



Are the long-term outcomes of En-bloc kidney transplantation from pediatric deceased donors comparable to those from adult donors?

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Introduction

- ✓ The prevalence of ESKD is growing in the world
- ✓ Kidney transplantation represents the **optimal approach** for kidney replacement therapy in patients with ESKD.
- ✓ It provides the best outcomes in terms of **survival and quality of life**
- ✓ Kidney transplantation is facing a **shortage of grafts**.
- ✓ An important effort has been made in recent decades in an attempt to increase donations and reduce the number of patients on the waiting list
- ✓ The use of expanded criteria donors is increasing, and the use of kidneys from **pediatric donors** is considered.



- ✓ Initially, the use of kidneys from pediatric donors (<5 years of age or whose weight is <15 kg or with kidneys size <6 cm) into adult recipients was associated with some complications, with the consequent decrease in graft survival and poor functional results.
- ✓ Higher incidence of acute rejection, lower nephron mass in donors, risk of hyperfiltration injury, delayed graft function, and vascular and urological complications, especially in early the postoperative period
- ✓ Hyperfiltration, a consequence of the dissimilarity between donor and recipient weight, is one of the causes of late graft failure in recipients of pediatric donor kidneys.
- ✓ The use of pediatric En bloc grafts attempts to minimize some of these risks by providing greater nephron mass and a larger caliber of the implanted blood vessels
- ✓ It offers a potential solution to broaden the pool of available kidney donors.
- ✓ In general, donors weighing less than 8 kg could increase the risk of complications despite en bloc transplantation

- ✓ It was first performed successfully in humans by Martin et al in 1969 (when a child received an 'en bloc 'kidney graft from an anencephalic infant which has functioned for more than 30 years)
- ✓ The surgical technique consists of **using the aorta and vena cava of the donor** as one vascular tree which is anastomosed directly to the recipient's vessels, and long-length ureters and bladder path



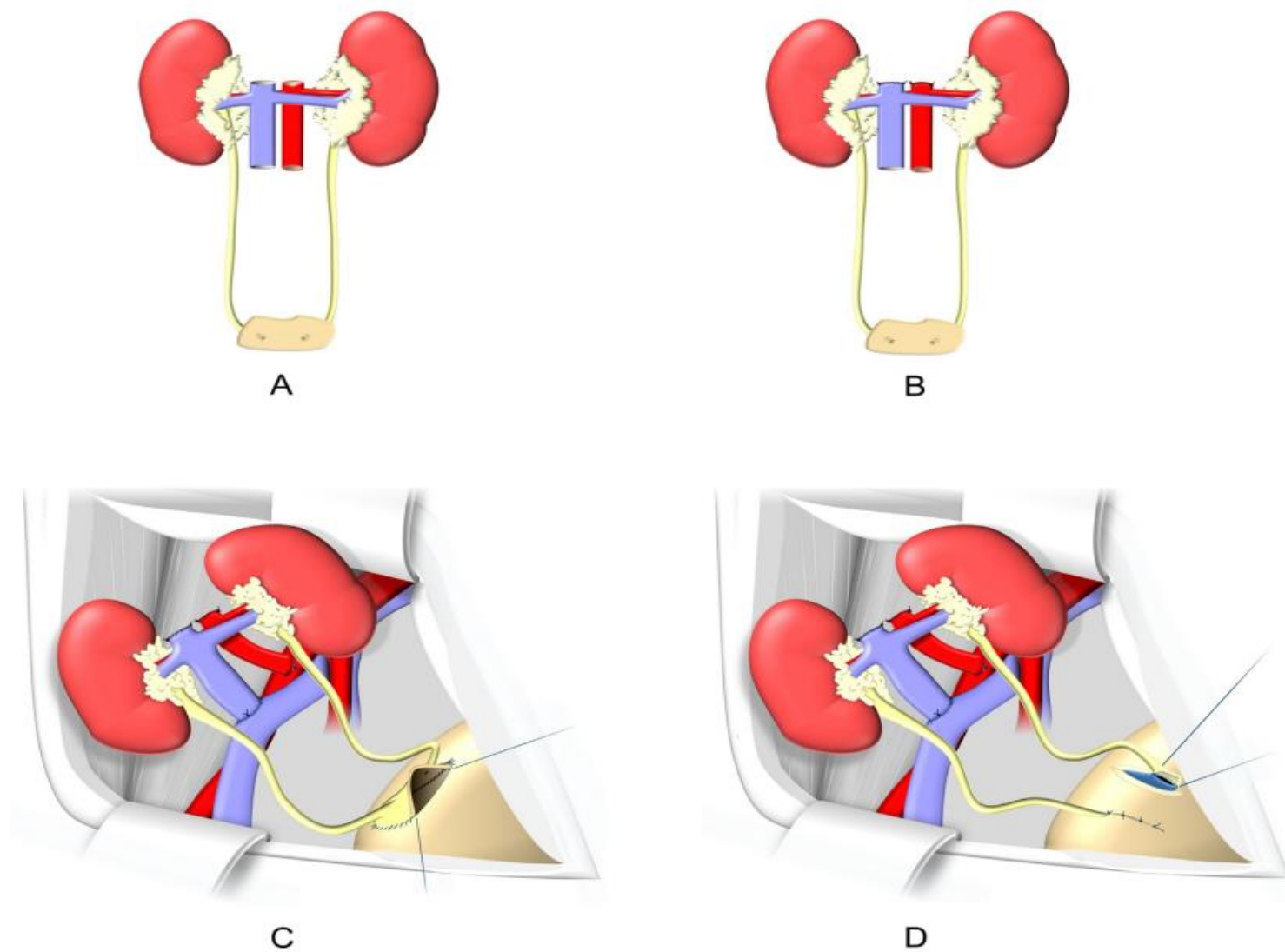


Fig. 1 – (A) En bloc procurement. (B) Suprarenal aorta and vena cava sealing. (C) Bladder patch technique. (D) Liech-Gregoire anastomoses.

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- ✓ In general, the age of the recipient is an important factor in the use of pediatric grafts. (kidneys with high long-term survival)
- ✓ The optimal recipient is a **young, low-weight person, with low immunological risk, without cardiovascular risk factors, and without a history of abdominal surgeries** that increase surgical complexity
- ✓ EBKT has more recently been reported to **have excellent outcomes.**
- ✓ Long-term results of EBKT are scarce



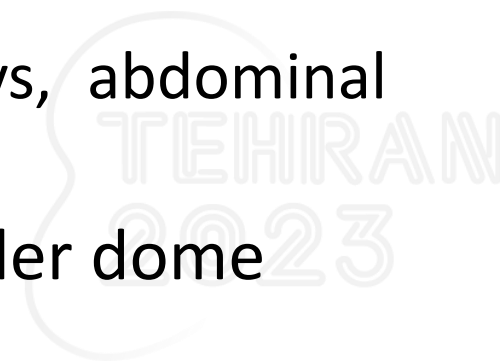
Objective

- ✓ The objective of our study was to assess and compare the long-term outcomes of En-bloc kidney transplantation from pediatric donors to the recipients from adult donors.



Materials and methods

- ✓ We conduct a retrospective cohort study of all the EBKT procedures performed in our kidney transplant center since 2015
- ✓ 13 En-bloc kidney transplants from pediatric donors to adults compared to 52 age and gender-matched recipients from adult donors (33 living donors and 19 deceased donors)
- ✓ Donors were exclusively pediatric brain-dead donors
- ✓ No donor presented AKI
- ✓ Ideal procurement was performed En bloc with both kidneys, abdominal aorta, vena cava, the ureters, and the bladder patch
- ✓ An anastomosis of the trigonal patch to the recipient's bladder dome



- ✓ The recipient's iliac fossa was approached in the standard fashion, preferably on the right side
- ✓ The surgery was performed in almost all cases by the **same highly experienced surgeons**
- ✓ **Anti-thymocyte globulin** was used for induction therapy followed by triple therapy with **mycophenolate mofetil, steroids, CNIs**
- ✓ Regarding follow-up, serum creatinine (mg/dL), and **eGFR** were determined to assess graft function.
- ✓ The study was conducted in accordance with the ethical principles outlined in the **Declaration of Helsinki** and received approval from the ethics committee of Tehran University of Medical Sciences

- ✓ Statistical analysis was performed with the SPSS Statistics version 26
- ✓ Continuous variables are expressed as means and standard deviations, and categorical variables are expressed as numbers and percentages. A **two-sided p value of < 0.05** was considered significant
- ✓ Correlation between variables was identified with **Pearson and Spearman correlation tests**
- ✓ The **Mann-Whitney U test** was utilized to Determine a significant difference between the two groups

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Results

- ✓ 13 En-bloc kidney transplants from pediatric donors to adults compared to 52 age and gender-matched recipients from adult donors (33 living donors and 19 deceased donors)
- ✓ The duration of follow-up was 60 to 90 months (5-7.5 years)



Donor characteristics

Group	En bloc graft (N=13)	Adult donor (N=52)
Gender (Male / Female)	4 / 4	34 / 6
Age (Mean±Sd , Median)	3.2 ± 1.5 , 4.0	31.1 ± 9.7 , 29.5

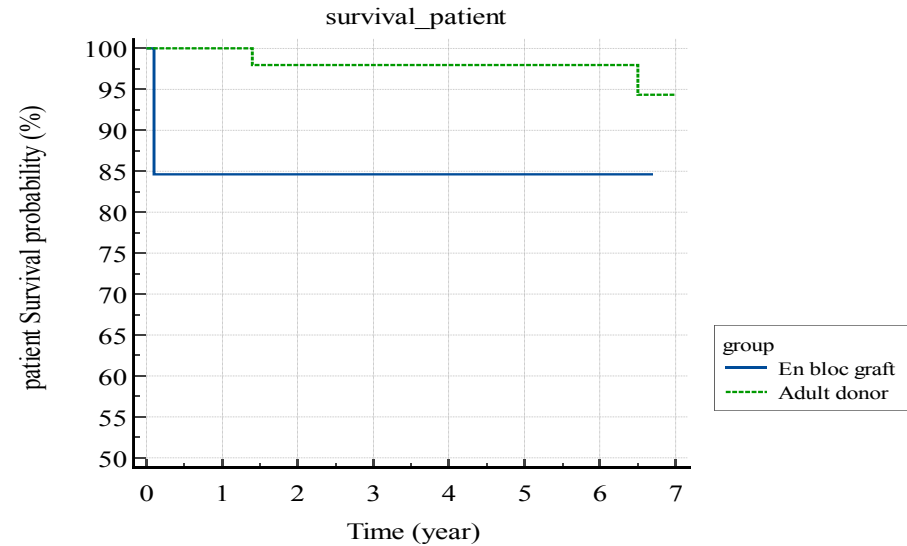


Recipients characteristics	Group	En bloc graft (N=13)	Adult donor (N=52)	P-value
Gender (Male)		8 (61.5 %)	32 (61.5 %)	1.00
Age (Mean±Sd , Median)		44.1 ± 9.4 , 40.0	40.1 ±10.4 , 38.0	0.168
Cause of kidney dysfunction				0.739
HTN		7 (58.3 %)	16 (34.8 %)	
DM		1 (8.3 %)	5 (10.9 %)	
polycystic kidney disease		1 (8.3 %)	5 (10.9 %)	
infection		1 (8.3 %)	2 (4.3 %)	
Lupus		1 (8.3 %)	1 (2.2 %)	
Horseshoe kidney		1 (8.3 %)	0	
Glomerulonep hritis or CKD		0	5 (10.9 %)	
Proteinuria		0	3 (6.5 %)	
Alport syndrome		0	2 (4.3 %)	
Rejection Previous graft		0	2 (4.3 %)	
reflux nephropathy		0	2 (4.3 %)	
FSGS		0	1 (2.2 %)	
Fibrous of kidney		0	1 (2.2 %)	
kidney stone		0	1 (2.2 %)	

Patient survival

Group	Estimate	Std. Error	95% Confidence Interval		P-value
			Lower Bound	Upper Bound	
En bloc graft	5.69	0.66	4.39	6.98	0.056
Adult donor	7.43	0.13	7.18	7.69	

Group	En bloc graft (N=13)	Adult donor (N=52)	P-value
Patient survival			0.176
1 month	84.6 %	100.0 %	
1 year	84.6 %	98.1 %	
5 year	84.6 %	96.2 %	

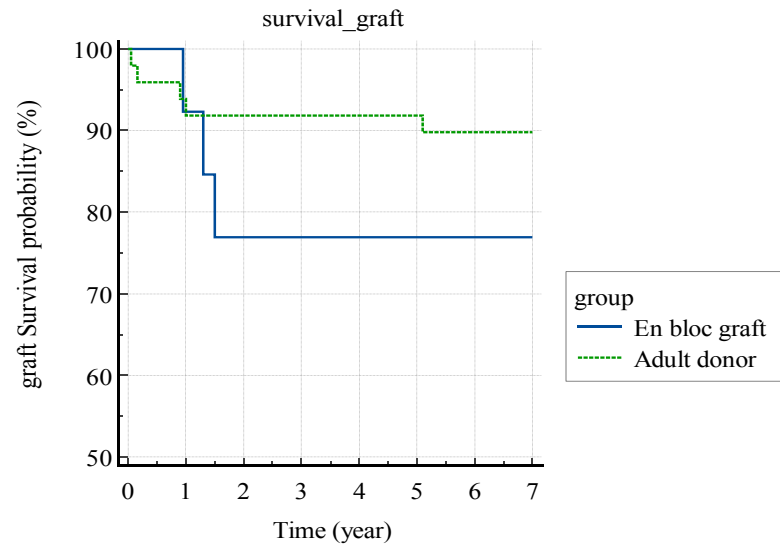


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Graft survival

Group	Estimate	Std. Error	95% Confidence Interval		P-value
			Lower Bound	Upper Bound	
En bloc graft	5.90	0.81	4.30	7.50	0.074
Adult donor	6.97	0.28	6.42	7.52	

Group	En bloc graft (N=13)	Adult donor (N=52)	P-value
Graft survival			0.070
1 month	84.6 %	98.1 %	
1 year	76.9 %	94.2 %	
5 year	69.2 %	90.4 %	



Complications of kidney transplantation

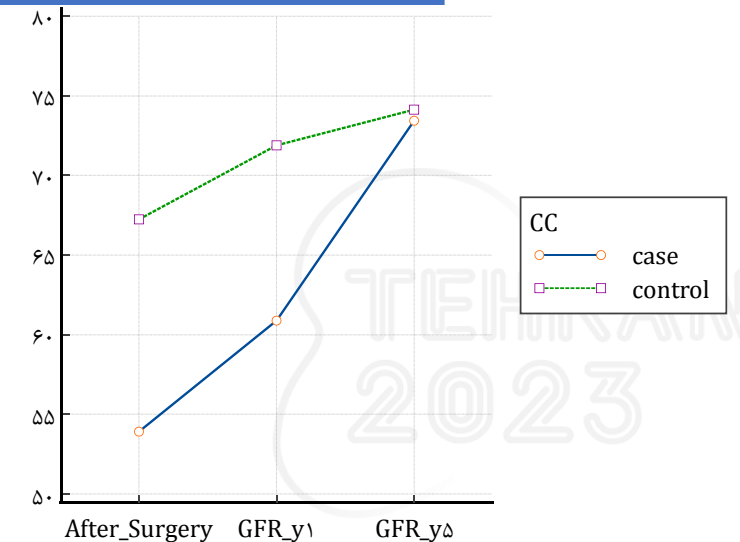
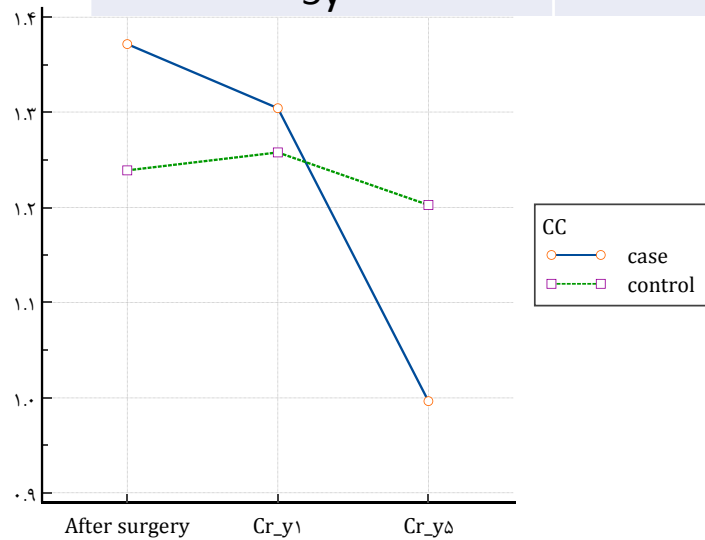
Group	En bloc graft (N=13)	Adult donor (N=52)	P-value
Complications			
Acute Rejection	2 (15.4 %)	2 (3.8 %)	0.18
Vascular Thrombosis	2 (15.4 %)	0	0.037
Ureteral stenosis	1 (7.7 %)	2 (3.8 %)	0.49
UTI	1 (7.7 %)	2 (3.8 %)	0.49
Lymphocele	1 (7.7 %)	0	0.20

The sole significant finding in this study was a higher incidence of vascular thrombosis in the En-bloc transplant group when contrasted with the conventional transplant group.



eGFR change during years

Group	En bloc graft	Adult donor	P-value
Cr			
At Discharge	1.37 ± 0.2	1.24 ± 0.2	0.067
1y	1.30 ± 0.5	1.26 ± 0.7	0.864
5y	1.00 ± 0.2	1.16 ± 0.4	0.386
eGFR			
At Discharge	54 ± 13	67 ± 16	0.014
1y	61 ± 20	72 ± 22	0.222
5y	73 ± 12	74 ± 20	0.925



- ✓ There was no significant correlation between the age of recipients and eGFR, and patient and graft survival in both group
- ✓ There was no significant correlation between the gender of recipients and eGFR in the En bloc group, but eGFR was higher among male patients in the adult recipient group (P=0.001)
- ✓ In contrast, with increasing the age at the time of kidney transplantation, graft survival decreased in the En bloc group, not in the adult recipient Group (p=0.021) (low number of participants)



Discussion

- ✓ The studies reporting results on EBKT are scarce.
- ✓ The historical **first negative results** have contributed to the **rejection of the technique** in the past.
- ✓ lower survival was seen for EBKT in the old transplant era (before 1997)
- ✓ All recent studies have reported **favorable outcomes with EBKT**.

- ✓ Kizilbash SJ, Evans MD, Chinnakotla S, Chavers BM. Survival benefit of en bloc transplantation of small pediatric kidneys in children. Transplantation 2020;104:2435–43.



- ✓ Several studies have shown the **superiority of EBKT over single kidneys from very small pediatric donors**
- ✓ Double ‘en bloc’ transplanted kidneys from the youngest donor group, have **similar graft survival as ideal donors.**
- ✓ It was even reported a **significantly better long-term outcome** for ‘en bloc’ transplanted double pediatric kidneys compared **to standard single kidney recipients**
- ✓ Sureshkumar KK, Reddy CS, Nghiem DD, Sandroni SE, Carpenter BJ (2006) Superiority of pediatric en bloc renal allografts over living donor kidneys: a long-term functional study. *Transplantation* 82(3):348–353. doi:10.1097/01.tp.0000228872.89572.d3
- ✓ Sanchez-Fructuoso AI, Prats D, Perez-Contin MJ, Marques M, Torrente J, Conesa J et al (2003) Increasing the donor pool using en bloc pediatric kidneys for transplant. *Transplantation* 76(8): 1180–1184. doi:10.1097/01.TP.0000090395.98045.09
- ✓ Mohanka R, Basu A, Shapiro R, Kayler LK (2008) Single versus en bloc kidney transplantation from pediatric donors less than or equal to 15 kg. *Transplantation* 86(2):264–268

- ✓ Very few studies have evaluated **graft size after pediatric kidney transplantation** in adults and concerned mostly single kidneys with a mean follow-up rarely over 24 months.
- ✓ It was found a **2.6-fold increase** in volume at 12 months
- ✓ Graft size increased rapidly after transplantation and reached normal size at 3 months.

- ✓ Sanchez-Fructuoso AI, Prats D, Perez-Contin MJ, et al. Increasing the donor pool using en bloc pediatric kidneys for transplant. *Transplantation* 2003;76:1180–4
- ✓ Foss A, Line P-D, Brabrand K, Midtvedt K, Hartmann A, et al. A prospective study on size and function of paediatric kidneys (<10 years) years) transplanted to adults. *Nephrol Dialysis Transplant* 2007;22: 1738–42.
- ✓ Zhu L, Fu C, Chen S, et al. Successful single-kidney transplantation in adult recipients using pediatric donors aged 8 to 36 months: comparable outcomes with those using pediatric donors aged >3 years. *Transplantation* 2019;103:2388–96

- ✓ There was a greater number of **vascular complications** compared to adult kidney transplantation, such as **graft thrombosis and renal artery stenosis**
- ✓ Most complications occurred in the **immediate postoperative period**
- ✓ **Graft thrombosis** was reported in **3.1–12.5%** of the cases
- ✓ The possible causes of graft thrombosis include a **difference in blood pressure and vessel size between the donor and the recipient with turbulent and inadequate perfusion of the graft, torsion of the kidney and progressive thrombosis of a blind end of the aorta in ‘En-bloc’ transplanted double kidneys**

- ✓ Hafner-Giessauf Hildegard, Mauric A, Müller H, Eller P, Zigeuner R, Iberer F, et al. Long-term outcome of en bloc pediatric kidney transplantation in adult recipients ---- up to years of center experience. Ann Transplant. 2013;18:101---7, <http://dx.doi.org/10.12659/AOT.883845>.
- ✓ Smyth G, Eng M, Power R, Hickey DD. Long-term outcome of cadaveric pediatric en bloc showed transplantation ---- A 15-year experience. Transplant Proc. 2005;37:4228---9, <http://dx.doi.org/10.1016/j.transproceed.2005.11.019>.
- ✓ Thomusch O, Tittelbach-Helmrich D, Meyer S, Drognitz O, Pisarski P. Twenty-year graft survival and graft function analysis by a matched pair study between pediatric en bloc kidney and deceased adult donors grafts. Transplantation. 2009;88:920---5, <http://dx.doi.org/10.1097/TP.0b013e3181b74e84>.

- ✓ The most frequently described major urological complications after en bloc pediatric kidney transplantation are **stenosis of the ureterovesical anastomosis**, the appearance of **lymphocele**, and **urine leak**
- ✓ It is demonstrated that however common in EBKT, urological complications **did not have an impact on graft survival**.
- ✓ Fananapazir G, Tse G, Di Geronimo R, et al. Urologic complications after transplantation of 225 en bloc kidneys from small pediatric donors 20 kg: incidence, management, and impact on graft survival. Am J Transplant 2020;20:2126–32.



Renal Disease

En Bloc Kidney Transplantation: A Retrospective Study of an 18-year Experience in a Single Institution

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- ✓ 21 EBKT (2002-2020), with a mean follow-up of 65 months
- ✓ Graft loss: 1 (5%)
- ✓ Excellent patient (100%) and graft (93%) survival after EBKT
- ✓ Vascular thrombosis: 2 (10%)
- ✓ 33% of urological complications including Ureteral stenosis:1 (5%)
- ✓ UTI: 9 (43%)
- ✓ Acute rejection: 2 (10%).

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Evolution of plasmatic creatinine and creatinine clearance

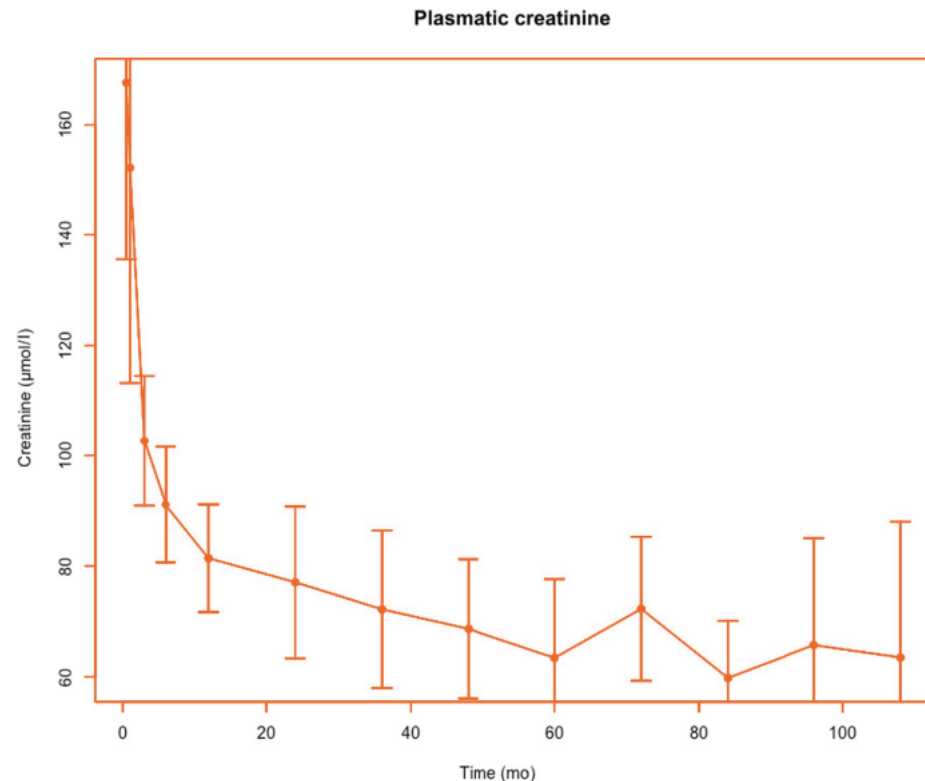


Fig. 2 - Mean plasmatic creatinine over time with 95% confidence interval.

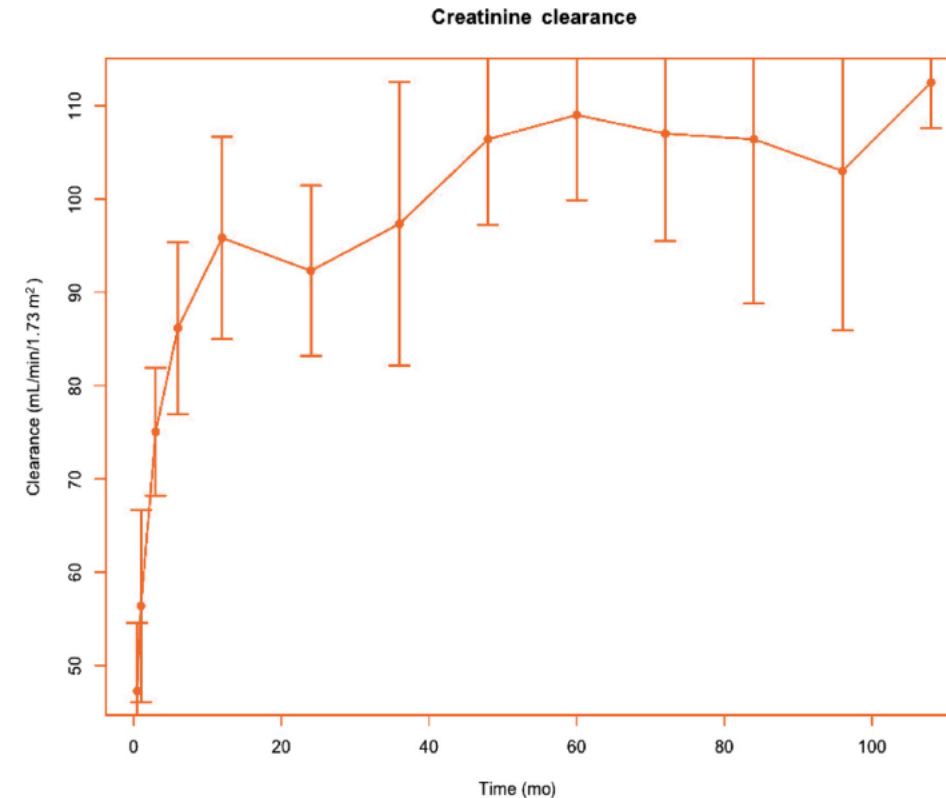


Fig. 3 - Mean creatinine clearance over time with 95% confidence interval.

Creatinine clearance increased during the first 3 yr before reaching stabilization. At 10 yr, the mean creatinine clearance was 112 ml/min (95% confidence interval 107–117)

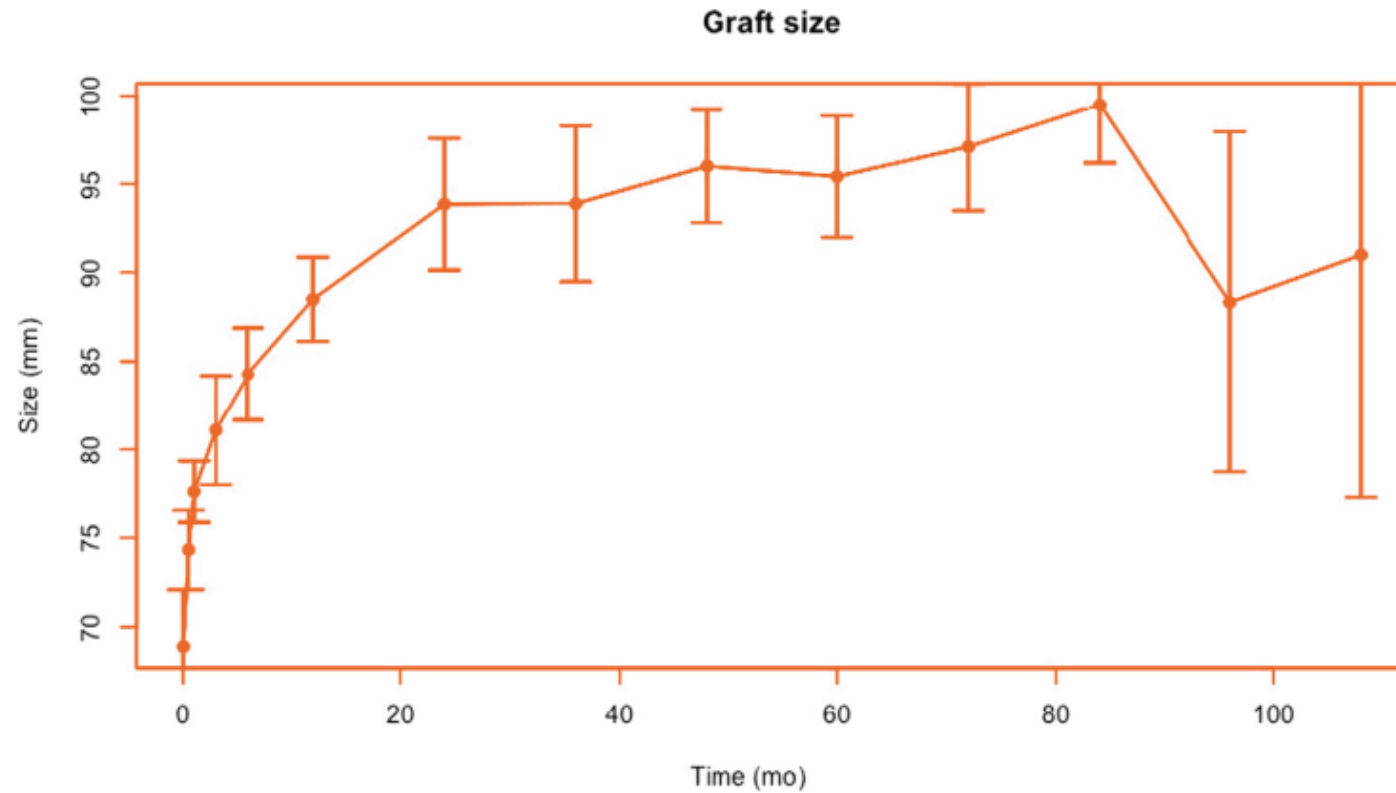


Fig. 4 – Mean graft size over time with 95% confidence interval.

As for graft size, the mean graft size increased in the first 2 yr after transplantation until reaching an adult size a rapid growth in the 1st year, before reaching the final size at 24 months and remaining stable thereafter





ORIGINAL ARTICLE

A 20-year experience in cadaveric pediatric en bloc kidney transplantation in adult recipients[☆]



J.A. López-González^{*}, M. Beamud-Cortés, L. Bermell-Marco, M.A. Pérez-Martínez, M.D. Cuenca-Ramírez, L.M. Moratalla-Charcos, J. Planelles-Gómez, M. Sánchez-Sanchís, J.F. Vidal-Moreno

- ✓ 42 patients who received en bloc kidney transplantation from a pediatric cadaveric donor in our center between 1999 and 2019.
- ✓ vascular complication rate of 23.8% (4 (9%) with graft thrombosis) and 16.7% of graft loss
- ✓ Graft function after this period was adequate in 83.3% of grafts (35/42)
- ✓ The main surgical complications occurred in the immediate postoperative period.



Figure 4 Graft survival. The graph shows how most graft losses occur in the immediate postoperative period while survival is maintained in the remaining period.



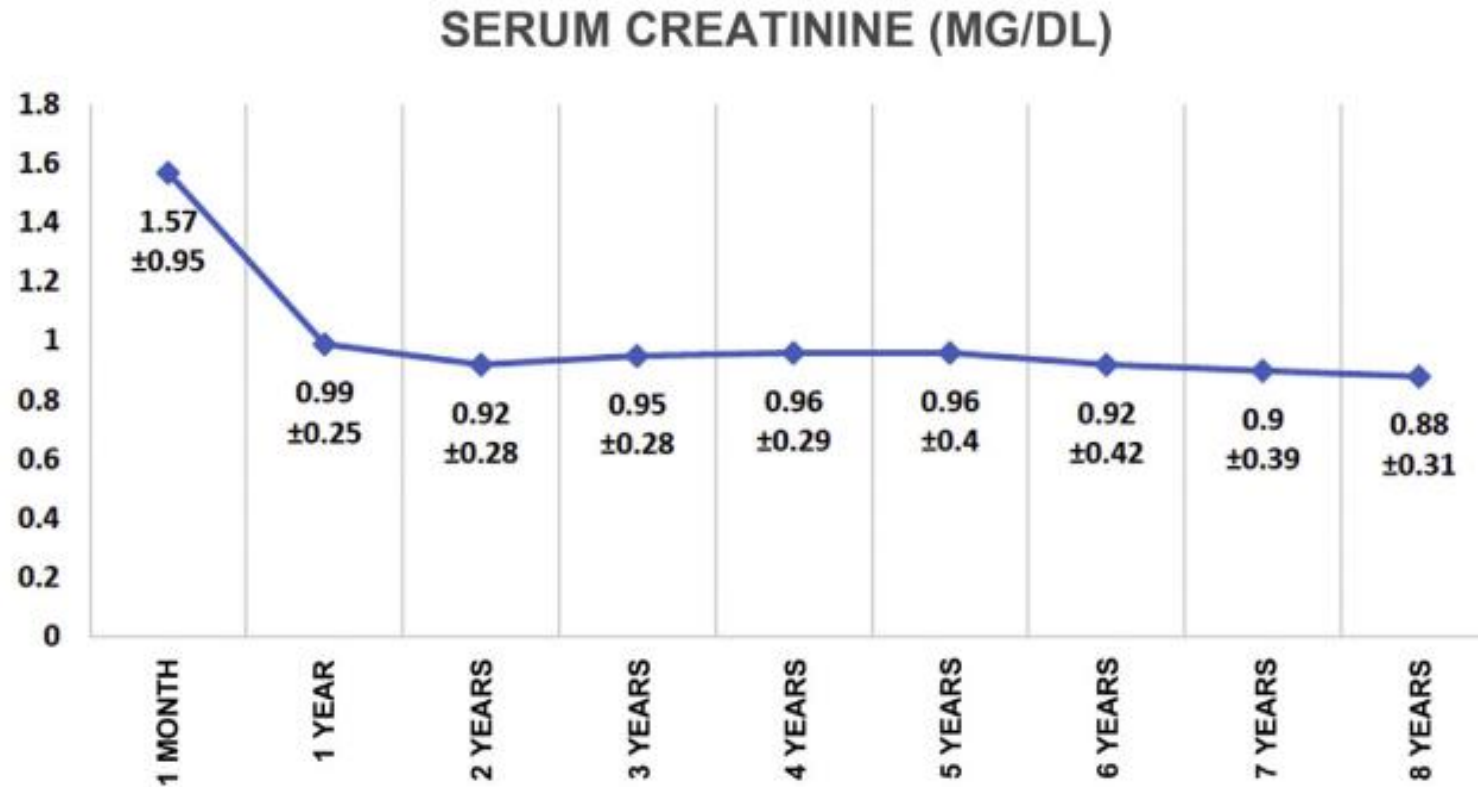


Figure 5 Mean serum creatinine values (mg/dL) during follow-up. At one year, creatinine values reach the normal range and remain stable over time.

It remained stable over time and even improved progressively

Long-term outcomes of en-bloc renal transplantation from paediatric donors into adult recipients[☆]

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Department of Transplant Surgery and Urology, Beaumont Hospital, Dublin, Ireland

Methods: Twenty-three paediatric to adult EBKTs were performed by the Irish National Kidney Transplant Service between 1990 and 2016. The primary outcome variable was long-term en-bloc allograft survival rate. Secondary outcome variables were incidence of allograft thrombosis, incidence of delayed graft function, overall patient survival and serum creatinine at most recent follow-up. Outcomes were compared to single kidney transplant recipients from the same time period.

Results: Mean donor age was 1.8 ± 0.97 years (range: 7 months to 3 years). Recipient age was 46 ± 12 years. Mean follow-up was 133 ± 64 months (range: 36–264). Overall graft survival was 100%, 91% and 80% after 1, 5 and 10 years respectively, compared to 92%, 79% and 61% in single kidney transplant recipients ($p = 0.04$). There were 5 cases of allograft failure, 3 due to death from unrelated causes. Median time to graft failure was 108 months (range: 36–172). Mean serum creatinine was 72.6 ± 21.6 $\mu\text{mol/l}$ after the follow-up period. There were no cases of graft thrombosis or delayed graft function. Overall survival was 96.4%, 88.0%, 76.23% and 50.5% at 1, 5, 10 and 20 years respectively.

Conclusion: En-bloc paediatric kidney transplantation is associated with excellent long-term allograft and patient survival and is a feasible strategy for increasing the transplant donor pool in carefully selected recipients.

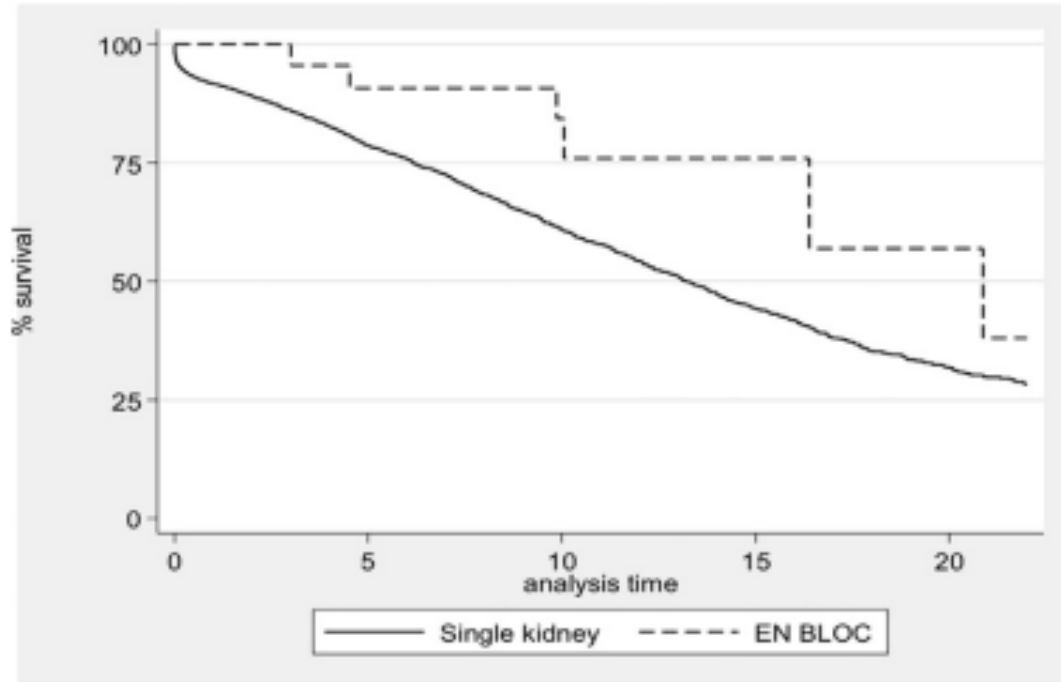


Fig. 2 – Kaplan–Meier curve of overall graft survival.

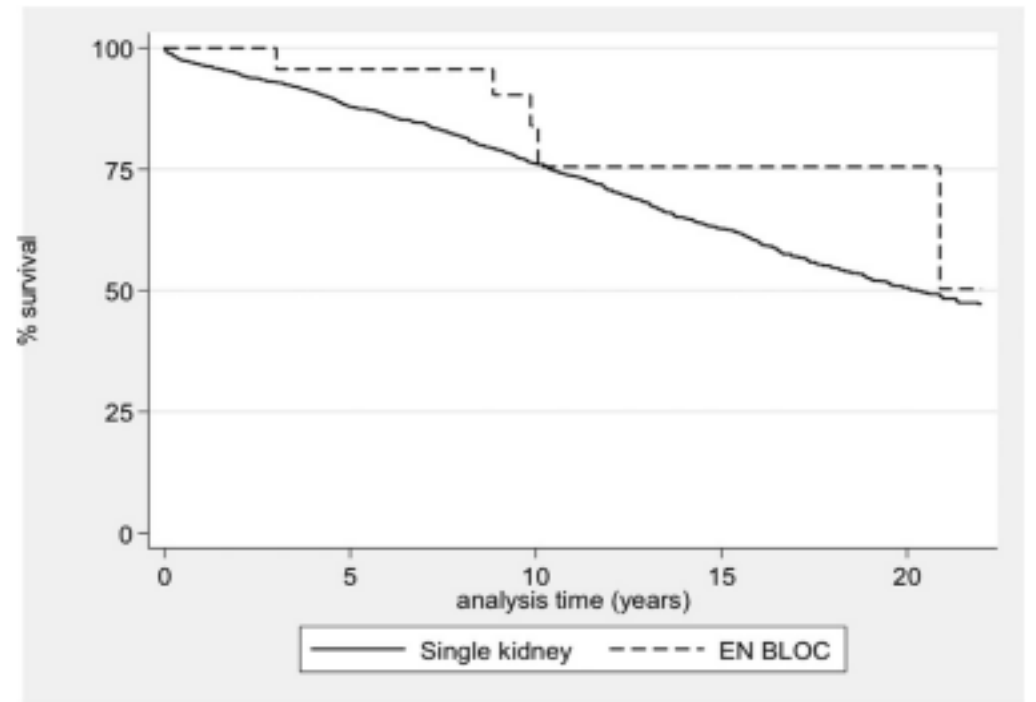


Fig. 4 – Kaplan–Meier curve of overall survival.

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- ✓ 72 pediatric en bloc and 75 living donor kidney recipients.
- ✓ It was revealed **similar graft survival between the groups up to 27 years** of follow up (log rank $p = 0.78$).
- ✓ Estimated **GFR** was **significantly higher in pediatric en bloc kidney recipients from years five through 17 posttransplantation**.
- ✓ **Conclusions:** Pediatric en bloc kidneys conferred **long-term graft survival similar to living donor kidneys over a 25-year period following transplantation** along with **superior graft function**. These findings support improved utilization of pediatric kidneys for transplantation into adults which not only helps to alleviate organ shortage but also provide excellent long-term function.

Sureshkumar KK, Habbach A, Tang A, Chopra B. Long-term Outcomes of Pediatric En Bloc Compared to Living Donor Kidney Transplantation: A Single-Center Experience With 25 Years Follow-Up. *Transplantation*. 2018;102(5):e245-e8.

Limitations of the study

- ✓ Low sample size
- ✓ Retrospective nature of the study
- ✓ Absence of electronic records and difficulties in data gathering
- ✓ Some missing data such as mean weight of donors, BMI of recipients, cold ischemia time



Conclusion

- ✓ EBKT can be considered as a valid option to expand the donor pool.
- ✓ Long-term function and survival are excellent.
- ✓ There was a high rate of postoperative complications.
- ✓ Improved surgical technique together with adequate selection of donors and recipients can lower complications





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