Long-term risks for kidney donors

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Previous studies have suggested that living kidney donors maintain long-term renal function and experience no increase in cardiovascular or all-cause mortality. However, most analyses have included control groups less healthy than the living donor population and have had relatively short follow-up periods. Here we compared long-term renal function and cardiovascular and all-cause mortality in living kidney donors compared with a control group of individuals who would have been eligible for donation. All-cause mortality, cardiovascular mortality, and end-stage renal disease (ESRD) was identified in 1901 individuals who donated a kidney during 1963 through 2007 with a median follow-up of 15.1 years. A control group of 32,621 potentially eligible kidney donors was selected, with a median follow-up of 24.9 years. Hazard ratio for all-cause death was significantly increased to 1.30 (95% confidence interval 1.11–1.52) for donors compared with controls. There was a significant corresponding increase in cardiovascular death to 1.40 (1.03–1.91), while the risk of ESRD was greatly and significantly increased to 11.38 (4.37–29.6). The overall incidence of ESRD among donors was 302 cases per million and might have been influenced by hereditary factors. Immunological renal disease was the cause of ESRD in the donors. Thus, kidney donors are at increased long-term risk for ESRD, cardiovascular, and all-cause mortality compared with a control group of non-donors who would have been eligible for donation.

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Living donor kidney transplantation is the preferred treatment for end-stage renal disease (ESRD), because it is associated with improved graft and patient survival compared with transplantation from a deceased donor.[1] Living kidney donation, however, requires that healthy individuals voluntarily undergo major surgery with no physical health benefit to themselves. Although rare, perioperative mortality does occur during organ retrieval from living donors and have been estimated to occur in 0.2% of liver donors and 0.03% of kidney donors.[2,3] Less serious perioperative risks are accepted and well documented.[3,4] Kidney donation inevitably leads to reduced renal function and is associated with an increase in proteinuria, as well as a rise in blood pressure (BP) greater than that attributable to normal aging.[5,6] These factors are associated with an increased risk for cardiovascular and all-cause mortality in the general population.[7–9]

Follow-up studies of living organ donors have not reported increased cardiovascular and all-cause mortality, but results may have been confounded by selection bias in the control groups. In most studies, controls were selected from the general population, which includes adults with medical conditions that would make them ineligible for kidney donation.[10–12] As a result, these controls would have been less healthy than the living donors and an effect of organ donation on all-cause and cardiovascular mortality could have been underestimated. Three studies have included control groups selected to have comparable health status to the living donors, and each of these demonstrated no increase in cardiovascular disease or mortality over a follow-up time of approximately 6 years.[3,13,14] It is possible, however, that living donors may be at increased risk of death for many years beyond the period that has been investigated to date. Thus an analysis with a longer follow-up time may be necessary to examine the possible impact of living donor nephrectomy. Occurrence of ESRD in living donors has also been observed long term after kidney donation although the absolute number of cases presented has been very low, and it is uncertain whether the statistical assessment used has been sufficient.

The aim of the present study was to estimate long-term all-cause mortality, cardiovascular mortality, and risk for ESRD in kidney donors compared with a selected control group screened for eligibility for live-kidney donation.

RESULTS

During 1963–2007, 2269 live-kidney donations were performed at Oslo University Hospital. After excluding marginal donors, 1901 donors were included (Figure 1). Among these, 1519 were first-degree relatives, 89 were other relatives, and 293 were unrelated. Median follow-up time was 15.1 (1.5–43.9) years. Mean estimated glomerular filtration rate (eGFR) at donation was 104.7 ml/min per 1.73 m^2 ($n = 1766$, s.d. 13.7). All donors were Caucasians.

Controls were included from the Health Study of Nord-Trøndelag (HUNT) population study. Out of the 74,991 individuals participating in this population-based survey, a control group of 32,621 was constructed to fit criteria for kidney donation (Table 1). Median follow-up time for the control group was 24.9 (0.1–26.0) years.

For donors, outcome data on all-cause mortality and renal replacement therapy were ascertained as of January 2010 and cardiovascular mortality as of January 2008. For controls, all outcome data were ascertained as of January 2010.

During the observation period, there were 224 deaths among 1901 kidney donors from the initial inclusion group, 68 (30.4%) of which were due to cardiovascular disease. There were 2425 deaths among the 32,621 controls, 688 (28.4%) of which were due to cardiovascular disease. No donors died during or immediately after the surgical procedure. Figure 2 shows the survival data for donors and controls. The survival curves were significantly different ($P < 0.001$).

Table 2a shows the hazard ratio (HR) for death by any cause in kidney donors compared with controls. The unadjusted risk associated with kidney donation was 2.49 (95% confidence interval (CI), 2.13–2.91, $P < 0.001$). In adjusted complete case analysis, the HR for kidney donors was 1.48 (95% CI, 1.17–1.88, $P = 0.001$). After multiple imputation, HR was 1.30 (95% CI, 1.11–1.52, $P = 0.001$). There was a corresponding increase in cardiovascular mortality (HR 1.40, 95% CI 1.03–1.91, $P = 0.03$) (Table 2b).

A total of nine donors (0.47%) developed ESRD. All were family members. Median time from donation was 18.7 (10.3–24.3) years. Renal failure in donors was mainly caused by immunological diseases: glomerulonephritis ($n = 3$), systemic lupus erythematosus ($n = 1$), Wegener's granulomatosis ($n = 1$), ANCA (anti-neutrophil cytoplasmic antibodies)-positive vasculitis ($n = 1$), sarcoidosis ($n = 1$), and diabetes/nephrosclerosis ($n = 2$). In the control group, 22 individuals developed ESRD. Reported causes were glomerulonephritis ($n = 5$), pyelonephritis ($n = 4$), polycystic kidney disease ($n = 4$), hypertension ($n = 3$), diabetes ($n = 1$), amyloidosis ($n = 1$), systemic lupus erythematosus ($n = 1$),

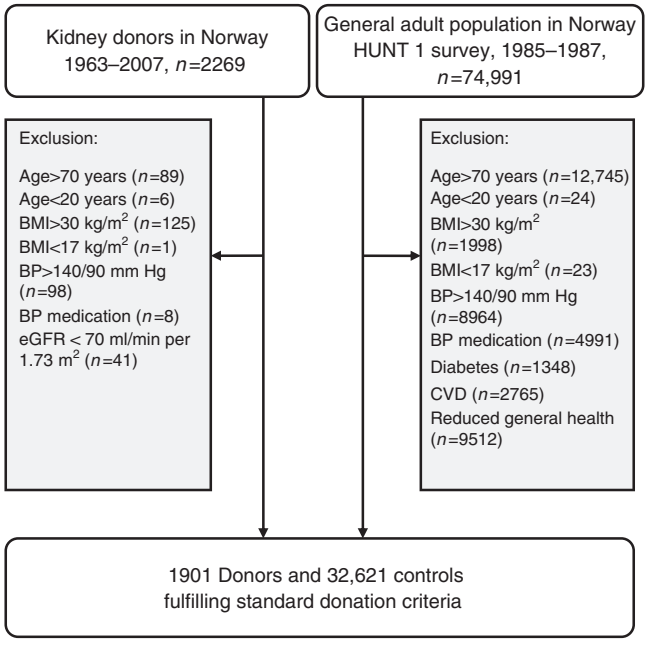

Figure 1 | Flow chart showing inclusion and exclusion of kidney donors and controls. BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HUNT 1, Health Study of Nord-Trøndelag.

Table 1 | Baseline characteristics of kidney donors and controls

	Kidney donors	Controls
Age, years	46.0 ± 11.5	37.6 ± 11.7
	$n = 1901$	$n = 32,621$
Male gender, %	41.0	46.9
	$n = 1901$	$n = 32,621$
Current smoking, %	41.5	39.5
	$n = 1375$	$n = 25,993$
Systolic BP, mm Hg	123.3 ± 10.0	121.4 ± 10.4
	$n = 1768$	$n = 31,398$
Diastolic BP, mm Hg	77.4 ± 7.2	77.2 ± 7.9
	$n = 1768$	$n = 31,394$
BMI, kg/m^2	24.2 ± 2.8	23.5 ± 2.6
	$n = 1558$	$n = 31,421$

Abbreviations: BMI, body mass index; BP, blood pressure.

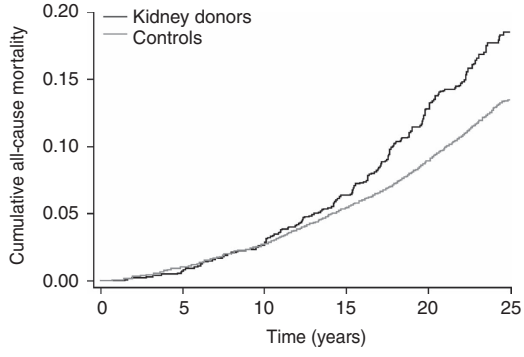

Figure 2 | Cumulative mortality risk in kidney donors and controls, adjusted for year of donation. Controls are matched to donors for age, sex, systolic blood pressure, body mass index, and smoking status.