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Laterality of live-donor nephrectomy: does it have a urologic impact on post-donation pregnancy?

Ahmed Farouk Donia[1,2*], Eman Elrefaie[1], Ayman Refaie[1], Moatasem Ghoneim[1], Yasser Osman[3] and Bedeir Ali-El-Dein[3]

Abstract

Background Our center policy is to promote right nephrectomy for pre-menopausal live donor donors. This is based on the traditional belief that ureteral obstruction and subsequent urinary tract infections (UTIs) of post-donation pregnancies would be more frequent among female donors with a solitary right (compared to left) kidney. Studies that support or dismiss our policy are lacking. Therefore, we conducted this study.

Methods 100 donors who had post-donation pregnancy were included. They underwent an updated clinical, laboratory and ultrasound assessment. They were classified into two groups: right and left nephrectomy groups. Both groups were compared relative to pre- and post-donation data, urinary troubles during or after post-donation pregnancies as well as their current kidney function.

Results Right nephrectomy was carried-out in 60 donors (60%). Post-donation acute pyelonephritis was not reported in either group. Unexpectedly, right nephrectomy group had a slightly higher (yet insignificant) lower UTIs during post-donation pregnancy. Furthermore, obstructive uropathy {two donors) and end stage renal disease (one donor) were only reported among right nephrectomy group. Both groups were comparable in terms of their current kidney function.

Conclusion Despite that the endeavor to retrieve the right rather than the left kidney among premenopausal women could give them the benefit of doubt in regard to possible obstructive uropathy and UTIs during their subsequent pregnancies, this policy is likely an overdoing practice. Larger-scale studies are needed.

Keywords Live kidney donor, Pregnancy, Nephrectomy laterality, Urologic problems, Renal outcome

*Correspondence:
Ahmed Farouk Donia
afdonia@hotmail.com
[1]Nephrology and transplant unit, urology and nephrology center, Mansoura University, Mansoura, Egypt
[2]Renal unit, Altnagelvin hospital, Londonderry, Northern Ireland, UK
[3]Department of urology, Faculty of Medicine, Mansoura University, Mansoura, Egypt

Introduction

Kidney transplantation is the best currently available treatment modality for patients with end stage kidney disease and pregnancy after kidney transplantation if planned and followed in coordination within an experienced center, both the pregnancy period and the birth process can occur without distress [1]. In Egypt, the only source of transplanted kidneys is live donors in view of absent cadaveric program. At our center, female donors constituted 1734 (55.5%) out of 3126 donors over the period between 1976 and 2020 [2].

Throughout this period, our center policy concerning females who donate a kidney during their child-bearing period has been to prefer right donor nephrectomy whenever possible. The left kidney has been only retrieved if it has an anatomical abnormality or its split function on isotope study is significantly lower compared to the right kidney (provided that it is still suitable for transplantation), or if the right kidney has multiple renal arteries making its retrieval a complex surgery. This policy has been adopted despite the preference of our transplant surgeons to retrieve the left kidney as transplantation mostly occurs on the right side of the recipient and it is, therefore, technically easier to transplant the left kidney. The rationale behind this policy is the belief that if pregnancy occurs after donation, female kidney donors with a solitary right kidney will be subjected to more ureteral obstruction and subsequent UTIs compared to those with a solitary left kidney. This belief is based on the well-known information that hydronephrosis during pregnancy is more pronounced on the right side [3]. Nevertheless, such practice may create an extra-pressure on the transplant team especially in the context of the rapidly growing minimally invasive laparoscopic donor nephrectomy technique which seemed to be a reliable solution with fewer complications and higher satisfaction rates. However, right nephrectomy is generally not preferred in such a technique [4].

As we know that there is no robust evidence to support or dismiss our left-kidney sparing policy among female kidney donors who may get pregnant after donation and because studies in this area are lacking, we conducted this study in order to assess the impact of laterality of donor nephrectomy among premenopausal female donors on the occurrence of urinary troubles during their post-donation pregnancy and subsequent renal outcome.

Materials and methods

This retrospective cohort study was conducted at the urology and nephrology center, Mansoura University, Egypt. It included 100 females who donated a kidney over the period between 1976 and 2020 at our center and had one or more post-donation pregnancy after donation. They were either picked up during their regular visit to our post-donation clinic or retrieved after a phone call for those who lost follow up. Females who donated their kidneys after menopause or those who donated their kidneys during the child-bearing period but didn't get pregnant thereafter were excluded from the study.

The included premenopausal women underwent clinical, laboratory and ultrasound assessment and their files were retrieved in order to obtain obstetric and urologic data. They were classified according to the side of donor nephrectomy into right and left donor nephrectomy groups. Laparoscopic donor nephrectomy has been exclusively performed on the left side. A special sheet designed for the study was filled in.

In terms of the relation of our premenopausal women to their recipients, 51 (51%) were sisters, 44 (44%) were wives and 5 (5%) were mothers. The accepted age of potential kidney donors at our center is 21–60 years [2]. While the lower age limit has been strict, parents above the age of 60 years are increasingly accepted as a donor for their offsprings if they are completely healthy and are the only available donor.

Lower urinary tract infection was diagnosed if there are symptoms suggestive of acute cystitis including dysuria, frequency and urgency without fever or flank pain. Acute pyelonephritis was diagnosed if there are flank pain and fever/chills with or without symptoms of acute cystitis. All methods were carried out in accordance with relevant guidelines and regulations.

Data of the premenopausal women included in the study were exported to SPSS program. Continuous data were expressed as mean±standard deviation and were compared using T-test while nominal data were expressed as numbers (percentages) and were compared using Chi-square test.

Sample size calculation

The effect size utilized in this study was derived from the findings of Marleen C. van Buren et al., 2023. Using these calculated effect sizes, we determined the appropriate sample size for our study. This calculation was performed using G*Power software, version 3.19.4, resulting in a total required sample size of 66 patients, with 33 patients in each group. In this study, we examined a total of 100 patients.

Results

Right nephrectomy was carried-out in 60 of out of the studied 100 donors (60%). Table 1 shows that both right and left donor nephrectomy groups were comparable in terms of pre-donation characteristics including age, number of pre-donation pregnancies and kidney function. Apart from family history of renal failure (the recipient), medical history was irrelevant in both donor groups except for bronchial asthma and mild hypertension in

Table 1 Pre-donation characteristics of right and left donor nephrectomy groups

	Right donor nephrectomy group (N = 60)	Left donor nephrectomy group (N = 40)	P value
Age at donation in years	27.85 ± 5.73	29.25 ± 4.57	0.198
Number of pregnancies before donation			
M ± SD	1.83 ± 1.45	2.3 ± 1.83	0.159
Median (min.-max.)	2 (0–5)	2 (0–8)	0.16
Frequency			0.741
None	15 (25%)	8 (20%)	
One	10 (16.7%)	6 (15%)	
Two	16 (26.7%)	10 (25%)	
Three	10 (16.7%)	5 (12.5%)	
Four	7 (11.6%)	7 (17.5%)	
Five	2 (3.3%)	3 (7.5%)	
Eight	0 (0%)	1 (2.5%)	
Lower UT symptoms during pre-donation pregnancies			0.73
No	56 (93.3%)	38 (95%)	
Yes	4 (6.7%)	2 (5%)	
Relevant medical history before donation			
None	59 (98.4%)	39 (97.5%)	
Bronchial asthma	1 (1.6%)	0 (0%)	0.338
Mild hypertension	0 (0%)	1 (2.5%)	
Pre-donation surgical history			
Tonsillectomy	1 (1.6%)	1 (2.5%)	0.771
Caesarean section	10 (16.6%)	3 (7.5%)	0.182
Cholecystectomy	1 (1.6%)	0 (0%)	0.412
Appendectomy	1 (1.6%)	0 (0%)	0.412
Disc prolapse	0 (0%)	1 (2.5%)	0.412
Systolic blood pressure before donation (mm Hg)	117.50 ± 8.36	118.75 ± 8.53	0.469
Diastolic blood pressure before donation (mm Hg)	77.50 ± 10.02	79.25 ± 8.59	0.366
Body mass index before donation (kg/m^2)			
18.5–24.9	15 (25%)	11 (27.5%)	
25-29.9	29 (48.3%)	25 (62.5%)	0.117
≥ 30	16 (26.7%)	4 (10%)	
Fasting blood sugar before donation (mg/dl)	88.97 ± 9.36	87.36 ± 8.01	0.380
Hemoglobin before donation (g%)	12.06 ± 0.96	12.26 ± 0.86	0.589
Serum creatinine (mg/dl) before donation (M ± SD)	0.73 ± 0.14	0.68 ± 0.16	0.08

one donor of the right and left nephrectomy groups respectively.

Table 2 shows post-donation data of both groups. The number of post-donation pregnancies was comparable in both groups. Almost half of the donors in both groups got more than one pregnancy after donation. Right and left nephrectomy group donors had a total of 108 and 62 post-donation pregnancies respectively. Post-donation acute pyelonephritis was not reported in either group. Among both groups, 40% had lower urinary tract infection during more than one pregnancy after donation. A total of 23 lower urinary tract infections occurred in both groups during a total number of 170 post-donation pregnancies. Unexpectedly, lower urinary tract infection during post-donation pregnancy occurred among 16.7% of individuals of the right nephrectomy group compared to 12.5% in the left nephrectomy group yet this difference was statistically insignificant ($p=0.776$). Furthermore, one of the right nephrectomy group donors developed post-donation ureteral obstruction with DJ insertion and subsequent successful stone extraction and resolution of obstructive uropathy and another donor developed end stage renal disease 21 years after donation due to a non-urologic etiology (likely related to toxemia of pregnancy) and has been unfortunately maintained on hemodialysis since 16 years despite that her donated kidney to her sister is currently perfect. Among all donors in both groups, the current urinary tract ultrasound doesn't show obstructive uropathy of the remaining kidney. Updated urine analysis showed asymptomatic pyuria in two donors of the right nephrectomy group. Serum creatinine at last follow-up was higher, yet statistically insignificant, among the right nephrectomy group donors. After exclusion of end stage renal disease donor in the

Table 2 Post-donation characteristics of right and left donor nephrectomy groups

	Right donor nephrectomy group (N = 60)	Left donor nephrectomy group (N = 40)	P value
Age at last follow up in years	41.45 ± 7.95	42.98 ± 9.46	0.39
Post-donation follow up period (years)	13.60 ± 8.98	13.73 ± 9.10	0.95
Number of pregnancies after donation			
M ± SD	1.8 ± 1.25	1.55 ± 0.71	0.25
Median (min.-max.)	1 (1–7)	1 (1–3)	0.26
Frequency			0.46
- One	34 (56.7%)	23 (57.5%)	
- Two	15 (25%)	12 (30%)	
- Three	5 (8.3%)	5 (12.5%)	
- Four	3 (5%)	0 (0%)	
- Five	2 (3.3%)	0 (0%)	
- Seven	1 (1.7%)	0 (0%)	
Lower UT symptoms during post-donation pregnancies			0.413
No	50 (83.3%)	35 (87.5%)	
Yes	10 (16.7%)	5 (12.5%)	
Number of post-donation pregnancies with Lower UT symptoms			0.47
One pregnancy	6 (60%)	3 (60%)	
Two pregnancies	2 (20%)	2 (40%)	
Three pregnancies	2 (20%)	0 (0%)	
Acute pyelonephritis during post-donation pregnancies			
No	60 (100%)	40 (100%)	
Yes	0	0	
Post-donation medical diseases			
Hypertension	15 (25%)	9 (22.5%)	0.675
Diabetes mellitus	6 (10%)	5 (12.5%)	0.695
Ischemic heart disease	3 (5%)	0	0.151
Bronchial asthma	1 (1.6%)	0	0.412
Hyperthyroidism	1 (1.6%)	0	0.412
ESRD	1 (1.6%)	0	0.412
Cancer			0.338
Breast	1 (1.6%)	0	
Bladder	0	1 (2.5%)	
Systolic blood pressure at last follow up (mm Hg)	121.83 ± 13.21	122.50 ± 14.63	0.813
Diastolic blood pressure at last follow up (mm Hg)	78.17 ± 10.97	77.75 ± 11.87	0.857
Body mass index at last follow up (kg/m^2)			
18.5–24.9	3 (5%)	4 (10%)	
25-29.9	16 (26.7%)	9 (22.5%)	0.599
≥ 30	41 (68.3%)	21 (67.5%)	
Fasting blood sugar at last follow up (mg/dl)	95.08 ± 20.93	94.78 ± 18.72	0.94
Hemoglobin at last follow up (g%)	12.06 ± 0.96	12.26 ± 0.86	0.285
Serum creatinine (mg/dl) at last follow up (M ± SD)	0.93 ± 1.45	0.78 ± 0.12	0.502
Urine analysis at last follow up			0.503
Free	54 (90%)	35 (87.5%)	
Non-nephrotic proteinuria	2 (3.33%)	3 (7.5%)	
Non-nephrotic proteinuria + microscopic hematuria	2 (3.33%)	2 (5%)	
Asymptomatic pyuria	2 (3.33%)	0 (0%)	

right nephrectomy group, serum creatinine at last follow-up becomes slightly lower in the right (0.75 ± 0.11 mg/dl) compared to the left (0.78 ± 0.12 mg/dl) nephrectomy group yet without statistical significance ($p = 0.163$).

Discussion

To the best of our knowledge, this is the first study that evaluates the impact of donor nephrectomy laterality on future pregnancy as well as future kidney function

among donors. In our study, we investigated the hypothesized benefit of right over left donor nephrectomy from the donor perspective. Conversely, the potential advantage of left over right donor nephrectomy was previously studied; mainly from the recipient perspective. Traditionally, surgeons prefer to transplant the left kidney as it has a longer renal vein. In an analysis of OPTN/UNOS database that included about 60,000 live-donor transplants, right donor nephrectomy recipients had significantly higher conversion from laparoscopic to open donor nephrectomy, delayed graft function and graft thrombosis as a cause of graft failure, and significantly lower graft survival. Nevertheless, the authors concluded that as these differences are small, the choice of nephrectomy side should be primarily dictated by surgical team preference and experience [5]. A meta-analysis of laparoscopic donor nephrectomy that included 15 studies and more than 3000 kidney transplants conversely showed that left laparoscopic donor nephrectomy was associated with significantly longer operative time, more blood loss and more donor intraoperative complications. However, both sides were comparable relative to the rate of conversion to open nephrectomy, delayed graft function, recipient and donor post-operative complications and one year graft survival and recommended left donor nephrectomy whenever possible due to longer renal vein making surgery easier [6]. It is interesting that the majority of donor nephrectomy in both studies were left sided (86.1% and 78% respectively) reflecting the general trend of surgeons to perform left donor nephrectomy. On the other hand, retrieval of the available data of our all transplant series showed that left donor nephrectomy was performed in only 1403 (60.4%) out of 2323 kidney transplants. The relatively lower percentage of left donor nephrectomy among our series compared to the previous two large studies may be attributed to our preference to perform right nephrectomy among female donors who have the potential to get pregnant after donation and to our routine use of donor renal isotope scan as a contributing tool in choosing the side of donor nephrectomy [7].

Interestingly, an abstract published in 2017 explored the impact of donor nephrectomy side on long-term donor outcome in terms of suprarenal function and suggested that left (compared to right) donor nephrectomy may predispose live donors to future adrenal insufficiency with more fatigue and poorer quality of life [8]. In addition, there was a report on a young female donor who got pregnant shortly after undergoing left donor nephrectomy with subsequent acute kidney injury late during pregnancy presumably due to pregnancy-related right hydronephrosis [9]. More than half of pregnant donors develop hydronephrosis late during pregnancy due to both mechanical and hormonal causes [3]. Hydronephrosis is more pronounced on the right side due to different anatomy of the right compared to the left ureter making the right ureter more liable to compression as it crosses the iliac artery at the pelvic brim and crossed by the right ovarian vein, compression by the dextrorotated uterus and crossing right ovarian vein and protection of the left ureter by the gas-filled sigmoid colon [10, 11] .However, laterality difference in terms of urologic complications during pregnancy is rarely evaluated [9, 11]. Contrary to our expectation, our study showed that right and left donor nephrectomy group premenopausal donors were comparable in terms of UTIs during post-donation pregnancy as well as their last follow up blood pressure, kidney function, urine analysis and ultrasound findings. Nevertheless, our results could be supported by extrapolation from studies of the general population that did not show an increased prevalence of urinary tract infection [12] or stone kidney disease [13–15] during pregnancy despite the known anatomic and physiologic effects of pregnancy on the urinary system. In addition, donors included in our study didn't have a periodic follow up renal ultrasound throughout pregnancy and we, therefore, are not confident whether they experienced hydronephrosis and whether those with a solitary right (compared to left) kidney had a significantly higher prevalence and/or degree of hydronephrosis during their post-donation pregnancy. Moreover, no other specific studies among kidney donors or even among single-kidney premenopausal females are available for comparison.

The overall prevalence of lower urinary tract infection among our premenopausal kidney donors was 13.5% during their post-donation pregnancies (23 infections in 170 pregnancies); much higher than that reported among other premenopausal donors. Although the prevalence of symptomatic urinary tract infection among donors of the general population during pregnancy is not exactly known, it is suggested to be 1-2.3% [3, 16, 17]. This difference may be attributed to the method of diagnosis being mainly on clinical basis among our donors. It may also reflect a real increase in prevalence of urinary tract infection in post-kidney donation pregnancy. Moreover, it is likely that socioeconomic standard might affect the occurrence of urinary tract infection among our pregnant donors as our reported prevalence was closer to that (8.9%) reported in a cohort of more than 4000 pregnant donors from Bangladesh [18]. This could explain the wide range of prevalence (3–35%) in a study which included pregnant donors from five continents [19].

Minimally invasive donor nephrectomy is gaining more popularity. Laparoscopic donor nephrectomy has become the standard of care in some centers. Nevertheless, left nephrectomy is more preferred for laparoscopic compared to open nephrectomy due to technical aspects [4]. At our center, laparoscopic donor nephrectomy has been exclusively performed on the left side [20]. Our

results may increase the use of laparoscopic nephrectomy among our premenopausal donors with possible improvement of post-donation morbidity and hospitalization period.

Our study has a number of limitations. It is a low-numbered cohort retrospective study. In addition, urine analysis/culture as well as ultrasound weren`t routinely performed during pregnancy to document UTIs and/or hydronephrosis respectively. Therefore, we believe that larger-scale, preferably multicenter, studies are worthwhile.

Conclusion

In our strive towards achieving the best recipient outcome as well as the best donor outcome in terms of better postoperative recovery (minimal invasive surgery), avoidance of any problems after donation and assuring the best quality of life, we could not observe a notable difference regarding pregnancy-related urinary troubles or long-term renal outcome among premenopausal donors who have a remaining right kidney after kidney donation. Despite that the endeavor to retrieve the right rather than the left kidney among female kidney donors could give them the benefit of the doubt in regard to possible ureteral obstruction/UTIs during their subsequent pregnancies, this policy is likely an overdoing practice and would only be adopted when it doesn't jeopardize the decision based on any other factor which could affect both recipient and donor outcomes. Larger-scale studies are needed to support this conclusion.

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Author contributions
AD: Data analysis and interpretation and writing the article. EE: Participated in data collection. AR: Revision of the final version to be published and Providing a clinical experience to the work described. MG: Participated in data collection. YO: Revision of the final version to be published and providing a clinical experience to the work described. BA: Revision of the final version to be published and Providing a clinical experience to the work described.

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Data availability
All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Declarations

Ethical approval and consent to participate
Ethical approval was waived by the local Ethics Committee of Urology and Nephrology Center, Mansoura University in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. Freely-given, written informed consent to participate in the research studies conducted by Urology and Nephrology Center was obtained from the recipients and donors before transplantation who are also free to get back in this consent at any time after transplantation. We also declare that no kidneys were donated by prisoners and all the kidney transplant surgeries were conducted under the supervision of the national committee of organ transplantation and Mansoura University. As regard the vulnerable groups, female donors who donated their kidneys were relatives to the recipients and we exhausted ourselves to make sure that they are free from coercion and donated their kidneys by their free well giving them the chance to stop at any time before the surgery.

Consent for publication
Freely-given, written informed consent for data publication after being involved in the research studies conducted by Urology and Nephrology Center was obtained from the recipients and donors before transplantation who are also free to get back in this consent at any time after transplantation.

Competing interests
The authors declare no competing interests.

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