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Home Hemodialysis: Clinical Benefits, Risks, Target Populations

(Hémodialyse à domicile: Bénéfices cliniques, risques, populations cibles)

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Summary

Home hemodialysis, and in particular intensive home hemodialysis, has seen renewed development since the early 2010s, linked to low-flow dialysate techniques and the use of more manageable monitors. A number of studies have demonstrated a clinical benefit in terms of survival and cardiovascular risk reduction, pointing in particular to this technique in patients at high cardiovascular risk and with difficult access to renal transplantation. However, these benefits must be balanced against potential risks linked essentially to the increased frequency of sessions rather than being at home: increased complications of vascular access, loss of residual renal function, and burnout. Optimal patient selection, appropriate training, and regular follow-up will optimize the benefits relative to the potential risks.

Résumé

L'hémodialyse à domicile et en particulier l'hémodialyse intensive à domicile a connu un regain de développement depuis le début des années 2010, lié aux techniques de bas débit de dialysat et à l'utilisation de moniteurs plus maniables. Plusieurs études ont montré un bénéfice clinique en terme de survie et de diminution du risque cardiovasculaire indiquant tout particulièrement cette technique chez les patients à haut risque cardiovasculaire et avec des difficultés d'accès à la greffe rénale. Ces bénéfices sont à contrebalancer avec de potentiels risques reliés essentiellement à l'augmentation de la fréquence des séances, plutôt qu'au domicile : augmentation des complications des voies d'abord vasculaire, perte de fonction rénale résiduelle et burn-out. Une sélection optimale des patients, une formation adéquate avec un suivi régulier permettent d'optimiser les bénéfices par rapport aux risques potentiels.

Keywords: home hemodialysis (HHD), conventional hemodialysis (CHD), intensive home hemodialysis (IHHD), long nocturnal hemodialysis (LNHD), short daily hemodialysis (SDHD), survival, mortality, target population

Mots-clés : hémodialyse à domicile (HDD), hémodialyse conventionnelle (HDC), hémodialyse intensive à domicile (HDID), hémodialyse longue nocturne (HDLN), hémodialyse quotidienne à domicile (HDDQ), survie, mortalité, population cible

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Introduction

Conventional in-center hemodialysis is associated over the long term with a high rate of cardiovascular complications and poor quality of life. Renal transplantation remains the treatment guaranteeing the best survival but has an average waiting time of over 2 years and restricted access for certain populations, notably elderly patients, those at high immunological risk, those with severe cardiovascular comorbidities, and obese patients. These difficulties of access to transplantation underline the importance of developing alternatives to conventional hemodialysis in order to optimize chronic dialysis patients' quantity and quality of life.

Home hemodialysis (HHD) was first introduced in the 1960s, with rapid expansion due to dialysis units' inability to meet patient demand. A marked decline was then observed with the development of self-dialysis units and changes in reimbursement policies. Since the 2010s, there has been a resurgence in HHD linked to the demonstrated clinical benefits of intensive hemodialysis and technical innovations including the use of low-flow dialysate [1]. However, HHD remains largely underutilized, accounting for just 1% of hemodialysis patients in France. This underutilization is mainly due to a lack of training for caregivers and information for patients, as well as a lack of incentive policies.

This review aims to reiterate the proven clinical benefits of HHD versus the potential risks and to reiterate patient eligibility criteria and contraindications.

Clinical Benefits

The clinical benefits of HHD are essentially related to the intensity of dialysis, which for logistical reasons is more easily achieved at home. Intensive home hemodialysis (IHHD) is defined as either an increase in the frequency of sessions (minimum of 5 sessions per week) with a reduction in their duration (2-3 h, short daily hemodialysis (SDHD)) or an increase in the duration of sessions to more than 5,5 h, 3-4 times per week, generally performed at night (long nocturnal hemodialysis, LNHD), or an increase in both the duration and frequency of sessions *(Table I)*. The technique most widely used in the United States and France is SDHD.

Table I. Home hemodialysis procedures, adapted from [16].

Terms and conditions	Sessions /week	Session duration (h)	Qs (ml/min)	Qd (ml/min)	Base (mmol/l)	K+ (mmol/l)	Ca2+ (mmol/l)	Add P0[4]
CHD	3-3,5	3-5	300-400	500-800	HC03-, 32-36	2	1,25	No
Alternating LNHD	3,5	6-8	250-350	300-500	HC03-, 28-35	2	1,25	Rarely
Traditional SDHD	5-6	2,5-3,5	350-400	350-600	HC03-, 32-36	2	1,25	No
Traditional LNHD	4-6	6-8	250-300	300	HC03-, 28-35	3	1,5-1,75	20-30% sessions
LFD SDHD	5-6	2,5-4	300-400	90-300	lactate, 40-45	1-2	1,5	No
LFD LNHD	4-6	6-8	300-350	83-166	lactate, 40-45	2	1,75	No

Qs: blood flow; Qd: dialysate flow; HC03-: bicarbonate concentration of dialysis bath; K+: potassium concentration of dialysis bath; Ca2+: calcium concentration of dialysis bath; P0[4]: phosphorus; CHD: conventional in-center hemodialysis; LNHD: long nocturnal hemodialysis; SDHD: short daily hemodialysis; LFD SDHD: low-flow dialysate SDHD; LFD LNHD: low-flow dialysate LNHD

Survival

To date, no randomized controlled trial has demonstrated a significant survival advantage for IHHD over conventional hemodialysis (CHD). Survival data from randomized trials on this subject come from the Frequent Hemodialysis Network (FHN) studies. The FHN daily study [2] found a significant difference in the primary composite endpoint of fewer deaths and less left ventricular hypertrophy (LVH) in the frequent hemodialysis group (center-based) compared with the conventional hemodialysis group. This study was then extended over a median period of 3,6 years (range 1,5 to 5,3 years) after randomization, with the observation of lower mortality and a relative risk (RR) of mortality for frequent hemodialysis versus conventional hemodialysis of 0,54 [3]. With regard to LNHD, the FHN nocturnal study [4] found no difference in terms of survival or reduction in LVH. These negative results were possibly linked to the high proportion of residual renal function (RRF) loss in the LNHD group (compared with an unusually high RRF in the CHD group) and, above all, to underpowering of the mortality study (low mortality in the CHD group, small number of patients, insufficient compliance with nocturnal treatment). The study was then extended to 5 years [5], with an increase in mortality observed in the LNHD group, but with an increase in the dialysis dose for a large number of patients in the CHD group, with more than 3 sessions per week and more than 27 hours of dialysis per week after the first 12 months, making any final interpretation difficult.

Other survival data on IHHD are derived from observational studies, with all the limitations inherent to these studies' characteristics, but partly offset by the large number of studies showing a survival benefit of IHHD over CHD. In particular, LNHD was found to be beneficial in several studies, with a reduction in the RR of mortality [6-8]. In the case of SDHD, Blagg et al. found a reduction in mortality with an RR reduction of 0,39 in comparison with incident patients from the United States Renal Data System (USRDS) registry [9]. Kjellstrand et al. observed a 2- to 3-fold increase in survival compared with a group of CHD patients [9,10]. Marshall et al. reviewed the Australian and New Zealand registries comparing CHD with different HHD modalities and found a nonsignificant survival advantage for IHHD (RR 0,56) versus CHD, while home CHD had the same mortality rate [11, 12]. Rydell et al. carried out a cohort study with 152 incident patients receiving home hemodialysis (15 hours per week) at high flow, performed diurnally and nocturnally, compared with 608 patients on CHD and 456 on peritoneal dialysis (PD) over a mean duration of 10,4 years, and observed an increase in survival in the HHD group compared with the CHD and PD groups [13].

With regard to SDHD at low dialysate flow, the main study is that of Weinhandl et al., which is a prospective observational study comparing 1873 patients on SDHD with the NxStage™ monitor versus 9365 patients on CHD (3 times a week) over 3 years: they observed a 13% reduction in mortality (RR 0,87) with an RR of 0,92 for cardiovascular mortality and a more marked benefit on the diabetic and obese population. The SDHD group was younger and less comorbid, but this difference was offset by matching [14].

Finally, a 2018 Canadian meta-analysis included 23 studies comparing CHD with different IHHD techniques (home and center) and found lower mortality in IHHD compared with CHD (RR of LNHD = 0,46, RR of SDHD = 0,54) [15].

Lockridge et al. estimated the results of different dialysis techniques compared with renal

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transplantation to tailor dialysis prescriptions as closely as possible to patients' needs *(Table II)* [16].

Table II. Comparison of different dialysis techniques in kidney transplantation, adapted from [16]

	Treatment intensity		Efficacy relative to transplantation (5= transplanted, 0= no treatment)			
Renal purification treatment	Sessions /week	Session duration (h)	Volume control	PO4 control4	Minimum purification dose[a]	Optimum purification dose[b]
Kidney transplantation	-	-	5	5	4	5
DPCA/ DPA without RRF	-	-	1	1	4	0
CHD	3	3-5	2	1	4	1
	3,5	3-5	3	2	4	2
SDHD	5-6	2,5-3,5	5	3	4	3
LNHD	3,5	6-8	4	4	4	4
	5-6	6-8	5	5	4	5
LFD SDHD	5-6	2,5-3,5	5	2	4	3
LFD LNHD	5-6	6-8	5	4	4	4

Note: the data available for direct comparisons of different renal replacement therapy modalities are limited. Relative efficacy values are estimates largely derived from opinion studies with a low level of evidence.
a The minimum purification dose is the minimum dialysis dose defined in the KDOQI (Kidney Disease Outcomes Quality Initiative) recommendations on the adequacy of hemodialysis (2015 update).
b The optimal purification dose is the dialysis dose after increasing the duration and frequency of sessions.
P0^4: phosphorus; CHD: conventional in-center hemodialysis; LNHD: long nocturnal hemodialysis; SDHD: short daily hemodialysis; LFD SDHD: low-flow dialysate SDHD; LFD LNHD: low-flow dialysate LNHD

Lower Cardiovascular Risk

Chronic hemodialysis patients are at high cardiovascular risk, with an excess risk of cardiovascular morbidity and mortality 10 to 30 times higher than in the general population. Controlling cardiovascular risk is therefore particularly important in this population.

Hypertension control is one of the particularly beneficial effects of IHHD, with a high level of evidence for both SDHD and LNHD. A significant reduction in blood pressure (BP) and a reduction in treatment were found in the FHN studies, as well as in the randomized ACTIVE and ALBERTA studies [17, 18]. This beneficial effect was found in several other non-randomized studies [19-21], and notably in the European retrospective cohort study KIDHNEy involving 104 SDHD patients with the NxStage™ monitor followed over 6 months [22]. The improvement in BP control observed with IHHD is probably related to volume control and reduction in peripheral vascular resistance [19, 23, 24].

The reduction in LVH also benefits from a high level of evidence, with a significant drop in the FHN daily study and in the LNHD group of the randomized ALBERTA study [2, 18]. No difference was found in the FHN nocturnal study, with the limitations cited above, or in the ACTIVE study [4, 17]. Several observational studies have observed a decrease in LVH in both diurnal SDHD [19, 21, 25] and LNHD [18, 26].

IHHD's positive effect on increased phosphoremia control has also been observed. This effect has been observed in SDHD [2, 27], extended hemodialysis [8, 17], and especially LNHD [4, 18, 28], with discontinuation of phosphorus binders and sometimes the need for per-session

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phosphorus supplementation.

Another major aspect described with frequent hemodialysis is the reduction in the effect of per-session myocardial sideration of dialysis, resulting from segmental and global cardiac ischemic damage and leading to long-term cardiac dysfunction. This positive impact was found in the observational cross-sectional study by Jefferies et al. [29], who carried out per-session cardiac echocardiography in 4 groups of hemodialysis patients (CHD, frequent in-center hemodialysis, home SDHD, home LNHD) and found a reduction in segmental and global kinetic disorders in the frequent hemodialysis groups, associated with a fall in ultrafiltration levels and cardiac markers (BNP and troponin).

The final aspect is the observation of a reduction in cardiovascular hospitalizations with both LNHD [29, 30] and SDHD [14, 32].

Quality of Life, Fertility

One of HHD's key advantages is its flexibility, giving patients the freedom to carry out their sessions according to the demands of their daily lives, dietary deviations, and leisure activities. HHD's influence on quality of life has been evaluated in numerous studies [4, 18, 33-35], with a positive impact on the experience of the burden of kidney disease. In addition to an increase in quality of life, the FREEDOM study found a significant improvement at 1 year in the depression inventory after switching patients to home SDHD on NxStage™ [27] and a reduction in restless leg syndrome associated with an increase in sleep quality.

The other major aspect is fertility, which is greatly reduced in CHD. Few data have been published, but IHHD, in particular LNHD, seems to increase the chances of successfully carrying a pregnancy to term [36].

Risks

Similarly to the benefits, the risks of HHD are essentially related to the intensity of dialysis. These risks are mainly increased vascular access (VA) complications, loss of RRF, and patients' exhaustion, sometimes associated with that of their caregivers. Some of these risks can be prevented and must be balanced against the expected benefits of IHHD.

Vascular access complications

The increased risk of VA complications has been described in the FHN studies. Suri et al. reported the FHN cohort data, observing a 76% increase in the risk of VA complications with 55% thrombectomy and revision surgery. The risk of complications was higher for arteriovenous fistulas (AVFs). However, there was no difference in VA loss or the infection rate [36,37]. Three VA-related deaths were described: one in each group of the FNH diurnal study and one in the LNHD group on gas embolism (presence of a central venous catheter (CVC)).

Weinhandl et al. found a nonsignificant increase in infectious mortality [14] but no direct causal relationship with an increase in VA infections.

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The impact of HHD on the increase in VA complications remains controversial, with an increase observed in several observational studies [38, 39] but not found in the randomized ALBERTA and ACTIVE studies [17, 18]. Nor was any difference observed in Achinger et al.'s prospective study [40].

This heterogeneity of results is probably linked to various factors: firstly, the difference in VA used for HHD, whether AVF or CVC, and when using AVF, the practice of the buttonhole technique. The latter is associated with an increased risk of infection, with an RR of 3,18 compared with the cord technique in Muir et al.'s review [40]. The risk of infection can be reduced by the systematic use of mupirocin [42, 43]: the application of this preventive measure, combined with optimal patient training and regular follow-up, is probably a second factor that may explain the discrepant results in terms of VA complications. Prevention remains essential, not only in terms of infection, but also in terms of AVF thrombosis and CVC dysfunction. A survey of 19 HHD centers in the USA revealed inadequate training of nurses and patients, which may increase the risk of infection [44].

Loss of Residual Renal Function

Loss of RRF has been mainly described in LNHD. The FHN cohort study found a 67% loss of RRF in the LNHD group versus 36% in the CHD group (P = 0,06), but there was no difference in the FHN daily study, subject to a majority of anuric patients in the 2 groups (72% in the IHHD group, 60% in the CHD group) [45].

The mechanisms potentially involved in this loss of RRF are better volemic and osmotic control, better blood pressure control with lower BPs, and discontinuation of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) with significantly lower prescribing in IHHD [46].

Burnout

Analysis of the FHN studies found an increase in caregiver burden in the LNHD group [47]. Walker et al.'s review of 24 studies found greater anxiety and apprehension among patients and caregivers, particularly in countries less accustomed to SDHD [48], suggesting once again that burnout could be prevented by optimizing patient training and follow-up.

Eligibility Criteria and Target Populations

Contraindications

The essential criteria for HHD are patient motivation and autonomy. Apart from the absence of these criteria, there are very few contraindications to HHD. Other barriers to IHHD include lack of compliance, cluttered and/or unhealthy housing, and VA difficulties. For the time being, dependent people cannot benefit from a home nurse, unlike PD patients in France.

The absence of a caregiver is theoretically a contraindication in France, since the presence of a third party during the dialysis session is mandatory by law, unlike in other countries. This

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obligation is regularly circumvented, with 95% of home hemodialysis patients declaring that their designated caregiver is not present during their dialysis session. Several nephrologists and patient associations have called for this obligation to be abolished, as it potentially deprives patients living alone of being placed on IHHD.

Bypassable Barriers

For Patients

Fear of puncture, isolation, and being a burden on the caregiver are frequently cited barriers to HHD [49-51]. These fears can be overcome by providing adequate information on HHD techniques, meeting expert patients who can allay certain apprehensions, and making a home visit to provide a personalized response to the patient's fears.

Advanced age, in particular >75 years, is not a contraindication in itself. There are few studies on the feasibility and potential benefits of HHD for elderly patients. A multicenter feasibility study including 79 patients aged over 65 years with an average age of 68 years showed positive survival results, with 92% and 83% event-free survival 1 and 2 years after initiation of HHD [52]. The major obstacle encountered with increasing age is the increase in physical, cognitive, social, and psychological frailties. These frailties can be explored by a multidisciplinary team, including a geriatrician, with corrective actions being taken in some cases to increase autonomy and make HHD feasible in some cases [53].

For Caregivers

There are also barriers related to caregivers, particularly nephrologists, who remain apprehensive about placing certain fragile patients on HHD due to a lack of training and experience. Several training projects have been developed in France to optimize the training of nephrologists and nurses, such as the international ECHO home dialysis project [54], the French Prodiadom module created by nephrologists with expertise in home dialysis [55], and online training courses and seminars offered by HHD machines (Physidia™ , Fresenius™).

The lack of adequate training, the lack of dedicated and motivated nurses, and the absence of a multidisciplinary team are also obstacles that can be overcome when setting up an HHD project [56].

Target Populations

Classic Preferred Indications

As we have seen, IHHD offers better control of cardiovascular risk factors than CHD and therefore represents a preferred indication for patients with resistant hypertension with refractory hydro-sodium overload, hyperphosphatemia, and severe obstructive sleep apnea-hypopnea syndrome.

Similarly, dialysis-treated women planning to conceive, or those who are pregnant, benefit from improved fertility and fewer obstetric-fetal complications with IHHD [36].

Given the flexibility with which dialysis sessions can be organized, HHD remains a preferred

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indication for professionally active patients. The employment rate for patients on HHD is higher than for those on in center CHD [57].
HHD also remains an interesting option, despite the paucity of evidence, for patients who have failed transplants and PD and wish to preserve their autonomy.

Heart Failure

While IHHD helps reduce cardiovascular risk, it is also a preferred indication in cases of prevalent heart failure.

Few studies have looked specifically at the effect of HHD in patients with congestive heart failure (CHF). A Canadian team published a small observational study including 6 patients with severe congestive heart failure (mean left ventricular ejection fraction (LVEF) 28%) on LNHD, with an improvement in LVEF to 41% at 3 years [58]. The same team subsequently published 2 retrospective studies showing an improvement in LVEF and right ventricular systolic pressure in 150 and 108 LNHD patients, respectively, after 4 years of follow-up [59, 60]. They also published a case report of a 76-year-old patient with severe pulmonary hypertension, congestive heart failure, end-stage renal failure, diabetic nephropathy, and cardio-renal syndrome placed on LNHD with a decrease in right ventricular systolic pressure and right atrial pressure, an increase in right LVEF, a decrease in left ventricular mass, and normalization of LVEF observed at 1 year [61].

Despite the low level of evidence, with few randomized studies demonstrating a cardiovascular benefit from HHD, the American Society of Cardiology issued recommendations in 2022 to optimize cardiovascular risk in dialysis patients, including encouraging the use of frequent home dialysis techniques in patients at cardiovascular risk and those with CHF [62].
Several mechanisms have been described that may explain this cardioprotective effect of IHHD, including the role of normalization of extracellular volume [63], improved purification of uremic toxins with a negative inotropic effect [59], a reduction in peripheral vascular resistance with the purification of vasoconstrictor substances, an improvement in endothelial dysfunction [24, 64], a reduction in the risk of per-session myocardial sideration [29, 58], and an improvement in severe obstructive sleep apnea-hypopnea syndrome [24, 65].

Obesity

Obesity is a real public health problem, with a growing proportion of obese patients undergoing dialysis. The administration of adequate replacement therapy is often more complicated in this population, given the difficulties of the dialysis access (increased risk of delayed AVF maturation and complications [66], increased risk of PD catheter dysfunction) and of suboptimal dialysis due to increased purification volume. The impact of suboptimal dialysis is all the more important as obesity is an obstacle to renal transplantation, currently representing the third cause of contraindication in the USA [67].

The solution to an insufficient dialysis dose is to increase the duration and frequency of hemodialysis sessions. This can have a significant impact on patients' quality of life, particularly in the center. Few studies have been carried out on the impact of IHHD in this population. An Australian team described an LNHD program for 23 obese patients with a body mass index between 34,9 and 71, followed up over 8 years; the average weekly dialysis time was 27 h, with a

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duration of 7,5 h per session and a urea purification rate within the target range with well-tolerated sessions [68]. As for studies on low-flow dialysate SDHD, we find an English cohort study from 2023 involving 105 patients followed for a minimum of 6 months with a significant increase in standard Kt/V and a drop in phosphoremia [69]. In addition, the RECAP and KIDHNEy studies showed a significant percentage of obese patients (13% and 22%, respectively) [22, 25].

Although there are few studies with a low level of evidence, these data suggest the feasibility of IHHD with a benefit in terms of purification in this population.

Conclusion

IHHD offers a number of advantages, with eligibility criteria broadened to include not only high-risk cardiovascular patients but also obese patients and younger patients concerned with preserving their fertility, autonomy, work, and quality of life. The potential risks described, including complications of VA, loss of RRF, and burnout, can be partially reduced with adequate patient training, regular reassessment of practices, medical and multidisciplinary follow-up, and, above all, optimal patient selection, focusing on autonomy, motivation, and compliance *(Figure 1)*.

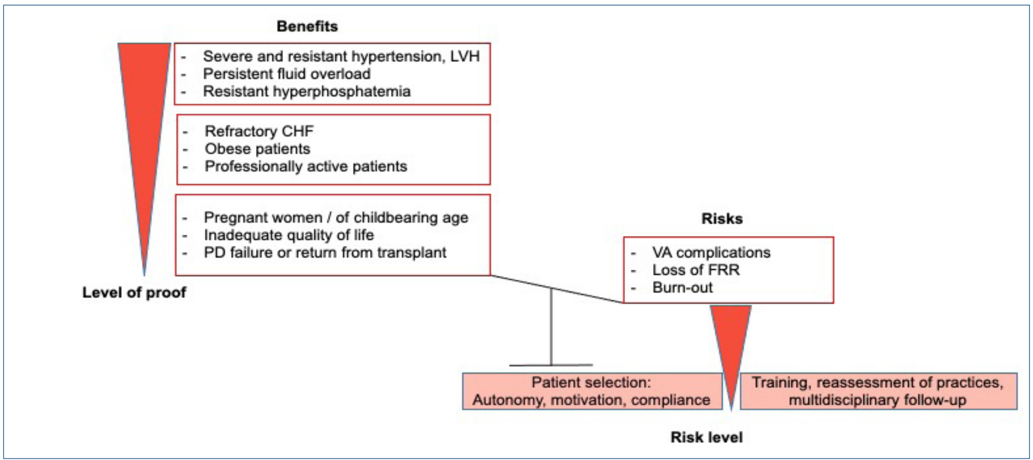

Figure 1. Indications for HDID according to benefit-risk of target populations

Ethical Considerations

Not applicable.

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The author has not received any funding for this work.

Conflicts of Interest

The author declares that she has no conflicts of interest.

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