

Supplementary Material

Supplementary Methods

Study Design

This was a retrospective analysis using structured data from two international prospective cohort studies: the Dialysis Outcomes and Practice Patterns Study (DOPPS) and the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS).^{4,6,S1,S2,S3,S4} The study objective was to describe rates of bleeding events leading to death or hospitalization in a global population of patients with ESKD, by dialysis modality and various subgroups of interest.

Dialysis Outcomes and Practice Patterns Study (DOPPS)

- Prospective cohort study of adult, in-center patients receiving hemodialysis ongoing since 1996; this analysis utilized data from DOPPS phases 4-7 (2009-2022).^{4,6,S1,S2,S3,S4}
- Each phase lasted approximately 3 years and data were collected every 4 months during follow-up.^{6,S2}
- Includes participants from 21 countries.^A
- Includes data on patient demographics, comorbidities, laboratory measures, medication prescriptions, patient-reported outcomes, and prospective follow-up for hospitalization and mortality.

Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS)

- Prospective cohort study of adult patients receiving peritoneal dialysis ongoing since 2014; this analysis utilized data from PDOPPS phases 1-2 (2014-2022).²
- Patient information was updated every 4 months.²
- Includes participants from 8 countries.^B

^A Australia, New Zealand, Japan, China, Belgium, France, Germany, Italy, Spain, Sweden, United Kingdom, Russia, Turkey, GCC, United States, Canada.

^B Australia, New Zealand, Japan, Thailand, South Korea, United Kingdom, United States, Canada.

- Includes data on patient demographics, comorbidities, laboratory measures, medication prescriptions, patient-reported outcomes, and prospective follow-up for hospitalization and mortality.

Patient Inclusion & Exclusion Criteria

All patients enrolled in DOPPS phases 4–7 (2009–2022) and PDOPPS phases 1–2 (2014–2022) were considered for inclusion. A subset of dialysis facilities from each cohort was excluded due to poor capture of cause-specific mortality and hospitalization. Supplemental Table S1 gives a breakdown of baseline patient characteristics at the time of study enrollment.

Analyses

Results were stratified by type of dialysis (hemodialysis [HD], peritoneal dialysis [PD]). Bleeding event rates were analyzed by geographical region, age, sex, history of comorbidities (any cardiovascular disease, atrial fibrillation, cerebrovascular disease, other atherothrombotic disease, other cardiovascular disease, and diabetes), and history of bleeding.

The outcome measures were a composite bleeding event rate and cause-specific bleeding event rates. The composite major bleed endpoint comprised any nonfatal bleeding event that resulted in hospitalization and any bleed event that resulted in death. Nonfatal bleeding events that resulted in hospitalization included epistaxis, subdural hematoma, cerebral hemorrhage, evacuation of hematoma, abnormal bleeding, hemoptysis, hematuria, and vascular access bleeding. Any bleeding event that resulted in death included gastrointestinal (GI) hemorrhage, hemorrhage from vascular access, hemorrhage from ruptured vascular aneurysm, hemorrhage from surgery, and other hemorrhage. Cause-specific bleeding events presented had the highest individual event rates and included: GI bleeding leading to hospitalization, vascular access-related bleeding leading to hospitalization (for HD only), and fatal intracerebral hemorrhage.

Supplemental Table S1: Baseline patient characteristics

	Overall	HD	PD
	N = 38,466	n = 32,396 (84%)	n = 6,070 (16%)
Region ^A			
Australia-New Zealand	4%	3%	8%
Europe	44%	51%	7%
Gulf Cooperation Council (GCC)	3%	4%	-
North America	16%	14%	26%
Other Asia-Pacific	33%	28%	60%
Age (mean ± SD)	64 ± 15	64 ± 15	59 ± 14
Age category (years)			
18-49	18%	16%	24%
50-59	18%	17%	24%
60-69	26%	25%	28%
70-79	25%	27%	17%
≥80	14%	15%	7%
Sex (% male)	61%	62%	59%
Race			
Asian	36%	31%	63%
Black	4%	3%	4%
Other	7%	8%	5%
White	53%	58%	27%
Primary cause of end-stage kidney disease, %			
Diabetes	33%	31%	40%
Glomerulonephritis/ vasculitis	22%	22%	19%
Hypertension/ large vessel disease	17%	17%	22%
Other	28%	30%	18%
Comorbidity history			
Diabetes	43%	42%	45%
Hypertension	88%	87%	91%
Any cardiovascular disease	58%	62%	38%
Atrial fibrillation	12%	13%	6%
Cerebrovascular disease	15%	16%	9%
Other atherothrombotic disease	41%	44%	23%
Other cardiovascular disease	32%	35%	20%
History of hospitalization due to any bleeding	5%	5%	3%
Gastrointestinal bleeding	4%	4%	2%
Cerebral hemorrhage	2%	2%	2%
Medication use^B			
Oral anticoagulant therapy	9%	9%	4%
Vitamin K antagonists	8%	9%	4%
Antiplatelets ^C	9%	10%	7%
Clopidogrel	9%	9%	6%

HD, hemodialysis. PD, peritoneal dialysis.

^AThe countries in each global region are as follows. North America: Canada and the United States. GCC: Bahrain, Saudi Arabia, Kuwait, United Arab Emirates, Oman, and Qatar. Europe: Belgium, France, Germany, Italy, Spain, Sweden, Russia, Turkey, and the United Kingdom. Other Asia-Pacific: Japan, China, Thailand, and South Korea.

^BThe denominators used to calculate the proportion of specific medication use included only those with prescription data available: n=32,901, 27,612, 5,289 for the overall patients, HD, and PD patients respectively.

^CExcluding aspirin. Aspirin use was not included because most aspirin use is over-the-counter. Since the drug utilization data for this study were based on prescription records, aspirin use would be significantly underestimated in prescription records.

Supplementary References

- S1.** Perl J, Karaboyas A, Morgenstern H, et al. Association between changes in quality of life and mortality in hemodialysis patients: results from the DOPPS. *Nephrol Dial Transplant*. Mar 1 2017;32(3):521-527.
- S2.** Pisoni RL, Gillespie BW, Dickinson DM, Chen K, Kutner MH, Wolfe RA. The Dialysis Outcomes and Practice Patterns Study (DOPPS): design, data elements, and methodology. *Am J Kidney Dis*. Nov 2004;44(5 Suppl 2):7-15.
- S3.** Rayner HC, Pisoni RL, Bommer J, et al. Mortality and hospitalization in haemodialysis patients in five European countries: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dial Transplant*. Jan 2004;19(1):108-120.
- S4.** Young E, Goodkin D, Mapes D, et al. The Dialysis Outcomes and Practice Patterns Study (DOPPS): An international hemodialysis study. *Kidney International*. 2000;57:S74-81.