AUCTORES
Globalize your Research

International Journal of Clinical Nephrology

Morched Haddad *

Open Access

Case Report

The Role of Cystatin C and the CKD-EPICr-Cyst equation in evaluating Glomerular Filtration Rate in Kidney Transplant Donors

Morched Haddad *

Néphrologie, Transplantation, Alger, Algérie.

***Corresponding Author:** Morched Haddad, Néphrologie, transplantation, Alger, Algérie.

Received Date: May 04, 2023; Accepted Date: 26 may 2023; Published Date: 08 June 2023

Citation: Morched Haddad (2023), The Role of Cystatin C and the CKD-EPICr-Cyst equation in evaluating Glomerular Filtration Rate in Kidney Transplant Donors, *International Journal of Clinical Nephrology*. 5(3); **DOI:10.31579/2834-5142/054**

Keywords: kidney; urolithiasis; kidney stone disease (ksd); glomerular filtration rate (gfr);chronic kidney disease (ckd); extracorporeal shock wave lithotripsy (eswl); ureteroscopy, percutaneous nephrolithotomy (pcnl); retrograde intra renal surgery (rirs) and mini percutaneous nephrolithotomy (mpnl)

Introduction

The incidence of chronic kidneydisease has increased markedly in recent years, with these serious complications, especially in the terminal stage, requiring treatment with dialysis and kidney transplantation (1). The latter, made from a living donor, remains the ideal treatment for IRCT; It offers a better quality of life for patients (2). S he realization from a living donor is based on strict and well-defined selection criteria, which concern both the donor and the recipient. One of the main criteria is the evaluation of the glomerular filtration rate (GFR) before donation, this is done by different evaluation methods from one country to another: GFR measurement methods, isotopic methods and GFR estimation methods by specific equations (4,5). In our country, the only transplant that is done is from a living donor, hence the interest of a good evaluation of the donor (2,3). The eGFR is calculated by the MDRD and CKD-EPICr equations according to the habits of the transplant teams without having a clear idea of the superiority of one over the other. The objective of our study is the evaluation of GFR in pre- and post-donation donors, using cystatin C and the equations CKDEPIcyst and CKDEPICr-cyst.

Cystatin C (cyst C) has been known since 1961. The two techniques for the determination of cystatin C are: immuno-nephelometry and immuno-turbidimetry. The sample can be stored for at least 48 hours at room temperature, 7 days at + 4 ° C and several months or even several years at - 80 C °. Several cycles (3-10) of freeze-thaw can be done. Blood is collected on either heparin or EDTA(6,7,8,9,10).

Recent guidelines from KDIGO 2012(11) suggest the use of cyst C to validate CKD in patients considered as such on the basis of a GFR < 60 ml.mn.1.73m² without albuminuria or other markers of kidney damage. The KDIGO2017 (3) followed by the application of the KDIGO 2020 (12) concerning the assessment of GFR in living donors recommend: the measurement of GFR by reference methods. If no: an initial test using creatinine equations and a confirmatory test using CKDEPICr-cyst(mixed) if reference methods are not available. The purpose of the evaluation is to authorize the donation according to the well-defined threshold (90 ml.mn.1.73m²). The addition of cystatin C to creatinine as a variable in the CKD PPE formula improved its effectiveness especially in terms of GFR accuracy.

Problematic:

The eGFR before authorizing donation requires a rigorous assessment, to allow the donor to be selected safely. Recommendations suggest measuring GFR by reference methods or measuring by isotopic method. The unavailability of these techniques and the practical difficulty of their realization, have led to the development of other methods such as the online calculator. In our country, we use creatinine equations, but these equations are still insufficient. Lack of access to the above methods; which led us to use other equations based on the combination of creatinine and cystatin C. The objective of our study is the usefulness of hepatitis C in the evaluation of GFR by the mixed CKD-PPE equation in living donors before donation and after kidney donation, to select the donor in the absence of reference measurement methods.

Materials and Methods:

It is a prospective follow-up, longitudinal, descriptive and analytical, multicenter study involving three nephrology teams . We recruited 55 couples (55 donors and 55 recipients), then we excluded 04 recipients because of their ages, note that: The sample size is calculated: n = P (1-P) X (Z/d) 2.P: prevalence: 1,025%. Z: 1.96 with an alfa risk of 5%. D: accuracy: 3%.n: 43.3.

After rigorous interrogation and clinical examination. eGFR was calculated using equations (MDRD, CKD-EPICr, CKD-EPICyst and CKD-EPICr-cyst) using an online calculator "06 GFR equations" before donation, 3 months and 6 months after donation.

Results:

In our study **(Table 01)** we have 55 donors, among them 53.6% women, the average age is: 47.8±11.78 years, the average BMI is 25.56±2.94 kg/m² and donors are classified according to age with a Cut-off: 40 years:

30 donors (representing 75% of donors over 40 years of age) have a BMI between 25-29.9 kg/m² donation they are overweight.

3 donors out of 55 have a BMI >30 kg/m² considered obese, two of them are over 40 years old

The different means of the eGFR calculated by the 04 equations (MDRD; CKDEPICr, CKDEPIcyst, CKDEPICr-cyst) which are: 103.67±28.2;101.15±18.77;99.58±21.25 and 98.07±19.53 respectively. By the ANOVA test: there is no significant difference between the means of GFR by the 04 equations before donation.52 donors out of 55 are normo tense and 03 hypertensive donors balanced under monotherapy without visceral impact, which represents 5.4% of all donors.

The mean cystatin C prior to donation was: 0.81±0.21mg/l **(Table 01**). There is a significant difference between the pre-donation means of creatinine and cystatin C by sex, the hourshad higher means of creatinine and cystatin C than women respectively: 7.13±1.91 and 8.52±1.70 with a P<0.01 and cystatin C values 0.92±0.19 and 0.71±0.18 with a P<0.01. There is no significant difference by age, hypertension, and microalbuminuria.

With regard to the eGFR averages calculated by the different equations: there is a highly significant difference between the age-specific eGFR averages for a cut-off: 40 years calculated by CKD-EPICr-cyst and CKD-EPIcyst, donors aged less than 40 years had higher averages compared to donors over 40 years of age with a P of 0.002. While the eGFR averages that are calculated by MDRD there is no significant difference. Also there is a significant difference between eGFR averages by sex,

Table 01:

Variables	Averagee m±SD	Mediane	Min	Max	Centile 25	Centile 50	centile 75
Age (an)	47,8±11,78	50	29	73	37	50	58
SexeH/F	25/30						
BMI (Kg/m2)	25,56±2,94	26	19,64	33	23	26	28
TA system	123,92±9,08	125	110	145	120	125	130
TA diast	69,3±7,21	70	60	90	65	70	75
Cyst (mg/l)	0,81±0,21	0,81	0,38	1,4	0,65	0,81	0,96
Creatinine(mg/l)	7.7mg/l±1.94	7.7	4	12	3.95	7.7	9.80

Table No.:02

	Average±SD	Median	min	Max	Centile25	Centile50	Centile75
DFG (ml/mn/1.73 m2) (MDRD)	103,67±28,2	105	58	184	82	105	120
DFG (ml/mn/1.73 m2) (CKDEPImixte)	101,15±18,77	100	68	158	86	100	114
DFG (ml/mn/1.73 m2) (CKD EPIcystC)	99,58±21,25	100	54	144	86	100	116
DFG (ml/mn/1.73 m2) (CKD EPI CR)	98,07±19,53	99	62	141	83	99	111

Which are calculated by CKD-EPICr-cyst and CKD-EPIcyst with a P of 0.03 and 0.004 respectively, while those calculated by MDRD and CKD-EPICr have no significant difference.18 candidates out of 55 donors representing 32.72% are excluded from donation by the MDRD equation according to the authorized donation threshold defined by the KDIGO 2017 recommendations. the mixed CKDEPI equation made it possible to reclassify 08 candidates out of 18, they were recovered and accepted. It misranked 10 donors who represent 18.18%. There is a strong relationship between the two equations with a highly significant P while the concordance with Kappa is equal to 0.4. These 10 donors were collected and did not definitively

exclude themselves from donation because we cannot exclude a healthy donor candidate who has no uronephrological abnormalities on the basis of an estimated GFR figure. GFR calculation equations may underestimate or overestimate GFR. 04 out of 10 donors had an eGFR calculated by CKDEPI cyst >90 ml.mn.1.73m² beforedonation

Discussion:

Several studies have demonstrated that cystatin C is an endogenous marker and a more appropriate alternative to creatinine in potential donors and therefore a creatinine-based eGFR is susceptible to bias due to changes in creatinineconcentration. They demonstrated the superiority of mixed CKDEPIwith more precision and less bias than MDRD and CKDEPICr.the study by Huang et al (13) proposed a strategy for assessing GFR in potential donors in 2015 subsequently validated by KDIGO2017(3), it consists of using creatinine-based eGFR as an initial assessment test and possibly supplemented by GFR calculated by equations based on creatinine and cystatin C, as confirmatory tests. They suggested the use of the CKDEPICr-cyst equation, for making decisions to accept or reject donor candidates without having mGFR measured by exogenous markers 126.Gaillard et al in France (14) (2016), suggested the use of CKDEPCr and MDRD and the use of web application in the absence of cystatin C measurement, they found relevant thresholds of MDRD and CKDEPICr, with an eGFR>100 ml.mn.1 .73m² per CKDEPI Cr, and >104 ml.mn.1.73m² per MDRD for an initial threshold of mGFR> 80 ml.mn.173m².and which resulted in good overall diagnostic performance. Another study published in 2019 by the same team (Gaillard et al in France), showed that MDRD misranked 33% of potential donors; they had a mGFR (measured) greater than 90 ml.mn.1.73m², while their eGFR calculated by MDRD was less than 90 ml.mn.1.73m²; these donors were accepted for donation according to their mGFR but were excluded from donation according to MDRD. In the same study, the CKDEPICr equation misranked only 26% of potential donors, their conclusion was that this equation CKDEPICr performed better than MDRD, and they stated that the non-evaluation of equations based on cystatin C is considered one of the limitations of this study. A study published by a Spanish team Ana Gonzalez-Rinne et al in 2019 (15) investigated the impact of creatinine and cystatin C in assessing GFR prior to donation. This study involved candidate donors accepted for donation with an mGFR> 90 ml.mn.173m² among them donors refused because of their GFR estimated by several estimation equations.These equations rejected donors with eGFR below the threshold of 90 for donation, (29 donors out of 93 which represents 31.18%). MDRD alone excluded 23 donors out of the 29 who had a GFR<90 by all equations, according to the eGFR criterion <90 ml.mn.173m². While the two equations based on the combination of the two markers creatinine and cystatin C: Stevens' equation Cr-cyst and CKDEPICr-cyst have recalibrated only 04 and 03 donation candidates because of their eGFR calculated by these two equations which were < 90 ml.mn.173m², while their mfr> 90 ml.mn.1.73m². They concluded that creatinine equations are unreliable for making decisions about donor acceptance or rejection, hence the value of an appropriate estimate of renal function, which is fundamental before donor selection. They also noticed that cystatin C equations recalibrate fewer donation candidates compared to creatinine equations. In our study we found: 18 out of 55 donors who had an eGFR less than 90 ml.mn.1.73² and 37 donors had an eGFR plus 90 ml.mn.1.73m² according to the MDRD equation. The MDRD equation excluded 18 candidates for donation. We reassessed the eGFR of this group of 18 donors which represents 32.72% of the total number of donors by the mixed CKDEPIequation, we found: 10 donors with an eGFR less than 90 ml.mn.1.73m² and 08 donors had an eGFR greater than or equal to 90 ml.mn.1. 73m². The 08 donors excluded from donation by the MDRD were reclassified and recovered by the mixed CKDEPI.

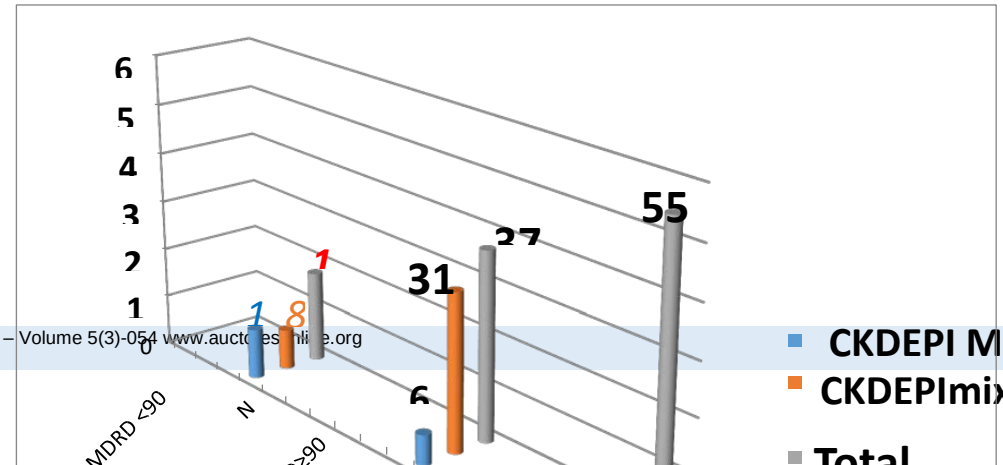
Conclusion :

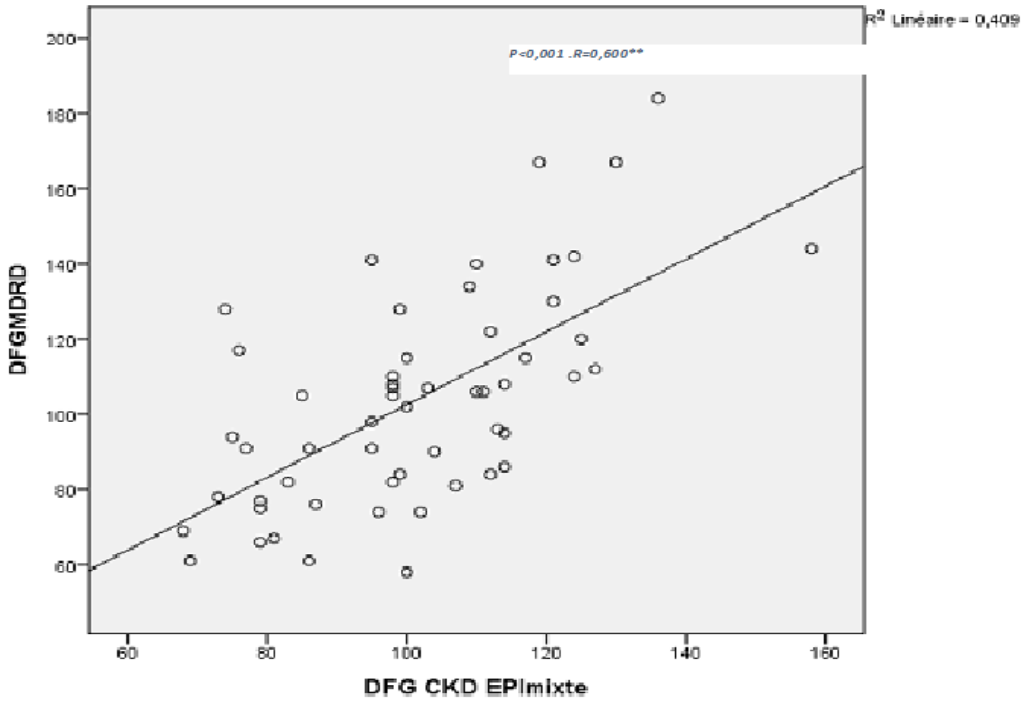
The determination of cystatin C and the use of mixed CKDEPIis essential for the proper assessment of GFR. This equation is able to assess GFR in the closest way to actual GFR because it is based on two endogenous markers. It recovered 08 donors out of 18 who were rejected for donation by the MDRD without any nephrological biological or radiological abnormalities. The CKD-PPE Cr-cyst equation has proven its effectiveness in readjusting the GFR assessment by the MDRD equation for a donation threshold (Cut-off: 90 ml.mn.1.73m²). It acceptedmore donors than MDRD, with good quality graft and remaining kidney function in the donor

Collaborators:

Kidney transplant teams in 03 kidney transplant centers at 03 hospitals:

Nephrology department at their t,Pr RAYANE, and Mazari at the University Hospital of Nafisa Hamoud (Ex Parnet): nephrologists, general practitioners The vascular surgeons of the vascular surgery department of the EHS of Maouche Mohand Amokrane..The renal transplant team of the nephrology department of the Central Hospital of the Army headed by Professor BOULAHIA and all the medical and paramedical staff, as well as the urological surgeons and vascular surgeons at their head Pr GAACHI. Thekidney transplant team of the CHU Batna: at their head Pr BOUGROURA and Pr Missoum with the entire medical team: general practitioners and nephrologists.As well as the surgical team headed by Professor Chaouche, and Professor Ourlent.





There is a correlation between the GFR calculated by MDRD and CKD mixed PPE (R=0, 6, P<0.001), but the intensity is not strong (R^2=0.409)

The concordance between the different equations of the calculation of GFR before donation in donors, calculated by the two equations MDRD and mixed ckdepi:

	CKDEPI mixed<90	CKDEPImixte≥90	Total	X2	P	K
MDRD <90 N	10	08	18	9,08	0,003	0,4
%	55,6	44,8	100			
MDRD≥90						
N	06	31	37			
%	16,2	88,8	100			
Total N	16	39	55			
%	29,1%	70,9%	100%			

References :

1. Masson E., (2021).Treatment of chronic renal failure: therapeutic strategy [Internet]. EM-CONSULT.
2. Kessler M., Büchler M., Durand D., Kolko-Labadens A., Lefrançois G., Menoyo V, et al. (2008). When should a patient be placed on the kidney transplant waiting list? Therapeutic nephrology. Jun 1;4(3):1559.
3. Lentine KL., Kasiske BL., Levey AS., Adams PL, Alberú J, Bakr MA, et al. (2016). KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors. Transplantation;101(8S Suppl 1):S1109.
4. Huang N., Foster MC., Lentine KL., Garg AX., Poggio ED, Kasiske BL., et al. (2016).Estimated GFR for Living Kidney Donor Evaluation. Am J Transplant. janv;16(1):17180.
5. Gaillard F., Courbebaisse M., Kamar N., Rostaing L., Jacquemont L., Hourmant M., et al. (2019). Impact of estimation versus direct measurement of predonation glomerular filtration rate on the eligibility of potential living kidney donors. Kidney Int. avr;95(4):896904.
6. Barrett A, Davies ME., Grubb A., (1984) The place of human γ-trace (cystatin C) amongst the cystein proteinase inhibitors. Biochem Biophys Res Commun. 1 mai;120:6316.
7. Bargnoux A-S., Barguil Y., Cavalier E, Cristol J-P. (2019).Estimation of glomerular filtration rate using cystatin C. Ann Biol Clin (Paris). 1 août;77(4):37580.
8. Delanaye P.(2003).,The interest of cystatin C in the assessment of renal function.;24:12.
9. Biomarkers in acute renal failure [Internet]. Swiss Medical Journal. [cited 2021 Oct 3].
10. Haase M., Bellomo R., Devarajan P., Ma Q., Bennett MR., Möckel M., et al. (2009). Novel biomarkers early predict the severity of acute kidney injury after cardiac surgery in adults. Ann Thorac Surg. juill;88(1):12430.
11. Andrassy KM.,M (2013).Comments on « KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease ». Kidney Int. sept;84(3):6223.
12. Application of the 2017 KDIGO Guideline for the Evaluation and Care of Living Kidney Donors to Clinical Practice Amit X. Garg,1 Andrew S. Levey,2 Bertram L. Kasiske,3 Michael Cheung,4 and Krista L. Lentine,5 on behalf of the KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors Work Group and Evidence Review Team.
13. Huang N., Foster MC., Lentine KL., Garg AX., Poggio ED., Kasiske BL., et al. (2016).Estimated GFR for Living Kidney Donor Evaluation. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. janv;16(1):17180.
14. Gaillard F., Flamant M, Lemoine S., Baron S., Timsit M-O., Eladari D., et al. (2016).Estimated or Measured GFR in Living Kidney Donors Work-up? Am J Transplant. oct;16(10):302432.
15. https://academic.oup.com/ckj/article-abstract/12/5/748/5384507

DOI: 10.37579/2834-5142/057