



ISPD Asia-Pacific Chapter Newsletter, August 2022

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Prepared by Chia-Te LIAO and Cheuk-Chun SZETO

News from the ISPD

International Society for Peritoneal Dialysis 2022 Congress



The ISPD Congress will be celebrated from 11-14 August 2022 in Singapore. We have everything ready for all the ISPD members to meet face to face with colleagues from other countries and regions, after two years when these opportunities have been scarce. It will be the first global event for the PD Community to rebuild our connections away from screens and online calls.

The Scientific Committee has prepared a fantastic program focusing on these key themes:

Basic Science
Epidemiology/Economics
PD Catheters/AKI
PD Outcomes/Technique Survival
Public Policy Forum
Supportive Care/PROM

PD Infections
Prescribing
Allied Health/Nursing
PD in Special Populations/Pediatrics
PD in Low and Middle Income Countries
Technology & Innovation/PD Solutions

This great program would not be possible without our prestigious conference speakers, coming from all parts of the world to share their experience and knowledge. We have also received dozens of high-quality abstracts that showcase the latest research from participants from across the world.

We are looking forward to welcoming you to our 2022 Congress to learn, exchange, cooperate and celebrate the achievements of the worldwide PD community while we enjoy the hospitality and the social program that the Singapore Society of Nephrology and the ISPD have prepared for the occasion.

ISPD Asia-Pacific Chapter Scholarship

This is a scholarship to support up to 3 months training in clinical PD for doctors and nurses from Asia-Pacific region. Deadline for application for each round: twice a year at 30 June or 31 December. **The next deadline is 31 August 2022.** Details and application procedures can be found under the Regional Chapters – Asia-Pacific Chapter, at the ISPD website.

For full details and application form: [click here](#) ➡

Upcoming Meetings

ANZ PD Academy 2022

August 27, 2022 - August 28, 2022 (hybrid event)

PARKROYAL Parramata 30 Philip Street, Parramata, NSW

Website: <http://www.eventful.com.au/pdacademy2022>

IPNA 2022 Congress

September 7, 2022 - September 11, 2022

Calgary TELUS Convention Center 136 8 Ave SE, Calgary, Alberta

Website: <https://www.ipna2022.org/>

10th International Society for Peritoneal Dialysis Asia Pacific Chapter meeting

22-24 September 2023, New Delhi, India

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Research News from Asia-Pacific Region

Burden of kidney disease in peritoneal dialysis and hemodialysis patients

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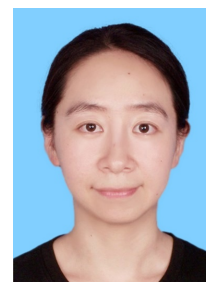


Photo: Li Fan

End stage kidney disease (ESKD) continues to increase worldwide and up to 5.4 million patients are expected to require treatment by 2030 [1]. Kidney failure is an important cause of patient life-years lost and reduced health-related quality of life (HRQoL) [2,3]. With the increase in life expectancy of dialysis patients, patient-centered outcomes are receiving more attention. Dialysis patient management have moved forwards from removing uremic toxins and prolonging life to improving quality of life in the past few years.

A few studies have done to evaluate the impact of dialysis mortality on quality of life in both dialysis patients and their caregivers. We have conducted a non-inferiority randomized controlled trial to compare the impact of peritoneal dialysis (PD) and conventional in-center hemodialysis (HD) on HRQoL [4]. A total of 1082 newly diagnosed kidney failure patients from 36 sites in China were randomly assigned to either PD or in-center HD. HRQoL was assessed using Kidney Disease Quality of Life-Short Form (KDQoL-SF) at the first day of dialysis initiation and 48 weeks after dialysis initiation. The primary outcome was the "Burden of Kidney Disease" scale of KDQoL-SF. We also compared the impact of PD and in-center HD on remaining scales of KDQoL-SF. The primary outcome analysis was conducted in 725 subjects who completed measures on the "Burden of Kidney Disease" at both baseline and 48 weeks. The mean (SD) change in the "Burden of Kidney Disease" score over 48 weeks was 2.61 (1.27) in the PD group and 2.58 (1.35) in the HD group, respectively; and the difference (95% CI) in "Burden of Kidney Disease" from baseline to 48 weeks was 0.03 (-3.29, 3.35) between the PD and HD groups. The changes of "Burden of Kidney Disease" from baseline to 48 weeks was not different between PD and HD group and satisfied non-inferiority for PD. For secondary analysis, although remaining scales of KDQoL-SF were not significant different between PD and HD after adjustment of multiple comparisons, our trial demonstrated PD may improve scores of "Symptoms of Kidney Disease", "Sleep" and "Pain", which need further studies to explore.

In addition to our study, many other studies have reported the impact of dialysis modality on HRQoL evaluated using different survey. A cross-sectional study including 356 Chinese dialysis patients (253 HD and 103 PD) found physical HRQoL of dialysis patients was worse than age- and sex- matched general population, the mental HRQoL was similar [3]. PD patients had better HRQoL with higher mean KDQoL-36 subscores and SF-6D scores than HD patients, except for mental component summary score; the "effects of kidney disease on daily life" had less impact on PD than HD patients. However, only one assessment of HRQoL survey was performed in this study, therefore the impact of PD vs. HD on the changes of HRQoL did not compare in this study. A meta-analysis including 190 studies with over 56,000 patients showed that PD had higher utility-based quality of life versus HD (effect size 0.03, 95% CI 0.00 - 0.06, $P=0.08$) [5]. This study also showed mean health utility was significantly higher in patients treated with automated PD (0.80, 95% CI 0.69, 0.91) than those on CAPD (0.72, 95% CI: 0.60, 0.85; interaction $p=0.02$). Zazzeroni et al also performed a systematic review and meta-analysis including 7 articles consisting of 1857 patients (1165 HD and 692 PD) [6]. One study included the analysis observed superiority for PD versus HD for the "Effect of Kidney Disease" scale of the KDQoL, but this meta-analysis did not lead a unanimous conclusion. Another meta-analysis by Chuasuwan et al also reported PD had better HRQoL measured by SF-36 and EQ-5D than HD patients; as well as better in subdomain of "physical functioning", "role limitations due to emotional problems", "effect of kidney disease" and "burden of kidney disease" using KDQoL than HD [7]. Bonenkamp et al, in meta-analysis, compared HRQoL between home dialysis defined as both PD and home HD and in-center HD [8]. Home dialysis had marginally better physical HRQoL scores compared to in-center HD patient, although heterogeneity was high. Mental HRQoL scores were not different between home dialysis and in-center HD. Dialysis is a long journey, caregivers and family member play a critical role in dialysis patients management. Burden of quality of life of dialysis caregivers and family member also affected dialysis modality selection. A meta-analysis found caregiver quality of life was poor than general population, but better than dialysis they cared for. Caregiver quality of life was not different between PD and HD [9].

Guidelines recommend that dialysis modality selection should be a shared decision-making between physicians and patients [10]. We should discuss with patients and their family regarding on the impact of dialysis modality on quality of life, survival and other implications and to help patients to choose dialysis modality with their own goals and minimize quality of life and treatment burden for both patient and caregivers.

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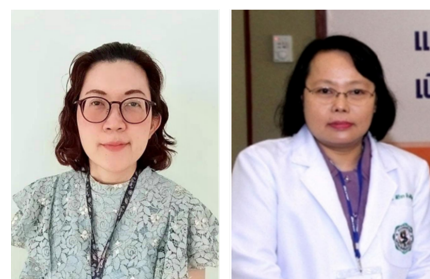
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Perspective to decrease rates of transferring to hemodialysis: a lesson from studying time-dependent incidence rates and risk factors in patients on peritoneal dialysis under the Thai PD-First Policy.

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Photos: Pornpen Sangthawan (left),
Siribha Changsirikulchai (right)

The incidence of end stage kidney disease (ESKD) is rising worldwide. Home dialysis is the preferred choice of kidney replacement therapy (KRT) due to the high cost of in-center hemodialysis (HD) and the various restrictions on health care the last 2 years because of the COVID- 19 pandemic. Peritoneal dialysis (PD) is the major home-based dialysis modality in Thailand and in many other developing countries. Permanent hemodialysis transfer (HDT) is the main challenge in PD care because it is an important cause of PD dropout. The identification of causes and risk factors for HDT is essential to design strategies for prevention and intervention to maintain patients with PD. A previous study from the Netherlands, a developed country, found that the incidence rates, causes, and risk factors for HDT differed according to the time on PD [1]. The main reason for PD dropout was kidney transplantation [1]. We postulate that the reasons for PD dropout would be different among countries. Therefore, we analyzed HDT by using a time-dependent analysis and it was recently published in the *Peritoneal Dialysis International* journal this year [2].

We conducted a retrospective analysis of 20,545 incident PD patients who were voluntarily registered in the Database of Peritoneal Dialysis in the Excel (DPEX) from January 2008 to June 2018 to determine the incidence rates and risk factors

of HDT among PD patients under the Thai PD-First Policy. DPEX is a web-based program, developed by an academic center in Thailand with the principal objective to provide a tool that each PD unit can use to monitor and improve the quality of care of these patients.

Our study found that the cumulative number of patients who discontinued PD due to HDT was 3,563 (17.4%). The incidence of HDT increased over time. The median time to HDT was 18.5 (95% CI 17.8-19.3) months. The reasons for HDT differed according to the time on PD. Mechanical complications due to catheters were the main reason during the first 3 months of PD, while peritonitis was the main cause in the later period of PD vintage. The results of our study emphasize that the causes of HDT should be defined in a time-dependent pattern.

A recent study from a Dutch cohort found causes of PD dropout similar to our results. They found that leakage and catheter problems were the main causes of PD dropout during the first 6 months while infections were the major risk during the entire follow-up [3]. These findings are helpful for designing strategies to prevent HDT as they are preventable causes.

Another previous study found that insufficient experience in catheter care and insertion was the main reason for early catheter problems [4]. PD centers should follow the International Society for Peritoneal Dialysis (ISPD) guideline recommendations regarding best practices in patient preparation, catheter selection, and peritoneal catheter placement procedures [5]. The recent 2022 ISPD guideline update recommends administration of systemic antibiotics immediately before catheter placement, monitoring and correcting for hypokalemia, and avoiding or limiting the use of histamine-2 receptor antagonists to prevent peritonitis [6]. The guideline also emphasizes the regular reassessment and updating of PD exchange techniques including ensuring any involved personnel have current knowledge of these things by direct inspection of PD practice and retraining [6]. Another study found that the knowledge of patients about PD had a significant impact on adherence to the treatment protocol and reduction of infections [7]. PD patients who are old with multiple comorbidities and problems with dexterity, vision and/or hearing impairment, frailty, cognitive function problems, and/or lower socioeconomic status will need extra support [8,9]. Home visit programs are another measure for continuing assessment of a patient's condition and needs. PD centers should consider assisted PD or automated PD (APD) as alternative modalities for HD in elderly or frail patients. In Thailand, the APD was currently approved for reimbursement under the Universal Health Coverage in February 2022. Continuing education courses focusing on practical training to improve the processes of care and clinical skills should be provided to PD care teams. A combination of these strategies would reduce rates and preventable risks of HDT and increase the number of patients continuing on PD.

Acknowledgements

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Increasing utilisation of PD driven by nephrologist-led intervention in Singapore

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Photo: Allen Yan Lun Liu

In 2019, five out of the top six countries or regions with the highest prevalence of treated End Stage Kidney Disease (ESKD) were from Asia (Taiwan, Japan, Singapore, South Korea and Thailand) [1]. Singapore is a multi-ethics city-state country with a 5.7-million population. Over the past decade, there was a 67.8% increase in the number of prevalent dialysis patients (4895 in 2011 and 8211 in 2020), equivalent to a 57.2% increase in crude prevalence rate (1291.8 patient-per-million-population [pmp] to 2030.3 pmp) or a 23.2% increase in age-standardised prevalence rate (919.2 pmp to 1132 pmp) (2). Despite the remarkable increase in the dialysis population, the utilisation of peritoneal dialysis (PD) among ESKD patients has been persistently low over the past decade (annual rate ranged from 11.6 to 13.6%) [2]. Multiple reasons explain the persistent low percentage of PD uptake nationwide [3]. The potential obstacle was difficulty accessing PD catheter insertion service that can be amendable by interventional nephrologist-led service and multidisciplinary collaboration model [4].

Established in 2010, Khoo Teck Puat Hospital (KTPH) is a 550-bed tertiary public health institution (PHI) serving the population of the northern part of Singapore. Nephrologists at KTPH have been performing all interventional nephrology (IN) procedures, including ultrasound (US) doppler of arteriovenous dialysis access, US-guided kidney biopsy, arteriovenous fistula or graft angiogram, angioplasty and salvage, and tunnelled dialysis catheter insertion since 2013 [5]. Like in other PHIs in the early 2010s, PD catheter insertion service had been predominately provided by surgeons. Nephrologists in KTPH had neither credentials for PD catheter insertion nor access rights to the Operation Theatre Scheduling System (OTS). This strategy posed a logistical challenge, as the service could not be available right at the time when ESKD patients had to initiate urgent dialysis, subject to the availability of the surgeons, outpatient clinic and operation theatre slots. In January 2015, we restructured our IN model of care for ESKD patients, who were indicated and willing to initiate PD, to transit through a seamless care pathway from pre-dialysis counselling, education on dialysis modality of choice, and assessment for PD eligibility to insertion of PD catheter. This approach was based on the following three steps:

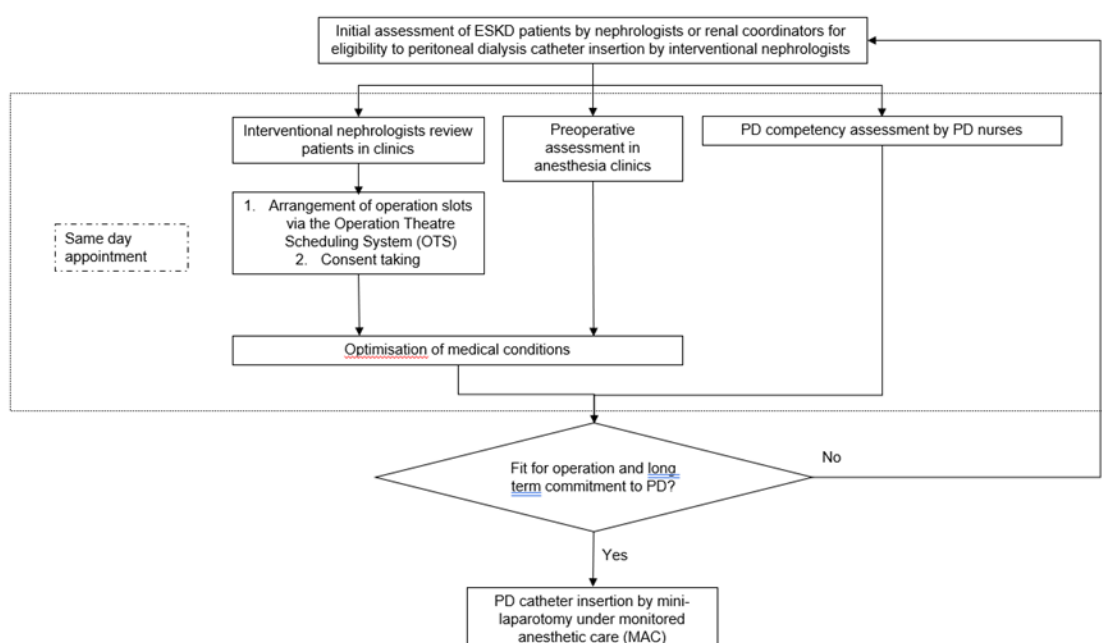
1. Nephrologist-led PD catheter insertion service

Interventional nephrologists received a 6-month training by fellow urologists in KTPH on surgical techniques and had been credentialed by hospital management to operate on PD catheter insertion by open, mini-laparotomy independently since January 2015. The interventional nephrologist was granted direct access rights to the OTS to list PD catheter insertion with this approach.

2. IN and coordination of care

The new care model emphasised the importance of renal coordinators (nursing background) working with primary nephrologists and interventional nephrologists. Instead of initiating urology referral, primary nephrologists and renal coordinators directly liaise with interventional nephrologists on patient eligibility, optimisation of medical conditions and OT listing in OTS. Renal coordinators could also arrange PD competency assessment and appointments for anaesthesia assessment in a timely and synchronised manner before operation (see Figure 1). All the pre-operative assessments and appointments could be arranged within the same day, shortening patients' waiting time and reducing the frequency of hospital visits.

Figure 1. Workflow for IN service in PD catheter insertion

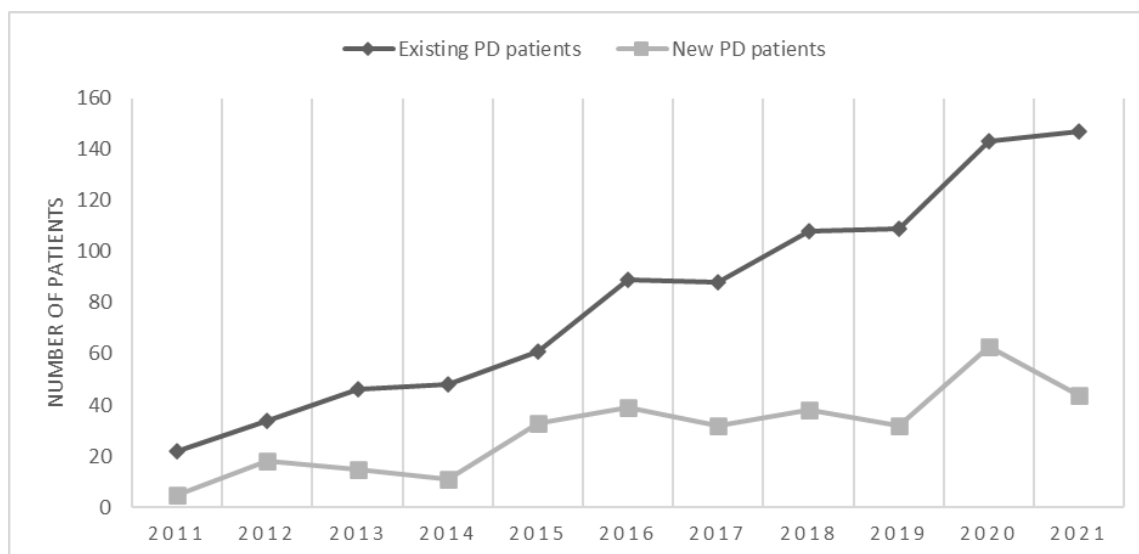


3. Interim service for urgent initiation of PD

We provided urgent PD support for eligible patients right after PD catheter insertion. With clinical indications for initiation of urgent dialysis (e.g. hyperkalaemia, acidosis, symptomatic uraemia and/or fluid retention), PD was started immediately after insertion of the PD catheter. A low-volume peritoneal dialysate (1-1.2L) was infused for the first week, followed by incremental volume adjustment to 2L or above (maximal tolerated volume according to body surface area). Intermittent PD 2-3 times per week, each with 8-10 hours of therapy for 5-10L dialysate, was performed for 2-3 weeks until PD training to patients and/or caregivers was accomplished. The whole process could avoid unnecessary haemodialysis (HD) catheter insertion and hospital admissions and potentially minimised switch of the modality of choice for dialysis.

The new service orientation increased utilisation, both in the growth of PD take-up rate and the percentage of ESKD patients on PD over HD. Our prevalent PD patients steadily increased from 48 in 2014 to 147 in 2020 (Figure 2).

Figure 2. Number of PD patients by years in Khoo Teck Puat Hospital, Singapore



Our annual rate of incident ESKD patients who chose PD as the dialysis modality increased from 15.6% (2011-2014) to 27.5% (2015-2020). In 2020, 34.9% of ESKD patients decided on PD as their dialysis modality. The percentage was the highest among all PHIs in Singapore for the past decades.

IN practice has grown steadily over the past 2-3 decades in Southeast Asia for HD and PD procedures [6]. In Singapore, many PHIs already have the intra-structure and expertise to establish nephrologist-led PD catheter insertion [7,8] and urgent-start PD services [9,10]. Our service provision shows that care coordination and collaboration with different disciplines were equally important as technical advancements in dialysis access management. While accreditation, turf issues, lack of peer support and lack of facilities are always the challenges to be encountered, we focus on improving patient outcomes, engagement with other specialty colleagues, providing efficient service with reasonable safety and efficacy, teamwork and support from within the nephrology team to achieve our goal.

The role of IN in PD should be multi-faceted and holistic. An integrated approach with collaborative and coordinated care orchestrated by interventional nephrologists provides a steady and remarkable growth of PD patients in a dialysis program, and it is achievable in other institutions in Asia as well.

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Immunogenicity and safety of COVID-19 vaccine in dialysis patients

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Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), continues to be a global public health threat causing significant patient morbidity and mortality. Patients on chronic dialysis are at increased risk of COVID-19 infection, severe complications and death, and thus effective and safe vaccination is particularly important for these patients. However, it is well recognized that patients on dialysis have reduced vaccine response due to altered innate, cellular and humoral immunity.

Why dialysis patients have reduced response to vaccination?

Both innate and adaptive immunity are required for an effective response to vaccination. After inoculation, the epitopes of the vaccine antigens are recognized by signal-pattern recognition receptors expressed on dendritic cells and macrophages. Activated antigen presenting cells then migrate to regional lymphoid organs to activate naïve T cells. Interaction of B and T cells results in somatic hypermutation and class-switch recombination to enhance the affinity and repertoire of the antibodies. Naïve B cells mature to antibody-producing cells, memory B cells or long-lived plasma cells. Various immunological dysfunctions in patients on dialysis contribute to reduced vaccination response [1]. Monocytes isolated from patients on dialysis showed impaired maturation and activation. Reduced expression of signal-pattern recognition receptors results in defective antigen presentation. There is also reduced T cell activation and proliferation due to autocrine dysfunction, and B cell lymphopenia due to increased apoptosis in uremic patients [2].

Dialysis patients showed reduced humoral response to COVID-19 vaccines

Humoral response to COVID-19 vaccination is reflected by the level of antibodies to the receptor-binding domain of the spike protein of SARS-CoV-2. Systemic review and meta-analysis data demonstrated that in patients on chronic HD, the overall seropositivity after two-dose COVID-19 vaccination was 84.3% (95% CI: 79.1%, 89.4%) at 7 days to 42 days after the second dose [3]. Compared to general population, patients receiving chronic HD were 18% less likely to achieve seropositivity (95%CI: -9%, -27%; $p < 0.001$). For patients on peritoneal dialysis (PD), meta-analysis data showed a seropositivity rate of 92.4% after two-dose COVID-19 vaccination (95% CI: 88.3%, 96.6%). Compared to healthy subjects, patients on PD were 11% less likely to become seropositive though not reaching statistical significance (95% CI: -1%, -21%; $p = 0.39$). Pooled data demonstrated that patients on PD developed comparable levels of anti-SARS-CoV-2 antibodies with patients receiving chronic HD. Age, presence of diabetes mellitus and dialysis vintage demonstrated no statistically significant correlation with anti-SARS-CoV-2 seropositivity among patients receiving longterm dialysis. Despite this seemingly reassuring data, patients on dialysis showed a greater decline of antibodies titre with time, compared to healthy controls, supporting the need for booster vaccination [4]. Third dose vaccination significantly increased the antibody levels in patients receiving maintenance dialysis and among non-responders after the second dose of vaccine, a significant portion, ranged from 33.3% to 54.5% reported in literature, seroconverted after the third dose [5]. Meta-analysis data on immunogenicity of third dose COVID-19 vaccination in dialysis patients is eagerly awaited.

Cellular response is impaired in dialysis patients

Cellular response to COVID-19 vaccination is reflected by the CD4+ T cell response. T cell activation was observed in 31-78% of dialysis cohort after two-dose COVID-19 vaccination, which is lower compared to the general population (88.2%) [6]. The suboptimal cellular response after COVID-19 vaccination in patients on chronic dialysis is consistent with the impaired immune response after hepatitis B vaccination. There were no correlations found between cellular and humoral response, nor with other studied predictors like age or immunosuppressive therapy [7].

Are COVID-19 vaccines still effective in dialysis patients?

Despite altered immunologic responses in dialysis patients, COVID-19 vaccination demonstrated a protective effect against severe forms of COVID-19. Vaccine exposure in dialysis patients was independently associated with lower hospitalization rate and mortality [8]. Ashby et al demonstrated that prior two-dose COVID-19 vaccination was associated with a 75% (95% CI: 56%, 86%) lower risk of admission and 88% (95% CI: 70%, 95%) fewer deaths in HD patients compared with unvaccinated patients [9].

Are COVID-19 vaccines safe in dialysis patients?

COVID-19 vaccination appears safe in patients receiving chronic dialysis. Meta-analysis demonstrated an overall adverse event rate of 2.1% after two-dose COVID-19 vaccination. None of these adverse events resulted in emergency department attendance or hospitalization [3]. The third dose COVID-19 vaccine also demonstrated safety data in dialysis cohort, with pain over injection site and fatigue being the most common local and systemic event reported respectively [10].

Any novel approaches to enhance immunogenicity of COVID vaccines in dialysis patients?

Novel strategies to boost vaccine immunogenicity are needed to better protect patients on chronic dialysis. Existing evidence on fourth dose COVID-19 vaccination were mainly derived from kidney transplant recipients but data on patients receiving chronic dialysis is lacking. Other approaches such as heterologous vaccination with alternative vaccine platforms, intradermal or intranasal route of vaccine administration and use of adjuvants are currently under evaluation in the general population. It is hoped that these immunogenicity data in patients receiving chronic dialysis will be available shortly.

Conclusion

Despite a reduced immunogenicity compared to general population, the three-dose COVID-19 vaccination regimen in patients on maintenance dialysis is generally safe and effective for prevention of severe disease. Further studies are needed to determine the optimal vaccination strategies in this vulnerable population.

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