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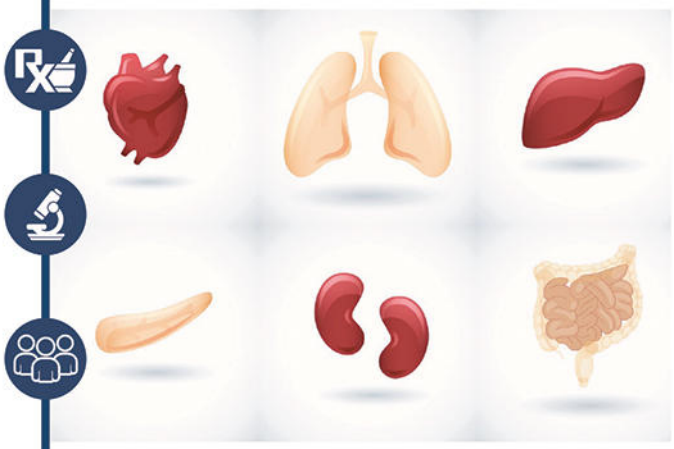

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BRIEF COMMUNICATION

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Fortuitous benefits of living kidney donation: Diagnosis of serious medical conditions during the living donor evaluation

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Abstract

Background: All living kidney donors are counseled about the possible surgical and medical risks associated with donation. Only a minority of transplant centers discuss the potential benefit of discovering undiagnosed medical conditions in the donor during evaluation, as part of their consent process.

Methods: We retrospectively investigated all potential living kidney donors evaluated over a 10-year period at a single center to characterize incidentally diagnosed serious medical conditions.

Results: Sixty-five of the 762 potential donors (8.5%) were not approved for donation because of a newly diagnosed serious medical condition discovered during their evaluation. This included six patients diagnosed with malignancies, five of which required operative intervention, six patients diagnosed with transmittable diseases requiring follow-up and treatment, four patients were found to have bilateral renal stones with significant stone burden, and two patients diagnosed with IgA nephropathy. Additionally, four patients were diagnosed with significant heart disease, and one of those patients subsequently required a coronary artery bypass surgery.

Conclusions: The evaluation process can diagnose serious medical conditions in a significant minority of donors that would have otherwise been unrecognized. The benefit associated with the donor evaluation should be considered an important part of the consent process.

KEYWORDS
living donor evaluation, transplantation

1 | INTRODUCTION

Transplant programs have an obligation to screen potential living kidney donors for medical conditions that could place them at risk for future complications.[1] Although the live kidney donor evaluation process is not standardized between institutions, the Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) does hold transplant centers uniformly responsible to perform certain medical review and testing.[1,2] This includes collection of basic demographic and medical information on all potential donors, with those who pass initial screening continuing on to a more comprehensive evaluation including a medical, surgical, and psychological interview as well as laboratory and radiographic testing. This comprehensive evaluation may reveal undiagnosed medical conditions that require further workup and potentially treatment.

The OPTN also has requirements for the consent of living donors that include voluntariness, confidentiality, disclosure of potential health risks, and recommendations for follow-up.[3] Living kidney donors are extensively counseled about the risk of surgery and long-term risks associated with kidney donation. Additionally, most potential

TABLE 1 Diagnosis of medical condition during the living donor evaluation

(a) Incidental finding	Finding	Age	Race	Sex	Relationship
Renal	Bilateral renal stones	42	White	Male	Unrelated
	Solitary kidney	64	White	Male	Related
	Papillary necrosis	23	White	Female	Related
	Bilateral peripelvic renal cyst	59	White	Female	Related
	Bilateral renal stones/hydronephrosis	33	White	Female	Related
	Bilateral renal stones	37	White	Female	Related
	Bilateral renal stones (>8 stones)	36	White	Female	Related
	Dysplastic left kidney	40	White	Female	Related
	Congenital UPJ obstruction	70	White	Male	Related
	Fibromuscular dysplasia	55	White	Female	Related
	Fibromuscular dysplasia	34	White	Female	Unrelated
	Horseshoe kidney	42	White	Female	Related
	Horseshoe kidney	32	White	Female	Related
Viral screening	Hepatitis B and C	60	White	Female	Related
	Hepatitis C	50	Black	Female	Related
	Hepatitis C	60	White	Female	Related
	Hepatitis C	30	White	Female	Related
	Hepatitis B	50	Black	Female	Unrelated
	Hepatitis C	36	White	Male	Unrelated
Malignant	Left breast adenocarcinoma	49	White	Female	Related
	Right renal cell carcinoma	57	White	Male	Unrelated
	Right renal cell carcinoma	39	White	Male	Unrelated
	Colon adenocarcinoma	52	White	Male	Unrelated
	IPMN	49	White	Female	Related
	Germ cell tumor	32	White	Female	Unrelated
	Prostate cancer	50	White	Male	Unknown
Cardiac conditions	Coronary artery disease	55	White	Female	Related
	Concentric LVH	50	White	Male	Related
	LVH/diastolic dysfunction	57	Hispanic	Female	Related
	Concentric LVH	50	White	Male	Related
Incidentaloma	Adrenal nodule, staghorn renal stones	59	White	Male	Related
	Adrenal nodule	48	White	Male	Unrelated
Hematuria	Alport syndrome	39	White	Female	Related
	TBMD[a]	49	White	Male	Related
	IgA nephropathy[b]	48	White	Female	Unrelated
	IgA nephropathy	50	White	Female	Related
	TBMD	54	White	Female	Related
Incidental/NOS	Monoclonal B-cell proliferation	68	White	Female	Unrelated
	Autoimmune hepatitis	55	White	Female	Related

(b) Hypertension	Newly diagnosed[c] N = 17	Preexisting hypertension N = 21	*P* value
Median age	40.8 years	47.6 years	.6691
Male	41.1%	47.6%	.6925
White race	94.1%	90.5%	.6863
Relationship (related)	47.0%	57.1%	.5447

(Continues)

TABLE 1 (Continued)

(c) Impaired glucose tolerance (N = 9)	Newly diagnosed
Median age	36.3 years
Male	33.3%
White race	77.7%
Relationship (related)	66.6%

[a]Thin basement membrane disease (TBMD) discovered on renal biopsy.
[b]Segmental mesangial IgA deposits discovered on renal biopsy.
[c]Patients with newly diagnosed hypertension presented to clinic with elevated blood pressure on the intake assessment and were subsequently given ambulatory blood pressure monitoring, which confirmed a new diagnosis of hypertension.

donors are educated that there is no obvious medical benefit associated with kidney donation. Nearly all transplant centers performing living donor transplant have a written consent form describing the required medical and psychological risk associated with donation, while only 30% of consent forms list discovering previously undiagnosed health problems as a benefit to the donor.[3] In fact, more transplant centers listed the satisfaction of helping others as a potential benefit to the donor. However, the exact extent of medical benefit for the donor, in the form of incidental discovery of disease, associated with the evaluation process is unknown as data on this topic are sparse.

We therefore sought to characterize the frequency and nature of incidentally diagnosed serious medical condition among potential living donors during the evaluation process.

2 | METHODS

A retrospective study of all living kidney donor evaluations between January 1, 2006 and December 31, 2015 at the University of Nebraska Medical Center was performed. Serious medical condition was defined as a diagnosis that was of sufficient severity that resulted in a decision of the institutional donor selection committee to deem the individual ineligible to be a living kidney donor and required further testing and/or treatment. For the purpose of this analysis, previously undiagnosed medical conditions discovered as a direct result of the living donor evaluation were considered to be incidental.

3 | RESULTS

Of the 762 individuals completing living donor evaluation during the study period, 324 were determined to be ineligible by the donor selection committee. Of these, 65 individuals were found to have incidental serious medical conditions (that is 20.0% of ineligible donors and 8.5% of all individuals evaluated), (Table 1). The most common incidental diagnosis in a potential donor was hypertension based on ambulatory blood pressure monitoring (26%) (Table 1b). Impaired glucose tolerance was found in nine of the 65 potential donors excluded for an incidental finding (13.8%) (Table 1c). An analysis of these 65 declined potential donors, all accepted donors, and all ineligible donors due to preexisting conditions is seen in Table 2. There was no significant difference between the median age, gender, or race in the study population. However, a diagnosis of a serious medical condition at the time of the living donor evaluation was significantly more likely to occur in potential donors who were related to their recipient ($P = .0004$). Psychological conditions were the most common reason for a potential donor to be declined for a preexisting condition (11.7%) (Table 3). The second most common reason was obesity (9.0%).

All 65 potential donors with serious medical conditions were referred for evaluation and/or treatment. Six of the 65 (9.2%) potential donors were found to have an undiagnosed malignancy.

The potential donors who were found to have malignancies are described below. A 49-year-old woman was diagnosed with stage IIB left breast adenocarcinoma discovered on screening mammogram and underwent a left radical mastectomy followed by adjuvant chemotherapy. A 57-year-old man was diagnosed with right T1a (3.1 cm) renal cell carcinoma. He underwent a radical nephrectomy approximately 1 month after his initial evaluation. A 39-year-old man who was also diagnosed with right T1a renal cell carcinoma underwent a partial nephrectomy approximately 2 months after the initial donor evaluation. A 50-year-old man was diagnosed with prostate cancer due to an elevated PSA level during screening. He subsequently underwent a radical prostatectomy. A 52-year-old man was diagnosed with colon adenocarcinoma discovered on colonoscopy after his CT angiography revealed mesenteric adenitis and fullness in the ascending colon. The biopsy performed during colonoscopy revealed poorly differentiated adenocarcinoma. He was referred to a local surgeon for treatment. A 49-year-old woman was diagnosed with cystic neoplasm of the pancreas on CT angiography. She underwent a pylorus-preserving pancreaticoduodenectomy. A 36-year-old woman was diagnosed with a mediastinal germ cell tumor when a 7.9 cm × 4.4 cm mass was partially viewed on CT angiography. She was referred to a center within her hometown for treatment.

Five of the 65 (7.6%) were found to have persistent hematuria during the donor evaluation. All five patients underwent a renal biopsy in which two of the five were diagnosed with IgA nephropathy. One patient was diagnosed with Alport syndrome.

Six of the 65 (9.2%) potential donors were found to have transmittable diseases, most commonly hepatitis C. Four potential donors

TABLE 2 Analysis of study population

	All accepted donors	Declined donors: preexisting conditions	Declined donors: incidental findings	*P* value donors with incidental findings vs donors without incidental findings
Number	438	259	65	
Median age	43 years	42.3 years	44.5 years	.808
Male	36%	37.5%	34.7%	.827
White race	87%	84.6%	91.2%	.204
Related	61.0%	54.2%	79%	.0004
Unrelated spouse	11.0%	9.9%	8.7%	.635
Other unrelated	22.1%	33.0%	11.2%	.002
Anonymous	4.3%	3.1%	1.1%	.253

TABLE 3 Analysis of ineligible donors due to preexisting conditions

Preexisting conditions N = 259	Ineligible donors
Cardiac	2.2%
Hypertension	8.3%
Obesity	9.0%
Psych/SW denial	11.7%
Renal function[a]	1.3%
Failure to complete additional testing	5.4%
Anomaly NOS[b]	13.1%

[a]Renal function refers to donors who were ineligible because their renal function was not appropriate for the recipient size and the donor did not want to enter a paired exchange.
[b]Anomaly NOS includes potential donors with previous cancer, renal vascular anomalies on CT angiography, pulmonary abnormalities, and patients with tobacco abuse.

were found to have significant cardiac disease. One of the patients was found to have asymptomatic coronary artery disease diagnosed after a positive stress test performed during the evaluation process. Her strong family history of coronary artery disease in three first degree relatives prompted a stress echocardiogram. She subsequently underwent a coronary artery bypass graft surgery 15 days later. One patient was found to have left ventricular hypertrophy and diastolic dysfunction after a diagnosis of hypertension during the evaluation appointment led to an echocardiogram. Concentric left ventricular hypertrophy was diagnosed in two potential donors after an EKG showed minimal voltage criteria.

One patient was diagnosed with autoimmune hepatitis after being found to have abnormal liver function studies. Her workup included a liver biopsy and referral to a gastroenterologist. She was treated initially with steroids and then azathioprine. Both patients diagnosed with adrenal nodules underwent biochemical analysis, and no operative intervention was indicated. One patient had bilateral staghorn renal stones in addition to the incidentaloma and was ultimately declined as a donor. The other patient was followed with Endocrinology for repeat biochemical testing for 1 year, but ultimately was denied for psychological reasons.

4 | DISCUSSION

The OPTN requires that all consent forms for living donor renal transplant include the statement "the potential donor understands that he or she will undertake risk and will receive no medical benefit from the operative procedure of donation."[3] As the largest single-center analysis of serious medical conditions diagnosed during the evaluation process, this study suggests that living kidney donation could have benefits for both the donor and recipient. Most of the emerging data to date, supporting this idea, have been in the setting of incidental renal masses.[4,5] The discovery of incidentally discovered malignancy in the evaluated donor population has been previously described. The reported rate of incidental diagnosis of malignancy during donor evaluation is 0.2%-0.8%, and our study corroborates these data with a rate of incidental malignancy diagnosis of 0.5%.[6,7]

We found kidney stones that precluded donation in five patients (1.5% of excluded potential donors; 0.6% of overall donors). The risk of clinical stone recurrence in donors and recipients is low, and thus, small stones are not an exclusion for living kidney donation.[8] However, according to Amsterdam guidelines, bilateral kidney stones precludes donation,[9] which led to the exclusion of these subjects in our database.

Hepatitis B and/or C was identified in six subjects in our cohort (1.8% of excluded donors; 0.8% of the entire cohort). These included four patients with hepatitis C, one with hepatitis B, and one with both hepatitis B and C. To our knowledge, there are no data on the prevalence of hepatitis in living kidney donors. According to the Amsterdam guidelines, hepatitis C-positive donors should be excluded if the recipient is negative.[9] However, with the development of newer curative options for hepatitis C, these individuals could potentially be considered for potential donation after completion of a curative course of therapy.[10]

Multiple studies have examined medical barriers to donation, and one study reported a new diagnosis of hypertension was found during

the evaluation in 25% of excluded donors.[11] We found no significant difference in the demographics of potential donors who had preexisting hypertension and those who were newly diagnosed. Even though no significant difference was found in the median age of the two groups, potential donors with a new diagnosis of hypertension tended to be younger. Not only does the donor evaluation diagnose individuals with hypertension, impaired glucose tolerance, and adrenal incidentaloma, but it can discover other serious medical conditions that may require surgical intervention, long-term follow-up, and treatment in otherwise asymptomatic individuals. We propose that all transplant centers discuss the potential for direct medical benefit to the donor candidate as a result of the living donor evaluation.

CONFLICT OF INTEREST

None.

AUTHORS' CONTRIBUTIONS

Arika Hoffman: participated in the concept, performance of research, article writing, and research design; Ketki Tendulkar: participated in the concept, article writing, and critical review of article; Shaheed Merani: participated in the performance of the research, article writing, and critical review of article; Alexander Maskin: participated in concept of research, drafting article, and approval of article; Alan Langnas: participated in research design, research concept, and critical review of article.

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