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Worldwide, mortality risk is high soon after initiation of hemodialysis

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Mortality rates for maintenance hemodialysis patients are much higher than the general population and are even greater soon after starting dialysis. Here we analyzed mortality patterns in 86,886 patients in 11 countries focusing on the early dialysis period using data from the Dialysis Outcomes and Practice Patterns Study, a prospective cohort study of in-center hemodialysis. The primary outcome was all-cause mortality, using time-dependent Cox regression, stratified by study phase adjusted for age, sex, race, and diabetes. The main predictor was time since dialysis start as divided into early (up to 120 days), intermediate (121–365 days), and late (over 365 days) periods. Mortality rates (deaths/100 patient-years) were 26.7 (95% confidence intervals 25.6–27.9), 16.9 (16.2–17.6), and 13.7 (13.5–14.0) in the early, intermediate, and late periods, respectively. In each country, mortality was higher in the early compared to the intermediate period, with a range of adjusted mortality ratios from 3.10 (2.22–4.32) in Japan to 1.15 (0.87–1.53) in the United Kingdom. Adjusted mortality rates were similar for intermediate and late periods. The ratio of elevated mortality rates in the early to the intermediate period increased with age. Within each period, mortality was higher in the United States than in most other countries. Thus, internationally, the early hemodialysis period is a high-risk time for all countries studied, with substantial differences in mortality between countries. Efforts to improve outcomes should focus on the transition period and the first few months of dialysis.

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Annual mortality rates for patients on maintenance hemodialysis (HD) are several times higher than those of the general population.[1] Compared with prevalent dialysis patients, patients new to dialysis (incident patients) experience an even higher mortality within the first few months after the initiation of dialysis.[1–3]

Many of the earlier studies that had assessed early mortality for incident dialysis patients reported an elevated mortality within the first 90 days after the initiation of dialysis.[4–6] However, the pattern of early mortality, and whether such an elevation was limited to the first 90 days, was unclear. Subsequently, using the US cohort of the Dialysis Outcomes and Practice Patterns Study (DOPPS), Bradbury *et al.*[2] showed that the elevated early mortality rate appeared to be maintained throughout the first 120 days after HD initiation, with mortality rates declining thereafter. Evidence from large national and regional renal registries suggested that the period of elevated mortality rate continues beyond the first 90 days,[1,3,7] and the degree and duration of elevation were more pronounced among elderly patients.[1,3] However, studies of early dialysis mortality have focused primarily on a few countries, such as the United States and United Kingdom. To our knowledge, mortality in the first few months after HD initiation has not been otherwise studied and compared across regions of the world.

The main purpose of this study was to evaluate mortality patterns over the course of HD treatment in 11 countries participating in the DOPPS, with particular focus on the elevated mortality rate soon after the initiation of HD. We hypothesized that the elevated early mortality rate is universal in all DOPPS countries, but that the degree of elevation may differ by country. We also examined the degree of elevated early mortality by patient age, and we hypothesized that, across countries, older HD patients are less able to tolerate the initial impact of starting HD and thus have relatively higher early mortality.

Table 1 | Patient characteristics by country (DOPPS 2 and 3 combined)

	DOPPS country									
	Australia–New Zealand	Belgium	Canada	France	Germany	Italy	Japan	Sweden	UK	US
Number of patients	5951	5544	10,102	5956	5589	4288	16,033	4600	5592	23,231
Age (mean)	59.6	66.8	63.1	63.7	63.7	65.6	62.8	63.6	61.4	62.3
<45	17.2	7.9	13.8	13.1	11.9	9.5	8.7	12.3	16.8	14.5
45–54	17.6	10.5	13.4	13.5	13.2	11.6	16.8	14.0	14.1	15.9
55–64	22.1	17.1	20.4	18.0	19.5	18.0	27.8	20.2	19.1	21.1
65–74	26.0	29.6	25.0	26.6	30.7	31.3	27.2	24.9	27.0	22.9
⩾75	17.1	34.9	27.4	28.8	24.8	29.5	19.4	28.7	23.0	25.7
Male (%)	58.7	58.0	58.4	59.7	59.3	59.2	61.8	63.8	61.9	55.4
Black (%)	0.4	2.5	4.8	4.7	0.3	0.6	0.0	0.9	5.1	29.8
Diabetes as cause of ESRD (%)	33.2	28.6	40.1	22.8	31.9	19.1	32.6	28.9	23.1	49.1

Abbreviations: DOPPS, Dialysis Outcomes and Practice Patterns Study; ESRD, end-stage renal disease.

RESULTS

Study population

Among the 86,886 participants, the median follow-up time was 1.2 years (range: 0–3.9 years), and 47,621 patients remained in the study up to the end of follow-up. Among 22,172 patients who were censored, the causes of censoring included the following: switch to peritoneal dialysis ($n = 1957$), kidney transplant ($n = 3594$), recovery of kidney function ($n = 1052$), transfer out of a DOPPS dialysis facility ($n = 15{,}565$), and other ($n = 4$). There were 16,907 deaths (overall mortality rate = 15.0 per 100 patient-years (95% confidence interval (CI) = 14.7, 15.2). Of these, 1939 deaths occurred in the early period, 2299 in the intermediate period, and 12,669 in the late period. Mortality rates, in deaths per 100 patient-years, were 26.7 (95% CI = 25.6, 27.9) in the early period, 16.9 (95% CI = 16.2, 17.6) in the intermediate period, and 13.7 (95% CI = 13.5, 14.0) in the late period.

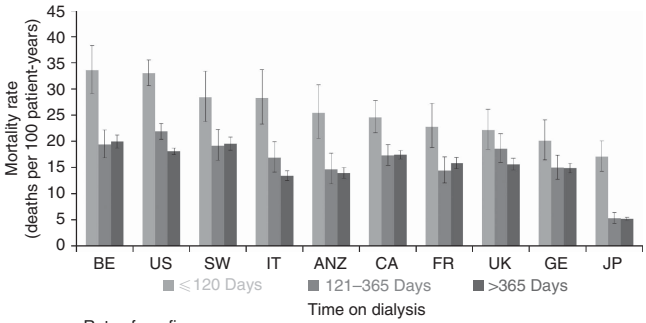
Demographics

Patient demographics by country are shown in Table 1. The mean age overall was 62.9 years, ranging from 59.6 years in Australia/New Zealand (ANZ) to 66.8 years in Belgium. There were 58.9% male patients, ranging from 55.4% in the United States to 63.8% in Sweden. In the United States, 29.8% of patients were black as compared with 0% in Japan and 2.7% in other countries. Diabetes was the cause of end-stage renal disease (ESRD) for 35.5% of patients, ranging from 19.1% in Italy to 49.1% in the United States. As expected, higher mortality was observed in patients who were older (adjusted hazard ratio (HR) per 5 years = 1.22, 95% CI = 1.21, 1.23, $P < 0.001$), male (HR = 1.05, 95% CI = 1.02, 1.09, $P = 0.001$), non-black (HR = 1.26, 95% CI = 1.14, 1.38, $P < 0.001$), and for whom diabetes was the cause of ESRD (HR = 1.27, 95% CI = 1.23, 1.32, $P < 0.001$). The interaction between the covariate black (vs. non-black) and country was not significant ($P = 0.70$).

Mortality at the early and late (vs. intermediate) period of dialysis

Crude mortality rates were highest in the early dialysis period (⩽120 days) in all countries (Figure 1). Mortality rates in the intermediate period (121–365 days) were similar to those in the late (>365 days) period. A sensitivity analysis limited to patients incident to dialysis at DOPPS enrollment resulted in rates that followed a similar pattern, with higher rates in the early dialysis period in every country. Table 2 shows the adjusted HRs for the early and late (vs. intermediate) period for each country. The adjusted HRs for the early period versus the intermediate period were 3.1 in Japan; 1.6–1.8 in ANZ, Belgium, and Italy; 1.3–1.5 in Canada, France, Germany, Sweden, and the United States; and 1.2 in the United Kingdom. The adjusted HRs for the late period versus the intermediate period were closer to 1, ranging from 0.92 (95% CI = 0.77, 1.09) in Italy to 1.25 (95% CI = 1.03, 1.52) in France.

The percentage of patients who switched modality was ⩽4% in all countries except ANZ (8%), and most of these patients switched before 120 days. If these patients were excluded from the analysis, the adjusted HRs comparing the early period with the intermediate period were substantially similar to the results presented in Table 2.



Rates from figure

DOPPS country	BE	US	SW	IT	ANZ	CA	FR	UK	GE	JP
⩽120 Days	33.5	33.0	28.4	28.3	25.4	24.6	22.8	22.1	20.1	17.0
121–365 Days	19.4	21.8	19.2	16.9	14.6	17.3	14.4	18.6	14.9	5.3
>365 Days	19.9	18.1	19.5	13.4	13.9	17.4	15.8	15.6	14.8	5.2

Figure 1 | Mortality after the start of dialysis. Countries were ordered by mortality rate at ⩽120 days. ANZ, Australia and New Zealand; BE, Belgium; CA, Canada; DOPPS, Dialysis Outcomes and Practice Patterns Study; FR, France; GE, Germany; IT, Italy; JP, Japan; SW, Sweden; UK, United Kingdom; US, United States. Error bars correspond to 95% confidence intervals calculated using the Byar approximation.