



# Practice Patterns in the Acceptance of Medically Complex Living Kidney Donors with Obesity, Hypertension, Family History of Kidney Disease, or Donor-Recipient Age Discrepancy

Ziad Arabi<sup>1</sup> Muhammad Bukhari<sup>2</sup> Abdullah Hamad<sup>3</sup> Abdulrahman Altheaby<sup>1</sup> Saleh Kaysi<sup>4</sup>

<sup>1</sup>Department of the Organ Transplant Center, Division of Adult Transplant Nephrology, King Abdulaziz Medical City, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

<sup>2</sup>Department of Medicine, Division of Adult Nephrology, Taif University, Taif, Saudi Arabia

<sup>3</sup>Department of Medicine, Division of Nephrology, Regional Medical Center of Orangeburg and Calhoun Counties, Orangeburg, South Carolina, United States

<sup>4</sup>Department of Medicine, Division of Nephrology, CHU, Clermont-Ferrand, France

**Address for correspondence** Ziad Arabi, MD, Department of the Organ Transplant Center, Division of Adult Transplant Nephrology, King Abdulaziz Medical City, Riyadh, Saudi Arabia (e-mail: ziadarabi@yahoo.com).

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## Abstract

**Background** To assess the practice patterns of the acceptance of medically complex living kidney donors (MCLKDs).

**Methods** We distributed a survey to nephrologists and transplant surgeons (TS) across the world through major international transplant societies. The survey contained questions regarding obesity, abnormal blood glucose profile, mild hypertension, donor-recipient age discrepancy, or family history of kidney disease of unknown etiology.

**Results** In total, 239 respondents from 29 countries (42% were nephrologists and 58% were TS).

Most respondents would allow donations from obese donors, especially if they intended to lose weight but would be cautious if these donors had abnormal blood glucose or family history of diabetes mellitus. In hypertensive donors, future pregnancy plans mattered in decisions regarding the acceptance of female donors. Most respondents would allow young donors but would be more cautious if they had a future risk of hypertension or a family history of kidney disease of unknown etiology. They would also allow donations from an older person if prolonged waiting time was anticipated. We found multiple areas of consensus of practice among the diverse members of international transplant societies, with some interesting variations among nephrologists and TS.

**Conclusions** This survey highlights the practice patterns of the acceptance of MCLKDs among the international community. In the absence of clear guidelines, this survey provides additional information to counsel kidney donors with these conditions.

## Keywords

- ▶ Age
- ▶ Diabetes
- ▶ Extended criteria
- ▶ Family history of kidney disease
- ▶ Gender
- ▶ Hypertension
- ▶ Living kidney donor
- ▶ Metabolic syndrome
- ▶ Obesity
- ▶ Pregnancy
- ▶ Survey

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## Introduction

Potential living kidney donors (LKDs) are frequently found to have borderline medical or surgical abnormalities, complicating the evaluation of kidney donation. These donors are often referred to as medically complex living kidney donors (MCLKDs). MCLKDs have many medical conditions such as obesity, mildly abnormal glucose profile, mild hypertension, or family history (FH) of kidney disease.<sup>1</sup> Although the exact prevalence of MCLKDs in an entire pool of donors is unknown, they constitute approximately at least 25% of LKDs.<sup>2</sup>

Kidney donations carry potential risks long-term risks, especially end-stage kidney disease (ESKD) for donors.<sup>3-6</sup> These risks are potentially higher in MCLKDs. The guidelines for kidney donation do not adequately address several controversial issues of MCLKDs due to lack of evidence-based data.<sup>7-9</sup> Similarly, online risk calculators can provide general estimations of risk of ESKD after kidney donation<sup>10,11</sup> but this does not apply to MCLKDs. The renal functional reserve of donors in the long-term cannot be accurately predicted at the time of donation.<sup>12</sup> Thus, experts' perspectives on the utility and acceptance of MCLKDs may vary.<sup>13,14</sup>

This study aimed to assess the practice patterns of the acceptance of MCLKDs with obesity, abnormal glucose profile, hypertension, FH of kidney disease of unknown etiology and donor-recipient age discrepancy, and to explore the areas of practice where guidelines are most needed.

## Materials and Methods

The survey was based on a thorough literature review of studies on LKDs with complex medical problems,<sup>1,2,13-16</sup> group discussion with expert transplant specialists (from nephrology and surgical fields), clinical experiences of dealing with these difficult cases, trends of transplant societies, and controversies arising in conferences. Our survey consisted of 31 questions. The first five questions focused on the demographic characteristics of the participants. The first 17 questions of the survey are discussed in this paper, and the remaining 9 questions are discussed in our concurrent submission. The questions discussed in this paper were grouped into four domains, representing the most frequently encountered and challenging issues about suitability and acceptance of MCLKDs: (1) obesity or abnormal glucose profile (8 questions), (2) mild hypertension (3 questions), (3) donor-recipient age discrepancy (4 questions), and (4) donors with FH of kidney disease of unknown origin (2 questions).

The cross-sectional survey was distributed to participants using SurveyMonkey after obtaining approval from the Institutional Review Board (IRB) (RC19/149/R). Six international transplant societies were contacted to distribute the survey to their members, including nephrologists and transplant surgeons (TS). However, only the American Society of Transplantation (AST), the American Society of Transplant Surgeons (ASTS), and the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) responded. Three transplant societies did not participate due to not responding.

The survey was distributed between June 2019 and February 2020 by the participating societies according to their respective policies. (AST: through the society email and directly to the members with five subsequent reminders, ERA-EDTA: by publishing the survey on its Web site, and ASTS: by using the "survey rental" of the society to email the questionnaires to the members with five subsequent reminders).

The inclusion criteria were as follows: practicing nephrologists and TS. In training or nonpracticing nephrologists or TS were requested not to participate. After obtaining informed consent online, participants were requested to choose the best option for the given scenarios. The frequency of the total responses to the questions was reported as the number and percentage of the total number of participants, nephrologists, and TS. SPSS (version 24) was used for data analysis. Comparisons were performed using  $\chi^2$  test or Fisher's exact test as appropriate. Two-sided *p*-values of less than 0.05 were defined as statistically significant.

## Results

### Demographic Characteristics of Participants

A total of 239 nephrologists and TS from 29 countries responded to the survey; 64% ( $n = 154$ ) of the respondents were from the United States. Among these, 42% ( $n = 100$ ) were nephrologists and 58% ( $n = 139$ ) were TS. Majority of the respondents (77%) had many years of work experience (> 6 years in practice) and were also heavily involved in pretransplant evaluations of donors and recipients. **Table 1** summarizes the demographic characteristics of the respondents.

Among the respondents, compared with nephrologists, TS had more years of work experience and were more involved in pretransplant evaluations of donors and recipients. Moreover, TS were more likely to be practicing in the United States ( $p < 0.05$ ), as shown in **Table 1**.

The response rate of the living donor and kidney and pancreas committee members of AST was 5.5%. The response rate of ASTS members was 10.4. Due to the nature of the survey distribution method by web posting through EDTA-ERA, the response rate could not be attained. The total responses from ERA-EDTA constituted 19% of the entire responses of the survey though. The survey completion rate (the rate at which the respondents completed the survey entirely) was 99%.

### Evaluation of Medically Complex Donors

#### Obesity or Abnormal Glucose Profile

From the data analysis, we found that obesity stage I (body mass index [BMI] 30-35) was not considered as a major challenge for kidney donation. Of the respondents, 75% answered that they would accept obese donors if they showed some weight loss before donation or if they were at least committed to losing weight in the future. In contrast, 76% felt that donors with obesity stage II (BMI 36-40) would require some weight loss or reduction of BMI to 30.

**Table 1** The characteristics of participants

Characteristic	Answers	Nephrologists	TS	p-Value	Total
		100 (41.5%)	139 (57.7%)		239 (100%)
Practice	< 1 year	3 3%	2 1.4%	0.022	5 2.1%
	1–5 years	29 29%	19 13.7%		48 20.1%
	6–10 years	14 14%	24 17.3%		38 15.9%
	More than 10 years.	54 54.4%	94 67.6%		148 61.9%
Do you assess donors for pretransplant workup?	On a weekly basis.	50 50%	77 55.4%	0.006	127 53.1%
	On a monthly basis.	15 15%	36 25.9%		51 21.3%
	Not on a regular basis.	21 21%	21 15.1%		42 17.6%
	I do not do donor assessment.	14 14%	5 3.6%		19 7.9%
Do you assess recipients for pretransplant workup?	On a weekly basis.	55 55%	113 81.9%	< 0.001	168 70.6%
	On a monthly basis.	16 16%	15 10.9%		31 13%
	Not on a regular basis.	11 11%	8 5.8%		19 8%
	I do not do a pretransplant assessment, but I see postrenal transplant patients.	6 6%	1 0.7%		7 2.9%
	I do not do a pretransplant assessment and I do not follow renal transplant patients.	12 12%	1 0.7%		13 5.5%
Country	United States	42 42.4%	112 81.8%	< 0.001	154 65.3%
	Saudi Arabia	9 9.1%	4 2.9%		13 5.5%
	Pakistan	10 10.1%	2 1.5%		12 5.1%
	Sudan	8 8.1%	1 0.7%		9 3.8%
	Canada	4 4%	4 2.9%		8 3.4%
	Other	26 26.3%	14 10.2%		40 15.9%

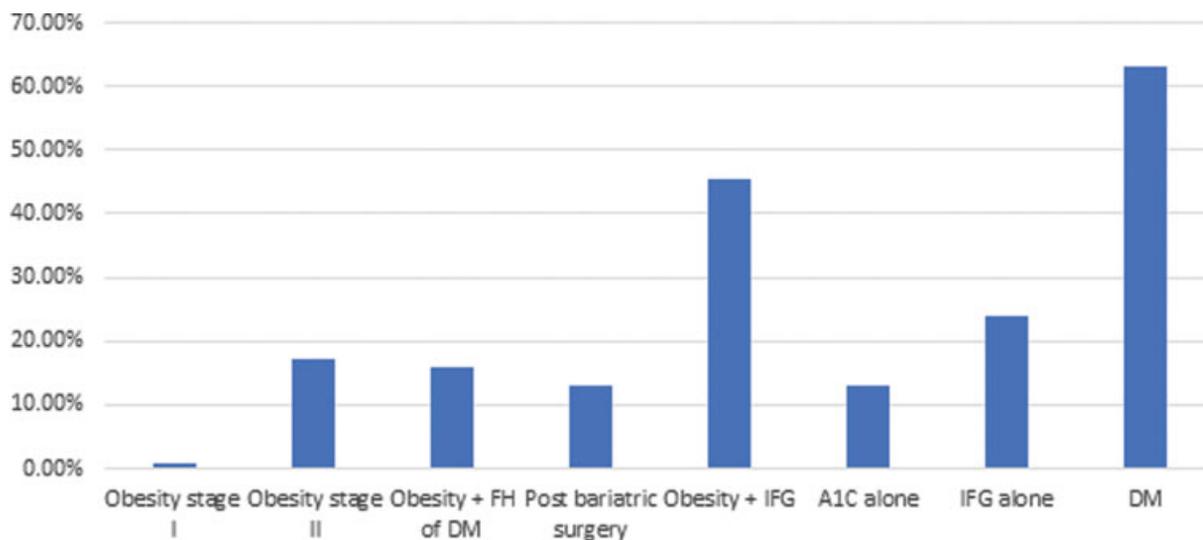
Abbreviation: TS, transplant surgeon.

Moreover, 17% of the respondents answered that they would decline such donors without considering weight reduction due to the risk of relapse of obesity.

Only 45% of the respondents would accept obese candidates with a strong FH of diabetes mellitus (DM), including those with normal fasting glucose (FG) and hemoglobin A1C (HgbA1C). Moreover, a significant number of respondents would not accept such candidates unless they lost weight and reduced their BMI to an acceptable level of 30 (32%) or 25 (7%). Only < 1% answered that they would decline an obese donor candidate (BMI if 30–35) with normal glucose profile.

However, the decline rate significantly increased to 16% for the same donor if they had a strong FH, as obesity is likely to relapse in such a case ( $p < 0.001$ ).

Regarding obese donors with impaired fasting glucose (IFG), 45% of the respondents would decline the kidney donation. Among the respondents, 32% would delay kidney donation until BMI is reduced to below 30 with resolution of impaired fasting glucose (IFG) which is secondary to weight reduction. More than half of the respondents (55%) would not rely solely on isolated mildly elevated Hgb A1C or isolated IFG as the critical indicator for declining a young donor with



**Fig. 1** The decline rate of medically complex donors with obesity or abnormal glucose profile.

normal weight and normal FG, but they would include a glucose tolerance test (GTT) to decide on whether to accept such donors.

Of the respondents, 63% indicated that the presence of even mild and controlled diabetes in a middle age-old donor was a contraindication for kidney donation. However, such donors might be allowed to donate if no alternative donor was available after counseling them about the risks involved (24%). Regarding potential donors with resolved DM due to weight loss after bariatric surgery, 36% of the respondents would consider them for donation if obesity did not relapse 2 years after the surgery. Additionally, 47% may consider such donors earlier (once BMI is below 30, 29%), while 18% may consider them immediately after bariatric surgery.

Isolated obesity stage I (with normal blood profile) was not considered an absolute contraindication for kidney donation (only < 1% of the respondents would decline such candidates). However, the decline rate increased significantly when other risk factors were included (up to 16% in the presence of FH [ $p < 0.001$ ], 17% in obesity stage II [ $p < 0.001$ ], and 45% in IFG [ $p < .0001$ ]). Only 13% of the respondents would immediately decline a young donor based on Hgb A1C alone, but almost twice as many (24.5%) would rely on IFG alone to decline a similar donor ( $p = 0.001$ ), as indicated in **Fig. 1**.

Compared with nephrologists, TS were more likely to accept obese donor candidates, obese candidates with an FH of DM, or postgastric sleeve ( $p < 0.05$ ). **Table 2** summarizes the survey data regarding donors with obesity or abnormal glucose profile.

#### Mild Hypertension

Majority of the respondents ( $n = 165$ , 69%) would allow a multiparous woman with hypertension to donate if she had mild and controlled hypertension (on single blood pressure [BP] medication) and was not planning on having more children. The remaining respondents would either advise

against donation unless there is no alternative donor ( $n = 39$ , 16%) or decline the donation ( $n = 33$ , 13.9%). In contrast, more respondents would reject a primiparous woman to donate in the same clinical scenario if she was considering having children ( $n = 103$ , 43%) or accept her only if there was no alternative donor ( $n = 74$ , 31%).

Most respondents would not allow a 20-year-old man to donate with apparent white coat hypertension if his 24-hour ambulatory BP monitoring (ABPM) showed a nondipping nocturnal pattern ( $n = 130$ , 54.6%) or they would accept him only if there was no alternative donor ( $n = 64$ , 26.9%). No differences were observed between the opinions of nephrologists and surgeons regarding these three questions. **Table 3** summarizes the survey data regarding donors with hypertension issues.

#### Donor-Recipient Age Discrepancy

Most respondents ( $n = 170$ , 71.1%) would allow an 18-year-old man to donate after counseling. However, this percentage decreased ( $n = 136$ , 57.1%) if it was an 18-year-old female candidate ( $p = 0.001$ ), which reflects the impact of childbearing as a major concern in considering kidney donation. On the contrary, approximately 20% of the respondents would decline the donor regardless of the donor's gender. The acceptance rate of an 18-year-old donor dropped significantly to 43% ( $n = 102$ ) if the recipient was a 75-year-old. However, in the case of a donor over 65 years, and an 18-year-old recipient, with expected prolonged waiting time for a deceased donor, 66% ( $n = 157$ ) of the respondents would advise finding an alternative donor but allow the donation if no alternative donor was available. Of the respondents, 28% would decline an 18-year-old donor for a 75-year-old recipient but only 9% would decline 65-year-old donor for an 18-year-old recipient ( $p < 0.001$ ). **Table 4** summarizes the responses to questions regarding donor-recipient age discrepancy.

**Table 2** The acceptance of the MLKD with obesity or abnormal glucose profile

Question	Answer choices	Nephrologist	TS	p-Value	Total
Q1. The donor is <b>obese</b> (BMI 30–35) with normal (fasting blood sugar and hemoglobin A1C) and no family history of diabetes):	I will allow this donor to donate now if the donor is intending to lose weight later.	34 34.00%	74 53.60%	0.030	108 45.4%
	I will allow this donor to donate once he/she demonstrates some weight loss.	38 38.00%	34 24.6%		72 30.3%
	I will NOT consider this donor to donate until he achieves a BMI: 30.	22 22.0%	25 18.1%		47 19.7%
	I will NOT consider this donor to donate until he achieves a BMI: 25.	5 5.0%	4 2.9%		9 3.8%
	I will deny this donor because obesity is a chronic problem and relapse is likely.	1 1.0%	1 0.7%		2 0.8%
Q2. The donor is <b>obese and has a strong family history of diabetes</b> (but normal fasting blood sugar and hemoglobin A1C):	I will allow this donor to donate now if the donor is intending to lose weight later.	10 10.0%	35 25.4%	0.004	45 18.9%
	I will allow this donor to donate once he/she demonstrates some weight loss.	21 21.0%	41 29.7%		62 26.1%
	I will NOT consider this donor to donate until he achieves a BMI: 30.	40 40.0%	36 26.1%		76 31.9%
	I will NOT consider this donor to donate until he achieves a BMI: 25.	10 10.0%	7 5.1%		17 7.1%
	I will deny this donor because obesity is a chronic problem and obese donors tend to regain weight after donation.	19 19.0%	19 13.8%		38 16.0%
Q3. The donor is <b>obese stage 2</b> (BMI 36–40) with normal fasting blood sugar, hemoglobin A1C and Negative family history of diabetes	I will allow this donor to donate now if the donor is intending to lose weight later.	2 2.0%	8 5.8%	0.020	10 4.2%
	I will allow this donor to donate once he/ she demonstrates some weight loss.	24 24.0%	55 39.9%		79 33.2%
	I will NOT consider this donor to donate until he achieves a BMI: 30.	49 49.0%	53 38.4%		102 42.9%
	I will NOT consider this donor to donate until he achieves a BMI: 25.	2 2.0%	4 2.9%		6 2.5%
	I will decline this donor because obesity is a chronic problem and obese donors tend to regain weight after donation.	23 23.0%	18 13.0%		41 17.2%
Q4. The donor is <b>obese and has impaired fasting blood sugar</b> :	I will allow this donor to donate now but the donor needs to lose weight later and to follow his/her blood sugar.	1 1.0%	1 0.7%	0.225	2 0.8%
	I will allow this donor to donate once impaired BS is resolved due to some weight reduction.	11 11.1%	29 21.0%		40 16.9%
	I will allow this donor to donate once impaired BS is resolved and BMI is below 30 due to weight reduction.	31 31.3%	45 32.6%		76 32.1%
	I will allow this donor to donate once impaired BS is resolved and	6 6.1%	5 3.6%		11 4.6%

Table 2 (Continued)

Question	Answer choices	Nephrologist	TS	p-Value	Total
	BMI is below 25 due to weight reduction.				
	I will decline this donor because this donor is at high risk to develop diabetes.	50 50.5%	58 42.0%		108 45.6%
Q5. A young donor with normal weight and normal fasting blood sugar but <b>mildly elevated HbA1C</b> (e.g., HbA1C = 5.7–6)	I will allow this donor to donate now after giving him/her the appropriate advice to manage prediabetes.	13 13.1%	20 14.4%	0.264	33 13.9%
	I will repeat A1C in 3 months and I will decline the donor if still elevated.	16 16.2%	25 18%		41 17.2%
	I will ask for 2 hour. GTT and I'll decline the donor if both GTT and HbA1C are elevated.	52 52.5%	81 58.3%		133 55.9%
	I will decline this donor donate due to his/her A1C and young age.	18 18.2%	13 9.4%		31 13.0%
Q6. A young donor with normal weight and normal HbA1C but <b>impaired fasting blood sugar</b>	I will allow this donor to donate now after giving him/her the appropriate advice to manage prediabetes.	13 13.3%	12 8.6%	0.066	25 10.5%
	I will repeat A1C in 3 months and I will decline the donor if still elevated.	8 8.2%	14 10.1%		22 9.3%
	I will ask for 2 hour. GTT and I'll decline the donor if both GTT and HbA1C are elevated.	46 46.9%	86 61.9%		132 55.7%
	I will decline this donor donate due to his/her impaired fasting sugar and young age.	31 31.6%	27 19.4%		58 24.5%
Q7. A <b>middle age</b> (e.g., 55 years old) donor <b>with diabetes</b> for one year and controlled with monotherapy and diet.	I will allow this donor to donate now.	6 6.0%	9 6.5%	0.629	15 6.3%
	I will allow this donor to donate if his diabetes gets controlled without any medication (with diet only).	8 8.0%	6 4.3%		14 5.9%
	I will advise him against donation, but I may allow him/her to donate if no alternative donor is available.	22 22.0%	36 25.9%		58 24.3%
	I will not clear this donor to donate even if there is no alternative living-donor is available.	64 64.0%	88 63.3%		152 63.6%
Q8. The donor is <b>postgastric sleeve</b> due to stage II obesity (BMI 36–40) and his diabetes has resolved with weight loss:	I will accept this donor for immediate donation (once surgically doable).	9 9.0%	34 24.5%	0.001	43 18.0%
	I will consider this donor for donation once BMI is below 30.	24 24.0%	46 33.1%		70 29.3%
	I will consider this donor for donation once BMI is down to 25.	6 6.0%	1 0.7%		7 2.9%
	I will consider this donor for donation if two years passed after bariatric surgery without obesity relapse.	44 44.0%	43 30.9%		87 36.4%
	I will not consider this donor for donation.	17 17.0%	15 10.8%		32 13.4%

Abbreviations: BMI, body mass index; BS, blood sugar; GTT, glucose tolerance test; MCLKD, medically complex living kidney donors; TS, transplant surgeon.

**Table 3** The acceptance of MCKLD with mild hypertension

Question	Answer choices	Nephrologists	TS	p-Value	Total
Q9. The donor is <b>multiparous women with mild and controlled hypertension</b> (only on one BP medication). She is NOT planning to have more children.	I allow her to donate after counselling her about the future risk after donation.	69 69.0%	96 70.1%	0.302	165 69.6%
	I will advise her not to donate but I will allow the donation if no alternative donor is available.	20 20.0%	19 13.9%		39 16.5%
	I will DECLINE this donor.	11 11.0%	22 16.1%		33 13.9%
Q10. The donor is <b>primiparous women with mild and controlled hypertension</b> (only one BP medication). She is considering having children later.	I allow her to donate after counselling her about the future risk after donation.	21 21.2%	40 28.8%	0.417	61 25.6%
	I will advise her not to donate but I will allow the donation if no alternative donor is available.	33 33.3%	41 29.5%		74 31.1%
	I will DECLINE this donor.	45 45.5%	58 41.7%		103 43.3%
Q11. A 20-year-old man with <b>high BP readings at the office</b> and a non-dipping pattern at night on his 24 hour ambulatory BP monitoring which is otherwise normal.	I allow him to donate after counselling.	13 13.0%	31 22.5%	0.178	44 18.5%
	I will advise him not to donate. However, I will allow the donation if no alternative donor is available.	29 29.0%	35 25.4%		64 26.9%
	I will DECLINE this donor.	58 58.0%	72 52.2%		130 54.6%

Abbreviations: BP, blood pressure; MCKLD, medically complex living kidney donors; TS, transplant surgeon.

### Family History of Kidney Disease of Unknown Etiology

Almost half of the respondents ( $n = 122$ , 47%) would not accept a young donor with a strong FH of kidney disease of unknown etiology despite negative evaluation. The rate of approval increased slightly when there was no alternative donor and the donor insisted on donating due to being a closer relative (e.g., mother) ( $n = 125$ , 53% to  $n = 157$ , 67%;  $p = 0.004$ ). The difference in the views of nephrologists and TS were not statistically significant. **Table 5** summarizes the responses to questions regarding donors with an FH of kidney disease of unknown etiology.

### Discussion

Evaluating LKDs with obesity is challenging. Obesity is commonly divided into the following three categories: stage I (BMI of 30 to <35), stage II (35 to <40), and stage III ( $\geq 40$ ).<sup>17,18</sup> Obesity is a major risk factor for type 2 DM and having a higher BMI increases this risk.<sup>19,20</sup> Additionally, obese patients are at an increased risk of developing proteinuria after unilateral nephrectomy.<sup>21</sup> For obesity stages I, II, and III, the adjusted relative risk for ESKD is increased to 3, 6, and 7, respectively, compared with people who had normal weight (BMI < 25).<sup>22</sup> In contrast, studies showed that MCKLDs with obesity exhibited a similar compensatory increase in function and volume of the remaining kidney compared with nonobese donors 5 years after the dona-

tion<sup>23</sup>; obese donors are not at increased risk for long-term reduced renal function compared with nonobese donors with a mean follow-up of 11 years.<sup>24</sup> These findings support the current practice of using otherwise healthy obese donors while emphasizing the need for more intensive preoperative and postoperative weight loss in such donors. Potential donors with obesity should be counseled about the higher risk of developing diabetes and consequential diabetic kidney disease.<sup>25</sup> Potential donors with FH of diabetes are at a higher risk of developing diabetes. The risk is even higher if their parent had DM at a younger age (< 50 years; hazard ratio [HR]: 4.7).<sup>26</sup> In our survey, the majority (75%) of respondents would allow a potential obese donor (BMI 30–35) to donate if they started to demonstrate some weight loss or intention to lose weight. However, only 45% of the respondents would allow a potential obese donor with a strong FH of DM to donate without further requirements or an intention to lose weight. These findings are comparable to those of one survey conducted in the United States in 2017.<sup>27</sup>

Donor nephrectomy in obese donors (stage II or more) is surgically challenging, with longer operation time, more wound complications, and higher risk of delayed graft function (odds ratio [OR]: 2.16,  $p = 0.01$ ).<sup>28</sup> However, additional serious complications are infrequent, especially at centers with higher annual transplant volume.<sup>29</sup> The risk of graft failure or recipient mortality is similar across donor BMI groups at the 6th or 11th month follow-up.<sup>28,30,31</sup> In our

**Table 4** The acceptance of the MCLKD with regard to age discrepancy

Question	Answer choices	Nephrologists	TS	p-Value	Total
Q12. Just turned <b>18-year-old man</b> who wants to donate his older sibling:	I allow him to donate after counselling him about the future risk after donation.	72 72.0%	98 70.5%	0.668	170 71.1%
	I will advise him not to donate because of his young age and the future risks of CKD and ESKD.	11 11.0%	12 8.6%		23 9.6%
	I will not consider him for donation at this age.	17 17.0%	29 20.9%		46 19.2%
Q13. Just turned <b>18-year-old woman</b> wants to donate her older sibling:	I will accept her for donation after counselling her about the increased risks of preeclampsia after donation.	56 56.6%	80 57.6%	0.768	136 57.1%
	I will advise her not to donate because of the increased risk of preeclampsia but I will allow her to donate if she insists and accepts the risks.	22 22.2%	26 18.7%		48 20.2%
	I will not consider her for donation at this age.	21 21.2%	33 23.7%		54 22.7%
Q14. 18-year-old man wants to donate to his <b>75-year-old</b> father.	I allow him to donate after counselling him about the future risk after donation.	35 35.4%	67 48.6%	0.081	102 43.0%
	I will advise him not to donate because of the CKD risk and since the recipient might not get the mortality benefit given his age.	35 35.4%	33 23.9%		68 28.7%
	I will not consider him for donation under the current age and circumstances.	29 29.3%	38 27.5%		67 28.3%
Q15. Donor > <b>65-year-old</b> man to <b>18-year-old</b> recipient and expected prolonged waiting time for deceased donor	I allow him to donate after counselling.	24 24.0%	35 25.4%	0.960	59 24.8%
	I will advise him to find a younger donor, but I will allow the donation if no alternative donor is available.	67 67.0%	90 65.2%		157 66.0%
	I will not consider him for donation at this age.	9 9.0%	13 9.4%		22 9.2%

Abbreviations: CKD, chronic kidney disease; ESKD, end-stage kidney disease; MCLKD, medically complex living kidney donors; TS, transplant surgeon.

survey, 62% of the respondents would decline LKDs with obesity stage II (unchanged rate from a United States survey in 2007).<sup>32</sup>

Donors would be considered at “increased risk for diabetes” or to have “prediabetes” if they meet any of the following three criteria: IFG—100 to 125 mg/dl (5.6–6.9 mmol/l), impaired oral glucose tolerance—140 to 199 mg/dl (7.8–11.0 mmol/l), or A1C 5.7 to 6.4%. For all three criteria, the risk is continuous, extending below the lower limit of the range and disproportionately increasing at the higher limit of the range.<sup>33</sup> Many programs consider potential LKDs with prediabetes. However, they individualize the decision based on the donors’ health profile regarding the acceptable risk threshold of the transplant program.<sup>8,9</sup> In our survey, potential donors with obesity and IFG could donate only if IFG was resolved due to weight reduction, according to half of the respondents.

The cutoff for IFG may vary, but 45% of the respondents stated it is IFG of > 100 mg/dl, which seems unchanged from 2007.<sup>32</sup>

Previous studies examining the use of HbA1C versus glucose cut points for the diagnosis of DM or IFG found that HbA1C has the least sensitivity for DM diagnosis in comparison to FG and GTT, which has the highest sensitivity.<sup>34</sup> The concordance rate of the criteria between the methods used to diagnose diabetes is low,<sup>35</sup> and it is even lower when the diagnosis is “pre-DM.” The oral GTT should be performed for the confirmation of DM among patients with IFG who have an HbA1C between 5.6% and 6.4%.<sup>36,37</sup> In our survey, more than half of the respondents would request GTT to verify isolated and mildly elevated A1C or IFG in a potential donor before deciding donation.

DM is considered as an absolute contraindication for kidney donation, according to the European Renal Best Practice Guideline 2014.<sup>9</sup> Kidney Disease: Improving Global Outcomes (KDIGO) 2017 advises to individualize the decision regarding donor candidates with prediabetes or type 2 DM based on their health profile and the acceptable risk threshold of the transplant program.<sup>8</sup> In our survey, most respondents would decline a middle-age donor candidate

**Table 5** The acceptance of the MCKLD with family history of kidney disease

Question	Answer choices	Nephrologist	TS	p-Value	Total
Q16. If an 18-year-old wants to donate to his brother (40 years old) and with a <b>family history</b> on two uncles with unknown etiology of ESKD at 40 years. Donor evaluation is normal otherwise.	I will clear him to can donate after counselling.	19 19.0%	42 30.4%	0.133	61 25.6%
	I will advise him against donation. However, I will allow the donation if no alternative donor is available.	29 29.0%	36 26.1%		65 27.3%
	I will not clear him.	52 52.0%	60 43.5%		112 47.1%
Q17. An 18-year-old wants to donate to his mother 40 years and with a <b>family history</b> on two uncles with ESKD at 40 years. Donor evaluation is negative otherwise. He understands the risks of donation, but he insists to donate to his mother since he is the only available donor.	I will clear him to can donate after counselling.	24 24.0%	47 33.8%	0.211	71 29.7%
	I will advise him against donation. However, I will allow the donation if no alternative donor is available.	41 41.0%	45 32.4%		86 36.0%
	I will not clear him.	35 35.0%	47 33.8%		82 34.3%

Abbreviations: ESKD, end-stage kidney disease; MCKLD, medically complex living kidney donors; TS, transplant surgeons.

with DM for 1 year, even if it was controlled with monotherapy or diet.

Our study's findings regarding the acceptance rate of donors with stage I obesity, decline rate of obese candidates with FH of DM, exclusion rate of candidates based only on FG values, and the rate of pursuing GTT for elevated I HbA1C are comparable to the findings of Garg et al in 2017.<sup>15</sup>

While programs are becoming less restrictive about accepting donors with BMI more than 35 or 40,<sup>15</sup> bariatric surgery prior to living donor nephrectomy may be a solution to expand the living donor kidney pool. In a study of 22 donors who had bariatric surgery, donors had waited 0.7 to 22 years prior to laparoscopic living donor nephrectomy. Eighteen donors would have been excluded from donation prior to bariatric surgery, as their BMI was more than 40 and 17 reached a BMI of less than 35 after bariatric surgery.<sup>38</sup> Nguyen et al advocated that bariatric surgery should be considered in preparation for donation in morbidly obese candidates, since this can positively alter their candidacy without significantly impacting the subsequent living donor nephrectomy and early outcomes.<sup>38</sup> In another study, bariatric surgery prior to living kidney donation by an obese donor was also found to be cost-effective (with a ratio of 3.64 vs. a kidney transplant from a deceased donor).<sup>39</sup> In our survey, donor candidates with resolved DM postbariatric surgery due to weight reduction could be considered for donation as soon as surgery was possible or when their BMI reduced to less than 30. However, more respondents (44%) preferred to have a waiting period postbariatric surgery to ensure no relapse.

According to our survey, potential donors with isolated obesity, IFG, mildly abnormal HgbA1C, or history of bariatric surgery were considered for kidney donation by many

respondents. However, donors with more than one abnormality, especially young donors, were not likely to be considered for donation.

Donor candidates with hypertension that can be controlled to systolic BP < 140 mm Hg and diastolic BP < 90 mm Hg using one or two antihypertensive agents, with no evidence of target organ damage, may be acceptable for donation.<sup>8,40</sup> In 2017, 65% of the renal transplant programs in the United States accepted donors with monotherapy-controlled hypertension, and only 10% of programs considered donor candidates on two antihypertensive medications.<sup>32</sup> The decision to approve donor candidates with hypertension should be individualized, based on the health profile of the donor and in consideration of the acceptable risk threshold of the transplant program.<sup>8,40,41</sup>

Female LKDs are 2.4 times more likely to develop gestational hypertension or preeclampsia (95% CI 1.2 to 5.0) compared with healthy nondonors.<sup>42</sup> However, most donor pregnancies remain uncomplicated with no significant neonatal or maternal gestational complications.<sup>42</sup> Thus, females of childbearing age should be counseled about these risks before donation. In our survey, we found that the majority of respondents would allow women with mild and controlled hypertension to proceed with living kidney donation only if they had no future plans for pregnancy.

In addition, normotensive LKDs may have a 5-mm Hg greater increase in BP than the increase anticipated with normal aging.<sup>43</sup> After kidney donation, up to 3%, 4%, 10%, and 51% of LKDs may develop hypertension at 2, 5, 10, and 40 years, respectively.<sup>44,45</sup> Donors who are male, obese, and who have a first-degree relationship are at higher risk.<sup>44</sup> The risk of developing hypertension after donation is increased by a HR (1.19; 95% CI, 1.01 to 1.41;  $p = 0.04$ ).<sup>46</sup>

Hypertension after donation may contribute to the increased risk of ESKD, cardiovascular, and all-cause mortality of donors compared with healthy nondonors.<sup>4,47</sup> The risk is also higher in healthy young donors than healthy older candidates.<sup>48</sup>

Up to 10% of donors have white coat hypertension (elevated BP readings measured in the clinic but normal BP by ABPM).<sup>8,40,41</sup> White coat hypertension and abnormal ABPM patterns such as nondipping BP at night are potentially associated with increased cardiovascular risk.<sup>49,50</sup> Neither white coat syndrome nor abnormal patterns of ABPM per se are contraindications for kidney donation. However, they are considered as indicators of increased risk, especially in young donors who are already at higher risk than their older counterparts.

The donor-recipient age discrepancy comprises another dilemma in deciding kidney transplantation. A very young age (18 to 21 years) is viewed as a relative contraindication for kidney donation by many programs (23% of programs in the United States).<sup>16,51,52</sup>

Programs are more restrictive in applying exclusion criteria for younger donors than older donors when it comes to renal risk factors.<sup>48</sup> This is because young LKDs are expected to have more years of exposure to renal risk factors post-kidney donation than older donors.<sup>4,47,48</sup> Young female donors of childbearing age are also prone to the potential risks associated with future pregnancies, including gestational hypertension or preeclampsia.<sup>42</sup>

In our survey, the majority of respondents would accept a very young potential donor, especially if they were males. However, up to 20% would decline them regardless of the donor's gender. Plans for future pregnancies were also an important factor when counseling a potential female donor of childbearing age.

In contrast, most transplant programs in the United States have no upper age limit for accepting donors,<sup>32</sup> but they require careful assessment of risk factors, especially for donors over 65 years, since these grafts can be associated with poorer outcomes.<sup>53,54</sup> The donor and recipient should be advised that grafts from LKD who are 65 to 69 years have similar (but not better) graft survival of standard criteria donor (SCD) and grafts from donors aged more than 70 years have worse graft survival of SCD.<sup>53</sup> In our survey, the majority of respondents would accept a donor over 65 years to donate to an 18-year-old recipient with expected prolonged waiting time for a deceased donor.

LKD transplantation in a recipient over 70 years is also challenging, especially if the donor is very young. Renal transplantation decreases all-cause mortality in elderly patients when compared with dialysis.<sup>54</sup> While graft survival may be similar, older transplant recipients have a higher mortality risk than their younger counterparts.<sup>55</sup> LKD transplantation for recipients over 70 years is associated with lower mortality than observed with SCD or expanded criteria donor (ECD).<sup>53</sup> However, higher age of the recipient (e.g., 60–70 years vs. 70–80 or over 80 years) is a strong, independent risk factor for death after kidney transplantation.<sup>53</sup> Criteria for and appropriateness of renal transplantation in elderly

patients with ESKD should be based on frailty score, comorbidities, and potential life expectancy.<sup>56</sup> In our survey, we found that the opinions about allowing a very young donor to donate to a very old recipient were divided in the transplant community.

The acceptance of LKDs with FH of kidney disease of unknown etiology is challenging. Up to 40% of LKDs are close biological relatives to the recipients.<sup>57</sup> Many of those biologically related donors are also in their 30s and 40s. This makes it more difficult to predict future risk of kidney disease, especially if the cause of kidney failure of the potential recipient is unknown and genetic etiology cannot be ruled out. Genetic screening for a specific disorder such as polycystic kidney disease, Alport disease, or atypical hemolytic uremic syndrome is typically guided by clinical indications. There is uncertainty about the interpretation of APOL1 status and its renal risk, and there is no consensus about its utility of the evaluation of potential LKD.<sup>16,58–61</sup>

Comprehensive genetic screening of LKDs with FH of chronic kidney disease with unknown etiology has several limitations. First, the majority of kidney diseases are polygenic or secondary to known risk factors of chronic kidney disease such as diabetes or hypertension.<sup>62</sup> Second, not all genetic variants are identified by targeted next-generation sequencing panels (or whole-exome sequencing).<sup>62</sup> Finally, significant variants unrelated to the phenotype (unsolicited but medically significant discoveries) may be identified.<sup>62–64</sup>

In one recent study, family members of patients with ESKD from “nonhereditary” causes of ESKD had increased relative risk of ESKD when compared with those with no FH of renal disease (risk ratio [RR]: 3.7; 95% CI: 3.1 to 4.4). The study identified glomerular disease, interstitial disease, diabetic nephropathy, and hypertensive nephrosclerosis among “nonhereditary” causes of ESKD.<sup>65</sup>

In our survey, FH of kidney disease of unknown etiology was a significant determining factor to decline young donors.

► **Table 6** summarizes the findings of the survey.

There are several strengths and limitations in our study. The survey was answered by 239 respondents, including 100 nephrologists and 139 TSs, from 29 countries through three major international transplant societies (AST, ASTS, and ERA-EDTA). The number of participants in our survey was much larger than that of previous surveys distributed through UNOS in 2007 and 2017 (for instance, the survey distributed through UNOS in 2017 had 72 responses, with 44 medical directors and 28 surgical directors). This was due to the multinational nature of our study and the fact that we did not restrict participation to the directors of the transplant units.

Our survey also covered several challenging areas that had not been addressed by previous guidelines or surveys. Potential living donors and recipients are typically assessed by separate health care teams to avoid any conflict of interest (75). Our survey was unique in exploring the difference between nephrologists and TS, although the main objective of our survey was exploring the opinions of nephrologists and TS as a unified group, since the decisions of accepting MCLKDs are typically addressed through a multidisciplinary approach.

**Table 6** Summary of the survey findings

1-	The vast majority (75%) of the respondents would allow an obese potential donor (BMI 30–35) to donate if the donor started to demonstrate some weight loss or intention to lose weight.
2-	Only 45% of the respondents will allow an obese potential donor with a strong FH of DM to donate if there were no alternative donor without further requirements or she/he intends to lose weight.
3-	Stage II obese potential donors have to demonstrate some weight loss or even reach a BMI of 30 before being considered for kidney donation by most of the respondents.
4-	Potential donors with obesity and IFG can donate only if impaired BS is resolved due to weight reduction according to half of the respondents.
5-	More than half of the respondents request GTT to verify isolated and mildly elevated A1C or IFG in a potential donor before deciding on candidacy.
6-	Most respondents would decline a middle-age donor candidate with diabetes for one year even if it was controlled with just monotherapy or diet.
7-	Donation candidates with resolved DM postbariatric surgery due to weight reduction can be considered for donation as soon as surgery is possible or when the BMI reduces to less than 30. Other respondents preferred a waiting period postbariatric surgery to ensure no relapse.
8-	Potential donors with isolated obesity, IFG, mildly abnormal HgbA1C or history of bariatric surgery are still considered for kidney donation by many respondents. However, donors with more than one abnormality especially at a young are likely not to be considered for donation.
9-	A majority of respondents would allow women with mild and controlled hypertension to proceed with living donation only if they have no future plans for pregnancy.
10-	Plan of future pregnancies is an important factor when counseling a potential female donor of childbearing age.
11-	Most respondents are reluctant to accept very young male donors if they show higher risk of developing hypertension in the future.
12-	The majority of respondents will allow very young donor candidates to donate especially in males. However up to 20% will decline this donation regardless of the gender of the donor.
13-	The transplant community is divided about allowing a very young donor to donate to a very old recipient.
14-	The majority will accept a > 65-year-old donor to donate to an 18-year-old recipient with expected prolonged waiting time for a deceased donor.
15-	FH of kidney disease of unknown etiology is an important factor to decline young donors.

Abbreviations: BMI, body mass index; DM, diabetes mellitus; FH, family history; GTT, glucose tolerance test; IFG, impaired fasting glucose.

One of the limitations of our study is that respondents practicing in the United States were overrepresented (65% of the total respondents were from the United States, whereas only 25% of worldwide renal transplantations occurred in the United States in 2019) (76–77). This is because we did not have official access to directly approach the renal transplant units globally, and the respondents were reached through the international societies, many of which did not have any means to distribute the external studies.

Other potential limitations of the survey are the unknown response rate of EDTA members and the fact that we did not account for multiple replies from the same unit. Again, this was due to the distribution of our survey through transplant societies by email and web posting. These do not critically affect the validity of our study, since it was designed to explore the general opinions of the transplant providers in the international community and not the formal policies of the transplant units. Other assuring factors include the high completion rate of 99% and the comparisons made between our results and previous surveys, as outlined throughout the discussion.

## Conclusion

This survey highlights the practice patterns of the acceptance of MCLKDs among the international community. In the absence of clear guidelines, this survey provides additional information to counsel kidney donors with obesity, hypertension, FH of kidney disease, and donor-recipient age discrepancy.

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