Median IgG at diagnosis	0.234	0.99 (0.99-1.00)
Median IgA at diagnosis	0.436	1.01 (0.99-1.02)
Median IgM at diagnosis	0.619	1.00 (0.99-1.00)
Median IgG TL	0.825	1.00 (0.99-1.00)

Median IgRT mg/kg/month	0.662	1.00 (0.99-1.00)
Changes in cortico-medullary differentiation and longitudinal bipolar diameters at Ultrasound	0.003	18.34 (2.65-127)
Any other US abnormalities*	0.217	1.80 (0.71-4.55)
ALC median [IQR]	0.302	1.00 (0.99-1.00)
Median T cells %	0.429	1.01 (0.98-1.03)
Median CD4+T cells %	0.855	0.99 (0.94-1.05)
Median CD8+T cells %	0.178	1.03 (0.99-1.08)
Median B cells %	0.017	0.85 (0.75-0.97)
Median Sm B cells %	0.491	0.93 (0.76-1.14)
Median CD21low B cells %	0.916	1.00 (0.95-1.05)
Median Mz B cells %	0.547	0.98 (0.93-1.03)
Median Tr B cells %	0.153	5.08 ⁻⁴ (1.55 ⁻⁸ -16.65)
Median Naive B cells %	0.780	1.00 (0.98-1.03)
Median neutrophil-to-lymphocyte ratio	0.010	1.17 (1.04-1.32)
Median platelet-to-lymphocytes ratio	0.704	1.00 (0.99-1.00)

*mild pyelectasis, nephrolithiasis, cysts.

B cells sub-populations were identified according to EUROclass study: Sm B cells: Switched memory IgD-IgM-CD27+; CD21low B cells: Activated CD21lowCD38low; MZ B cell: Marginal zone IgD+IgM+CD27+; Tr B cells: Transitional CD38++IgMhigh; Naive B cells: Naive IgD+IgM+CD27- [22]. Statistically significant results in bold.

Table S4

	p value	OR [IC95%]
Age	0.089	1.055 [0.99-1.13]
Neutrophil-to-lymphocytes ratio	0.188	1.341 [0.87-2.07]
B cell %	0.263	0.890 [0.73-1.09]
AI cytopenia	0.024	21.391 [1.41-136.80]
Trimethoprim-sulfamethoxazole antibiotic prophylaxis	0.771	1.441 [0.12-16.96]

Statistically significant results in bold. AUC 0.889