



# Impact of Incidental Findings During the Evaluation of Live Kidney Donors on Post-Transplant Outcomes: A Single Center Analysis

Ester De Marco<sup>a</sup>, Daniela Corona<sup>b</sup>, Flavio Origlio<sup>a</sup>, Giuseppe Giuffrida<sup>c</sup>, Rossella Gioco<sup>a</sup>, Chiara Palermo<sup>a</sup>, Francesca Privitera<sup>d</sup>, Alessia Giaquinta<sup>a</sup>, Alba Ilari<sup>d</sup>, Sara D'Errico<sup>d</sup>, Flavia Pinto<sup>d</sup>, Fausto Carbone<sup>a</sup>, Anna Carbonaro<sup>a</sup>, Pierfrancesco Veroux<sup>a</sup>, and Massimiliano Veroux<sup>a,d,\*</sup>

<sup>a</sup>Organ Transplant Unit, Department of Surgical and Medical Sciences and Advanced Technologies, University Hospital of Catania, Catania, Italy; <sup>b</sup>Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy; <sup>c</sup>Manchester Royal Infirmary Organ Transplant Unit, Manchester, UK; and <sup>d</sup>Endocrine Surgery Unit, Department of Surgical and Medical Sciences and Advanced Technologies, University Hospital of Catania, Catania, Italy

## ABSTRACT

**Background.** A careful assessment of a living donor is mandatory to minimize the short- and long-term risk related to kidney donation. In this study, we evaluated the incidence of incidental findings (IFs) in a large population of potential living kidney donors. Moreover, this study evaluated if the presence of IFs could influence the chance of living kidney donation and post-transplant outcomes.

**Methods.** One hundred and sixty consecutive potential prospective living kidney transplant donors, who underwent a multidetector computed tomography angiography (MDCTA), were included in the study. An IF was defined as an incidentally discovered mass or lesion, detected by computed tomography angiography during the imaging evaluation of potential living donors. Clinical outcomes of living donors with IF were compared with those without IF.

**Results.** In 10 patients (6.2%) an incidental finding was detected at MDCTA assessment. Among the 10 patients presenting with an IF, 7 patients (4.3%) were excluded from the living donation: 2 patients with an adrenal lesion, 3 patients with cancer, and 2 patients with a large (>8 cm) renal cyst. Graft and patient survival of kidney transplant recipients of donors with IFs were not significantly different to those receiving a kidney from living donors without IFs.

**Conclusions.** Incidental findings are frequently discovered during living kidney donor evaluation. Whereas most are asymptomatic or not clinically relevant, predonation screening could identify potentially life-threatening diseases at an earlier stage, allowing for a more radical treatment.

**K**IDNEY transplantation is the best replacement therapy for patients with end-stage renal disease [1], as it is associated with better survival and quality of life when compared with patients remaining on dialysis [2,3]. However, this created a great disparity between the available organs and the number of patients on the waiting list. Living donor kidney transplantation offers an alternative source of organs [4], as it is associated with significantly better long-term allograft function when compared with a deceased donor transplant [4,5], thanks to the minimal cold ischemia time, the elective procedure, and use of healthy donors [6].

Kidney donor evaluation is a complex process in which assessment of potential harm to the donor relative to the potential benefit to the recipient should be carefully balanced. Because of the severe imbalance between patients

\*Address correspondence to Massimiliano Veroux, MD, PhD, Endocrine Surgery Unit, Organ Transplant Unit; Department of Medical and Surgical Sciences and Advanced Technologies, University Hospital of Catania, Via Santa Sofia, 84 95123, Catania, Italy. Tel: +39 095 3782206; Fax: +39 0953782206. E-mail: [veroux@unict.it](mailto:veroux@unict.it)

in need of transplantation and donor supply, medically complex donors are increasingly considered for potential donation [7]. A careful selection of healthy individuals suitable for donation is mandatory to reduce the potential risk related to kidney donation. Imaging is of utmost importance in selecting donors and, before donor nephrectomy, all donors should undergo an assessment of vasculature and ureteric anatomy by multidetector computed tomography angiography (MDCTA), which allows visualization of not only the renal parenchyma, collecting system, and renal vasculature, but also a portion of the lower thoracic cavity and the entire abdomen and pelvis [8–11], thereby potentially increasing the rate of incidentally discovered mass or lesion, known as incidentaloma or incidental findings (IFs). Whereas in most cases IFs have a limited clinical impact and are usually asymptomatic, in the setting of living kidney transplantation, unfavorable findings, such as anatomic, vascular, and collecting duct abnormalities, may lead to exclusion from donor nephrectomy. On the other hand, asymptomatic disease may be detected at an early and potentially curable stage [12,13], and this may result in decreased patient morbidity and mortality, as well as overall savings in downstream health care costs [14].

In this study, we evaluated the incidence of IFs in a population of potential living kidney donors. Moreover, this study evaluated if the presence of IFs could influence the chance of living kidney donation and post-transplant outcomes.

## METHODS

The study was performed on 160 consecutive potential prospective living kidney transplant donors, who underwent an MDCTA, as part of a standard preoperative evaluation for renal donation, from November 2000 to April 2017, at the University Hospital of Catania. All potential living donor candidates underwent a standardized preoperative protocol to evaluate the potential suitability for kidney donation [4,15,16], including an MDCTA for the assessment of vasculature and ureteric anatomy. All scans were obtained with either a 32-slice or 64-slice MDCT scanner (Optima, General Electric Healthcare Italia, Milano, Italy). The protocol included unenhanced and intravenous contrast-enhanced scans from the second cervical vertebrae to iliac crest [17]. All image data are reconstructed with a body soft-tissue algorithm in 1-mm-thick and 3-mm-thick sections. All CT angiograms are interpreted in axial, sagittal, and coronal reformations. An expert radiologist systematically reviewed the CT reports and a shared electronic database was created to record the imaging findings and identify patients who had incidentalomas. An IF was defined as an incidentally discovered mass or lesion, detected by CT-angiography during the imaging evaluation of potential living donors. Comments about past surgical interventions, nonpathologic anatomic variations, and vascular abnormalities were not considered IFs. The decision as to which kidney can safely be donated is dependent on the combination of imaging results and functional studies [4,18], and intraoperative management of donors during nephrectomy followed a standardized protocol [18,19].

Kidney transplant recipients received a standard 3-drug immunosuppressive therapy, with or without induction therapy, as previously described [20].

We evaluated which donors proceeded to kidney donation and which donors were excluded. Potential donors with IFs who did not proceed to kidney donation were further investigated for the reason and categorized accordingly.

The primary endpoints were to determine the incidence of IF in potential living kidney donors, the discard rate of living donor owing to the presence of IF, and the outcome of kidney transplant recipients of donors with IFs compared with those without IFs.

## STATISTICAL ANALYSIS

Categorical variables were analyzed using  $\chi^2$  test or Fisher contingency tables. Results and patients characteristics are reported as mean  $\pm$  standard deviation. Comparison of means and percentages was estimated by the unpaired 2 Student's *t* test or Mann-Whitney *U* test, as appropriate. A *P* value  $< .05$  was considered as statistically significant. All calculations were performed using SPSS, version 12.0 (SPSS, Inc, Chicago, Ill, United States).

## RESULTS

During the study period, 160 consecutive potential living kidney donors (74 [46.2%] men and 86 [53.8%] women; mean age 46.6 years, range, 19–85 years) were systematically reviewed. Overall 45 (28%) potential kidney living donors were deemed unsuitable for donor nephrectomy (Table 1). Ten individuals (6.2%) presented an incidentaloma at CT angiography. The risk of antibody-mediated acute rejection (11.1%) and the low glomerular filtration rate (33.3%) were the most frequent reasons for not proceeding to donation, and an IF was the cause of discarding the living donor in 7 subjects (15.5%).

## IFs

A total of 20 IFs were discovered among 160 potential kidney donors. IFs were equally distributed among sex (10 male and 10 female), and patients with IFs had a mean age of  $45 \pm 12.1$  years. Among the 20 patients presenting with an incidentaloma, 7 patients were excluded from the living donation. These included 3 incidentally detected, pathologically proven malignancies in 3 potential donors (1.8%):

**Table 1. Causes of Exclusion From Living Donation**

Reasons of Exclusion	No. (45)	
	No.	%
Risk of antibody mediated rejection - positive CM	5	11.1%
Donor declined to proceed for personal reasons	4	8.8%
Complex donor anatomy	3	6.6%
Diabetes risk	1	2.2%
Hypertension	3	6.6%
Recipient contraindication	3	6.6%
Low GFR	15	33.3%
Incidental finding	7	15.5%
Recipient received deceased donor	3	6.6%
Another donor was selected	1	3%
No reasons specified	1	2.2%

Abbreviations: CM, cross-match; GFR, glomerular filtration rate.

2 patients had a lung cancer tumor of 3 and 4 cm, and survived 3 and 4 years, respectively. One patient with a 4-cm cholangiocarcinoma underwent a right hepatic bisegmentectomy and survived 3 years after surgical intervention. Other causes of exclusion from living donation were an adrenal mass in 2 patients and a large renal cyst in 2 other patients. Patients with large renal cysts required sonographic follow-up, and the 2 patients with adrenal lesion underwent a left surrenalectomy. All these patients were completely asymptomatic at the time of diagnosis.

Thirteen patients with an IF (10 renal cysts < 5 cm, 3 adrenal masses < 2 cm) completed the evaluation and successfully donated the kidney.

Kidney transplant recipients from donors with an IF had similar outcomes compared with recipients of donors without an associated IF: 1-year patient survival was 100% for both groups, and 1-year graft survival was 99% for recipients of a donor with an IF and 99.7% for recipients of donors without associated diseases ( $P = NS$ ).

One-year mean serum creatinine was similar between the 2 groups: 1.23 mg/dL for recipients of donors with incidental findings and 1.28 mg/dL for recipients of donors without IFs ( $P = NS$ ).

At a mean follow-up of 4.2 years, all living kidney donors are alive with a good renal function.

## DISCUSSION

The increasing shortage of organ donors for kidney transplantation has led most transplant centers to increase the utilization of living donors to try to close the increasing gap between the number of patients on the waiting list and the available donors. However, living donor transplantation poses some ethical issues related to maintaining the pre-donation health status of the donor and to prevent the potential long-term complications, including end-stage renal disease. In this setting, a careful evaluation of potential comorbidities and an evaluation of the renal anatomy and vasculature of prospective donors is important for planning surgery, anticipating intraoperative difficulties, and preventing postoperative complications [17].

MDCTA is the imaging modality of choice for preoperative evaluation of living renal donors, as it includes arterial, venous phase, and delayed urographic images, offering minimally invasive and accurate evaluation of renal donors with an accuracy of 95% to 100% [10,11,17]. However, the evaluation of potential living donors may lead to the serendipitous finding of previously undiscovered conditions that may impact donation [6].

The prevalence of IFs in prospective living donors have been reported with an incidence varying from 42% to 74.9% [6,11,21,22], depending on the findings considered as pathologic disease. In our overall study cohort of 160 prospective living donors, the incidence of the IFs was lower than reported in literature, and we were able to identify 20 subjects with an IF, with an overall incidence of 12.5%. This is probably related to the exclusion from the analysis of many

diseases that did not have a clinical impact (eg, hepatic steatosis), and to the exclusion of potential donors with known diseases (eg, renal stones) from the evaluation for kidney donation.

In the largest series reported in literature, Tan et al [21] evaluated 1597 potential living donors undergoing assessment with CT scan, and they found an incidental finding in the 74.9% of patients. However, among the total of 1195 incidental findings evaluated, the 95.4% were characterized as benign or low importance, leaving only 4.5% of incidental findings warranting additional workup.

Whereas most of these conditions are asymptomatic or clinically not relevant, IFs may require additional follow-up investigations in the 1.1% to 7.5% of patients [6,11,21], as reported in our study. This may determine anxiety for patients and referring physicians and could require additional and potentially unnecessary tests with increased costs and procedure-associated complications [22–24]. This is particularly true in patients who are definitely excluded from donation owing to an IF. In these subjects the fear for the uncertain prognosis of a potential life-threatening disease is added to the frustration related to the impossibility to proceed with the donation, and this would definitely increase the anxiety of these individuals.

Significant imaging findings contributed to the exclusion of 7 potential donors (4.3%) who were finally deemed unsuitable for donation. This is consistent with data reported in literature, where IFs were a cause of exclusion in up to 4.1% of patients [11,25,26].

The most common causes of exclusion were renal stones, renal scarring, and, in our experience, malignancy and large renal cysts. The prevalence of malignancy in our series was 1.8%, higher than previously reported by Tan et al [21], who reported an overall incidence of malignancy in the prospective renal donor population of 0.1%, and than that of O'Neill et al [6], who recently reported a potential donor with a superficial urothelial carcinoma (overall prevalence 0.3%).

In our population, 2 patients with lung tumor underwent a surgical resection, and the third potential donor with a cholangiocarcinoma underwent a right lobar bisegmentectomy. Interestingly, in these patients, the evaluation for potential living donation allowed for a diagnosis at an earlier stage in asymptomatic patients, allowing for a more radical surgery.

The presence of an IF did not affect survival of living donors, and there was no significant difference in terms of graft and patients survival for those patients receiving grafts from donors with an IF compared with kidney transplants from donors without IFs.

Although the presence of large renal cysts may not constitute an absolute contraindication to living donation and may be in some cases curative of donor's hypertension [27,28], the presence of a large renal cyst may reduce the normal functioning parenchyma, thereby reducing the likelihood of utilizing the kidney for living donation.

Although this study reported interesting results, we are conscious of its limitations. First, it is a retrospective review

of prospectively acquired data; however, the study population is homogeneous, thereby reducing the potential confounding factors. Second, the incidence of IFs in our population is probably underestimated, as we have a priori excluded the diseases with limited clinical impact and those patients with known comorbidities that could be considered a contraindication to living donation.

In conclusion, IFs diagnosed at CT scan during potential living donor evaluation are common. Most are not perceived to be harmful enough to prevent kidney donation, but predonation screening could identify potentially life-threatening diseases at an earlier stage, allowing for a more radical treatment.

The referring physician and the patient should be aware of the medical, economic, and ethical implications of extensive evaluation in the potential donor population.

## REFERENCES

- [1] Veroux M, Corona D, Veroux P. Kidney transplantation: future challenges. *Minerva Chir.* 2009;64:75–100.
- [2] Port FK, Wolfe RA, Mauger EA, Berling DP, Jiang K. Comparison of survival probabilities for dialysis patients vs cadaveric renal transplant recipients. *JAMA.* 1993;270:1339–1343.
- [3] Coemans M, Süsal C, Döhler B, et al. Analyses of the short- and long-term graft survival after kidney transplantation in Europe between 1986 and 2015. *Kidney Int.* 2018;94:964–973.
- [4] Veroux P, Veroux M, Puliatti C, et al. Living kidney transplantation: a starting experience. *Transplant Proc.* 2004;36:475–478.
- [5] Nemati E, Einollahi B, Lesan Pezeshki M, Porfarziani V, Fattahi MR. Does kidney transplantation with deceased or living donor affect graft survival? *Nephrourol Mon.* 2014;6: e12182.
- [6] O'Neill DC, Davis NF, Murray TÉ, Lee MJ, Little D, Morrin MM. Prevalence of incidental findings on multidetector computed tomography in potential nephrectomy donors: a prospective observational study. *Exp Clin Transplant.* 2019;17:177–182.
- [7] Kim IK, Tan JC, Lapasia J, Elihu A, Busque S, Melcher ML. Incidental kidney stones: a single center experience with kidney donor selection. *Clin Transplant.* 2012;26:558–563.
- [8] Valastro M, Veroux M, Macarone M, et al. Multi-detector row CT scanner angiography in the evaluation of living kidney donors. *Chir Ital.* 2007;59:337–341.
- [9] Lentine KL, Kasiske BL, Levey AS, et al. KDIGO clinical practice guideline on the evaluation and care of living kidney donors. *Transplantation.* 2017;101:S1–109.
- [10] Gulati M, Dermendjian H, Gómez AM, et al. 3.0 Tesla magnetic resonance angiography (MRA) for comprehensive renal evaluation of living renal donors: pilot study with computerized tomography angiography (CTA) comparison. *Clin Imaging.* 2016;40:370–377.
- [11] Chu LC, Sheth S, Segev DL, Montgomery RA, Fishman EK. Role of MDCT angiography in selection and presurgical planning of potential renal donors. *AJR Am J Roentgenol.* 2012;199:1035–1041. <https://doi.org/10.2214/AJR.11.8058>.
- [12] Rajapaksa RC, Macari M, Bini EJ. Prevalence and impact of extracolonic findings in patients undergoing CT colonography. *J Clin Gastroenterol.* 2004;38:767.
- [13] Hara AK, Johnson CD, MacCarty RL, Welch TJ. Incidental extracolonic findings at CT colonography. *Radiology.* 2000;215:353–357.
- [14] Berland LL, Silverman SG, Gore RM, et al. Managing incidental findings on abdominal CT: white paper of the ACR incidental findings committee. *J Am Coll Radiol.* 2010;7:754–773.
- [15] De Pasquale C, Veroux M, Corona D, et al. The concept of self and emotional involvement in living kidney donation: a psychometric investigation. *Transplant Proc.* 2013;45:2604–2606.
- [16] De Pasquale C, Veroux M, Sinagra N, et al. Patterns of personality in living kidney donors. *Transplant Proc.* 2016;48:319–322.
- [17] Kawamoto S, Fishman EK. MDCT angiography of living laparoscopic renal donors. *Abdom Imaging.* 2006;31:361–373.
- [18] Sorbello M, Morello G, Paratore A, et al. Fenoldopam vs dopamine as a nephroprotective strategy during living donor kidney transplantation: preliminary data. *Transplant Proc.* 2007;39:1794–1796.
- [19] Cavaleri M, Veroux M, Palermo F, et al. Perioperative goal-directed therapy during kidney transplantation: an impact evaluation on the major postoperative complications. *J Clin Med.* 2019;8:E80. <https://doi.org/10.3390/jcm8010080>.
- [20] Veroux M, Zerbo D, Basile G, et al. Simultaneous native nephrectomy and kidney transplantation in patients with autosomal dominant polycystic kidney disease. *PLoS One.* 2016;11: e0155481.
- [21] Tan N, Charoensak A, Ajwichai K, et al. Prevalence of incidental findings on abdominal computed tomography angiograms on prospective renal donors. *Transplantation.* 2015;99:1203–1207.
- [22] Mutneja A, Saling L, Yano M, Vijayan A. Financial impact of incidental radiologic findings during living kidney donor evaluation. *Transplant Proc.* 2017;49:2007–2010.
- [23] Strang AM, Lockhart ME, Kenney PJ, et al. Computerized tomographic angiography for renal donor evaluation leads to a higher exclusion rate. *J Urol.* 2007;177:1826–1829.
- [24] Maizlin ZV, Barnard SA, Gourlay WA, Brown JA. Economic and ethical impact of extrarenal findings on potential living kidney donor assessment with computed tomography angiography. *Transpl Int.* 2007;20:338–342.
- [25] Hsu TH, Su LM, Ratner LE, Kavoussi LR. Laparoscopic donor nephrectomy in the elderly patient. *Urology.* 2002;60:398–401.
- [26] The British Transplantation Society and The Renal Association. *United Kingdom Guidelines for Living Donor Kidney Donation.* 4th ed; 2018 [accessed November 2018]. <https://bts.org.uk/wp-content/uploads/2016/09/LDKidneyDonation.pdf>.
- [27] Veroux P, Veroux M. Complete remission of hypertension after successful living donation of a kidney with a large benign cyst. *Transplantation.* 2002;74:744.
- [28] Veroux P, Veroux M, Puliatti C, et al. Living transplantation using a kidney with a large cyst as curative treatment of donor's hypertension. *Nephrol Dial Transplant.* 2002;17:2258.