Letters

RESEARCH LETTER

Thirty-Year Trends in Perioperative Mortality Risk for Living Kidney Donors

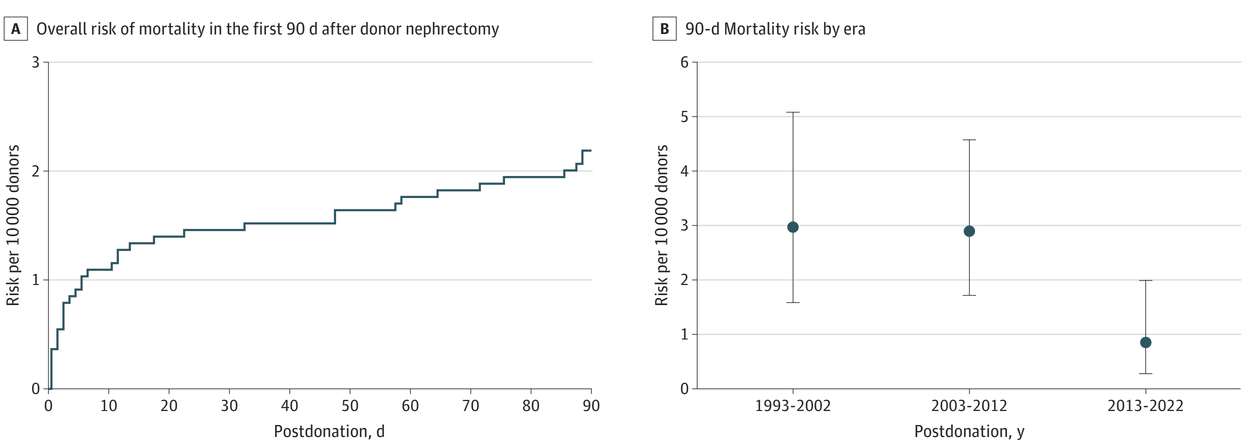
Living kidney donor candidates must be accurately informed of the risks of perioperative mortality. The best current estimate, 3.1 deaths within 90 days per 10 000 donations, comes from a study of donors from 1994 to 2009.[1] Open donor nephrectomy, standard of care in the 1990s, has now been replaced almost completely by laparoscopic nephrectomy.[2,3] Because of this transition, as well as improvements in donor selection, perioperative care, and surgical technique,[4] prior estimates of perioperative mortality may not accurately represent current risk to donors. We performed a national registry study to characterize temporal trends in perioperative mortality in donors and risk factors associated with this event.

Supplemental content

Methods | Using Scientific Registry of Transplant Recipients data on living kidney donors from 1993 to 2022, we calculated mortality ratios within 90 days of donation, stratified across 3 eras: 1993 through 2002, 2003 through 2012, and 2013 through 2022. Death events were captured from Organ Procurement and Transplantation Network (OPTN) living donor follow-up reported by transplant programs; National Technical Information Service Limited Access Death Master File; and deaths made available to the OPTN contractor through an interagency data sharing agreement between the Centers for Medicare & Medicaid Services and the Health Resources and Services Administration, and secondarily verified by the OPTN contractor. Per OPTN policy, all donor deaths within 2 years of donation must be reported within 72 hours of the hospital's becoming aware of the death. The institutional review board of NYU Langone Health determined that this study of deidentified data did not constitute human subjects research and waived consent. We compared mortality across eras and across subgroups of donors by age, sex, race, ethnicity, procedure type, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), and hypertension, using Fisher exact tests and reporting Clopper-Pearson exact CIs. Subgroups by procedure type and BMI category were analyzed during 1999-2022 and by history of hypertension during 2004-2022, when these variables were reliably captured in the registry. Owing to the small number of events, we did not conduct multivariable analyses. Analyses were conducted with Stata 17, using 2-sided tests with $\alpha = .05$.

Results | There were 164 593 donors in our study, of whom 36 died within 90 days postdonation (2.2 per 10 000 cases); 50% of deaths occurred within the first 7 days (**Figure**, A). When cause-of-death data were available, the most common cause was hemorrhage (8 deaths of 19 with reported cause of death). Mortality was comparable in 1993-2002 (13 deaths, 3.0 [95% CI, 1.6-5.1] per 10 000) and 2003-2012 (18 deaths, 2.9 [95% CI, 1.7-4.6] per 10 000) and then declined statistically significantly in 2013-2022 (5 deaths, 0.9 [95% CI, 0.3-2.0] per 10 000; *P* = .01) (Figure, B). There were no statistically significant differences across subgroups of age, race, and ethnicity; compared with that of White donors (2.0 per 10 000), mortality was higher for Black donors (4.2 per 10 000) and lower among donors who were neither Black nor White (1.3 per 10 000; *P* = .12) (**Table**). Male donors were at higher risk than female donors (4.0 vs 1.0 per

Figure. Perioperative Mortality and Donor Nephrectomy



A, Eight individuals died due to hemorrhage; 2, due to infection; 2, due to pulmonary embolism; 2, due to cardiovascular causes; 1, due to cerebrovascular accident; 1, due to homicide; and 3, due to other reasons not specified.

B, Vertical lines denote 95% confidence bars. Cause-of-death information was available for 19 of the 28 deaths that occurred in 2000 or later.

Table. Donor Characteristics 1993-2022 and Risk of Mortality

	No. of donors	No. (per 10 000) who died within 90 d	*P* value
Overall	164 593	36 (2.2)	NA
Era			
1993-2002	43 752	13 (3)	.01
2003-2012	62 185	18 (2.9)	
2013-2022	58 656	5 (0.9)	
Age, y[a]			
≤40	74 421	14 (1.9)	.25
40-49	47 308	15 (3.2)	
≥50	58 656	7 (1.6)	
Sex[a]			
Male	64 703	26 (4)	<.001
Female	99 890	10 (1)	
Race[a]			
Black	19 011	8 (4.2)	.12
Other or multiracial[b]	22 994	3 (1.3)	
White	122 525	25 (2)	
Ethnicity (any race)[a]			
Hispanic/Latino	22 379	4 (1.8)	.81
Non-Hispanic/non-Latino	142 214	32 (2.3)	
Among donors 1999-2022			
Procedure type[a]			
Open	16 447	7 (4.3)	.08
Laparoscopic	124 771	24 (1.9)	
BMI category[a]			
Underweight or healthy weight	46 338	6 (1.3)	.59
Overweight	54 775	12 (2.2)	
Obese	32 417	6 (1.9)	
Among donors 2004-2022			
Predonation hypertension[a]			
No	106 967	15 (1.4)	.03
Yes	4006	3 (7.5)	

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NA, not applicable.

[a] Missingness is as follows: age, 7 donors; sex, 0; race, 63; ethnicity, 0; era, 0; procedure type (among donors 1999-2022), 2121; BMI (among donors 1999-2022), 9808; and predonation hypertension (among donors 2004-2022), 3399.

[b] Race and ethnicity were assessed to investigate whether risk of perioperative mortality differentially affects members of minority groups. Race and ethnicity were self-reported, with options defined by the Organ Procurement and Transplantation Network. The "other" category includes American Indian or Alaska Native, Asian, multiracial, Native Hawaiian or Other Pacific Islander, and unknown.

10 000). Mortality was higher for donors who had open (vs laparoscopic) procedures, although not statistically significant (4.3 vs 1.9 per 10 000; *P* = .08). Mortality was consistent across categories of BMI. Mortality was higher for donors with a history of predonation hypertension (7.5 vs 1.4 per 10 000; *P* = .03).

Discussion | Perioperative mortality after living donation declined substantially in the past decade compared with prior decades, to fewer than 1 event per 10 000 donations. Risk was higher for male donors and donors with a history of hypertension. Current guidelines[5] for donor informed consent, based on 2009 data, should be updated to reflect this information.

Study limitations include that with only 36 perioperative deaths in 30 years, power to estimate relative risks is limited. Additionally, follow-up may be incomplete. However, OPTN requirements for donor follow-up have grown stricter, with 6-month follow-up required for donors since 2013; as such, missingness would bias toward lower mortality in earlier eras, the opposite of what the study found.

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Data Sharing Statement: See the Supplement.

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CLIMATE CHANGE AND HEALTH

Greenhouse Gas Emissions and Costs of Inhaler Devices in the US

Metered-dose inhalers prescribed for asthma and chronic obstructive pulmonary disease contain hydrofluorocarbon propellants, potent greenhouse gases that trap heat in the atmosphere thousands of times more powerfully than carbon dioxide. In England, these inhalers contribute an estimated 0.8 million metric tons (MMT) of annual carbon dioxide equivalent (CO_2e) emissions,[1] equivalent to 157 885 US homes' yearly electricity use.[2] In response, the National Health Service (NHS) has encouraged switching from propellant-containing metered-dose inhalers to propellant-free alternatives such as dry-powder and soft-mist inhalers.[1]

Supplemental content

The US health care system produces 550 MMT of CO_2e emissions annually[3] vs 30.4 MMT of CO_2e for NHS England,[1] yet efforts to reduce inhaler-related emissions in the US have been hindered by limited data on the carbon footprint of US inhalers. We assessed mean emissions and costs and estimated total yearly emissions and costs for US brand-name inhalers prescribed to Medicare Part D and Medicaid beneficiaries. Medicare Part D and Medicaid account for approximately 40% of US retail prescription drug spending.[4]

Methods | All brand-name and generic inhaler prescriptions filled by Medicare Part D and Medicaid beneficiaries in 2022 were included. Emissions associated with the use and disposal of each metered-dose inhaler were calculated with the following formula: Weight of Inhaler Contents × Propellant Percentage × 100-Year Global Warming Potential of the Propellant. Inhaler weight was obtained from the package insert; the percentage and type of propellant were obtained from McKesson material safety data sheets; and the 100-year global warming potential, which represents the earth-warming effect of a gas relative to CO_2 during 100 years, was obtained from the Sixth Assessment Report of the Intergovernmental Panel on Climate Change. Manufacturing and active pharmaceutical ingredient emissions for all inhalers were derived from prior European studies (eAppendix in Supplement 1).[5,6] Mean emissions for each inhaler and by inhaler class (metered-dose, dry-powder, and soft-mist) were calculated. To estimate total emissions in 2022, mean emissions per class were multiplied by number of claims per class. Inhaler claims and costs were extracted from the Centers for Medicare & Medicaid Services (CMS) summary and statistics database. Analyses were performed with Microsoft Excel version 2308.

Results | Mean (SD) estimated emissions per inhaler by device class were 23.1 (11.3) kg of CO_2e for metered-dose inhalers (n = 14), 0.79 (0.06) kg CO_2e for dry-powder inhalers (n = 19), and 0.78 (0.0) kg CO_2e for soft-mist inhalers (n = 4), where 10 kg CO_2e equals 41.2 km driven in an average gasoline-powered passenger vehicle. The inhaled corticosteroid, long-acting β-agonist, metered-dose inhaler Dulera (mometasone/formoterol) had the highest emissions per inhaler, at 48.1 kg CO_2e, and cost $444.37 per Medicare claim vs analogous inhaled corticosteroid, long-acting β-agonist, dry-powder inhaler Advair Diskus (fluticasone/salmeterol), which had 0.898 kg CO_2e emissions per inhaler and cost $581.60 per Medicare claim. Among metered-dose inhalers, short-acting β-agonists were the most prescribed medication category, with 35.3 million claims. Within short-acting β-agonist medications, Ventolin HFA (albuterol sulfate) had the highest emissions, 28.7 kg CO_2e per inhaler (**Table**).

In total, 69.8 million CMS inhaler claims in 2022 resulted in an estimated 1.15 MMT of CO_2e emissions. Metered-dose inhalers accounted for 49.0 million claims (70.2%), 1.13 MMT CO_2e emissions (98.3%), and $7.5 billion of spending (37.9%); dry-powder inhalers accounted for 17.1 million claims (24.5%), 0.014 MMT CO_2e emissions (1.22%), and $10.0 billion of spending (50.8%); and soft-mist inhalers accounted