

Global Dialysis Perspective: Japan

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Introduction

Hemodialysis therapy was first performed in Japan at United States military base hospitals during the Korean War (1950–1953) to treat injured American soldiers with crush syndrome transferred from the combat zone. Encouraged by such experiences, several university hospitals started to offer acute hemodialysis treatment in 1955 and chronic hemodialysis treatment in the early 1960s. The health insurance program started to cover chronic hemodialysis treatment in 1967. Initially, the costs were not fully covered by the program: a 30% to even 50% copayment was required for patients who were not beneficiaries of the public insurance plan. In 1972, the national government started a program that also covered copayment on the basis of the Basic Act for Persons with Disabilities as a result of lobbying activities by patient groups and academic societies. Since then, hemodialysis treatment has become almost free of charge, except for high-income patients (up to 20,000 Japanese Yen [JPY] or approximately United States \$200 per month).

A History of Dialysis Therapy and the Reimbursement System in Japan

Typically, the total monthly cost for a patient on maintenance dialysis is approximately 320,000 JPY or approximately United States \$3000, excluding any additional fees or medications. The cost consists of the medical management fee, including routine laboratory tests (22,500 JPY per month), and technical fees (21,400 JPY × approximately 14/mo). The reimbursement system is updated every 2 years. In April 2006, the costs for erythropoiesis-stimulating agents were bundled with the technical fees of hemodialysis and with anti-coagulant and normal saline for rinsing. Roxadustat has recently been approved and bundled.

Current Status of Dialysis Therapy in Japan

According to the recent annual report of the Japanese Society for Dialysis Therapy Renal Data Registry (JRDR) (1), a total of 334,505 patients (2640.0 per million people in the general population) are receiving dialysis treatment in Japan as of 2017. In 40,959 incident patients (323 per million people in the general population), the average eGFR at the start of dialysis therapy was 5.43 ± 3.43 ml/min per 1.73 m^2 (2). As

detailed in Tables 1 and 2 (1), most of the patients are treated with hemodialysis, and only a few (2.7%) are treated with peritoneal dialysis. Reasons for such low numbers of patients on peritoneal dialysis may include concerns about encapsulating peritoneal sclerosis, longer dialysis vintage, and easy access to hemodialysis facilities. (According to the Global Kidney Health Atlas of the International Society of Nephrology, the number of facilities per patient is the highest in Japan.) Recently, the population receiving online hemodiafiltration, especially the predilution method, has remarkably increased because all patients became potentially eligible for therapy in 2012 as long as the water purity of the facility meets the standard set by the Japanese Society for Dialysis Therapy (JSDT). The number of patients on home hemodialysis therapy is still limited (684 as of 2017) but is gradually increasing (1).

The dialysis unit team in Japan is usually composed of several health care professionals, such as doctors, clinical engineers (CEs), nurses, pharmacists, dietitians, social workers, and physical therapists. The doctors are typically physicians (including board-certified nephrologists endorsed by the Japanese Society of Nephrology), surgeons, or urologists. Among them, 6000 are also qualified as fellows of the JSDT.

CEs specializing in the operation and maintenance of life-supporting devices or machines used for RRT have been endorsed by national licenses on the basis of the Clinical Engineers Act since 1987. Twenty-three thousand CEs had jobs in dialysis facilities as of 2016 (2). They not only support the maintenance and performance of dialysis machines but are also highly responsible for maintaining dialysate quality, including water purity. This is quite important because dialysis fluid is delivered from a central system in most facilities in Japan, except for a few patients who need special prescriptions. For the nursing care of patients on dialysis, a total of 43,000 registered nurses were involved in dialysis therapy as of 2016 (2) (*i.e.*, 1 nurse for every eight patients). The Japanese Nursing Association accredits the title of certified nurse to leaders in the field of dialysis nursing, but only approximately 300 nurses have been accredited.

In Japan, a total of 4413 facilities were providing dialysis treatment as of 2017 (1). There are many groups of facilities, usually owned by private health care corporations. However, the size of each group is

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Table 1. Summary of dialysis therapy in Japan as of 2017 (summarized from ref. 1)

Modalities	No. (%)
Prevalence	
Hemodialysis	228,089 (68.2)
Hemodiafiltration	95,140 (28.4)
Other blood purification types	1502 (0.4)
Home hemodialysis	684 (0.2)
Peritoneal dialysis	9090 (2.7)
Total	334,505 (2640.0 per million people in the general population)
Incidence	
Hemodialysis	38,842 (94.8)
Peritoneal dialysis	2117 (5.2)
Total	40,959 (323 per million people in the general population)
Deceased patients	32,532

Table 2. Summary of dialysis therapy in Japan as of 2017 (summarized from ref. 1)

Patient Backgrounds	Prevalent Patients	Incident Patients
Age, yr	68.4±12.5	69.7±13.4
Sex, men/women	208,870 (65.0%)/ 112,648 (35.0%)	26,677 (68.8%)/ 12,109 (31.2%)
Diabetes as the primary diagnosis of ESKD	125,247 (39.0%)	16,492 (42.5%)

usually small with several facilities, except for very few with several thousand patients. According to a JRDR report, 1.2%, 19.4%, 1.7%, 30.3%, and 47.4% of the total facilities were national university hospitals, public hospitals, private university hospitals, private hospitals, and private clinics, respectively (2). Because the Medical Care Act of Japan prohibits paying any dividend to shareholders, all medical corporations in Japan are technically nonprofit organizations.

Table 3. Characteristics of clinical practice patterns in Japanese dialysis therapy

Factors	Values
eGFR at the start of dialysis therapy	5.43±3.43 ml/min per 1.73 m ² (2)
Percentage of home dialysis	2.9% (9774; 9090 on PD and 684 on HHD) (1)
Insurance coverage	Almost 100% (out-of-pocket payment of up to 20,000 JPY for the high-income patients)
Hospital affiliated or free standing	Hospital affiliated 52.6%; free standing 47.4% (2)
For profit/nonprofit	Entirely nonprofit; the national government does not allow for-profit medical facilities in Japan
Basic cost to be reimbursed for a single hemodialysis session	Approximately United States \$200
Professionals managing patients	Doctors and government-licensed clinical engineers as well as registered nurses
Patient-nurse ratio	7.8 patients per nurse (2)
Length of session, mean ± SD (min)	239.3±32.9 (2)
Times of nephrologist consultation	Every session: dialysis therapy without consultation with a doctor is prohibited by the law
Types of vascular access	AVF 89.0%, AVG 7.3%, CVC (both temporary and cuffed) 1.8%, superficialized artery 1.8%, others 0.1% (1)
Blood flow rate, ml/min	206.5±36.5 (lower) (1)
Kt/V	1.51±0.30 (lower) (1)
Bicarbonate levels in dialysis fluid, meq/L	25–30 for acetate-containing DF, 35 for acetate-free DF (lower)
ESA use, kU/wk	6±5 (lower) (4)
Iron use	33% (lower) (4)
Iron dose among treated, mg/wk	32±21 (lower) (4)
Serum ferritin level, ng/ml	145±205 (lower) (4)
Inflammation status, mg/L, median (IQR)	1 (1–3) (lower) (4)
ESA responsiveness	Higher (ESA dose is much smaller, whereas hemoglobin of 10.7 g/dl is almost equivalent or slightly lower [4])
PTH target, pg/ml	60–240 (lower) (6,8)
Adherence of the patients to therapies (represented by the proportion of missed treatment; in the text)	Higher (0.4% in Japan, whereas 24% in the United States [10])

The factors potentially related to the better clinical outcome of Japanese patients on dialysis are listed. PD, peritoneal dialysis; HHD, home hemodialysis; JPY, Japanese Yen; AVF, arteriovenous fistula; AVG, arteriovenous graft; CVC, central venous catheter; DF, dialysis fluid; ESA, erythropoiesis-stimulating agent; IQR, interquartile range; PTH, parathyroid hormone.

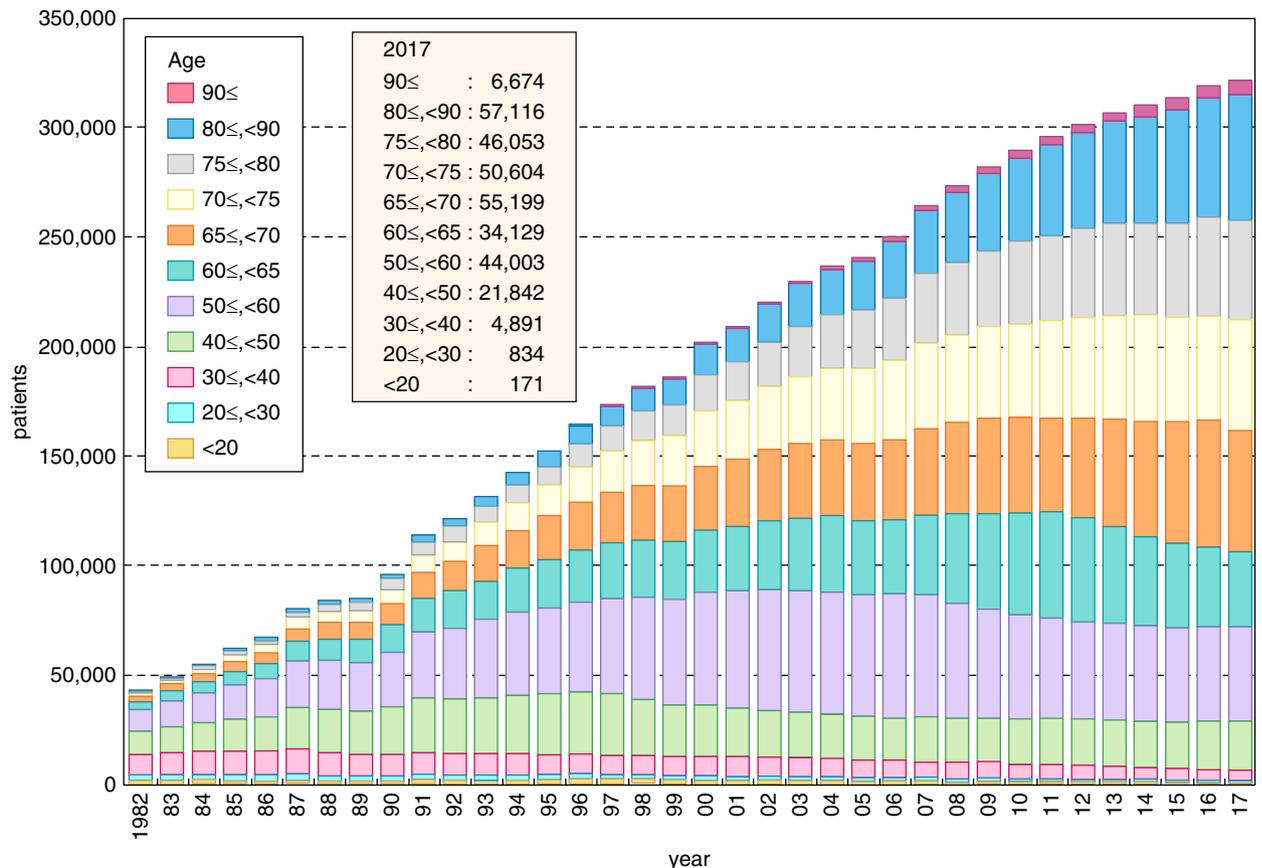


Figure 1. | The trend of patients on prevalent dialysis by age. Reprinted from ref. 1, which is available under the terms of the Creative Commons Attribution License 4.0.

Practice Pattern and Prognosis of Japanese Patients on Dialysis

The survival of Japanese patients on dialysis is reportedly one of the best in the world (3). The survival of the entire Japanese dialysis population may be superior to that of healthier patients on the waiting list in the United States. The JRDR in 2007 demonstrated that patients aged 60–74 years old had a crude 5-year mortality rate of 40.7%, whereas patients aged 60–64 years old who were on the waiting list between 1995 and 2007 experienced a 5-year mortality rate of 49% in the United States (4). These data suggest that the survival advantage of Japanese patients may not be due to the lower incidence of kidney transplantation. Many attempts have been made to elucidate the reasons for the longevity of Japanese patients on dialysis, including the Dialysis Outcomes and Practice Patterns Study (DOPPS). It has been reported that several clinical practice patterns in Japan are different from those in other countries (Table 3).

The causes of death are different between Japan and other countries, partly due to the definitions. The Annual Data Report of the US Renal Data System in 2017 delineates that the leading cause of death was arrhythmia or cardiac arrest (40%) followed by withdrawal (18%) and septicemia (8%). Congestive heart failure comprised only 3% of the total deaths. In contrast, the most prevalent cause in Japan is congestive heart failure (24.0%) followed by infection

(21.1%) and malignancy (9.0%). Withholding or foregoing dialysis therapy is rare in Japan compared with in the United States, but it is currently under detailed discussion.

Another striking difference in clinical practice is the proportions of vascular access used for hemodialysis. Almost all vascular access is arteriovenous fistula with native veins; 89.0%, 7.3%, and 1.4% of the patients had arteriovenous fistula, arteriovenous graft, and tunneled catheter procedures, respectively (1). In addition, elevated or superficialized brachial arteries are occasionally (1.8%) used in patients with reduced cardiac function. Regarding the dialysis prescription, the blood flow rate is lower in Japanese patients than in patients in other countries, which might be a reflection of the smaller body size of the Japanese dialysis population. The dialysis duration is 239 ± 33 minutes per session on average (2).

Anemia management in Japan is also different from that in other countries. The hemoglobin level was lower in the early 2000s (10.2 ± 1.4 and 10.9 ± 1.3 g/dl in 2005 and 2017, respectively), probably due to a limitation on epoetin for use in patients on dialysis (up to 9000 U/wk). Even after erythropoiesis-stimulating agents with longer half-lives have become available in higher doses than epoetin, the doses are still kept low in Japan. This trend might be explained by the fact that erythropoiesis-stimulating agent responsiveness has been reported to be higher in Japan than in other DOPPS countries (5). Furthermore, as proposed by

the JSDT guidelines (6), the target level of parathyroid hormone is also kept lower at 60–240 pg/ml than that recommended by other guidelines. Accordingly, the median parathyroid hormone level was 126 pg/ml, much lower than that in Europe (233 pg/ml) or North America (283 pg/ml) (7). The reasons may include racial differences in skeletal resistance to parathyroid hormone, drug availability, and the health care system; however, these explanations still remain to be elucidated (8).

The law, namely the Medical Practitioners' Act of Japan, prohibits the provision of treatment without examination by any doctor. Therefore, every patient must legally be seen by a doctor at every dialysis session, although not necessarily by a full-time nephrologist; part-time nephrologists or doctors with various backgrounds, including surgeons, are also acceptable. Although each patient is seen by a doctor for just 5 minutes (9), this consultation might be a reason for the better clinical outcomes of Japanese patients on dialysis. Additionally, the adherence of the patients is higher in Japan; only 0.4% of patients skipped one or more sessions over 4 months according to the DOPPS data, whereas 24% of patients skipped sessions in the United States (10).

Future Perspectives

Many factors can account for the better prognosis of Japanese patients on dialysis, including more intensive care and the broader coverage of drugs by the health insurance system. Nevertheless, the number of patients on dialysis continues to increase, especially older diabetic patients with lower physical activity (Figure 1, Table 2). The expansion of this older population in Japan can also lead to an increase in the number of frail people in terms of physical, mental, cognitive, and social functioning. Moreover, there will be fewer health care workers caring for such patients with multiple comorbidities.

According to the estimates of national medical care expenditure by the Ministry of Health, Labor, and Welfare, Japan, the total cost of hemodialysis therapy currently accounts for 5% of the total medical expenditure in Japan. Thus, it is mandatory for Japanese society to find a solution to these issues for sustainability. The increase in the number of peritoneal dialysis procedures (1) and kidney transplants (still fewer than 2000/yr and nearly 90% from living donors) (11) might be one of the keys.

Author Contributions

M. Fukagawa and N. Hanafusa conceptualized the study, wrote the original draft, and reviewed and edited the manuscript.

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