# Outcome of Live-Donor Renal Transplants With Incidentally Diagnosed Renal Angiomyolipoma in the Donor

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ABSTRACT

Introduction. Accepting donors with renal lesion amenable for pre-transplant management with no suspected long-term harm seems to expand the live-donor pool. We aimed to assess the long-term outcome of live-donor renal transplantation with incidentally discovered renal angiomyolipoma (AML) during routine evaluation of donors.

Patients and Methods. A retrospective evaluation of incidentally discovered AML, during live-related-donor evaluation, was performed. The tumor criteria were retrieved. In cases with exophytic tumor, a back-table, partial nephrectomy was done with frozen section to exclude malignancy. Endophytic lesions were kept in situ and transplanted. Both donor and recipient were followed up by periodic imaging.

Results. Among 2925 cases, 6 AML with a median volume of 0.96 (range, 0.5–2) $cm^2$ were identified. The median recipients' age was 21 (range, 10–38) years and the median donors' age was 48 (range, 45–50). Two AML were exophytic and back-table partial nephrectomy was performed, while 4 were endophytic and kept in situ, and the kidney was transplanted. After a median follow-up of 82 (range, 25–150) months, 4 patients were alive with functioning grafts and 2 resumed hemodialysis 5 and 7 years after transplantation. There was no evidence of increase in the AML size or newly developed AML in the grafts. All donors were alive with normal renal function (mean ± standard deviation, serum creatinine was 0.9 ± 0.2 mg/dL) and none developed new AML in the remaining kidney.

Conclusion. Incidentally discovered AML during live-donor evaluation is not a contraindication of donation after proper counseling of the couples and regular, periodic follow-up.

RENAL transplantation remains the gold standard treatment for patients with end stage renal disease (ESRD), as it increases life expectancy by 3 to 15 years in comparison to other forms of renal replacement therapy [1]. However, the number of patients awaiting renal transplantation increases over time, but the available number of donors does not increase at a parallel rate. This leads to expanding the donor pool by accepting more donors with marginal criteria, as well as donors with circulatory death. Consequently, the number of the available deceased donors increases to some extent, but there is still a shortage of available live donors, especially in countries where a deceased-donor program is not available. It is not unusual to find suspicious renal lesions on preoperative imaging of potential kidney donors. So, accepting donors with renal lesions, who are amenable for pretransplant management with no suspected long-term harm to the immunocompromised recipients, seems to expand the live-donor pool [2].

Renal angiomyolipoma (AML) is the most common benign renal tumor, and the second most common cause of

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retroperitoneal hemorrhage after renal cell carcinoma. It is not an uncommon, incidental finding in the general population. The diagnosis can be confirmed with contrast-enhanced computed tomography (CT) and magnetic resonance imaging by the high propensity of fat content. As a benign disease, small (<4 cm) asymptomatic tumor does not require intervention [3,4]. Several reports of successful renal transplantation with AML were reported with either pretransplantation excision (in vivo or ex vivo) or keeping in situ. However, all case reports illustrated 1 or at maximum 2 cases.

Herein, we retrospectively reviewed our prospectively followed cases of live-donor renal transplantation and report the long-term outcome of a series of live-donor renal transplants with incidentally discovered renal AML that were ex vivo excised and/or in situ transplanted.

## PATIENTS AND METHODS

After obtaining approval from the local institutional research board (MFM/IRB no: R.18.07.245), the dedicated electronic database of live-donor renal transplant cases were retrospectively reviewed. Patients who received kidneys with incidentally diagnosed AML at preoperative evaluation, whether the tumor was excised on back-table or left in situ and transplanted, were eligible for analysis.

As a routine, all potential donors were fully evaluated by a team including a nephrologist, a urologist, and a psychiatrist, where full medical history, thorough examination, and laboratory investigations were carefully evaluated. In all cases, a contrast-enhanced CT scan was performed to evaluate renal parenchymal and vascular morphology and identify any condition that could hamper donation. All images were reviewed by a special radiologist and both donor and recipient surgeons. All prepared, renal transplant couples were discussed at the weekly, multidisciplinary evaluation meeting. In the case of detected renal masses, all investigations were exhausted to confirm diagnosis of malignancy and exclude the donor upon confirmation. In case of AML, radiological diagnosis was made by CT imaging, based on the density of fatty content. Despite its benign nature, we excluded cases unless there was no other available donor and the recipients were suffering from uncontrolled, dialysis-related complications. All possible risks and benefits of using this kidney were explained to both donor and recipient, and written informed consent was obtained.

In all cases with diagnosed AML, the kidney was dissected from the surrounding perinephric fat with excision of the fat overlying the tumor, if exophytic. Selective control of the artery, vein, and ureter was done. The kidney was placed immediately in ice and flushed with cold saline containing unfractionated heparin, verapamil, and papaverine. The renal mass was exposed and sharply dissected with adequate margin. Frozen section was sent from both the lesion and the base to exclude malignancy or residual tumor. Once the pathologists confirmed the absence of malignancy or residual tumor, the renal parenchymal defect was closed using 4/0 and 2/0 Vicryl sutures. The mass was sent for final histopathological examination. Heterotopic renal transplantation in the right iliac fossa was done in all cases. All patients received induction immunotherapy using basiliximab (anti-interlukin-2 receptor monoclonal antibody) and maintained on tacrolimus and mycophenolate mofetil with steroid maintenance or with rapid steroid withdrawal. For those maintained on a steroid-free regimen, once an episode of rejection was diagnosed, steroid maintenance therapy resumed.

All patients were followed regularly after discharge, twice weekly for 3 months, monthly for 1 year, then every 3 months. Follow-up ultrasound was performed every 3 months in the first year, then every 6 months for both donor and recipients. Specific data were obtained from the electronic database including age, sex, original kidney disease, date of transplant, preoperative donor imaging, and perioperative complications. Follow-up graft function and imaging data were obtained from the outpatient clinic registered data. Rejection episodes were confirmed by histopathological evaluation of biopsied renal specimens and reassessed according to revised Banff 2017 classification [5]. Estimated glomerular filtration rate (GFR) before and after transplantation was calculated using Modification of Diet in Renal Disease equation [6].

## RESULTS

The study included 6 live, related-donor renal transplants with a median age of 21 (range, 10–38) years. The donors were healthy individuals with no comorbidities with a median age of 48 (range, 45–50) years at the time of donation. The causes of ESRD were unknown in 1, glomerulonephritis in 1, hypertensive nephropathy in 1, posterior urethral valve in 1, and vesicoureteral reflux in 2 patients. Table 1 illustrates patients' demographics.

In 2 cases, where the tumor was exophytic, ex vivo excision of the tumor was done on back-table before transplantation. In 4 cases, the tumor was kept in situ and transplanted because of the central location of the tumor. The mean ± standard deviation (SD) ischemia time was 50.3 ± 10.8 minutes. All patients had immediate graft function. None reported postoperative bleeding or urinary leakage. Final histopathological examination of the excised 2 tumors revealed tumor proliferation formed of variable amounts of adipose tissue, smooth muscles, and thickened and hyalinized blood vessels. The adipose tissue was the predominant element and consisted of mature fat cells. The diagnosis of AML was confirmed.

After renal transplantation, the median estimated GFR increased from 5.5 (range, 4–12) mL/min/1.73 $m^2$ before transplantation to 74.8 (29–130), 64.5 (39.7–114), and 52 (33–109) mL/min/1.73 $m^2$ at 1 month, 1, and 3 years, respectively (Fig 1). Similarly, serum creatinine decreased in the same pattern (Table 1). Episodes of rejection were encountered in 4 patients. Patient 1 developed 1 attack of mixed acute cellular and acute humoral rejection in the first month after transplantation and responded to antithymocyte globulin and plasma exchanges therapy. Patient 2 developed 1 episode of acute T cell mediated rejection and 2 episodes of borderline changes at 2, 3, and 4 years of follow-up. Patient 4 developed borderline changes in the biopsied specimens taken at 1 and 6 years of follow-up. Whereas patient 6 developed an attack of acute T cell-mediated rejection 9 months posttransplant, all episodes of rejection were managed with pulse steroid therapy and recovered.

**Table 1. Demographic Criteria and Outcome in 6 Live-Donor Renal Transplant Recipients With Angiomyolipoma in Their Donors**

| | Patient | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| Age | 21 | 26 | 21 | 19 | 38 | 10 |
| Sex | Female | Male | Female | Male | Male | Male |
| Cause of ESRD | VUR | GN | Hypertensive nephropathy | Unknown | VUR | PUV |
| Donor age | 48 | 50 | 49 | 49 | 45 | 47 |
| Donor sex | Female | Female | Male | Female | Female | Male |
| Relation | Parent | Parent | Parent | Parent | Sibling | Parent |
| AML size (cm) | 1.5 × 1 | 0.7 × 0.9 | 1 × 0.5 | 2 × 1 | 0.8 × 01 | 0.8 × 0.8 |
| Ex vivo excision or left in situ | Left in situ | Left in situ | Ex vivo excision | Ex vivo excision | Left in situ | Left in situ |
| Recurrence or increase size | No | No | No | No | No | No |
| Perioperative complications | No | No | No | No | No | No |
| GFR of donated kidney (mL/min) | 44 | 42 | 67 | 49 | 45.3 | 50.5 |
| Follow-up (mo) | 86 | 150 | 96 | 80 | 46 | 25 |
| Serum Cr (mg/dL) | | | | | | |
| 1 mo | 2.2 | 1.6 | 0.9 | 1 | 1.3 | 0.3 |
| 1 y | 1.4 | 1.9 | 0.8 | 1.2 | 2.2 | 1 |
| 3 y | 1.3 | 2 | 0.7 | 1.4 | 2.3 | 1.1 |
| 5 y | 1.7 | 4.3 | 0.9 | 1.4 | | |
| Last follow-up | 6.5 | 11.5 | 1.3 | 1.4 | 2.3 | 1.1 |

Abbreviations: AML, angiomyolipoma; Cr, creatinine; ESRD, end-stage renal disease; GFR, glomerular filtration rate; GN, glomerulonephritis; PUV, posterior urethral valve; VUR, vesicoureteral reflux.

At median follow-up of 82 (range, 25–150) months, 4 cases were alive with functioning graft, while the first 2 cases have impaired graft function and resumed hemodialysis 5 and 7 years after transplantation, respectively. In those with ex vivo partial nephrectomy, no evidence of recurrence or newly developed graft AML was detected on the last follow-up images. For patients who received a kidney with small AML, there was no increase in the tumor size or developing new lesions at the last follow-up and no evidence of microscopic or macroscopic hematuria. Furthermore, in the patient with graft failure, there was no need for graft nephrectomy (Fig 2).

After a median follow-up of 50 (range, 19–154) months, all donors were alive with normal renal function with a mean (SD, range) serum creatinine of 0.9 (0.2, 0.7–1.2) mg/dL. None developed new AML in the remaining kidney.

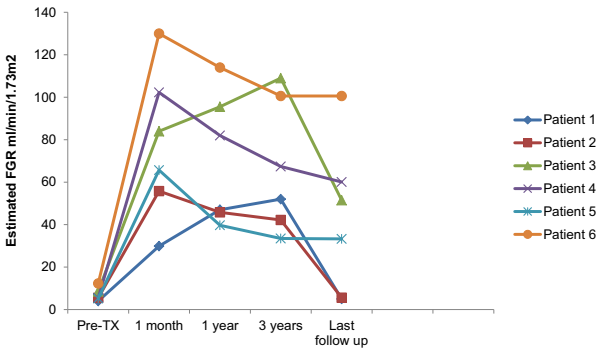


**Fig 1.** Estimated-GFR measured before and at different times after live-donor renal allotransplants.

## DISCUSSION

The reported prevalence of ESRD in Egypt was 375 patients per million people with a yearly incidence of 74 patients per million people [7]. Hemodialysis is the predominant form of renal replacement therapy. This may be attributed to the shortage of available live donors and the absence of a national deceased-donor program. Consequently, this increases the economic burden on both the health care system and diseased individuals. Thus, the need to expand the base of live donation is a necessary strategy that should be adopted by governmental health system. One method is to accept marginal living donors willing to donate their kidneys to genetically or emotionally related recipients. Till now, the definition of marginal living donor is not well defined. Yet, these donors can include elderly, obese, hypertensive, diabetic, or those with renal anomalies like nephrolithiasis, ureteropelvic junction obstruction, cysts, benign tumors, or even small, incidentally discovered renal cell carcinoma [8].

Herein, in 4 cases the AML were kept in situ without excision and transplanted. The median age of the recipient was 23.5 years. The mean (SD, range) tumor volume was 0.89 (0.4, 0.63–1.5) $cm^3$. After a median follow-up of 65 (range, 25–150) months, there was no increase in the tumor size or development of new lesions. Fritsche et al reported the first case of a successful live-donor renal transplantation with a 1 cm AML in situ from a 59-year-old mother to her 39-year-old son. The AML remained asymptomatic with no change in the size for 18 months [9]. In a recent report, a 27-year-old woman received a live-donor kidney with a lower polar AML (1.5 × 1 cm) from her mother. Follow-up for 5 years was uneventful with no change in the size of the AML on follow-up CT scan [10]. The assumption was to avoid possible complications of tumor excision like hemorrhage or

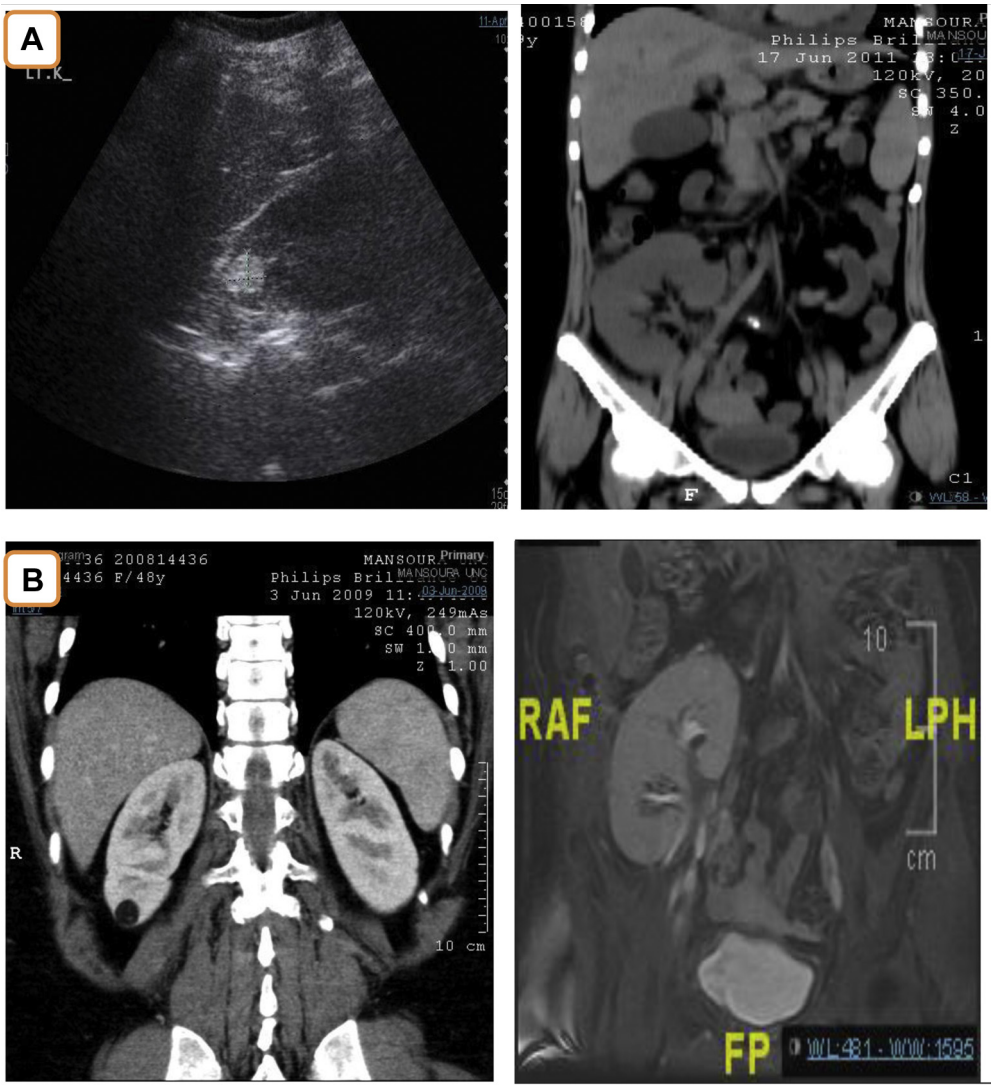


**Fig 2.** Illustrates the angiomyolipoma in both donor and related recipient. **(A)** Ultrasonography illustrates upper polar AML in the upper pole of the donor kidney and the CT image revealed no changes in the size after 6 years of transplantation. **(B)** CT revealed lower polar AML that was excised on back-table at time of transplantation and the magnetic resonance imaging follow-up of the recipient showed no recurrence of the lesion.

vascular malformation development. But this carries the potential risk of complications of spontaneous hemorrhage and tumor enlargement. However, this is a remote possibility in such a small lesion, as it has a slow and constant growth rate and the major risk factors for bleeding are tumor size, grade of the angiogenic component, and the presence of tuberous sclerosis. Moreover, mammalian target of rapamycin inhibitors like sirolimus and everolimus therapy were found to be associated with a reduction in AML size [11].

In 2 cases, the AML was excised at the bench side before transplantation. This was because they were exophytic and it was feasible to excise the lesions safely without increased risk of hemorrhage, renal damage, or prolongation of the ischemia time. The first reported case of direct live-donor renal transplantation after ex vivo excision of AML was performed in 1993 [12]. Sener et al reported 2 successful live-donor renal transplantations after ex vivo excision of 1 and 2.3 cm AML with no postoperative bleeding or urine leakage from the allograft. After 1 and 49 months of follow-up, patients were alive with a functioning graft and no evidence of tumor recurrence [13]. Similarly, ex vivo excision of a 7 cm AML in an emotionally related live donor was reported without perioperative complications. After 36 months, the graft was functioning with no evidence of tumor recurrence [3]. Recently, Nyame et al reported a successful

ex vivo excision of a 2.6 cm lower polar AML before transplantation. Although the recipient developed deep venous thrombosis posttransplant and was maintained on warfarin therapy, no perioperative bleeding or urinary leakage occurred. The graft function remained stable for 24 months with no evidence of tumor recurrence on radiological images [14].

Chen et al reported on successful renal transplantation after in vivo excision of a 7 cm AML between a genetically related couple. Partial nephrectomy was performed under cold ischemia for 10 minutes. Once the frozen section confirmed the benign pathology and the clear margins, donor nephrectomy was performed for transplantation. This enabled extensive evaluation of the repair of the tumor bed at the theoretical expense of an additional re-perfusion episode after cold ischemia. There was no delay in graft function and the patient's convalescence was unremarkable. He was discharged with proper graft function [15]. Similarly, in vivo excision of AML was performed safely, and the donor nephrectomy was completed. Then the graft was successfully transplanted. There were no postoperative complications. The recipient remains off dialysis at 18 months of follow-up [16].

The present study and the previous reports' results suggest that a donated kidney with incidentally diagnosed AML should not be prohibited from donation. This, together with other kidneys harboring small incidentally diagnosed renal cell carcinoma, might be a potential solution for the ongoing shortage of available kidney donors. Detection of AML in the donated kidney could be managed by 1 of the following methods. First, endophytic inaccessible lesions less than 4 cm can be left in situ and the kidney transplanted with regular follow-up imaging and, with the use of mammalian target of rapamycin inhibitors as immunosuppressive drugs, AML is expected to regress in size. Second, an exophytic lesion can be enucleated, whether in vivo or ex vivo, before transplantation. Ex vivo partial nephrectomy is a safe and straightforward procedure. It provides a bloodless field without significant increase in the warm ischemia time. Moreover, none of the reported cases were complicated with postoperative bleeding, urinary leakage, or unfavorable outcome.

To the best of our knowledge, this is the largest, single-center series concerning the outcome of transplantation using AML-harboring kidneys. It presents the results of successful renal transplantation using kidneys previously considered unsuitable due to the presence of benign pathology. Proper understanding of the inherent nature of AML and advances in the surgical techniques helped with acceptance of these marginal, living donors. Although this will not solve the national problem of kidney shortage, it will provide a new track for those whose only available donors have benign renal pathology. However, the results should be taken in the context of the study limitations. It is a retrospective study with the inherent limitation to this design. The number of cases is limited because of the rarity of the condition and the real-life look to the donor with renal anomalies. Also, the results represent the experience of a single center, which does not reflect the perspectives of other transplantation centers in our locality toward the renal AML.

## CONCLUSION

Presence of incidentally discovered renal AML should not prohibit donation. Tumor excision (if exophytic) or keeping in situ (if small endophytic) and completing the procedure of transplantation is not associated with an increased risk of long-term complications or unfavorable graft function outcome. It might expand the criteria for accepting marginal donors in an attempt to overcome the problem of organ shortage.

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