Nephrology and Transplantation Department
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Social Security Organization of Islamic Repoblic of Iran

COVID-19 AFTER KIDNEY TRANSPLANTATION

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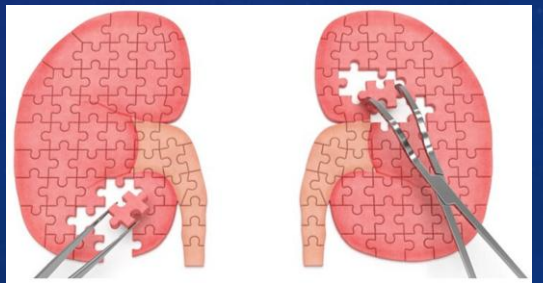

Special Article

Global Transplantation COVID Report March 2020

C. Ahn, H. Amer, D. Anglicheau, N. Ascher, C. Baan, B. Bat-Ireedui, T. Berney, M.G.H. Betjes, S. Bichu, H. Birn, D. Brennan, J. Bromberg, S. Caillard, R. Cannon, M. Cantarovich, A. Chan, Z. Chen, J.R. Chapman, E.H. Cole, N. Cross, F. Durand, H. Egawa, J. Emond, M. Farrero, P. Friend, E.K. Geissler, J. Ha, M. Haberal, M. Henderson, D.A. Hesselink, A. Humar, W. Jassem, J.C. Jeong, B. Kaplan, T. Kee, S.J. Kim, D. Kumar, C. Legendre, K. Man, B. Moulin, E. Muller, R. Munkhbat, L. Od-Erdene, P. Perrin, M. Rela, K. Tanabe, H. Tedesco Silva, K.T. Tinckam, S.G. Tullius, and G. Wong

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AUSTRALIA

Acute transplantation activity has substantively reduced nationally. Living donor kidney transplantation has stopped for the past few days, and deceased donor transplantation, which was being assessed on a case-by-case basis, has also stopped entirely for a period, depending on hospital Intensive Care and Emergency Department capacity. All deceased donors have required COVID testing, but the number of deceased donors has dropped dramatically. We have also slowed down all elective surgery, endoscopies, and bronchoscopies, as well as auxiliary and allied

CANADA, MONTREAL

We have stopped living donor kidney transplantation and are not accepting offers of deceased donor kidneys for recipients >70 years unless they are highly sensitized. All deceased donor kidney offers have been assessed on a case-by-case basis to assess individual risk/benefits for a transplant at this time, but we have now put a hold on transplants. We are planning to reassess that decision in 2 weeks. All donors must be tested for COVID-19 PCR before transplantation. All recipients have been screened

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CHINA, WUHAN

No organ transplant surgery was performed during the COVID-19 epidemic, even living donor organ transplantation between relatives, because we have been concerned about the risk of infection and we did not have sufficient medical resources. We now hope that the work of trans-

DENMARK

poned or canceled. Deceased donor kidney, liver, lung, and heart transplantations are being continued at all Danish centers performing these. Combined kidney-pancreas transplantation has been paused. Organ exchange within the Scandinavian deceased donor exchange program is maintained at present. The number of deceased donors currently appears to be stable. All potential deceased donors are tested for SARS-Co-2, and to date, no donor has tested positive. Scheduled living donor kidney transplants will proceed at some kidney renal transplant centers, while others have canceled these. No new living donor kidney transplantations are scheduled. A planned match

FRANCE, PARIS, KIDNEY

To prevent transplant patients coming to the transplant center, clinics are undertaken through the phone and we have created a file of all 2300 follow-up patients to send them information and new follow-up processes. The role of doctors has been modified to allow each of us to take care of a specific phase of care. Kidney transplantation with deceased and living donors has stopped until further notice. When transplant patients suspected of infection come to the hospital, they are seen in the infectious disease unit, tested by PCR, and then allocated to a COVID-19–positive hospital since ours has been designated COVID negative. In less than a week, 11 patients are positive, 10 tests are awaited, 3 patients are in intensive care, and 2 are in a very bad situation. With COVID-19–positive patients, we stop MMF and mTOR inhibitors. In patients with ARDS, we also stop tacrolimus so patients remain only on steroids. We call each positive patient every day to monitor

GERMANY

Throughout Germany, living kidney donor transplant procedures are mostly being postponed. Cadaveric transplantation activities are being performed as normal for the time being. Testing for COVID-19 will be performed on cadaveric donors, but the results will generally not be used to determine if the organ is transplanted; the testing is for the purpose of recording whether the donor was positive or negative for the virus.

JAPAN

Japan continues life-saving transplantation with informed consent about the risks for heart, lung, and status 1 liver recipients, but it has been recommended to postpone kidney, pancreas, and bowel transplants. We rec-

before the donation to avoid unnecessary exposure. Where testing is available, it is recommended 14 days and 1 day before transplantation in both donors and recipients. Chest CT scans are also recommended before transplantation in donors and recipients.

THE UNITED STATES, MIDWEST

In the past week, a hold has been placed on all living donor transplants initially, anticipating this to continue throughout April but to be reassessed depending on the spread of COVID-19 locally and nationally. Deceased donor transplants are currently ongoing but on a case-by-case basis. New donor and recipient evaluations are on

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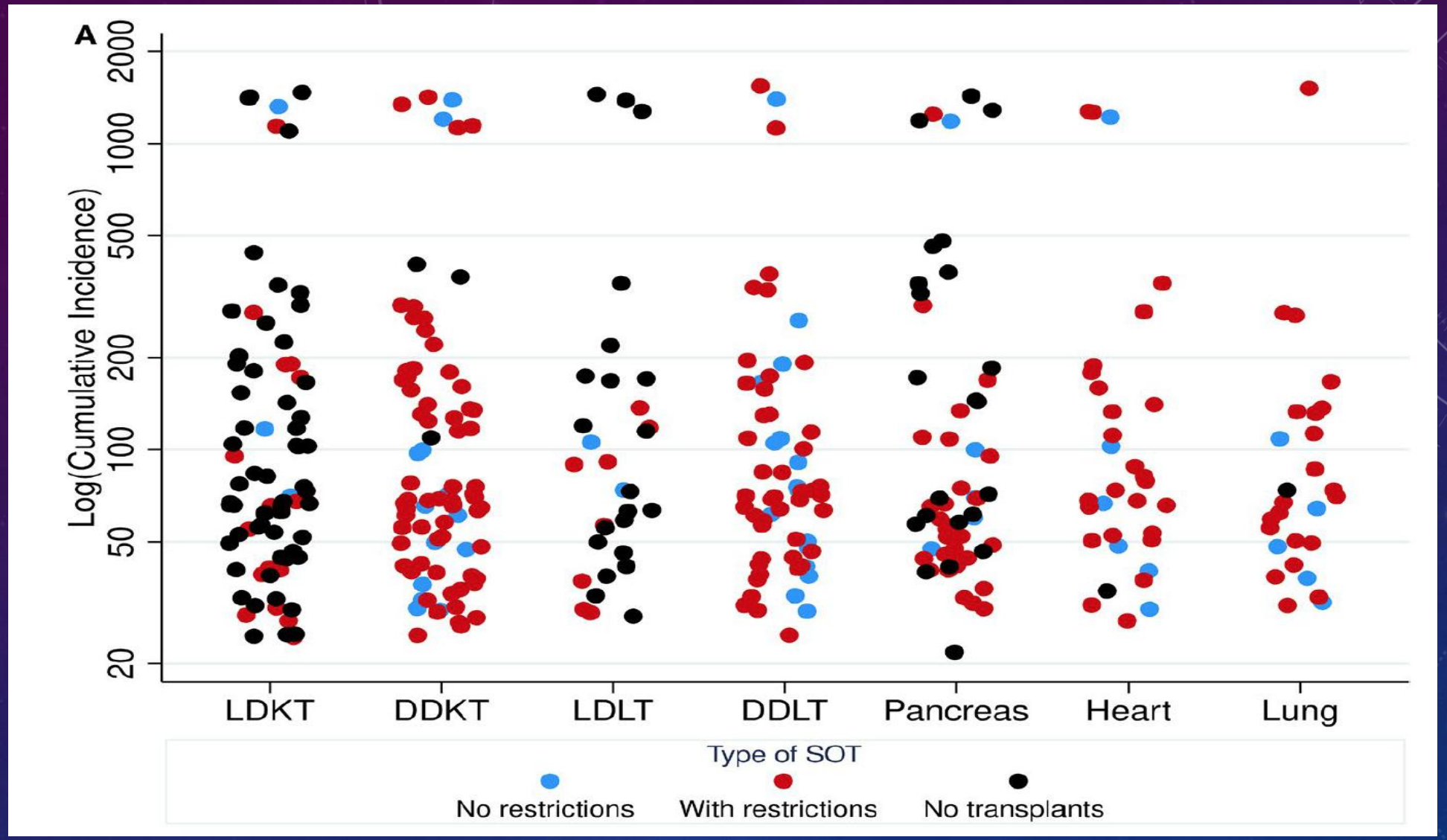

Complete suspension of live donor kidney transplantation was reported by 71.8%

Restrictions to deceased donor kidney transplantation were reported by 84.0%

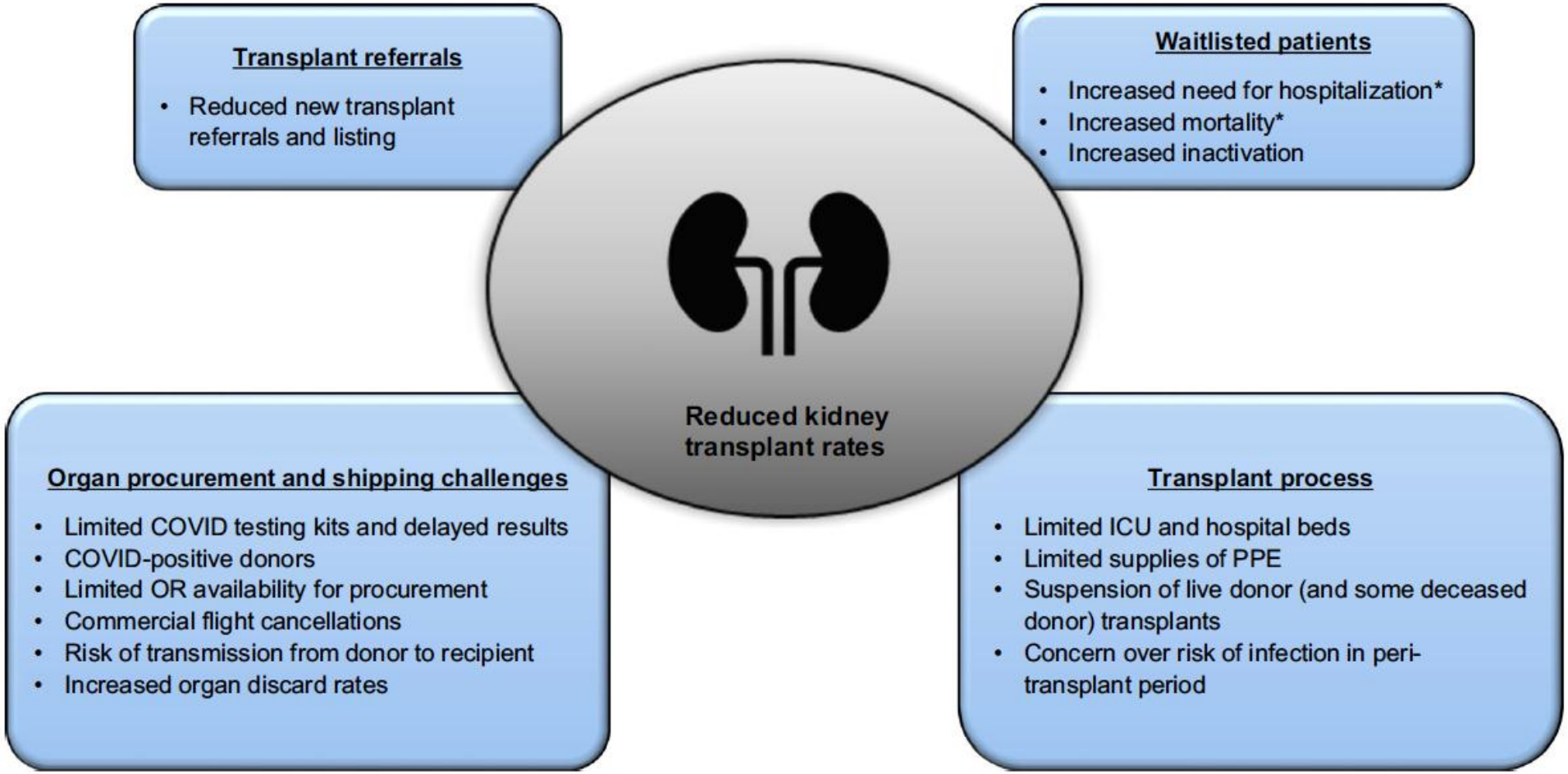

Figure 2 Factors affecting kidney transplant rates during the COVID-19 pandemic. ICU: intensive care unit; PPE: personal protective equipment. *Due to COVID-19 infection.

Table 2 Agreed statements for kidney transplant practice during COVID-19 pandemic

Domain	Statement	Agreement (%)
1. Kidney transplantation	**S1.1** During COVID-19 pandemic, live donor transplantation should be delayed, unless urgent conditions apply	98
	S1.2 During COVID-19 pandemic, deceased donor renal transplantation should be performed only if COVID-19 free pathways can be ensured	96
2. Screening for occult COVID-19 infection	**S2.1** During COVID-19 pandemic, asymptomatic patients should be screened by nasopharyngeal swabs before proceeding to renal transplantation	94
	S2.2 During COVID-19 pandemic, asymptomatic patients with acute rejection should be screened by nasopharyngeal swabs before administration of anti-rejection treatments	83
4. Other pharmacological agents	**S4.1** The use of Tocilizumab can be considered in kidney transplant recipients with severe pneumonia caused by SARS-CoV2 infection	98
	S4.2 Steroid boluses can be used in renal transplant recipients with severe pneumonia caused by SARS-CoV2 infection who need intensive care assistance	91

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ORIGINAL ARTICLE

AJT

Early impact of COVID-19 on transplant center practices and policies in the United States

[1]Department of Surgery, Johns Hopkins

Brian J. Boyarsky[1] | Teresa Po-Yu Chiang[1] | William A. Werbel[2] | Christine M. Durand[2] | Robin K. Avery[2] | Samantha N. Getsin[1] | Kyle R. Jackson[1] | Amber B. Kernodle[1] | Sarah E. Van Pilsum Rasmussen[2] | Allan B. Massie[1,3] | Dorry L. Segev[1,3] | Jacqueline M. Garonzik-Wang[1]

Changes in OP monitoring	n = 63 n (%)
Stopped visits	5 (7.9)
Limited visits	62 (98.4)
Limited laboratory draws	13 (20.6)
Telemedicine	61 (96.8)

Am J Transplant. 2020;20:1809–1818.

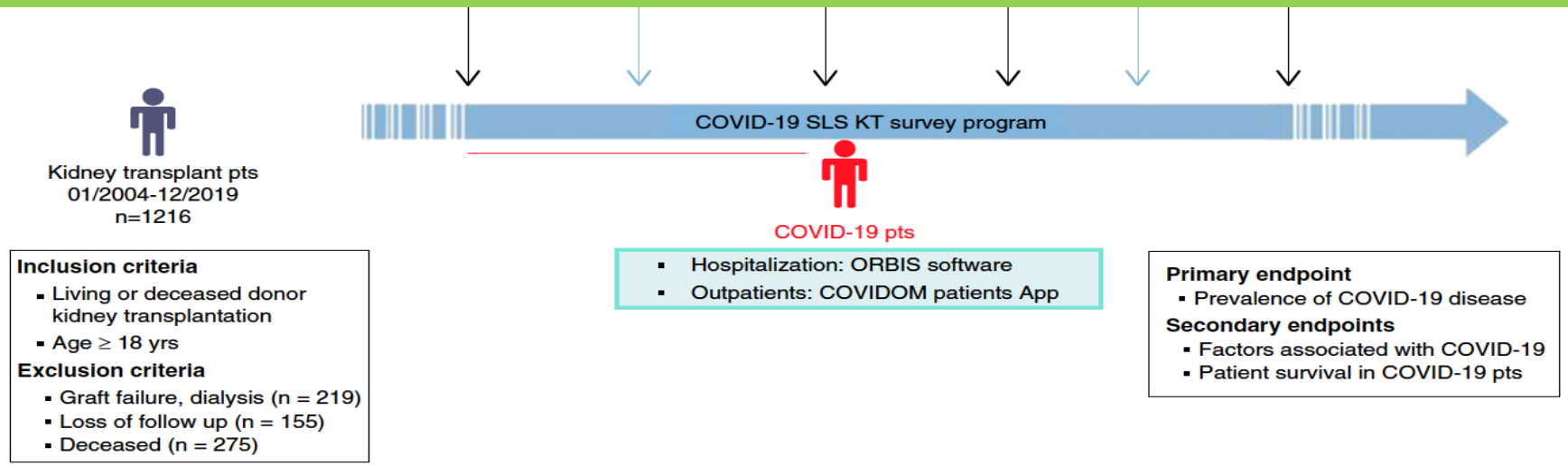
CLINICAL RESEARCH www.jasn.org

JASN 31: 2413–2423, 2020

COVID-19 Infection in Kidney Transplant Recipients: Disease Incidence and Clinical Outcomes

Michelle Elias,[1] Daniele Pievani,[1] Christine Randoux,[2] Kevin Louis,[3] Blandine Denis,[4] Alexandra Delion,[1] Océane Le Goff,[1] Corinne Antoine,[1] Clarisse Greze,[2] Evangeline Pillebout,[1] Imad Abboud,[1] Denis Glotz,[1,3] Eric Daugas,[2] and

Patients with kidney transplants display a high risk of mortality and comorbidities such as obesity, diabetes, asthma, and chronic pulmonary disease were associated with higher risk of developing COVID-19 disease



available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Case Series of the Month

Clinical Course, Imaging Features, and Outcomes of COVID-19 in Kidney Transplant Recipients

Alireza Abrishami [a,*], *Shiva Samavat* [b,c], *Behdad Behnam* [d], *Mehran Arab-Ahmadi* [e], *Mohsen Nafar* [b,c], *Morteza Sanei Taheri* [f]

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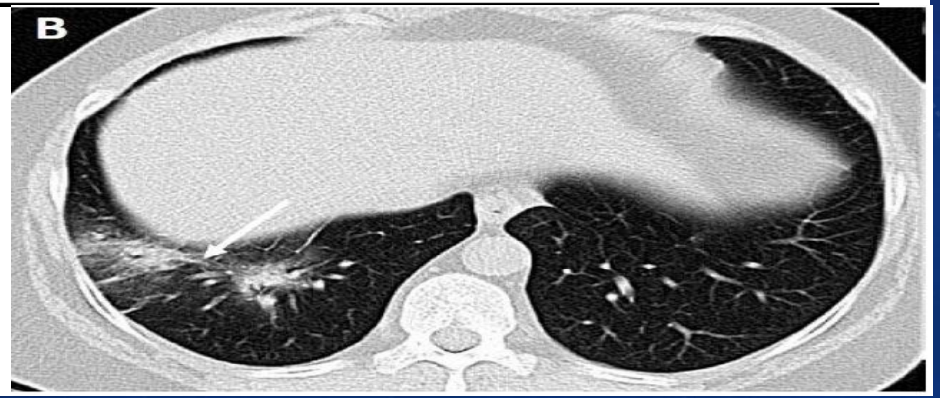
Table 3 – Frequency of chest computed tomography scan features in the 12 patients.

Parameter		Patients, *n* (%)
Lung involvement	Bilateral	8 (66.7)
	Unilateral	4 (33.3)
Lobar anatomy	Right upper lobe	9 (75)
	Right middle lobe	10 (83.3)
	Right lower lobe	11 (91.7)
	Left upper lobe	9 (75)
	Left lower lobe	11 (91.7)
Zonal anatomy	Upper	1 (8.3)
	Middle	3 (25)
	Lower	3 (25)
	Diffuse	5 (41.7)
Axial distribution	Peripheral	4 (33.3)
	Peripheral + central	8 (66.7)
Segmental distribution	Posterior	8 (66.7)
	Anterior	2 (16.7)
	Diffuse	2 (16.7)
Computed tomography features	Ground glass opacity	12 (100)
	Consolidation	9 (75)
	Interlobular septal thickening	5 (41.7)
	Dilated small vessels in the lesion	9 (75)
	Crazy-paving	2 (16.7)
	Pleural effusion	2 (16.7)
	Pericardial effusion	1 (8.3)

Table 4 – Chest computed tomography scores for each lobe and total lungs.

Lobar anatomy	Ground glass opacity	Consolidation	Total score
Right upper lobe	1.5	0.16	1.66
Right middle lobe	1.66	0	1.66
Right lower lobe	1.41	0.91	2.32
Left upper lobe	1.41	0.08	1.49
Left lower lobe	1.58	0.75	2.33
Total lungs	7.58	1.9	9.46



Original Clinical Science—General

Clinical Profile and Outcome of COVID-19 in 250 Kidney Transplant Recipients: A Multicenter Cohort Study From India

Vivek B. Kute, MD,[1] Anil K. Bhalla, MD,[2] Sandeep Guleria, MS,[3] Deepak S. Ray, MD,[4] Madan M. Bahadur, MD,[5] Ashay Shingare, MD,[5] Umapati Hegde, MD,[6] Sishir Gang, MD,[6] Sreebhushan Raju, MD,[7] Himanshu V. Patel, MD,[1] Siddharth Jain, MD,[8] Suraj Godara, MD,[9] Pranjal Modi, MS,[10] Manoj Gumber, MD,[11] Divyesh P. Engineer, MD,[1] Sonal Dalal, MD,[12] Prakash Darji, MD,[13] Manish Balwani, MD,[14] Ansy H. Patel, MBBS,[15] and Vineet V. Mishra, MS[16]

(*Transplantation* 2021;105: 851–860).

Risk factors for mortality included

older age; dyspnea; severe disease; obesity; allograft dysfunction before COVID-19 infection; acute kidney injury; higher levels of inflammatory markers including C-reactive protein, interleukin-6 level, and procalcitonin; chest X-ray abnormality, and intensive care unit/ventilator requirements.

ARTICLE IN PRESS

www.kidney-international.org

clinical investigation

COVID-19 infection in kidney transplant recipients at the epicenter of pandemics

Yorg Azzi[1,2], Michael Parides[3], Omar Alani[2], Pablo Loarte-Campos[1,2], Rachel Bartash[4], Stefanie Forest[5], Adriana Colovai[2], Maria Ajaimy[1,2], Luz Liriano-Ward[1,2], Cindy Pynadath[1,2], Jay Graham[2,3], Marie Le[2,3], Stuart Greenstein[2,3], Juan Rocca[2,3], Milan Kinkhabwala[2,3] and Enver Akalin[1,2]

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Older age, receipt of deceased donor transplantation, lack of influenza vaccination in the previous year and higher serum interleukine-6 levels were associated with mortality.

Characteristics	Total patients (*N* = 229)	COVID-19 RT-PCR–positive (*N* = 132)	SARS-CoV-2 IgG antibody–positive (*N* = 97)	*P* value	Survivors (*N* = 182)	Nonsurvivors (*N* = 47)	*P* value
Sex				0.84			
Male	141 (62)	82 (62)	59 (61)		113 (62)	28 (60)	0.75
Female	88 (38)	50 (38)	38 (39)		69 (38)	19 (40)	
Age, yr	59 [49–68]	62.5 [51–71]	57 [46–65]	0.0024	58 [46–66]	70 [58–74]	< 0.001
Race				0.87			0.53
Hispanic	125 (55)	74 (56)	51 (53)		74 (56)	51 (53)	
African American	74 (32)	41 (31)	33 (34)		41 (31)	33 (34)	
Other	30 (13)	17 (13)	13 (13)		17 (13)	13 (13)	
Type of transplant				0.039			
Deceased donor	165 (73)	101 (77)	64 (66)		124 (69)	41 (89)	0.0058
Living donor	61 (27)	28 (21)	33 (34)		56 (31)	5 (11)	
Time after transplantation, mo	58.2 [25.4–127.6]	60.8 [20–128.5]	57.7 [28.7–124.6]	0.9	57.7 [27.3–123.7]	65.2 [16.3–134.1]	0.82
Transplantation at <6 mo	13 (7)	9 (9)	4 (4)	0.49	10 (6)	3 (6)	0.21
Transplantation at <12 mo	18 (9)	11 (11)	7 (8)	0.97	13 (7)	5 (11)	0.43
Etiology of ESRD				0.005			
Diabetes mellitus	106 (47)	72 (55)	34 (35)		73 (40)	33 (70)	0.0065
Hypertension	49 (22)	21 (16)	28 (29)		45 (25)	4 (9)	
Glomerulonephritis	52 (23)	23 (18)	29 (30)		44 (24)	8 (17)	
Polycystic kidney disease	9 (4)	2 (2)	7 (5)		8 (4)	1 (2)	
Others	12 (5)	8 (6)	4 (4)		11 (6)	1 (2)	
Body mass index, kg/m^2	28.5 [24.2–32.6]	28.7 [23.7–32.5]	28.1 [24.7–32.6]	0.76	28.3 [24.2–32.3]	29.1 [23.7–34.3]	0.66
History of smoking	81 (36)	48 (37)	33 (34)	0.68	64 (35)	17 (36)	0.92
Influenza vaccination	193 (89)	102 (86)	91 (94)	0.055	162 (93)	31 (66)	0.0015
Comorbidities							
Hypertension	224 (98)	128 (98)	96 (99)	0.47	178 (98)	46 (98)	0.83
Diabetes mellitus	140 (61)	89 (68)	51 (53)	0.019	104 (58)	36 (77)	0.016
Heart disease	49 (22)	28 (21)	21 (22)	0.96	38 (21)	11 (23)	0.72
Lung disease	16 (7)	11 (8)	5 (5)	0.34	10 (6)	6 (13)	0.083
Cancer	23 (10)	12 (9)	11 (11)	0.59	18 (10)	5 (11)	0.89
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use	60 (26)	33 (25)	27 (28)	0.65	47 (26)	13 (28)	0.81
Statin use	143 (63)	84 (64)	59 (61)	0.61	113 (62)	30 (64)	0.86
Baseline serum creatinine, mg/dl	1.4 [1.0–1.7]	1.4 [1.1–1.8]	1.2 [1.0–1.5]	0.0048	1.3 [1.0–1.6]	1.5 [1.2–1.8]	0.032

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Table 2 | Laboratory values and inflammatory markers on admission of the patients admitted to Montefiore Medical Center

Laboratory values and inflammatory markers on admission	Total patients (*N* = 79)	Survivors (*N* = 51)	Nonsurvivors (*N* = 28)	*P* value
Hemoglobin, g/dl	12.1 [10.6–13.2]	12.2 [10.6–13.3]	11.8 [11.1–13]	0.94
WBC count, k/μl	6.2 [4.4–8.0]	5.8 [4.1–7.7]	6.4 [5.4–8.1]	0.23
WBC count <4 k/μl	12 (15)	11 (22)	1 (4)	
Lymphocytes, k/μl	0.6 [0.4–0.8]	0.6 [0.4–0.8]	0.7 [0.4–0.8]	0.96
Lymphocyte count <1 k/μl	67 (85)	42 (82)	25 (89)	
Platelets, k/μl	178 [132–240]	189 [132–241]	162 [118.5–205.5]	0.22
Platelets count <150 k/μl	30 (38)	18 (35)	12 (43)	
CD3 cell count, cells/μl	319 [205–552]	390 [226.5–574]	243 [158–529]	0.12
CD3 count <706 cells/μl	54 (68)	33 (65)	21 (75)	
CD4 cell count, cells/μl	147 [88–304]	178 [117–305]	120 [74–252]	0.085
CD4 count <344 cells/μl	52 (66)	31 (61)	21 (75)	
CD8 cell count, cells/μl	126 [83–272]	147 [87.5–263]	123 [71–272]	0.4
CD8 count <104 cells/μl	22 (28)	13 (26)	9 (32)	
CRP, mg/dl	9.9 [4.9–16.2]	7.2 [4.6–14.8]	11.3 [5.7–18.1]	0.25
CRP >10 mg/dl	38 (48)	23 (45)	15 (54)	
Procalcitonin, ng/ml	0.3 [0.1–1.7]	0.2 [0.1–1.6]	0.4 [0.2–2.9]	0.065
Procalcitonin >0.2 ng/ml	41 (52)	22 (43)	19 (68)	
Ferritin, ng/ml	1345 [681–2397]	1516 [713–3179]	1029 [629–1939]	0.16
Ferritin >900 ng/ml	50 (63)	35 (69)	15 (54)	
D-dimer, μg/ml	1.7 [0.8–3.3]	1.8 [0.7–3.5]	1.7 [1.1–2.2]	0.99
D-dimer >0.5 μg/ml	66 (84)	42 (82)	24 (86)	
D-dimer >3 μg/ml	20 (25)	15 (29)	5 (18)	
IL-6, pg/ml	54 [25–154]	47 [26–98]	101 [22–335]	0.036
IL-6 >60 pg/ml	32 (41)	15 (29)	17 (61)	
LDH, U/l	356 [274–414]	350 [271–406]	364 [286.5–433]	0.42
LDH >1.5 times upper limit of normal	53 (67)	33 (65)	20 (71)	
Creatine kinase, U/l	103 [56–204]	91 [55–143]	140 [68–362]	0.095
Creatine kinase >200 U/l	19 (24)	8 (16)	11 (39)	
Fibrinogen, mg/dl	605.5 [504.5–728.5]	606 [511–754]	605 [459–666]	0.46
Fibrinogen >500 mg/dl	49 (62)	33 (65)	16 (57)	
Pro-BNP, pg/ml	1785 [740–4987]	1278 [450–3234]	2380 [1152–9342]	0.031
Pro-BNP >900 pg/ml	43 (54)	24 (47)	29 (68)	
Serum creatinine, mg/dl	2.2 [1.5–3.0]	1.9 [1.3–3.0]	2.3 [1.7–2.9]	0.33

Table 4 | Clinical outcomes of the hospitalized patients

Clinical outcomes	Total patients ($N = 79$)	Survivors ($N = 51$)	Nonsurvivors ($N = 28$)	P value
Intubation	28 (35)	5 (10)	23 (82)	<0.001
Acute kidney injury requiring renal replacement therapy	18 (23)	9 (18)	9 (32)	0.15
Bacteremia	7 (9)	4 (8)	3 (6)	0.67
Urinary tract infection	9 (11)	5 (10)	4 (14)	0.55
Bacterial pneumonia	4 (5)	0 (0)	4 (14)	0.014
Fungal infection	4 (5)	1 (2)	3 (11)	0.12
Cytomegalovirus viremia	12 (15)	8 (16)	4 (14)	0.87
Deep venous thrombosis	10 (13)	6 (12)	4 (14)	0.75
Cerebrovascular accident	3 (4)	1 (2)	2 (7)	0.29

Data are *n* (%) unless otherwise noted.

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Check for updates

WILEY

ORIGINAL REPORT

Low rate of COVID-19 pneumonia in kidney transplant recipients–A battle between infection and immune response?

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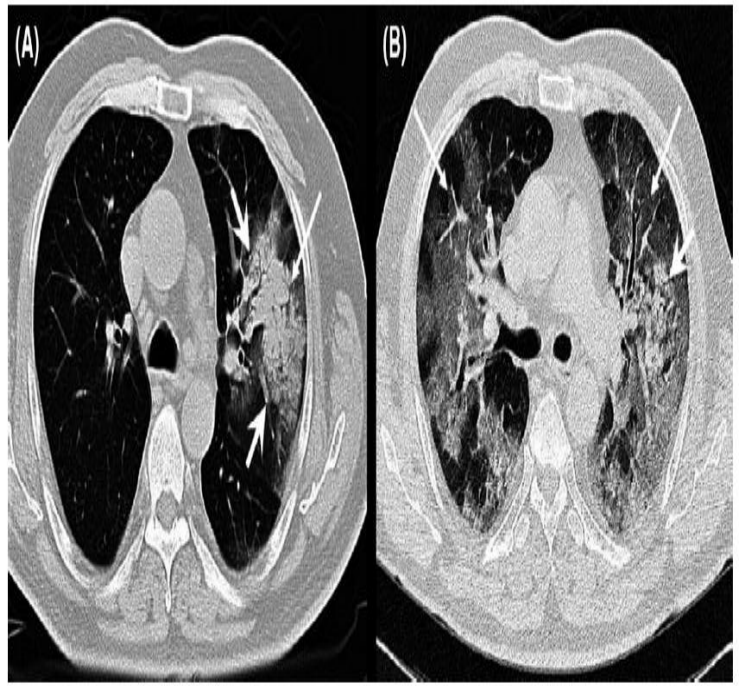

FIGURE 1 Fifty nine-year-old man with dry cough, fever, and history of three years kidney transplantation. A, CT images obtained on the day of admission show unilateral consolidation (*wide arrows*) with inside air bronchogram and ground-glass (*long arrows*) opacities in left upper lobe. B, Follow-up CT images (4 d later) show extensive bilateral ground-glass and consolidation opacities. Patient passed away after 17 d of hospitalization

TABLE 4 Treatments and clinical outcome

Characteristics	All patients (N = 19)	Hospital course		*P* value
		Death (N = 9)	Alive (N = 10)	
CNI dose reduction (%)	13 (68.4)	5 (55.6)	8 (80.0)	.25
CNI discontinuation (%)	11 (57.9)	9 (100.0)	2 (20.0)	.0001
Oseltamivir (%)	13 (68.4)	7 (77.8)	6 (60.0)	.40
Hydroxychloroquine (%)	18 (94.7)	8 (88.9)	10 (100.0)	.28
Lopinavir/ritonavir (%)	15 (78.9)	9 (100.0)	6 (60.0)	.03
Ribavirin (%)	15 (78.9)	9 (100.0)	6 (60.0)	.03
IVIG (%)	14 (73.7)	9 (100.0)	5 (50.0)	.01
Transplant to admission (mo), mean, SD	115.6 (70.3)	105.3 (75.4)	124.8 (68.2)	.55
Rejection To admission (mo), mean, SD	1.68 (5.6)	0.89 (1.7)	2.4 (7.6)	.50
Symptom to admission (d), mean, SD	4.21 (3.7)	4.8 (4.8)	3.7 (2.4)	1.0
Total hospital stay (days), mean, SD	13.0 (9.0)	17.1 (7.7)	9.3 (8.8)	.008

Abbreviations: CNI, calcineurin inhibitor; IVIG, intravenous immunoglobulin.

History of acute rejection during the past 12 months, diabetes, higher N/L ratio, lower platelet count, elevated N/L x CRP, higher levels of LDH, positive D-dimer, higher troponin, and prolonged PT were associated with mortality. Treatment with cyclosporine was associated with better clinical outcome.

Clinical Kidney Journal, 2021, vol. 14, Suppl 1, i21–i29

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CKJ Review

CKJ REVIEW

Kidney transplantation and COVID-19 renal and patient prognosis

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Although the number of renal transplant patients diagnosed with COVID-19 was higher than in the general population, the lower threshold for testing may have contributed to its better identification while many oligosymptomatic individuals in the general population were not tested

AKI IN RENAL TRANSPLANT PATIENTS WITH COVID-19

- The main risk factors associated with AKI are advanced age, male gender, severity of respiratory impairment, mechanical ventilation, pre-existing chronic renal failure, coinfection with other organisms and systemic inflammatory response.

Table 2. Incidence of AKI and need for RRT in hospitalized kidney transplant patients and in the general population with COVID-19 infection

	No. of patients	% AKI	% RRT
Kidney transplantation			
Marinaki *et al.* [33]	345	44.0	9.9
Favá *et al.* [12]	104	45.0	Not reported
Cravedi *et al.* [11]	144	52.0	Not reported
Elias *et al.* [14]	66	42.0	11.0
Weighted average	659	45.7	10.1
General population			
Chan *et al.* [25]	3993	46.0	8.7
Fisher *et al.* [23]	3345	56.9	4.9
Richardson *et al.* [26]	2351	22.2	3.2
Ng *et al.* [24]	9657	39.9	6.6
Weighted average	19 346	41.9	6.3

Incidence of AKI in studies including >1000 patients from the general population and studies including >50 kidney transplant patients. The incidence of AKI and the need for RRT was summarized as the weighted average.

Despite the fact that AKI incidence was higher in kidney transplant patients (27.5% versus 13.3%), as well as RRT (15.4% versus 3.3%), the mortality rate was similar between groups.

AKI AND HISTOLOGY

- Acute tubular necrosis is the main finding in patients with AKI.
- However, a high proportion of patients display proteinuria (44–66%) and micro hematuria (27–42%), suggesting that, in addition to classical factors leading to AKI, a direct cytopathic effect of the virus may contribute to renal damage .
- Angiotensin-converting enzyme 2 receptor is highly expressed in kidney podocytes and tubular cells, and viral particles have been observed in electron microscopy studies .
- In the vast majority of patients, hematuria and proteinuria rapidly disappeared; however, in patients with severe proteinuria, collapsing glomerulopathy , minimal change disease, thrombotic microangiopathy and pauci-immune crescentic glomerulonephritis have been described.
- In kidney transplant patients there is scarce information on histological findings. In patients with AKI, apart from acute tubular injury, minimal change disease , cortical necrosis and collapsing glomerulopathy have also been described. In addition, very few cases of T cell– or antibody-mediated rejection have been described, raising the question of whether COVID-19 infection may enhance the alloimmune response

ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN RENAL TRANSPLANT PATIENTS WITH COVID-19

- A trend for an increased risk of ARDS was recorded in patients on tacrolimus {OR 2.77 [95% confidence interval(CI) 0.91–8.9]}, whereas a protective trend towards the risk of ARDS was a transplant vintage >10 years [OR 0.37 [95% CI 0.12–1.1]) and the presence of GI symptoms at disease onset.
- During the first wave of the pandemic, the most widely used agents with presumed antiviral activity were hydroxychloroquine, antibiotics (azithromycin) and protease inhibitors, showing no benefit for prevention or treatment in both the general and SOT populations and increasing the risk of interactions with other drugs .
- In the general population, remdesivir has been shown to decrease the in-hospital stay, but with no effect on the mortality rate. Importantly, its use is contraindicated in patients with an estimated glomerular filtration rate (eGFR)<30mL/min/1.73 m2 and there are no studies on the use of remdesivir in the transplanted population.

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KI REPORTS
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CLINICAL RESEARCH

Use and Safety of Remdesivir in Kidney Transplant Recipients With COVID-19

Anna Buxeda[1,27], Carlos Arias-Cabrales[1,27], María José Pérez-Sáez[1], Judit Cacho[2],

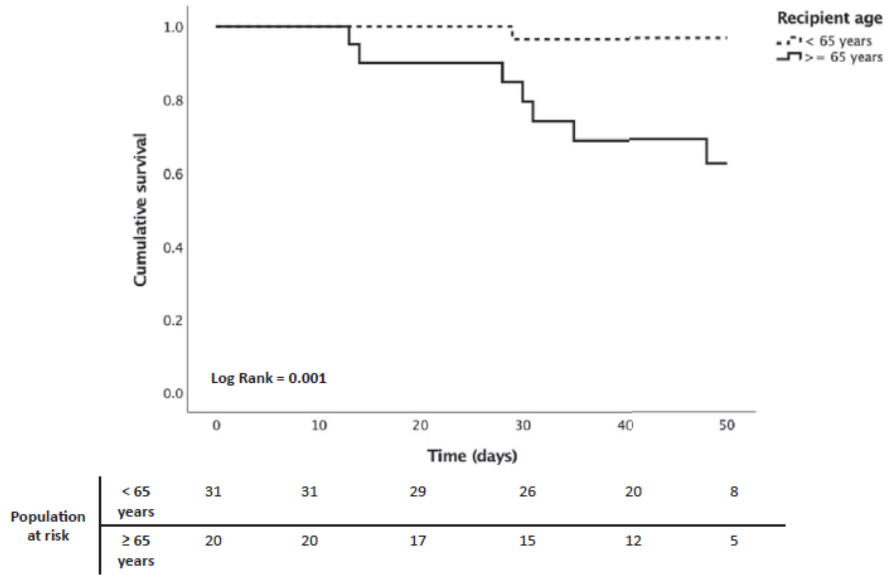

Figure 3. Patient survival according to age in kidney transplant recipient with COVID-19 treated with remdesivir. Kaplan-Meier curve shows mortality rates of kidney transplantation patients with COVID-19 according to recipient age (<65 years vs. ≥65 years). The median time between the onset of symptoms and the end of follow-up was 49 days (interquartile range, 34–68 days).

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- Non-randomized studies have shown that treatment with tocilizumab in critically ill patients may offer some benefit in both the general and kidney transplant population . However, prospective randomized studies in hospitalized patients with COVID-19 pneumonia showed that although tocilizumab may reduce the likelihood of progression to mechanical ventilation, it did not improve survival .

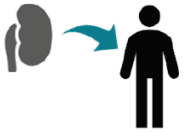
- The large RECOVERY trial showed that dexamethasone decreases 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone, but not among those receiving no respiratory support.

- An approach like that of other serious viral infections (mycophenolate withdrawal and calcineurin inhibitor reduction) seems a safe option.

Informing the risk of kidney transplantation versus remaining on the wait list in the COVID-19 era

STUDY POPULATION

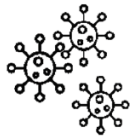
299 Patients on the wait list



237 Recent transplant recipients

897 Patients not on wait list

METHODS



All polymerase chain reaction (PRC) positive COVID-19 cases identified

Seroprevalence data collated

Clinical characteristics and outcomes collected

FINDINGS

Wait listed patients:
Higher infection rate 17.7 vs. 6.8%
(p = 0.001)

Transplant recipients:
Higher mortality rate 2.5 vs. 2.0%
(p = 0.015)

Relative risk of death following a diagnosis of COVID-19 higher in transplant recipients:
HR 3.36 (1.19-9.50, p=0.022)

CONCLUSION:
Although COVID-19 infection was more common in the wait list patients, a higher COVID-19 associated mortality rate was seen in transplant recipients, resulting in comparable overall mortality rates.

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Clarke, 2021

COVID-19–related Mortality During the First 60 Days After Kidney Transplantation

EUROPEAN UROLOGY 78 (2020) 637–643

[a]Department of Nephrology, Hospital del Mar, Barcelona, Spain

Julio Pascual [a,], Edoardo Melilli [b], Carlos Jiménez-Martín [c], Esther González-Monte [d], Sofía Zárraga [e],*

Table 1 – Characteristics of 24 patients who suffered from COVID-19 during the first 60 d after kidney transplantation.

Variable	Alive ($n = 13$)	Dead ($n = 11$)	p value
Male, n (%)	6 (46.2)	5 (45.5)	0.97
Median age, yr (range)	61.1 (40–74)	69.6 (60–75)	0.006
Age ≥65 yr, n (%)	4 (30.8)	8 (72.7)	0.04
Hypertension, n (%)	12 (92.3)	10 (90.9)	1
Diabetes, n (%)	8 (66,7)	4 (36.4)	0.15
Deceased donor, n (%)	13 (100)	10 (91)	0,46
Delayed graft function n (%)	5 (38.5)	7 (63.6)	0.41
Acute rejection, n (%)	2 (15.4)	0 (0)	0.48
Median time from KT to COVID-19 Dx, d (range)	39 (15–59)	28.8 (8–56)	0.07
Baseline immunosuppressive treatment, n (%)			
Prednisone	13 (100)	11 (100)	1
Tacrolimus	13 (100)	11 (100)	1
Mycophenolate	12 (92,3)	9 (81.8)	0.58
mTOR inhibitors	0 (0)	2 (18.2)	0.2
Fever, n (%)	9 (69.2)	6 (54.5)	0.67
Cough, expectoration, and/or rhinorrhea, n (%)	6 (46.2)	8 (72.7)	0.24
Dyspnea, n (%)	6 (46.2)	8 (72.7)	0.24
Pneumonia, n (%)	12 (92.3)	10 (90.9)	1
Digestive symptoms, n (%)	1 (7.7)	2 (18.2)	0.58
Lymphopenia, n (%)	13 (100)	11 (100)	1
Hospitalization, n (%)	13 (100)	11 (100)	1
Renal failure, n (%)	6 (46.2)	7 (63.6)	0.26
Ventilator support, n (%)	2 (15.4)	7 (77.8)	0.007
Intensive care unit admission, n (%)	2 (15.4)	2 (18.2)	1
COVID-19 treatment, n (%)			
Hydroxychloroquine	12 (92.3)	10 (90.9)	1
Glucocorticoids	3 (25)	9 (81.8)	0.006
Lopinavir/ritonavir	4 (30.8)	4 (36.4)	1
Tocilizumab	5 (38.5)	3 (27.3)	0.68
Median time from admission to death or recovery, d (range)	23 (4–48)	13.7 (6–36)	0.08

KT = kidney transplantation; Dx = diagnosis.

OUTCOMES IN KIDNEY RECIPIENTS VERSUS PATIENTS ON THE WAITING LIST

- Kidney transplant recipients experience a high mortality rate compared with the general population, especially during the very early post-transplant period.
- Despite the fact that some studies report more favorable outcomes in patients with a kidney transplant than in patients on the kidney waiting list, the higher mortality described in the very early post-transplant period would advise against performing a kidney transplant in areas where the spread of infection is high, especially in recipients >60 years of age.

Oto *et al. BMC Nephrology* (2021) 22:100
https://doi.org/10.1186/s12882-021-02299-w

BMC Nephrology

RESEARCH ARTICLE Open Access

Predicting the outcome of COVID-19 infection in kidney transplant recipients

Ozgur Akin Oto[1*], Savas Ozturk[2], Kenan Turgutalp[3], Mustafa Arici[4], Nadir Alpay[5], Ozgur Merhametsiz[6], Savas Sipahi[7], Melike Betul Ogutmen[8], Berna Yelken[9], Mehmet Riza Altiparmak[10], Numan Gorgulu[11], Erhan Tatar[12], Oktay Ozka Demir[6], Ali Riza Oda

Table 4 Univariate and multivariate logistic regression analysis of the parameters related to mortality

	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (95% CI)	***p*-value**	**Odds Ratio (95% CI)**	***p*-value**
Age > 60 years	2.743 (0.811–9.274)	0.104		
Male gender	0.500 (0.161–1.556)	0.231		
Presence of diabetes mellitus	1.371 (0.390–4.822)	0.622		
Presence of hypertension	1.152 (0.295–4.506)	0.838		
Presence of ischemic heart disease	3.702 (1.047–13.083)	0.042	**4.129 (1.104–15.442)**	**0.035**
Initial lymphocyte count	0.999 (0.998–1.000)	0.222		
Initial serum ferritin level	1.000 (1.000–1.001)	0.373		
Initial serum albumin level	0.492 (0.178–1.360)	0.172		
Initial serum creatinine level	1.520 (1.016–2.274)	0.042	**1.681 (1.083–2.608)**	**0.021**

Abbreviations: CI confidence interval

Nephron

Clinical Practice: Case Report

Nephron 2021;145:192–198
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Published online: December 8, 2020

COVID-19 in Renal Transplant Recipients: Case Series and a Brief Review of Current Evidence

Supportive treatment could be sufficient for the management or to be tried first.

Short hospital stay with self-isolation on discharge reduces the burden on the health service and protect the staff and the public.

Patient	Chest X-ray	Management	Length of hospital stay	Outcome
1	Clear	Discontinue MMF + supportive treatment	2 days	Discharged, asymptomatic
2	Bilateral patchy consolidation	Discontinue MMF + supportive treatment	2 days	Discharged, asymptomatic
3	Clear	Discontinue MMF + self-isolation at home	2 h	Stayed at home, full recovery
4	Bilateral patchy consolidation	Discontinue MMF + supportive treatment	7 days	Discharged, asymptomatic
5	Bilateral patchy consolidation	Discontinue MMF + mechanical ventilation + CVVH	21 days	Discharged, asymptomatic
6	Bilateral patchy consolidation	Discontinue MMF + supportive treatment	4 days	Discharged, asymptomatic
7	na	Discontinue MMF + supportive treatment	4 days	Discharged, asymptomatic
8	Bilateral patchy consolidation	Discontinue Aza + oxygen therapy	2 days	Discharged, still has a cough

na, not applicable; MMF, mycophenolate mofetil; Aza, azathioprine; ITU, intensive therapy unit; CVVH, continuous veno-venous hemofiltration.

NATURE REVIEWS | NEPHROLOGY
VOLUME 16 | JULY 2020

COMMENT

Check for updates

COVID-19: implications for immunosuppression in kidney disease and transplantation

Andreas Kronbichler[1] ✉, Philipp Gauckler[1], Martin Windpessl[2,3], Jae Il Shin[4,5,6], Vivekanand Jha[7,8,9], Brad H. Rovin[10] and Rainer Oberbauer[11]

Non-immunosuppressive derivatives of ciclosporin decreased the expression of the N protein of human coronavirus 229E; this multifunctional protein is required for viral replication. Based on these in vitro data, it might be speculated that ciclosporin could be used as the preferred CNI during the COVID-19 pandemic.

No data are available on whether tacrolimus derivatives or metabolites exhibit similar in vitro activity.

IMPACT ON INDUCTION IMMUNOSUPPRESSION STRATEGIES

- Akalin et al reported infected KTRs had lower CD3, CD4, and CD8 cell counts and more rapid clinical progression than persons with COVID-19 in the general population.
- Although no definite recommendations can be provided, in case induction immunosuppression is indicated, it seems reasonable to consider non–T-cell depleting agents (basiliximab or other IL2 receptor antagonists), especially in low immunologic risk kidney transplant patients wherein the risk of acute rejection is lower.

(*Transplantation Direct* 2020;6: e582; doi: 10.1097/TXD.0000000000001031. Published online 15 July, 2020.)

IMMUNOSUPPRESSION

- Thymoglobulin, a T cell depleting agent, it makes sense to speculate that it will increase the rate and the severity of COVID-19 infections.
- Its advantage is that it decreases the rate of rejection and allows the use of lower CNI levels. If the recipient is of higher immunological risk, the importance of thymoglobulin induction rises.
- Therefore, should we avoid thymoglobulin and move to non-depleting regimens, e.g., Basiliximab or avoid induction at all? This will increase the risk of acute rejection, and if rejection occurs this could result in a whole anti-rejection treatment protocol accumulating to a much larger dose of immunosuppression.
- Perhaps there is logic in using induction for higher immunological risk recipients. Nevertheless, at this time, due to lack of evidence-based reports, we believe institutions should continue their induction practices as before.

World J Transplant 2020 September 18; 10(9): 223-229

Transplant International

REVIEW ARTICLE

The impact of COVID-19 on kidney transplantation and the kidney transplant recipient – One year into the pandemic

Pascale Khairallah[1], Nidhi Aggarwal[1,2], Ahmed A. Awan[1], Chandan Vangala[1,2], Medha Airy[1], Jenny S. Pan[1,2], Bhamidipati V. R. Murthy[1], Wolfgang C. Winkelmayer[1] & Venkat Ramanathan[1,2]

Transplant International 2021;

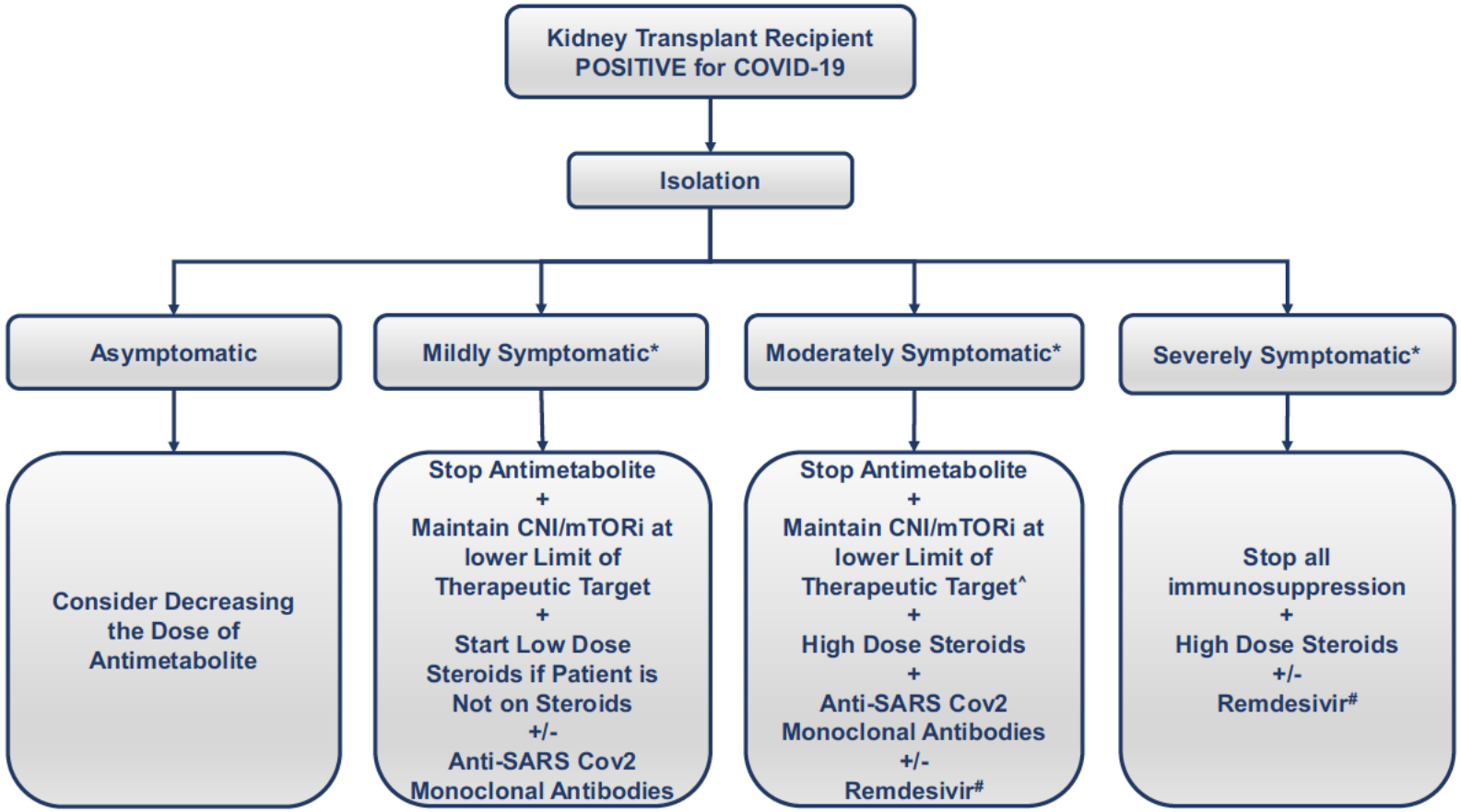

Figure 1 Suggested algorithm for the management of the COVID-19-positive kidney transplant recipient. *Symptoms of upper respiratory tract infection, gastrointestinal symptoms, and loss of taste or smell could be present in all patients. Mildly symptomatic is defined as a patient who has oxygen saturation > 95%, has no tachypnea, and has no evidence of COVID-19 on imaging. Moderately symptomatic is defined as a patient who has evidence of COVID-19 on imaging, but has an oxygen saturation > 94% and a respiratory rate < 30. Severely symptomatic is defined as a patient who has a low oxygen saturation < 94% or a respiratory rate > 30 despite supplemental oxygen, or respiratory failure requiring mechanical ventilation. ^Physicians can consider stopping CNI/mTORi in select patients who are at low risk for rejection. #There is significant variation between individual countries in Remdesivir indications.

PERSPECTIVES www.jasn.org

SARS-CoV-2 Vaccines in Kidney Transplant Recipients: Will They Be Safe and Effective and How Will We Know?

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Division of Allergy and Infectious Diseases, Department of Medicine, University of Washington, Seattle, Washington

JASN 32: 1021–1024, 2021. doi: https://doi.org/10.1681/ASN.2021010023

Table 1. Major SARS-CoV-2 platforms in development[a]

Vaccine Platform	Vaccine Name (Manufacturer)	Vehicle	Phase of Development	Adjuvant	Safety and Efficacy in the General Population	Specific Considerations for Kidney Transplant Recipients
mRNA	BNTb162b2 (Pfizer/BioNTech) mRNA-1273 (Moderna)	mRNA encapsulated in lipid nanoparticles	Authorized for emergency use in the United States and other countries	Unadjuvanted, but lipid nanoparticles possess natural adjuvant activity[7]	95% efficacy in phase 3 trials.[1] Anaphylaxis has been reported. Avoid in patients with a known allergy to a vaccine component (*e.g.*, polyethylene glycol). Close monitoring after administration for patients with a history of anaphylaxis to any food or drug.[3]	Does not contain live virus. No evidence of vaccine-induced off-target immune responses in large phase 3 clinical trials.[2,3]
Replication-defective viral vectors	AZD122 (Oxford/AstraZeneca)	Human-chimpanzee adenovirus (ChAdOx1)	Phase 3	Unadjuvanted	70%–90% efficacy depending on dose in phase 3 trials.[8] Transverse myelitis reported.[8]	Removal of genes necessary for replication reduces risk of vaccine-associated AdV disease.[9] Theoretical risk of emergence of new AdV type with replicative potential through homologous recombination, although this has never been demonstrated to occur with AdV-vectored vaccines.[9]
	JNJ78436735/Ad26.COV2.S (Janssen)	Human adenovirus (Ad26)	Phase 3	Unadjuvanted	Unknown	
	Convidecia (Ad5-nCov)	Human adenovirus (Ad5)	Approved for limited use in China	Unadjuvanted	Unknown	
	Sputnik V (Gamaleya)	Human adenovirus (Ad5 and Ad26 in consecutive doses)	Early use in Russia, Belarus, and Argentina	Unadjuvanted	Unknown	
Protein subunit	NVX-CoV2373 (Novavax)	Recombinant spike glycoprotein	Phase 3	Matrix-M1 system plus an additional, unnamed adjuvant	Unknown	Does not contain live virus. Matrix-M1 contains the same QS21 saponin as the AS01B adjuvant system contained in the recombinant varicella zoster vaccine.[7]
	SARS-CoV-2 recombinant protein formulation (GSK/Sanofi)	Recombinant spike protein	Phase 2	AS03 adjuvant	Unknown	High incidence of anti-HLA antibodies in KTR vaccinated with AS03-adjuvanted influenza vaccines, but no association between AS03 exposure and rejection.[3,10]
	EpiVacCorona (Vector Institute)	Peptide epitope	Early use in Russia	Unknown		Limited data available
Whole-inactivated (killed)	BBIBP-CoV (Sinopharm) CoronaVac (SinoVac)	Whole-inactivated SARS-CoV-2 viral particles	Limited use in China and other countries	Unknown	Unknown	Does not contain live virus. Limited data available in peer-reviewed literature.

GSK, GlaskoSmithKline; KTR, kidney transplant recipients.
[a]Does not include all candidate vaccines or platforms under investigation; limited to platforms in advanced stages of clinical development or authorized for use as of December 31, 2020.

- Vaccines are not recommended immediately post-transplant due to a presumed decrease in immunogenicity after recent high-level immunosuppression, when possible, SARS-CoV-2 vaccines should be given before transplantation.
- Expert opinion advises that delaying SARS-CoV-2 vaccination of vaccine naïve transplant recipients until 3 months after transplant or receipt of T cell or B cell ablative therapies may be appropriate; for patients who received a first dose before transplant, administration of the second dose should be delayed until at least 4 weeks post-transplant.
- In the post-transplant setting, age > 65 years, more recent transplantation, use of mycophenolate and mammalian target of rapamycin inhibitors, and lower graft function are associated with decreased serologic responses to influenza vaccines.

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients

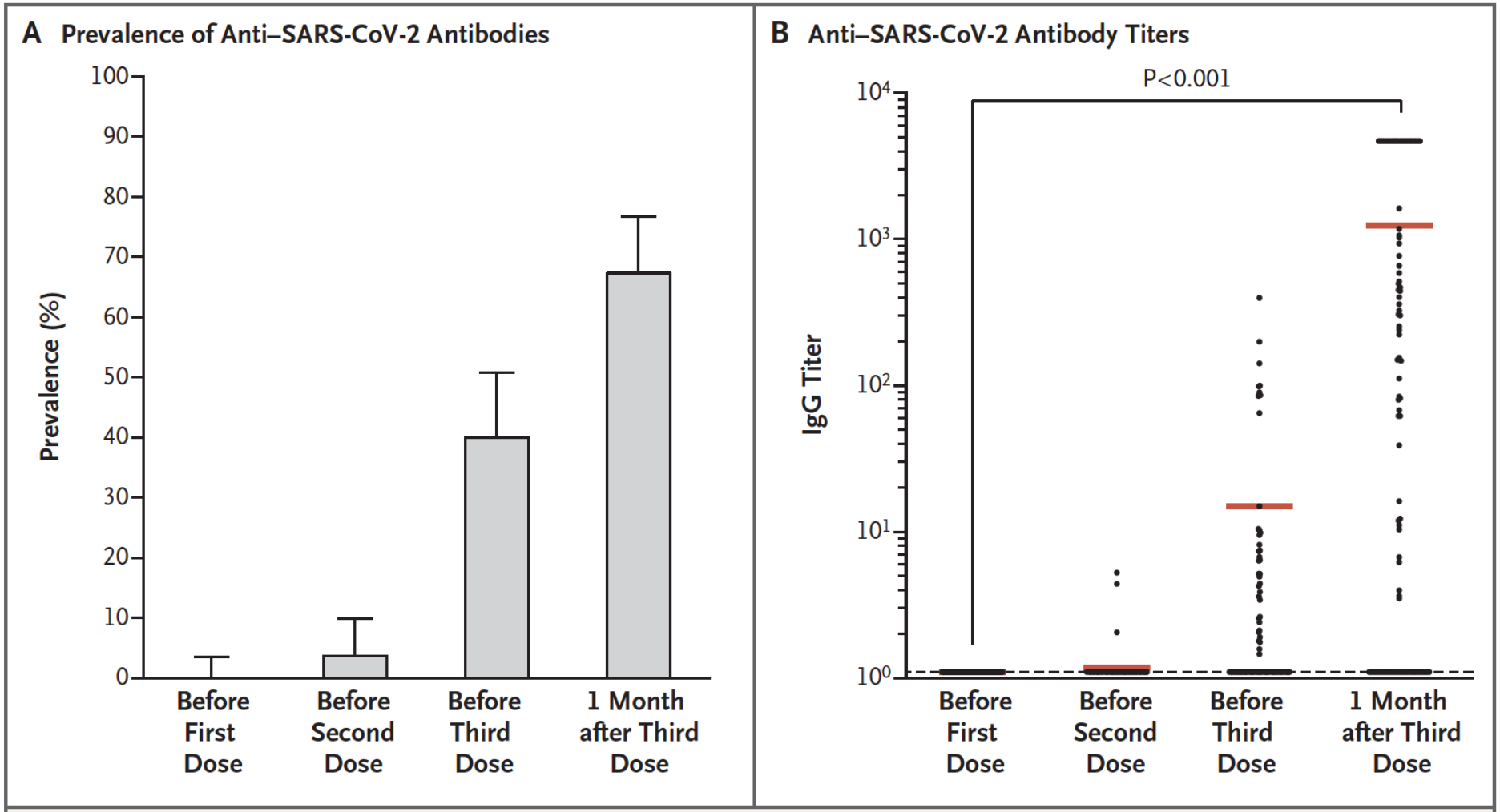


Figure 1. Immunogenicity.

Panel A shows the prevalence of anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies before and after vaccination in the study population. Panel B shows anti–SARS-CoV-2 antibody titers before and after vaccination in the study population.

Letters

RESEARCH LETTER

Antibody Response After a Third Dose of the mRNA-1273 SARS-CoV-2 Vaccine in Kidney Transplant Recipients With Minimal Serologic Response to 2 Doses

JAMA Published online July 23, 2021

Table. Association Between Patient Characteristics, Immunosuppression, and Antibody Titers After the Third Dose of a SARS-CoV-2 mRNA Vaccine in 159 Kidney Transplant Recipients

Variables	Sample, No. (%)	Antibody titers, mean (SD)	Adjusted mean difference (95% CI)[a]	*P* value
Age, y				
≤60	93 (58.5)	720.64 (1436.17)	−94.10 (−214 to 26)	.73
>60	66 (41.5)	777.77 (1974.04)		
Sex				
Male	98 (61.6)	1009.70 (1967.29)	280.22 (−240.59 to 801.03)	.29
Female	61 (38.4)	318.06 (910.83)		
BMI[b]				
<25	72 (45.3)	790.28 (1532.48)	98.57 (−394.18 to 591.32)	.69
≥25	87 (54.7)	706.34 (1791.95)		
Time from transplantation, y				
>3	102 (64.2)	882.33 (1847.79)	166.69 (−346.26 to 679.64)	.52
≤3	57 (35.8)	497.45 (1288.08)		
Donor type				
Living donor	36 (22.6)	596.54 (1273.02)	7.69 (−586.47 to 601.86)	.98
Deceased donor	123 (77.4)	787.61 (1777.45)		
Immunosuppression maintenance therapy				
Tacrolimus + MMF/MPA + steroids	84 (52.8)	316.72 (797.73)	−697.28 (−1193.00 to −201.56)	.006
All other regimens	75 (47.2)	1223.31 (2198.86)		
Serum creatinine, mg/dL				
<1.47	81 (50.9)	766.84 (1305.64)	153.26 (−350.37 to 656.89)	.55
≥1.47	78 (49.1)	721.00 (1995.83)		
Antibody titers after the second vaccine dose, AU/mL				
>6.8 and <50	64 (40.3)	1426.88 (1947.30)	894.89 (377.41 to 1410.37)	.001
≤6.8	95 (59.7)	284.55 (1281.55)		

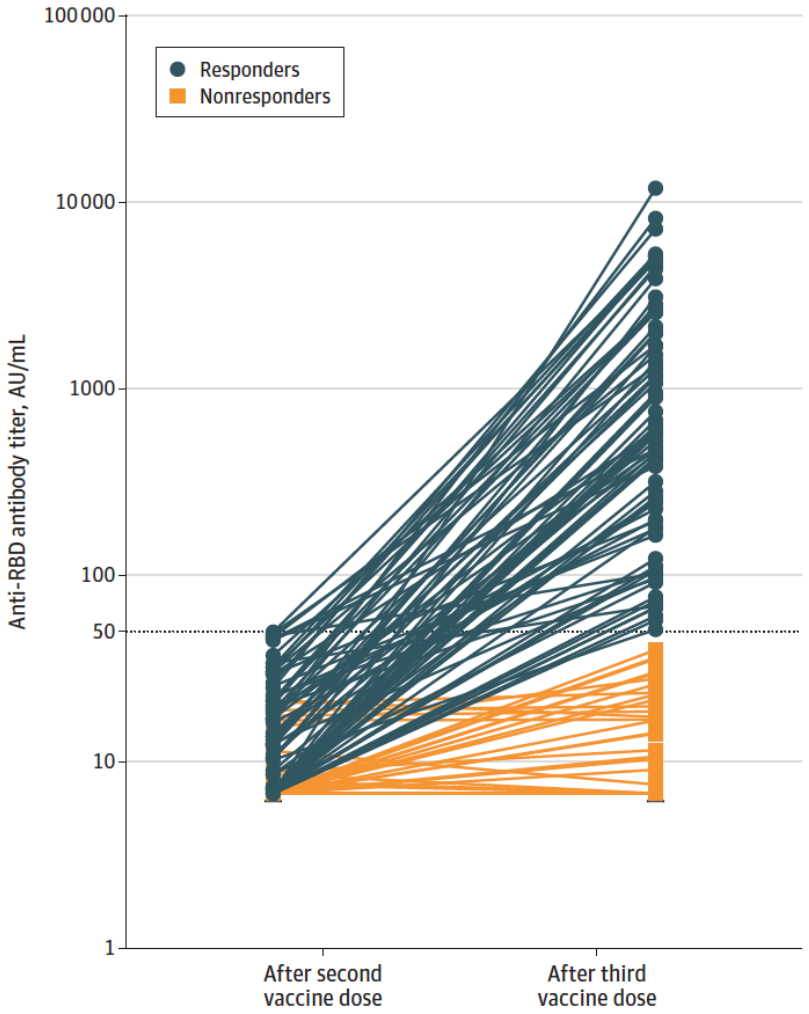
Abbreviations: AU, arbitrary units; BMI, body mass index; MMF, mycophenolate mofetil; MPA, mycophenolic acid; mRNA, messenger RNA.

SI conversion factor: To convert creatinine values to mmol/L, multiply by 88.4.

[a] Model adjusted for sex, BMI, donor type, time from kidney transplantation, serum creatinine level, triple immunosuppression (tacrolimus + MMF/MPA + steroids), and antibody titers after the second dose.

[b] Calculated as weight in kilograms divided by height in meters squared.

Figure. Anti-Receptor-Binding Domain (RBG) IgG Antibody Titers Measured 28 Days After the Third Dose of mRNA-1273 SARS-CoV-2 Vaccine in 159 Kidney Transplant Recipients



Horizontal dotted line indicates the cutoff for positivity (50 arbitrary units [AU]/mL). Blue lines indicate the antibody titers of kidney transplant recipients who seroconverted after the third dose (titers ≥50 AU/mL); orange lines, the evolution of antibody titers among nonresponders (titers <50 AU/mL). mRNA indicates messenger RNA.

- Patients who had a weak response after the second dose were more likely to develop an antibody response after the third dose compared with those without an antibody response.
- This study found that a third dose of mRNA-1273 vaccine induced a serologic response in 49%of kidney transplant recipients who did not respond after 2 doses.
- However, 51%of the patients did not develop anti–SARS-CoV-2 antibodies after the third dose, especially those receiving triple immunosuppression.

Thanks for Your Attention