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### Letter to the Editor

# Antibody response and safety of COVID-19 vaccine in peritoneal dialysis patients

#### To the Editor:

We read with interest a recent article reported by Ao et al.<sup>1</sup> The authors reported a meta-analysis describing the outcomes of hemodialysis patients infected with COVID-19 after SARS-CoV-2 double vaccination. They found that two doses of SARS-CoV-2 vaccination was associated with reduced mortality and need for oxygen supplementation in hemodialysis patients with COVID-19.

Peritoneal dialysis (PD) patients are another group of immunocompromised patients. They are vulnerable to COVID-19 infection like hemodialysis patients due to their immunocompromised state. They are also at increased risk of developing serious complications if they contract the virus. COVID-19 vaccine can contribute to reduce the risk of infection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, it is well recognized that chronic kidney disease patients have reduced vaccine response. Hence, meta-analysis of the antibody response and safety of COVID-19 vaccine in patients with PD is of great significance.

An extensive literature search was performed in PubMed, Web of Science, and EMBASE to find all relevant studies published from January 1, 2020, to October 05, 2022. We screened the references of the retrieved studies and restricted the language of the search to English. The following keywords were used in the search: COVID-19 vaccines (SARS-CoV-2 vaccines, SARS2 vaccines, SARS Coronavirus 2 vaccines, Coronavirus Disease 2019 vaccines, 2019-nCoV vaccine, and 2019 Novel Coronavirus vaccines) and peritoneal dialysis. The inclusion criteria included: (1) patients diagnosed with chronic kidney disease patients receiving PD and receiving COVID-19 vaccines, and (2) English article. The exclusion criteria were as follows: (1) irrelevant to the research direction, (2) no relevant data, (3) case reports, (4) repeated articles, and (5) review papers.

The analysis was conducted using Review Manager statistical software, version 5.3. A binary controlled study was used to calculate the number of positive rates of anti-SARS-CoV-2 spike protein IgG or adverse events. Odds ratio (OR) and 95% confidence interval (CI) were used to assess the effect in a whole random-effects meta-analysis model. The  $I^2$  and P value was used to quantify the heterogeneity of the effects among the included studies.

A total of eighteen studies involving 4434 patients were identified in the final analysis, and the details of the included studies are listed in Table 1.<sup>2–19</sup> Eighteen studies showed that the overall OR of positive rates of anti-SARS-CoV-2 spike protein IgG following COVID-19 vaccination in PD patients vs. healthy control subtyped for dose of vaccine was 0.36 (95% CI, 0.16–0.83, P = 0.02), the single dose vaccine was 0.44 (95% CI, 0.09–2.16, P = 0.31), and the double dose vaccine was 0.36 (95% CI, 0.13–0.98, P = 0.04) (Fig. 1). The positive rate in PD patients were significantly lower than that in healthy group, especially the double doses vaccine.

In sixteen studies, we found that the overall OR of positive rate of anti-SARS-CoV-2 spike protein IgG following COVID-19 vaccination in PD vs. hemodialysis patients subtyped for dose of vaccine was 1.64 (95% CI, 1.09–247, P = 0.02), the single dose vaccine was 2.43 (95% CI, 1.24–4.73, P = 0.009), and the double dose vaccine was 1.12(95% CI, 0.72–1.73, P = 0.62) (Fig. 2). The positive rate in PD patients were higher than that in hemodialysis patients. However, there was no significant difference in positive rate between PD patients and hemodialysis patients following the double dose COVID-19 vaccine.

In four studies, we found that the overall OR of adverse events following COVID-19 vaccine in PD patients vs. healthy control was 0.42 (95% CI, 0.15–1.13, P = 0.09), the OR of local adverse events was 0.52 (95% CI, 0.15–1.73, P = 0.28), and the OR of systemic adverse events was 0.32 (95% CI, 0.05–2.04, P = 0.23) Fig. 3. There was no significant difference in local and systemic adverse events in PD patients and healthy persons following COVID-19 vaccination.

In conclusion, our research showed that PD patients produced lower levels of anti-SARS-CoV-2 spike protein IgG after two doses of COVID-19 vaccine in comparison to healthy persons. However, our study also showed that the positive rate in PD patients were higher than hemodialysis patients. Hence, we think COVID-19 vaccine may serve as a sufficient protective role in reducing the severity of disease and likelihood of overall mortality in PD patients like hemodialysis patients. In addition, the current COVID-19 vaccine for patients with PD was safe. Future studies should determine adverse events of each vaccine type and critically identify mechanisms of severe adverse events following vaccination in PD patients.

#### **Declaration of Competing Interest**

All authors report that they have no potential conflicts of interest.

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Table 1Baseline characteristics of the included studies.

Study	Group	Events	Number of events (n)	Total (n)	Dose of vaccine
Bassi et al. <sup>2</sup>	PD	spike IgG	12	12	2
	Healthy	spike IgG	47	47	2
	Hemodialysis	spike IgG	114	121	2
Bruminhent et al. <sup>3</sup>	PD	spike IgG	23	28	2
	Healthy	spike IgG	16	16	2
	Hemodialysis	spike IgG	29	31	2
Crespo et al. <sup>4</sup>	PD	spike IgG	28	29	2
	Healthy	spike IgG	32	32	2
D 15	Hemodialysis	spike IgG	55	58	2
Duarte et al. <sup>5</sup>	PD	spike IgG	22	25	1
	Hemodialysis	spike IgG	21	42	1
	PD Harradiaharia	spike IgG	25	25	2
Unana at al 6	Hemodialysis	spike IgG	36	42	2
Haase et al. <sup>6</sup>	PD	spike IgG	21	21	2
	Healthy PD	spike IgG Local adverse events	24 10	24 28	2 1
	Healthy	Local adverse events	23	28	1
	PD	Local adverse events	7	23	2
	Healthy	Local adverse events	16	26	2
	PD	Systemic adverse events	3	28	1
	Healthy	Systemic adverse events	20	28	1
	PD	Systemic adverse events	2	23	2
	Healthy	Systemic adverse events	16	26	2
Lesny et al. <sup>7</sup>	PD	spike IgG	4	4	1
Leony et ui.	Healthy	spike IgG	8	4	1
	Hemodialysis	spike IgG	4	23	1
Longlune et al. <sup>8</sup>	PD	spike IgG	10	23	1
	Hemodialysis	spike IgG	17	80	1
	PD	spike IgG	17	20	2
	Hemodialysis	spike IgG	74	82	2
Matsunami et al. <sup>9</sup>	PD	spike IgG	26	27	2
	Healthy	spike IgG	38	38	2
	Hemodialysis	spike IgG	77	78	2
Murt et al. <sup>10</sup>	PD	spike IgG	19	20	2
	Healthy	spike IgG	54	61	2
	Hemodialysis	spike IgG	35	41	2
Murt et al. <sup>11</sup>	PD	spike IgG	22	23	2
	Healthy	spike IgG	28	29	2
	Hemodialysis	spike IgG	41	51	2
Nacasch et al. <sup>12</sup>	PD	spike IgG	52	64	2
	Hemodialysis	spike IgG	93	118	2
Patecki et al. <sup>13</sup>	PD	spike IgG	13	30	1
	Hemodialysis	spike IgG	15	30	1
	PD	spike IgG	26	30	2
	Hemodialysis	spike IgG	30	30	2
Piotrowska et al. <sup>14</sup>	PD	spike IgG	18	21	1
	Healthy	spike IgG	29	34	1
	PD	spike IgG	21	21	2
	Healthy	spike IgG	34	34	2
	Hemodialysis	spike IgG	20	35	1
	Hemodialysis	spike IgG	34	35	2
Polewska et al. <sup>15</sup>	PD	Local adverse events	16	20	1
	Healthy	Local adverse events	102	161	1
	PD	Local adverse events	12	20	2
	Healthy	Local adverse events	102	159	2
	PD	Systemic adverse events	6	20	1
	Healthy	Systemic adverse events	28	161	1
	PD	Systemic adverse events	7	20	2
Speen at al 16	Healthy	Systemic adverse events	48	159	2
Speer et al. <sup>16</sup>	PD	spike IgG	22	41	1
	Healthy	spike IgG	17	20	1
	PD	spike IgG	39	41	2
	Healthy	spike IgG	20	20	2
	Hemodialysis	spike IgG	44	124	1
Tylicki et al. <sup>17</sup>	Hemodialysis	spike IgG	109	124	2
I YIICKI CL dl.	PD Hemodialysis	spike IgG	18 20	21	1
	PD	spike IgG spike IgG	20 21	35 21	1 2
	Hemodialysis	spike IgG spike IgG	34	35	2
Wang et al. <sup>18</sup>	PD	spike IgG spike IgG	34 80	35 116	2
wang et di.	Healthy		80 33	34	1
	PD	spike IgG	108	34 116	2
		spike IgG			
	Healthy	spike IgG	34	34	2
	Hemodialysis	spike IgG	147	204	1
Versey et al 10	Hemodialysis	spike IgG	192	204	2
Yanay et al. <sup>19</sup>	PD	spike IgG	30	33	2 2
	Healthy	spike IgG	132	132	,

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	Peritoneal d		Healthy c			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
1.1.1 Dose=1							
Lesny P, 2021	4	4	8	14	5.8%	6.88 [0.31, 152.02]	
Piotrowska M, 2022	18	21	29	34	14.9%	1.03 [0.22, 4.86]	
Speer C, 2021	22	41	17	20	16.8%	0.20 [0.05, 0.81]	
Wang HH, 2022	80	116	33	34	10.8%	0.07 [0.01, 0.51]	← → → → → → → → → → → → → → → → → → → →
Subtotal (95% CI)		182		102	48.2%	0.44 [0.09, 2.16]	
Total events	124		87				
Heterogeneity: Tau <sup>2</sup> =	1.67; Chi <sup>2</sup> = 8.6	69, df = 3	(P = 0.03);	l² = 65%	6		
Test for overall effect:	Z = 1.01 (P = 0	.31)					
1.1.2 Dose=2							
Bassi J, 2021	12	12	47	47		Not estimable	
Bruminhent J. 2022	23	28	16	16	6.2%	0.13 [0.01, 2.51]	· · · · · · · · · · · · · · · · · · ·
Crespo M, 2022	28	29	32	32	5.3%	0.29 [0.01, 7.46]	
Haase M, 2022	21	21	24	24		Not estimable	
Matsunami M, 2021	26	27	38	38	5.3%	0.23 [0.01, 5.85]	· · · · · ·
Murt A, 2022a	22	23	28	29	6.7%	0.79 [0.05, 13.28]	
Murt A, 2022b	19	20	54	61	9.9%	2.46 [0.28, 21.35]	
Piotrowska M, 2022	21	21	34	34		Not estimable	
Speer C, 2021	39	41	20	20	5.8%	0.39 [0.02, 8.41]	
Wang HH, 2022	108	116	34	34	6.5%	0.18 [0.01, 3.29]	
Yanay NB, 2021	30	33	132	132	6.1%	0.03 [0.00, 0.65]	·
Subtotal (95% CI)		371		467	51.8%	0.36 [0.13, 0.98]	
Total events	349		459				
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> = 6.	56, df = 7	(P = 0.48);	l² = 0%			
Test for overall effect:	Z = 2.00 (P = 0	.04)					
Total (95% CI)		553		569	100.0%	0.36 [0.16, 0.83]	◆
Total events	473		546				
Heterogeneity: Tau <sup>2</sup> =	0.55; Chi <sup>2</sup> = 15	.23, df =	11 (P = 0.1	7); l <sup>2</sup> = 2	8%		
Test for overall effect:	Z = 2.42 (P = 0)	.02)					
Test for subaroup diffe	erences: Chi <sup>2</sup> =	0.05. df =	= 1 (P = 0.8)	3), $ ^2 = 0^4$	%		Peritoneal dialysis Healthy control

Fig. 1. Positive rates of anti-SARS-CoV-2 spike protein IgG following COVID-19 vaccination in patients with PD and healthy control subtyped for dose of vaccine.

	Peritoneal di		Hemodia			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
1.2.1 Dose=1							
Duarte R, 2021	22	25	21	42	5.4%	7.33 [1.90, 28.27]	
esny P, 2021	4	4	4	23	1.5%	39.00 [1.76, 862.54]	
onglune N, 2021	10	24	17	80	7.5%	2.65 [1.00, 7.00]	-
Patecki M, 2022	13	30	15	30	7.2%	0.76 [0.28, 2.11]	
Piotrowska M, 2022	18	21	20	35	5.2%	4.50 [1.12, 18.13]	
Speer C, 2021	22	41	44	124	9.3%	2.11 [1.03, 4.31]	
Tylicki L, 2021	18	21	20	35	5.2%	4.50 [1.12, 18.13]	
Vang HH, 2022	80	116	147	204	10.9%	0.86 [0.52, 1.42]	-
Subtotal (95% CI)		282		573	52.1%	2.43 [1.24, 4.73]	-
Total events	187		288				
Heterogeneity: Tau <sup>2</sup> =	0.56; Chi <sup>2</sup> = 22	.89, df = 1	7 (P = 0.00	02); I <sup>2</sup> =	69%		
Test for overall effect:	Z = 2.60 (P = 0	.009)					
l.2.2 Dose=2							
Bassi J. 2021	12	12	114	121	1.7%	1.64 [0.09, 30.41]	
Bruminhent J, 2022	23	28	29	31	3.9%	0.32 [0.06, 1.79]	
Crespo M, 2022	28	29	55	58	2.5%	1.53 [0.15, 15.36]	
Duarte R, 2021	25	25	36	42	1.7%	9.08 [0.49, 168.49]	
Longlune N, 2021	17	20	74	82	5.0%	0.61 [0.15, 2.55]	
Matsunami M, 2021	26	20	74	78	1.8%	0.34 [0.02, 5.59]	
Murt A, 2022a	20	27	41	51	2.9%	5.37 [0.64, 44.70]	
Murt A, 2022b	19	20	35	41	2.3%	3.26 [0.36, 29.09]	
Nacasch N, 2022	52	20 64	93	118	8.9%	1.16 [0.54, 2.51]	_ <b>_</b>
Patecki M, 2022	26	30	30	30	1.6%	0.10 [0.00, 1.88]	·
Piotrowska M, 2022	20	21	30	35	1.0%	1.87 [0.07, 48.00]	
Speer C, 2021	39	41	109	124	4.6%	2.68 [0.59, 12.27]	
Fylicki L, 2021	21	21	34	35	4.0%	1.87 [0.07, 48.00]	
Vang HH, 2022	108	116	192	204	7.8%	0.84 [0.33, 2.13]	
Subtotal (95% CI)	100	477	152	1050	47.9%	1.12 [0.72, 1.73]	<b>•</b>
Fotal events	439	411	953	1000	411070		ſ
Heterogeneity: Tau <sup>2</sup> =		10 df =		44)· 12 =	1%		
Test for overall effect:			10 (1 = 0.	,,	170		
「otal (95% CI)		759		1623	100.0%	1.64 [1.09, 2.47]	•
Total events	626	100	1241	1023	.00.070	1.04 [1.00, 2.47]	•
Heterogeneity: Tau <sup>2</sup> =		76 df -		01): 12 -	11%		· · · · · · · · · · · · · · · · · · ·
· ·	Z = 2.40 (P = 0)	,	21 (F = 0.0	ui), i= =	44 70		0.01 0.1 1 10 1

Fig. 2. Positive rates of anti-SARS-CoV-2 spike protein IgG following COVID-19 vaccination in patients with PD and hemodialysis subtyped for dose of vaccine.

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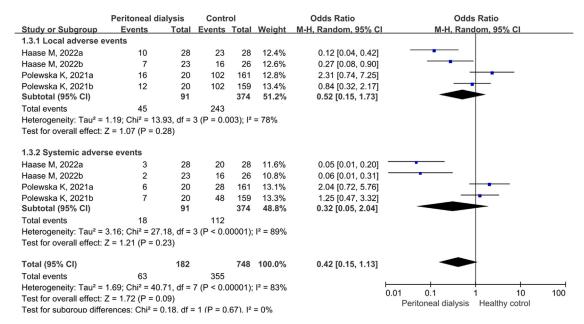


Fig. 3. Local adverse events and systemic adverse events following COVID-19 vaccination in patients with PD.

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