

Defining a Minimal Clinically Meaningful Difference (MCMD) in Estimated Glomerular Filtration Rate (eGFR) for Kidney Transplantation

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Background

Estimated glomerular filtration rate (eGFR) is the primary diagnostic test used to assess renal function in primary clinical care. However, a minimal clinically meaningful difference (MCMD) has not been established.

- MCMD is defined as the smallest difference in an outcome which is beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in patient management.
- KDIGO Guidelines state that a decline in eGFR of >5 mL/min/1.73m² per year indicates “rapid progression” of CKD, a meaningful event that requires clinical intervention; this served as an initial hypothesis for our analysis.
- There is clearly a need to define an MCMD for eGFR in patients undergoing renal transplantation to better evaluate new medical interventions.

Study Design

Data source: Organ Procurement and Transplantation Network (OPTN) registry database

Study population: Adults (> 18 years of age); received deceased donor kidney 01/01/2013 to 12/31/2018 with at least 12 months survival post-transplant; last follow-up date was 12/14/2019. Multi-organ and prior transplants were excluded.

Analysis: Cox proportional hazards regression

Primary outcome: Death-censored graft failure starting 12-months post-transplantation.

Predictors: Recipient, donor, and transplantation characteristics; 12-month eGFR (CKD-EPI), as shown in Table 1.

Analytic approach: 12-month eGFR was stratified by bands of 5, 7 or 10 mL/min/1.73m². Sequential regression models compared each band to the adjacent higher eGFR band. Results of regression models were adjusted hazard ratios (HRs) for 5, 7 or 10 mL/min/1.73m² increase in eGFR for each eGFR band. That is, HRs reflect incremental death-censored graft failure risk for the lower eGFR band. Finally, a weighted mean HR was calculated using the OPTN sub-population represented by each eGFR band.

Table 1: Sample Characteristics

Value	N	%
RECIPIENT PARAMETERS		
Gender		
F	21,842	39.9
M	32,943	60.1
Age		
<30	3,192	5.8
30-44	11,024	20.1
45-59	20,616	37.6
60-74	18,921	34.5
>=75	1,032	1.9
Race		
Non-black	36,642	66.9
Black	18,143	33.1
Diabetes		
No	35,204	64.3
Yes	19,525	35.6
Missing	56	0.1
BMI Mean (SD)	28.7	51.7
PRA Mean (SD)	25.0	37.4
DONOR PARAMETERS		
Age		
<=10	2,346	4.3
11-20	5,497	10
21-40	22,073	40.3
41-60	21,649	39.5
>60	3,220	5.9
Diabetes		
No	50,678	92.5
Yes	3,789	6.9
Missing	318	0.6
HTN		
No	39,746	72.5
Yes	14,660	26.8
Missing	379	0.7
Urine Protein		
No	28,920	52.8
Yes	25,538	46.6
Missing	327	0.6
TRANSPLANT PARAMETERS		
CIT		
≤40 hours	53,453	97.6
>40 hours	1,005	1.8
Missing	327	0.6
Received on pump		
No	28,983	52.9
Yes	25,802	47.1
DR Locus mismatch		
0	9,728	17.8
1	25,453	46.5
2	19,306	35.2
Missing	298	0.5
DGF		
No	40,383	73.7
Yes	14,399	26.3
Missing	3	0

Abbreviations: SD, standard deviation; BMI, body mass index; PRA, panel reactive antibody; HTN, hypertension; CIT, cold ischemia time; DR, donor-recipient; DGF, delayed graft function

Figure 1: Hazard Ratio for Death-Censored Graft Failure by 12-month eGFR Band with Percent of Population within Each eGFR Band

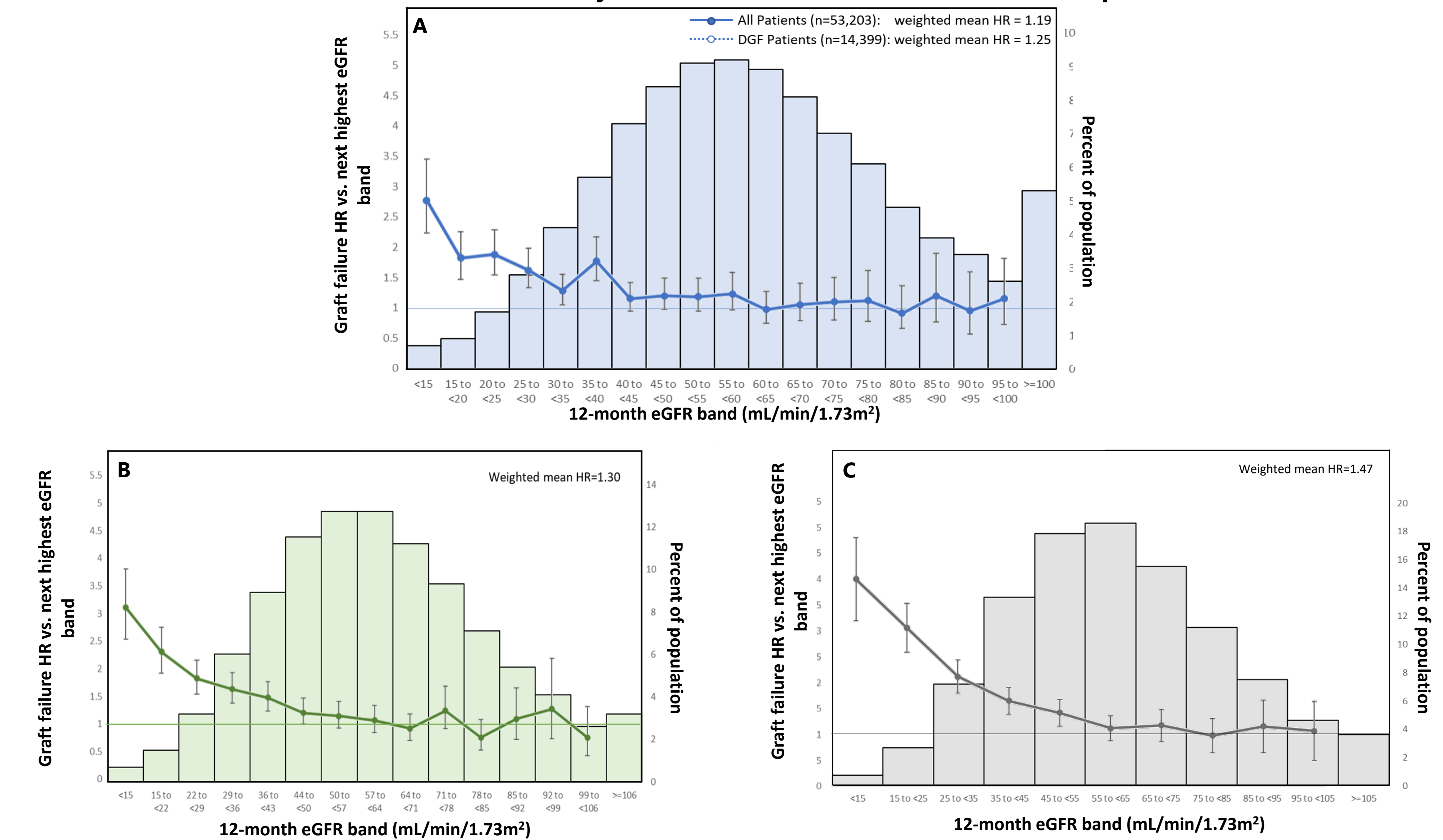


Table 2: 12-month eGFR Bands at 10, 7, and 5 mL/min/1.73m²

10 mL/min/1.73m ²			7 mL/min/1.73m ²			5 mL/min/1.73m ²		
Band	N	%	Band	N	%	Band	N	%
<15	360	0.7	<15	360	0.7	<15	360	0.7
15 to <25	1430	2.6	15 to <22	832	1.5	15 to <20	510	0.9
25 to <35	3831	7.0	22 to <29	1734	3.2	20 to <25	920	1.7
35 to <45	7147	13.0	29 to <36	3281	6.0	25 to <30	1519	2.8
45 to <55	9555	17.4	36 to <43	4849	8.9	30 to <35	2312	4.2
55 to <65	9909	18.1	44 to <50	6305	11.5	35 to <40	3149	5.7
65 to <75	8253	15.1	50 to <57	6937	12.7	40 to <45	3998	7.3
75 to <85	5969	10.9	57 to <64	6973	12.7	45 to <50	4596	8.4
85 to <95	3992	7.3	64 to <71	6160	11.2	50 to <55	4959	9.1
95 to <105	2443	4.5	71 to <78	5102	9.3	55 to <60	5019	9.2
≥105	1896	3.5	78 to <85	3913	7.1	60 to <65	4890	8.9
			85 to <92	2954	5.4	65 to <70	4443	8.1
			92 to <99	2224	4.1	70 to <75	3810	7.0
			99 to <106	1417	2.6	75 to <80	3357	6.1
			≥106	1736	3.2	80 to <85	2612	4.8
						85 to <90	2113	3.9
						90 to <95	1879	3.4
						95 to <100	1410	2.6
						≥100	2929	5.3

Results

54,785 renal transplant recipients were included; 2419 had a graft failure after 12 months (2.8%). **Table 1** lists sample characteristics, which are also predictors in regression models. **Table 2** reports eGFR bands for the analyses and proportions in eGFR bands. **Figure 1A** shows HRs for 5 mL/min/1.73m² 12-month eGFR bands versus next highest, with the higher band as reference. Incremental risk is highest (HR=1.23 to 2.77) in eGFR bands below 60 mL/min/1.73m². Weighted mean HR across all 5 mL/min/1.73m² bands was 1.19; for patients with DGF it was 1.25. **Figures 1B and 1C** show the HRs for the 7 and 10 mL/min/1.73m² eGFR bands. The weighted overall mean HRs were 1.30 for 1.47, respectively.

Conclusion

These results support 5 mL/min/1.73m² as the MCMD for 12-month eGFR in kidney transplantation. Higher 12-month eGFR is strongly associated with improved death-censored graft survival.

DISCLAIMER: The interpretation and reporting of these data are the responsibility of the authors & in no way should be seen as an official policy of or interpretation by the OPTN or the US Government.

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