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PERMANYER

EDITORIAL

Remembering Eduardo Slatopolsky

Recordando a Eduardo Slatopolsky

Alberto Alles

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There was nothing premonitory before that sad day when Jorge Cannata conveyed the news we couldn't have imagined. Eduardo had died; we had lost a true friend.

When the course of life brings us to the reality that we are closer to the end than the beginning, it becomes inevitable to talk about the end. And it was in those conversations that he mentioned he would like to be remembered simply as "a good guy," even above his undeniable achievements as a nephrologist and brilliant researcher. This is a curious emblem: those who aspire to be remembered in this way are generally good people.

And Eduardo was. I remember the day Pablo Massari introduced us. I approached this figure, who seemed to me imposing and almost inaccessible in the world of nephrology. We shook hands, and he introduced himself as Dr. Slatopolsky: a genuine mark of humility, as he did not assume that everyone should know who he was.

I presented to him the idea of organizing a Satellite Symposium of the World Congress of Nephrology in Buenos Aires, Argentina in 1999, on Bone and Mineral Metabolism, together with Jorge Cannata, another dear friend. He accepted immediately, hoping it would be the best congress on the topic ever held until then. And he got to work, aiming to invite the cream of the crop of the specialty at an international level and secure significant financial support. And so it happened. In Foz de Iguazú, Argentina everything went perfectly, thanks to his attention to the smallest details. He and Jorge agreed that all the profits would go to the Asociación de Nefrología de Santa fe. And so it happened: 15 nephrologists from Rosario and Santa Fe received scholarships for a 3-month stay, all expenses paid, at the Nephrology service in Santa Cruz de Tenerife, Spain thanks also to the invaluable and generous collaboration of another prominent Argentine nephrologist, Dr. Víctor Lorenzo.

Despite moving and settling in the United States at a young age, he never forgot his country of origin, where his parents had arrived from distant lands. He never turned down an invitation to participate in all kinds of scientific events, provincial and national conferences, without asking if logistical details were covered. He felt passionate about Buenos Aires, his hometown, and Rosario. He loved enjoying the Paraná River and watching the majestic passage of the grain ships.

He also had the courtesy to participate and be a reviewer for the Bone and Mineral Metabolism Guidelines developed by the respective Argentine Society of Nephrology Working Group.

Argentina pained him. He was perfectly informed about our reality throughout all those years. We shared the hope that, even if we weren't going to see it, we could eventually have a better country.

From that symposium, we began what became a 25-year uninterrupted friendship, during which time I had the immense fortune of enjoying and strengthening a true friendship and, most importantly, knowing him in

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his rich human facet: he was a tremendously educated man, never solemn, formal when appropriate, with an enviable sense of humor, sincere and honest, very generous in general, and even more so with those he cared about. A passionate defender of democratic ideas and respectful of different opinions.

My wife and I shared many pleasant and unforgettable moments with him and his wife Judith, the love of his life.

When we love someone dearly, we usually refuse to think that one day they will be gone. That's why I didn't imagine, or didn't want to, that Eduardo would leave us one day. It will be a little while until we meet again, savoring a Malbec.

See you soon, Eduardo, dear friend, thank you for being who you were and, on behalf of those who were lucky enough to be your friends, allowing us to enjoy and love you so much.

PERMANYER

EDITORIAL

Dr. Slatopolsky's Obituary

Obituario del Dr. Slatopolsky

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Last Wednesday, April 24th, the profound sorrow of facing the sad reality that Eduardo Slatopolsky will no longer accompany us on our convergent paths in nephrology, in science, and in life, was followed by an overwhelming flood of memories in my mind and heart from all the time shared since September 7th, 1985, when I joined his lab for a postdoc that was initially supposed to last two years.

Almost 40 years later, this tribute to Eduardo is aimed at briefly recalling the brilliant scientific career of a young doctor from Buenos Aires, who, after his nephrology residency at Cleveland Clinic, joined Dr. Neil Bricker's team at Washington University in St. Louis in 1963, initiating an uninterrupted series of contributions that marked "milestones" in the treatment of chronic kidney disease, starting with the development of the first method for determining parathyroid hormone levels across the United States. Each advance in the understanding of the pathophysiology of kidney disease was accompanied by a meticulous delineation of the molecular mechanisms that mediate the deleterious effects of phosphorus on the progression of kidney damage, secondary hyperparathyroidism, and vascular calcification, as well as the survival benefits of the appropriate use of calcitriol or its analogs, or a normal vitamin D status, just to mention a few. His hundreds of publications in the most prestigious scientific journals speak for themselves about the countless contributions from his laboratory to world nephrology.

Eduardo's passion for improving the lives of patients with advanced chronic kidney disease led him to make a titanic effort, both organizationally and in managing the financial resources needed to create the first dialysis center in St. Louis: the Chromalloy American Kidney Center, which he founded and directed for 30 years, and which still provides dialysis to the most disadvantaged sectors of the African American community in St. Louis.

But Eduardo's legacy extends far beyond his overwhelming contributions to nephrology. His zest for life was contagious, stimulating and supporting both his patients and the members of his team, which, over more than 50 years of active scientific life, brought together nephrologists and researchers of all races and creeds into a unique extended family. In his laboratory, the work was very hard, but collaboration took precedence over competition, and one person's success was a reason for everyone to celebrate. This particular blend of science and life, fostered for generations, transcended the gregarious spirit of Argentinians and Latin Americans, as his massive New Year parties or the fun barbecues at his house compensated with music, joy, and the eloquent affection of Eduardo and Judith for

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the nostalgia and uprooting felt by each foreign “apprentice” in his lab.

Even the ultra-respectful and conventional Japanese researchers suggested to their apprentices to choose St. Louis over Harvard because, with equally excellent science, the immense personal richness of their experiences in the Renal Division of Washington University would last them a lifetime.

With the certainty that one only truly dies when one’s memory fades, I am convinced that Eduardo Slatopolsky will continue to accompany us at every conference, in every effort to improve the quality of life for kidney disease patients, and in every attempt to provide, IN HIS HONOR, the best of ourselves to each nephrology or research apprentice that crosses our paths.

ORIGINAL ARTICLE

Kidney transplant under paired kidney donation program: experience of a tertiary hospital in Mexico

Trasplante renal bajo el programa de donación renal pareada: experiencia de un hospital de tercer nivel en México

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Abstract

Objective: *To demonstrate the experience acquired in a tertiary hospital in Mexico since the implementation of the paired kidney donation (KPD) program.* **Material and methods:** *Observational, analytical, longitudinal and prospective study from september 2018 to september 2022. All G5 KDIGO chronic kidney patients who were HLA or ABO incompatible with their original donors in the pretransplant protocol and who were transplanted under the KPD program were included.* **Results:** *Thirty-four kidney transplants were performed under this program. At one year after the transplant, graft survival was 97%, glomerular filtration rate was 76.18 (± 21.91) ml/min/1.73 m² SC and the incidence of rejection was 17.6%. These results were statistically better than those presented in a historical group of kidney transplant recipients after desensitization due to positive flow-crossmatch test: graft survival 51.1%, glomerular filtration rate 51.79 (± 26.29) ml/min/1.73 m² SC and rejection incidence 51.1%.* **Conclusions:** *In Mexico, transplantation under KPD program is a successful modality when there is HLA/ABO incompatibility or sensitization. The greater use and socialization of this program can increase the national kidney transplant rate, reducing the waiting list.*

Keywords: *Kidney paired donation. Kidney transplant. Plasmapheresis. Compatibility. HLA.*

Resumen

Objetivo: *Demostrar la experiencia adquirida en un hospital de tercer nivel de atención en México desde la implementación del programa de donación renal pareada (KPD).* **Material y métodos:** *Estudio observacional, analítico, longitudinal y prospectivo de septiembre de 2018 a septiembre de 2022. Se incluyeron todos los enfermos renales crónicos G5 KDIGO que en el protocolo pretrasplante resultaron HLA o ABO incompatibles con sus donantes originales y que fueron trasplantados bajo programa KPD.* **Resultados:** *Se realizaron 34 trasplantes renales bajo este programa. A un año postrasplante, la sobrevida del injerto fue del 97%, la tasa de filtración glomerular fue 76.18 (± 21.91) ml/min/1.73 m² SC y la incidencia de rechazos fue del 17.6%. Estos resultados fueron estadísticamente mejores que los presentados en un grupo histórico de trasplantados renales previa desensibilización por haber tenido una prueba cruzada originalmente incompatible: sobrevida del injerto 51.1% (p = 0.019), tasa de filtración glomerular 51.79 (± 26.29) ml/min/1.73 m² SC e incidencia de rechazos del 51.1%.*

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Conclusiones: *En México, el trasplante bajo programa de KPD constituye una modalidad exitosa cuando existe incompatibilidad HLA/ABO o sensibilización. La mayor utilización y la socialización de este programa puede aumentar la tasa de trasplante renal nacional, disminuyendo la lista de espera.*

Palabras clave: *Donación renal pareada. Trasplante renal. Plasmaféresis. Compatibilidad. HLA.*

Introduction

Kidney transplantation is the most cost-effective modality of renal replacement therapy that provides better survival and quality of life for both adult and pediatric patients compared to dialysis[1]. In Mexico, according to data from CENATRA (National Transplant Center), 2713 and 3082 renal patients were transplanted nationwide in 2022 and 2023, respectively, and by the end of 2023, there were 16,370 renal patients on the waiting list[2], highlighting a significant gap between supply and demand.

In terms of living donor kidney transplantation, 30% of pairs will have ABO blood group incompatibility or human leukocyte antigen (HLA) system incompatibility[3]. The most common practice is to discard these originally incompatible donors or accept the inherent risk of rejection and proceed to desensitize recipients through various immunosuppression schemes. Félix Rapaport proposed in 1986 the possibility of exchanging donors[4]; the first actual donor exchange procedure was performed in South Korea in 1991, followed by Europe in 1999 and then the United Sates in 2000, with slow acceptance primarily due to ethical and legal considerations[4].

Within Mexican national legislation, the donor exchange in the paired kidney transplant program is based on the administrative figure of the unrelated living donor. The acceptance of the expansion of the concept of the unrelated living donor to not only include spouses but also friends and even unrelated voluntary donors was published in the Official Gazette of the Federation on November 5th, 2004[5]. An essential requirement is the presentation of the notarized deed before the hospital's internal transplant committee to approve particular cases.

Kidney donor exchange is generically encompassed under the kidney paired donation (KPD) program, which has evolved internationally from its simplest form with pair exchanges[6-8] to the inter-hospital shipping of organs, variations that emerged to ensure that donors could not withdraw after their originally paired recipient received a kidney transplant[9].

Formal KPD programs now encourage compatible pairs to join, allowing the recipient to receive a kidney graft from a younger donor with better anthropometric matching, better HLA compatibility, or reduced antibody intensity against a cross-matched donor. Adding compatible pairs to the KPD increases the probability of matches for incompatible pairs or highly sensitized patients, thus improving the overall capacity of the program[8-9].

Each originally incompatible pair must necessarily have the triad of immunological studies (crossmatch, HLA typing, and single antigen reactive antibody panel) needed to perform basic calculations that justify the initial incompatibility and allow finding compatible donors with manual calculations when transplant centers perform fewer complex exchanges.

To overcome the multiple selection challenges in which there is greater immunological complexity or chain length, KPD programs use computer algorithms based on the donor-recipient blood group, body mass index (BMI), sensitization status, cytomegalovirus (CMV) status, and size of the pool of incompatible pairs, determining the best probability of matching and pairing donors and recipients[10] based on the principles of equity, utility, and justice[11].

The total number of possible combinations, assuming that "n" represents the total number of originally incompatible donor/recipient pairs within a potential exchange, is equal to $(n^2 - n)/2$, which represents the initial calculation to be performed[12].

Regardless of immunological complexity, there are also logistical challenges requiring efficient operating room availability, an adequate number of transplant surgeons, anesthesiologists, and nursing staff to perform multiple nephrectomies and kidney implants. Similarly, the participation of hospital administrative and legal areas is fundamental and must work perfectly in tandem with the clinical areas.

When performing living donor exchanges, the creation of chains takes time and is usually done electively so that donor and recipient operations can be performed sequentially and within a reasonably short period of time. It is recommended to gather incompatible pairs over a defined period (quarterly or every 4 months depending on each hospital logistics) and use those pairs to perform mathematical calculations to find matching through software.

On the other hand, when considering list exchanges or initiating a chain with a cadaveric donor, deceased donor transplants are performed semi-urgently, and chains starting with this type of donor must be mobilized urgently and not electively[13]. It is suggested to programmatically construct most of the chain (those highly sensitized patients who already have a compatible paired donor) and only leave the start of the chain for less sensitized patients who are inferred to have a rapid possibility of compatibility with the first cadaveric donors.

Table 1. Modalities of kidney transplantation via KPD in renal patients at Hospital Central Militar

Modality	Pairs (donor-renal patient) involved in each chain	Total recipients
2 crosses	2 pairs	4
3 chains	3 pairs	9
1 chain	4 pairs	4
1 chain	5 pairs	5
1 chain	12 pairs	12

Method

We conducted a prospective cohort study with patients transplanted under the paired kidney donation program at our hospital from September 2018 through September 2022. All pairs that entered the program completed the pre-transplant protocol, were evaluated, and authorized by the internal transplant committee upon presentation of the notarized deed. The donation risk for each donor was estimated. For each recipient and each crossmatch, the probability of matching compatibility was calculated[14]. All recipients were transplanted with a negative flow cytometry crossmatch (XM CF). Simultaneous nephrectomies of the donors were scheduled and performed in adjacent operating rooms when the crossmatches were simple; if the chains involved more than 3 pairs, the kidney transplants were performed with a 2-3 week interval between each recipient. The conventional technique was performed using open or laparoscopic nephrectomy, the kidneys were perfused ex vivo with preservation solution, and the implant was performed in the contralateral right iliac fossa of the obtained kidney. This implant was performed with end-to-side vascular anastomoses from the renal vein to the external iliac vein and from the renal artery to the external iliac artery; after reperfusion, neo-uretero-cysto-anastomosis was performed using the Leich-Gregor technique with stenting over a double J 6-Fr ureteral catheter.

Immunosuppression induction was performed using basiliximab or thymoglobulin, with maintenance completed with mycophenolic acid, tacrolimus, and prednisone. No renal patient was desensitized. The demographic, clinical, and biochemical characteristics of this patient group were determined basally and through post-transplant evaluations based on the hospital internal protocol; protocol biopsy of the renal allograft was performed between months 3 and 15, evaluated using Banff 2017 criteria. For each recipient, the glomerular filtration rate (GFR), rate of allograft rejection, and graft survival 1 year after transplantation were determined. The GFR was also determined for each donor in the post-transplant period.

Table 2. Clinical and biochemical characteristics of recipients under the Kidney Paired Donation transplant program

Variable	Mean (SD)
Recipient Age (years)	 35.24 (± 13.01)
Sex Male Female	 14 (41.2%) 20 (58.8%)
BMI (kg/m²)	24.77 (± 3.30)
Post-transplant Creatinine (mg/dl)	1.32 (± 0.37)
PRA Class I Class II	 25.51% 28.21%

SD: standard deviation; BMI: body mass index; PRA: panel of reactive antibodies.

The KPD group was compared with a historical control group of renal patients who had an initially incompatible crossmatch and were eventually transplanted at our center with their original donors after desensitization with plasmapheresis.

The variables managed in the database included: age, sex, etiology of chronic kidney disease (CKD), blood group and Rh, panel of reactive antibodies (determined by Luminex), type of immunosuppression induction, type and level of maintenance immunosuppression, serum creatinine, GFR in mL/min/1.73 m^2 BSA, complications, and graft status to date. Histological variables from the protocol biopsy of the renal allograft were obtained according to the Banff 2017 classification[15].

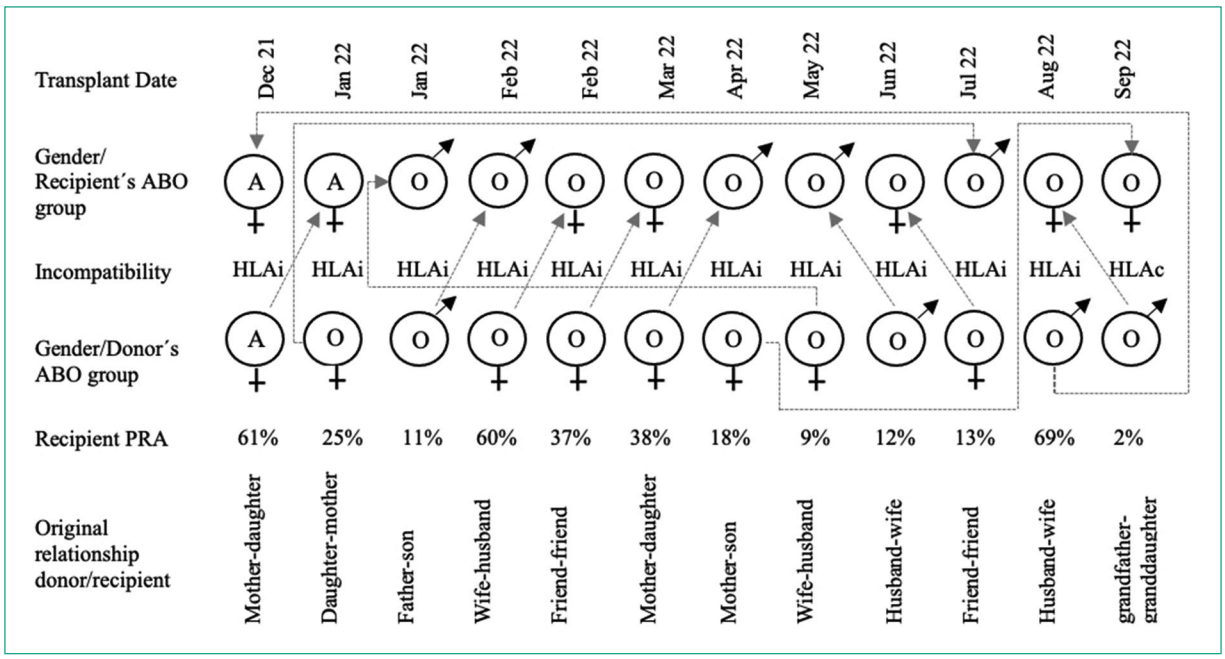

Figure 1. Kidney transplant chain under the donor exchange program (KPD), conducted in 2021-2022 at Hospital Central Militar. KPD: Kidney Paired Donation; HLAi: HLA incompatible; HLAc: HLA compatible; ABO: ABO blood group; PRA: panel of reactive antibodies.

Statistical analysis

Descriptive statistics were performed by determining means with standard deviation (SD) and percentages of the variables using SPSS 25. Regarding analytical statistics, normality of the data was determined using the Kolmogorov-Smirnov test; the chi-square and Mann-Whitney U tests were also performed. Graft survival analysis was conducted using the Kaplan-Meier method and curve comparison using the Log-rank method. A p-value < 0.05 was considered statistically significant.

Results

A total of 34 kidney transplant recipients were included, among which there were 4 pediatric recipients under this program (Table 1). The first 3 transplants with inter-hospital donor exchanges in Mexico were included in the 5-pair and 12-pair chains (Fig. 1).

The indication for entry into the KPD program for each of the renal patients was: 29 patients due to HLAi (85.3%), 3 patients due to ABOi (8.2%), 1 patient for immunological gain (3.25%), and 1 patient for anthropometric gain (3.25%).

None of the renal patients were desensitized pre-t or post-transplant). A total of 58.8% of participants were women (Table 2). Anticipated transplantation was performed in 5.9% of patients, and in 58.8% renal replacement therapy via hemodialysis. Table 3 includes the antibody levels reported by the panel of reactive antibodies (PRA) and the type of induction immunosuppression used. The most common etiology of CKD was not determined (ND) with 44.1%, and systemic arterial hypertension (SAH) with 17.6%. A total of 91.17% of patients were on the standard immunosuppression regimen with tacrolimus (FK)/mycophenolate mofetil (MMF)/prednisone (PDN), 5.9% on a minimized regimen (FK/mammalian target of rapamycin inhibitor [i-mTOR]/PDN), and 2.93% on a cyclosporine (CsA)/MMF/PDN regimen.

A total of 97% of the grafts were functional 1 year after the transplant: 1 graft lost function due to chronic active antibody-mediated rejection (ABMR) that did not respond to treatment (the patient exhibited non-adherence to immunosuppression, recipient No. 20). In the protocol biopsies, 5 other subclinical active ABMRs were documented (recipients No. 4, 8, 17, 26, and 34), which were treated with 2 steroid boluses + 500 mg of rituximab.

The mean waiting time from entry into the paired program to transplantation was 5.1 months; the mean post-transplant follow-up was 24.1 months.

A total of 10 sensitized patients (29.41%) with PRA ≥ 25% and 7 highly sensitized patients (20.59%) with

Table 3. Baseline demographic characteristics pre- and post-transplant and biochemical/histological progression of patients under the paired Kidney Donation Program 1 Year after the transplant

n	Sex	Age (years)	PRA class I/II	HLAmm with paired donor	Induction	IS	PrU (mg/day)	FK/CsA (ng/mL)	Cr (mg/dL)	Microvascular inflammation Banff 2017
1	M	11	98%/100%	1A/1B/1DR	ATG (4mg/kg)	FK/MMF/PDN	122	7.3	1.12	g1, ptc0, v0
2	W	60	7%/9%	1A/1B/1DR	Basiliximab	FK/MTOR/PDN	100	3.9	1.40	g1, ptc1, v0
3	M	29	5%/8%	2A/1B/1DR	Basiliximab	FK/MMF/PDN	199	6.4	1.2	g0, ptc0, v0
4	W	46	68%/44%	1A/1B/1DR	ATG (1mg/kg)	FK/MTOR/PDN	177	2.7	1.1	g2, ptc3, v0
5	W	44	6%/0%	1A/1B/2DR	Basiliximab	FK/MMF/PDN	150	5.6	1.0	g1, ptc0, v0
6	M	28	10%/5%	1A/1B/2DR	Basiliximab	FK/MMF/PDN	167	5.3	1.3	g1, ptc1, v0
7	W	37	6%/2%	1A/1B/1DR	Basiliximab	FK/MMF/PDN	248	4.5	1.1	g1, ptc0, v0
8	M	28	8%/14%	2A/1B/1DR	ATG (3.5mg/kg)	FK/MMF/PDN	139	6.3	1.5	g2, ptc3, v0
9	W	24	8%/5%	1A/1B/1DR	ATG (4mg/kg)	FK/MMF/PDN	136	8.2	0.9	g0, ptc0, v0
10	W	41	45%/84%	1A/1B/1DR	ATG (4.5mg/kg)	FK/MMF/PDN	229	7.2	0.8	g1, ptc0, v0
11	M	31	7%/10%	1A/1B/1DR	Basiliximab	FK/MMF/PDN	102	8	1.2	g1, ptc1, v0
12	W	49	4%/24%	1A/1B/1DR	Basiliximab	FK/MMF/PDN	262	5.6	0.8	g0, ptc0, v0
13	W	39	30%/16%	1A/1B/0DR	ATG (3mg/kg)	FK/MMF/PDN	116	4.1	1.3	g0, ptc0, v0
14	W	46	100%/99%	1A/0B/0DR	ATG (5.5mg/kg)	FK/MMF/PDN	232	8.1	0.9	g0, ptc0, v0
15	M	42	68%/82%	1A/2B/1DR	ATG (4mg/kg)	FK/MMF/PDN	186	12.6	1.7	g1, ptc1, v0
16	M	32	5%/8%	2A/2B/1DR	Basiliximab	FK/MMF/PDN	192	4.8	1.33	g0, ptc0, v0
17	W	40	52%/88%	2A/B/1DR	ATG (4.5mg/kg)	FK/MMF/PDN	77	5.3	1.28	g2, ptc3, v0
18	W	46	2%/7%	1A/1B/1DR	Basiliximab	FK/MMF/PDN	134	9	0.7	g1, ptc0, v0
19	W	30	9%/11%	1A/1B/1DR	Basiliximab	FK/MMF/PDN	165	7.7	1	g0, ptc0, v0
20	W	15	7%/5%	0A/1B/0DR	Basiliximab	FK/MMF/PDN	120	5.3	5.1	g2, ptc3, v1
21	M	13	4%/7%	2A/2B/1DR	Basiliximab	FK/MMF/PDN	126	5.1	0.7	g1, ptc1, v0
22	M	45	5%/3%	1A/1B/1DR	Basiliximab	FK/MMF/PDN	200	9.5	1.2	g0, ptc0, v0
23	W	24	80%/43%	1A/0B/1DR	Basiliximab	FK/MMF/PDN	80	9.2	0.84	g0, ptc0, v0
24	W	60	6%/19%	0A/0B/1DR	Basiliximab	FK/MMF/PDN	120	9.6	1.23	g1, ptc0, v0
25	M	19	10%/12%	2A/1B/1DR	Basiliximab	FK/MMF/PDN	150	13.9	0.9	g0, ptc0, v0
26	M	56	80%/43%	2A/2B/2DR	Basiliximab	CsA/MMF/PDN	190	237	0.8	g2 ptc1, v0
27	W	28	45%/29%	2A/2B/1DR	Basiliximab	FK/MMF/PDN	200	8.9	0.9	g1, ptc0, v0
28	W	22	27%/49%	1A/2B/0DR	Basiliximab	FK/MMF/PDN	145	9	0.8	g0, ptc0, v0
29	M	34	14%/22%	1A/1B/2DR	Basiliximab	FK/MMF/PDN	160	10.5	1.2	g0, ptc1, v0
30	M	34	12%/6%	2A/2B/1DR	Basiliximab	FK/MMF/PDN	145	9.4	1.3	g0, ptc0, v0
31	W	45	4%/22%	1A/0B/1DR	Basiliximab	FK/MMF/PDN	150	11.1	0.5	g0, ptc0, v0
32	M	35	15%/11%	1A/2B/2DR	Basiliximab	FK/MMF/PDN	100	11.3	1.3	g0, ptc0, v0
33	W	43	62%/77%	1A/2B/1DR	Basiliximab	FK/MMF/PDN	1000	10.3	1	g0, ptc0, v0
34	W	16	2%/0%	2A/1B/2DR	Basiliximab	FK/MMF/PDN	170	10.2	1.2	g2, ptc2, v0

PRA: panel of reactive antibodies; HLAmm: human leukocyte antigen mismatches; ATG: antithymocyte globulin; IS: maintenance immunosuppression; FK: tacrolimus; MMF: mycophenolate mofetil; MTOR: mTOR inhibitor; CsA: cyclosporine; PrU: 24-hour proteinuria; Cr: creatinine; g: glomerulitis; ptc: peritubular capillaritis; v: intimal arteritis; PDN: prednisone.

PRA ≥ 80% were included; that is, 50% of the patients transplanted under KPD were sensitized or highly sensitized. The rest of the recipients had a PRA < 25%.

There were 4 surgical complications (3 lymphoceles and 1 ureteral stenosis) and 2 medical complications (1 BK viremia and 1 patient with diabetic ketoacidosis), all of which were immediately resolved, with grafts fully functional to date.

Patient survival was 100% 1 year after the transplant and 94.1% to date (2 patients died after the first follow-up year with fully functional grafts due to severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] infection).

At Hospital Central Militar, 88 patients were transplanted during the study period, 44 of whom were from related/unrelated directed living donors, 10 from deceased donors, and 34 under the paired kidney donation program, indicating that the use of the KPD program represents a 38.6% increase in transplants at our hospital.

Regarding donors, the age was 42.93 (± 10.46) years, post-donation creatinine level was 1.17 (± 0.32) mg/dL, all were reported as healthy with adequate GFR 1 year after nephrectomy (75.47 ± 15.61 mL/min/1.73 m^2 BSA). One donor died at the 1-year follow-up due to SARS-CoV-2 infection during the COVID-19 pandemic.

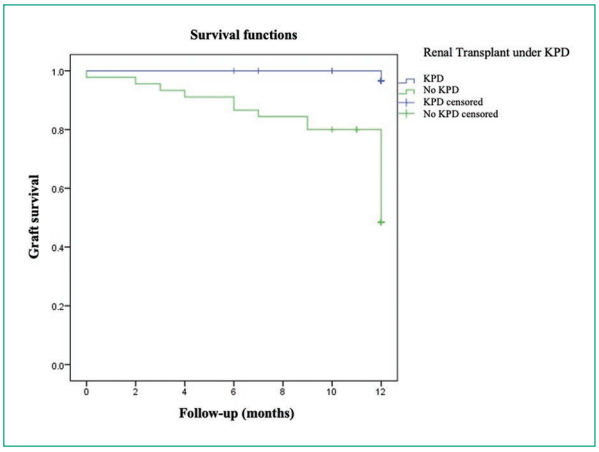

Figure 2. 1-year post-transplant kidney graft survival comparing the KPD (Kidney Paired Donation) group with the historical control group desensitized with plasmapheresis. Log rank (Mantel-Cox) = 0.019.

Discussion

Regionally, in Latin America, some reports claim Costa Rica reported 1 case of kidney paired donation in 2016[16], Guatemala reported a series of cases using this kidney transplantation modality in 2018[17], and Argentina performed its first case in 2015[18] and its second case in 2018 after the approval of the Justina Law[19].

According to the *Transplant Newsletter* 2022, there is already activity in the KPD program in Mexico[20]; in our country, the first kidney transplant with donor exchange was performed in 1996 at the Mexican Institute of Social Security (IMSS)[21]. However, due to its limited penetration among the medical community, this program was not resumed until 2016 by a few transplant centers that initiated it in an isolated manner (Instituto Nacional de Nutrición Salvador Zubirán, Hospital Juárez de México, Hospital Regional de Alta Especialidad de Yucatán, and Unidad Médica de Alta Especialidad No. 71 in Torreón, Coahuila; the latter reported having performed a total of 143 kidney transplants under the paired program by 2015)[22]. Our hospital formally started this program in the second half of 2018, and to date, the program has been systematically applied for 5 years[23].

Although our experience under the paired donation program is limited to 34 kidney transplant recipients, our hospital is classified according to Massie et al. as a center with very high utilization of the KPD program[24].

According to data from CENATRA, the mean waiting time to receive a kidney from a deceased donor nationwide in Mexico from 2018 through 2022 was 33.8 months[25], and for a living donor kidney transplant, it was 3.38 months[26]. In our cohort of patients transplanted under KPD, the mean waiting time from entering the program to transplantation was 5.1 months, shorter than being on the cadaveric waiting list. The reason for the longer waiting time for KPD vs the national average for living donor kidney transplantation is that this population is more sensitized than the directed living donor kidney recipients.

In the Canadian KPD program registry, the mean number of days from a candidate's participation in a compatibility cycle under paired kidney transplantation to transplantation was 182 days (range, 47-1,741; mean ± SD, 275 ± 17)[27], and the waiting time from enrollment in the program to transplantation at Mayo Clinic, United States, 330 days (178-539)[28]. Our hospital has a mean waiting time of 153 days from enrollment to transplantation under this program, which is shorter than reported in the literature.

When analyzing graft survival free of rejection in our pediatric recipients under the paired program, it was lower than reported by Sypek et al. in the Australian registry of the pediatric paired kidney exchange program[29], because 1 in 4 pediatric recipients experienced

Table 4. Baseline clinical characteristics and post-transplant biochemical outcomes of renal patients originally incompatible with their donors and transplanted under KPD vs a historical control group with pre-transplant desensitization

Variable	KPD kidney transplant recipients (HLA/ABO Incompatibility)	Kidney transplant recipients with plasmapheresis (HLA Incompatibility)	p
Age (years)	35.24 (± 13.01)	30.24 (± 12.44)	0.088
Etiology of CKD			
ND	15	17	0.270
CGN	5	16	
SAH	6	5	
DM	1	2	
Other	7	5	
Induction			
Basiliximab	25	8	0.000
ATG	9	22	
Daclizumab	0	12	
MPD	0	3	
Plasmapheresis	0	45	0.000
GFR (mL/min/1.73 m² BSA)*	76.18 (± 21.91)	51.79 (± 26.29)	0.000
Functional graft at 1 Year			
Yes	33	23	0.019
No	1	22	

KPD: kidney paired donation; HLA: human leukocyte antigen; ABO: ABO blood group; GFR: glomerular filtration rate; CKD: chronic kidney disease; ND: not determined; CGN: chronic glomerulonephritis; SAH: systemic arterial hypertension; DM: diabetes mellitus; ATG: antithymocyte globulin; MPD: methylprednisolone; p: statistical significance level.
*GFR calculated using the CKD-EPI equation.

graft loss due to non-adherence to immunosuppressive treatment.

Regarding graft survival at the follow-up, it was 97% in patients transplanted under the paired kidney program vs 95.45% in a cohort of 44 patients transplanted at our hospital during the same study period from directed living donors (p = 0.769); data similar to those reported by Kute et al., who demonstrated that graft survival is similar when using related living donation vs paired donation[30]. Additionally, in the 135 kidney recipients with a 1-year follow-up in the Canadian paired kidney donation registry, patient and allograft survival were 99% and 96%, respectively.

In that same Canadian cohort, the biopsy-confirmed acute rejection rate was 8%[27] vs 17.6% in our military hospital cohort; except for 1 patient treated with plasmapheresis, immunoglobulin, and rituximab, the rest of these rejections were only subclinical, and the grafts are functional; it is recommended, since most of our KPD patients are classified as high immunological risk, to perform protocol biopsies at 3 and 12 months post-transplant.

When the 1-year post-transplant adjusted graft survival of those renal patients in Canada was analyzed, it was 97.3%, 98.1%, and 97.7% for sensitized recipients with PRA in the groups of 0-79%, > 80%, and > 99.9%, respectively[27]. In our hospital, this survival rate was 96.3% in the PRA 0-79% groups, and 100% in the PRA > 80% group.

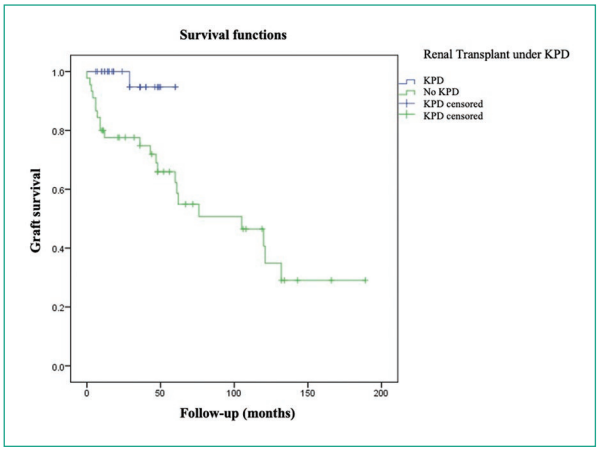

Figure 3. Kidney graft survival at the follow-up comparing the group transplanted under KPD (Kidney Paired Donation) with the historical control group transplanted after desensitization with plasmapheresis. Log rank (Mantel-Cox) = 0.007.

The results found in our recipients transplanted under the KPD program were compared with a historical control group of renal patients who were transplanted in our center from 1995 through 2017. These recipients had initially incompatible crossmatches with their original donors, were subsequently desensitized with 3 sessions of plasmapheresis plus IV immunoglobulin (patients who, by definition, had donor-specific antibodies), and finally had compatible crossmatches; both groups were considered sensitized patients. The results demonstrated that donor exchange to transplant recipients without donor-specific antibodies provides better GFR and graft survival (Table 4).

The analysis showed that 1-year post-transplant graft survival was statistically better when using donor exchange to transplant these renal patients vs desensitization for initially incompatible crossmatch with their original donor (Fig. 2).

When analyzing graft survival at the follow-up in the same 2 groups of patients, KPD transplantation proved superior with statistical significance vs pre-transplant plasmapheresis in sensitized patients (Fig. 3).

The dropout rate of donors in our cohort was 0% because bridge donors were used in only 13.6% of cases. Kher and Kumar recommend that paired donors should be counseled in advance to minimize the waiting time to donate their organ and thus avoid dropout[31].

Conclusions

The donor exchange program is an option to increase the probability of a successful kidney transplant in HLA/ABO incompatible patients with their original donors, but it must be conducted under strict in-hospital medical-ethical protocols, administrative and legal national regulations and in full compliance with the Declaration of Istanbul[32]. In high immunological risk patients, KPD is superior to desensitization, demonstrating better GFR and graft survival, as well as a lower rate of rejection. This program also promotes cost savings by reducing over-immunosuppression.

The results obtained can socialize and raise awareness of this program among the general population, as well as encourage transplant groups to use this modality and integrate regional or national donor exchange programs to reduce national waiting lists for renal patients in Mexico and Latin America.

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The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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PERMANYER

ORIGINAL ARTICLE

Urgent-start peritoneal dialysis for patients with end-stage renal disease. A health technology assessment

Diálisis peritoneal de inicio urgente para pacientes con enfermedad renal terminal. Una evaluación de tecnologías sanitarias

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Abstract

Objective: *To analyze the available evidence on the relevant clinical and economic aspects of urgent-start peritoneal dialysis (US-PD) compared to urgent-start hemodialysis (US-HD).* **Material and methods:** *Rapid systematic review with searches in: Medline, Embase, Cochrane Library and Clinicaltrials.gov. The included studies were evaluated with quality tools. Relative risk (RR) was summarized, and meta-analysis of results was performed, when possible.* **Results:** *1,303 articles were identified, 939 were screened by title and abstract, 29 were evaluated in full-text and 16 were selected. A total of 2,179 patients participated in the selected studies, 1,087 in the US-PD group, 915 in the US-HD group, and 177 in the PD after US-HD group. US-PD has beneficial effects, such as reducing one-year mortality (RR, 0.69; 95%CI: 0.51-0.92). There is no evidence to suggest US-PD increases the risk of complications in unplanned dialysis. On the contrary, there is an association between the practice of US-PD and a lower risk of undesirable outcomes compared to HD with a central venous catheter. Limited and heterogeneous economic evidence suggests that there is no incremental impact on costs.* **Conclusions:** *US-PD can be an effective, safe and accessible option for urgent initiation of dialysis in patients with chronic kidney disease who require unplanned initiation of dialysis.*

Keywords: *Peritoneal dialysis. Hemodialysis. Chronic renal disease. End-stage renal disease.*

Resumen

Objetivo: *Analizar la evidencia disponible sobre los aspectos clínicos y económicos relevantes de la diálisis peritoneal de inicio urgente (DP-IU) en comparación con la hemodiálisis de inicio urgente (HD-IU).* **Material y métodos:** *Revisión sistemática rápida con búsquedas en Medline, Embase, Cochrane Library y Clinicaltrials.gov. Los estudios incluidos fueron evaluados con herramientas de calidad. Los riesgos relativos (RR) fueron resumidos y se realizó metaanálisis de los resultados, cuando fue posible.* **Resultados:** *Se identificaron 1,303 artículos, 939 se tamizaron por título y resumen, 29 fueron evaluados en texto completo y 16 fueron seleccionados. En los estudios seleccionados participaron 2,179 pacientes en total, 1,087 en el grupo DP-IU, 915 en el grupo HD-IU y 177 en el grupo DP después de HD-IU. La DP-IU tiene efectos beneficiosos como la reducción de la mortalidad al año (RR, 0.69; IC95%: 0.51-0.92). No se evidenció que la DP-IU aumente el riesgo de complicaciones en diálisis no planificada. Por el contrario, existe una asociación entre la práctica de la DP-IU y un menor riesgo de resultados indeseables en comparación con la HD con catéter venoso central. La evidencia económica, limitada y heterogénea, sugiere que no hay un impacto incremental en*

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los costos. **Conclusiones:** *La DP-IU puede ser una opción efectiva, segura y accesible para el inicio urgente de diálisis en pacientes con enfermedad renal crónica que requieren inicio de diálisis no planificado.*

Palabras clave: *Peritoneal dialysis. Hemodialysis. Chronic renal disease. End-stage renal disease.*

Introduction

The rapid expansion of end-stage renal disease (ESRD) is a challenge for public health, budgetary impact control, and the capacity of health services to provide dialysis. Health systems must plan the supply and financing of different renal replacement therapy modalities[1]. Currently, there are more than 2.5 million patients on dialysis[2], and it is estimated that by 2030, this number will double[3].

Pre-dialysis care and early referral to a nephrologist are prognostic factors in patient survival and the success of the dialysis technique[4]. However, a large percentage of patients start dialysis in an unplanned or urgent manner[2,5], mainly through hemodialysis (HD), which increases the risk of complications, prolonged hospitalization, and mortality[6].

Urgent-start peritoneal dialysis (USPD) has been promoted as a feasible and equally effective unplanned alternative to planned-start PD[7-9]. In the long term, the survival rates of PD and HD are comparable, although some patient selection-biased studies indicate that PD tends to have better survival rates within the first two years of treatment[10], along with preservation of residual kidney function (diuresis)[11] and greater patient satisfaction compared to HD[12].

Economically, HD requires significant capital investment, more facility infrastructure, and personnel to operate[13]. Comparing the overall cost of in-hospital HD (not home HD) and continuous ambulatory and automated PD in 46 health systems, 70% of countries report higher costs for HD vs PD, with an incremental cost between 30% and 235%, demonstrating that PD can be more cost-effective by providing comparable results to HD at a lower total cost[14]. Additionally, maintaining patients with USPD has shown good long-term results[15].

Despite similar clinical outcomes and better humanistic and economic benefits associated with PD, HD remains the predominant modality[16]. This distribution does not reflect the preferences of patients, families, and caregivers[12], and may be related to the habitual practice of starting HD in urgent dialysis patients[17]. However, with appropriate protocols and training, a PD catheter can be quickly placed and used, avoiding the need for a central venous catheter (CVC)[18].

The practice of USPD could benefit health systems and patients with greater adoption of PD. This systematic review aims to analyze the evidence on the benefits, harms, and economic impact of USPD compared to urgent-start hemodialysis (USHD) in adults with ESRD requiring unplanned dialysis initiation to provide evidence-based recommendations for adopting this practice.

Method

This review was developed following the PRISMA Statement recommendations[19] and the Rapid Review Guide of the National Collaborating Centre for Methods and Tools[20].

From September through October 2020, a comprehensive search was conducted across the Medline, Embase, Cochrane Library, Cochrane Central Register of Controlled Trials (CENTRAL), and Clinicaltrials.gov databases. Two search strategies were implemented to identify clinical and economic evidence. Search strategies are presented in Appendix 1 (each appendix can be found in the supplementary data of this manuscript).

Randomized controlled clinical trials or non-randomized controlled observational trials published since 2000 were included. Meta-analyses, systematic reviews, and guidelines were considered sources to identify relevant individual studies. Full-text articles, abstracts, and conference papers providing sufficient information were included. Uncontrolled observational studies, case reports, review articles, protocols, and letters were excluded. For studies published in multiple articles, the one with the largest sample size and the most reported outcomes was included.

The target population included adults with a prior diagnosis of chronic kidney disease or ESRD requiring emergency renal replacement therapy for the first time[21,22], without a prior functional vascular access implant or PD catheter. USPD was defined as starting PD within 48 hours to 14 days after peritoneal catheter implantation before complete healing of the PD catheter cuff, including all peritoneal catheter implantation techniques (surgical and percutaneous) and all PD modalities (ambulatory peritoneal dialysis [APD], continuous ambulatory peritoneal dialysis [CAPD]). Daytime ambulatory peritoneal dialysis (DAPD) and intermittent peritoneal dialysis (IPD) were also considered interventions[22].

Patients who started any PD modality in a planned manner (patients with pre-established functional PD catheter implants or starting PD 14 days after catheter implantation) and patients with acute kidney injury undergoing intermittent hemodialysis, sustained low-efficiency dialysis, or continuous renal replacement therapy were excluded.

USHD was considered a comparator (defined as the emergency start of HD using a temporary CVC[21]) initiated within the first two weeks after the CVC was tunneled (permanent) or non-tunneled (temporary), including patients with USHD who converted to any other PD modality after the PD catheter cuff healed (PD after USHD).

The outcomes evaluated were all-cause mortality, infectious complications, bacteremia, non-infectious complications (hemorrhage, leaks, organ rupture, thrombosis, catheter self-extraction or malposition), other relevant findings (use of erythropoiesis-stimulating agents [ESA], antihypertensives, diuresis, phosphorus control, or hospitalization rates), and direct costs. Data extraction was performed using a form adapted from the Rapid Review Guide of the National Collaborating Centre for Methods and Tools[20], and findings were presented in summary tables.

The quality of evidence for observational studies was assessed using the Newcastle-Ottawa Scale (NOS)[23], the AMSTAR tool for systematic reviews[24], and the CHEERS checklist for economic studies[25].

For studies comparing USPD vs USHD, in which similarities in designs, interventions, comparators, endpoints, and follow-up were found, results were pooled using meta-analysis. Dichotomous outcomes were expressed as relative risks (RR) and continuous data with standardized mean differences, both with 95% confidence intervals (CI95%). Results were presented in tables and forest plots by author, year of publication, and country of origin. Adjusted effect estimates with CI95% from observational studies were combined and weighted using the generic inverse variance method. A random-effects model was preferred for observational studies due to the heterogeneity in study designs, patient profiles, and intervention characteristics, which may lead to high variance among studies. Heterogeneity was assessed using the chi-square test and the I^2 statistic. Meta-regressions were performed to evaluate the effect of some factors increasing heterogeneity by country, study design, dialysis modality, and catheter insertion technique for each outcome. STATA-16 software was used for meta-analysis functions. Egger's regression test was used to assess publication bias[26]. The certainty of the body of evidence was evaluated using the GRADE system[27]. A narrative synthesis of relevant aspects was used for economic studies.

Results

A total of 1303 articles were identified, of these, 16 were included in this review (Fig. 1). The selected studies were observational[22,28-38], including 3 economic studies[18,39,40] and 1 meta-analysis[7]. The main characteristics of the studies are presented in Table 1. A total of 2179 patients were included: 1087 in the USPD group, 915 in the USHD group, and 177 in the PD after USHD group. A total of 9 studies compared USPD vs USHD; 3 compared USPD with PD after USHD; 3 compared PD after USHD vs USHD, and 1 compared USPD with USHD and PD after USHD simultaneously.

The APD technique was reported in 5 studies, the CAPD technique in 1 study, and mixed PD techniques (APD, CAPD, DAPD, IPD) in 5 studies. Five studies did not report on the PD technique. The peritoneal catheter implantation technique was percutaneous in 3 studies and surgical in 9 (laparotomy or laparoscopic). Four studies did not report on the PD catheter implantation technique. The meta-analysis was conducted with 6 outcomes reported as dichotomous events and effect size as RR. GRADE tables are available in Appendix 2.

Mortality at six months and one year

Four observational studies (839 patients) evaluated all-cause mortality within the first six months[29,32,36,37]. The pooled estimate showed a 30% nonsignificant reduction in the 6-month mortality (RR, 0.70; CI95%, 0.48-1.01; I^2: 0%) (Fig. 1 in appendix 2). Five observational studies (1078 patients) evaluated all-cause mortality within the first year[29,34,36-38]. The pooled estimate demonstrated a 31% reduction in the 1-year mortality RR (RR, 0.69; CI95%, 0.51-0.92; I^2: 0%) (Fig. 2).

Dialysis-related complications

Four studies (894 patients) evaluated dialysis-related complications[29,34,36,37]. The pooled estimate demonstrated a 69% reduction in the RR of dialysis-related complications (RR, 0.31; CI95%, 0.20-0.48; I^2: 0%) (Fig. 3).

Infectious complications

Five studies (1078 patients) evaluated infectious complications[29,34,36-38]. The combined RR reduction in infectious complications was a non-statistically significant 51%

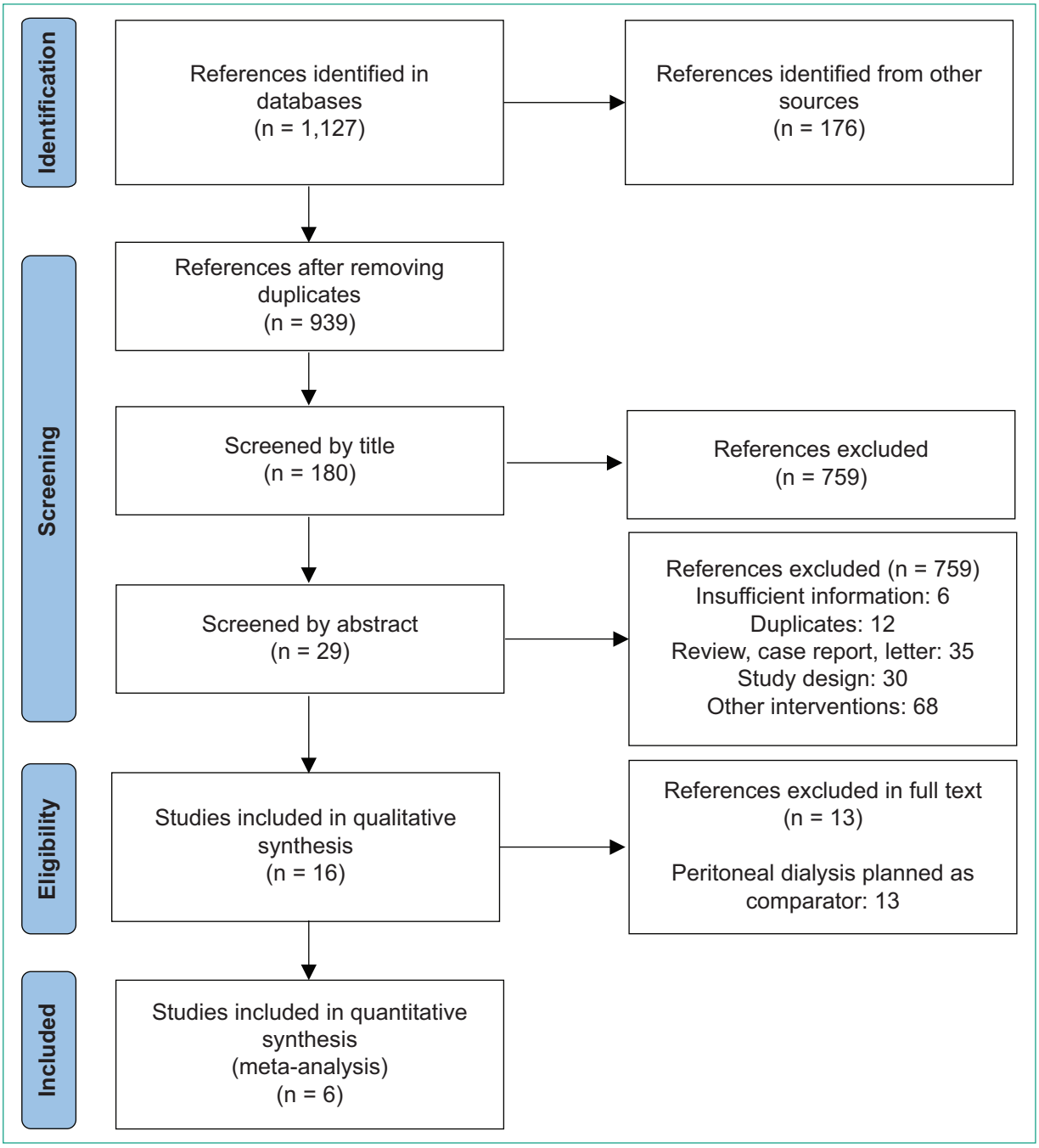

Figure 1. Literature search and selection.

(RR, 0.49; CI95%, 0.20-1.20; I^2: 63.8%). When considering only studies from China, the combined RR reduction was 69% (RR, 0.31; CI95%, 0.14-0.67; I^2: 0%) (Fig. 2).

Bacteremia

Five studies (1023 patients) evaluated bacteremia[29,32,36-38]. The pooled estimate showed a 72% reduction in the RR of bacteremia (RR, 0.28; CI95%, 0.16-0.47; I^2: 0%) (Fig. 3).

Non-infectious complications

Five studies (1078 patients) evaluated non-infectious complications[29,34,36-38]. The pooled estimate showed a 58% reduction in the RR of non-infectious complications

Table 1. Characteristics of the studies included

Author, year, country	Follow-up	Method	Intervention and PD modality	Comparator	PD catheter implantation	CASP quality assessment checklist	Quality assessment of studies
Lobbedez et al., 2008[31] France	– Up to 1.6 years – – Not reported mean follow-up	Prospective cohort study	– PD after USHD (n = 34) Modality of PD: APD	– USHD (n = 26)	– Surgical laparotomy	– 8/12 questions	High quality* – Selection 3 – Comparability 1 – Outcome 3
Koch et al., 2012[32] Germany	– Up to 0.5 years – 0.4 years on average	Prospective cohort study	– USPD (n = 57) Modality of PD: APD	– USHD (n = 57)	– Laparoscopic surgery	– 7/12 questions	Moderate quality* – Selection 3 – Comparability 1 – Outcome 2
Hernández et al., 2012[40] Mexico	Length of stay	Economic retrospective cohort study	– USPD (n = 25) Modality of PD: not reported	– PD after USHD (n = 25)	– Surgical laparotomy	– 7/12 questions	Moderate quality* – Selection 2 – Comparability 1 – Outcome 2
Liu et al., 2014[18] USA	– 0.25 years	Deterministic economic model	– USPD (dual) Modality of PD: not reported	– PD after USHD /dual) - USHD	– Not reported	– 6/12 questions	Evaluated with CHEERS
Ghaffari et al., 2015[33] USA	– 2.2 years on average	Prospective cohort study	– USPD (n = 78) Modality of PD: not reported	– USHD (n = 78)	– Not reported	– 7/12 questions	Moderate quality* – Selection 2 – Comparability 1 – Outcome 3
Jin et al., 2016[34] China	≥ 30 days – 1.6 years on average	Prospective cohort study	– USPD (n = 82) Modality of PD: APD, CAPD, DAPD, or IPD	– USHD (n = 82)	– Surgical laparotomy	– 7/12 questions	Moderate quality* – Selection 3 – Comparability 1 – Outcome 2
Li et al., 2017[35] Taiwan	– Up to 2 years – Follow-up not reported	Prospective cohort study	– PD AFTER USHD (n = 68) Modality of PD: CAPD	– USHD (n = 37)	– Surgical laparotomy	– 8/12 questions	High quality* – Selection 3 – Comparability 1 – Outcome 3
Brabo et al., 2018[41] Brazil	– 0.5 years	Economic prospective cohort study	– USPD (n = 20) Modality of PD: APD	– USHD (n = 20)	– Not reported	– 7/12 questions	Moderate quality* – Selection 3 – Comparability 1 – Outcome 2
Jin et al., 2018[36] China	≥ 30 days – Follow-up not reported	Prospective cohort study	– USPD (n = 41) Modality of PD: APD, CAPD, DAPD, or IPD	– USHD (n = 41)	– Surgical laparotomy	– 7/12 questions	Moderate quality* – Selection 3 – Comparability 1 – Outcome 2
Artunc et al., 2019[22] Germany	Up to 1 year	Prospective cohort study	– PD after USPD (n = 12) Modality of PD: APD	-PD after USHD (n = 6)	Surgical laparotomy	6/12 questions, Low quality	Selection: 2, Comparability: 0, Outcome: 1
Jin et al., 2019[38] China	≥ 30 days, average follow-up not reported	Prospective cohort study	USPD (n = 50), Modalities: ADP, DAPD, DAPD, IPD	-USHD (n = 30)	Surgical laparotomy	7/12 questions, Moderate quality	Selection: 3, Comparability: 1, Outcome: 2

(Continues)

Table 1. Characteristics of the studies included *(continued)*

Author, year, country	Follow-up	Method	Intervention and PD modality	Comparator	PD catheter implantation	CASP quality assessment checklist	Quality assessment of studies
Phang et al., 2019[28] Singapore	Not reported	Retrospective cohort study	USPD (n = 52), Modality not reported	PD after USHD (n = 26)	Not reported	7/12 questions, Moderate quality	Selection: 3, Comparability: 0, Outcome: 2
Bitencourt et al., 2020[17] Brazil	1.8 years on average	Prospective cohort study	USPD (n = 93), Modality: APD	USHD (n = 91)	Percutaneous	7/12 questions, High quality	Selection: 3, Comparability: 1, Outcome: 3
Wang et al., 2020[30] USA	Mean follow-up 1.25-1.5 years	Retrospective cohort study	PD after USHD (n = 18), Modality of PD: not reported	USHD (n = 18)	Not reported	7/12 questions, Moderate quality	Selection: 3, Comparability: 1, Outcome: 2
Xieyi et al., 2020[7] France, Germany, China, Taiwan	30 days 0.5 years, 1 year 2 years	Meta-analysis of 4 observational studies	USPD (n = 264)	HD-IU (n = 202)	3 studies not reported 1 study laparoscopic technique	8/12 questions, High quality	Evaluated with AMSTAR
Zang et al., 2020[29] China	Mean follow-up: 2 years	Retrospective cohort study	USPD (n = 309), Modality: DAPD	HD-IU (n = 233)	Percutaneous	8/12 questions,	High quality Selection: 3, Comparability: 2, Outcome: 2

*Newcastle-Ottawa Scale (NOS): the risk of bias was assessed based on 3 aspects: selection of the study group (0-4 points), comparability of the groups (0-2 points), and outcome measures (0-3 points). The overall quality of a study was defined as low (0-3 points), moderate (4-6 points), or high (7-9 points).
CASP: critical appraisal skills program; PD: peritoneal dialysis; APD: ambulatory peritoneal dialysis; CAPD: continuous ambulatory peritoneal dialysis; IPD: intermittent peritoneal dialysis; USPD: urgent-start peritoneal dialysis; USHD: urgent-start hemodialysis.

(RR, 0.42; CI95%, 0.24-0.73; I^2: 37.6%) (Fig. 4). Considering only studies from China, the meta-analysis showed that the risk of non-infectious complications was reduced by 67% (RR, 0.33; CI95%, 0.18-0.60; I^2: 0.5%).

Meta-regression analysis

A meta-regression analysis was performed to evaluate the effect of some factors increasing heterogeneity by country, study design, dialysis modality, and catheter insertion technique. Overall, there was no statistical evidence that any of these factors had an effect on the pooled estimate of the evaluated outcomes.

Other outcomes

Other clinical outcomes were reported in individual studies. Bitencourt et al.[38] showed that the USPD group vs the USHD group had a lower frequency of ESA use (25.8 vs 40.6%; p = 0.04), better diuresis at six months (700 vs 0.00 ml/day; p < 0.001), and phosphorus control levels < 5.5 mg/dL at six months (62.4 vs 41.8%; p = 0.008). The USPD group required fewer doses of erythropoietin (p < 0.001), phosphate binders (p < 0.001), and antihypertensives (p = 0.003), with statistically significant differences compared to USHD patients. Ghaffari et al.[33] showed a 43% higher adjusted hospitalization rate (RR, 1.43; CI95%, 1.105-1.849; p = 0.0045) and a 4.3 times higher adjusted bacteremia rate (RR, 4.32; CI95%, 1.48-12.62; p = 0.0074) in the USHD group vs the USPD. Jin et al.[34] showed that dialysis-related complications requiring catheter reinsertion (peritoneal catheter in USPD or CVC in USHD) were significantly lower in the USPD group (1.0 vs 24.4%; p < 0.001). Zang et al.[29] confirmed that 30-day complications requiring recatheterization were lower in USPD patients (1.6 vs 9.4%; p < 0.001).

Economic results

Due to the heterogeneous and scarce economic evidence obtained, the results are described narratively

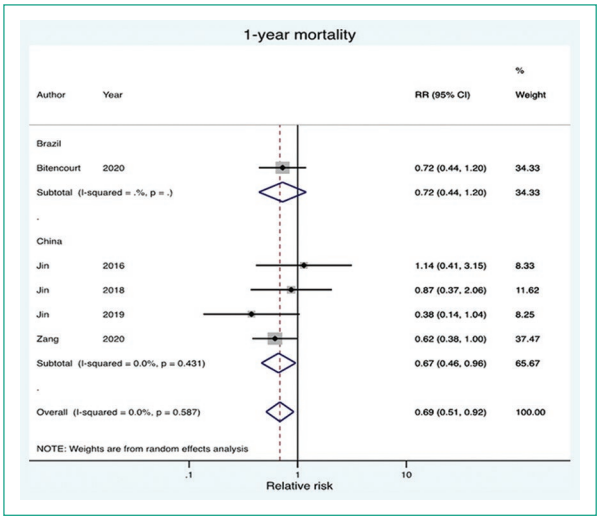

Figure 2. 1-Year mortality rate: USPD vs. USHD, urgent-start. USPD: urgent-start peritoneal dialysis; USHD: urgent-start hemodialysis.

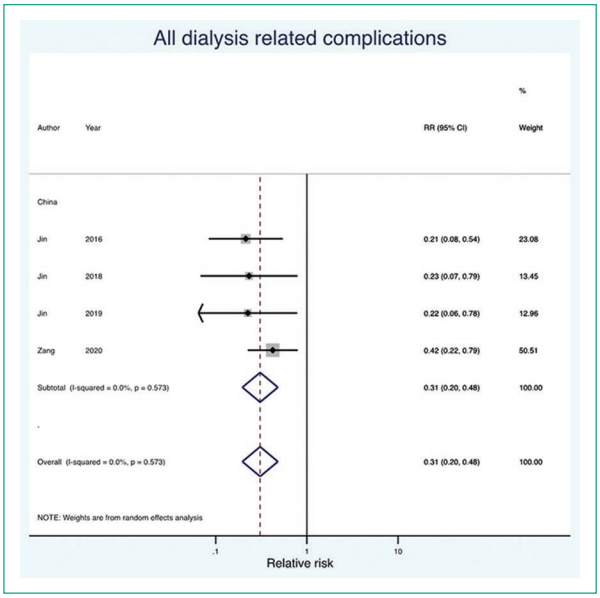

Figure 3. Dialysis-related complications: USPD vs. USHD. USPD: urgent-start peritoneal dialysis; USHD: urgent-start hemodialysis.

(see Appendix 2). From the Brazilian payer's perspective, Brabo et al.[40] compared USPD vs USHD and showed that overall direct costs at six months were similar between the groups ($6091.7 vs $6209; p = 0.45). However, an analysis of individual cost categories revealed different cost patterns between USPD and USHD. The main driver of direct costs by category was maintenance dialysis (80.3 vs 75.2%; p = 0.04), the

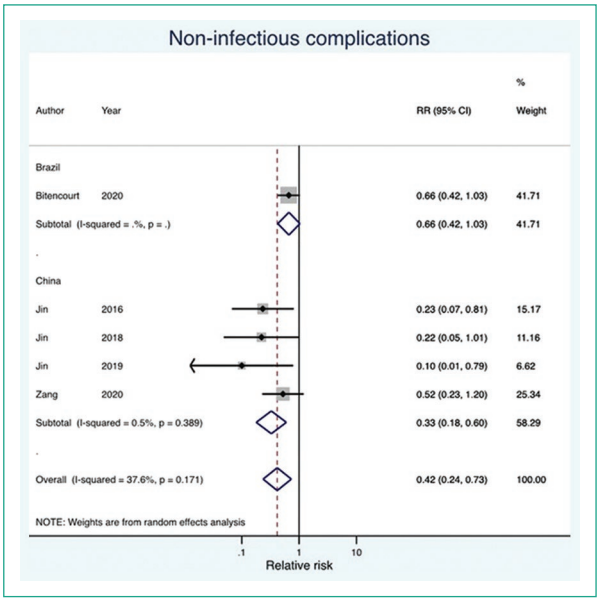

Figure 4. Non-infectious complications: USPD vs. USHD. USPD: urgent-start peritoneal dialysis; USHD: urgent-start hemodialysis.

length of stay (2.1 vs 0%; p < 0.001), the lab test results (1.7 vs 1.6%; p = 0.29), dialysis access/mechanical catheter complications (3.7 vs 9.3%; p < 0.001), antibiotic therapy (1.1 vs 2.54%; p = 0.94), and drugs (9.6 vs 12.3%; p = 0.15). There was a difference in the etiology of chronic kidney disease (diabetes in USPD 45 vs 10% in USHD; p = 0.03) that could be a relevant confounding factor for USPD.

Using a deterministic economic model, Liu et al.[18] estimated that over a 90-day time horizon, USPD could generate direct cost savings from the US payer's perspective vs USHD and PD after USHD. Resource utilization (personnel, supplies, drugs, and laboratories) and overhead costs were identified through interviews with staff at five dialysis clinics. When comparing cost categories between USPD vs USHD and PD after USHD. Potential differences in hospitalization costs and dialysis service costs were identified. Results showed that USPD was associated with the lowest costs within the first 90-day period. In the sensitivity analysis, the total cost of USPD ranged from $10,326 up to $20,446, USHD from $13,280 up to $23,400, and PD after USHD from $15,352 up to $27,496. Assumptions about the duration of initial hospitalization and infection rates had the most significant impact on costs. Even when model inputs were modified, including peritonitis rate, catheter replacement rate, duration of initial hospitalization, and supply and medication costs, USPD remained the lowest-cost modality.

Hernández et al.[39] showed that USPD vs PD after USHD was a cost-saving alternative from the Mexican public payer's perspective (total cost USPD $3645 vs PD after USHD $5710; p < 0.05). The cost of hospital beds (44% up to 45% of the overall cost), medical-surgical procedures (23% up to 27% of the overall cost), and diagnosis (10% up to 12% of the overall cost) were the main cost drivers, accounting for 80% or more of the total cost. In the generalized linear multivariate model, PD after USHD was independently associated with higher costs after controlling for demographics and comorbidities.

Certainty of the evidence and publication bias

The GRADE system was used to evaluate each meta-analysis outcome. Overall, the certainty of the evidence is low. This evidence comes only from observational studies. Groups were not fully comparable in terms of demographic and clinical characteristics, and selection bias was not consistently controlled. In some outcomes, heterogeneity reduced the certainty assessment. Egger's test showed strong suspicion of publication bias for bacteremia and infectious complications outcomes.

Discussion

This meta-analysis summarized the results of observational studies comparing USPD with USHD in adult ESRD patients. Overall, with low certainty, the risk-benefit balance of USPD is likely favorable vs USHD. There was a 31% reduction in 1-year mortality, a 69% reduction in all dialysis-related complications, and a 72% reduction in bacteremia risk. For 6-month mortality and infectious complications outcomes, the differences were not statistically significant. Other potential benefits associated with USPD described in the literature include a 37% reduction in ESA frequency and dosage, preservation of residual diuresis at six months, better phosphorus control at six months, fewer phosphate binder and antihypertensive doses, and fewer dialysis-related complications requiring catheter reinsertion[33,34,36-38]. These findings are relevant because USPD may imply a lower need to resolve complications and, therefore, lower resource use. Additionally, it offers patients a feasible and safe treatment that can predict kidney function recovery[38].

The growth of PD as a bridging therapy has advantages such as home implementation, no need to travel to a hemodialysis center, cost-effectiveness, reduced dietary restrictions, increased perception of freedom and patient satisfaction, less hemodynamic instability during dialysis, improved quality of life, and productivity[41]. Additionally, USPD improves the clearance of small and medium molecules and ultrafiltration in overloaded patients without affecting patient hemodynamics with a slow clearance rate compared to other dialysis modalities, providing adequate fill without causing organ ischemia[42].

Regarding economic impact, two studies showed that broader adoption of USPD could be a cost-saving alternative compared to USHD or PD after USHD. Economic findings are consistent with clinical results, reflecting how reducing dialysis complications could potentially affect resource use and costs. Considering that PD is less expensive than HD in some countries[14], broader practice of USPD could generate long-term savings. None of the economic evaluations indicated that USPD could increase healthcare system costs. Potential cost factors identified were mechanical catheter complications, infectious complications (bacteremia), length of stay, and chronic PD-HD treatment differences.

A similar meta-analysis by Xieyi et al.[7] showed that all-cause mortality could be reduced by 48% in the USPD group; however, this trend was not strong enough to demonstrate statistically significant differences (RR, 0.52; CI95%, 0.18-1.48) and heterogeneity was considerable (I^2: 73%; p = 0.01). The six-month rate of rehospitalization was similar between USPD and USHD (RR, 0.96; CI95%, 0.62-1.48). However, this meta-analysis demonstrated a significant 81% reduction in bacteremia risk in the USPD group (RR, 0.19; CI95%, 0.07-0.48), which is consistent with our results.

Factors interfering with the clinical implementation of USPD are related to wound healing or pericatheter tissue granulation, increasing the risk of leaks and other mechanical catheter complications[7]. Former guidelines recommended that PD should wait at least 15 days after catheter implantation to avoid risks, making USPD an unviable option for some patients[43,44]. However, this recommendation is based on weak evidence, and it is now known that fluid volume and intraperitoneal pressure are directly correlated with complications. Therefore, incremental PD using a small initial fill volume and proper USPD technique has drastically reduced catheter leakage[7].

Long-term survival of the USPD technique has shown good results, maintaining the patient in a safe modality.

A 10-year follow-up study of USPD patients reported a technique survival rate from 97.0% at 1 year to 58.8% at 10 years and catheter patency rates of 96.4% at 1 year and 96.2% at 3 and 5 years. During a median follow-up of 36.5 months (CI95%, 17.7-61.4), 14.1% were transferred to HD and 21% received a kidney transplant, making PD a sustainable long-term technique[15]. However, USPD programs are needed to ensure the advantages of USPD over USHD[45].

Successful USPD programs require multidisciplinary collaboration and commitment from the patient and caregivers to continue home therapy. The nephrologist or surgeon must be able to provide short-term catheter insertion, nursing staff must be prepared to perform PD and train the patient in a short time, social work or psychology must assess suitability for home PD, and administrative and nephrology leaders must promote the adoption of this practice[46]. However, in Latin America, challenges remain in nephrology due to the lack of training centers, barriers related to migration of those seeking training abroad, and inequity in the distribution of resources for health professional training[47].

Evidence on USPD practice is based on single-center observational studies with a significant risk of selection bias and confounding factors, limiting the results to showing association rather than causality. However, considering the long-term dialysis burden and the humanistic impact of therapy, randomization is not feasible because patient and caregiver preferences in dialysis modality selection must be considered. Additionally, blinding is not possible due to differences in techniques (USPD and USHD) and catheter characteristics. For these reasons, future evidence with better study designs is not expected, but better patient selection in these studies and more multicenter studies are needed.

Limitations of this study are that not all studies described the number of patients with diabetes or albumin levels, which are determinants of mortality in dialysis patients. In addition to the small number of studies included in the meta-analysis, most evidence came from Chinese cohorts, and other potential sources of gray literature were not considered, although the search strategy was highly sensitive, and the selection criteria were precise.

Future research should close evidence gaps by mitigating selection bias in observational studies through more robust statistical methods (propensity score matching) and maintaining consistency in follow-up periods, outcome definitions, and USPD technique standards to reduce study heterogeneity. Additionally, including other relevant outcomes supporting economic model conceptualization (indirect costs, cardiovascular events, rehospitalizations, length of stay, technique failure, survival, transplantation, quality of life, and utilities) is essential.

Conclusions

There is insufficient evidence to demonstrate that USPD increases the risk of complications for unplanned dialysis patients. On the contrary, there is an association between USPD and a lower risk of undesirable outcomes vs USHD with CVC. Available economic evidence, although heterogeneous and scarce, suggests no incremental impact on costs associated with the adoption of USPD.

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The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Patient's data protection. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Supplementary data

Supplementary data are available at DOI: 10.24875/NEFRO.23000053 . These data are provided by the

corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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REVIEW ARTICLE

Contributions to the creation of kidney health programs in Latin America, SLANH Kidney Health Committee

Aportes para la creación de programas de salud renal en Latinoamérica, Comité de Salud Renal de la SLANH

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Abstract

Chronic kidney disease (CKD) is silent and is characterized by its high prevalence, high morbidity and mortality, especially cardiovascular, and high health costs. In Latin America, the lack of resources and low awareness of the disease, not only in the population but also in health care teams, makes early diagnosis and timely treatment difficult. To reverse this reality, it is necessary to have kidney health care programs (KHP), designed and implemented by nephrologists in each country, focused on improving the health conditions of patients at risk or with CKD. This article develops Latin American strategies and experiences of proven effectiveness in the prevention of kidney disease collected by the Renal Health Committee of the Latin American Society of Nephrology and Hypertension (SLANH) and outlines fundamental steps for the implementation of a KHP adapted to the realities and resources of each country. There is a need to generate prevention policies, establish a strong educational component, create efficient CKD detection programs, and achieve timely and universal access to treatment.

Keywords: *Chronic kidney disease. Health plans and programs. Prevention. Latin America.*

Resumen

La enfermedad renal crónica (ERC) es silenciosa y se caracteriza por su elevada prevalencia, alta morbimortalidad, sobre todo cardiovascular, y altos costos en salud. En Latinoamérica la falta de recursos y la baja conciencia de la enfermedad,

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no solo en la población sino también en los equipos asistenciales, dificulta el diagnóstico temprano y el tratamiento oportuno. Para revertir esta realidad es necesario contar con programas de salud renal (PSR), diseñados e implementados por los nefrólogos de cada país, enfocados en mejorar las condiciones de salud de los pacientes con riesgo o portadores de ERC. En el presente artículo se exponen estrategias y experiencias latinoamericanas en la prevención de la enfermedad renal recogidas por el Comité de Salud Renal de la Sociedad Latinoamericana de Nefrología e Hipertensión (SLANH) y se delinean pasos fundamentales para la implementación de un programa de salud renal que deberán ser adaptados a las realidades y recursos de cada país. Se plantea la necesidad de generar políticas de prevención, establecer un fuerte componente educativo, gestar programas eficientes de detección de la ERC y lograr el acceso oportuno y universal al tratamiento.

Palabras clave: *Enfermedad renal crónica. Planes y programas de salud. Prevención. América Latina.*

Introduction

Chronic kidney disease (CKD) is a silent condition with high prevalence that causes significant morbidity and mortality, particularly cardiovascular, and results in high health care costs[1]. The figures related to CKD are especially concerning in Latin America (LA): the prevalence reaches 10.15%, the percentage of disability-adjusted life years (DALY) is estimated at 3.07%, and the annual mortality rate is 5.5%, compared to significantly lower global values of 9.5%, 1.5%, and 2.4%, respectively[2].

Additionally, the mean annual cost per patient on hemodialysis is USD 17,241, on peritoneal dialysis USD 15,846, and within the first year of kidney transplantation, USD 20,837. However, the per capita investment in health during 2021 was only USD 431, notably lower than the European per capita investment of USD 5088[2]. This results in heterogeneity in the prevalence of renal replacement therapy and even lack of access to treatment for a significant number of patients[3,4].

It has been demonstrated that the health actions of a structured renal health program (RHP) can stabilize and even improve renal function in most patients, and slow progression in others[5]. Early and timely diagnosis is essential and easily achievable through simple laboratory tests applied to high-risk populations, and current treatment is widely recognized and standardized.

For several decades, Latin American nephrology groups have been promoting various initiatives to prevent and treat CKD[6]. A rich history of registries[5,7], clinical practice guidelines[8], population and health care professional educational experiences[9-11], epidemiological studies and surveys, health policies to promote healthy lifestyles[12], and the application of new communication technologies such as telemedicine[13,14] have been generated. Prevention programs (regional, provincial, or national)[15-19] have been implemented and are currently at different stages of development.

This document from the Renal Health Committee of the Latin American Society of Nephrology and Hypertension (SLANH) provides concrete examples of various successful experiences and policies in the region, which can serve as an initial stimulus for the creation of an RHP in each country.

Towards the creation of a renal health program

Designing an RHP requires fulfilling a series of fundamental steps that must be adapted to the material and human resources of each country and their needs.

Definition of the target population and activities to be carried out

It is useful to define the population to which the RHP will be directed, particularly regarding the population that will require nephrological care, as well as the health policies directed at the general population and the population with renal risk factors.

- General population: Public health policies for the primary prevention of CKD, such as promoting healthy lifestyle habits (avoiding smoking, limiting salt and saturated and trans fats intake, encouraging the consumption of healthy foods and adequate physical activity), and screening programs for hypertension (HTN), diabetes (DM), and dyslipidemia, are shared with other non-communicable chronic diseases (NCDs) and are accompanied by population education campaigns. For example, in Argentina, there are campaigns to reduce alcohol intake[20] and promote healthy eating[21], and Uruguay has been a pioneer in the fight against smoking[22].
- Population with renal risk factors and screening: In this population with risk factors that have not yet developed CKD, there is rich experience in primary prevention policies and development of clinical practice guidelines for controlling these factors. Screening in CKD risk populations is the most cost-effective

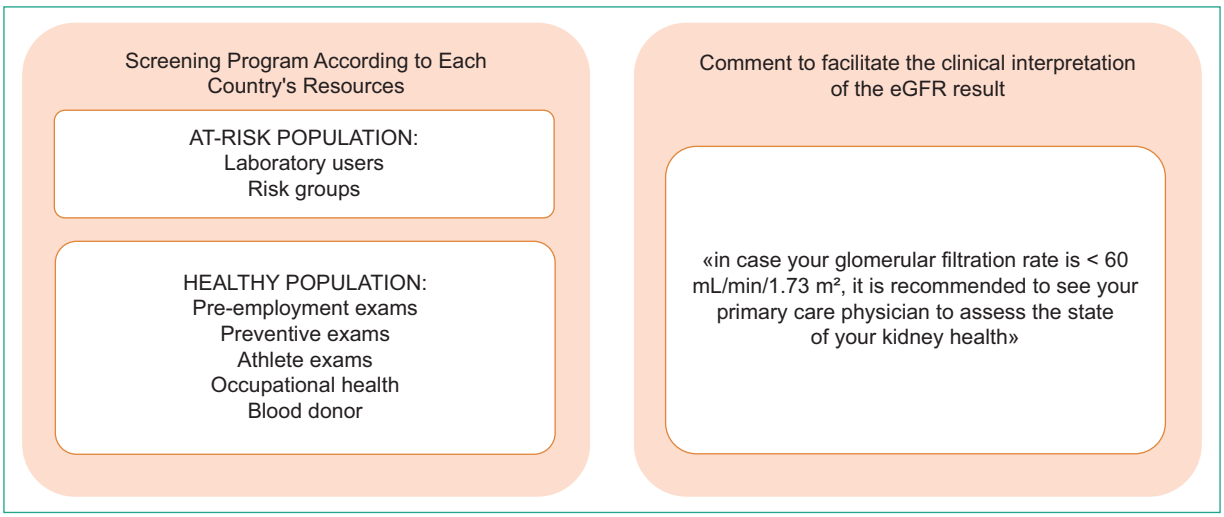

Figure 1. Early detection and standardization of the follow-up path for screened patients. Each country will define the target population for screening according to its resources and needs. The follow-up path for screened patients must be clearly established. eGFR: estimated glomerular filtration rate.

strategy[23], but few countries adopt strategies directed at the general population[24,25]. The screening program is usually linked to the DBT, HTN, and other NCD detection programs available in the country. Some Latin American countries promote screening in patients who have a spontaneous medical consultation, while others promote it in specific population groups, for example, those older than 60 years old, diabetics, or hypertensives (Fig. 1). In Uruguay, urine tests are conducted in the general population older than 18 years old[25], while in Chile, Colombia, Mexico, and Peru, patients with risk factors, mainly diabetics and hypertensives, are prioritized[10,16,18,19].

– Population with established CKD (secondary and tertiary prevention). Most Latin American countries follow the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines[26] and the Latin American Clinical Practice Guideline on CKD[8] to define and classify CKD, i.e., the presence of alterations in kidney structure or function lasting more than three months. Glomerular filtration rate (GFR) and albuminuria are the main determinants of the risk of death and kidney failure. The stage of CKD and its etiology are useful for planning care, defining management and prognosis[27,28]. Establishing the level of medical care, identifying the group of patients requiring nephrological care, therapeutic objectives, and the number of consultations per period for each stage also contributes to planning adequate management and follow-up[27]. Another useful prognostic tool is the Kidney Failure Risk Equation (KFRE), which helps identify patients at higher risk of end-stage kidney disease at 2 and 5 years[29], although it may need to be validated for our region, as shown by its application in Peru[30].

Systematization of the diagnostic methodology

Regarding CKD screening, we follow the SLANH-COLABIOCLI recommendations[31], which include:

– Estimating GFR from serum creatinine determination using the CKD-EPI 2021 equation (if creatinine determination is standardized), or the MDRD4 factor 186 equation (if creatinine determination is not standardized).
– Recommending that clinical laboratories always report the estimated GFR using equations along with the serum creatinine concentration report, even if not requested by the physician, as this allows early recognition of patients with reduced renal function (Fig. 2).
– Promoting clinical laboratories to establish processes for standardizing serum creatinine and for internal and external quality control to improve the quality of the results.

Furthermore, it is suggested to assess the presence of albuminuria and/or proteinuria using the albuminuria/creatininuria or proteinuria/creatininuria ratio, 24-hour proteinuria, or the presence of total proteins or albumin on urine dipsticks or test strips, in decreasing order of measurement reliability[32].

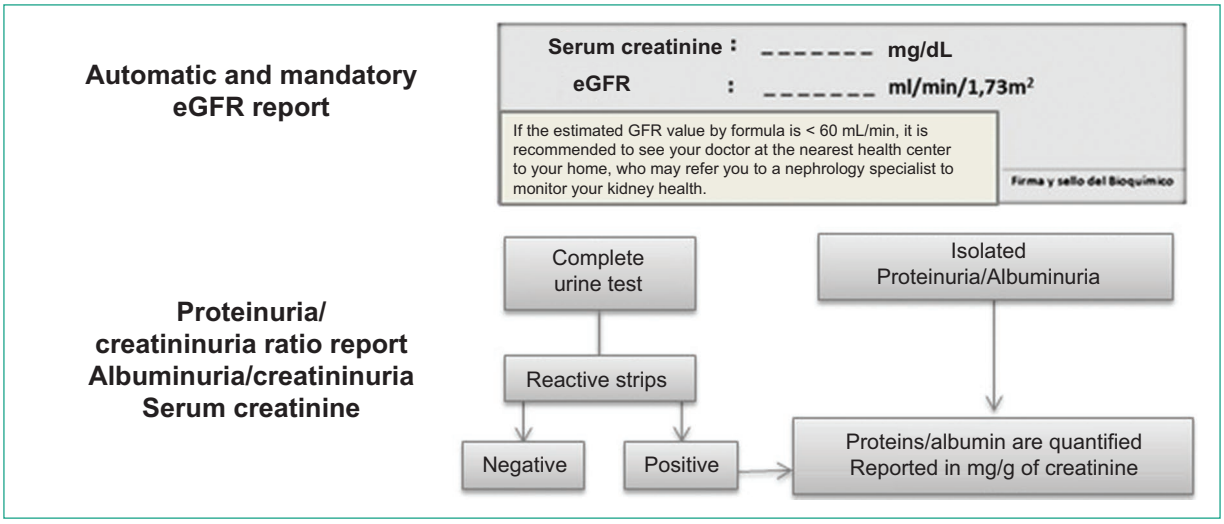

Figure 2. Systematization of the methodology for diagnosing chronic kidney disease. Automatically and mandatorily reporting eGFR by laboratories each time creatinine is determined is the key to the universal diagnosis of chronic kidney disease. It alerts the non-specialist doctor that the patient may have an underlying kidney problem. Proteinuria is an early marker of kidney damage and cardiovascular risk, and its systematic quantification is low-cost. eGFR: estimated glomerular filtration rate.

Structuring medical care and follow-up of patients with chronic kidney disease

It is desirable to clearly establish the pathway that a patient with detected CKD should follow. Given the limited number of nephrologists in LA, the initial assessment is likely to be carried out by the first-contact physician trained to determine the diagnosis, stage, and etiology of CKD. According to protocols, this physician will decide which patients require nephrological evaluation and who will continue under their care.

The commission leading the RHP generally outlines these referral protocols to the nephrologist (Fig. 3).

Chronic kidney disease integrated into other health care/timely referral to nephrology

Patients in the early stages of CKD are usually followed by primary care teams. The referral criteria to a nephrologist should consider not only the CKD stage but also its progression, the impact on the internal environment, and the etiology. Proteinuric nephropathies can progress rapidly and should be evaluated promptly by a specialist. Obstructive nephropathies will require urological attention.

Therefore, in countries like Peru[18], social security proposes coordinated management between primary care, responsible for patients in stages 1, 2, and 3a, and nephrologists, who take care of patients in CKD stages 3b, 4, 5, and certain nephropathies that specifically require nephrological care. In Colombia RHP[16], patients in CKD stages 1 and 2 are managed at the first level of care, and patients with an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 or with high-risk factors for CKD progression are referred for continued treatment with the multidisciplinary team led by the nephrologist.

A network of alerts and referrals to specialists for advanced cases or those requiring specific treatments implies organizing a referral and counter-referral system (both physical and virtual) and defining protocolized warning signs to send patients to nephrology, according to the available nephrological resources[17].

Advanced chronic kidney disease clinics

In patients at higher risk of progression, nephrological follow-up is associated with improved health outcomes. For example, in the KHP (kidney health care program) of Uruguay, in advanced chronic kidney disease (CKD) clinics (ERCA)[5], kidney function was stabilized in more than 50% of patients in stages 4-5. Establishing which patients will be referred to these clinics is crucial; for instance, patients with an eGFR < 30 mL/min/1.73 m^2, those with significant proteinuria, or those who progress despite correctly established treatment could be referred. These clinics are generally

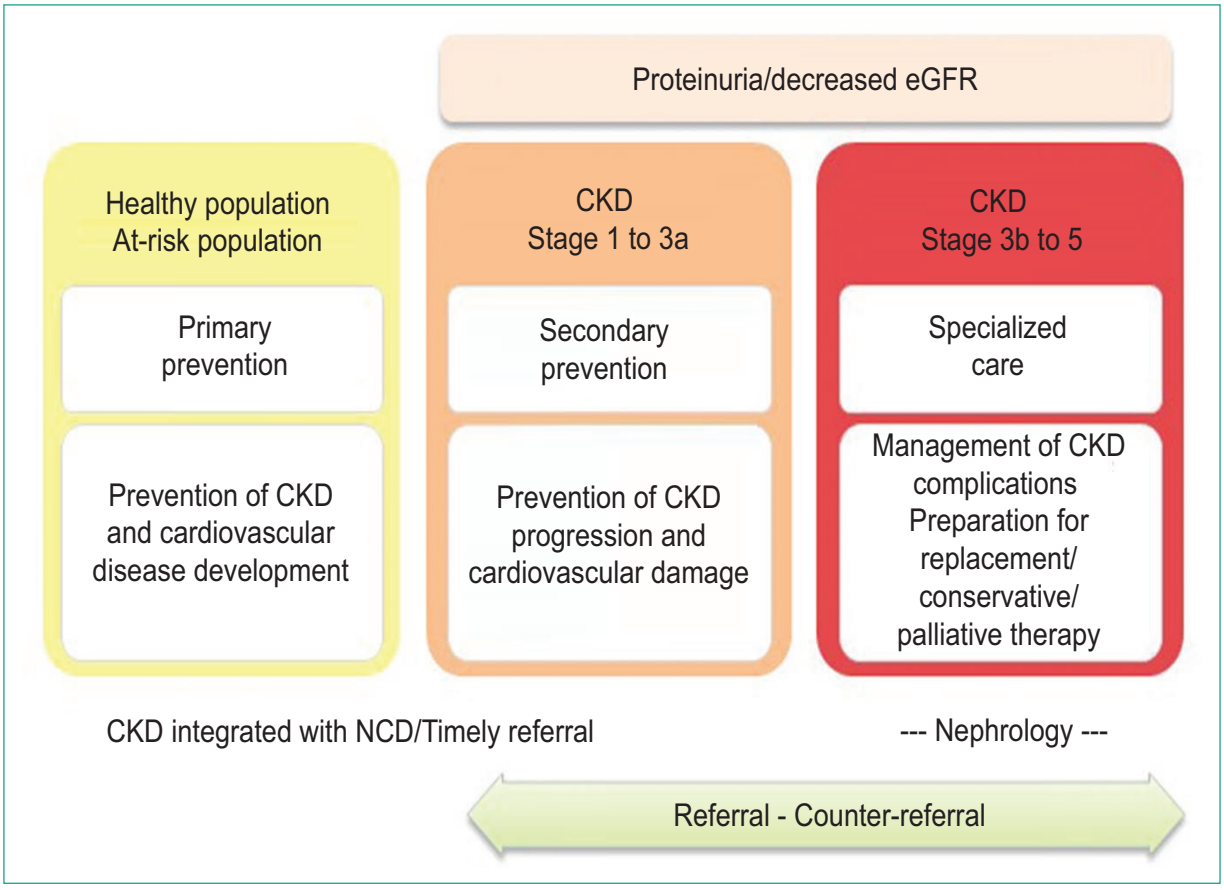

Figure 3. Structure of CKD prevention. The renal health program should plan actions grouped according to the stage* of CKD, covering from primary to specialized care. Initial stages can be managed by the primary level of care. Patients at higher risk of progression, needing specific treatment, and advanced stages benefit from nephrology follow-up. A coordinated referral/counter-referral system across different levels ensures continuity of care. NCD: non-communicable chronic disease; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate.
*Stages according to KDIGO 2012 guidelines.

multidisciplinary, composed of professionals specializing in the care of CKD patients (nephrologist, nurse, and nutritionist); they have access to basic tests (creatinine, blood count, blood glucose, sodium, potassium, chloride, glycosylated hemoglobin, serum calcium determination, phosphorus, parathyroid hormone, blood gas analysis, urinary tract ultrasound with post-void residual measurement), and histopathological studies. Additionally, they coordinate entry into renal replacement therapy or palliative care when necessary (Fig. 4).

Tele-nephrology: A strategy to improve access to nephrologists for people with chronic kidney disease from primary care

There is a growing number of publications related to telemedicine and particularly to tele-nephrology, reflecting the increasing interest in incorporating digitalization, especially in the prevention and comprehensive management of CKD[14,33]. Published reports indicate that telematic care would facilitate access, timely evaluation, and treatment of patients referred from the first level of care (FLC) (especially in rural areas) to the nephrologist and would allow prioritizing the face-to-face evaluation of those at higher risk or severity[34]. Similarly, telematic education for health teams by specialists would strengthen promotion, prevention, and care actions for CKD. The incorporation of this strategy in the cities of Concepción and Talcahuano in southern Chile[14] reduced the waiting time for specialist care from 225 days down to 2.5 days for telematic care and to 30 days for face-to-face care. A total of 57.3% of the evaluated patients did not require face-to-face evaluation by the nephrologist and were referred to the FLC

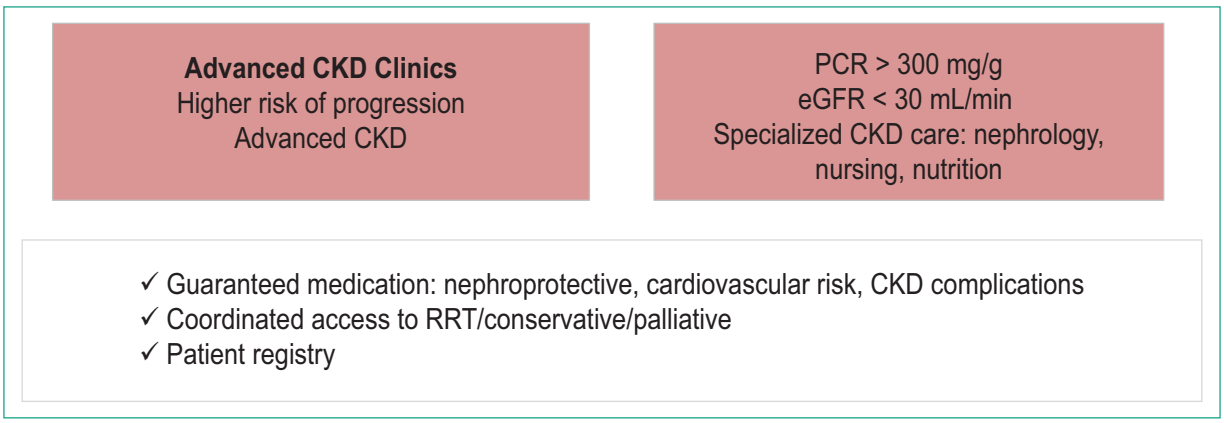

Figure 4. Advanced CKD clinics. In patients at higher risk of progression and with advanced CKD, nephrology follow-up is associated with improved health outcomes. The management of complications and final access to renal replacement therapy, palliative care, or conservative treatment should be coordinated by the nephrologist, ideally in multidisciplinary clinics (advanced CKD clinics), integrated by professionals specializing in the care of CKD patients (at least one nephrologist, nurse, and nutritionist). PCR: proteinuria/creatininuria ratio; advanced CKD: advanced chronic kidney disease; eGFR: estimated glomerular filtration rate; RRT: renal replacement therapy.

with therapeutic recommendations from the specialist. Timely telematic referral of patients with CKD stage 4-5 increased the choice of peritoneal dialysis from 5% up to 16.3%, the entry into hemodialysis with arteriovenous fistula from 28.3% up to 60.3% and minimized emergency dialysis entry without prior evaluation down to 0.9%. The satisfaction evaluation of the use of tele-nephrology by FLC doctors was 87%. SLANH, through its Renal Health Committee, has proposed promoting the use of digital technology for the management of CKD in the region[35].

Universal access to nephroprotective medication

Nephrologists must ensure that health authorities become aware that patients with established CKD should access nephroprotective medication at all stages of the disease: blockers of the renin-angiotensin-aldosterone system and other antihypertensives, statins, oral antidiabetics, and insulin. Sodium-glucose cotransporter type 2 inhibitors and other new drugs that have been shown to alter CKD progression and cardiovascular mortality should also be included. The release of payment for these drugs was used as an incentive for medical care centers to meet KHP indicators in Uruguay[17].

Information recording and outcome evaluation

Registers are an essential tool from both an epidemiological perspective and for evaluating the program as a whole and each renal health team individually[36]. They allow a real estimation of the nephrological problem and the corresponding health demand, patient follow-up, alerts and alarm generation, resource allocation (materials, human, organizational), and actions.

Adherence to the KHP by patients reduced the risk of progression and death[37]. A patient lost to follow-up has up to a 30% higher risk of death or earlier dialysis entry vs another patient in regular follow-up[5]. By recording consultations, patients lost to follow-up can be identified, and different appointment modalities (e.g., phone calls, SMS messages, emails, applications) can be used.

Four LA countries have registers of patients with CKD stages 1 to 5 without dialysis. The main difficulties are related to interoperability with the electronic health record, unification and governance, and the security of recorded data[38].

The stages of CKD included in the registry are defined according to the program target population. The data to be recorded will be performance indicators, and it is suggested to seek a balance between recording capacity and measurement precision (Fig. 5).

Communication and educational strategies

– Aimed at the general population. These are information strategies on the importance of kidney health and actions that contribute to the detection and proper management of CKD, aimed at all people, with an emphasis on those at risk of developing CKD. World Kidney Day is an appropriate and emblematic

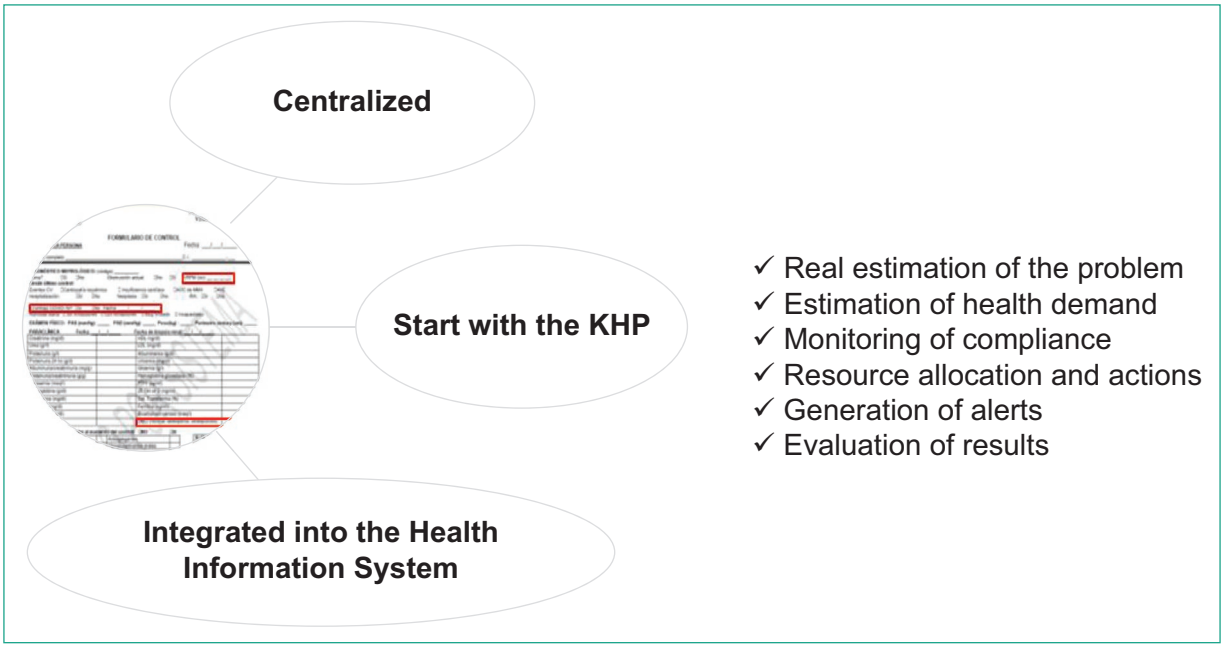

Figure 5. Importance of chronic kidney disease registries. Registries are an essential tool from both an epidemiological perspective and for evaluating the program as a whole and each renal health team individually. They allow the real estimation of the nephrological problem and the consequent health demand, follow-up of patients, generation of alerts and alarms, allocation of resources, and taking actions. KHP: kidney health care program.

date for such campaigns, which can include the promotion of health activities and dissemination in community participation spaces, press, radio, TV, and social media. Content and reminders in mass media. Training, promotion, and education workshops for CKD patients aimed at patients and caregivers.

– Aimed at the health care personnel. Continuous training of health teams at different stages of their training and care or management activity. Incorporation of concepts such as CKD as a cardiovascular risk factor, the need for early detection, and criteria for referral to nephrology, in the curriculum of medical, nutrition, nursing, biochemistry, and other related health science faculties and schools[39,40].

Sustainability and governance

It is essential that the KHP of each country achieves broad support from health authorities and the national (or local) nephrology community to ensure its longevity. Several experiences in Latin America (LA) confirm this[16,17].

– National Advisory Commission on Renal Health (CNASR). Experiences in this regard included the formation of a high-level nephrology working group which, together with health authorities, care centers, and with the support of patient organizations, will be responsible for designing and managing the KHP, as well as advising on the promotion of public health policies.
– Legal support and endorsement. Promoting a Renal Health Act or Decree that recognizes the KHP and CNASR, mandates CKD screening according to defined methodology, and even requires reporting high-risk ERCA situations to the Ministry of Health (e.g., cases of glomerulopathies or CKD stage 4 or 5).
– Public health policies. The promotion of population health policies through laws or decrees has seen significant development in several LA countries with nephrologist participation: anti-tobacco laws, reduction of sodium, saturated/trans fats, and sugar content in foods, front-of-package food labeling, and encouraging physical exercise at early ages[20,21].

One tool is the Framework Convention sponsored by the World Health Organization (WHO), which is in effect in 21 countries in Latin America and the Caribbean[41]. Regarding salt reduction in foods, the Pan American Health Organization (PAHO)-WHO established a regional social marketing and communication plan in 2015, with a series of creative concepts and communication strategies aimed at reducing the demand for salt and ingredients with high sodium content used in the preparation and consumption of foods in Latin American households[42].

Ten countries in Latin America and the Caribbean have passed legislation or regulations to address the increase in overweight and obesity, such as front-of-package nutritional labeling, which informs consumers about the nutritional content of food products and promotes the reduction of consumption of products with excessive critical nutrients[43].

Pilot program

Starting the KHP with a pilot experience, implemented by the CNASR, in a defined and reduced territory has been useful[17,44]. This pilot program has allowed for the implementation of all aspects related to the proper functioning of the KHP, evaluation of results, and necessary corrections. It requires ensuring financial and institutional support for its development.

Conclusions

Developing a KHP is a tough but immensely rewarding task, in which nephrologists must take the initiative, form a broad and committed working group, and work alongside national health authorities to create a series of conditions and measures that lead to improved renal health and quality of care for the population. This is not a one-day task; it requires a permanent working group to investigate and analyze the national nephrological situation and propose solutions appropriate to reality. CKD should be understood within the framework of NCDs and actions should be planned in that context, without neglecting its particularities. Improvement in the quality of care for CKD patients can be quickly reflected if information and results are adequately collected.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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CASE REPORT

Endovascular salvage of dysfunctional hemodialysis tunneled catheter in a patient with vascular access exhaustion

Salvamento endovascular de catéter tunelizado disfuncional para hemodiálisis en una paciente con agotamiento de accesos vasculares

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Abstract

Vascular access exhaustion is common in hemodialysis patients. It is important to have vascular access options for dialysis. The most common cause of tunneled catheter dysfunction is fibrin sheath formation. We report the case of a morbidly obese patient with exhaustion of vascular access who presents a dysfunctional tunneled catheter due to displacement of one of its branches and fibrin sheath that occludes the superior vena cava. Using an endovascular technique, the functionality of the catheter was recovered without the need to change it. The patient is on hemodialysis without complications.

Keywords: *Vascular access. Hemodialysis. Endovascular. Fibrin sheath.*

Resumen

El agotamiento de accesos vasculares es frecuente en los pacientes en hemodiálisis. Es importante tener opciones de acceso vascular para la diálisis. La causa más frecuente de disfunción de un catéter tunelizado es la formación de vaina de fibrina. Reportamos el caso de una paciente obesa mórbida, con agotamiento de accesos vasculares que presenta un catéter tunelizado disfuncionante por desplazamiento de una de sus ramas y vaina de fibrina que ocluye la vena cava superior. Mediante técnica endovascular se recuperó la funcionalidad del catéter, sin necesidad de cambiarlo. La paciente se encuentra en hemodiálisis sin complicaciones.

Palabras clave: *Acceso vascular. Hemodiálisis. Endovascular. Vaina de fibrina.*

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Introduction

Progressively increasing numbers and age of the hemodialysis population, along with improvements in nephrological care, lead to the belief that the number of patients with exhausted dialysis accesses will increase over time[1]. Patients with year-long dialysis through catheters often develop stenoses or central vein occlusions, and those dialyzed through native or prosthetic vascular accesses have depleted veins in their upper limbs[2].

The most common cause of hemodialysis catheter dysfunction is the formation of a fibrin sheath, which is composed of fibrinogen, lipoproteins, albumin, and coagulation factors and begins to form within 24 h of catheter placement[3].

The fibrin sheath covers the inlet and outlet orifices of the hemodialysis catheter, acting as a 1-way valve[4]. This deteriorates the quality of hemodialysis, triggering issues such as difficulty in aspiration despite being able to inject the catheter or else the impossibility of both due to catheter occlusion.

Dysfunctional catheters are often treated by exchanging them. However, this carries the risk of scarring, venous stenosis, potential loss of valuable access, and the risk of infection[5]. Endovascular removal of the fibrin sheath (fibrin sheath stripping) may be a better option if it was more readily available and cost-effective.

This is a case of a morbidly obese woman with exhausted vascular accesses due to central and peripheral vein occlusions and a dysfunctional left subclavian tunneled catheter due to displacement of one of its branches and a fibrin sheath occluding the superior vena cava (SVC). The arterial branch of the catheter was relocated, balloon angioplasty was performed to recanalize the superior vena cava and the peri-catheter fibrin sheath was removed with an endovascular snare, recovering the functionality of the catheter without having to change it.

Case report

A 65-year-old morbidly obese woman with a medical history of multiple catheter implants in the internal jugular, subclavian, and femoral veins, and occlusion of several native and prosthetic vascular accesses in both upper limbs was referred to our center with a dysfunctional tunneled catheter for hemodialysis (Tesio®). The catheter had been implanted in 2021 in the left subclavian vein due to the occlusion of both internal jugular veins in a procedure that required previous angioplasty with stenting in the left innominate trunk and SVC due to central venous occlusion, which ended up working properly (flow > 300 mL/min) for 16 months. In the dialysis center, catheter positioning maneuvers and vigorous saline infusion were performed without success, which is why the patient was referred for interventional treatment.

Fluoroscopy revealed the displacement of the catheter arterial branch (Fig. 1A).

Arterial branch aspiration with a 20 cc syringe was negative for obtaining blood.

Transcatheter phlebography revealed the occlusion of the SVC, and the retrograde contrast reflow along the catheter axis, which is characteristic of fibrin sheath formation. Retrograde flow was also seen in the azygos vein (Fig. 1B).

Therapeutic strategy

Ultrasound-guided puncture of the right common femoral vein was performed, followed by the insertion of an 8-Fr introducer sheath.

The attempts to cross the occlusion of the SVC with a 0.035 in hydrophilic Guidewire (Terumo®) through the distal orifice of the displaced branch proved unsuccessful. Afterward, the SVC was recanalized using the 0.035 in hydrophilic Guidewire through a lateral orifice in the displaced branch. The Guidewire was then externalized with a 15 mm endovascular snare (Amplatz Goose Neck, Medtronic) through the femoral introducer sheath to create a stable connection between the displaced branch and the femoral introducer sheath (through and through). An 8 mm × 40 mm balloon (Oceanus 35, iVascular) was advanced over the 0.035 in Guidewire to the displaced branch lateral orifice and inflated to 20 atm (Fig. 2A) to break the fibrin sheath and allow the catheter to descend and be repositioned using the endovascular snare. Afterward, the 0.035 in Guidewire was redirected through the distal orifice of the displaced branch and again externalized through the femoral introducer sheath. Afterward, a 10 mm × 40 mm balloon (Oceanus 35, iVascular) was advanced toward the catheter branch distal orifice and inflated at 12 atm (Fig. 2A). Finally, the displaced branch was correctly repositioned at the cavoatrial junction using the endovascular snare, and fibrin sheath stripping was performed on both catheter branches (Fig. 2B). The snare was, then, advanced as high as possible around the catheter axis in the SVC. Multiple passes were made with the snare around the axis of both catheter branches.

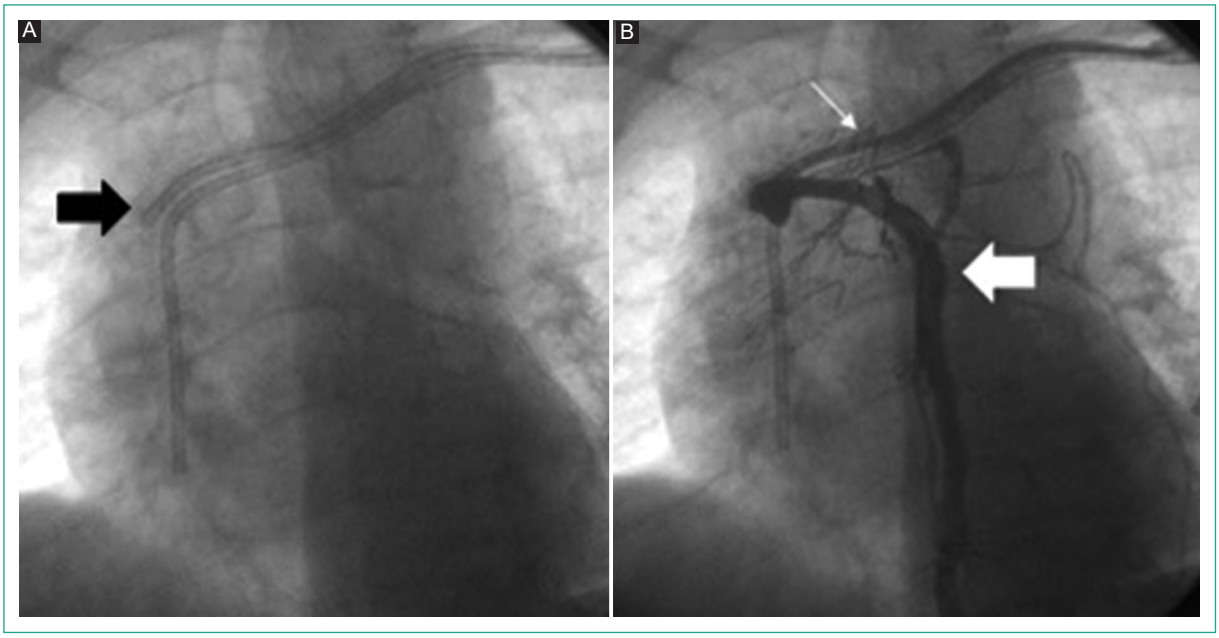

Figure 1. A: displacement of the tunnelized catheter arterial branch (black arrow). **B:** transcatheter phlebography: occlusion of the superior vena cava and retrograde contrast reflow along the catheter axis (thin white arrow). Azygos vein with retrograde flow (thick white arrow).

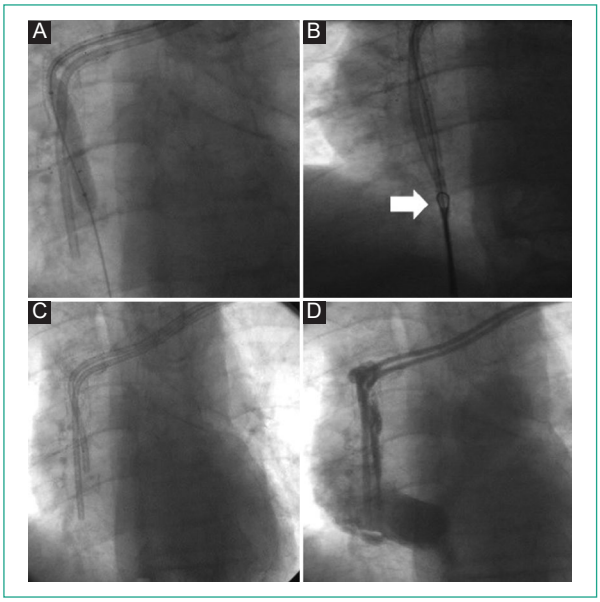

Figure 2. A: rupture of the fibrin sheath with balloon angioplasty. **B:** extraction of the fibrin sheath with an endovascular snare system (arrow). **C:** proper positioning of both catheter branches. **D:** transcatheter phlebography: Rapid jet flow running through the catheter orifices with resolution of the fibrin sheath.

The follow-up fluoroscopy showed the proper position of both catheter branches (Fig. 2C), and the transcatheter phlebography confirmed the rapid flow through the catheter orifices with the resolution of the fibrin sheath (Fig. 2D).

The patient did not experience any postoperative decrease in oxygen saturation.

Afterward, the patient was referred for hemodialysis with significant improvement in catheter flow to up to 300 mL/min. Proper catheter flow remained (> 300 mL/min) at the 12-month follow-up.

Discussion

The increased prevalence of patients with advanced chronic kidney disease who require hemodialysis, along with the aging of the hemodialysis population has led to a greater recognition of vascular access-related complications. In this context, the development of central venous stenoses or occlusions and the depletion of peripheral veins have led to the development of various techniques for creating vascular accesses[6].

Patients with exhausted vascular accesses have several options available, including various types of catheters (transfemoral, translumbar, transhepatic, and transatrial), various surgical techniques, and peritoneal dialysis[6].

In our case, we decided, together with nephrologists and vascular surgeons, to recover the dysfunctional catheter because the patient was old, morbidly obese, had exhausted

vascular accesses, and presented a high surgical risk for last-resort vascular access procedures.

The medical literature currently available on fibrin sheath stripping is mainly represented in the form of uncontrolled case reports, and case series reports with good safety rates and short-term success; however, long-term data on efficacy are lacking[7].

Conclusion

Most patients on hemodialysis undergo multiple catheter exchanges, and efforts should only be made to exchange the catheter when all other measures have failed. Venous stenosis, scarring, the formation of new tunnels, the potential loss of venous access, and patient anxiety are unwanted factors involved in catheter exchange. Performing complex endovascular techniques by interventionists trained in this condition may result in fewer catheter exchanges, especially in patients like the one described in our case, who lacked patent central and peripheral veins for vascular access formation in the upper limbs.

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Ethical disclosures

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Targeting the right spot: atypical presentation of infection in kidney transplant recipient

Apuntando al punto: presentación atípica de infección en un receptor de trasplante de riñón

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Introduction

Transplant recipients are at higher infection risk. Ecthyma gangrenosum occurs in the setting of severe Pseudomonas aeruginosa infection with bacteremia[1,2]. Immediate diagnosis is crucial[3].

Case

A 49-year-old kidney transplant recipient presented fever (T: 38.5°C), an abdominal pustule of 2 cm (Fig. 1), leukopenia (2.400/uL), and C-reactive protein of 4.7 mg/dL. Despite cefixime treatment, the lesion worsened (Fig. 2). Blood cultures confirmed P. aeruginosa with undetermined entry site. After 1 week, the

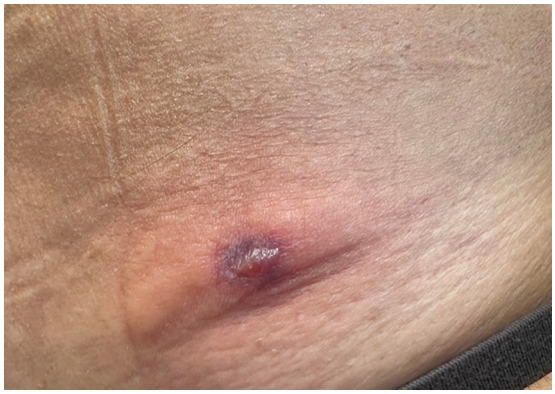

Figure 1. Ecthyma gangrenosum presenting with gunmetal gray, infarcted papule with surrounding erythema.

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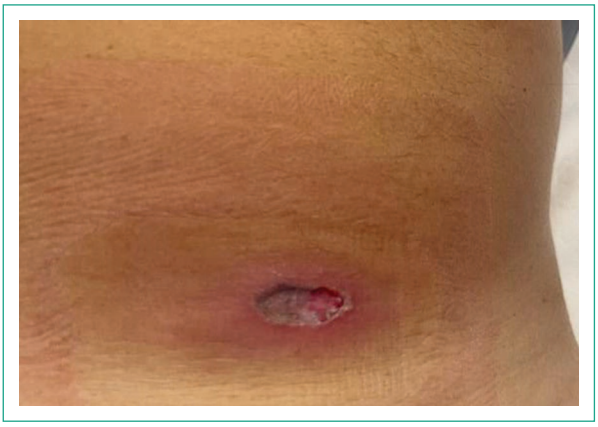

Figure 2. Ecthyma gangrenosum evolved into ulcerative eschar with erythematous halo.

ecthyma gangrenosum developed a necrotic, ulcerative eschar, and erythematous halo and worsening leukopenia (850/uL) and elevated C-reactive protein (7 mg/dL). Ceftazidime treatment led to recovery.

Conclusion

Early ecthyma gangrenosum recognition guides effective treatment[2]. Infection entry point detection may be especially challenging in immunosuppressed patients. Vigilant monitoring mitigates life-threatening risks associated with pseudomonas infection[2].

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Conflicts of interest

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Ethical disclosures

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