“T.E. STARZL”
SPRING MEETING SITO 2017
Linee Guida in Trapiantologia

Collegio SITO-SIN

Proposta per le raccomandazioni cliniche sulla valutazione e follow-up del donatore vivente di trapianto renale

GRUPPO 3

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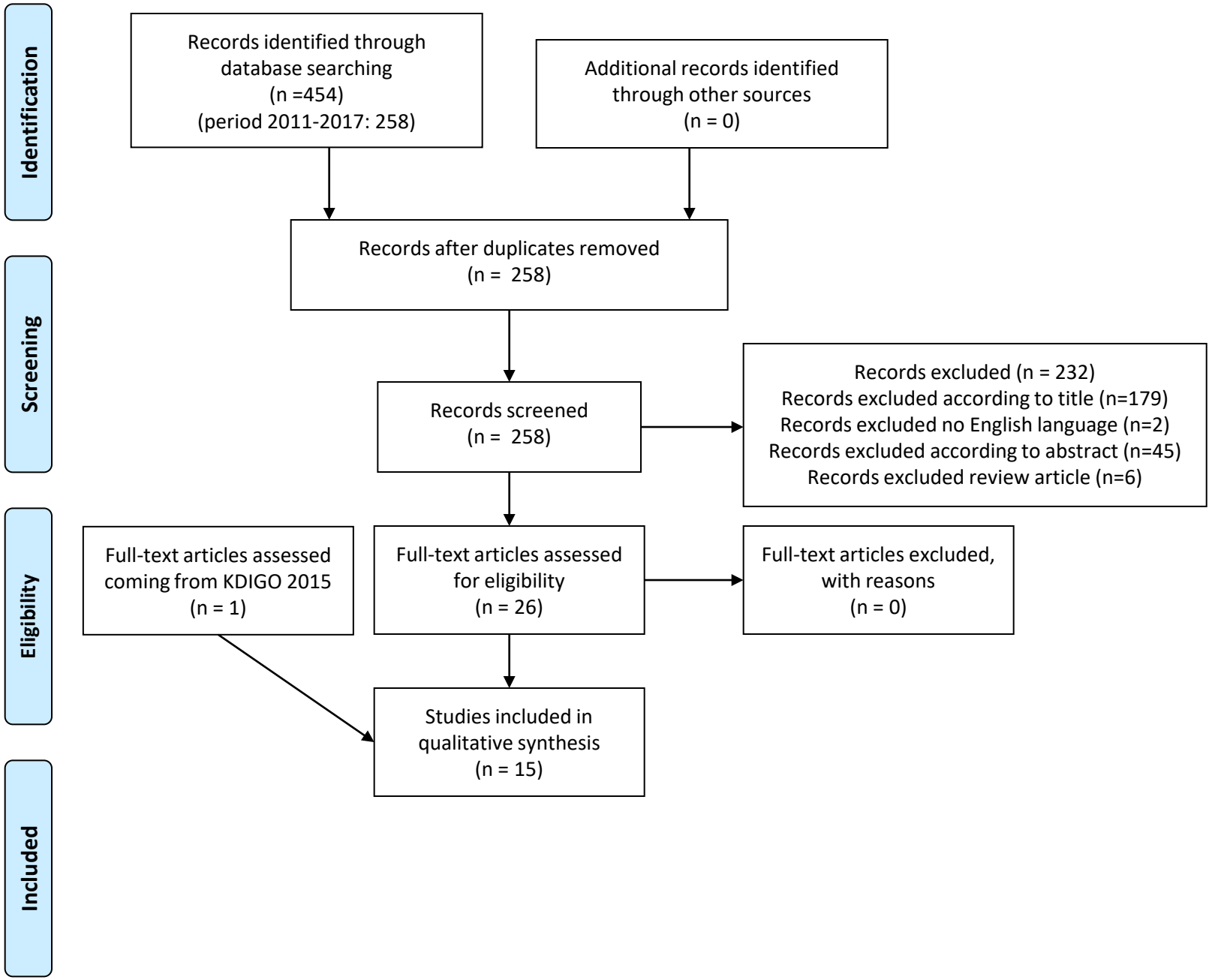
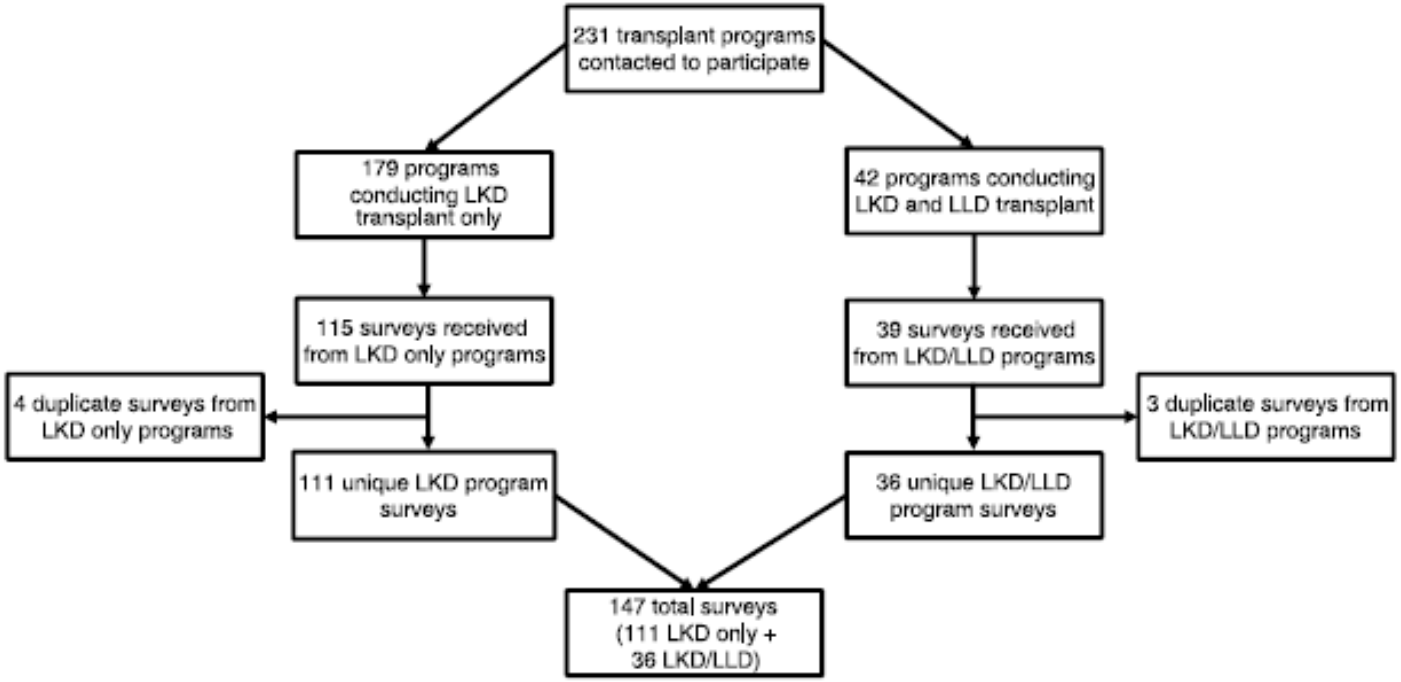
Follow-up del donatore


Identification
Screening
Eligibility
Included
Records identified through database searching (n =454) (period 2011-2017: 258)
Additional records identified through other sources (n = 0)
Records after duplicates removed (n = 258)
Records screened (n = 258)
Records excluded (n = 232)
Records excluded according to title (n=179)
Records excluded no English language (n=2)
Records excluded according to abstract (n=45)
Records excluded review article (n=6)
Full-text articles assessed coming from KDIGO 2015 (n = 1)
Full-text articles assessed for eligibility (n = 26)
Full-text articles excluded, with reasons (n = 0)
Studies included in qualitative synthesis (n = 15)

Waterman AD, et al. Living-Donor Follow-up Attitudes and Practices in U.S. Kidney and Liver Donor Programs. Transplantation 2013 Mar 27;95(6):883-8.



- ✓ **Approximately 40%** of programs lost contact with more than **75% of theirs donors by 2 years after donation**

- ✓ Whereas 92% of LKD and 96% LLD programs inform potential donors about follow-up requirements

- ✓ **67% LKD and 78% LLD programs** develop plans with donors to achieve follow-up

Waterman AD, et al. Living-Donor Follow-up Attitudes and Practices in U.S. Kidney and Liver Donor Programs. Transplantation 2013 Mar 27;95(6):883-8.

TABLE 1. Benefits and barriers to collecting LDF data

	% Respondents (n=147)
Benefits	
Improved information can be provided to prospective living donors about risks	94.8
Improved knowledge about health of living donors in their program	94.7
Improved national trust in the process of living donation	85.0
Improved donation outcomes for future living donors	86.5
Improved health for living donors nationally	86.1
Reduced medical risks associated with kidney donation	70.2
Reduced medical risks associated with liver donation	78.8
Barriers	
Donors do not want to return to the transplantation program for medical tests as time passes	86.8
Living donors' contact information becomes outdated	72.7
Lack of reimbursement to programs for LDF costs	53.7
Lack of reimbursement to donors for costs associated with follow-up	48.8
Cost of additional medical testing for living donors	45.5
Living donors do not want to be contacted	38.8
Lack of staff time to follow-up with or locate living donors by telephone	35.5
Lack of staff time to conduct ongoing medical assessments of living donors	28.1
Lack of staff time to complete OPTN LDF forms	19.8
Other barriers	11.6

LDF, living-donor follow-up; OPTN, Organ Procurement and Transplantation Network.

Ommen E.S., et al. When Good Intentions are not enough: obtaining follow-up data in Living Kindney Donors. Am J Transplant. 2011 Dec;11(12):2575-81.

- A national donor follow-up registry is essential to ensure transparency in ascertaining long-term health outcomes among all living donors and in providing assessments of quality assurance within transplant programs.

- Governmental agencies must allocate funding for a unified and centralized system for compensating direct and indirect costs of mandated donor follow-up.

- The federal government must provide funds to HHS to ensure that long-term health is followed in all donors and reported to a registry that will allow a thorough analysis.

" We believe that pre and post-donation education regarding the importance of follow-up evaluation, in combination with an elimination of expenses incurred by donors will serve, over time, to increase donor follow-up".

Kasiske L, et al. A Prospective Controlled Study of Living Kidney Donors: Three-Year Follow-up. Am J Kidney Dis 2015;66(1): 114-124

Prospective, controlled , observational cohort study .
At 36 months, 182 of 203 (89.7%) original donors and 173 of 201(86.1%) original controls continue to participate in follow-up visits.

Table 1. Heart Rate and BP

		Visit (time after donation)				*P*[a]		
Test	Group	6 mo	12 mo	24 mo	36 mo	Donors vs Controls[b]	Visit[c]	Interaction[d]
Heart rate (beats/min)	Controls	66.3 ± 10.0 (198)	66.6 ± 10.3 (193)	67.0 ± 9.3 (180)	66.7 ± 9.7 (169)	0.9	0.1	0.7
	Donors	66.3 ± 9.6 (200)	66.6 ± 9.5 (196)	66.9 ± 10.0 (184)	66.6 ± 9.2 (181)			
Systolic BP (mm Hg)	Controls	115.7 ± 12.2 (198)	116.2 ± 11.8 (193)	117.2 ± 13.3 (180)	117.3 ± 12.8 (170)	0.6	<0.001	0.8
	Donors	115.2 ± 11.3 (200)	116.4 ± 12.4 (196)	116.2 ± 11.6 (184)	117.5 ± 12.0 (182)			
Diastolic BP (mm Hg)	Controls	70.0 ± 8.5 (198)	70.1 ± 9.0 (193)	71.0 ± 9.1 (180)	71.6 ± 8.5 (170)	0.7	<0.001	0.8
	Donors	70.4 ± 8.5 (200)	70.3 ± 8.6 (196)	70.7 ± 8.3 (184)	72.1 ± 8.4 (182)			
Pulse pressure (mm Hg)	Controls	45.7 ± 8.8 (198)	46.2 ± 8.4 (193)	46.2 ± 9.7 (180)	45.7 ± 8.7 (170)	0.3	0.9	0.6
	Donors	44.8 ± 8.2 (200)	46.1 ± 8.6 (196)	45.5 ± 8.4 (184)	45.4 ± 8.9 (182)			

Note: Values are given as mean ± standard deviation (number sampled).
Abbreviation: BP, blood pressure.
[a]Analysis of variance with repeated measures. Each variable was analyzed separately and no adjustment was made for multiple comparisons. Values not normally distributed were logarithmically transformed before analysis.
[b]Donors versus controls, *P* values test overall differences between donors and controls.
[c]Visit *P* values test differences among the 4 visits.
[d]Interaction *P* values test the interaction between donors versus controls and between visits.

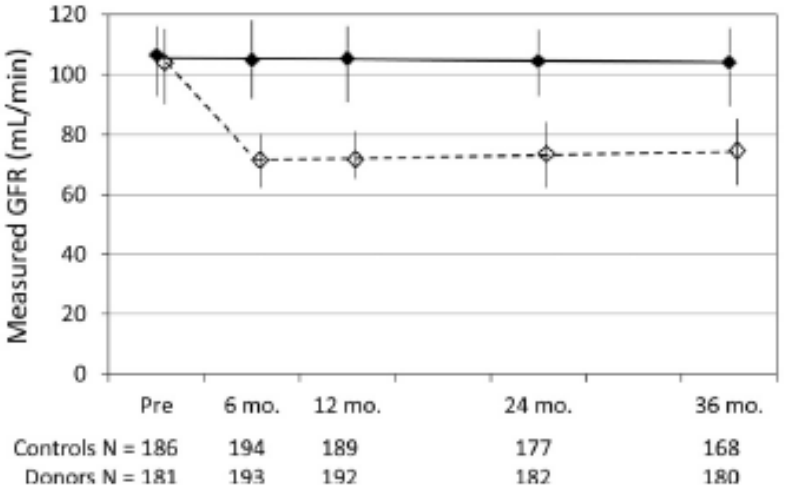
- ✓ Both systolic and diastolic BP increased slightly but significantly over time, but there were no differences between donors and controls
- ✓ There were no statistically significant differences between donors and controls in any of the 24-hour ambulatory BP parameters

Kasiske L, et al. A Prospective Controlled Study of Living Kidney Donors: Three-Year Follow-up. Am J Kidney Dis 2015;66(1): 114-124

Table 4. Changes in Kidney Function Over Time

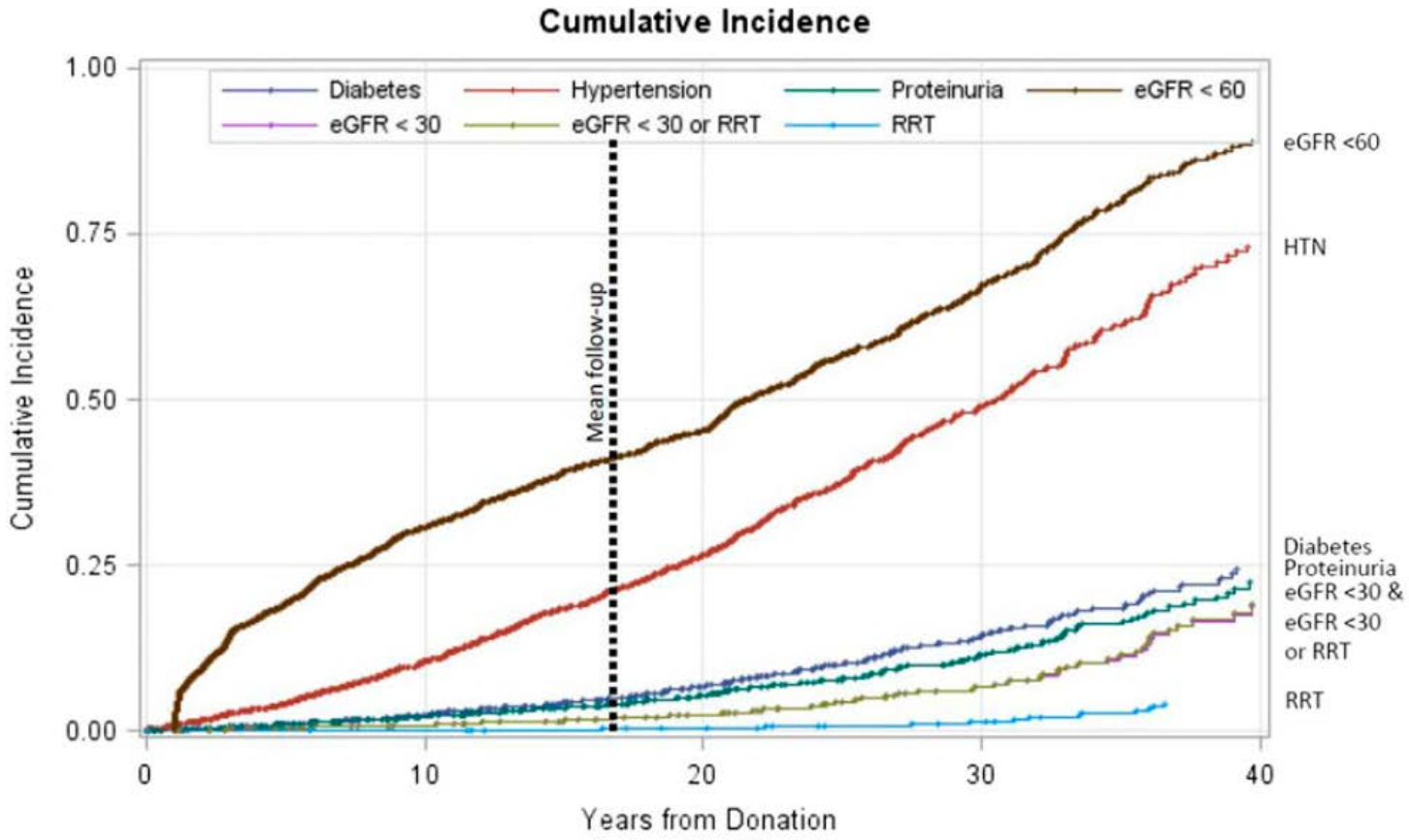
Measurement	Follow-up Duration (mo)	Group	Rate of Change in Kidney Function	P*
mGFR (mL/min per y)	12-36	Controls	−0.36 ± 7.55 (194)	0.005
		Donors	1.47 ± 5.02 (198)	
	36	Controls	−0.19 ± 5.31 (172)	0.002
		Donors	1.30 ± 3.49 (181)	
mGFR (mL/min/1.73 m^2 per y)	12-36	Controls	−0.44 ± 7.35 (194)	0.01
		Donors	1.09 ± 4.28 (198)	
	36	Controls	−0.39 ± 4.81 (172)	0.004
		Donors	0.84 ± 3.09 (181)	
$eGFR_{cr}$ (mL/min/1.73 m^2 per y)	12-36	Controls	−1.04 ± 6.16 (196)	<0.001
		Donors	1.82 ± 4.92 (200)	
	36	Controls	−0.46 ± 3.68 (173)	<0.001
		Donors	1.60 ± 3.75 (182)	
$eGFR_{cys}$ (mL/min/1.73 m^2 per y)	12-36	Controls	−0.33 ± 7.36 (196)	0.003
		Donors	1.82 ± 6.76 (200)	
	36	Controls	0.16 ± 4.68 (173)	0.04
		Donors	1.21 ± 5.06 (182)	
$eGFR_{cr\text{-}cys}$ (mL/min/1.73 m^2 per y)	12-36	Controls	−0.73 ± 6.38 (196)	<0.001
		Donors	1.89 ± 4.58 (200)	
	36	Controls	−0.07 ± 3.85 (173)	<0.001
		Donors	1.49 ± 3.81 (182)	

Both ,mGFR and eGFR declined in controls between 6 and 36 months, whereas they increased in donors.



Ibrahim N.H. et al., Renal Function Profile in White Kidney Donors: The First 4 Decades J Am Soc Nephrol 27: 2885–2893, 2016.

3596 white donors from US (median FU: 16.6±11.9 years).



Cumulative risk of reduced GFR and proteinuria. Kaplan–Meier time to development of hypertension, proteinuria, eGFR,60ml/min per 1.73 m2, eGFR,30ml/min per 1.73 m2, eGFR,30ml/min per 1.73 m2 or ESRD, and ESRD alone

Ibrahim N.H. et al., Renal Function Profile in White Kidney Donors: The First 4 Decades J Am Soc Nephrol 27: 2885–2893, 2016.

3596 white donors from US (median FU: 16.6±11.9 years).

Table 4. Postdonation events and risk of death, proteinuria, and eGFR<30ml/min per 1.73 m^2 or ESRD

Outcome	Time-Dependent Covariate	HR (95% CI)	*P* Value
Death	Diabetes	0.74 (0.48 to 1.14)	0.17
	New-onset hypertension	3.82 (2.97 to 4.91)	<0.001
	Proteinuria	2.25 (1.42 to 3.55)	<0.001
	eGFR<60[a]	4.62 (3.70 to 5.77)	<0.001
	eGFR<30[a]	2.99 (1.96 to 4.58)	<0.001
	eGFR<30[a] or ESRD	3.19 (2.20 to 4.62)	<0.001
Proteinuria	Diabetes	4.92 (3.43 to 7.05)	<0.001
	New-onset hypertension	3.9 (2.50 to 6.08)	<0.001
	eGFR<60[a]	3.94 (2.55 to 6.08)	<0.001
	eGFR<30[a]	6.45 (3.11 to 13.38)	<0.001
	eGFR<30[a] or ESRD	7.26 (3.63 to 14.48)	<0.001
eGFR<30[a] or ESRD	Diabetes	2.41 (1.42 to 4.09)	0.001
	New-onset hypertension	2.79 (1.55 to 5.03)	<0.001
	Proteinuria	4.11 (2.04 to 8.26)	<0.001
	eGFR<60[a]	4.22 (2.65 to 6.71)	<0.001
	eGFR<45[a]	6.82 (4.19 to 11.11)	<0.001

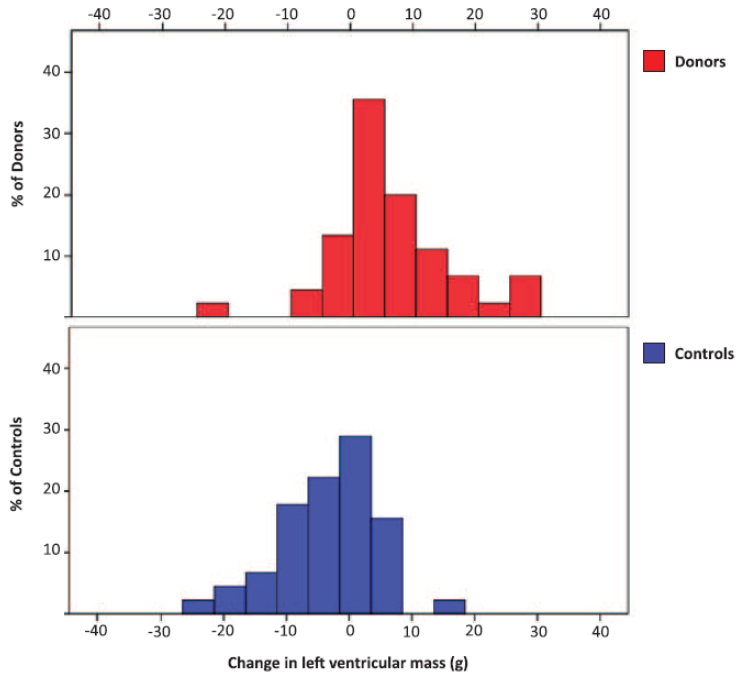
[a]eGFR given in ml/min per 1.73 m^2.

Moody E. W. Et al. Cardiovascular Effects of Unilateral Nephrectomy in living Kindey Donros. Hypertension 2016;67:368-377

Hematological and Biochemical Effects of a reduction in Kidney function:

There was a mean decrease in iGFR in donors of −30±12 mL/min/1.73m2 and no clinically significant change in controls (−1±10 mL/min/1.73m2; P<0.001).

At 12 months, over one third of donors (35%) had an iGFR <60 mL/min/1.73m2, whereas more than one half (53%) had an eGFR <60 mL/min/1.73m2.



There was a significant increase in left ventricular mass in donors vs controls at 12 mo with a mean difference in the change >12 mo of 9.8 g (95% confidence interval, 6.2–13.3; P<0.001).

Torres X., et al. Death of recipients after kidney living donation triples donors risk of dropping out from follow up a retrospective study Transplant Int 2017; 30:603-610

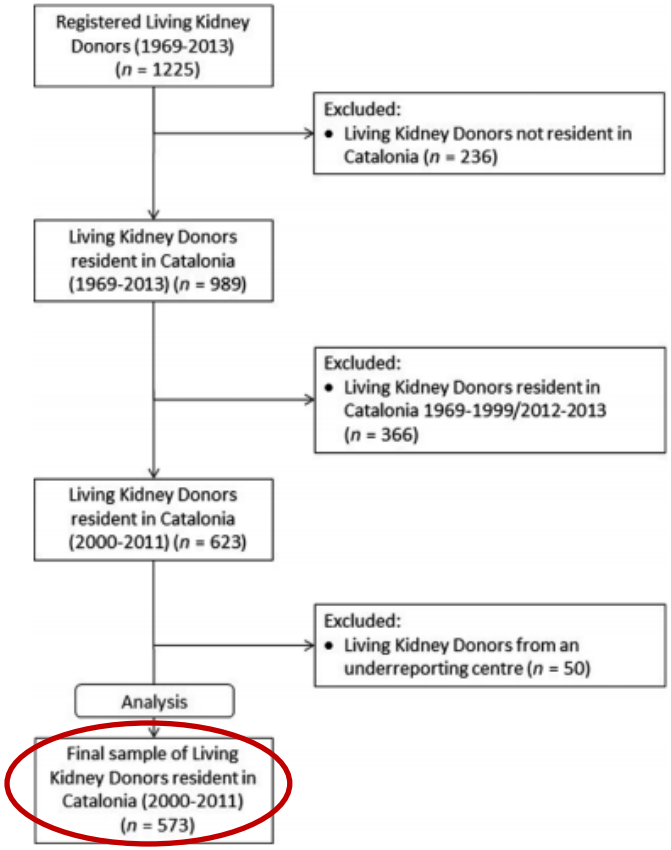
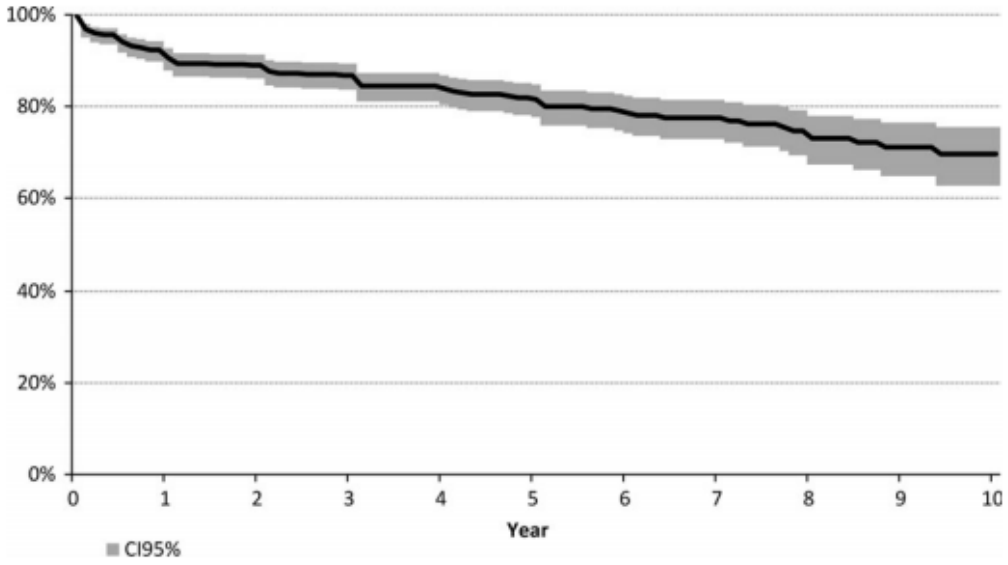


Figure 1 Flow diagram showing donors' selection.



Cumulative probability of loss to follow-up.

Torres X., et al. Death of recipients after kidney living donation triples donors risk of dropping out from follow up a retrospective study Transplant Int 2017; 30:603-610

Survival analysis of donor's lost-to-follow-up event.

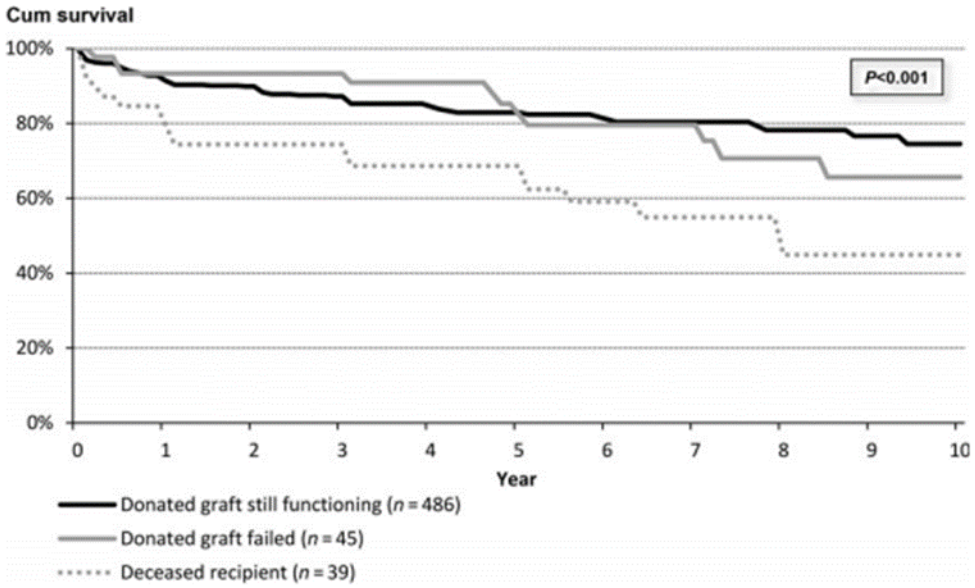


Table 2. Multivariate Cox analysis with variables related to living kidney donor loss-of-follow-up.

Variable	HR	CI 95%
Sex		
Male (reference)	1	
Female	0.83	0.56–1.23
Age group in the nephrectomy (in years)		
55–64 (reference)	1	
≤34	2.60*	1.33–5.07
35–54	1.58	0.98–2.55
≥65	2.69*	1.38–5.24
Period of donation		
2000–2007 (reference)	1	
2008–2011	1.75*	1.10–2.76
Follow-up centre		
Centre 1 (reference)	1	
Centre 3	3.33*	1.15–9.65
Centre 4	2.35*	1.04–5.32
Centre 5	3.49*	1.10–11.11
Centre 6	3.08*	1.36–6.93
Recipient status		
Functioning graft (reference)	1	
Lost graft	1.59	0.85–2.97
Deceased recipient	2.98*	1.73–5.11

*$P < 0.05$.