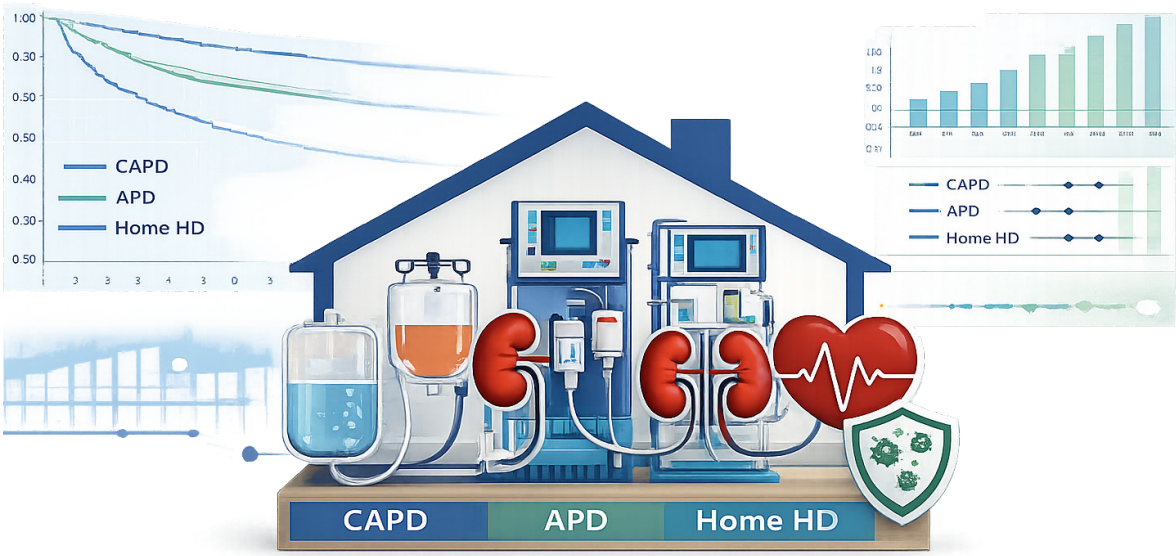


OUTCOMES OF HOME DIALYSIS MODALITIES

A comparative analysis of survival, infections, and cardiovascular events

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A COMPARATIVE ANALYSIS OF SURVIVAL, INFECTIONS, AND CARDIOVASCULAR EVENTS

Wisam Bitar

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To my parents and teachers, and to the cherished memory of my godfather

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LIST OF PUBLICATIONS

This thesis is based on the following publications:

I. Bitar W, Helve J, Honkanen E, Rauta V, Haapio M, Finne P. Similar survival on home haemodialysis and automated peritoneal dialysis: an inception cohort study. Nephrol Dial Transplant. 2022 Jul 26; doi:10.1093/ndt/gfab233.

II. Bitar W, Helve J, Kanerva M, Honkanen E, Rauta V, Haapio M, Finne P. Severe infections in peritoneal dialysis and home hemodialysis patients: an inception cohort study. PLoS One. 2023 Jun 14; doi:10.1371/journal.pone.0286579.

III. Bitar W, Helve J, Haapio M, Rauta V, Honkanen E, Finne P. Risk of major adverse cardiovascular events in home dialysis compared with in-center hemodialysis. Clin J Am Soc Nephrol. 2025 Jan 1; doi:10.2215/CJN.0000000579.

The publications are referred to in the text by their Roman numerals.

ABBREVIATIONS

ANOVA	Analysis of Variance
ANZDAT	Australia and New Zealand Dialysis and Transplant registry
APD	Automated peritoneal dialysis
AVF	Arteriovenous fistula
BP	Blood pressure
bpm	Beat per minute
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CAPD	Continuous ambulatory peritoneal dialysis
CI	Confidence intervals
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
CVA	Cerebrovascular accident
EKG	Electrocardiogram
ERA	European Renal Association
ESKD	End-stage kidney disease
FU	Follow-up
GFR	Glomerular filtration rate
HD	Hemodialysis
Home HD	Home hemodialysis
HR	Hazard ratio
In-center HD	In-center hemodialysis
IR	Incidence rate
IRR	Incidence rate ratio
ISPD	International Society for Peritoneal Dialysis
KDIGO	Kidney Disease: Improving Global Outcomes
KRT	Kidney replacement therapy
LBBB	Left bundle branch block
LVEDD	Left ventricular end diastolic diameter
LVESD	Left ventricular end systolic diameter
LVH	Left ventricular hypertrophy

LVPW	Left ventricular posterior wall
MACE	Major Adverse Cardiovascular Events
n.	Number
N/A	Not Available
NICE	National Institute for Health and Care Excellence
NIH	National Institutes of Health
PCI	Percutaneous coronary intervention
PD	Peritoneal dialysis
Pmp	Per million population
PRD	Primary renal disease
PVD	Peripheral vascular disease
SMTR	Finnish Registry for Kidney Diseases
SNY	Finnish Society of Nephrology
Tx	Kidney transplantation
USRDS	US Renal Data System

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Wisam Bitar

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ABSTRACT

Background

Home dialysis modalities—continuous ambulatory peritoneal dialysis (CAPD), automated peritoneal dialysis (APD), and home hemodialysis (home HD)—offer alternatives to in-center hemodialysis (HD) for patients with end-stage kidney disease (ESKD). However, the comparative outcomes of these home modalities remain insufficiently defined. This study evaluated survival, infection-related complications, and risk of major adverse cardiovascular events (MACE) among home dialysis patients, with comprehensive adjustment for potential confounding factors.

Methods

A retrospective cohort of 536 adult ESKD patients who initiated home dialysis in the Helsinki-Uusimaa healthcare district between 2004 and 2017 was followed until the end of 2019. Additionally, a randomly selected sample of 432 patients receiving in-center HD was included for comparison. Dialysis modality was determined at day 90 after initiation of kidney replacement therapy. Primary outcomes included all-cause mortality, severe infection episodes (defined by C-reactive protein ≥100 mg/L), and MACE. Analyses included Kaplan-Meier survival estimates, Cox proportional hazards models, and Fine-Gray competing risks models, with propensity score adjustment for baseline differences.

Results

Five-year survival rates were similar between APD (88%) and home HD (90%) patients but significantly lower for CAPD patients (56%). After adjustment, the survival disadvantage of CAPD was attenuated, suggesting it was largely driven by older age and greater comorbidity burden. Severe infections occurred more frequently in CAPD and APD patients—mainly due to peritonitis—while bloodstream infections were more common in home HD. MACE incidence was lowest in home HD (32 per 1,000 patient-years) and APD (50), and higher in CAPD (109) and in-center HD (91), although these differences diminished and became statistically insignificant after adjustment. A sex-based interaction was observed, with peritoneal dialysis associating with higher MACE risk in males.

Conclusions

Home HD and APD were associated with more favorable outcomes than CAPD, though much of this was explained by patient characteristics. These findings support individualized dialysis modality selection based on clinical risk profiles rather than presumed modality superiority. Targeted strategies to reduce infection in peritoneal dialysis and further research into sex-specific cardiovascular risks are warranted.

TIIVISTELMÄ (ABSTRACT IN FINNISH)

Tausta

Kotidialyysimuodot—käsinvaihdoin tehtävä vatsakalvo- eli peritoneaalidialyysi (CAPD), koneen avulla tehtävä peritoneaalidialyysi (APD) ja kotihemodialyysi (home HD)—tarjoavat vaihtoehtoja sairaalassa tehtävälle hemodialyysille (HD) loppuvaiheen munuaissairautta (ESKD) sairastaville potilaille. Kotidialyysimuotoja vertailevia hoitotuloksia on kuitenkin tutkittu aiemmin varsin vähän. Tässä tutkimuksessa arvioitiin kotidialyysipotilaiden eloonjäämistä, infektioiden esiintymistä sekä sydän- ja verisuonitapahtumia, ottaen kattavasti huomioon mahdollisia sekoittavia tekijöitä.

Menetelmät

Retrospektiiviseen kohorttiin kuului 536 aikuista ESKD-potilasta, jotka aloittivat kotidialyysin Helsingin ja Uudenmaan sairaanhoitopiirissä vuosina 2004–2017. Vertailuryhmäksi otettiin satunnaisesti valittu 432 sairaalahemodialyysipotilaan otos. Tutkimuksessa käytettiin sitä dialyysihoitomuotoa, jossa potilas oli 90. hoitopäivänä. Ensisijaiset päätetapahtumat olivat kokonaiskuolleisuus, vaikeat infektioepisodit (määritelty C-reaktiivisen proteiinin ≥100 mg/l perusteella) ja vakavat sydän- ja verisuonitapahtumat (MACE). Analyyseissä käytettiin Kaplan-Meierin eloonjäämiskäyriä, Coxin suhteellisten riskien malleja ja Fine-Grayn-kilpailevien riskien malleja. Tulokset vakioitiin lukuisien muuttujien suhteen potilasryhmien välisten lähtötilanteen erojen pienentämiseksi.

Tulokset

Viiden vuoden eloonjäämisluvut olivat samankaltaiset APD- (88 %) ja koti-HD-potilailla (90 %), mutta merkittävästi matalammat CAPD-potilailla (56 %). Vakioinnin jälkeen CAPD:hen liittynyt heikompi eloonjääminen lievittyi, mikä viittaa siihen, että ero johtui suurelta osin korkeammasta iästä ja liitännäissairauksien määrästä. Vaikeita infektioita esiintyi useammin CAPD- ja APD-potilailla—pääasiassa peritoneaalidialyysin komplikaationa tulleen peritoniitin vuoksi—kun taas veren bakteeri-infektiot olivat yleisempiä koti-HD:ssä. MACE:n ilmaantuvuus oli matalin koti-HD:ssä (32/1 000 potilasvuotta) ja APD:ssä (50), mutta korkeampi CAPD:ssä (109) ja sairaala-HD:ssä (91), vaikka erot pienenivät vakioinnin jälkeen. Sukupuolen havaittiin vaikuttavan tuloksiin: peritoneaalidialyysiin liittyi korkeampi MACE-riski vain miehillä.

Johtopäätökset

Koti-HD:ssä ja APD:ssä hoitotulokset olivat suotuisampia kuin CAPD:ssä, mutta suuri osa tästä selittyi potilasryhmien eroilla. Tulokset tukevat dialyysimuodon yksilöllistä valintaa eri hoitomuotojen potilaskohtaisia hyötyjä ja riskejä punniten. Peritoneaalidialyysipotilailla tulisi tehostaa infektioiden ennaltaehkäisyä. Heille tarvitaan myös lisää tutkimusta eri sukupuolten sydän- ja verisuonitautiriskeistä.

INTRODUCTION

Background

Chronic kidney disease (CKD) is a prevalent and progressive medical condition characterized by the gradual loss of kidney function over time (Bikbov et al. 2020; Lameire et al. 2021) . CKD affects approximately 10% of the global population, underscoring its widespread impact (Bikbov et al. 2020). The prevalence of CKD has been increasing worldwide, posing a serious public health challenge (Rao et al. 2025). Several factors contribute to this rising trend, including an aging population, the growing prevalence of diseases such as diabetes and hypertension, along with various lifestyle factors (Levey and Coresh 2012; Webster et al. 2017).

CKD is classified into five stages based on glomerular filtration rate (GFR) and the presence of kidney damage. The progression from early stages of CKD to end-stage kidney disease (ESKD) involves a complex interplay of risk factors and comorbidities. Several studies emphasize that early detection and management besides controlling risk factors, are crucial for slowing CKD progression (KDIGO 2013; Perkovic et al. 2013; Stevens and Levin 2013).

Kidney replacement therapy (KRT)

The primary modalities of KRT include dialysis therapy, and kidney transplantation.

Dialysis therapies can be classified into home-based and facility-based dialysis. Home-based dialysis includes PD and home HD, while facility-based dialysis consists of in-center HD.

PD includes two main forms: CAPD and APD. CAPD is manually performed by the patient throughout the day. APD involves the use of a machine to perform fluid exchanges, typically during the night while the patient sleeps. APD provides more consistent dialysis and greater freedom during the day compared to CAPD.

HD involves filtration of blood. Home HD is performed by patients in their own homes, while in-center HD is the traditional form of HD performed in a clinical setting and remains the most common dialysis modality. Kidney transplantation is the preferred modality for ESKD when feasible, as it generally offers the best outcomes in terms of survival, quality of life and costs (Huijben et al. 2023; Mohnen et al. 2019; Hariharan, Israni, and Danovitch 2021).

Patient outcomes across dialysis modalities

Dialysis is a crucial intervention both for patients who are awaiting kidney transplantation and those who are not candidates for it. Choosing the appropriate dialysis method requires careful consideration of various factors, including patient characteristics, comorbid conditions, and geographic and socioeconomic factors.

Despite the availability of multiple dialysis options, significant debate and variability persist in clinical practice regarding the optimal modality. Key clinical outcomes of paramount concern in managing ESKD include survival, infectious complications, and cardiovascular events (Mazzuchi, Fernández-Cean, and Carbonell 2000). Consequently, this research has focused on understanding how different dialysis modalities affect patient outcomes by evaluating survival rates, investigating the frequency and severity of infections, and assessing the incidence of cardiovascular events in patients undergoing various types of dialysis.

REVIEW OF THE LITERATURE

1 End-Stage Kidney Disease

1.1 Causes and epidemiology of ESKD

1.1.1 Causes of ESKD

ESKD is a critical health condition characterized by the irreversible loss of kidney function, typically evidenced by a glomerular filtration rate (GFR) of less than 15 mL/min/1.73 m² (KDIGO 2013), necessitating KRT through dialysis or transplantation. Nearly all studies on ESKD in the literature have focused on patients already on KRT.

Diabetes mellitus and hypertension remain the most prevalent causes of ESKD worldwide. Diabetes, particularly type 2 diabetes, is a leading contributor to the development of ESKD due to its association with diabetic nephropathy, which accelerates the decline in kidney function (Ghaderian et al. 2015). Hypertension also plays a critical role in the progression of CKD to ESKD, as high blood pressure exacerbates kidney damage and accelerates kidney function deterioration (Hsu et al. 2005).

In addition to diabetes and hypertension, glomerulonephritis represents a significant cause of ESKD, encompassing various forms of immune-mediated kidney diseases (Wetmore et al. 2016; Abd ElHafeez et al. 2024). Other causes include polycystic kidney disease, which is a genetic disorder leading to the formation of cysts in the kidneys and ultimately resulting in kidney failure (Bisceglia et al. 2006; Spithoven et al. 2014). The role of autoimmune diseases such as systemic lupus erythematosus in the development of ESKD has also been documented, particularly in younger populations (Wetmore et al. 2016; Derner et al. 2022). Notably, complex interplay between comorbid conditions, environmental factors, and genetic predisposition stand behind the pathogenesis of ESKD.

In high-income countries, such as the United States and those in Western Europe, diabetes and hypertension are the primary causes of ESKD. Data from the United States Renal Data System indicates that diabetes contributes to over 40% of new ESKD cases, while hypertension accounts for around 30% (USRDS 2023). In contrast, in many low- and middle-income countries, infectious diseases and chronic glomerulonephritis remain prevalent causes of ESKD (Jha et al. 2013).

1.1.2 Incidence and prevalence of ESKD

The distinction between incidence and prevalence is crucial in understanding the impact of ESKD on public health. Incidence refers to the number of new cases of ESKD diagnosed within a specific time period, while prevalence denotes the total number of individuals living with ESKD at a given time (Noordzij et al. 2010).

In 2021, the incidence of treated ESKD in European countries ranged between 53 per million population (pmp) in Ukraine and 283 pmp in Cyprus, with an average incidence of 145 pmp. On the other hand, the mean prevalence was 1040 pmp (Boerstra et al. 2024; ERA-Registry 2023).

Despite the increasing prevalence of ESKD until 2021, Finland had a relatively low incidence of ESKD in comparison to other European countries, with an incidence of approximately 82 pmp, and prevalence of 958 Pmp (Boerstra et al. 2024; ERA-Registry 2023).

Australia and New Zealand had a higher incidence and prevalence of ESKD in 2021 compared to Finland. The incidence in Australia was 127 pmp, while the prevalence was 1109 pmp. The incidence in New Zealand was 137 pmp, while the prevalence was 1054 pmp (ANZDATA-Registry 2022a, 2022b).

In the United States, the incidence of ESKD in 2021 was about 394 pmp and the prevalence of 2397 Pmp.

The disparity in ESKD incidence rates (IR) between countries can be attributed to a combination of socioeconomic, healthcare, and environmental factors (Ulasi et al. 2022). For instance, high-income countries often report higher ESKD incidence rates compared to low- and middle-income countries. This discrepancy is partly due to better diagnostic capabilities and more comprehensive health reporting systems. Moreover, lifestyle factors prevalent in high-income countries, such as sedentary behavior and dietary habits, contribute to a higher prevalence of diabetes and hypertension, both of which increase the risk of developing ESKD. (Burrows NR 2022; Thurlow et al. 2021). Additionally, since aging is a risk factor for ESKD, people in high-income countries, who typically have longer life expectancies, are more likely to live long enough to develop ESKD. (O'Hare et al. 2007; Beltrán-Sánchez and Subramanian 2019).

Conversely, in low- and middle-income countries, limited access to healthcare services and inadequate management of chronic diseases result in lower reported rates of ESKD. However, these regions face a different challenge, such as an underestimation of ESKD prevalence due to less developed healthcare infrastructure and diagnostic limitations. Many patients in these regions cannot access KRT, leading to lower reported ESKD incidence rates, despite a potentially higher true disease burden due to lack of diagnosis and treatment (Thurlow et al. 2021).

The differences in ESKD incidence also reflect variations in public health policies and healthcare systems. Countries with established KRT programs and

advanced dialysis technologies tend to have higher reported ESKD rates. Despite this, access to universal healthcare systems, such as those in Nordic countries, contributes to lower ESKD rates by providing earlier interventions for chronic kidney disease, which may slow disease progression and reduce ESKD incidence (Thurlow et al. 2021). In contrast, countries with limited resources and reduced access to dialysis services may report lower incidences—not necessarily due to a truly lower prevalence, but rather because of limited detection and treatment capacity. Alternatively, they may have a genuinely lower prevalence as a result of increased mortality among individuals in need of kidney replacement therapy (KRT), which is not readily available (Ulasi et al. 2022).

1.2 Outcomes of ESKD

1.2.1 Mortality of ESKD

Studies indicate that the mortality rate in patients with ESKD is 10 to 20 times higher than that of the general population, underscoring the severity of the condition and its challenging management (de Jager et al. 2009; Pippias et al. 2016; Chantrel et al. 2013). Several factors contribute to the high mortality rates in patients with ESKD. While cardiovascular disease is the leading cause of death in this population (Cozzolino et al. 2018; Khou et al. 2022), infectious complications are the second most common cause (Mailloux et al. 1991; Dalrymple and Go 2008; Vogelzang et al. 2015).

1.2.2 Factors affecting the outcome of ESKD

The outcomes of ESKD encompass a wide range of factors, including survival rates, quality of life, and cardiovascular morbidity. Survival rates among ESKD patients vary significantly and are influenced by both clinical and demographic factors. Additionally, patients with ESKD often experience a diminished quality of life, affected by both physical and psychological burdens (Mbeje 2022).

Comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease play a critical role in the outcomes of ESKD (Helve et al. 2021). Diabetes mellitus often leads to poorer outcomes due to its associated complications, such as cardiovascular disease and increased susceptibility to infections. Hypertension, which is both a cause and a consequence of kidney disease, can exacerbate ESKD and further deteriorate patient outcomes. Age also significantly affects prognosis, as older ESKD patients generally fare worse due to age-related health decline and other chronic conditions (Prichard 2000).

Access to healthcare is crucial, as patients with more comprehensive care, including specialized nephrology services, tend to experience better outcomes. Patients with higher income and education levels often have better access to healthcare, which facilitates adherence to treatment plans. Furthermore, in

countries without universal healthcare, insurance coverage becomes a decisive factor in determining access to essential treatments and medications, thereby influencing patient health (Robinson et al. 2016; Jurkovitz et al. 2013; Narva, Norton, and Boulware 2016).

Diet and nutrition also play an essential role, as poor dietary habits can worsen kidney function and overall health (Crews et al. 2015). Similarly, regular physical activity improves cardiovascular health and well-being, positively affecting ESKD outcomes (Mallamaci, Pisano, and Tripepi 2020). On the contrary, unhealthy behaviors like smoking and excessive alcohol use can worsen kidney function (Perneger et al. 1999) and increase the risk of cardiovascular disease (Provenzano et al. 2021), leading to poorer outcomes.

Adherence to treatment plans is critical for managing ESKD. Patients who strictly follow their treatment schedules, medication regimens, and dietary restrictions typically have better outcomes, whereas non-adherence increases the risk of complications and mortality (Denhaerynck et al. 2007). Mental health is another important factor, as depression and anxiety can negatively impact adherence and overall health in ESKD patients (Lee et al. 2022).

Additionally, social support from family, friends, and healthcare providers can enhance emotional well-being and provide practical help in managing the disease, leading to better outcomes (Plantinga et al. 2010).

1.2.3 Causes of death in ESKD

ESKD presents a substantial challenge in nephrology, with mortality being a critical aspect of patient outcomes. In addition to fluid overload, electrolyte imbalances, and uremia-related complications, several factors influence mortality in ESKD patients.

Cardiovascular complications, including heart failure and acute coronary syndrome, are the leading cause of death among ESKD patients. Several factors contribute to this increased risk of cardiovascular events (Poli et al. 2019).

Infections are another major cause of death in ESKD patients (Vogelzang et al. 2015). The risk of infections is compounded by immunocompromised states, frequent hospitalizations, and the presence of comorbid conditions (Dalrymple and Go 2008; KDIGO 2013; Li, Tai, et al. 2022).

The incidence of cancer is also elevated in ESKD patients, attributed to factors such as chronic inflammation, and oxidative stress (Lee et al. 2021; Vogelzang et al. 2015). Studies have shown that the risk of specific cancers, such as renal cell carcinoma and lymphomas, is higher in ESKD population (Shirazian, Starakiewicz, and Latcha 2021).

Metabolic disorders, including diabetes and malnutrition, contribute significantly to mortality in ESKD patients. Diabetes, a common comorbidity

in ESKD, exacerbates the progression of kidney disease and complicates overall patient management (Kumar et al. 2023). Malnutrition, commonly observed in ESKD patients, impairs immune function, increases susceptibility to infections, and further worsens overall health outcomes (Sungjin Chung 2012; Rashid et al. 2024; Kato et al. 2008).

2 ESKD management approaches

2.1 Dialysis

Dialysis for ESKD patients is a critical life-sustaining therapy that partially replaces the filtering function of the kidneys, by artificially removing waste products and excess fluids from the blood. Dialysis is indicated for patients with ESKD who exhibit symptoms of uremia, including nausea, vomiting, anorexia, fatigue, and altered mental status. It is also necessary for those with refractory hyperkalemia, severe acidosis, fluid overload unresponsive to diuretics, and uremic pericarditis. The decision to initiate dialysis is individualized, taking into account patient symptoms, biochemical parameters, and overall health status. Absolute contraindications to dialysis are rare but may include severe dementia or irreversible coma, which preclude informed consent and cooperation. Relative contraindications include severe cardiovascular instability, which may be exacerbated by the hemodynamic shifts during dialysis sessions, as well as significantly reduced functional capacity, severe frailty, and a limited life expectancy due to other underlying illnesses (NICE 2018).

Dialysis is broadly categorized into peritoneal dialysis (PD) and hemodialysis (HD), each with specific techniques and settings.

PD involves the use of the patient's peritoneum as a natural filter across which fluids and dissolved substances are exchanged from the blood. The peritoneal membrane acts as a semi-permeable barrier, facilitating the exchange of waste products and electrolytes between the blood and the dialysis solution (dialysate). A catheter is surgically implanted into the peritoneal cavity, and dialysis solution is infused through the catheter. The solution absorbs waste products and excess fluids, which are then drained and replaced with fresh solution. PD offers flexibility and is associated with better preservation of residual kidney function. However, it carries risks such as peritonitis and requires patient or caregiver training (Szeto and Li 2019). PD can be performed manually (CAPD) or using a machine (APD) (Rabindranath et al. 2007).

CAPD involves the manual infusion and drainage of dialysate fluid into the peritoneal cavity through the placed catheter. Patients typically perform four exchanges throughout the day. Each exchange takes about 30–40 minutes, and the

fluid remains in the abdomen for several hours between exchanges. Thus, CAPD provides continuous clearance of solutes and fluid, potentially leading to better preservation of residual renal function (Nongnuch et al. 2015). Additionally, CAPD allows for greater patient mobility and independence but requires adherence to strict aseptic techniques to prevent peritonitis (Mawar, Gupta, and Mahajan 2012).

APD employs a machine (cycler) to perform exchanges automatically, usually at night while the patient sleeps. Typically, APD involves a longer dwell time during the day when the fluid stays in the abdomen. The cycler infuses and drains the dialysate fluid multiple times, providing the benefits of PD with reduced manual intervention. APD can offer better fluid management and improved quality of life. However, it requires access to electricity and a stable home environment; and may be associated with higher costs and regular machine maintenance (Domenici and Giuliani 2021; Rivero-Urzua et al. 2022).

HD is the most common dialysis modality. The process uses a dialysis machine for extracorporeal removal of waste products, toxins, and excess fluids from the blood through a dialyzer. The dialysis machine is connected to the patient via vascular access, typically through an arteriovenous fistula, graft, or catheter (NIH 2018). HD typically occurs in two settings: home HD and in-center HD, each with distinct benefits and challenges.

Home HD allows patients to perform hemodialysis at home, providing greater flexibility and autonomy, and the potential for more frequent dialysis sessions or longer durations (e.g., nocturnal dialysis). Patients are trained to manage the dialysis process and related challenges such as vascular access and preventing infections, independently or with the assistance of a caregiver (Walker et al. 2015; Wu et al. 2023). Home HD can provide better control of blood pressure and phosphorus levels but requires significant patient training, home modifications, and the availability of a supportive caregiver (Bieber and Young 2021). Studies have shown that while home HD improves quality of life, technique survival can be compromised by issues like patient burnout, inadequate social support, and medical complications (Tran et al. 2023).

In-center HD is the most common dialysis modality, typically performed three times a week, with each session lasting around four hours in a clinical or hospital setting. In-center HD offers regular medical supervision and opportunities for social interaction but limits patient autonomy and can cause fatigue due to rapid fluid shifts during treatment (Park and Jung 2025; Harwood et al. 2012; Bossola et al. 2023). Additionally, it requires travel to the dialysis center and adherence to a fixed schedule, which can be time-consuming and negatively impact quality of life (Diamant et al. 2010; McDonald et al. 2023).

2.2 Kidney Transplantation

Kidney transplantation is considered the most effective treatment for ESKD, offering the potential for a near-normal quality of life and improved survival rates compared to dialysis. The procedure involves surgically placing a healthy kidney from a living or deceased donor into the patient's body. The transplant surgery typically involves placing the donor kidney in the iliac fossa, anastomosing the renal artery and vein to the recipient's iliac vessels, and connecting the ureter to the bladder. The transplanted kidney takes over the function of filtering blood, producing urine, and maintaining electrolyte balance. Postoperative care includes monitoring for complications such as rejection, infection, and surgical issues. Regular follow-up and adherence to immunosuppressive therapy are crucial for maintaining graft function (Zachcial et al. 2022). Kidney transplantation can restore normal kidney function, freeing patients from dialysis and improving life expectancy and quality of life. The success of kidney transplantation depends on factors such as donor organ quality, recipient health, and immunosuppressive therapy.

While lifelong immunosuppressive therapy is required to prevent rejection of the transplanted kidney, immunosuppressive medications themselves carry risks of rejection or complications as infections and malignancies. Consequently, regular follow-up is necessary to monitor kidney function and detect any complications (Hariharan 2006). Kidney transplantation remains the most effective form of KRT in terms of survival and functional benefits, despite the challenges associated with organ availability and post-transplant complications (Abecassis et al. 2008). Advances in surgical techniques, immunosuppressive regimens, and donor matching have improved long-term graft survival and patient outcomes (Thongprayoon et al. 2020).

The indication for kidney transplantation is ESKD, irrespective of the underlying cause. Candidates must be free from severe cardiovascular disease, infections, malignancies, and other conditions that could impair transplant success. Key considerations include the patient's age, overall health, and the presence of a suitable donor. Absolute contraindications for kidney transplantation include active malignancy, active or chronic infection, untreated significant cardiac or peripheral vascular disease, ongoing substance abuse, and significant non-compliance with medical therapy. Relative contraindications include advanced age, severe obesity, multiple comorbid conditions and psychosocial issues that may impact post-transplant care (Chadban et al. 2020).

2.3 Conservative Management

Conservative management refers to the approach of managing ESKD without dialysis or kidney transplantation, with an emphasis on symptom control, quality

of life, and psychosocial support. It is an option for patients who opt not to undergo dialysis or transplantation and is often considered for frail elderly patients or those with significant comorbidities, where the burden of dialysis may outweigh its potential benefits. Conservative management emphasizes patient-centered care and includes lifestyle modifications, pharmacological interventions, and palliative care to improve quality of life and manage symptoms such as pain, anemia, electrolyte imbalances, and fluid overload (NICE 2018).

3 Home Dialysis Modalities

3.1 Epidemiology of home dialysis modalities

Home dialysis modalities have seen a variable adoption rate across different regions and countries. The adoption rates have been influenced by factors such as healthcare policies, patient preferences, and the availability of training and support services (Thongprayoon et al. 2024).

Home HD is less common compared to PD. However, in countries like Australia and Canada, home HD rates are relatively higher due to robust support systems and patient education programs. In contrast, home HD adoption remains limited in many low- and middle-income countries due to logistical and resource constraints.

PD has been more widely adopted due to its lower cost and ease of implementation compared to home HD. In 2022 PD constituted about 12.3% of dialysis population in USA and Canada, 17% in Australia, and 24% in New Zealand (ERA-Registry 2024; ANZDATA-Registry 2023; USRDS 2025).

Figure 1 compares the prevalence of home dialysis modalities across several countries in Europe.

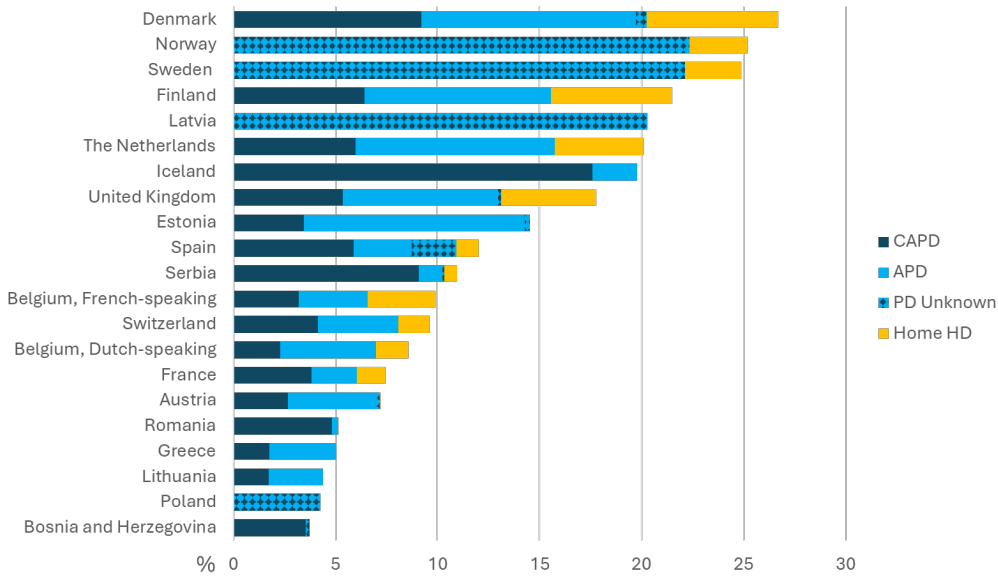


Figure 1. The proportion of home dialysis modalities out of all patients on dialysis at the end of year 2021 in several European countries from the ERA Registry Annual Report 2021

3.2 Characteristics of home dialysis modalities

Home dialysis modalities, both home HD and PD, offer advantages in treatment flexibility and frequency compared to in-center HD. Patients undergoing home HD can schedule more frequent sessions, which allows for better fluid and electrolyte management and improved clinical outcomes. In contrast, in-center HD typically involves three fixed sessions per week, each lasting 4–5 hours, which may be rigid and less adaptable to individual patient needs.

Beyond clinical outcomes, home dialysis modalities also contribute to improved quality of life and higher patient satisfaction (Kraus et al. 2016). The ability to manage treatment at home not only aligns with patients' lifestyles but also allows for greater autonomy. Patients on home dialysis report fewer dietary restrictions, reduced travel burdens, and a more normal lifestyle, with the ability to work and engage in social activities (Helantera et al. 2012). This enhanced sense of control and flexibility results in higher patient engagement and satisfaction. Increased autonomy and personalization of care is a primary reason patients favor home dialysis over in-center treatment (Perl et al. 2023). These modalities foster a patient-centered approach, contributing to better overall well-being and long-term adherence to treatment.

While home dialysis presents numerous benefits, it also demands a higher level of patient responsibility and self-management. The safety and complication profiles differ from those of in-center HD, which is continuously monitored by

healthcare professionals. Home dialysis can reduce the risk of cardiovascular complications and improve blood pressure control, but it requires rigorous training and self-care skills to manage potential risks, such as infections in PD or vascular access complications in home HD. Despite these challenges, with proper training and support, many patients successfully manage their treatments at home, demonstrating fewer hospitalizations and better overall outcomes (Ishani A 2015).

From an economic standpoint, home dialysis is often more cost-effective than in-center HD, primarily due to reduced transportation needs and lower hospitalization rates (Couchoud et al. 2015). Although initial setup costs for home dialysis may be high, the long-term savings associated with better management of ESKD can offset these expenses (Krahn et al. 2019). Recent technological advances, such as innovations in home HD machines, PD solutions, and remote monitoring via telemedicine, have further enhanced the safety, efficacy, and convenience of home dialysis (Lew et al. 2024). These developments not only improve patient adherence but also expand the feasibility of home dialysis for a broader range of patients, making it an increasingly attractive option for ESKD management.

Despite its advantages, home dialysis is not without challenges. Several barriers to widespread adoption of home dialysis, including the need for patient training, the requirement for a supportive home environment, and potential issues related to access to medical support and equipment (Perl et al. 2023; Hope 2013).

3.3 Strategies for home dialysis across different regions

In high-income countries like the United States, there has been a gradual increase in the adoption of home dialysis modalities (Rivara and Mehrotra 2014).

In Hong Kong, recent guidelines from the Hong Kong Society of Nephrology advocate for increased use of PD due to its cost-effectiveness and patient preference. There is a strong focus on training programs and patient support networks (Li and Chow 2013; Li, Lu, et al. 2022).

In Taiwan, Taiwanese guidelines emphasize a balanced approach to home dialysis, with particular attention to ensuring patient safety and effective training. Recent policies support increased funding and infrastructure for home dialysis programs (Kwong and Li 2015).

In Thailand, Thailand's nephrology guidelines advocate for PD as a first-line home dialysis option due to its feasibility and lower cost compared to home HD (Chuengsaman and Kasemsup 2017).

New Zealand promotes both PD and home HD as viable home dialysis options. Strategies include patient-centered care, community support, and comprehensive training programs.

In Australia, Australian guidelines emphasize the importance of patient choice and support for home dialysis. The Australian government provides

financial incentives and support programs to encourage home dialysis adoption (Fortnum and Ludlow 2014).

Nordic countries (Denmark, Finland, Iceland, Norway, Sweden) have implemented progressive strategies to promote home dialysis, including patient education, support networks, and integration with primary care. There is a strong emphasis on patient autonomy and choice (SNY 2021).

3.4 Peritoneal dialysis

PD provides advantages in terms of lifestyle flexibility and patient autonomy. Studies have consistently shown that patients undergoing PD often experience improvements in quality of life compared to those on in-center HD (Noshad et al. 2009; Hsu et al. 2020; Jung et al. 2019). PD enables patients to manage their treatments at home, reducing the need for frequent hospital visits and offering greater control over their daily routines.

One of the notable benefits of PD is the preservation of residual renal function (Liu and Dai 2017). Residual renal function is crucial for maintaining fluid and electrolyte balance and may contribute to better overall outcomes and reduced mortality rates (van der Wal et al. 2011; Shemin et al. 2001; Suda et al. 2000; Termorshuizen et al. 2003). Studies have shown differing results regarding the rate of residual renal function decline between CAPD and APD. Hufnagel et al. observed a slower decline in residual renal function among patients using CAPD (Hufnagel et al. 1999), while other studies did not find any significant difference between the two methods (van der Wal et al. 2011; Shemin et al. 2001; Suda et al. 2000; Termorshuizen et al. 2003).

Advances in PD technology have led to improvements in both equipment and dialysis solutions. APD machines have become more sophisticated, offering enhanced user interfaces and automated processes that improve patient safety and ease of use (Maliha, Burke, and Reddy 2023). Innovations in dialysate solutions, such as those with improved biocompatibility and reduced glucose load, have also contributed to better patient outcomes (Bonomini et al. 2021).

Recent research has focused on tailoring PD regimens to individual patient needs. This includes adjustments in dialysate composition and the frequency of exchanges based on patient-specific factors such as body size, residual renal function, and comorbid conditions (Slon-Roblero, Sanchez-Alvarez, and Bajo-Rubio 2024). Personalized approaches aim to optimize dialysis efficacy while minimizing complications.

Complications such as peritonitis, catheter-related issues, and ultrafiltration failure remain significant challenges in PD (Chaudhary 2011; Peppelenbosch et al. 2008). Research continues to address these challenges through improved catheter

designs, infection prevention strategies, and novel therapeutic approaches for managing complications (Crabtree et al. 2019).

3.5 Home hemodialysis

Home HD is a modality that allows patients to perform hemodialysis in the comfort of their own homes. This approach can offer several advantages over traditional in-center HD. Literature has highlighted both the promising outcomes, and the challenges associated with home HD (Ishani A 2015).

Studies have shown that the flexibility in scheduling afforded by home HD with the potential for more frequent sessions might contribute to improved long-term health outcomes compared to conventional in-center HD (Palmer et al. 2014). The benefits of home HD extend to include improvements in quality of life (Punal et al. 2008).

Technological innovations have played a crucial role in advancing the feasibility and effectiveness of home HD. Technological advancements, such as the development of more user-friendly dialysis machines and remote monitoring systems, have the potential to enhance the safety and convenience of home HD (Farrington and Greenwood 2011).

4 Survival Outcomes in Dialysis

4.1 Survival in dialysis patients

The survival rates of patients undergoing different dialysis modalities have been a significant focus of nephrology research.

Research indicates variation in survival outcomes for PD compared to in-center HD. However, USRDS annual report consistently shows a survival advantage for PD in the first few years of therapy, particularly in younger patients and those without significant comorbidities (USRDS 2021). Other studies reported similar findings, with PD showing better survival than HD in the initial years but comparable survival later on (Heaf, Løkkegaard, and Madsen 2002; McDonald et al. 2009; Korevaar et al. 2003). The survival rate was found to be better in PD patients with residual kidney function compared to in-center HD patients (Heaf, Løkkegaard, and Madsen 2002; Chandna and Farrington 2004; Lysaght et al. 1991; Moist et al. 2000). Other studies found no significant difference in survival between PD and HD after adjusting for confounders, suggesting that the choice between these modalities can be based on other factors rather than survival outcomes (Jager et al. 1999; Haapio et al. 2013).

Home HD has gained increasing attention due to its potential for improving patient outcomes and quality of life. Its survival benefit may be attributed to the increased frequency and duration of dialysis sessions, which more closely mimic the natural kidney function. Additionally, studies have suggested that more frequent dialysis can lead to better outcomes by reducing fluid overload and improving blood pressure control (Weinhandl et al. 2012).

In-center HD remains the most common modality for dialysis worldwide. Despite its widespread use, studies have shown varying results regarding its survival outcomes compared to home-based therapies. While several studies show better survival in home-based dialysis (Vinson, Perl, and Tennankore 2019), others show similar outcomes (Ishani A 2015).

4.2 Factors influencing survival

Age is a critical determinant of survival in dialysis patients. Older patients tend to have poorer survival outcomes regardless of the dialysis modality (Chandna et al. 2011; Byrne, Vernon, and Cohen 1994). Sex also may play a role, with some studies suggesting that females on PD may have better survival rates compared to males, although the evidence is mixed (Danneville et al. 2022).

Comorbid conditions such as diabetes, cardiovascular disease, and hypertension critically influence survival outcomes in dialysis patients (Gomez et al. 2015). Diabetic patients, for example, have been found to have poorer survival rates on PD compared to HD (Vonesh et al. 2004).

Adherence to prescribed dialysis regimens and associated treatments is paramount for improving survival outcomes. Non-adherence to dialysis schedules, dietary restrictions, and medication regimens has been linked to increased mortality rates in both PD and HD patients (Griva et al. 2014; Denhaerynck et al. 2007).

Socioeconomic factors, including income, education level, and insurance status, affect survival outcomes. Patients from lower socioeconomic backgrounds often face barriers to accessing consistent and high-quality care, leading to poorer outcomes (Nicholas, Kalantar-Zadeh, and Norris 2015).

5 Infectious Complications Associated with Dialysis

5.1 Burden of infections in dialysis patients

Infections represent the second leading cause of death among KRT patients, 10% to 13% of all deaths, following cardiovascular diseases (USRDS 2021; Vogelzang et al. 2015).

ESKD itself is associated with an impaired immune response. Uremia has been shown to negatively impact both the innate and adaptive immune systems. This includes dysfunctions in neutrophil and monocyte activity, lymphocyte proliferation, and the production of critical cytokines necessary for mounting an effective immune response (Cohen 2020). The immunocompromised state of ESKD patients is exacerbated by comorbid conditions common in this population, such as diabetes mellitus, cardiovascular disease, and malnutrition, all of which further impair immune function. Additionally, the frequent healthcare interactions and hospitalizations inherent in the management of ESKD and its complications increase exposure to nosocomial pathogens.

Dialysis introduces additional risks for infection. The dialysis process, whether through PD or HD, involves peritoneal access or repeated vascular access, providing potential entry points for pathogens.

For instance, PD involves the insertion of a catheter into the peritoneal cavity, which provides a direct pathway for pathogens to enter. The most common infectious complication in PD is peritonitis, which can lead to significant morbidity and even technique failure.

The incidence of peritonitis is a crucial metric for assessing PD efficacy and patient safety. The overall incidence of peritonitis in PD patients ranges from 0.2 to 0.4 episodes per patient-year (Li, Chow, et al. 2022; SMTR 2022). Peritonitis rates may have declined due to improvements in PD sterile techniques, patient education and antimicrobial prophylaxis (Campbell et al. 2017), but it remains a significant concern due to its potential to lead to catheter removal and transition to hemodialysis (Al Sahlawi and Perl 2022; Brown et al. 2011). The pathogenesis of peritonitis often involves skin flora, such as Staphylococcus epidermidis and Staphylococcus aureus, and enteric organisms, including Escherichia coli and Klebsiella pneumoniae (Salzer 2018). Key risk factors include poor catheter care, contamination during exchanges, and the presence of comorbid conditions. Infections at the exit site or within the tunnel of the PD catheter can lead to peritonitis or systemic infections. Thus, proper catheter exit site care and prophylactic measures are crucial in preventing these infections (Gursu et al. 2023).

In HD, vascular access is essential for the treatment and can be achieved through arteriovenous fistulas, grafts, or central venous catheters. Each type of access has its associated infection risks. Central venous catheters, in particular, are associated with a high risk of bloodstream infections due to their direct access to the bloodstream and frequent handling, in addition to their potential for biofilm formation, which can harbor bacteria and resist antimicrobial treatment (Gominet et al. 2017; Esposito et al. 2013; El Khudari et al. 2022; Soi et al. 2016). The risk of bloodstream infections is a major concern in HD patients, with the highest infection rates associated with catheters, followed by grafts, while arteriovenous

fistulas (AVF) carry the lowest risk (Allon and Lok 2010). Current guidelines strongly recommend the use of AVF whenever possible to minimize infection risk (Lee et al. 2018).

5.2 Infectious complication endpoints in dialysis studies

The two most assessed infection endpoints in clinical studies are infection-related hospitalization and mortality.

In patients undergoing PD, peritonitis remains the most frequent and severe infectious complication, often necessitating hospitalization. Among HD patients, particularly those with central venous catheters, hospitalization rates are elevated due to catheter-related bloodstream infections (Gahlot et al. 2014).

Peritonitis and its progression to sepsis represent major contributors to infection-related mortality in PD patients. A review by Li et al. reported that peritonitis accounts for up to 16% of all deaths in this population (Li et al. 2010).

In HD patients, infection-related mortality is most often attributed to sepsis secondary to catheter-related bloodstream infections (Locham et al. 2021).

5.3 Strategies for reducing infectious complications

In PD patients, protocols to reduce the risk of peritonitis include the use of prophylactic antibiotics, adherence to sterile techniques during catheter exchanges, and comprehensive patient education on hygiene practices. Proper care of the PD catheter exit site and tunnel is also essential; recommendations include regular cleaning with antiseptics and monitoring for signs of infection (Li, Chow, et al. 2022).

For home HD patients, thorough training in infection prevention and home hygiene is essential. Structured training programs and regular follow-up can significantly lower infection rates (Al Sahlawi, Chan, and Perl 2025). Additionally, the use of infection-resistant materials and devices in home HD setups may further contribute to lowering infection risks. Earlier research highlighted the potential of innovations in catheter materials to reduce infection rates (Timsit et al. 2011).

In in-center HD patients, strategies to reduce catheter-related infections include the use of antibiotic locks, routine catheter site disinfection, and strict adherence to aseptic techniques during catheter insertion and maintenance (Vanholder et al. 2010).

6 Cardiovascular Adverse Events in Dialysis

6.1 Cardiovascular disease burden in dialysis patients

Cardiovascular disease is the leading cause of morbidity and mortality among patients with ESKD (Cozzolino et al. 2018). These patients experience cardiovascular events such as myocardial infarction, stroke, and heart failure at rates approximately 10 to 20 times higher than those in the general population (Echefu et al. 2023; KDIGO 2024). The mechanisms that drive cardiovascular risk in ESKD patients are multifactorial (Yamamoto and Kon 2009; Wanner, Amann, and Shoji 2016). Dysregulation in calcium and phosphate metabolism contributes to vascular calcification, a common issue in this population (Dube et al. 2021). Additionally, systemic inflammation and oxidative stress are significant contributors to cardiovascular pathology in ESKD (Wang and Gao 2022). Studies have identified elevated levels of inflammatory markers, such as C-reactive protein (CRP) and interleukin-6, which link inflammation to poor cardiovascular outcomes (Held et al. 2017).

Volume overload plays a critical role in worsening cardiovascular conditions. Dysregulated fluid balance not only elevates blood pressure but also increases the cardiac workload, accelerating LVH and the progression of heart failure (Byoung-Geun Han 2020; Tangwonglert and Davenport 2021). In turn, LVH and arterial stiffness contribute to cardiovascular events in ESKD patients (Inserra et al. 2021; Paoletti et al. 2004).

The type of dialysis modality plays a crucial role in the cardiovascular risk profile, as both PD and HD have unique cardiovascular challenges (Johnson et al. 2009).

HD patients, especially those undergoing in-center treatment, face a high incidence of cardiovascular complications, particularly myocardial infarction and heart failure. The fluid overload and fluctuating blood pressure associated with rapid fluid shifts during dialysis place a stress on cardiovascular system (Chirakarnjanakorn et al. 2017). Such hemodynamic instability and stress contribute to the faster worsening of LVH.

Home dialysis, on the other hand, provides a more physiological approach to dialysis and, under many circumstances, can lead to improved cardiovascular outcomes compared with traditional thrice-weekly in-center hemodialysis (Sarnak et al. 2022).

6.2 Cardiovascular endpoints in dialysis studies

Cardiovascular hospitalization is a key endpoint for evaluating the burden of cardiovascular events in dialysis patients. It includes hospital admissions due to conditions such as acute myocardial infarction, heart failure, and unstable

angina. Given its direct impact on patient quality of life and healthcare costs, cardiovascular hospitalization is frequently used as a surrogate marker for adverse cardiovascular outcomes (Lui et al. 2023). Likewise, cardiovascular death—defined as mortality resulting from cardiovascular causes such as myocardial infarction, stroke, and heart failure—serves as a critical endpoint for assessing the long-term effects of different dialysis modalities on patient survival and cardiovascular health (Khoo et al. 2022).

In clinical research, major adverse cardiovascular events (MACE) are commonly used to evaluate cardiovascular risk. The three-point MACE endpoint includes myocardial infarction, stroke, and cardiovascular death, whereas additional MACE endpoints expand upon this by also incorporating cardiovascular hospitalization due to unstable angina or heart failure. This composite measure provides a comprehensive assessment of severe cardiovascular outcomes and is widely used in clinical trials to evaluate interventions aimed at improving cardiovascular health (Bosco et al. 2021; Rastogi et al. 2023).

6.3 Methods of cardiovascular protection specific to dialysis modalities

Effective fluid management is a fundamental mechanism through which certain dialysis modalities confer cardiovascular protection. PD, characterized by gradual and continuous fluid removal, and home HD, which often involves more frequent sessions, both contribute to improved fluid balance. Maintaining this stability reduces the risk of fluid overload, hypertension, and subsequent cardiovascular stress, thereby lowering the incidence of heart failure and related complications (Canaud et al. 2019).

Stability in blood pressure during dialysis is also critical, as fluctuations can exacerbate cardiovascular complications. Home HD, with the potential for longer and more frequent sessions, offers superior intradialytic and interdialytic blood pressure control compared with conventional in-center HD. Enhanced hemodynamic stability has been shown to decrease the risk of LVH and ischemic heart disease (Richardson, Gardner, and Salani 2025).

Chronic inflammation represents another important pathway contributing to cardiovascular disease among dialysis patients. In PD, continuous exposure to dialysate and recurrent episodes of peritoneal irritation may promote a persistent inflammatory state and metabolic burden (Roumeliotis et al. 2020). Similarly, HD is also associated with elevated levels of pro-inflammatory cytokines, largely resulting from repeated interaction between blood and the dialysis membrane (Wang and Gao 2022).

Finally, the frequency and intensity of dialysis sessions influence cardiac workload. Home HD allows for more frequent treatments with less intensive fluid removal per session, thereby alleviating the hemodynamic stress commonly observed in conventional thrice-weekly HD. This approach minimizes large volume shifts and rapid blood pressure changes, reducing cardiac strain and ultimately improving cardiovascular outcomes (Canaud et al. 2021; McCullough et al. 2016).

AIMS OF THE STUDY

The primary aim of this study is to evaluate the prognostic outcomes associated with different home dialysis modalities in ESKD patients, with particular attention to survival, infection-related complications, and cardiovascular events. To address this aim, analyses were performed with comprehensive adjustment for potential confounding factors. The specific objectives are as follows:

1. **Survival Outcomes**
   Evaluating the impact of home dialysis modalities (CAPD, APD, and home HD) on overall survival rates.

2. **Infectious Outcomes**
   Assessing the effect of home dialysis modalities on the risk of severe infections.

3. **Cardiovascular Outcomes**
   Determining the impact of home dialysis modalities on cardiovascular risk compared with conventional in-center hemodialysis.

METHODS

1 Study Population

These studies included patients who initiated KRT between 2004 and 2017 in the Helsinki-Uusimaa healthcare district. This district serves a population of 1.7 million people, approximately 30% of Finland's total population. A total of 536 adult patients (aged 18 years or older) were identified as being on home dialysis (either PD or home HD) at day 90 from the start of KRT (31% of all dialysis patients). These patients were followed up until December 31, 2019, or until they moved out of the district, died, or received a kidney transplant. In addition to the home dialysis patients, in Study III 432 patients who were on in-center HD at day 90 from starting dialysis were randomly selected to represent the entire group of in-center HD patients (n=1211), resulting in a total study population of 968. The random selection was made to ensure a representative and manageable data set, as all data were manually collected from patient files.

Table 1 displays the main characteristics of patients in the dialysis modality groups.

During the entire study period, the Helsinki-Uusimaa district has had a "home first" policy when dialysis modality was selected, which means that both PD and home HD were equally prioritized. Patients were informed about their dialysis options through lectures, on-spot information, and videos before making their choice. A multidisciplinary team, including a nephrologist and a dialysis nurse, evaluated the patients for contraindications and suitability for home dialysis. Patients who selected PD underwent training by specialized nurses for at least one week, with a focus on peritonitis prevention. Home HD patients received about six to eight weeks of training to perform dialysis at home, and most (91%) used a fistula for vascular access.

Table 1. Main characteristics of patient populations across different studies.

Patient characteristics	CAPD	APD	Home HD	In-center HD
Number of patients	162	229	145	432
Male sex (%)	70	66	68	64
Median age (years)	65	50	50	66
Primary kidney disease (%)				
Glomerulonephritis	17	22	24	8
Polycystic kidney disease	6	15	31	8
Diabetes	39	30	22	33
Others	39	33	23	51
At least one comorbidity (%)	29	13	13	32
Study I				
Median FU-time (years)	2.8	1.9	1.6	N/A
Deaths in 5 years (n.)	66	26	12	N/A
Death IR*	252	108	87	N/A
Study II				
Median FU-time (years)	2.0	1.6	1.4	N/A
At least one infection episode (%)	62	35	21	N/A
Infection episode IR*	540	371	197	N/A
Number of Infection episodes	197	158	52	N/A
Hospitalization needed (n.)	178	142	38	N/A
Study III				
Median FU-time (years) (IQR)	2.7	1.9	1.6	2.6
At least one MACE event (%)	21	9.6	7.6	24
MACE IR*	109	50	32	91

* Incidence rate (IR) per 1000 patient-years.

2 Study Design

All three studies were observational, retrospective incidence cohort studies, with data retrieved from HUS patient records and the data lake. The studies did not involve patient contact or intervention. Patients were followed up from start of dialysis to the event or censoring for various reasons as appears in Table 2.

Table 2. Comparing methodology in the three studies.

Study Variables	Study I	Study II	Study III
Patients (n.)	536	536	968
Compared groups	CAPD, APD versus home HD	CAPD, APD versus home HD	CAPD, APD, home HD versus in-center HD
Outcome	Survival	Risk of severe infections	Risk of MACE
Event	Death	Severe infection	MACE
Adjustments	Propensity scores	Propensity scores	Propensity scores
Main analysis censoring points		Change from PD to home HD or vice versa	
		Transfer to in-center HD	
		Death	Non-cardiac death
		Kidney transplantation	Kidney transplantation
	Loss of follow-up	Loss of follow-up	Loss of follow-up
	Kidney function recovery	Kidney function recovery	Kidney function recovery
	Five-year follow-up	Five-year follow-up	Five-year follow-up
	December 31, 2019	December 31, 2019	December 31, 2019
Main statistical analyses	Kaplan-Meier curves	Cumulative incidence analysis considering death as a competing risk	Cumulative incidence analysis considering non-cardiac death as a competing risk
	Cox regression models	Cox regression models	Cox regression models
		IR and IRR	IR and IRR
Sensitivity analyses	Censoring at kidney transplantation or transfer from home dialysis to in-center HD	Fine-Gray regression considering competing risks, such as death, transfer to in-center HD, and kidney transplantation. Additional adjustment for prognostic variables.	Exploring different subgroups, such as sex and cardiovascular comorbidity status

3 Data Collection

Data for these studies were extracted retrospectively from the patient data system of Helsinki University Hospital, encompassing a wide range of variables. These included demographic information, clinical characteristics, comorbidities, primary renal disease (PRD), laboratory results, blood pressure, electrocardiogram (EKG) and echocardiography findings, and social factors (Table 3). Specific to Study II, plasma C-reactive protein (CRP) levels were collected from the data lake of the Helsinki-Uusimaa healthcare district, because this marker is virtually always

analyzed when a severe infection is suspected. A structured research database was established using Microsoft Access to handle the extensive data collection.

Severe infections in Study II were identified using a CRP cutoff level of 100 mg/l. All CRP values for study patients were systematically reviewed, and patients with CRP values of 100 mg/L or higher were selected for further investigation. The underlying causes of elevated CRP levels were then classified as either infectious or non-infectious. Subsequently, specific types of infections were identified. Study III focused on Major Adverse Cardiovascular Events (MACE), which included myocardial infarction, ischemic or hemorrhagic stroke, and death due to cardiovascular causes.

Table 3. Variables collected at start of dialysis treatment.

Variables	CAPD	APD	Home HD	In-center HD
Number of patients	162	229	145	432
Categorical variables (%)				
Male sex	70	66	68	64
Primary kidney disease				
Glomerulonephritis	17	22	24	8
Polycystic kidney disease	6	15	31	8
Diabetes	39	30	22	33
Others	39	33	23	51
Comorbid conditions				
Angina pectoris / CAD	12	8	5	16
Coronary angiography	16	5.7	6.2	13
Coronary intervention (CABG/PCI)	11	7.4	5.5	13
Acute myocardial infarction	11	5	6	13
Ischemic CVA	1.2	0.4	1.4	1.4
Bleeding CVA	0.6	0.0	0.0	0.9
Transient ischemic attack	4	1	1	N/A
Peripheral vascular disease (PVD)	6.8	3.5	2.8	11
PVD with surgical intervention	6	1	4	10
Amputation due to PVD	1.9	1.3	0.7	5.8
Congestive heart failure	6.8	3.1	0.7	12
LVH	33	21	17	31
Pulmonary embolism	9.9	4.8	3.4	10
Deep vein thrombosis	2.5	0.0	2.1	1.2
Antithrombotic treatment	96	93	79	83

Variables	CAPD	APD	Home HD	In-center HD
LVH on EKG	3.1	4.8	6.9	7.4
LBBB on EKG	3.1	1.7	2.1	2.8
Malignancy	11	5	10	N/A
Type 1 diabetes	21	21	17	N/A
Type 2 diabetes	21	9	10	N/A
Liver disease	1	4	2	N/A
COPD / Asthma	9	8	10	N/A
Gastrointestinal bleeding	0	0	0.7	N/A
Dementia	0.6	0	0	N/A
Connective tissue disease	0	0.9	0	N/A
Vasculitis	1	2	1	N/A
Depression	8	12	9	N/A
Hypertension	82	84	89	N/A
Dyslipidemia	41	41	41	N/A
Sarcoidosis	0.6	0	0.7	N/A
Obesity	22	17	34	N/A
Other rheumatologic diseases	4	1	0	N/A
Other immunological diseases	0.6	0.9	1	N/A
Other psychological/ neurological/ developmental diseases	6	5	3	N/A
Atrial fibrillation	15	5	5	N/A
Hearing problems	6	3	1	N/A
Visual problems	29	26	14	N/A
Current smoker	15	11	18	N/A
Support in daily activities	30	9	8	N/A
Living alone	22	17	19	N/A
Compliance problem	14	15	10	N/A
Three or more comorbidities	67	54	51	N/A
Dialysis assistance				
by professional	4.9	1.7	0.7	N/A
by family member	18.5	4.4	4.1	N/A
Continuous variables (median)				
Age (years)	65	50	50	66
Echocardiography parameters				
Ejection fraction	60	62	65	60
LVEDD (mm)	49	50	52	51
LVESD (mm)	32	32	32	33

Variables	CAPD	APD	Home HD	In-center HD
LVPW (mm)	11	11	11	11
Septum (mm)	12	12	12	13
Electrocardiogram parameters				
Heart rate (bpm)	67	67	68	71
PR-interval (ms)	176	162	161	168
QRS-duration (ms)	94	96	94	96
QT-interval (ms)	416	412	404	414
Corrected QT-interval (ms)	435	435	430	453
P-Axis (degree)	51	53	51	51
R-Axis (degree)	17	22	19	17
T-Axis (degree)	54	49	48	58
Laboratory findings at start of dialysis				
P-Creatinine (μmol/l)	557	582	621	556
P-Urea (mmol/l)	26	27	28	25
P-Albumin (g/l)	36	36	36	30
P-ionized calcium (mmol/l)	1.2	1.2	1.2	1.2
P-Phosphate (mmol/l)	1.7	1.7	1.8	1.7
Hemoglobin (g/l)	114	111	109	100
P-C-reactive protein (mg/l)	5	4	4	8
Total P-Cholesterol (mmol/l)	4.0	4.2	4.0	3.7
High density lipoprotein (mmol/l)	1.3	1.2	1.2	1.1
P-Triglycerides (mmol/l)	1.6	1.4	1.4	1.4
Hemoglobin A1C (mmol/l)	7	7	6	6
Systolic BP (mmHg)	149	144	148	147
Diastolic BP (mmHg)	84	88	84	79
Height (cm)	170	173	174	171
Weight (kg)	75	77	80	77
Body mass index (kg/m2)	25.7	24.9	26.4	25.9

4 Statistical Analysis

Incidence rates (IR) and incidence rate ratios (IRR) and their 95% confidence intervals (CI) were calculated for infection episodes and MACE across the different dialysis modalities. The cumulative incidence was estimated using the R Software (version Ri386 3.6.0, the cmprsk package, cuminc function), and calculations accounted for competing risk events, such as death, in Studies II and III.

All other statistical analyses were performed using SPSS (version 25). P Values for comparing categorical variables between groups were calculated using the Independent Samples T Test and continuous variables were assessed with the One-Way ANOVA. Kaplan-Meier curves and Cox regression analyses were used across the studies to estimate survival probabilities and hazard ratios for different outcomes, including death, infection episodes, and cardiovascular events.
Table 2 displays the methodology of the three studies.

5 Confounding Factors and Propensity Score Adjustment

All three studies acknowledged the potential for confounding factors that could influence the outcomes associated with different dialysis modalities. These factors included demographic variables, comorbidities, laboratory parameters, and social factors and are detailed in Table 3. To address potential confounding factors, propensity scores were developed using binary logistic regression for pairwise comparisons between different dialysis modalities (e.g., CAPD vs. home HD, APD vs. home HD, and PD vs. home HD). Variables were selected using a stepwise forward procedure from the patient characteristics and comorbidities listed in Table 3.

In Studies I and II, propensity scores were calculated separately for each pairwise comparison (APD vs. home HD, CAPD vs. home HD, and combined PD vs. home HD). Study III extended this approach to include comparisons between in-center HD and home dialysis modalities (CAPD, APD, and home HD).

6 Censoring and Sensitivity Analyses

In the main analysis of Study I, patients were followed up until death (the outcome), or censoring at five years, the end of the study period (December 31, 2019), or at the time of moving outside the healthcare district (n=13). Importantly, several sensitivity analyses were conducted, including censoring at kidney transplantation or transfer from home dialysis to in-center hemodialysis (HD), to ensure the robustness of the findings. These analyses helped address potential biases introduced by different censoring points and ensured that the results were consistent across various scenarios.

In Study II infection episodes were the primary outcome. The censoring points included the end of the follow-up period (five years or December 31, 2019), kidney transplantation, transfer to in-center HD, change between home dialysis modalities (not between CAPD and APD), and death. In sensitivity analyses using

Fine-Gray regression, the study took into account the competing risk events death, transfer to in-center HD, and kidney transplantation. This approach acknowledged that patients might experience other events that preclude the occurrence of the infection episode.

Study III expanded the population to include, in addition to home dialysis patients, a randomly selected sample of in-center HD patients. The study primarily examined MACE and censored for kidney transplantation, recovery of kidney function, loss of follow-up, death due to non-cardiac causes, and the end of the follow-up period (December 31, 2019). The study's approach to censoring was similar to the previous studies. As the MACE event included death due to cardiovascular disease, the cumulative incidence analysis accounted for the competing risk of non-cardiac death events. Sensitivity analyses were also conducted to explore various subgroups, such as sex and cardiovascular comorbidity status, ensuring that the findings were consistent across these different patient populations.

7 Outcome Variables

The primary outcome variables varied across the studies:

Study I examined survival, and the risk of all-cause death associated with different dialysis modalities

Study II investigated risk of getting a severe infection. The study also presented IR and IRR of infections.

Study III evaluated the risk of MACE. IR and IRRs of MACE were also assessed.

8 Explanatory Variables

The explanatory variables in each study were the types of dialysis modalities used by patients at 90 days from the start of KRT. These modalities included CAPD, APD, and home HD. In Study III, in-center HD was also included as an additional modality for comparison.

RESULTS

Study I

1 Population Characteristics

The study evaluated patients on CAPD, APD, and home HD (Figure 2), showing comparable baseline characteristics among home HD and APD patients, with a median age of 50 years at the start of KRT. The proportion of patients with three or more comorbidities was similar in both groups (51 and 54%). The proportion of patients waitlisted for kidney transplantation (88 and 85%) or who received a transplant (81 and 73%) during the follow-up was also similar across these groups. CAPD patients were older (median age 65 years), had a higher prevalence of comorbidities (67% with three or more), and required more support in daily activities and dialysis (Table 3).

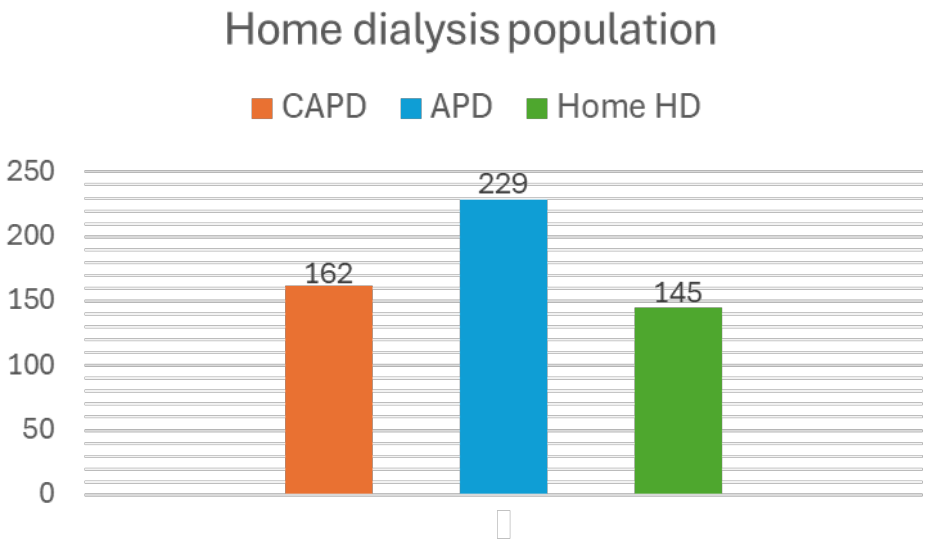


Figure 2. Number of patients who were on home dialysis at day 90 from start of KRT in 2004 to 2017

2 Survival Analysis

Kaplan-Meier curves revealed similar survival probabilities for patients on home HD and APD, while those on CAPD exhibited significantly lower survival rates (Figure 3). The five-year survival rates were 90% for home HD, 88% for APD, and 56% for CAPD patients, with a combined five-year survival rate of 75% for all PD patients (Figure 4).

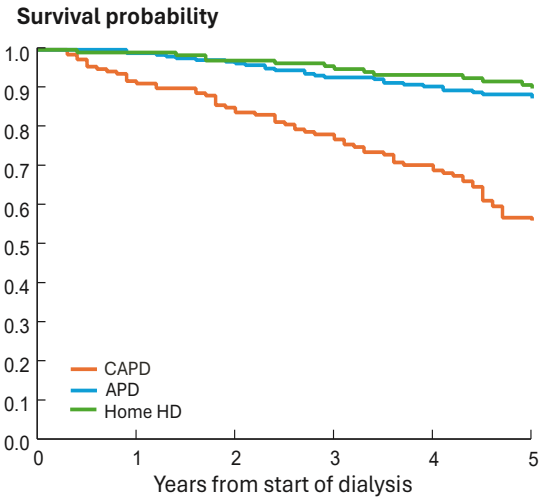


Figure 3. Kaplan-Meier survival curves of home dialysis patients.

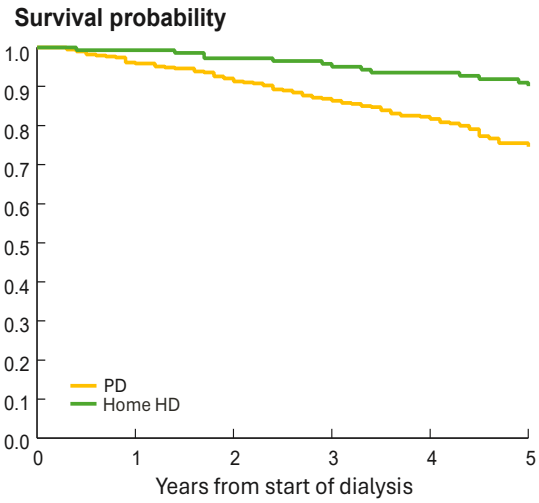


Figure 4. Kaplan-Meier survival curves of PD and home HD patients

3 Hazard Ratios of Death

Cox regression analyses, both unadjusted and adjusted for age and sex, indicated no significant difference in the risk of death between APD and home HD patients (Table 4). Propensity score adjustment yielded a hazard ratio of 1.1 (95% CI 0.52–2.4) for APD compared to home HD, still showing no significant difference. CAPD was associated with a 5.9-fold unadjusted risk of death compared to home HD, which reduced to 1.6 (95% CI 0.74–2.6) after propensity score adjustment, indicating no statistically significant difference.

Table 4. Hazard ratios for mortality in home dialysis patients.

Adjustment of Cox regression	CAPD	APD	PD
	HR (95% CI) compared to home HD		
Unadjusted	5.9 (3.2–10.9)	1.4 (0.69–2.7)	3.1 (1.7–5.6)
Age and sex	3.5 (1.8–6.7)	1.4 (0.69–2.7)	2.2 (1.2–4.1)
Propensity score	1.6 (0.74–3.6)	1.1 (0.52–2.4)	1.5 (0.81–2.9)

4 Sensitivity Analyses

Sensitivity analyses, including censoring at the time of transfer to in-center HD or kidney transplantation, confirmed that the hazard ratio of death for APD compared to home HD remained statistically insignificant (Table 5). Additional adjustments for need for assistance in dialysis and removal of the five-year censoring threshold yielded similar results.

Table 5. Sensitivity analyses of survival in home dialysis.

Sensitivity analysis* Adjusted for propensity score	CAPD	APD	PD
	HR (95% CI) compared to home HD		
Censoring at transfer to in-center HD or at transplantation	1.1 (0.40–2.9)	1.3 (0.51–3.3)	1.4 (0.63–3.1)
Tx waitlisting as a time-dependent variable	1.5 (0.68–3.2)	1.2 (0.57–2.6)	1.5 (0.81–2.9)
Tx as a time-dependent variable	1.4 (0.63–2.9)	0.96 (0.44–2.1)	1.3 (0.66–2.4)

*Censored at 5 years since start of KRT.

Study II

1 Population Characteristics

The study population, which consisted of the same patients studied in Study I, comprised 536 patients on home dialysis at day 90 from the start of KRT, distributed as in Figure 2. CAPD patients were generally older, had more comorbidities, and required more dialysis assistance compared to home HD patients. APD patients had characteristics similar to those of home HD patients (Table 3).

2 Cumulative Incidence of Severe Infections

During the follow-up, 213 patients (40%) experienced at least one severe infection episode. The cumulative incidence of a first severe infection episode at one year was 35% for CAPD, 25% for APD, and 11% for home HD patients (Figure 5), with CAPD and APD patients exhibiting a 2–3-fold increased risk of a first infection compared to home HD (Table 6).

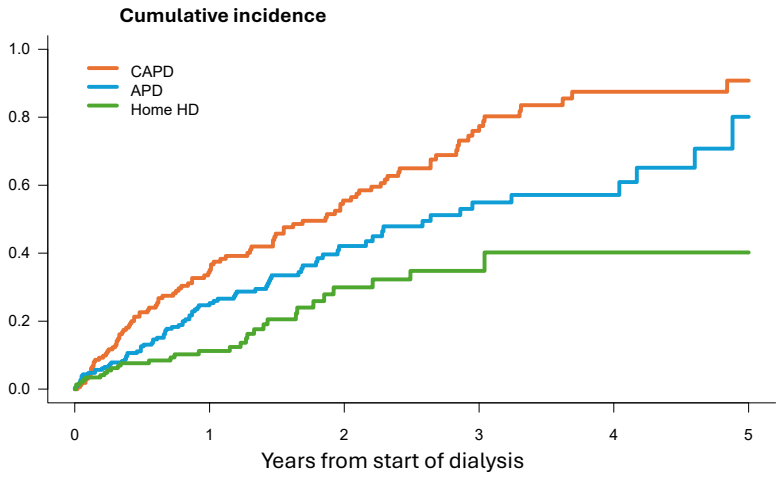


Figure 5. Cumulative incidence of the first severe infection in home dialysis patients.

Table 6. Hazard ratios for the first severe infection episode in home dialysis patients.

Cox regression analysis adjustment	CAPD	APD
	compared to home HD HR (95% CI)	
Unadjusted	3.2 (2.1–4.8)	1.9 (1.2–2.8)
Age and sex	2.7 (1.7–4.1)	1.9 (1.2–2.8)
Propensity score	2.8 (1.6–4.8)	2.2 (1.4–3.5)

3 Incidence Rate of Severe Infections

The overall IR of severe infections was highest among CAPD patients, with 540 episodes per 1000 patient-years, followed by APD patients at 371 episodes and home HD patients at 197 episodes (Figure 6, Table 7). In patients undergoing PD, severe infections were considered dialysis-related if they occurred in conjunction with peritonitis, or with PD catheter or exit site infections.

In home HD patients, bloodstream infections were classified as dialysis-related if they were clearly linked to the dialysis access site or if the source of infection was unclear (e.g., not attributable to other sites such as the urinary tract).

CAPD patients had a significantly higher IRR of 14 (95% CI 6.7–31) for dialysis-related infections compared to home HD patients, while APD patients had an IRR of 9.7 (95% CI 4.5–21).

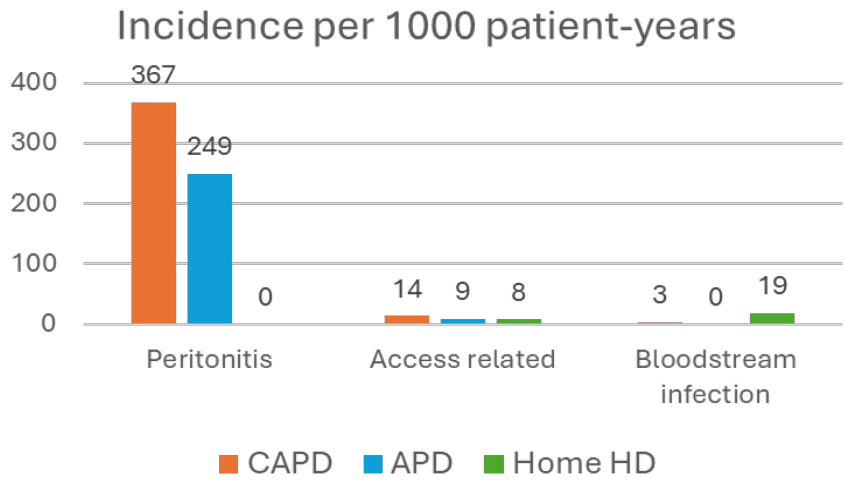


Figure 6. Incidence of dialysis-related infections in home dialysis patients

Table 7. Incidence of all severe infections in home dialysis patients.

Home dialysis modality		CAPD	APD	Home HD
Patient-years		365	426	264
All infections	IR* (n.)	540 (197)	371 (158)	197 (52)
	IRR (95% CI)	2.7 (2.0–3.7)	1.9 (1.4–2.6)	1 (reference)
Dialysis-related infections	IR* (n.)	383 (140)	258 (110)	27 (7)
	IRR (95% CI)	14 (6.7–31)	9.7 (4.5–21)	1 (reference)
Bloodstream infections	IR* (n.)	16 (7)	12 (5)	42 (11)
	IRR (95% CI)	0.46 (0.25–0.85)	0.28 (0.15–0.52)	1 (reference)
Non-dialysis-related infections	IR* (n.)	156 (57)	113 (48)	170 (45)
	IRR (95% CI)	0.90 (0.65–1.2)	0.65 (0.47–0.89)	1 (reference)
Infectious hospitalization	IR* (n.)	488 (178)	333 (142)	144 (38)
	IRR (95% CI)	2.5 (1.8–3.4)	1.7 (1.2–2.3)	1 (reference)
Fatal infections	IR* (n.)	41 (15)	9 (4)	4 (1)
	IRR (95% CI)	11 (1.5–80)	2.5 (0.33–18)	1 (reference)

*Incidence rate (IR) per 1000 patient-years.

4 Causes of Severe Infections

Peritonitis was the predominant cause of infection among CAPD and APD patients, accounting for 68% and 67% of episodes, respectively. Bloodstream infections were more common in home HD patients (21% of all severe infections) compared to PD patients (3%). The IRR for all bloodstream infections was 0.46 for CAPD and 0.28 for APD compared to home HD. Among non-dialysis-related infections, skin/soft tissue and respiratory infections were the most common causes (Figure 7). Staphylococcus aureus was the most common causative organism (24%) in peritonitis cases, followed by Coagulase-negative Staphylococcus (17%) (Figure 8).

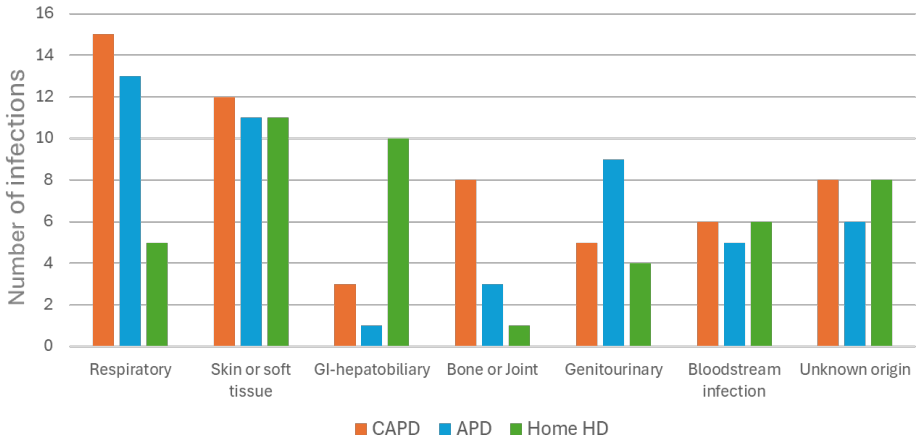


Figure 7. Distribution of non-dialysis-related severe infection events in home dialysis patients.

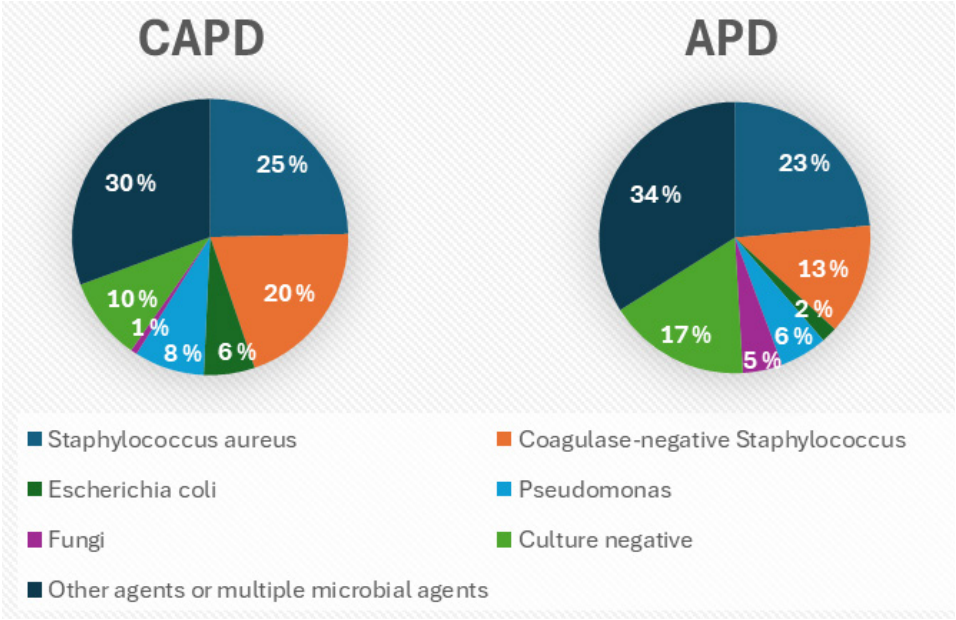


Figure 8. Distribution of Organisms Causing Peritonitis in PD Patients.

5 Hospitalization Due to Severe Infections

Of the 407 severe infection episodes, 88% required hospitalization, with 90% of CAPD and APD patients and 73% of home HD patients requiring hospital care (Table 1). The median hospital stay was 6 days for CAPD and APD patients and

8 days for home HD patients. CRP levels correlated with the length of hospital stay and the need for intensive care, particularly in cases where CRP was 200 mg/L or higher.

6 Severe Infection Episodes Before Dialysis Start

Both PD and home HD patients had higher infection rates after starting KRT than before (Figure 9). There was no significant difference in infection rates during the two years prior to KRT among the groups.

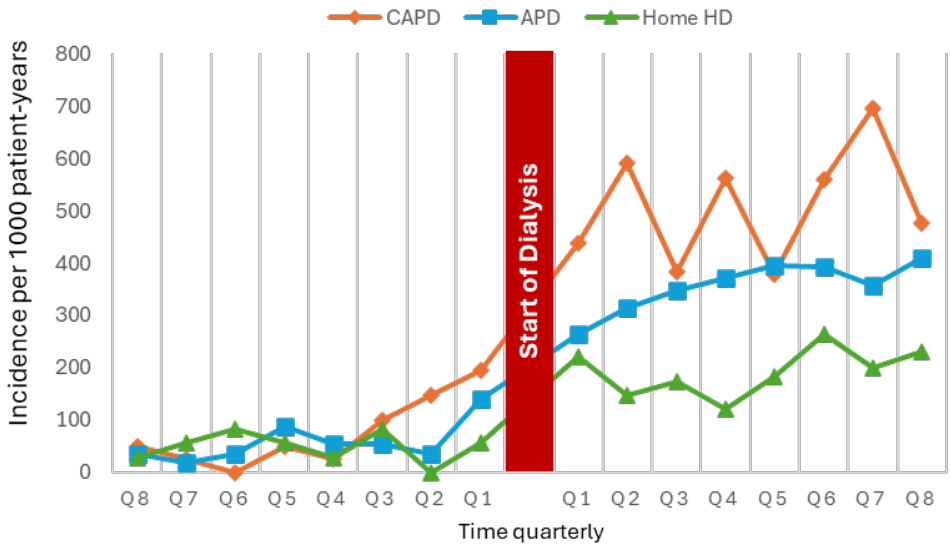


Figure 9. Incidence rate of severe infection episodes before and after the start of dialysis in home dialysis patients.

Study III

1 Population Characteristics

This study included 968 patients, comprising those from Studies I and II (162 on CAPD, 229 on APD, and 145 on home HD), along with 432 patients on in-center HD at day 90 following dialysis initiation (Figure 10). CAPD and in-center HD patients were generally older and had more cardiovascular comorbidities compared to those on APD or home HD (Table 1). In-center HD patients had a higher prevalence of diabetes and a lower prevalence of glomerulonephritis or polycystic kidney disease.

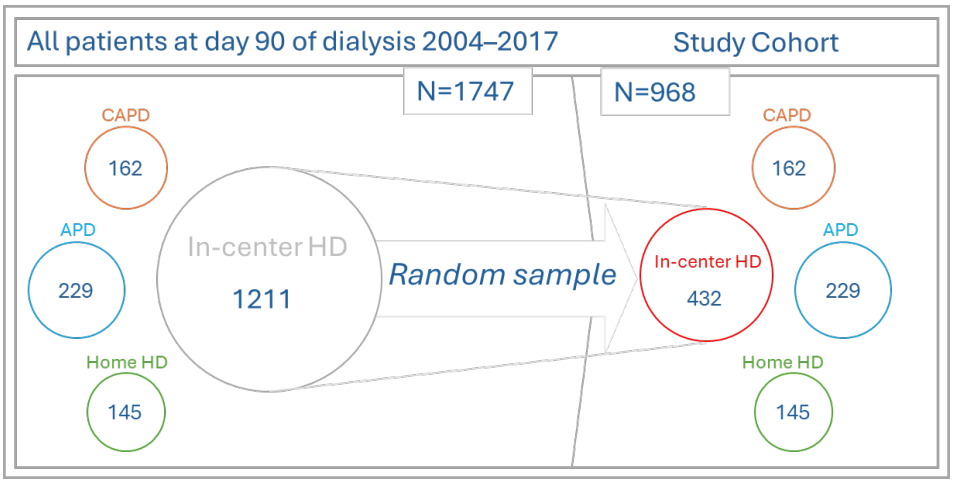


Figure 10. Study cohort

2 Cumulative Incidence of First MACE

A total of 172 patients (18%) experienced at least one MACE during the follow-up. The cumulative incidence of the first MACE at one year was highest in in-center HD patients (10%), followed by CAPD (8%), APD (3%), and home HD (2%) patients (Figure 11). APD and home HD patients had a lower risk of getting a MACE compared to in-center HD patients, although these differences became statistically insignificant after propensity score adjustment (Table 8).

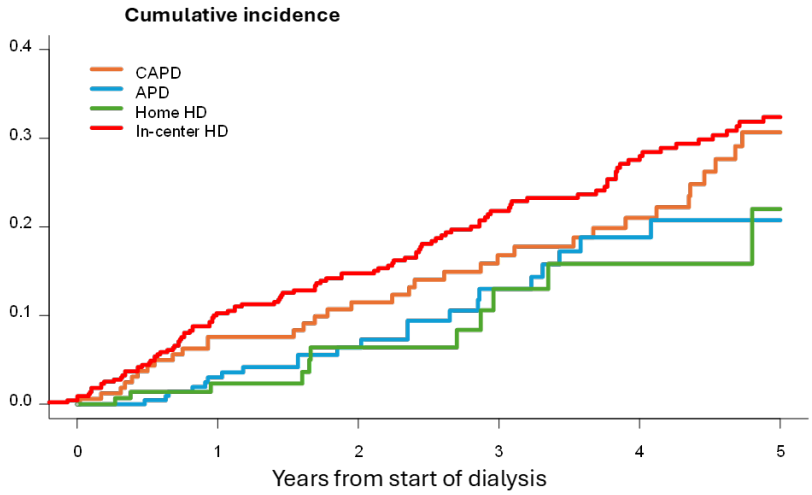


Figure 11. Cumulative incidence of the first MACE in dialysis patients.

Table 8. Hazard ratios of the first MACE in dialysis patients.

Adjustment of Cox regression	CAPD	APD	Home HD
	HR (95% CI) compared to in-center HD		
Unadjusted	0.83 (0.56–1.22)	0.49 (0.31–0.77)	0.42 (0.23–0.78)
Age and sex	0.81 (0.55–1.20)	0.62 (0.38–1.00)	0.53 (0.28–1.00)
Propensity score	1.22 (0.73–2.05)	0.86 (0.47–1.57)	0.67 (0.30–1.50)

3 Incidence Rate of MACE

The IR of MACE was highest in CAPD patients at 109 events per 1000 patient-years, followed by in-center HD at 91, APD at 50, and home HD at 32 (Table 9). The IRR was 1.20 (95% CI 0.99–1.46) for CAPD, 0.55 (95% CI 0.45–0.67) for APD, and 0.35 (95% CI 0.29–0.43) for home HD compared to in-center HD patients.

Table 9. Incidence rate and incidence rate ratios for all MACE events in dialysis patients.

Dialysis modality	CAPD	APD	Home HD	In-center HD
MACE events (n.)	41	26	11	115
Patient-years	375	522	345	1266
IR* of MACE	109	50	32	91
IRR of MACE (95% CI)	1.20 (0.99–1.46)	0.55 (0.45–0.67)	0.35 (0.29–0.43)	1 (reference)

*Incidence rate (IR) per 1000 patient-years.

4 Sensitivity Analyses

Sensitivity analyses revealed that the risk of the first MACE did not significantly differ between patients with or without pre-existing cardiovascular comorbidities when adjusted for propensity scores. There was a notable interaction between sex and treatment modality, with PD being associated with a higher risk of MACE in males and a lower risk in females compared to in-center HD or home HD (Table 10). Additional analyses were consistent with the main findings, even when censoring for modality changes during the follow-up.

Table 10. Hazard ratios of the first MACE in males and females with propensity score adjustment in dialysis patients.

Gender	CAPD	APD	PD	Home HD
HR (95% CI) compared to in-center HD				
Males	1.78 (1.02–3.09)	1.26 (0.65–2.45)	1.80 (1.11–2.92)	0.62 (0.21–1.80)
Females	0.25 (0.07–0.93)	0.22 (0.05–0.94)	0.37 (0.14–0.99)	0.73 (0.20–2.57)
Interaction p value	0.04	0.06	0.006	0.33
HR (95% CI) compared to home HD				
Males	2.09 (0.72–6.08)	1.73 (0.59–5.01)	2.06 (0.82–5.21)	
Females	0.09 (0.01–0.79)	0.33 (0.07–1.58)	0.32 (0.09–1.17)	
Interaction p value	0.01	0.02	0.01	

DISCUSSION

The selection of dialysis modality is a pivotal decision in the management of patients with ESKD, impacting their overall health and quality of life. This investigation aims to assess how different home dialysis modalities––namely CAPD, APD, and home HD–– affect key patient outcomes, including survival, infection risk, and cardiovascular events. Survival represents a fundamental measure of the long-term effectiveness of dialysis therapy. Infections, a common and serious complication in dialysis patient, vary in frequency and severity depending on the modality used. Cardiovascular events, the leading cause of death among dialysis patients, are particularly critical in shaping overall prognosis and may also be influenced by the choice of dialysis modality. Together, these outcomes offer a comprehensive framework for understanding the relative benefits and risks associated with each treatment approach.

1 Comparative survival outcomes

Study I primarily focused on comparing survival rates among patients on home HD, APD, and CAPD. Notably, crude analysis suggested that survival rates were similar between patients on home HD and APD, while those on CAPD exhibited lower survival rates. However, this disparity diminished and became statistically insignificant after adjusting for confounding factors using propensity scores. This suggests that the survival disparity could be attributed to the older age and greater frailty of CAPD patients rather than the dialysis modality itself.

One of the critical insights from this study is the importance of adjusting for a comprehensive range of confounders when comparing different dialysis modalities. Since randomized trial protocols are practically impossible in this context, a well-designed standardized cohort study represents the best available approach. Previous studies that reported a survival advantage for home HD over PD often lacked the depth of confounder adjustment seen here (Nitsch et al. 2011; Marshall et al. 2011; Marshall et al. 2014; Nadeau-Fredette et al. 2015; Weinhandl, Gilbertson, and Collins 2016; Rydell et al. 2019). The inclusion of 34 different comorbidities, along with factors such as patient compliance and the need for daily assistance, enabled a detailed analysis that more accurately considers the differences between patient groups. This level of detail helps to clarify why earlier studies found a survival benefit for home HD that was not observed in this study after adjustment.

Moreover, the present study is notable in that it separates APD and CAPD—an approach that has seldom been applied in earlier research. The findings suggest that APD patients share more characteristics with home HD patients than with CAPD patients, which may help explain the observed similarity in survival outcomes between APD and home HD. This distinction underscores the need for future studies to continue treating APD and CAPD as separate entities when analyzing outcomes.

Overall, this study suggests that survival should not be the only consideration when selecting a dialysis modality, as the differences between home HD and APD were minimal after adjusting for confounding factors. This finding supports the view that patient preferences, quality of life, and other clinical outcomes should also be taken into account when choosing a dialysis modality.

2 Infection risks across dialysis modalities

Study II focused on the incidence of severe infections among patients undergoing CAPD, APD, and home HD. The findings reveal that patients on CAPD and APD had a significantly higher risk of severe infections compared to home HD patients, primarily driven by peritonitis in PD patients. The cumulative incidence of the first severe infection episode was 35% for CAPD, 25% for APD, and 11% for home HD at one year from the start of dialysis. Even after adjusting for confounding factors, CAPD and APD patients had a 2-3-fold risk of severe infections compared to home HD patients. In previous studies, comparisons between CAPD and APD have yielded contradictory results. Some studies reported a higher incidence of peritonitis in CAPD patients compared to those on APD (Rabindranath et al. 2007; Rodríguez-Carmona et al. 1999; Kokubu et al. 2020), while others found no significant difference (Bieber et al. 2014; Mehrotra 2009; Cnossen et al. 2011; Lan et al. 2014).

The high incidence of peritonitis among CAPD and APD patients was a major contributor to this increased infection risk. Interestingly, when dialysis-related infections were excluded, the infection burden between the modalities was similar, with CAPD and APD patients even showing a lower risk of bloodstream infections compared to home HD patients. This suggests that while PD modalities are associated with higher peritonitis rates, their infection profile may be otherwise comparable to home HD.

Notably, the infection risk was higher in CAPD patients, who also had a greater need for dialysis assistance and more comorbidities compared to APD and home HD patients. Moreover, the nature of CAPD might increase exposure to infection and attribute to the higher incidence of peritonitis in CAPD patients compared to APD. However, despite the lower overall infection rate in home HD, the risk of

bloodstream infections remains a concern, although it was not associated with increased mortality in this study.

Our findings emphasize the importance of preventing peritonitis in PD patients and suggest that home HD may be a preferable option for those at high risk of developing peritonitis. Unfortunately, there is no definitive method to identify patients at an increased risk of peritonitis, which could serve as a potential area for further research.

3 Cardiovascular outcomes and MACE incidence

The third study investigated the incidence of major adverse cardiovascular events (MACE) among patients on CAPD, APD, home HD, and in-center HD. The cumulative incidence of MACE was highest among in-center HD patients, followed by CAPD, with APD and home HD patients showing the lowest incidence. At one year from the start of dialysis, the cumulative incidence of the first MACE was lowest in home HD patients (2%) and highest in in-center HD patients (10%). After adjusting for potential confounders using propensity scores, the differences in unadjusted risk of MACE between the modalities were no longer statistically significant, although the trend favored home-based dialysis.

Previous studies have compared cardiovascular risk and mortality across different dialysis modalities. Hu et al. reported that PD was associated with a slightly higher risk of cardiovascular events compared to in-center HD (Hu et al. 2020), but highlighted the need for studies that adjust for confounding factors such as cardiovascular comorbidities and diagnostic findings––factors that were accounted for in our study. A 2019 meta-analysis of five studies (Wang et al. 2016; Refaat et al. 2016; Kim et al. 2015; LOCATELLI et al. 2001; Borràs Sans M 2017) found no significant difference in cardiovascular events between PD and HD (Lozier et al. 2019), although one study suggested a lower risk with PD (Wang et al. 2016). Additionally, PD was associated with lower hospitalization rates for heart failure compared to in-center HD (Sun CY 2019). Frequent home HD has been linked to reduced cardiovascular hospitalizations compared to PD (Suri, Li, and Nesrallah 2015; Weinhandl, Gilbertson, and Collins 2016; McCullough et al. 2016).

The reduced cardiovascular risk associated with home dialysis modalities, particularly APD and home HD, could be attributed possibly to the more stable hemodynamic profiles and the ability to tailor dialysis schedules to patient needs. Home dialysis patients often have more control over their treatment schedule, allowing for more frequent and longer dialysis sessions, which could lead to better fluid management and reduced cardiovascular stress. Additionally, patients on APD and home HD are typically younger and have fewer comorbidities, which also contributes to their lower cardiovascular risk.

However, the lack of statistically significant differences after adjustment suggests that the initial differences are likely due to underlying patient characteristics rather than the dialysis modality itself. Additionally, the fact that cardiovascular comorbidities were more prevalent among in-center HD and CAPD patients supports the notion that sicker patients are more likely to be treated with these modalities, leading to worse unadjusted outcomes. The similar outcomes between home dialysis, and in-center HD after adjustment emphasize the importance of individualized patient care and selection.

Finally, this study presents a novel finding that PD is associated with a higher risk of MACE than in-center HD among males while the finding is the opposite among females, suggesting a sex-specific disparity in cardiovascular outcomes. The observed difference in MACE risk between sexes could partially be explained by biological differences and the potential influence of dialysis modality on cardiovascular health. While previous studies have highlighted sex-related differences among PD patients, a similar comparison has not been extensively reported (Kitterer et al. 2017; Danneville et al. 2022). This finding underscores the need for a more personalized approach to dialysis care, considering sex-specific factors that might influence outcomes. Further research is necessary to confirm these findings and to guide the development of strategies to reduce the cardiovascular burden in this vulnerable population.

4 Strengths

The studies employed comprehensive population-based cohorts, which included large samples of patients across various dialysis modalities such as CAPD, APD, home HD, and in-center HD. Notably, a significant strength of the studies was the relatively large cohort of patients receiving home HD, as this treatment modality has been offered to patients at our institution for an extended period. This broad sampling enhances the external validity of the results and minimizes selection bias, as all patients within a specific healthcare district were included at day 90 of KRT initiation, reflecting real-world clinical practices.

The studies provided extensive data on patient demographics, comorbidities, and dialysis modalities, which allowed comprehensive adjustment for potential confounding factors using propensity score analysis.

Another strength is the distinction between APD and CAPD. Unlike previous research that often grouped all peritoneal dialysis patients together, these studies separately analyzed APD and CAPD patients, which is crucial given the different technical requirements and patient profiles associated with each modality. This separation led to more precise insights into the outcomes associated with each

method, such as the observation that APD and home HD had similar survival rates, highlighting the importance of considering specific PD modalities individually.

The studies also featured robust outcome measures, assessing critical clinical outcomes such as overall survival, severe infections, and major adverse cardiovascular events (MACE).

Finally, several sensitivity analyses were performed and they showed similar results in various scenarios, for example when using different censoring techniques in the Cox regression.

5 Limitations

The studies are subject to certain limitations. First, the observational design inherently limits the ability to establish causality. Despite extensive adjustments for confounders, residual confounding may persist due to unmeasured factors such as patient adherence, social support, and specific health behaviors, which could influence the observed outcomes.

Another limitation is the relatively small number of patients, that may limit the statistical power to detect differences, especially in subgroup analyses involving rare events like MACE or specific severe infections.

The selection process and distribution of dialysis modalities vary between countries and healthcare settings, which may limit the applicability of the findings to other populations. For instance, the high proportion of home HD patients in these studies, compared to other regions where home HD is less common, could affect the generalizability of the results.

Additionally, the studies lacked reliable individual data on residual kidney function and on the intensity, frequency, and duration of dialysis. The absence of such information could introduce variability in the results, as residual kidney function is an important determinant of patient outcomes. For example, preserved residual function may allow lighter dialysis regimens to be sufficient when the overall prognosis is favorable, whereas differences in dialysis intensity and frequency can otherwise have a significant impact on outcomes such as survival and infection rates.

Moreover, there was no information on quality of life and some other outcomes. While the studies focused on survival, severe infections, and MACE, they did not extensively explore other important patient-centered outcomes such as patient satisfaction, and long-term functional status. These aspects are crucial for making informed decisions about dialysis modality, particularly regarding patient preferences and overall well-being.

Finally, there may be heterogeneity in infection management practices between countries. Studies have shown that hospitalization rates for peritonitis

may not be generalizable due to variations in local practices. For instance, in some regions, most peritonitis treatments are initiated in the hospital, whereas in others, treatment may begin in outpatient settings. Such differences in infection management protocols across centers could influence the observed incidence rates of hospitalisations, thereby limiting the applicability of the findings to settings with differing practices.

6 Clinical implications

For patients who have technical ability and adequate support to manage more complex home dialysis, both home HD and APD provide comparable survival outcomes and may lower the risk of cardiovascular events compared with in-center HD. Home HD may be particularly beneficial for patients at higher risk of infections, as it is associated with significantly lower infection rates. By contrast, CAPD can be a suitable option for older or frailer patients who may not be able to manage the demands of home HD or APD. However, the higher infection risk associated with CAPD should be clearly discussed with these patients, while the greater convenience and less intensive nature of CAPD remain important considerations in weighing this modality.

Given the elevated risk of peritonitis among CAPD and APD patients, robust infection prevention measures are essential. These should include comprehensive patient education, regular monitoring, and clearly defined early intervention protocols. Patients with a history of peritonitis or other significant risk factors require particularly close follow-up. Where feasible, home HD may be considered as an alternative to reduce infection risk.

Comprehensive management of cardiovascular risk remains critical in patients with ESKD. Although differences in MACE risk between home-based modalities and in-center HD appear to diminish after adjustment, the potential cardiovascular advantages of home HD and APD should still be taken into account. Observed sex differences in MACE further underscore the need for additional research to clarify these patterns.

Ultimately, the choice of dialysis modality should be guided by patient counseling and shared decision-making, with careful consideration of the patient's lifestyle and the practical feasibility of treatment. In the light of current evidence, a personalized approach is warranted, balancing patient preferences with clinical indications and considering the risk of peritonitis in PD.

CONCLUSIONS

Survival outcomes varied significantly among the different home dialysis modalities. Patients on home HD and APD exhibited comparable survival rates, whereas patients on CAPD had significantly lower survival. However, after adjusting for confounders such as age, comorbidities, and the need for assistance with dialysis, the survival differences between CAPD and home HD diminished and lost statistical significance. This suggests that the observed survival disparity was primarily due to patient characteristics rather than the dialysis modality itself. Consequently, the choice between home dialysis modalities should be guided by other factors than survival.

The risk of severe infections differed markedly across modalities. CAPD and APD patients had a significantly higher risk of severe infections, due to peritonitis associated with PD, compared to home HD patients. Even after adjusting for confounders, the elevated risk of severe infection persisted for CAPD and APD patients. This underscores the need for further research to identify patients at higher risk of peritonitis and develop targeted preventative strategies.

Cardiovascular outcomes, particularly the incidence of MACE, also showed variability between modalities. Home HD and APD patients experienced a lower cumulative incidence of MACE compared to CAPD and in-center HD patients. However, after adjusting for confounders, the initial differences in MACE risk between home HD/APD and in-center HD patients were attenuated. Additionally, sex differences in cardiovascular outcomes on HD and PD warrant further investigation to better inform clinical decision-making.

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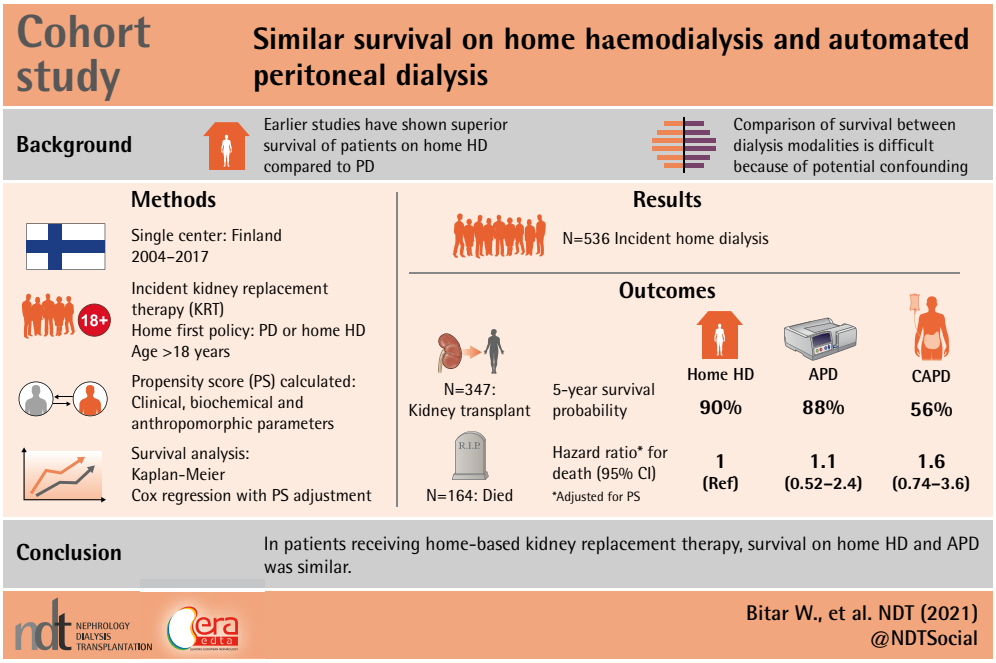
Similar survival on home haemodialysis and automated peritoneal dialysis: an inception cohort study

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GRAPHICAL ABSTRACT



ABSTRACT

Background. Several studies have shown superior survival of patients on home haemodialysis (HD) compared with peritoneal dialysis (PD), but patients on automated PD (APD) and continuous ambulatory PD (CAPD) have not been considered separately. As APD allows larger fluid volumes and may be more efficient than CAPD, we primarily compared patient survival between APD and home HD.

Methods. All adult patients who started kidney replacement therapy (KRT) between 2004 and 2017 in the district of

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ORIGINAL ARTICLE
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KEY LEARNING POINTS

What is already known about this subject?

- Earlier studies have shown superior survival of patients on home haemodialysis (HD) compared with peritoneal dialysis (PD), but automated PD (APD) and continuous ambulatory PD have not been considered separately.
- Comparison of survival between dialysis modalities is difficult because of potential confounding.

What this study adds?

- Patients on APD and home HD have similar survival outcomes.

What impact this may have on practice or policy?

- This study provides information on survival outcomes, which is important for healthcare professionals and patients when choosing the type of home dialysis modality.

Helsinki-Uusimaa in Finland and who were on one of the home dialysis modalities at 90 days from starting KRT were included. We used intention-to-treat analysis. Survival of home HD, APD and CAPD patients was studied using Kaplan–Meier curves and Cox regression with adjustment for propensity scores that were based on extensive data on possible confounding factors.

Results. The probability of surviving 5 years was 90% for home HD, 88% for APD and 56% for CAPD patients. After adjustment for propensity scores, the hazard ratio of death was 1.1 [95% confidence interval (CI) 0.52–2.4] for APD and 1.6 (95% CI 0.74–3.6) for CAPD compared with home HD. Censoring at the time of kidney transplantation (KTx) or at transfer to in-centre HD did not change the results. Characteristics of home HD and APD patients at the start of dialysis were similar, whereas patients on CAPD had higher median age and more comorbidities and received KTx less frequently.

Conclusions. Home HD and APD patients had comparable characteristics and their survival appeared similar.

Keywords: home dialysis, home haemodialysis, kidney replacement therapy, peritoneal dialysis, survival

INTRODUCTION

Since home dialysis has been associated with lower costs, higher participation in working life and better quality of life [1–3], many centres have a home-first policy. However, the proportion of patients on peritoneal dialysis (PD) and home haemodialysis (HD) varies markedly between countries, for instance, 3% in Japan, 7% in France, 12% in the USA, 26% in Finland, 47% in New Zealand and 74% in Hong Kong [4].

Several studies have compared survival of patients on PD and HD [5–8]. PD appears to be associated with better survival during the first 2 years of kidney replacement therapy (KRT), but the difference disappears thereafter. However, a reliable comparison is difficult because randomized trials of dialysis modalities have not been feasible. Outcomes of various types of dialysis are compared in observational studies, which require adequate adjustment for confounding, because patient characteristics typically differ considerably between dialysis modalities.

To our knowledge, six studies have compared the survival prognosis between patients on home HD and PD [9–14]. In all of these studies, home HD was associated with lower mortality compared with PD. Notably, none of the studies analysed automated PD (APD) and continuous ambulatory PD (CAPD) separately. As APD allows more flexible adjustment of dialysis treatment, e.g. by easily increasing the number and volume of fluid exchanges, it may improve dialysis accuracy, and some studies have shown improved patient survival on APD compared with CAPD [15, 16], whereas others have not [17, 18]. APD requires more technical skills of the patient than CAPD, and in that regard APD and home HD patients can be expected to share similar characteristics. Therefore, when comparing outcomes of patients on home HD with those on PD, selection bias may be reduced if specifically comparing with patients on APD.

In this study performed in an academic hospital with a long commitment to home dialysis, we investigated patient survival in home therapies. We used comprehensive data to adjust for putative confounding factors and we primarily compared APD with home HD.

MATERIALS AND METHODS

Study design and population

Of 1640 patients ≥18 years of age who started KRT in 2004–2017 in the healthcare district of Helsinki-Uusimaa, Finland, 536 patients were on home dialysis 90 days after initiating KRT and were included in the analysis. This healthcare district serves 1.7 million inhabitants, which is 30% of Finland's population. All home dialysis patients in the district are treated and followed up centrally at Helsinki University Hospital. The follow-up data were complete until moving outside the district (n = 13), return of kidney function (n = 0), death (n = 164) or end of follow-up on 31 December 2019 (n = 359). During the follow-up, 347 patients received a kidney transplant.

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During the study period in the healthcare district of Helsinki-Uusimaa, there was a systematic dialysis modality selection with a 'home-first' policy. This means that both PD and home HD were equally prioritized. Patients were informed about dialysis modalities by lectures and on-spot information before the modality choice was made. The medical team evaluated the patients for contraindications and suitability for various modalities and informed the patients accordingly. If there were no medical contraindications, the patient could choose the modality that was most suitable with regard to working life, social life, hobbies, etc. The decision was made in a multidisciplinary manner together with a dialysis nurse, nephrologist, the patient and family members.

Data collection

We established a structured research database and collected extensive data from the patient data system of the entire healthcare district. We collected data retrospectively on 34 various comorbidities, primary renal disease (PRD), laboratory results, blood pressure (BP), electrocardiogram (ECG) parameters, findings on heart ultrasound and social variables (Supplementary data, Table S1).

Statistical analysis

Survival probabilities were calculated using Kaplan–Meier curves according to the type of dialysis treatment (home HD, CAPD or APD) at 90 days from the start of KRT. Patients were followed up from the start of KRT until death (the event) or the end of follow-up, and if follow-up was >5 years, they were censored at 5 years from the start of KRT. Hazard ratios (HRs) of death associated with dialysis modality were assessed using Cox regression with adjustment for propensity scores [19, 20]. The proportional hazards assumption was assessed graphically.

Propensity scores were developed pairwise for APD versus home HD, CAPD versus home HD and PD (APD and CAPD as one group) versus home HD using binary logistic regression. Explanatory variables were selected from those listed in Supplementary data, Table S1 using a stepwise forward procedure. The variables human immunodeficiency virus and Parkinson's disease were not included due to the small number of affected patients. The P-value for inclusion was <0.10. Missing values were statistically imputed using predictors as indicated in Supplementary data, Table S1. Additionally, the events waitlisting for kidney transplantation (KTx), KTx and death were used as predictors in the imputation. There were no missing data for comorbidities because each comorbidity was analysed as either found or not found in the patient files before the start of KRT. Table 1 displays the variables that were finally included for calculation of the propensity scores and Supplementary data, Table S1 further indicates which variables were used for calculating propensity scores for APD versus home HD, CAPD versus home HD and PD versus home HD.

To ensure the robustness of the results, several sensitivity analyses were conducted. Cox regression was performed with censoring at either transplantation or transfer from home dialysis to in-centre HD. Additionally, models that included either KTx or waitlisting for transplantation as time-dependent variables were evaluated (Table 3). Models were also constructed without propensity score adjustment (data not shown).

RESULTS

Patients on home HD and APD showed similar characteristics. The median age in both patient groups was 50 years at the start of KRT and 51–54% had three or more comorbidities. In addition, the proportion of those waitlisted for KTx or of those receiving a transplant during the follow-up was similar (Supplementary data, Table S1). CAPD patients were older (65 years), 67% had three or more comorbidities and they more often needed support in daily activities and assistance in dialysis.

In unadjusted analyses, Kaplan–Meier curves showed similar survival probability for APD and home HD patients, whereas CAPD patients had lower survival probability (Figure 1). The 5-year survival was 90% for home HD, 88% for APD and 56% for CAPD patients. The 5-year survival for all PD patients was 75% (Figure 2).

Both in unadjusted and in age- and sex-adjusted Cox regression analyses, the risks of death did not differ significantly between patients on APD and home HD (Table 2). Adjustment for propensity scores did not alter the result with an HR of death of 1.1 [95% confidence interval (CI) 0.52–2.4] for APD compared with home HD. The unadjusted HR of death associated with CAPD was almost 5.9-fold, while age- and sex-adjusted risk was 3.5-fold compared with that associated with home HD. However, after adjustment for propensity score, the HR of death diminished to 1.6 (95% CI 0.74–3.6), showing no statistically significant difference between CAPD and home HD. We also compared survival of all PD patients (both APD and CAPD) to that of home HD patients. With adjustment for propensity scores, the HR of death was 1.5 (95% CI 0.81–2.9) for PD compared with home HD.

We did several sensitivity analyses. When censoring at the time of transfer to in-centre HD or KTx, the HR of death for APD compared with home HD was 1.3 and the difference between the treatment modalities remained statistically insignificant (Table 3). Including waitlisting or KTx as a time-dependent variable in the model did not alter the results as compared with the propensity score–adjusted analysis in Table 2. We also performed an analysis with additional adjustment for the need for assistance in dialysis, but this did not alter the results. In addition, we included a sensitivity analysis without censoring at 5 years from the start of KRT, and this gave similar results.

DISCUSSION

In this study of 536 consecutive patients who entered home dialysis in 2004–2017, we observed similar survival among home HD and APD patients. After adjusting for potential confounders, this finding remained virtually unchanged, which was expected as these two patient groups showed many similar characteristics, e.g. age and number of comorbidities. Our study suggests that the choice between home HD and APD does not

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Table 1. Patient characteristics that were used for propensity scores

Characteristics	APD	CAPD	PD	Home HD
Patients, *n*	229	162	391	145
Total deaths[a], *n*	46	90	136	28
Deaths in 5 years[b], *n*	26	66	92	12
Deaths per 1000 patient-years[b], *n*	108	252	146	87
PRD, %				
Glomerulonephritis	22	17	20	24
Cystic kidney disease	15	6	11	31
Type 1 diabetes	21	19	21	17
Type 2 diabetes	9	20	13	5
Interstitial nephritis	4	4	4	1
Hypertension	4	5	4	2
Unknown	13	20	16	10
Others	12	11	12	9
Comorbidities, %				
Malignancy	5	11	7	10
Obesity	17	22	19	34
Atrial fibrillation	5	15	9	5
Visual problems	26	29	27	14
Type 2 diabetes	9	21	14	10
Hypertension	84	82	83	89
Compliance problem, %	15	14	15	10
Support in daily activities, %	9	30	18	8
Dialysis assistance, %[b]				
By professional	1.7	4.9	3.1	0.7
By family member	4.4	18.5	10.2	4.1
KTx-listed, %[a,b]	85	51	71	88
KTx, %[a,b]	73	38	59	81
Continuous variables, median (IQR)				
Age (years)	50 (40–61)	65 (52–74)	55 (43–68)	50 (42–60)
QT-interval on ECG (ms)	412 (386–440)	416 (390–440)	413 (386–440)	404 (381–436)
Systolic BP (mmHg)	144 (132–159)	148 (132–168)	146 (132–161)	148 (132–168)
Diastolic BP (mmHg)	89 (79–95)	85 (76–92)	87 (78–94)	84 (76–93)
Height (cm)	173 (165–180)	170 (164–178)	173 (164–180)	174 (168–180)
Weight (kg)	77 (66–87)	75 (63–85)	77 (65–87)	80 (70–93)
Body mass index (kg/m^2)	25 (23–28)	26 (22–28)	25 (23–28)	26 (23–31)
Laboratory findings, median (IQR)				
P-creatinine (mmol/L)	583 (484–708)	558 (470–660)	573 (480–689)	621 (532–712)
P-albumin (g/L)	36 (33–39)	36 (32–38)	36 (32–39)	36 (33–38)
P-ionized calcium (mmol/L)	1.2 (1.1–1.3)	1.2 (1.2–1.3)	1.2 (1.2–1.3)	1.2 (1.1–1.2)
B-haemoglobin (g/L)	111 (103–120)	114 (105–122)	113 (104–121)	109 (100–118)
P-C-reactive protein (mg/L)	3 (<3–5)	5 (<3–7)	4 (<3–7)	4 (<3–5)
Total P-cholesterol (mmol/L)	4.2 (3.5–5.0)	4.0 (3.4–4.6)	4.1 (3.4–4.8)	3.9 (3.3–4.8)
P-triglycerides (mmol/L)	1.4 (1.0–2.0)	1.6 (1.1–2.0)	1.5 (1.1–2.0)	1.4 (0.97–1.9)

IQR, interquartile range; CAD, coronary artery disease. [a]During the entire follow-up period. [b]Not included in propensity scores.

affect patients' survival. CAPD patients showed worse survival, but the difference compared with home HD diminished and was not statistically significant after accounting for confounders. CAPD patients were significantly older and frailer and consequently the comparison of their survival with that of patients on other modalities was challenging, despite abundant data on confounders.

All earlier studies comparing home HD and PD have shown better patient survival on home HD. Studies from the UK, Australia, New Zealand and Sweden observed 30–40% lower risk of death associated with home HD compared with PD after adjustment for confounding factors [9–11, 14]. Our study also showed a survival advantage of home HD patients compared with PD patients in unadjusted analysis, but the difference disappeared after we accounted for confounding factors by propensity score adjustment. Two previous studies have also applied propensity scores when comparing survival on PD and home HD. In a study from Australia and New Zealand, home HD patients had 52% lower risk of premature death than PD patients in an analysis with propensity score matching [12]. In a study based on data from the US Renal Data System, Weinhandl *et al.* [13] showed a 20% lower mortality risk in 4201 daily home HD patients compared with a group of propensity score–matched PD patients. Our study took into account an exceptionally large number of confounders, among which there were 34 different comorbidities. Many of the potential confounders used in the analyses of our study, like patient compliance, need for support in daily activities, ECG findings and C-reactive protein, were assessed in earlier studies, and this might explain why adjustment for confounders made

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the survival difference disappear in our study, unlike in the earlier ones. There may be other explanations as well. When Weinhandl *et al.* [13] included only the patients who initiated home dialysis within 6 months from start of dialysis therapy, a situation more like that in our study, the survival difference between home HD and PD disappeared. Furthermore, a notable difference between our study and some of the earlier ones is the proportion of home HD patients out of all patients who entered chronic dialysis treatment. This proportion was 8% in our study and similar in the studies from Australia and New Zealand [10–12], but in all other studies [9, 13, 14] the proportion was <1%. A very small proportion of home HD probably indicates strict selection, meaning that only the fittest patients enter this treatment modality. A strong selection will favour home HD compared with PD and may be difficult to fully account for when adjusting for confounders.

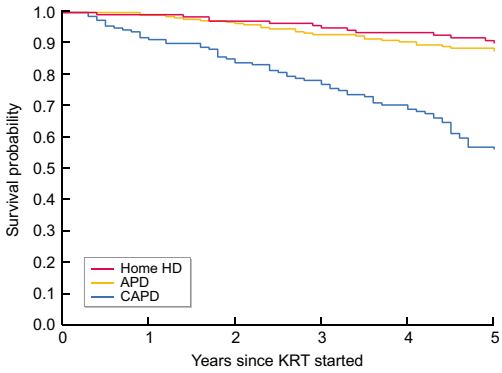


FIGURE 1: Survival of patients on home HD, APD or CAPD.

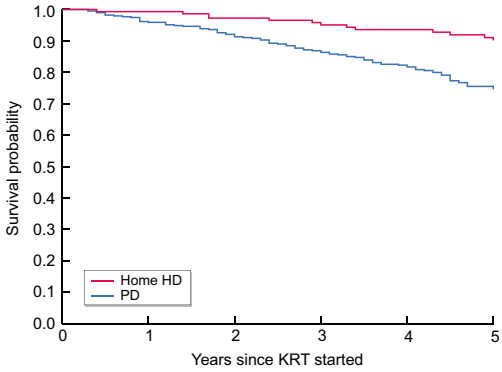


FIGURE 2: Survival of patients on home HD or PD.

Our study is unique in that it considered APD and CAPD separately. All earlier studies analysed PD patients as one group without distinction between CAPD and APD. Of the two types of PD, APD resembles home HD more in many aspects: both APD and home HD require the patient to manage a dialysis device independently at home with a certain degree of technical skills and sufficient physical and cognitive capacity. Thus it may be assumed that patients who select home HD have more characteristics in common with APD than with CAPD patients, which was also observed in our study. Consequently the similarity between home HD and APD patients may make the statistical comparison between these two groups more reliable.

When interpreting survival outcomes of home HD patients, it is important to have information about the frequency and duration of the dialysis sessions. These data were not directly available in our research database, but according to data collected by the Finnish Registry for Kidney Diseases about the home HD patients in our district, 76% had more than three weekly sessions, 53% had at least five sessions per week, 32% did >15 h of dialysis per week and 16% did nocturnal dialysis. Thus home HD patients in our cohort typically used more intense HD than just thrice-weekly 3- to 5-h sessions. In most of the earlier studies, the type of home HD was unspecified, except in one study that implied a similarity in survival between conventional and frequent/extended home HD [10]. The results may also be affected by the type of home HD device. In our study, all patients used conventional dialysis machines, whereas, for example, in the study of Weinhandl *et al.* [13], all home HD patients used one specific type of HD device with low dialysate volumes.

Table 2. HR of death in 5 years according to home dialysis modality

Explanatory variable	Hazard ratio	95% CI of hazard ratio
Unadjusted 5-year risk of death		
Home HD (reference)		
APD	1.4	0.69–2.7
CAPD	5.9	3.2–10.9
PD	3.1	1.7–5.6
Adjusted for age and sex 5-year risk of death		
Home HD (reference)		
APD	1.4	0.69–2.7
CAPD	3.5	1.8–6.7
PD	2.2	1.2–4.1
5-year risk of death adjusted for propensity score		
APD (compared with Home HD)	1.1	0.52–2.4
CAPD (compared with Home HD)	1.6	0.74–3.6
PD (compared with Home HD)	1.5	0.81–2.9

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Table 3. HR of death according to home dialysis modality (sensitivity analyses with propensity score adjustment)

Explanatory variable	Hazard ratio	95% CI for hazard ratio
Censoring at transfer to in-centre HD or at transplantation[a]		
APD (compared with home HD)	1.3	0.51–3.3
CAPD (compared with home HD)	1.1	0.40–2.9
PD (compared with home HD)	1.4	0.63–3.1
KTx waitlisting as a time-dependent variable[a]		
APD (compared with home HD)	1.2	0.57–2.6
CAPD (compared with home HD)	1.5	0.68–3.2
PD (compared with home HD)	1.5	0.81–2.9
KTx as a time-dependent variable[a]		
APD (compared with home HD)	0.96	0.44–2.1
CAPD (compared with home HD)	1.4	0.63–2.9
PD (compared with home HD)	1.3	0.66–2.4
For the total study period, not censoring at 5 years		
APD (compared with home HD)	0.87	0.51–1.5
CAPD (compared with home HD)	1.3	0.74–2.3
PD (compared with home HD)	1.1	0.72–1.7

[a]Censored at 5 years since the start of KRT.

Our study has many strengths. The study is population-based, as we were able to include all patients in the healthcare district who were on home dialysis at 90 days from start of KRT. Comparing home HD patients separately with patients on APD and CAPD is unique for our study. Furthermore, the high proportion of home HD patients may reduce selection bias. We had complete data on the outcome and exceptionally extensive data on confounders. A lack of sufficient data on confounders was considered a concern by some of the earlier studies [10, 11, 13]. The observational nature of our study represents a limitation and leaves the possibility of residual confounding. Additionally, the relatively small number of patients makes analysis of subgroups difficult. Finally, patient selection differs between countries and centres, and our results may not be generalizable to other settings.

CONCLUSIONS

The results of our study may help healthcare professionals when counselling patients about selection of dialysis modalities. Our study suggests that patients' survival may not be affected by the choice between home HD and APD. Consequently, factors other than survival should be considered when choosing dialysis modality. Further studies are needed to investigate outcomes other than survival, such as infections, cardiovascular events, hospitalizations and quality of life.

SUPPLEMENTARY DATA

Supplementary data are available at ndt online.

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AUTHORS' CONTRIBUTIONS

P.F. was responsible for the research idea. B.W., J.H. and P.F. were responsible for the study design and data analysis. B.W. and P.F. were responsible for data acquisition. B.W., J.H., E.H., V.R., M.H. and P.F. were responsible for data interpretation. J.H. and P.F. were responsible for supervision. Each author contributed important intellectual content during manuscript drafting and revision. All authors accept accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST STATEMENT

P.F. has received honoraria for lectures and membership in advisory board from Baxter. V.R. has received honoraria for lectures from Baxter and Fresenius and research funding (not for this project) from Business Finland. The findings, results and conclusions in this report are those of the authors and are independent from the funding sources.

DATA AVAILABILITY STATEMENT

The data underlying this article cannot be shared publicly because this was not allowed in the research permission provided by the Helsinki University Hospital.

(See related article by Wang. Comparing survival between home hemodialysis and peritoneal dialysis—is the controversy over? *Nephrol Dial Transplant* 2022; 37: 1393–1395)

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II

PLOS ONE

RESEARCH ARTICLE

Severe infections in peritoneal dialysis and home hemodialysis patients: An inception cohort study

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Abstract

Objectives

Infections are the most common non-cardiovascular cause of death among dialysis patients. Earlier studies have shown similar or higher risk of infectious complications in peritoneal dialysis (PD) compared to hemodialysis (HD) patients, but comparisons to home HD patients have been rare. We investigated the risk of severe infections after start of continuous ambulatory PD (CAPD) and automated PD (APD) as compared to home HD.

Methods

All adult patients (n = 536), who were on home dialysis at day 90 from starting kidney replacement therapy (KRT) between 2004 and 2017 in Helsinki healthcare district, were included. We defined severe infection as an infection with C-reactive protein of 100 mg/l or higher. Cumulative incidence of first severe infection was assessed considering death as a competing risk. Hazard ratios were estimated using Cox regression with propensity score adjustment.

Results

The risk of getting a severe infection during the first year of dialysis was 35% for CAPD, 25% for APD and 11% for home HD patients. During five years of follow-up, the hazard ratio of severe infection was 2.8 [95% CI 1.6–4.8] for CAPD and 2.2 [95% CI 1.4–3.5] for APD in comparison to home HD. Incidence rate of severe infections per 1000 patient-years was 537 for CAPD, 371 for APD, and 197 for home HD patients. When excluding peritonitis, the incidence rate was not higher among PD than home HD patients.

individual patients' data. Our research permission granted by Helsinki University Hospital does not either allow sharing of individual patients' data. Researchers can submit a research application to the Helsinki University Hospital in order to get access to the data. The contact person: Professor, chief physician Pauli Puolakkainen, Helsinki University Hospital, email: Pauli.puolakkainen@hus.fi.

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Conclusions

CAPD and APD patients had higher risk of severe infections than home HD patients. This was explained by PD-associated peritonitis.

Introduction

Infections are the most common cause of death among dialysis patients next to cardiovascular disease [1, 2]. Dialysis patients have been reported to carry an 82-fold risk of dying of infections compared to the general population [3]. Earlier studies have shown that patients on peritoneal dialysis (PD) and hemodialysis (HD) have similar risks of infection [4–6], whereas one study showed increased risk of infection-related hospitalization among PD compared to HD patients [7]. When comparing patients on continuous ambulatory PD (CAPD) and automated PD (APD) some studies have not found a difference in risk of infections [8–11], while others have indicated higher risk in CAPD than APD patients [12–14]. Infections have been reported to be the most common cause of hospital admissions among home HD patients [15]. Two studies have compared infection-related hospitalization between PD and home HD, and they have given contradicting results. The first one demonstrated no difference between the treatment modalities in an intention-to-treat analysis [16], whereas the other one showed that patients who entered PD had higher risk of infection-related hospitalization than those who entered home HD [17]. Neither study considered CAPD and APD separately.

For patients who are eligible for home dialysis, there are three options: CAPD, APD and home HD. We have recently reported similar survival of patients on APD and home HD [18], whereas earlier studies have reported somewhat less favorable survival in PD compared to home HD [16, 19–24]. However, when considering which type of home dialysis to choose, other issues than survival are important as well. While peritonitis is a well-known problem in PD, there is scarce and contradicting information about the difference in infection-burden between PD and home HD. We investigated the risk of severe infections after start of CAPD or APD as compared to home HD.

Materials and methods

Study design and population

The Helsinki-Uusimaa healthcare district covers 1.7 million inhabitants, representing about 30% of Finland's population. In this healthcare district, 1747 adult patients started dialysis treatment between 2004 and 2017. Of these, 536 patients were on home dialysis at day 90 from initiating kidney replacement therapy (KRT) and they were included in this study. Patients' follow-up data were available until December 31, 2019.

When the dialysis modality is selected, our healthcare district applies a "home first"-policy, with equal priority given to PD and home HD. The patients are informed using on-spot and video information, and they are evaluated by a multidisciplinary team for home dialysis suitability. According to surveillance data from our healthcare district, the frequency of PD peritonitis was 530/1000 patient-years in 2011–2020 which is slightly above the target of less than 500 PD peritonitis episodes/1000 patient-years according to the ISPD guideline 2016 [25] and clearly above the newest target of 400/1000 patient-years in the ISPD guideline 2022 [26]. Our unit has a protocol for peritonitis prevention that includes education of patients by specialized PD nurses, exit-site care, surveillance of PD peritonitis frequency and regular follow-up meetings with infection diseases specialists. All patients who start PD are trained by a PD nurse for

at least one week, and retraining is provided if needed. Prophylactic antibiotics are used at PD catheter insertion and prior to dental and endoscopic procedures. Decolonization is performed after Staphylococcus aureus infection, and topical prophylactic antibiotic is used on exit-site based on clinical assessment. All home HD patients were trained during an average of six weeks to perform hemodialysis at home and all patients used the button-hole technique for cannulation. On average, at the end of the years 2004 to 2019, 91% of the home HD patients had a fistula, 4% had a graft and 5% had a tunneled hemodialysis catheter.

As the study subjects were not contacted and no intervention was performed, no consent from the patients nor permission from an Ethics committee were needed. The study was approved by the Helsinki University Hospital, permission number HUS/459/2018.

Data collection

A structured research database was established, and extensive data were extracted from the patient data system. The retrospectively collected data comprised 34 various comorbidities, primary renal disease (PRD), laboratory results, blood pressure, ECG parameters, findings on heart ultrasound, and social variables (S1 Table). Additionally, data on all values of plasma C-reactive protein (CRP) of the study patients were retrieved from the data pool of the Helsinki-Uusimaa healthcare district. In Finnish medical practice, CRP has for decades been used as a key infection marker for the assessment of infection severity and bacterial origin, and its predictability is often appreciated over the blood leucocyte count. CRP is also used to guide antibiotic therapy. Therefore, several measurements per patient are usually available during an infection episode.

Identification of severe infections

We defined severe infection as an infection accompanied with a plasma CRP level of 100 mg/l or higher. Although several studies have shown that CRP correlates with severity of infections [27, 28], there is no general recommendation in the literature for the cutoff of CRP to determine the severity. We chose the cutoff of 100 mg/l because a CRP value under this level has been strongly associated with low infection mortality [29] and among HD patients a CRP value higher than 100 mg/l has been correlated with risk of infection mortality [30]. In our study, a severe infection episode was recorded when CRP was 100 mg/l or higher, and the cause was an infection. Two different episodes were recorded if the time interval between elevated CRP values was at least 21 days without CRP measurements, or 30 days with at least one CRP value less than 50 mg/l in between. The cause of elevated CRP was checked from the patient's medical records and defined as infectious or non-infectious. The cause of infection, including types of infections and infectious agents, was collected. For PD patients, peritonitis and PD-catheter related infections were defined as dialysis-related. Bloodstream infection was considered dialysis-related only if accompanied by peritonitis or PD access site infection. For home HD patients, bloodstream infections were considered dialysis-related if the source was clearly related to the dialysis access site infection or if it was unknown (i.e., not related to other infection foci such as urinary tract infections). We also collected data on hospitalization, length of hospitalization and need for intensive care in connection to the infection episode. Infections were defined as fatal if the patient died within 30 days from the infection regardless of the cause of death.

Statistical analyses

The probability of the first infection episode was estimated considering death as a competing risk event according to type of home dialysis treatment (CAPD, APD or home HD) at day 90

from the beginning of KRT. Patients were followed up for five years from the beginning of KRT until kidney transplantation (n = 285), transfer to in-center HD (n = 122, of whom 58 were on CAPD, 49 on APD and 15 on home HD, and 35% of the PD patients had transferred because of peritonitis), change from CAPD or APD to home HD (n = 4), change from home HD to CAPD or APD (n = 1), transfer to conservative treatment (n = 2) loss of follow up (n = 1), death (n = 71) or end of follow-up at 5 years or 31 December 2019 (n = 50). Hazard ratios of first infection episode associated with each home dialysis modality were assessed using Cox regression. The event was the first infection episode and patients were censored at end of follow-up. As the research question was aetiological (to study association between dialysis modality and infection risk) we selected Cox regression without taking competing risk into account [31]. We further did sensitivity analyses using Fine-Gray regression in which 1) death, 2) both death and kidney transplantation or 3) death, kidney transplantation and transfer to in-center HD were defined as competing risk events. In all analyses we also adjusted for propensity scores [32, 33] to account for a possible confounding effect of age, comorbidities, primary renal disease, and other factors (S1 Table). The proportional hazards assumption was assessed graphically by inspecting the cumulative hazards of first infections episodes among CAPD, APD and home HD patients. In addition, the proportional hazards assumption was tested statistically (using the estat phtest) in the Stata software Version 17.

We imputed missing values using predictors as indicated in S1 Table. In addition, waitlisting for kidney transplantation, kidney transplantation, and death were included as predictors in the imputation. Each comorbidity was analyzed as either found or not found in the patient files before the beginning of KRT. Consequently, there were no missing data for comorbidities.

We used binary logistic regression to develop propensity scores for CAPD vs. home HD, APD vs. home HD and PD (CAPD and APD as one group) vs. home HD pairwise. S1 Table displays all the variables from which the explanatory variables for the propensity scores were selected by a stepwise forward procedure. The *P* value for inclusion was less than 0.1. As a sensitivity analysis we adjusted, on top of the propensity score adjustment, for prognostic variables, which predicted infections but were not included in the propensity scores. These variables were selected from the variables in S1 Table using stepwise forward Cox regression. Four statistically significant prognostic variables were identified: plasma phosphate, history of coronary intervention, stroke, and vasculitis.

Incidence rate (IR) and IR ratios (IRR) of infections were assessed for CAPD, APD and home HD patients. Confidence intervals (95% CI) of IRR were calculated [34]. The cumulative incidence was estimated using the R Software (version Ri386 3.6.0, the cmprsk package, cuminc function), while all other statistical analyses were performed using SPSS (version 25).

Results

Population characteristics

Of the patients who were on home dialysis modality at day 90 from starting KRT, 162 (30%) were on CAPD, 229 (43%) on APD and 145 (27%) on home HD (Table 1). Compared to home HD patients, CAPD patients were older and had a larger number of comorbidities, whereas the characteristics of APD patients were similar to those of home HD patients. CAPD patients more often needed dialysis assistance and they were less often waitlisted for kidney transplantation. At the time of start of dialysis, the median plasma CRP was 4 mg/l, with an interquartile range of 3–7 mg/l and a 90-percentile of 15 mg/l, which means that 90% of the patients had a baseline CRP value lower than 15 mg/l.

Table 1. Patient characteristics.

Home dialysis modality	CAPD	APD	Home HD	P-value	
				CAPD vs Home HD	APD vs Home HD
Number of patients	162	229	145		
Male Gender (%)	70	66	68	0.691	0.703
Median FU-time (years)	2.0 (0.97–3.4)	1.6 (0.86–2.5)	1.4 (0.73–2.7)	0.013	0.499
Number of Patient-years	365	426	264		
Number of Infection episodes	197	158	52		
Hospitalization needed (n)	178	142	38		
Infection episode IR	540	371	197		
At least one episode (%)	62	35	21		
Number of deaths in 5 years*	66	26	12	<0.001	0.330
Number of infection deaths*	18	12	5	0.011	0.418
Median age (years)	65 (52–74)	50 (40–61)	50 (42–60)	<0.001	0.832
Primary renal disease (%)				<0.001	0.017
Glomerulonephritis	17	22	24		
Cystic kidney disease	6	15	31		
Type 1 diabetes	19	21	17		
Type 2 diabetes	20	9	5		
Interstitial nephritis	4	4	1		
Hypertension	5	4	2		
Unknown	20	13	10		
Others	11	12	9		
Number of comorbidities (%)				0.001	0.305
0	1.2	2.2	0.0		
1–2	32	44	48		
3–4	40	42	41		
> = 5	27	12	11		
Dialysis assistance (%)				<0.001	0.061
by professional	4.9	1.7	0.7		
by family member	18.5	4.4	4.1		
KTx-listed (%) *	39	75	74	<0.001	0.776
KTx (%) *	25	58	66	<0.001	0.116

Abbreviations: HD, hemodialysis; PD, peritoneal dialysis; APD, automated PD; CAPD, continuous ambulatory PD; (%), (percentage); FU, follow-up; IQR, interquartile range; IR, incidence rate per 1000 patient-years; KTx, kidney transplantation;

*During the follow-up period.

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Cumulative incidence and hazard ratio of the first severe infection episode

Of the 536 patients, 213 (40%) experienced at least one severe infection episode during the follow-up. Cumulative incidence of a first infection episode was 35% for CAPD, 25% for APD and 11% for home HD patients at one year from start of dialysis (Fig 1) ($P < 0.001$). Both in unadjusted and in age- and sex-adjusted analyses, CAPD and APD patients had a 2–3-fold risk of a first infection episode compared to home HD patients (Table 2). Similarly, after adjustment for propensity scores, the hazard ratio of a first infection episode was 2.8 (95% CI 1.6–4.8) for CAPD patients and 2.2 (95% CI 1.4–3.5) for APD patients compared to home HD patients. We tested statistically that the proportional hazards' assumption was not violated ($P = 0.469$). We further performed four sensitivity analyses in which, instead of censoring, we

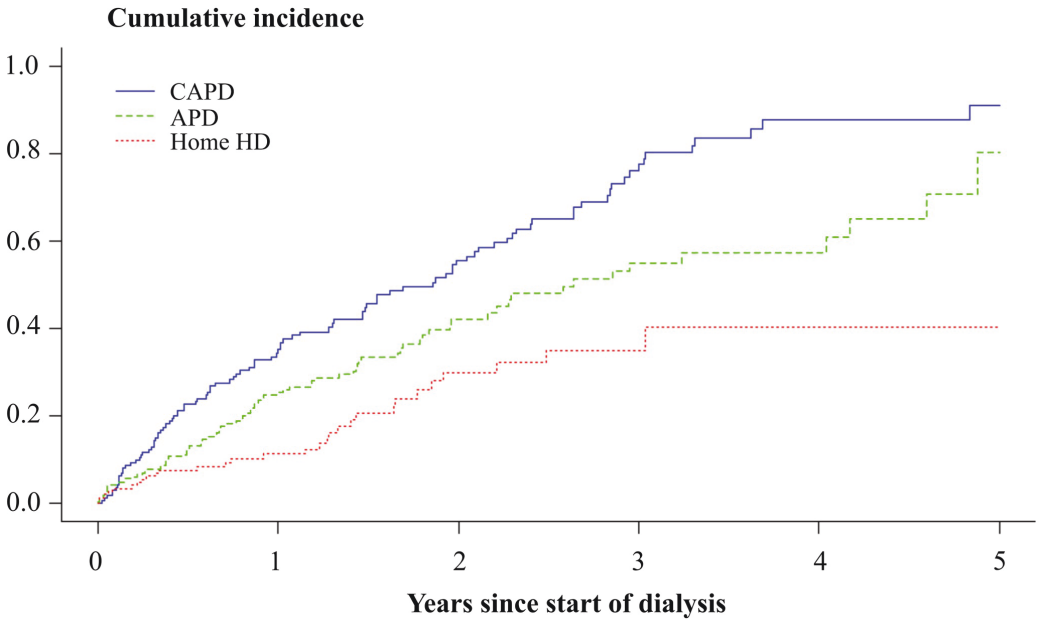


Fig 1. Cumulative incidence of the first severe infection episodes.

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defined 1) death, 2) both death and kidney transplantation or 3) death, kidney transplantation and transfer to in-center HD as competing risk events in Fine-Gray regression, but the hazard ratios remained virtually unchanged. In the fourth sensitivity analysis, we adjusted for prognostic variables in addition to the propensity scores, but the results remained virtually

Table 2. Hazard ratios of first infection according to home dialysis modality during 5 years from the start of KRT.

	HR of first infection episode	95% CI of HR	
		Lower	Upper
HR of first infection episode incidence, unadjusted			
Home HD (reference)			
CAPD	3.2	2.1	4.8
APD	1.9	1.2	2.8
HR of first infection episode incidence, adjusted for age and sex			
Home HD (reference)			
CAPD	2.7	1.7	4.1
APD	1.9	1.2	2.8
HR of first infection episode incidence, adjusted for propensity score			
CAPD (compared to Home HD)	2.8	1.6	4.8
APD (compared to Home HD)	2.2	1.4	3.5

Abbreviations: KRT, kidney replacement therapy; HR, hazard ratio; CI, confidence interval; HD, hemodialysis; PD, peritoneal dialysis; APD, automated PD; CAPD, continuous ambulatory PD.

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unchanged: hazard ratio 2.6 (95% CI 1.5–4.5) for CAPD patients and 2.0 (95% CI 1.3–3.3) for APD patients compared to home HD patients. We also did an additional analysis comparing the risk of a first infection episode between APD and CAPD and found that the difference was not significant after adjusting for propensity scores, HR 1.3 (95% CI 0.94–1.9).

Incidence rate of severe infection episodes

Calculation of the incidence rate allows considering all severe infection episodes, not only the first infection of each patient. The incidence rate was 537 infection episodes per 1000 patient-years for CAPD patients while it was 371 for APD and 197 for home HD patients (Table 3). The incidence rate ratio (IRR) was 2.7 (95% CI 2.0–3.7) for CAPD and 1.9 (95% CI 1.4–2.6) for APD compared to home HD patients. If excluding dialysis-related infections, the corresponding IRR was 0.90 (95% CI 0.65–1.2) for CAPD and 0.65 (95% CI 0.47–0.89) for APD. On the other hand, if analyzing only the dialysis-related infections, CAPD patients had an IRR of 14 (95% CI 6.7–31) and APD patients an IRR of 9.7 (95% CI 4.5–21) compared to home HD patients. Of all the 407 severe infection episodes, 5% were fatal, i.e., the patient died within 30 days.

Causes of severe infection episodes

Peritonitis constituted 68% of the infection episodes among CAPD patients (incidence rate 367 per 1000 patient-years) and 67% of the episodes among APD patients (incidence rate 249 per 1000 patient-years) (Table 3). Bloodstream infections accounted for 21% of the infection episodes among home HD patients, but only 3% of the CAPD and APD patients' episodes. The IRR of all bloodstream infections was 0.39 (95% CI 0.21–0.73) for CAPD and 0.28 (95% CI 0.15–0.52) for APD patients compared to home HD patients.

Table 3. Type and incidence rate of infections according to type of home dialysis modality.

Type and incidence rate of infections IR per 1000 patient-years (number of infections)				
Home dialysis modality		**CAPD**	**APD**	**Home HD**
Number of patient-years		365	426	264
IR of all infections (n)		540 (197)	371 (158)	197 (52)
IRR of all infections (95% CI)		2.7 (2.0–3.7)	1.9 (1.4–2.6)	1 (reference)
IR of dialysis- related infections (n)	Peritonitis	367 (134)	249 (106)	0 (0)
	Access related	14 (5)	9.4 (4)	8 (2)
	Bloodstream infection	2.7 (1)	0 (0)	19 (5)
IR of dialysis-related infections (n)		383 (140)	258 (110)	27 (7)
IRR of dialysis-related infections (95%CI)		14 (6.7–31)	9.7 (4.5–21)	1 (reference)
IR of all bloodstream infections (n)		16 (7)	12 (5)	42 (11)
IRR of all bloodstream infections (95% CI)		0.46 (0.25–0.85)	0.28 (0.15–0.52)	1 (reference)
IR of non-dialysis-related infections (n)		156 (57)	113 (48)	170 (45)
IRR of non-dialysis-related infections (95% CI)		0.90 (0.65–1.2)	0.65 (0.47–0.89)	1 (reference)
IR of infections needed hospitalization (n)		488 (178)	333 (142)	144 (38)
IRR of infections needed hospitalization (95% CI)		2.5 (1.8–3.4)	1.7 (1.2–2.3)	1 (reference)
IR of fatal infections (n)		41 (15)	9 (4)	4 (1)
IRR of fatal infections (95% CI)		11 (1.5–80)	2.5 (0.33–18)	1 (reference)

Abbreviations: IR, incidence rate; n, number of infections; PD, peritoneal dialysis; CAPD, continuous ambulatory PD; APD, automated PD; HD, hemodialysis; IRR, incidence rate ratio; CI, confidence interval.

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Table 4. Types of non-dialysis-related infections.

Infection Type	CAPD	APD	Home HD	Total
Upper or lower respiratory airways	15	13	5	33
Skin or soft tissue	12	11	11	34
Gastrointestinal or hepatobiliary	3	1	10	14
Bone or Joint	8	3	1	12
Genitourinary	5	9	4	18
Bloodstream infection	6	5	6	17
Unknown origin	8	6	8	22
Total	57	48	45	150

Abbreviations: PD, peritoneal dialysis; CAPD, continuous ambulatory PD; APD, automated PD; HD, hemodialysis.

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Of the 150 non-dialysis-related infection episodes 34 (23%) were caused by skin or soft tissue infections and 33 (22%) by respiratory infections (Table 4).

The most common causative organism of peritonitis was Staphylococcus Aureus (24%), and the second most common cause Coagulase-negative Staphylococcus (17%) (Table 5).

Hospitalization in connection to severe infection episodes

Of all the 407 severe infection episodes, 358 (88%) led to hospitalization. Among CAPD and APD patients 90% (320 of 355) and among home HD patients 73% (38 of 52) of the episodes required hospitalization ($P < 0.001$, Table 1). Overall, the median duration of hospital stay was 6 days for CAPD and APD patients and 8 days for home HD patients ($P = 0.25$). Regardless of CRP level, hospitalization was needed in 86–90% of the infection episodes. However, CRP level associated with the proportion of infection episodes requiring more than 7 days of hospital care: 32% if CRP level was 100–149 mg/L, 43% if 150–199 mg/L and 60% if 200 mg/L or higher ($P < 0.001$). Intensive care was needed in 2.2% of all the 407 infection episodes, in 4.9% of the 103 episodes with a CRP of 200 mg/l or higher and in 1.3% of the 304 episodes with a lower CRP level ($P = 0.049$). Among PD patients, 98% of the infection episodes caused by peritonitis and 75% of the non-peritonitis infection episodes required hospitalization. Of the 240 infection episodes caused by peritonitis, PD-catheter was removed in 12%, and this proportion increased with increasing CRP level ($P = 0.040$).

Table 5. Causative organisms of the peritonitis episodes.

Causative organism	CAPD	APD	Total (%)
Staphylococcus Aureus	33	25	58 (24)
Coagulase-negative Staphylococcus	27	14	41 (17)
Escherichia coli	8	2	10 (4)
Pseudomonas	11	6	17 (7)
Fungi	1	5	6 (3)
Culture negative	13	18	31 (13)
Other agents or multiple microbial agents	41	36	77 (32)
Total	134	106	240 (100)

Abbreviations: PD, peritoneal dialysis; CAPD, continuous ambulatory PD; APD, automated PD.

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Severe infection episodes before start of dialysis

Both in PD patients and home HD patients the incidence rate of infections was clearly higher after the start of KRT than before (Fig 2). Among PD patients a slight increase in incidence rate could be noticed already half a year prior to start of dialysis. However, if analyzing the whole two-year period before start of KRT, infection rate did not differ significantly between groups with an IRR of 1.5 (95% CI 0.89–2.7) for CAPD and 1.2 (95% CI 0.68–2.0) for APD patients in comparison to home HD patients.

Discussion

In this study of patients who started home dialysis, we found that CAPD and APD patients have a 2–3-fold risk of getting severe infections compared to home HD patients. This was mainly explained by the numerous peritonitis episodes occurring among PD patients. Infections that were unrelated to dialysis were not more frequent among PD than home HD patients, and PD patients had lower risk of bloodstream infection. Although infections that raised plasma CRP to a level of 100 mg/L or higher were frequent and occurred among 40% of the patients, only 5% died within 30 days from an infection episode.

There is limited information about the infection burden among home HD patients compared to PD patients, and no study has compared home HD to CAPD and APD separately. However, comparisons have been made between CAPD and APD, showing contradicting results. Some studies showed a higher incidence of peritonitis among CAPD than APD patients [12–14], whereas others did not [8–11]. Although this was not the primary comparison in our study, we observed a tendency towards higher risk of peritonitis in CAPD than APD patients. A few studies have shown similar or increased infection burden among PD compared to in-center HD patients [4–7].

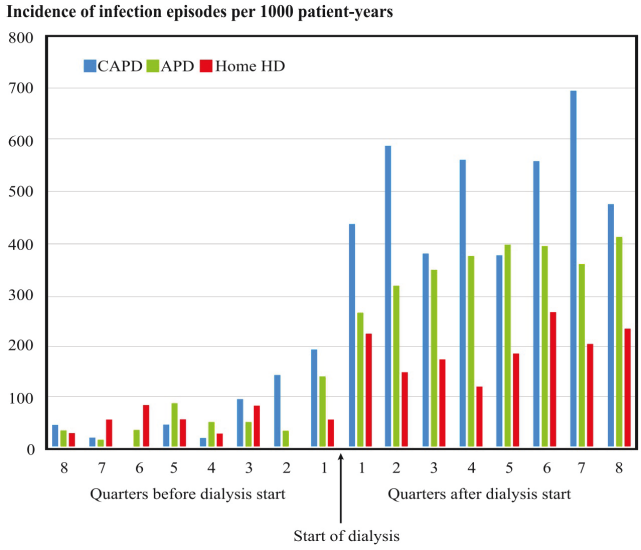


Fig 2. Incidence of severe infection episodes per 1000 patient-years quarter-yearly before and after the start of dialysis.

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Rydell et al. [17] studied hospitalizations among 152 home HD patients compared to 456 matched PD patients. Home HD patients had a lower infection-related hospitalization rate, which is in line with our results on severe infections. However, Rydell et al. did not present type of infections or to what extent this difference was due to peritonitis. Weinhandl et al. [16] compared US home HD patients with matched PD patients, and in intention-to-treat analysis they did not find differences in overall risk of infection-related hospitalizations between the groups. Home HD patients had higher risk of bloodstream infection and lower risk of dialysis-access site infection including peritonitis, which is comparable to our results.

The strength of this population-based study was that all patients in the healthcare district who were on home dialysis at day 90 from the start of KRT were included, thus minimizing selection bias. As we had data on all patients' CRP values, the data on infection episodes with a CRP of 100 mg/l or higher were complete and assessed in the same way regardless of dialysis modality. A CRP value of 100 mg/l or higher has not been validated as a marker of severe infections. Notably, our results indicate that CRP level associates with infection severity with regard to longer hospitalization and need for intensive care, and in case of peritonitis, with removal of PD catheter. Thus, identifying severe infections based on CRP value appears sensible. Another strength is that we had extensive data on putative confounding factors, which were used for propensity score adjustment when comparing the dialysis modalities. Furthermore, the main characteristics of patients on APD and home HD were similar, which should reduce bias in this comparison. Nevertheless, in observational studies like this, there is still a possibility of residual confounding. Furthermore, the distribution of patients in various dialysis modalities differs between countries and centers, and the proportion of home HD patients is often lower than in this study, which may limit the generalizability of our results. On the other hand, the large proportion of home HD patients in our study implies a less strict selection of patient to this modality, and may improve comparability with PD. We reported a high frequency of hospitalization for peritonitis due to the policy of our unit to start most peritonitis treatments in the hospital. Thus, hospitalization rates for peritonitis cannot be generalized to units with other policies. Notably, our analysis included only peritonitis episodes accompanied with a plasma CRP of 100 mg/l or higher. If not restricting to elevated CRP, the peritonitis rate is higher, i.e., it was 530 episodes per 1000 patient-years in 2011–2020 in our district. This peritonitis rate was higher than recommended by ISPD, which may hamper generalization of the results to centers with lower peritonitis rates. In addition, 95% of the home HD patients had a fistula or graft which probably contributes to their low risk of severe infections.

Our study provides new knowledge about risk of infections in the different home dialysis modalities. Accurate information about both advantages and disadvantages of the various dialysis types is important when choosing dialysis modality. PD-related infections have been identified as a major problem among PD patients and it has been considered as one of the most important outcomes in studies on PD patients [35]. We show that home HD patients had a clearly lower risk of severe infections overall, even if their risk of bloodstream infection was higher. Notably, of the 11 bloodstream infection episodes observed among the home HD patients, no one lead to death within 30 days. Thus, our findings would favor the choice of home HD to reduce the burden of infections. However, we have earlier shown, in the same patient cohort, that PD patients did not have higher risk of death. In this study, we observed an increased mortality rate of severe infections among CAPD patients compared to home HD patients, but this comparison was unadjusted and the confidence intervals were broad, and the observation will require validation in a larger patient cohort. Many aspects need to be considered when selecting home dialysis modality. Home HD is technically more difficult, and not possible for all patients for whom PD is an option. Based on our results, the infection burden was similar for home HD and PD patients, and even lower for APD patients, when peritonitis

was excluded. It would be important to know more about risk factors for peritonitis, so that especially patients at high risk of peritonitis could be advised to choose home HD.

To conclude, CAPD and APD patients in our study had higher risk of severe infections than home HD patients. This was explained by PD-associated peritonitis. Thus, our results emphasize the importance of peritonitis prevention measures for PD patients.

Supporting information

S1 Table. Characteristics of home dialysis patients.
(DOCX)

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III

OPEN

Risk of Major Adverse Cardiovascular Events in Home Dialysis Compared With In-Center Hemodialysis

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Key Points

- We observed a comparable cumulative incidence of major adverse cardiovascular event (MACE) in in-center hemodialysis (IC-HD) and continuous ambulatory peritoneal dialysis (PD) patients, which was higher than in automated PD and home hemodialysis patients.
- After adjustment for confounders, there was no difference in risk of MACE between patients on home dialysis modalities and IC-HD.
- Compared with IC-HD, PD was associated with lower risk of MACE among female patients and higher risk among male patients.

Abstract

Background Among dialysis patients, cardiovascular events are the leading cause of death. Little is known about how the frequency and type of cardiovascular events differ between various dialysis modalities. We compared risk of major adverse cardiovascular events (MACEs) in patients who started continuous ambulatory peritoneal dialysis (CAPD), automated peritoneal dialysis (APD), and home hemodialysis with in-center hemodialysis (IC-HD) patients.

Methods We included 968 patients who entered dialysis in the Helsinki-Uusimaa health care district in Finland from 2004 to 2017, of whom 162 were on CAPD, 229 on APD, 145 on home hemodialysis, and 432 on IC-HD at day 90 from the start of dialysis. MACE was defined as acute myocardial infarction, stroke, or death due to cardiovascular disease. The cumulative incidence of the first MACE was calculated. Cox regression was used to compare risk of MACE between dialysis modalities with adjustment for potential confounding factors.

Results Of all 968 patients, 195 (20%) experienced a MACE during the entire follow-up and 62 (6%) during the first year of follow-up. The cumulative incidence of first MACE was similar in IC-HD and CAPD patients and higher than that in APD and home hemodialysis patients. After adjustment for possible confounders, the hazard ratio (HR) of MACE was 1.22 (95% confidence intervals [CIs], 0.73 to 2.05) for CAPD, 0.86 (95% CI, 0.47 to 1.57) for APD and 0.67 (95% CI, 0.30 to 1.50) for home hemodialysis compared with IC-HD. Unexpectedly, compared with IC-HD, peritoneal dialysis associated with lower risk of MACE among female patients (HR, 0.37; 95% CI, 0.14 to 0.99) and higher risk among male patients (HR, 1.80; 95% CI, 1.11 to 2.92).

Conclusions In this cohort, the risk of MACE was comparable across in-center and home dialysis modalities. However, the result differed between male patients and female patients, which requires further research.

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Introduction

Cardiovascular disease is the most common cause of death among dialysis patients and causes approximately 40% of the deaths.[1] Dialysis patients have been shown to have a 10-fold to 20-fold risk of dying from cardiovascular diseases compared with general population.[2,3]

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The increased cardiovascular mortality observed in the dialysis population could be explained in part by factors related to uremia such as oxidative stress and inflammation.[4] Compared with hemodialysis, peritoneal dialysis (PD) provides more stable removal of uremic products and fluid, contributing to reduced hemodynamic stress. This could theoretically contribute to lower risk of cardiovascular events. In addition, the longer preservation of residual kidney function observed in PD[5] has been connected to improved cardiac parameters[6,7] and reduction in cardiovascular events and mortality.[8,9] On the other hand, PD may increase cardiovascular risk by causing hyperglycemia, obesity, or dyslipidemia.

Home hemodialysis typically allows more frequent dialysis than three times a week in-center hemodialysis (IC-HD). Patients on more frequent hemodialysis have been shown to have better BP control, left ventricular mass reduction, and less often intradialytic hypotension than patients on thrice-weekly IC-HD.[10,11] Risk of cardiac death has been observed to vary from day to day among thrice-weekly IC-HD patients, but not among home hemodialysis and PD patients.[12,13]

Several studies have compared mortality and morbidity due to cardiovascular disease between PD and IC-HD patients, but results have been conflicting. In addition, some studies have shown lower risk of cardiovascular related hospitalization or death in frequent home hemodialysis compared with PD and also compared with IC-HD.[14–16] Compared with IC-HD, PD has been associated with higher risk of emergency hospitalization and mortality due to cardiovascular disease,[17] but on the other hand, PD has also been associated with lower incidence of congestive heart failure.[18] A large population-based study showed that PD was noninferior to hemodialysis with regard to cardiovascular mortality.[19] Notably, all studies have been observational, and the results may have been affected by differences in patient selection to the dialysis modalities and patient characteristics. This underlines the importance of comprehensive adjustment for confounding factors.

We have earlier shown that patients entering automated PD (APD) have similar survival compared with those who enter home hemodialysis.[20] However, it is not well understood how these dialysis modalities affect patients' risk of cardiovascular events. To investigate this, we collected, in addition to data on dialysis, comprehensive information on various other factors possibly affecting cardiovascular risk. This enabled thorough adjustment for potential confounders when comparing the risk of major adverse cardiovascular event (MACE) in patients on home hemodialysis, APD, continuous ambulatory PD (CAPD), and IC-HD.

Methods

Study Design and Population

All patients aged 18 years or older who were on one of the home dialysis modalities at day 90 from the beginning of the dialysis therapy in the Helsinki-Uusimaa health care district in Finland were included (N=536). In addition, we used Microsoft Excel (the random command) to select a random sample of patients who were on IC-HD at day 90 from starting dialysis (N=432) to represent the whole group of IC-HD patients (N=1211) (Supplemental Figure 1). The reason for selecting a random sample was that the number of IC-HD patients was much larger than that of home dialysis patients, and all data were collected manually from the patient files. All study patients (N=968) had started their dialysis therapy between 2004 and 2017 (Supplemental Table 1).

Data Collection

Data were extracted retrospectively from the patient data system of Helsinki University Hospital into a structural database. The last available data before start of dialysis were collected on cardiovascular and other comorbidities, primary kidney disease, electrocardiogram and echocardiography parameters, BP, and laboratory tests. A summary of the data are displayed in Supplemental Table 2. MACE was defined as myocardial infarction, ischemic or hemorrhagic cerebrovascular stroke, or death due to cardiovascular causes.

Statistical Analyses

The cumulative incidence of first MACE was estimated considering death due to noncardiac causes as a competing risk event according to dialysis modality (CAPD, APD, home hemodialysis, and IC-HD) at day 90 from the beginning of dialysis (Figure 1).

We used Cox regression to assess hazard ratios (HRs) of first MACE associated with the dialysis treatment modality at 90 days from start of dialysis. Patients were censored at kidney transplantation (N=444), 5 years from starting dialysis (N=141), recovery of kidney function (N=7), loss of follow-up (FU) (N=3), and end of the year 2019 (N=92) or death due to noncardiac causes (N=151).

Missing values were imputed using predicting variables as appears in Supplemental Table 2. The multiple imputation tool in SPSS was used to impute one dataset with complete information for all analyzed variables. To adjust for confounding, we developed propensity scores using binary logistic regression for CAPD versus IC-HD, APD versus IC-HD and home hemodialysis versus IC-HD pairwise. All explanatory variables for the propensity scores were selected by a stepwise forward procedure. Supplemental Table 2 displays the related variables.

The incidence rate and incidence rate ratios (IRRs) of MACE were assessed for CAPD, APD, home hemodialysis, and IC-HD patients. This analysis included also subsequent events, not only the first MACE of each patient. Confidence intervals (CIs) of IRR were calculated.[21] Sensitivity analyses were conducted to ensure that the main result did not change by alternative analytic strategies. These included doing separate analyses for male patients and female patients and for patients with or without cardiovascular comorbidities before start of dialysis.

The cumulative incidence was estimated using the R Software (version Ri386 3.6.0, the cmprsk package, cuminc function), while the other statistical analyses were performed using SPSS (version 25).

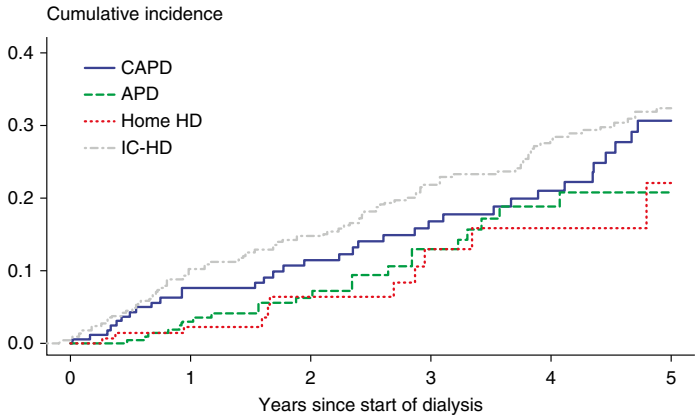


Figure 1. Cumulative incidence of the first MACE according to dialysis modality. APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; HD, hemodialysis; IC-HD, in-center hemodialysis; MACE, major adverse cardiovascular event; PD, peritoneal dialysis.

Results

Population Characteristics

A total of 968 patients were included in the study cohort. At day 90 from the beginning of dialysis, 162 were on CAPD, 229 on APD, 145 on home hemodialysis, and 432 on IC-hemodialysis. Patients on CAPD and IC-hemodialysis were older and had more often cardiovascular comorbidities before dialysis start compared with patients on APD or home hemodialysis (Table 1). IC-HD patients more often had diabetes and less often GN or polycystic kidney degeneration compared with home dialysis patients. More detailed patient characteristics are shown in Supplemental Table 2.

Cumulative Incidence and HR of the First MACE

Of the 968 patients, 172 (18%) experienced at least one MACE event during the FU. The cumulative incidence of a first MACE was 8% for CAPD, 3% for APD, 2% for home hemodialysis, and 10% for IC-HD patients at 1 year from the beginning of dialysis (Figure 1). In unadjusted and in age-adjusted and sex-adjusted analyses, APD and home hemodialysis patients had a lower risk of a first MACE compared with IC-HD patients (Table 2). However, after adjustment for propensity scores, these differences diminished and were no longer statistically significant, HR 0.86 (95% CI, 0.47 to 1.57) for APD and HR 0.67 (95% CI, 0.30 to 1.50) for home hemodialysis compared with IC-HD. When comparing CAPD with IC-HD, there was no statistically significant difference between hazards of first MACE.

IR of MACE

By calculating the IR, we considered all MACE events, not only the first MACE event of each patient. The IR was 109 MACE per 1000 patient-years for CAPD patients while it was 50 for APD, 32 for home hemodialysis, and 91 for IC-HD patients (Table 3). The corresponding IRR was 1.20 (95% CI, 0.99 to 1.46) for CAPD, 0.55 (95% CI, 0.45 to 0.67) for APD, and 0.35 (95% CI, 0.29 to 0.43) for home hemodialysis compared with IC-HD patients. Death due to cardiovascular disease comprised 52% of all MACE events during the study FU period, followed by myocardial infarction (27%) and cerebrovascular infarction (17%) and cerebrovascular bleeding (4%) (Supplemental Table 3).

Sensitivity Analyses

As a sensitivity analysis, we assessed the risk of getting the first MACE separately in patients with and without cardiovascular comorbidities at the time of dialysis initiation. With propensity score adjustment, the results were similar to those shown in Table 2, and there were no significant interactions between cardiovascular comorbidities and treatment modalities. For patients without prior cardiovascular comorbidities and compared with IC-HD, the HR for MACE was 0.97 (95% CI, 0.44 to 2.13) for CAPD, 0.97 (0.44 to 2.15) for APD, and 1.00 (0.37 to 2.72) for home hemodialysis.

When analyzed separately by sex, and with adjustment for propensity scores, the HR of MACE was 1.80 (95% CI, 1.11 to 2.92) for male patients and 0.37 (0.14 to 0.99) for female patients among those who started PD compared with IC-HD. The interaction between sex and treatment modality was statistically significant ($P = 0.006$). We also analyzed separately CAPD and APD: The difference between sexes remained similar in both PD modalities, thus PD associating with a higher risk of MACE among male patients and a lower risk among female patients (Supplemental Table 4). We further compared PD, CAPD, and APD with home hemodialysis separately by sex, and the result was similar to the comparison with IC-HD. We also analyzed separately patients who had or had not a history of cardiovascular comorbidities before start of dialysis, and again the difference between sexes was observed in both groups: compared with IC-HD, PD associated with higher risk of MACE among male patients and lower risk among female patients as compared with IC-HD.

In the main analysis, we did not censor at time of dialysis modality change. Of the patients who were on

Table 1. Baseline patient characteristics according to dialysis modality

Dialysis Modality[a]	CAPD	APD	Home Hemodialysis	IC-HD	*P* Value		
					CAPD versus IC-HD	APD versus IC-HD	Home Hemodialysis versus IC-HD
Number of patients	162	229	145	432			
Male sex, %	70	66	68	64	0.17	0.60	0.39
Age, yr, median (IQR)	65 (52–74)	50 (40–61)	50 (42–60)	66 (56–73)	0.50	<0.001	<0.001
Primary kidney disease, %					0.003	<0.001	<0.001
GN	17	22	24	8	[b]	[b]	[b]
Polycystic kidney disease	6	15	31	8		[b]	[b]
Diabetes	19	21	17	33			[b]
Others	11	12	9	51	[b]	[b]	[b]
A history of at least one comorbidity, %	29	13	13	32	0.56	<0.001	<0.001
Myocardial infarction	11	5	6	13	0.64	0.003	0.04
Cerebrovascular infarction	1.2	0.4	1.4	1.4	0.88	0.26	0.99
Cerebrovascular bleeding	0.6	0.0	0.0	0.9	0.71	0.14	0.25
FU-time, yr, median (IQR)	2.7 (1.4–4.4)	1.9 (1.1–3.6)	1.6 (0.88–3.0)	2.6 (1.4–4.4)	0.60	0.001	<0.001
At least one MACE event, %	21	9.6	7.6	24	0.40	<0.001	<0.001
Deaths in 5 yr[c], *N*	63	25	10	174	0.76	<0.001	<0.001
Cardiovascular deaths[c], *N*	22	10	5	70	0.43	<0.001	<0.001

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; FU, follow-up; IC-HD, in-center hemodialysis; IQR, interquartile range; MACE, major adverse cardiovascular event; *N*, number; PD, peritoneal dialysis; %, percentage.
[a]Dialysis modality at 90 days from start of KRT.
[b]Points with statistically significant differences in the primary kidney disease group.
[c]During follow-up period.

PD at day 90, 24% had transferred to IC-HD before the end FU, and of the patients who were on IC-HD, 5% transferred to PD and 5% to home hemodialysis. We performed a sensitivity analysis, with censoring also at the time of dialysis modality change (PD, home hemodialysis, or IC-HD). The results were comparable with the main analysis (Supplemental Table 5).

Discussion

We observed that patients who started APD or home hemodialysis had lower risk of MACE compared with those who started IC-HD, but after adjustment for confounding factors, the difference was no longer significant. Patients on APD and home hemodialysis showed similar characteristics, and they were younger and had fewer comorbidities than patients on CAPD and IC-HD. During the 5-year FU, 18% of the patients experienced at least one MACE, cardiovascular deaths comprising half of them.

Several earlier studies have compared risk of cardiovascular events and mortality between dialysis modalities. Hu *et al.* showed that PD was not inferior to IC-HD regarding cardiovascular events.[19] The authors used propensity score matching with comorbidities but

Table 2. Hazard ratios of first major adverse cardiovascular event according to dialysis modality during 5 years from the start of KRT

Analysis	HR of First MACE	95% CI of HR	
		Lower	Upper
HR of first MACE, unadjusted			
IC-HD (reference)			
CAPD	0.83	0.56	1.22
APD	0.49	0.31	0.77
Home hemodialysis	0.42	0.23	0.78
HR of first MACE, adjusted for age and sex			
IC-HD (reference)			
CAPD	0.81	0.55	1.20
APD	0.62	0.38	1.00
Home hemodialysis	0.53	0.28	1.00
HR of first MACE, adjusted for propensity score			
CAPD (compared with IC-HD)	1.22	0.73	2.05
APD (compared with IC-HD)	0.86	0.47	1.57
Home hemodialysis (compared with IC-HD)	0.67	0.30	1.50

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; CI, confidence interval; HR, hazard ratio; IC-HD, in-center hemodialysis; MACE, major adverse cardiovascular event; PD, peritoneal dialysis.

Table 3. Incidence rate and incidence rate ratio of major adverse cardiovascular event

Dialysis Modality	CAPD	APD	Home Hemodialysis	IC-HD
Number of PY	375	522	345	1266
Number of MACE events	41	26	11	115
IR (per 1000 PY) of MACE	109	50	32	91
IRR of MACE (95% CI)	1.20 (0.99–1.46)	0.55 (0.45–0.67)	0.35 (0.29–0.43)	1 (reference)

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; CI, confidence interval; IC-HD, in-center hemodialysis; IR, incidence rate per 1000 patient-years; IRR, incidence rate ratio; MACE, major adverse cardiovascular events; PD, peritoneal dialysis; PY, patient-years.

recommended to include more information on confounding factors in future studies. For example, their study did not have detailed data on cardiovascular comorbidities, laboratory results, electrocardiogram, and cardiac ultrasound findings, which all were available in our study. A meta-analysis published in 2019 based on five studies[22–26] compared cardiovascular adverse events between patients who started PD with those who started hemodialysis,[27] showing no difference between the treatment modalities. However, one of the included studies showed a lower risk of cardiovascular events among PD compared with hemodialysis patients.[22] Notably, only one of the included studies[23] contained data on both laboratory values and prior cardiovascular comorbidities. Some studies have shown lower risk of hospitalization for cardiovascular events among patients on frequent home dialysis compared with PD patients.[14–16] Compared with IC-HD, PD has been connected to higher risk of emergency hospitalization for cardiovascular disease[17] and lower risk of hospitalization for congestive heart failure.[18] We did not have data on hospitalizations, but we analyzed the risk of cardiovascular death, which was in line with that of MACE.

Unexpectedly, we observed that among females, PD associated with a clearly lower risk of MACE compared with IC-HD or home hemodialysis, while the association was the opposite among males. Earlier studies have not analyzed separately for male patients and female patients how various dialysis modalities associate with risk of MACE. Hu *et al.* observed a higher HR of death for PD compared with hemodialysis among female patients than male patients but did not present results on cardiovascular events by sex.[19] The reason for the different finding between male patients and female patients in our study remains unclear. We also found a similar tendency, but statistically nonsignificant, for risk of cardiovascular death. Regarding all-cause death, we observed no difference between sexes when comparing PD and hemodialysis. Based on our findings, we suggest that future studies compare outcomes of PD and hemodialysis separately by sex.

There are many strengths in our study. As a population-based study, it included all patients in Helsinki-Uusimaa health care district who were on home dialysis at day 90 and a randomly selected sample of IC-HD patients. Of all patients who entered KRT, the proportion of home dialysis patients was relatively high. As a result, these patients were not highly selected, and this may have reduced selection bias. Furthermore, we had complete data on MACE and comprehensive data on possible confounders. For most variables, <10% of data were missing, but for some variables, the level of missingness was higher. Statistical imputation was used to replace missing values, to include all patients and avoid selection bias. Notably, our study is observational, and despite adjusting for a large number of confounders, the results may still be affected by residual confounding. For example, we did not have information on fluid status or residual kidney function. As the numbers of patients and cardiovascular events were rather low, our study does not have the statistical power to show small differences between the dialysis modalities. In addition, the results may not be generalized to other settings in which, for instance, different selection criteria are applied for patients to receive home dialysis. Thus, it is important that these results are validated in other datasets in the future.

Regarding choosing between dialysis modalities, many nephrological centers have a PD first or home first policy, and the Finnish Society of Nephrology has published a strategy for increasing the proportion of home dialysis in Finland.[28] When deciding the dialysis modality, it is important that the patient is involved and well-informed. An important piece of information is how the dialysis modality affects various aspects of the patient's outcome. We have earlier shown that APD, and home hemodialysis are similar, and not statistically different than CAPD, with regard to survival. Our study does not demonstrate significant differences in risk of MACE between various dialysis modalities, which is important information for both health care professionals and patients when selecting the most appropriate dialysis modality. Notably, we found a difference between the sexes, so that PD, as compared with IC-HD, was connected to higher risk of MACE among male patients than female patients. This finding needs to be evaluated in further studies.

In conclusion, the risk of MACE was comparable across in-center and home dialysis modalities in this cohort study suggesting that the risk of cardiovascular events may not be a decisive factor when selecting a particular dialysis modality. Unexpectedly, we observed that PD is associated with lower risk of MACE among female patients and higher risk among male patients compared with IC-HD. Further research is needed to evaluate these findings and explore additional clinical outcomes associated with different dialysis modalities to guide informed decision-making in clinical practice.

Disclosures

Disclosure forms, as provided by each author, are available with the online version of the article at http://links.lww.com/CJN/C103.

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Ethical Consideration

We received a research permission by the Helsinki University Hospital (HUS/23/2024). Approval by an Ethics Committee was not required because no clinical experimentation was performed, and the patients were not contacted.

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Data Sharing Statement

Data cannot be shared. The data protection law of Finland (December 5, 2018/1050), which is based on the General Data Protection Regulation of European Union, does not allow public (or any) sharing of individual patients' data. Our research permission granted by Helsinki University Hospital does not allow sharing of individual patients' data. Researchers can submit a research application to the Helsinki University Hospital in order to get access to the data.

Supplemental Material

This article contains the following supplemental material online at http://links.lww.com/CJN/C102.

Supplemental Figure 1. Study cohort according to dialysis modality at day 90 from starting dialysis treatment.

Supplemental Table 1. Yearly distribution of patients according to dialysis modality at day 90 from starting dialysis treatment over the study period.

Supplemental Table 2. Detailed characteristics of the study population.

Supplemental Table 3. Distribution of MACE according to dialysis modality.

Supplemental Table 4. Comparison of HRs of MACE between male patients and female patients with propensity score adjustment.

Supplemental Table 5. HRs of the first MACE according to dialysis modality during 5 years from the start of KRT, with censoring at change of dialysis modality, kidney transplantation, loss of FU, recovery of kidney function, noncardiac death, and end of FU.

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