## The Clinical Appraisal of On-Line Hemodiafiltration

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# Utilization of Hemodiafiltration as Treatment Modality in Renal Replacement Therapy for End-Stage Renal Disease Patients – A Global Perspective

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## Abstract

The worldwide demand for renal replacement therapy (RRT) is constantly rising. In order to support both medical communities and healthcare authorities in their decisionmaking processes, it has become increasingly interesting to provide guantitative overviews on the global development of the number of end-stage renal disease (ESRD) patients, as well as information on the quantitative development of individual treatment modalities. Worldwide, numerous registries and studies contribute to establishing a reliable base for understanding ESRD patient numbers. Supplementary, Fresenius Medical Care maintains an ESRD information system that enables reporting of the most recent numbers on a global scale. The Fresenius Medical Care Market & Competitor Survey (MCS) provides ESRD-related data from more than 140 countries on a yearly basis. With a combined population of around 6.7 billion, these countries represented around 97% of the world population and covered more than 99% of all treated ESRD patients at the end of 2010. The survey results can be interpreted as providing a global picture of ESRD demographics in 2010, including the number and distribution of patients on individual treatment modalities such as hemodiafiltration (HDF). The following HDF-related results are presented here: the global HDF patient population treated, the HDF patient distribution in various regions/countries, and the growth patterns of HDF and on-line HDF. The treatment of ESRD patients by HDF has gained significantly in popularity over recent years. In some regions, more patients are treated by HDF than by peritoneal dialysis and, in selected countries, HDF accounts for more than 25% of all extracorporeal dialysis treatments for ESRD patients.

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End-stage renal disease (ESRD) is a chronic condition with the need for lifesaving medical intervention in the form of dialysis or renal transplantation. Worldwide, the size of the prevalent ESRD population is constantly increasing – since the beginning of maintenance therapy for ESRD in the 1960s the number of patients treated for terminal kidney failure has continued to significantly exceed the growth rate of the general population. Consequently, the worldwide demand for renal replacement therapy (RRT) is set to rise and ESRD is increasingly considered an emerging public health problem that requires attention in the medical field as well as in health policy. Therefore, it becomes increasingly interesting to provide quantitative overviews on the global development of ESRD patients as well as information on the quantitative development of individual treatment modalities.

A growing number of national and international renal registries worldwide provide demographic and epidemiologic information on renal patients. The US Renal Data System (USRDS) [1], the multinational European database organized by the ERA/EDTA [2] or the Australia & New Zealand Dialysis and Transplant Registry [3] - to name only a few - contribute to establishing reliable and consolidated information on ESRD patient demographics. An alternative approach to reporting international ESRD-relevant data is pursued in the Dialysis Outcomes and Practice Patterns Study (DOPPS) [4]. These registries and studies constitute an important and well-established base for understanding ESRD treatment practices and policies. However, even at a national level, the maintenance of an information system that enables fast and reliable reporting of the most recent renal patient numbers is particularly challenging. The collection of records reflecting the situation in a large group of countries means a further enhancement of this difficulty. A time lag between data gathering and publication through the registries is inevitable and can be significant at times. Furthermore, national or regional registry data alone cannot offer a complete global picture as the majority of countries providing RRT either do not have official registries or do not publish the corresponding data. (Based on internal Fresenius Medical Care analysis, in 2011 the number of countries publishing information either directly through a national renal registry or indirectly through a multinational organization was 37 while 147 countries are reported to provide renal replacement therapy.) Fresenius Medical Care, the largest dialysis care company worldwide, operating on a global scale, maintains an annually updated database addressing international ESRD data. Through its worldwide network, Fresenius Medical Care is in a unique position to efficiently retrieve and process global ESRDrelated information, such as an insight into patient demographics, various aspects associated with the regional patient distribution, treatment practices and trends.

## Methods

Details of the data collection and validation process of the Fresenius Medical Care Market & Competitor Survey (MCS) have been described in earlier publications referring to the status in the years 2001, 2004 and 2005 [5–7]. The MCS provides annual data from more than 140 countries (or areas of special sovereignty) with established dialysis programs. With a combined population of around 6.7 billion, these countries represented around 97% of the world population and were estimated to cover more than 99% of all treated ESRD patients at the end of 2010. As such, the survey results can be interpreted as providing a global picture of ESRD demographics in the corresponding year.

The country-by-country survey, consisting of a catalogue of several thematic areas relevant to the treatment of ESRD patients, focuses on the total number of patients treated, the modality selected, trends in treatment practices and products used, treatment location, ESRD patient care structures and funding. Whereas the degree of detail concerning the information requested on ESRD patients and treatment practices varies among different countries depending on maturity and size of their national ESRD patient care program and infrastructure, the modular design of the survey allows the global consolidation and compilation of the gained information in one central database. Before being entered in the database, the surveyed demographic and economic data are additionally validated by means of cross-reference with the most recent sources of national ESRD information (e.g. registry data) and with the results of earlier such surveys performed during previous years. In addition, the collected data are subjected to comprehensive consistency tests. The regular ex-post validations of the survey demonstrate a consecutively high reliability of the acquired data and a systematic bias can be excluded.

In the following, focus is primarily on ESRD patient-related figures at year-end 2010. Results are presented for the subgroup of patients undergoing hemodiafiltration (HDF). The numbers presented are rounded in a consistent and common sense manner.

# Results

The utilization of HDF as a treatment modality is quite diverse between the various regions worldwide. Comparing the ratio of HDF patients in a region to the total number of ESRD patients treated by extracorporeal dialysis (here denominated as HD for hemodialysis), Europe is the most relevant HDF region in the world with a share of 15%. Furthermore, Europe also accounts for over 60% of the global HDF population. While the region Asia-Pacific (AP) has a 5% share of its HD patients treated with HDF, the treatment modality is almost non-existent in African, Middle East, Latin and North American countries (table 1).

In terms of absolute numbers, China has become the country with the highest HDF population (13,000 patients), followed by Japan and Germany (each around 10,000 patients).

With 90%, the vast majority of HDF patients receive on-line HDF as defined by the on-line preparation of the substitution fluid by the dialysis machine.

#### Table 1. Distribution of HD and HDF patients in 2010

	HD patients, n	HD patients on HDF, n	HD patients on HDF, %	HDF patients on conventional HDF, %	HDF patients on on-line HDF, %
Europe total	390,000	57,000	15	5	95
Africa + Middle East + Latin America	330,000	2,000	1	0	100
North America	420,000	300	0	0	100
AP total	680,000	31,000	5	15	85
Global	1,810,000	90,000	5	10	90

**Table 2.** Distribution of HDF patients in the top ten European countries with largest relative

 HDF populations in 2010

Country	HD patients n	Patients on HDF total, n	Patients on HDF %		
Switzerland	3,000	2,000	>60		
Slovenia	1,400	900	>60		
Slovakia	2,900	1,600	>50		
Portugal	9,900	4,800	>40		
Hungary	5,500	2,300	>40		
Czech Republic	5,300	1,800	>30		
Belgium	6,800	2,000	>30		
Greece	8,900	2,600	>25		
Sweden	2,900	800	>25		
Austria	4,000	1,100	>25		

Conventional HDF, as defined by the delivery of substitution fluid from bags, accounted only for 10% of global HDF treatments in 2010.

There were more than 45 countries within the region Europe/Middle East/ Africa (EMEA) where HDF treatments were performed in 2010. Table 2 lists the key HDF countries, i.e. those countries where HDF patients account for more than 25% of all HD patients. Switzerland and Slovenia have the highest relative utilization of HDF worldwide, treating more than 60% of all their HD patients with HDF.

It is interesting to see that some of the countries have registered significant increases in HDF utilization over the last years. Between 2004 and 2010, the share of HDF patients increased in Switzerland from ~40% to over 60%, in

Country	Patients on HDF total n	Patients on conventional HDF %	Patients on on-line HDF %
Germany	9,800		100
Italy	7,600	25	75
France	4,900		100
Portugal	4,800		100
Spain	3,900	5	95
United Kingdom	3,400		100
Greece	2,600	50	50
Hungary	2,300		100
Belgium	2,000		100
Switzerland	2,000		100

**Table 3.** Distribution of conventional and on-line HDF patients in the top ten European countries with largest HDF populations in 2010

Table 4. Growth of HDF patients from 2004 to 2010

HDF patients	2004	2005	2006	2007	2008	2009	2010	CAGR 04-07	CAGR 07-10	CAGR 04-10
Global total	44,000	47,000	50,000	59,000	66,000	77,000	90,000	11%	15%	13%
EMEA total	25,000	27,000	29,000	36,000	43,000	50,000	59,000	13%	18%	15%
Asia-Pacific total	19,000	20,000	21,000	23,000	22,000	27,000	31,000	5%	11%	8%

Slovenia from more than 20% to over 60%, and in Hungary from around 10% to over 40%.

With regard to the absolute numbers of HDF patients in the EMEA region, Germany and Italy are the countries with the largest HDF patient populations (table 3).

What becomes obvious is that, within the top ten EMEA countries with the largest HDF populations, only two countries have considerable numbers of patients on conventional HDF (Italy and Greece). As a result, the predominant HDF treatment mode within EMEA is on-line HDF with a share of around 95% of all HDF patients being treated with on-line HDF.

Observing the development of HDF patient numbers on a global scale between 2004 and 2010, the number of HDF patients increased by around 13% on average per year (table 4). While between 2004 and 2007 the average growth was only around 11% per year, there was a reported growth of around 15% on average per year between 2007 and 2010. All in all, the number of HDF patients grew about twice as fast as the number of HD patients over the last years.



Fig. 1. Development of HDF patients from 2004 to 2010.

In EMEA and AP, the growth of the number of HDF patients between 2007 and 2010 was considerably higher than the corresponding growth between 2004 and 2007. While the HDF patient growth in AP between 2004 and 2007 was still below the HD patient growth on standard HD, in the region EMEA the HDF patient growth significantly exceeded the standard HD patient growth already at that time.

In EMEA, the number of patients treated by HDF (59,000 patients in 2010) is significantly higher than the number of patients treated by peritoneal dialysis (43,000 patients in 2010).

The two HDF modalities (i.e. conventional and on-line) display opposite trends. While on-line HDF patient numbers have increased strongly over the last 7 years at a rate of around 20% per annum, the number of patients treated with conventional HDF has decreased by around 11% per year. On-line HDF patient numbers increased in this period from around 27,000 patients to around 82,000. In the meantime, the number of patients treated with conventional HDF dropped from almost 17,000 patients in 2004 to around 8,500 in 2010 (fig. 1).

## Conclusion

Use of HDF has increased consistently over the last years. In the majority of the countries analyzed, access to HDF therapy is still restricted due to various regulatory issues. Nevertheless, the percentage of chronic patients receiving HDF treatment grew by 13% per year on average between 2004 and 2010, which is about double the growth of the number of dialysis patients. In some regions and countries, more patients receive HDF nowadays than peritoneal dialysis and,

in selected countries, HDF accounts for more than 25% of all extracorporeal dialysis treatments for ESRD patients. Besides the growing acceptance in the medical communities [8, 9], the positive development of this therapy option can also be seen as having been facilitated by the increasing availability of convenient technical solutions that support the administration of HDF in a resource-saving manner. In 2010, on-line HDF was by far the predominant mode of HDF therapy, being applied to around 90% of the global HDF patients.

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# **Disclosure Statement**

Both authors are employees of Fresenius Medical Care.

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