Global Dialysis Perspective: Spain

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Introduction
Spain is a country in Southwestern Europe with a population of 46.7 million in 2018. Its territory is organized into seventeen Autonomous Communities, formed in turn by fifty provinces, and two autonomous cities (Ceuta and Melilla) in the north of Africa. According to the principle of decentralization promulgated by the Spanish Constitution, health competence is transferred to each of these Autonomous Communities. Health care in Spain, paid for by public funds, is guaranteed to those persons who pay into the system or are its beneficiaries within the National Health System.

Treated kidney failure patients in Spain
Most data shown here were presented during the XLIX meeting of the Spanish Society of Nephrology (A Coruña, October 2019) and obtained from the Spanish Registry of Renal Patients (Registro Español de Enfermos Renales, REER, http://www.registrorenal.es/) which collects the information of treated kidney failure patients registered by the seventeen Autonomous Communities and the two autonomous cities of Spain (1). In addition, some data from regional registries of kidney patients were also added (2-5).

Incidence
According to the REER, 6,883 kidney failure patients started kidney replacement therapy (KRT) in 2018 representing an incidence rate of 147.3 per million population (pmp). Considering the regional distribution, the highest incidence rate was in Ceuta (258.4 pmp) followed by Catalonia (183.4 pmp) and Asturias (166.3 pmp) (1). In addition, some data from regional registries of kidney patients were also added (2-5).

Regarding the evolution of the incidence rate for treated kidney failure in Spain, it remained between 128-130 pmp from 2006 to 2008, decreased to 120-121 pmp from 2009 to 2012 and then progressively increased from 2013 (125.4 pmp) to 2018, year with the highest recorded incidence rate. This upward trend in the incidence rate since 2013 has occurred along with the progressive growth of the number of kidney failure patients older than 65 years who have started KRT, the highest rate of which (496 pmp) was recorded during 2018 in patients older than 75 years. Year after year, diabetic nephropathy remained the most frequent aetiology of kidney failure patients to start KRT (about 25% of cases per year) (1).

The most frequent modality to start KRT in Spain from 2006 to 2018 was hemodialysis
(HD, around 100-116 pmp), well above that of peritoneal dialysis or pre-emptive kidney transplantation. However, these two modalities of KRT have increased during this period of time as follows (pmp): from 17.2 to 24.1 and from 1.8 to 7.0, respectively (1).

**Prevalence**

On December 31, 2018, there were 61,764 kidney failure patients on KRT in Spain, accounting for a prevalence rate of 1,321.9 pmp, which was the highest prevalence rate ever reached in our country (1). In fact, the prevalence rate in Spain did not stop growing progressively over the 10 years from 994.8 pmp (2008) to the current top-level (2018). The highest prevalence rate in 2018 was recorded in Catalonia (1,469 pmp) followed by Canary Islands (1,449 pmp) and Valencia Community (1,445 pmp). Considering five age groups between 2013 and 2018, mostly KRT patients were in the age bracket of 65-74 years-old (1).

Regarding the distribution of the KRT modality in 2018, most kidney failure patients were treated with kidney transplantation (33,766 patients, 722.7 pmp), followed by HD (24,900 patients, 532.9 pmp) and peritoneal dialysis (3,098 patients, 66.5 pmp) (1). The most impressive change in the KRT modality over time in Spain has been evidenced by the number of prevalent kidney failure patients having a functioning kidney graft that has increased from 490.2 pmp in 2006 to the historical maximum of 2018 (1). In fact, the majority of prevalent kidney failure patients in 2018 had a functioning kidney graft (54.7%) and the remaining ones were treated through some kind of dialysis technique (HD 40.3%, peritoneal dialysis 5.0%). According the Global Observatory on Donation and Transplantation, Spain registered the highest worldwide kidney transplantation rate in 2018 (3,313 patients, 70.8 pmp) (1).

**Mortality**

The all-cause mortality rate of kidney failure patients on KRT in Spain during the period 2007 to 2018 remained between 8% and 9% annually (1). During these years, the mortality rate was associated to KRT modality: kidney failure patients treated with HD and kidney transplantation showed the highest (around 15%/year) and the lowest (<3%/year) mortality rate, respectively; patients treated with peritoneal dialysis showed an in-between mortality rate (around 9%/year). The maximum mortality rate was recorded in patients older than 75 years for all KRT modalities. The all-cause mortality rate was
8.3% in 2018 (5,128 deaths over 61,764 prevalent KRT patients) and distributed as follows (%): HD 15.9, peritoneal dialysis 9.6 and kidney transplantation 2.6 (1).

Considering only data of the registry from Catalonia, 1,024 treated kidney failure patients died during 2018 and cardiovascular disease was the main known cause of death (35%) followed by infection (18.5%) (2). Regarding the evolution of the annual all-cause mortality rate over time per 100 KRT pts/year in Catalonia, there was a significant decreasing trend in all age groups throughout the period 1986-2018 (2).

Survival
The median of survival analyzed in 77,629 incident dialysis patients (HD 84.3%, peritoneal dialysis 15.7%) during the period 2004-2018 in Spain was 6.55 years (95% confidence interval: 6.45–6.65) (1). The overall survival of incident patients who started KRT in Catalonia during the period 1984-2018 (n= 30,986) at 1, 3, 5, 10, 15, 20, 25 and 30 years was 87.3%, 69.3%, 55.1%, 34.7%, 25.0%, 18.9%, 14.5% and 10.9%, respectively (2).

According to a multivariate survival analysis of 19,874 incident KRT patients from 2000 to 2018 in Catalonia, survival was associated to age group, gender, primary kidney disease, functional status, situation on the waiting list for kidney transplantation and comorbidity at starting KRT (2). In addition, survival of patients treated with HD was also associated to the first vascular access used: starting HD through a central vein catheter was associated with a 1.36-fold higher risk for all-cause mortality over time than when using an arteriovenous fistula (2).

Dialysis treatment according regional registries from Andalusia and Catalonia during 2018

A) Hemodialysis
Data from Autonomous Communities showed that 1,181 and 1,392 kidney failure patients started KRT in Andalusia and Catalonia, respectively (incidence rate: 140.9 and 183.2 pmp, respectively) and most of them through HD (79.9 % and 79.1%, respectively) (2,3).

On December 31, 2018 there were 10,430 and 11,162 kidney failure patients on KRT in Andalusia and Catalonia, respectively (prevalence rate: 1,244 pmp and 1,468.7 pmp,
respectively) and most of them had a functioning kidney graft (around 57% in both Communities). HD treatment accounted for 39.3% and 38.3% in Andalusia and Catalonia, respectively (2,3). The proportion of HD patients treated with on-line hemodiafiltration in Spain is variable between Autonomous Communities and also among HD Units of each Community (2,4).

Regarding the duration of the HD session, most HD patients were treated for 12 hours/week in Catalonia (80.8%) (2). The percentage of HD patients treated for more than 12 hours/week in Catalonia (8.6%) varied according to gender, age and body mass index: men, from 15 to 64 years with a body mass index over 29 are those who had longer HD sessions in Catalonia (2).

The mean prescribed pump speed was 378.5±62.0 ml/min in Andalusia and it was higher for patients dialyzed through an arteriovenous fistula than a tunnelled catheter (393 vs 353 ml/min, respectively) (4).

Regarding HD adequacy, mean spKt/V and urea reduction ratio in Andalusia were 1.76±0.45 and 76.3±7.8%, respectively (4). Mean equilibrated Kt/V reported in Catalonia over the last 5 years was around 1.6 and women over 75 years-old with a body mass index under 20 treated by on-line hemodiafiltration through fistula was the patient’s profile showing the highest equilibrated Kt/V level (2).

**B) Peritoneal dialysis**

From the statistical reports, 14.6% and 13.6% kidney failure patients started KRT during 2018 through peritoneal dialysis in Andalusia and Catalonia, respectively (2,5). On December 31, 2018, only 3.5% and 3.9% of kidney failure patients were treated with peritoneal dialysis in Andalusia and Catalonia, respectively (2,5). Continuous Ambulatory Peritoneal Dialysis was slightly more commonly used than Automated Peritoneal Dialysis in Catalonia (52.7% versus 47.3%) during 2018 (2).

Peritonitis rate (cases/patient/year) was 0.30 and 0.20 in Andalusia and Catalonia, respectively (2,5). When considered separately, Automated Peritoneal Dialysis and Continuous Ambulatory Peritoneal Dialysis techniques in Catalonia, comprised 0.13 and 0.25 cases/patient/year, respectively (2).
**Vascular access for HD**

Most kidney failure patients started HD through a catheter in Catalonia (59.4%) and only 39.9% through a mature arteriovenous fistula in 2018 (2). This percentage of fistula as the first vascular access decreased progressively in Catalonia over the last 20 years from 1998 (around 50%) to 2018 (around 40%) (2). The factors associated with the probability of starting HD through a mature arteriovenous fistula in Catalonia were previously analyzed (6).

Considering a quality indicator of the current Spanish Guidelines (nephrology predialysis care higher than 6 months) (7), most kidney failure patients started HD in Andalusia through a mature fistula (61.9%) and the remaining ones through a catheter (tunnelled catheter 23.4% and untunnelled catheter 14.7%) (3).

The proportion of prevalent HD patients dialyzed though a mature fistula in Spain is variable between Autonomous Communities and also among HD Units of each Community. On December 31, 2018, 63.7% of HD patients were dialyzed through a fistula in Andalusia (4) and 59.8% in Catalonia (2). The factors related to the likelihood of the prevalent patient being dialyzed through a fistula in Catalonia have recently been analyzed (8). According to the Dialysis Outcomes and Practice Patterns Study (DOPPS 5, 2012-2014), the vascular access distribution in prevalent HD patients in Spain was as follows: 65% arteriovenous fistula, 6% arteriovenous graft and 29% central vein catheter (Table 1) (9).

Considering four types of vascular access (arteriovenous fistula, arteriovenous graft, tunnelled catheter and untunnelled catheter, the fistula was the vascular access associated with the lowest incidence of hospital admissions due to complications in Catalonia during 2018 (7.7 % with ≥1 admissions) while the arteriovenous graft showed the highest (33.6 % with ≥ 1 admissions). Furthermore, arteriovenous graft showed the highest incidence of outpatient procedures for the treatment of any complication (37.3% of cases) (2).

**Medication utilization patterns for HD patients**

An observational study of 7,316 patients on HD in Spain, performed in a network of
clinics from an international dialysis organization, showed the following distribution of medication from both incident (n=2,637) and prevalent (n=4,679) HD patients (%): erythropoiesis-stimulating agents 97.4 and 92.7, statins 57.8 and 53.3, angiotensin converting enzyme inhibitors 44.7 and 34.2, other anti-hypertensives 76.6 and 60.3, insulin 22.5 and 16.5, oral antidiabetics 4.2 and 2.5, oral vitamin D (calcitriol or paricalcitol or vitamin D native) 61.6 and 66.9, phosphate binders 79.8 and 82.6, cinacalcet 26.5 and 41.7, respectively (10).

From the DOPPS phase 4 (2009-2011), the mean number of prescribed phosphate binder was 5.1 pills/day in Spain, but 39% of them skipped taking their phosphate binder medication at least once in the previous month (11). According to DOPPS phase 5 (2012-2015), only 13.1% out of 526 Spanish maintenance HD patients were not treated with erythropoiesis-stimulating agents at DOPPS study entry and, from the remaining HD patients, the patient erythropoiesis-stimulating agent type distribution was the following (%): darbepoetin alfa 31, continuous erythropoietin receptor agonist CERA 4, epoetin beta 29 and epoetin alfa 36 (12).

**Hypertension and volume management of maintenance dialysis patients**

According to data from a cross-section of DOPPS II, including 600 Spanish HD patients, 50.8% of them were prescribed any antihypertensive agent, being long-acting dihydropyridines the main class of drug prescribed (26.7%) (13). Data of EURODOPPS (DOPPS phase 4, 2009-2011), referring to 1,073 maintenance HD patients from Spain, showed that around 40% of them attained the target blood pressure and the number of antihypertensive drugs taken was the following (%): zero 25, one 35, two 25 and three or more 15 (14).

The utilization of objective measures of volume status on HD or peritoneal dialysis patients is spreading in Spanish Dialysis Units. In recent years, numerous studies have been published on the benefit of the bioimpedance technique to assess the degree of hydration of Spanish maintenance dialysis patients, which allows us to introduce changes in the treatment schedule for dialysis and, therefore, manage a better blood pressure control (15-17). In this way, Vega et al., analyzed the hydration status by bioimpedance in 128 maintenance HD patients showing 96 patients (75%) with hypertension, of whom 85% were overhydrated and, therefore, had volume-dependent hypertension (16). In the
same line, ambulatory blood pressure monitoring and bioimpedance usefulness for the treatment and control of hypertension in Spanish maintenance HD patients has recently been reported (18). In addition, the role of ultrasound in inferior vena cava and lungs for the patient’s hydration assessment has been highlighted in the Spanish consensus document for ultrasound training in the specialty of Nephrology (19).

**Home HD**

Home HD is a minority treatment in Spain. The cumulative incidence of home HD in Spain was reported during the 2019 meeting of the Spanish Society of Nephrology (20). Two hundred and forty-two incident home HD patients were analyzed (mean age 54.4±14 years, 71% male) with a variable distribution according to the Autonomous Community considered. Most patients were dialyzed at home using a portable HD machine (71.3%) and with a short daily treatment time schedule (69.3%). Vascular access distribution was catheter and fistula at fifty percent each. Buttonhole technique was the method most frequently used for fistula needling (69%). At the end of the follow-up period, 56.2% (n=136) were still on the home HD program; of the remaining patients who did not continue on home HD (106, 43.8%), most of them (61, 57.5%) received a kidney graft (20).

**Characteristics of dialysis treatment in Spain, 2018 (Table 1)**

All HD sessions are covered by the National Health System. Home dialysis is a minority treatment in Spain and very few patients are treated using home HD. Most HD patients were dialyzed in a Dialysis Unit inside the Hospital (public or subsidized HD Unit, both non-profit) or in a private Dialysis Center (mostly out-of-hospital and for-profit by international dialysis organizations).

Regarding HD reimbursement, sanitary agreements between the health administration and the HD Units have been subscribed in each Autonomous Community, and they can differ depending on whether it is a public hospital, a subsidized private hospital or a Dialysis Center. For this reason, there is significant variability in the reimbursement per HD session between the different HD Units of Spain. For instance, the reimbursement established for an HD session in public hospital HD Units is different when comparing Asturias (192.8$, single fee), Cantabria (261.8$ for outpatient session), Catalonia (196.6$ and 180.8$ for inpatient and outpatient session, respectively) and País Vasco (201.4$, single fee) (21-24). Another example of heterogeneous reimbursement for HD
session in Spain lies within the Valladolid province, where the reimbursement to two different companies hired to manage two private Dialysis Center was different for Valladolid capital (133.7$–130.7$ according to the number of HD sessions per month) and for Medina del Campo (166.5$–150.8$ according to the number of HD sessions per month) (25). In addition, the reimbursement per session can also be different depending on the HD modality performed and can be 39$ higher through on-line hemodiafiltration (23,25). In summary, there is no fixed rate for all of Spain.

Each dialysis Center has a reference Hospital where it is possible to refer the patient anytime when any complication occurs. The staff who perform HD are exclusively made up of registered nurses specialized in HD and the figure of the dialysis technician does not exist in Spain. In general, the patient-to-nurse ratio is 4:1 for non-profit Dialysis Units and 5:1 for-profit Dialysis Units. The average length of a dialysis session is equal to or greater than 4 hours for most HD patients. A nephrologist rounds sees patients on each HD session.

Areas for improvement in Spain and potential strategies to address them
Although the kidney transplantation rate is excellent in Spain, the pre-emptive kidney transplantation rate has room for improvement. Regarding dialysis treatment, there are some aspects that can be improved, such as the following:

1) Increase the percentage of patients who start KRT by using peritoneal dialysis
2) Decrease the percentage of patients starting HD using a catheter.
3) Increase the percentage of prevalent HD patients dialyzed through a mature fistula
4) Increase the percentage of prevalent HD patients treated with home HD
5) Generalize the on-line hemodiafiltration technique

It’s necessary to take a step forward regarding the current role of home-based dialysis therapies in Spain because they are associated with clinical, social, and economic benefits (26-28). It’s essential to adequately inform the kidney failure patient about these techniques in pre-dialysis check-ups, to carry out specific training courses in their use for the professionals who care for these patients and to encourage health administrations to increase resources to definitively promote these therapies in Spain (26-28)
Regarding vascular access issues in Spain, the following fourteen key points for improvement have previously been highlighted and are fully in force today (29):

1) Establish a multidisciplinary team.
2) Set up a structured advanced kidney failure outpatients’ clinic.
3) Achieve full commitment of the vascular surgeon in vascular access management.
4) Introduce vascular mapping by using Doppler ultrasound in the advanced kidney failure outpatients’ clinic.
5) Early arteriovenous access creation 4-6 months before the first HD.
6) Close monitoring of arteriovenous access maturation from creation to the first needling.
7) Ensure treatment for the non-matured arteriovenous access of incident HD patients through interventional radiology and/or revision surgery in order to try starting HD by using this access.
8) Minimize the cases of arteriovenous access thrombosis not related to stenosis.
9) Include each prevalent HD patient in protocolized vascular access follow-up programs.
10) Upgrade HD units by introducing second-generation follow-up methods for early detection of arteriovenous access stenosis.
11) Increase the diffusion of screening techniques for stenosis based on the indirect determination of arteriovenous access blood flow rate.
12) Introduce the portable Doppler ultrasound machine in all HD rooms.
13) Ensure elective or salvage treatment through interventional radiology and/or revision surgery for the arteriovenous access of prevalent HD patients with stenosis or thrombosis, respectively.
14) Specific kidney failure patient education related to their vascular access.

Given the increasing body of evidence on the benefits of on-line hemodiafiltration (30), the Spanish healthcare authorities should increase economic resources so that as many HD patients as possible use this HD modality.
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J Ibeas: Conceptualization; Formal analysis; Investigation; Supervision; Validation; Writing - review and editing
E Sanchez: Conceptualization; Formal analysis; Investigation; Supervision; Validation; Writing - review and editing
References


### Table 1. Characteristics of dialysis in Spain, 2018

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Description</th>
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<tbody>
<tr>
<td>Number of patients on dialysis (per million population)</td>
<td>27,998 (5,994)</td>
</tr>
<tr>
<td>Percentage of patients on home dialysis (%)</td>
<td>5.2</td>
</tr>
<tr>
<td>Dialysis sessions: covered by insurance vs patients pays</td>
<td>100% covered by the National Health System</td>
</tr>
<tr>
<td>Dialysis units: hospital-based or freestanding</td>
<td>Both</td>
</tr>
<tr>
<td>Dialysis Units: economic model</td>
<td>Private, mostly for profit. Public, none for profit.</td>
</tr>
<tr>
<td>Reimbursement per hemodialysis session*</td>
<td>Variable according the Autonomous Community, no fixed rate for all of Spain</td>
</tr>
<tr>
<td>Dialysis delivery staff</td>
<td>Only dialysis nurses</td>
</tr>
<tr>
<td>Nurse to patient ratio in the dialysis units*</td>
<td>1:4 – 1:5</td>
</tr>
<tr>
<td>Hemodialysis session length (min)</td>
<td>≥ 240 for most patients</td>
</tr>
<tr>
<td>Frequency that patient is seen by a nephrologist</td>
<td>Each hemodialysis session</td>
</tr>
<tr>
<td>Vascular access for hemodialysis (%)**</td>
<td>Arteriovenous fistula 65, Arteriovenous graft 6, Central vein catheter 29</td>
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*See the text  
**See the reference 9