61ST ERA CONGRESS
STOCKHOLM & VIRTUAL
MAY 23-26, 2024

2024 pearls of CKJ

Pierre Delanaye, MD, PhD
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Statement about the financial Interest (COI - Conflict of Interest)

Do you have, or have you had during the past 2 years, received any non-financial support from an entity?	**No**	
Do you have, or have you had during the past 2 years, received any grants from an entity?	**No**	
Are you a member (current) of any kind of committee, board, WG, etc. of another scientific association with similar aims as ERA?	**Yes**	Board of the European Kidney Function Consortium Board of Renadaptor
Do you have, or have you had during the past 2 years, received any personal fees from an entity?	**Yes**	Nephrolyx IDS AstraZeneca GPR Astellas Alentis Fresenius Fresenius Kabi Bayer ARK

We have selected among (original) articles published in 2023:

- The most downloaded
- The most cited

Thanks to Caroline Vinck for your help in the selection

Clinical Kidney Journal, 2023, vol. 16, no. 5, 835–844

https://doi.org/10.1093/ckj/sfad004
Advance Access Publication Date: 5 January 2023
Original Article

ORIGINAL ARTICLE

Direct oral anticoagulants versus warfarin in patients with non-valvular atrial fibrillation and CKD G3–G5D

Frida Welander [1], Henrik Renlund [2], Emöke Dimény [3], Henrik Holmberg [4] and Anders Själander [3]

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Context

- Non-valvular atrial fibrillation
- The use of direct oral anticoagulants in CKD patients is still controversial

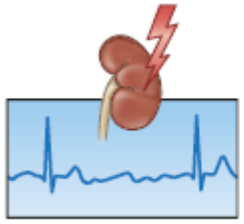
- DOAC seems safe and efficient in non-dialysis CKD (stage 3)
- Evidence is decreasing at lower CKD stages
- At worse, similar results as warfarin
- At best, better results than warfarin

(except for dabigatran)

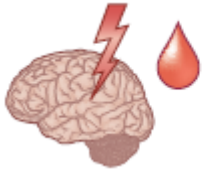
Methods

Swedish register-based study 2009–2018

- Swedish Renal Registry (Stage 3b (80%) to dialysis(>90%))
- Swedish National Patient Register (all hospital admission, 97% of AF)
- Stroke register (acute stroke 94%)
- AuriculA (AF and anticoagulation, treatment, dosage, INR)
- Swedish Prescribed Drug Register (dispenses at Swedish pharmacies, 100%)
- Cause of Death Register



Population:
CKD G3–G5D + atrial fibrillation with DOAC or warfarin



Outcomes:
Major bleeding and ischemic stroke

- T0 = AF, G3-G5D and treatment
- Primary outcomes = hospitalization for stroke or bleeding

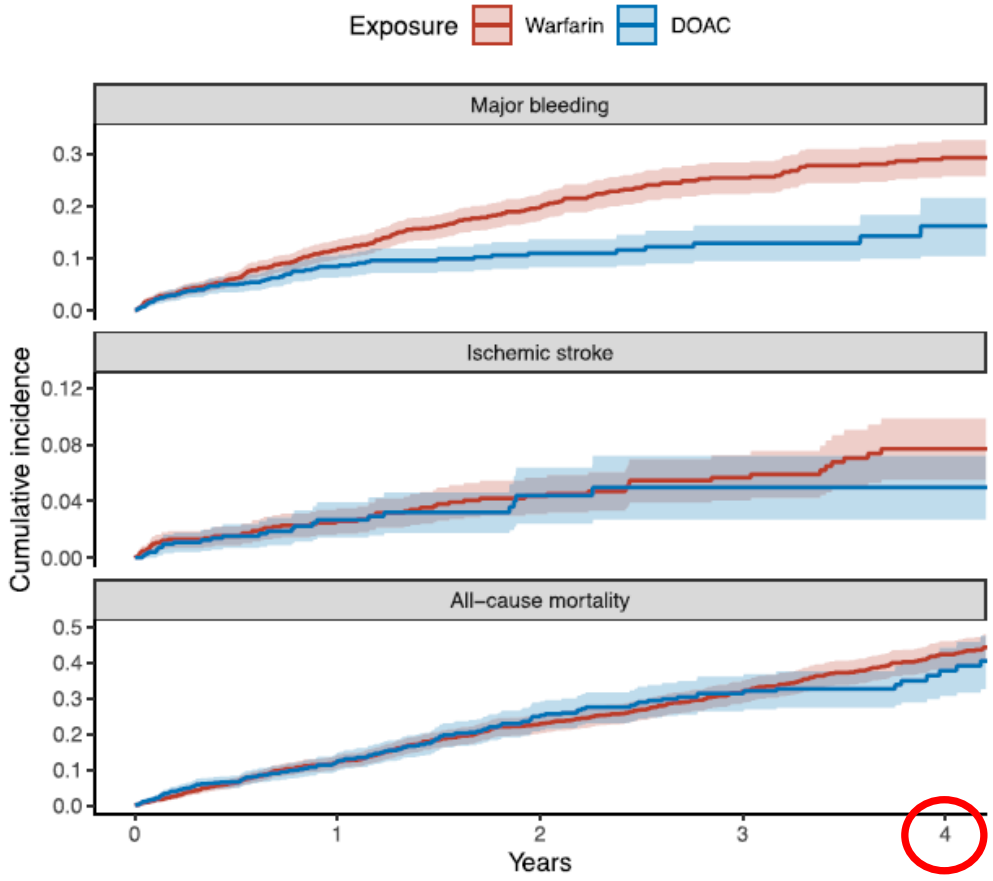
Analysis:
Cox regression analysis

- age, sex, GFR category, years from study start, diabetes mellitus, hypertension, congestive heart failure, stroke or transient ischemic attack , vascular disease, major bleeding, myocardial infarction, percutaneous coronary intervention and excessive alcohol use
- Sensitivity analyses: new treatment, only G3-G5, only correct dose of apixaban

Results

- N=12,106 with CKD and non-valvular-AF
- 8,318 excluded because no treatment (!)
- 1,335 excluded because long-term use
- N=2,453
- At T0: 59% treated with warfarin 41% with DOAC
- G3: W: 63% D: 27% G4: W: 56% D: 44%
  G5: W: 86% D: 14% G5D: W: 92% D: 8%
- DOAC: 81% apixa, 15%: rivaro, 3%: dabigatran
  1% edoxa
- W: Mean Time in Therapeutic Range (TTR): 67%

Characteristics	Total (N = 2453)
Demographics	
Age, years	76.7 (70.9–81.8)
Female	783 (31.9)
CKD G3	693 (28.3)
CKD G4	1113 (45.4)
CKD G5	222 (9.1)
CKD G5D	425 (17.3)
Medical history	
Diabetes mellitus	1180 (48.1)
Hypertension	2288 (93.3)
Stroke	507 (20.7)
TIA	230 (9.4)
COPD	364 (14.8)
Cancer	704 (28.7)
Congestive heart failure	1326 (54.1)
Myocardial infarction	832 (33.9)
Anaemia	911 (37.1)
Dementia	20 (0.82)
Liver disease	92 (3.8)
Excessive alcohol use	88 (3.6)
History of falls	289 (11.8)
Any previous major bleeding	979 (39.9)
Gastrointestinal bleeding	338 (13.8)
Intracranial bleeding	94 (3.8)
CHA2DS2-VASC	5 (4–6)



Major bleeding: Warfarin	1448	863	534	353	213
: DOAC	1005	412	209	104	45
Ischemic stroke: Warfarin	1448	919	597	402	241
: DOAC	1005	424	213	108	45
All–cause mortality: Warfarin	1448	933	613	419	255
: DOAC	1005	434	219	111	48

Figure 1: Unadjusted Kaplan–Meier curves for primary and secondary outcomes comparing all treatment periods of warfarin (red) and DOAC (blue). Graphs presented with years since entry (up to 4 years) on the x-axis and cumulative incidence on the y-axis.

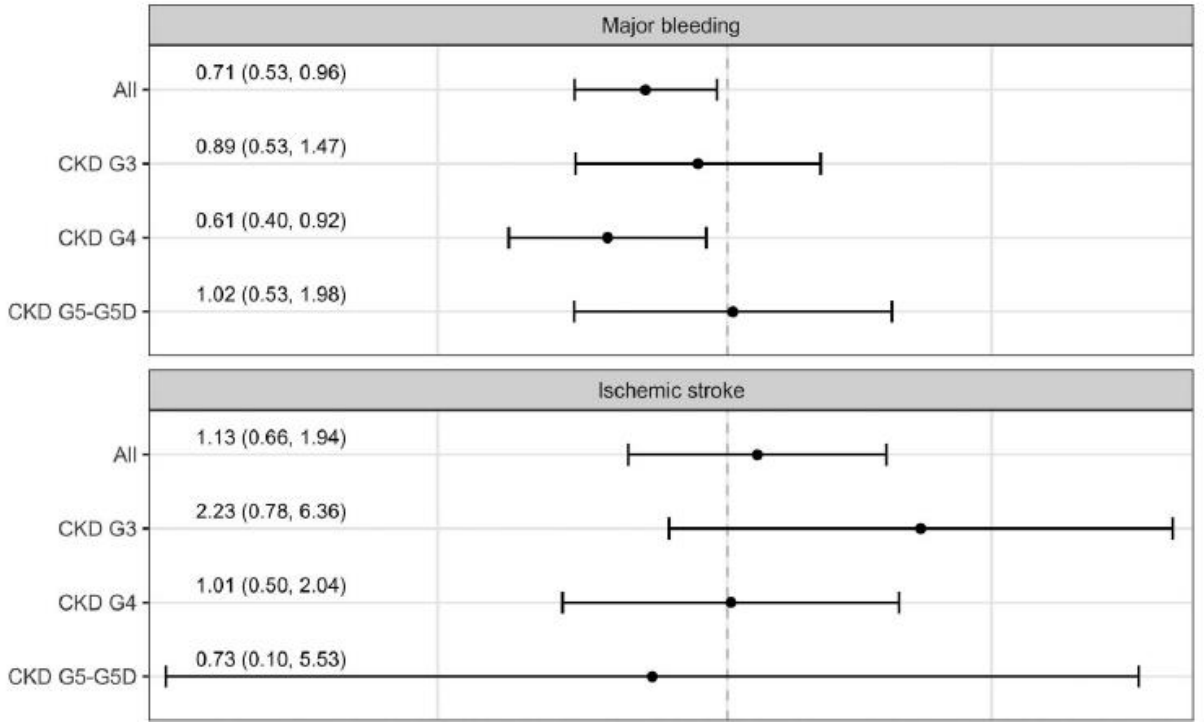


Figure 2: Adjusted models for DOAC vs warfarin. Data presented as HR (95% CI). 'All patients' with all 2453 patients (Model 1), and 'CKD G3–G5/5D' (Model 2) created by adding GFR category as an interaction to Model 1. Models 1 and 2 are adjusted for sex, age, GFR category, years from study start and for any prior presence of the following: congestive heart failure, diabetes mellitus, hypertension, stroke or TIA, vascular disease, major bleeding, myocardial infarction, PCI and excessive alcohol use.

Same results in sensitivity analyses

Discussion

- Retrospective
- Small sample size
- TTR available and high
- Bias by indication (all patients on transplantation list are on warfarin)
- Call for further studies
- At least, (it seems) we are not "assassins" if we prescribed DOAC in severe CKD
- Should we use anticoagulation for non-valvular AF in CKD5D?

Clinical Kidney Journal, 2023, vol. 17, no. 1, 1–15

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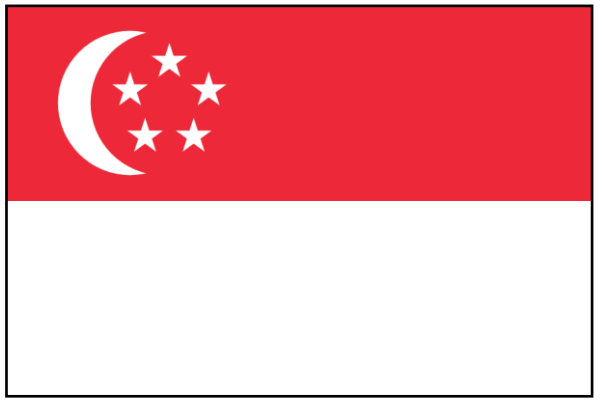
Original Article



ORIGINAL ARTICLE

Cost-effectiveness of screening for chronic kidney disease in the general adult population: a systematic review

See Cheng Yeo[1], Hankun Wang[1], Yee Gary Ang[2], Chee Kong Lim[3] and Xi Yan Ooi[1]

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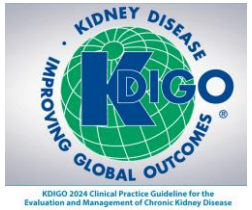
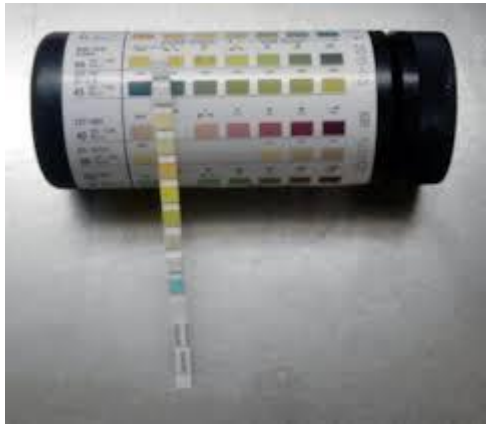
Context

- Systematic screening for CKD is still controversial

Screening. Despite the increasing recognition of the true burden of CKD, there remains controversy and lack of consensus as to the utility of population screening for CKD[1] or targeted screening programs[2] due to the complexity of the underlying sociopolitical and resource environment.



- It is (potentially) not very costly: creatinine and dipstick



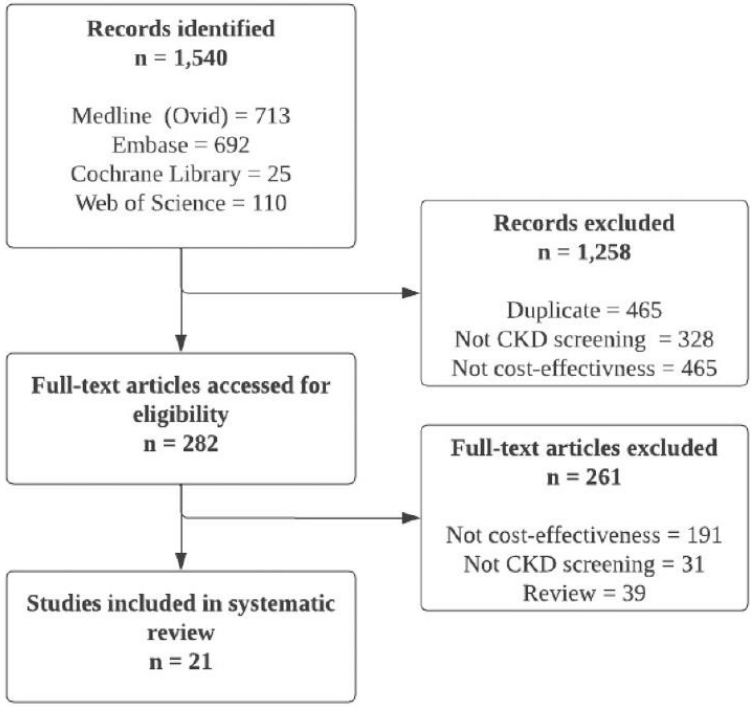
Systematic Review and meta-analysis

- Inclusion criteria:

adult individuals, full or partial health economic evaluation (including cost-effectiveness, cost-utility, cost-benefit, cost-minimization, cost-description, cost-consequence or cost-outcome) using societal or healthcare payer perspective, CKD screening strategies available

- Outcomes

Incremental cost-effectiveness ratio (ICER)
=cost per quality-adjusted life year (QALY)
or cost per life-year gain (LYG)



Results

- 13 in targeted populations and 8 in general population
- 9 in USA, 5 each in Europe and Asia and 2 in Australia
- UACR or UPCR only n=13, eGFR only n=3, both n=3

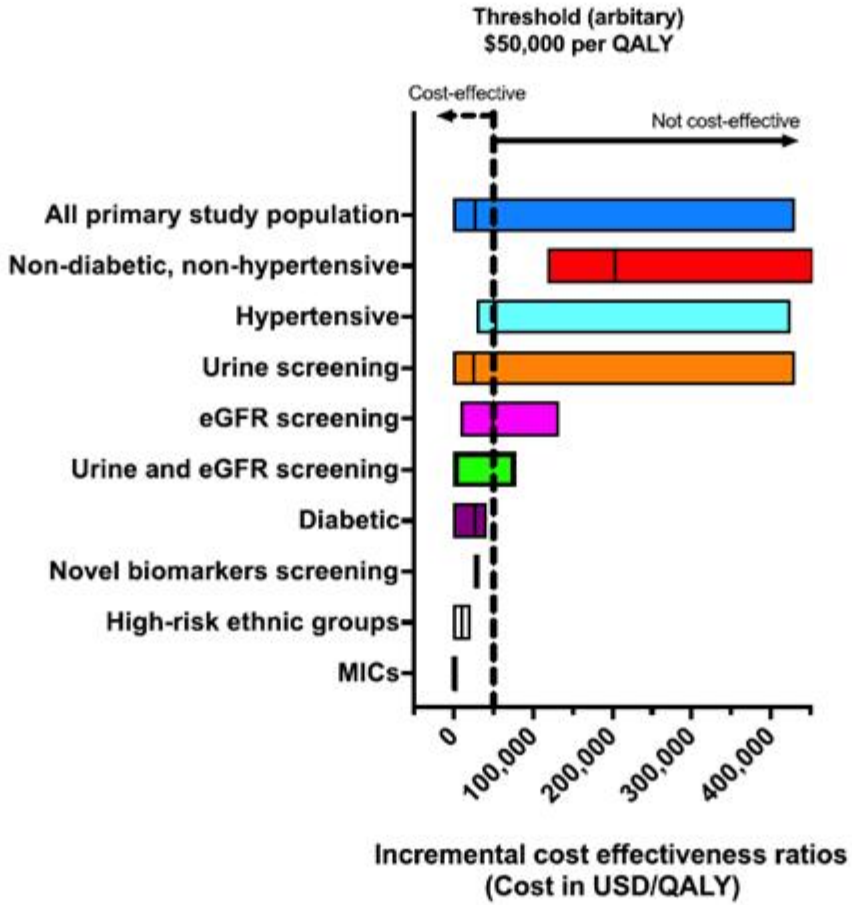
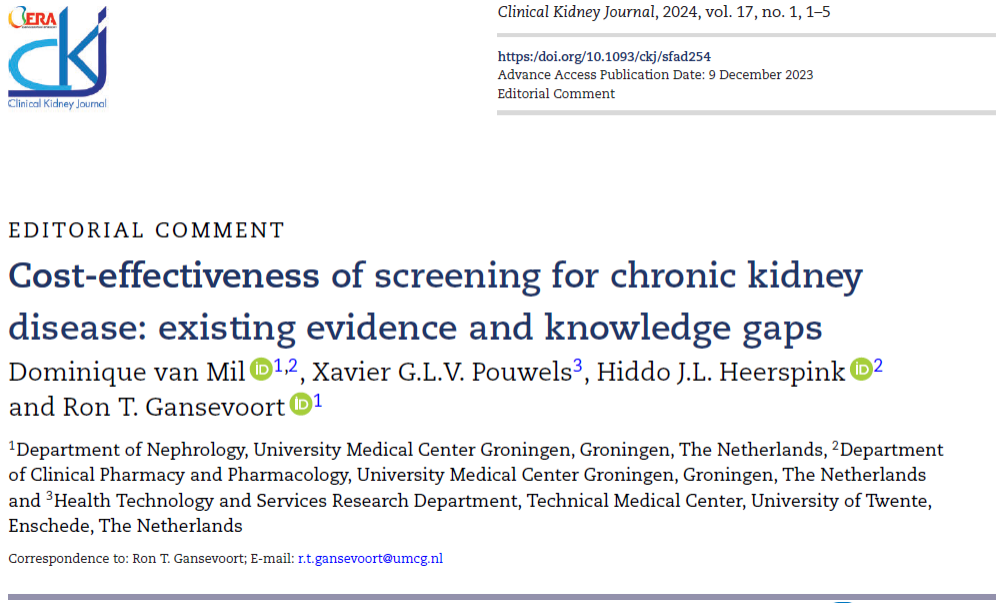


Figure 2: Plot comparing reported incremental cost-effectiveness ratios in selected sub-populations. Each bar represents the range of ICERs reported with the line showing the median value. The $50000 ICER threshold was pre-defined to demonstrate cost-effectiveness (left of vertical line) or not cost-effective (right of vertical line). MICs, middle-income countries.

Discussion

- Cost-effectiveness varies widely…
- Targeted screening is more cost-effective
- Which setting? (primary care or home-based)
- Which outcome? (renal and/or CV)
- Which method? albuminuria and/or eGFR
- Role of the fixed threshold for eGFR?
- Repeated measurements?
- We have new (very) effective drugs



Clinical Kidney Journal, 2024, vol. 17, no. 1, 1–5

https://doi.org/10.1093/ckj/sfad254
Advance Access Publication Date: 9 December 2023
Editorial Comment

EDITORIAL COMMENT

Cost-effectiveness of screening for chronic kidney disease: existing evidence and knowledge gaps

Dominique van Mil[1,2], Xavier G.L.V. Pouwels[3], Hiddo J.L. Heerspink[2] and Ron T. Gansevoort[1]

[1]Department of Nephrology, University Medical Center Groningen, Groningen, The Netherlands, [2]Department of Clinical Pharmacy and Pharmacology, University Medical Center Groningen, Groningen, The Netherlands and [3]Health Technology and Services Research Department, Technical Medical Center, University of Twente, Enschede, The Netherlands

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Clinical Kidney Journal, 2023, vol. 17, no. 1, 1–13

https://doi.org/10.1093/ckj/sfad143
Advance Access Publication Date: 22 June 2023
Original Article

ORIGINAL ARTICLE

Efficacy and safety of hypoxia-inducible factor prolyl hydroxylase inhibitors in patients with chronic kidney disease: meta-analysis of phase 3 randomized controlled trials

Roberto Minutolo[1], Maria Elena Liberti[1], Vittorio Simeon[2], Ferdinando C. Sasso[3], Silvio Borrelli[1], Luca De Nicola[1] and Carlo Garofalo[1]

[1]Nephrology Unit, University of Campania "Luigi Vanvitelli", Naples, Italy, [2]Medical Statistic Unit, University of Campania "Luigi Vanvitelli", Naples, Italy and [3]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy

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Clinical Kidney Journal, 2023, vol. 16, no. 5, 845–858

https://doi.org/10.1093/ckj/sfac271
Advance Access Publication Date: 24 January 2023
Original Article

ORIGINAL ARTICLE

The impacts of hypoxia-inducible factor stabilizers on laboratory parameters and clinical outcomes in chronic kidney disease patients with renal anemia: a systematic review and meta-analysis

Kullaya Takkavatakarn[1,*], Theerachai Thammathiwat[1,2,*], Jeerath Phannajit[1], Pisut Katavetin[1], Kearkiat Praditpornsilpa[1], Somchai Eiam-Ong[1] and Paweena Susantitaphong[1,3]

[1]Division of Nephrology, Department of Medicine, King Chulalongkorn Memorial Hospital, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [2]Division of Nephrology, Department of Medicine, Naresuan University, Phitsanulok, Thailand and [3]Research Unit for Metabolic Bone Disease in CKD patients, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

*These authors contributed equally to this work.
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Meta-analyses

- RCT, HIFs vs ESAs, dialysis or non dialysis
- ΔHg, Δhepcidin, Δserum iron, ΔTIBC, ΔTSAT, Δferritin
- K, MACE, MACE+, thrombotic events, AVF thrombosis, death

- Published and unpublished articles, dialysis or non dialysis, HIFs vs placebo vs ESAs
- ΔHg, Δhepcidin, ΔTSAT, Δferritin
- K, MACE, MACE+, thrombotic events, AKI, death

Results

- 26 RCTs, n=24,387, median FU: 16,5 m

Hemoglobin (Hb)
- ΔHb from BL 0.10 g/dL (0.02–0.17)
- Hb target OR 1.04, (95% CI 0.88–1.22)

Iron parameters
- Decline of hepcidin and ferritin
- Increase of serum iron and TIBC
- No change in TSAT

Safety (*HIF-PHIs* vs. ESA)


Rate ratio of cancer risk
0.93, 95% CI: 0.76–1.13


Rate ratio of MACE
1.00, 95% CI: 0.94–1.07

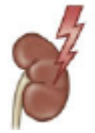

Rate ratio of AVF thrombosis
1.00, 95% CI: 0.94–1.07

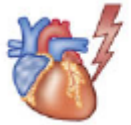
Rate ratio of all-cause death
1.02, 95% CI: 0.95–1.09

- 46 RCTs, n=27,338, FU: 4 to 104 w


Hemoglobin
Significantly increased Hb levels (MD 0.659 g/dL) compared with the control group (ESA or placebo)


Iron parameters
> Significantly decreased ferritin, TSAT, and hepcidin
> Significantly increased TIBC


AKI
RR 1.28 (1.00–1.64)
P = 0.04


MACE
RR 1.00 (0.94–1.07)
P = 0.71

Mortality
RR 0.91 (0.78–1.07)
P = 0.89

Results

- 26 RCTs, n=24,387, **median FU: 16,5 m**

Hemoglobin (Hb)
- ΔHb from BL 0.10 g/dL (0.02–0.17)
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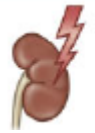
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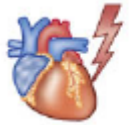
MACE
RR 1.00 (0.94–1.07)
P = 0.71

Mortality
RR 0.91 (0.78–1.07)
P = 0.89

Reassuring? Yes…maybe

CLINICAL KIDNEY JOURNAL

Clinical Kidney Journal

Clinical Kidney Journal, 2023, vol. 16, no. 5, 776–779

https://doi.org/10.1093/ckj/sfad026
Advance Access Publication Date: 1 March 2023
Editorial Comment

EDITORIAL COMMENT

Hypoxia-inducible factor stabilizers: 27 228 patients studied, yet a role still undefined

Steven Fishbane, Deepa A. Malieckal and Ji H. Ng

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Clinical Kidney Journal, 2023, vol. 16, no. 8, 1265–1277

https://doi.org/10.1093/ckj/sfad012
Advance Access Publication Date: 20 January 2023
Original Article

ORIGINAL ARTICLE

Development and validation of a new equation based on plasma creatinine and muscle mass assessed by CT scan to estimate glomerular filtration rate: a cross-sectional study

Thomas Stehlé[1,2], Yaniss Ouamri[1,3], Antoine Morel[1,4], Emmanuelle Vidal-Petiot[5,6], Soraya Fellahi[7,8], Lauriane Segaux[1,4], Dominique Prié[9,10], Philippe Grimbert[1,2], Alain Luciani[1,3], Vincent Audard[1,2], Jean Philippe Haymann[11,12], Sébastien Mulé[1,3], Eric De Kerviler[13], Marie-Noëlle Peraldi[14], Anne Boutten[15], Marie Matignon[1,2], Florence Canouï-Poitrine[1,4], Martin Flamant[5,6] and Frédéric Pigneur[1,3]

Context

- GFR is estimated in clinical practice by serum creatinine
- Muscular mass is the main non-GFR determinant of creatinine
- Developing an equation with “muscle mass” measured by CT-Scan (MMB-eGFR)

Methods

- GFR measured with a reference method (iohexol or ^{51}Cr-EDTA)
- Serum creatinine and cystatin C
- Development in 118 kidney donors and validation in

1) 114 other donors,
2) 55 with CKD
3) 60 with discrepant $eGFR_{crea}$ and $eGFR_{cys}$ (≠ of 30%)

- Bias, precision, P30
- New variable = total lumbar muscle cross sectional area by CT-Scan at the third lumbar vertebra

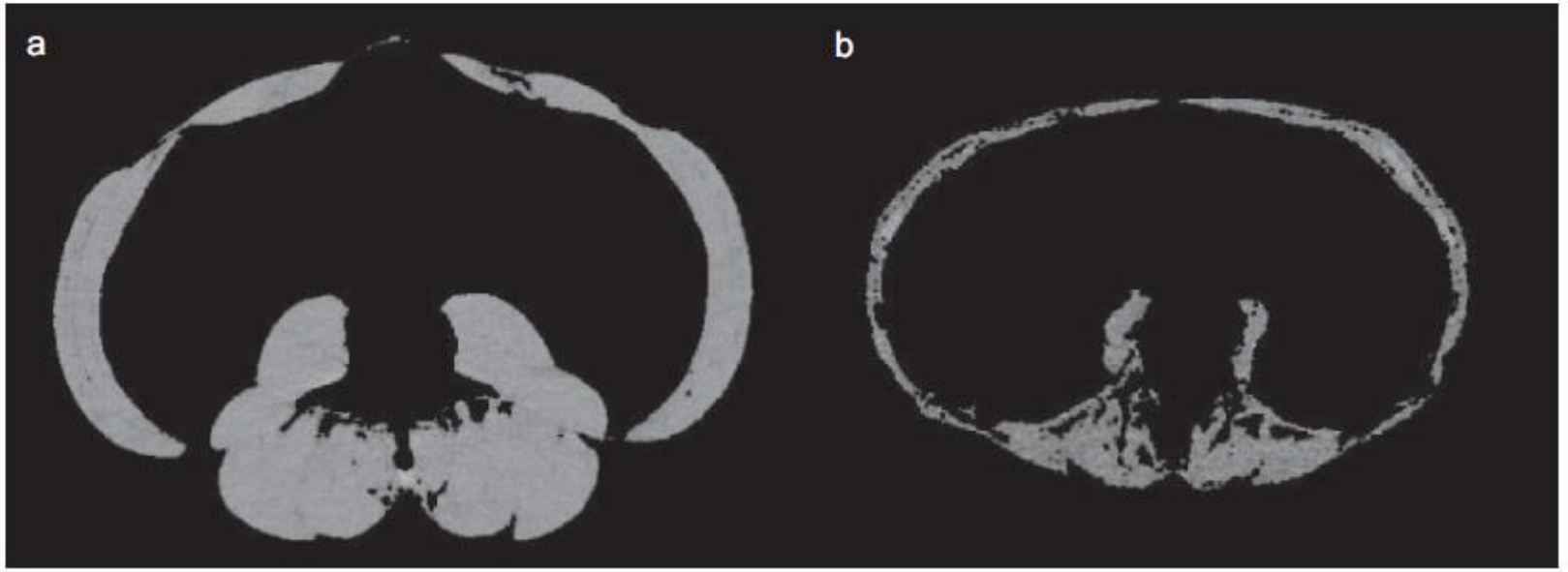

Figure 1: Unenhanced CT scan section taken at the level of the middle of the third lumbar vertebra, after segmentation of total lumbar muscle cross-sectional area. (**a**) A 61-year-old man with localized kidney cancer. Total lumbar MCSA is 208 cm^2. (**b**) A 70-year-old, kidney donor candidate woman whose past medical history includes only parathyroidectomy for primary hyperparathyroidism complicated by osteoporosis. Total lumbar MCSA is 84 cm^2.

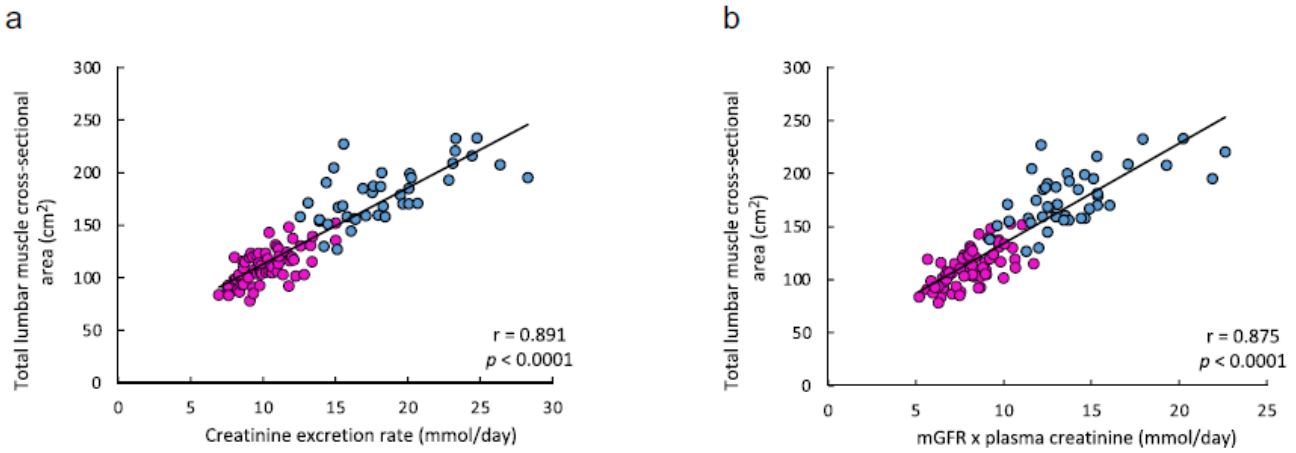

Figure 3: Correlation between creatinine urinary excretion and muscle mass assessed by CT scan, in the development population. Correlation between creatinine excretion rate and total lumbar MCSA (**a**), and between urinary creatinine excretion derived from glomerular filtration (mGFR × plasma creatinine) and MCSA (**b**). Pink and blue dots represent women and men, respectively. The solid lines represent the linear regressions between the variables. The Pearson correlation coefficient r are reported on the graphs, with the related P-values.

MMBeGFR:
-522,4 + 55,8 x MACS (cm^2)/serum creatinine (micromole/L)

Results

Table 1: Characteristics of participants of the development population and the validation populations.

	Development population	Validation population 1	Validation population 2	Validation population 3
Number of patients	118	114	55	60
Age, years, mean ± SD	50.6 ± 12.4	45.1 ± 10.6*	55.5 ± 15.7*	52.7 ± 15.2
Female, N (%)	75 (63)	62 (54)	20 (36)*	27 (45)*
African or Caribbean ancestry, N (%)	32 (27)	14 (12)*	20 (36)	14(23)
Body weight, kg, mean ± SD	74.0 ± 14.3	73.1 ± 13.6	76.7 ± 19.2	72.9 ± 18.3
Height, cm, median (IQR)	168 (160–175)	168 (161–176)	170 (163–175)	170 (160–177)
BMI, kg/m^2, mean ± SD	26.1 ± 3.9	25.5 ± 4.1	26.5 ± 6.0	26.0 ± 6.0
mGFR (mL/min/1.73 m^2)	97.4 ± 18.8	95.9 ± 13.6	60.9 ± 30.5*	54.6 ± 21.7*
Total lumbar MCSA, cm^2, median (IQR)	124 (106–159)	128 (108–169)	139 (109–166)	127 (105–158)

P-values were calculated between each validation population and development population using a Chi^2 test for categorial variables and t-test or Mann–Whitney test as appropriate for quantitative variables. *P < .05.
BMI, body mass index.

	Mean bias (95% CI) (mL/min/1.73 m^2)	SD of the bias (mL/min/1.73 m^2)	Accuracy within 30% (95% CI) (%)
Development population ($n = 118$)			
MMB-eGFR	0.8 (−1.9 to 3.4)	14.7	95.8 (92.1 to 99.4)
CKD-EPI$_{Cr2009}$	0.7 (−2.1 to 3.5)	15.5	93.2 (88.7 to 97.8)
CKD-EPI$_{Cr2021}$	4.0 (1.2 to 6.8)	15.4	90.7 (85.4 to 95.9)
EKFC	−4.0 (−6.6 to −1.2)	15.0	94.1 (89.8 to 98.3)
Validation population 1 ($n = 114$)			
MMB-eGFR	−1.1 (−3.7 to 1.5)	14.2	96.5 (93.1 to 99.9)
CKD-EPI$_{Cr2009}$	3.7 (1.2 to 6.2)	13.6	96.5 (93.1 to 99.9)
CKD-EPI$_{Cr2021}$	7.0 (4.5 to 9.4)	13.3	96.5 (93.1 to 99.9)
EKFC	0.1 (−2.3 to 2.5)	13.0	98.2 (95.8 to 100)
Validation population 2 ($n = 55$)			
MMB-eGFR	−2.3 (−5.8 to 1.6)	13.1	80.0 (69.4 to 90.6)
CKD-EPI$_{Cr2009}$	−1.1 (−5.4 to 3.3)	16.5*	80.0 (69.4 to 90.6)
CKD-EPI$_{Cr2021}$	1.6 (−2.7 to 6.1)	16.8*	80.0 (69.4 to 90.6)
EKFC	−3.1 (−7.3 to 1.1)	15.9*	83.6 (73.9 to 94.4)
Validation population 3 ($n = 60$)			
MMB-eGFR	7.4 (3.2 to 11.5)	16.3	75.0 (64.0 to 86.0)
CKD-EPI$_{Cr2009}$	9.5 (4.4 to 14.5)	20.0*	51.7 (39.0 to 64.3)*
CKD-EPI$_{Cr2021}$	12.3 (7.2 to 17.4)	20.2*	43.3 (31.0 to 55.9)*
EKFC	7.7 (3.1 to 12.2)	18.0	53.3 (40.7 to 66.0)*

	Mean bias (95% CI) (mL/min/1.73 m^2)	SD of the bias (mL/min/1.73 m^2	Accuracy within 30% (95% CI) (%)
Development population ($n = 117$)			
MMB-eGFR	0.8 (−1.9 to 3.5)	14.8	95.7 (92.1 to 99.4)
Mean MMB-eGFR/CKD-EPI$_{Cys}$	−2.0 (−4.2 to 0.2)	12.5	99.1 (97.5 to 100)
CKD-EPI$_{Cys}$	−5.0 (−8.0 to −2.0)	16.6	91.5 (86.4 to 96.5)
CKD-EPI$_{Cr\text{-}Cys\,2021}$	2.5 (0.0 to 5.1)	14.2†	94.9 (90.9 to 98.9)
FAS$_{combi}$	−4.5 (−7.2 to −1.7)	15.0†	94.0 (89.7 to 98.3)†
Validation population 1 ($n = 110$)			
MMB-eGFR	−1.1 (−3.7 to 1.5)	14.4	96.4 (92.9 to 99.9)
Mean MMB-eGFR/CKD-EPI$_{Cys}$	3.0 (1.1 to 4.9)	10.2	99.1 (97.3 to 100)
CKD-EPI$_{Cys}$	7.1 (4.7 to 9.4)	12.7	92.7 (87.9 to 97.6)
CKD-EPI$_{Cr\text{-}Cys\,2021}$	10.6 (8.5 to 12.6)	11.1*	90.9 (85.5 to 96.3)†
FAS$_{combi}$	4.5 (1.8 to 7.2)	14.5†	92.7 (87.9 to 97.6)†
Validation population 2 ($n = 54$)			
MMB-eGFR	−2.3 (−5.8 to 1.2)	13.2	79.6 (68.9 to 90.4)
Mean MMB-eGFR/CKD-EPI$_{Cys}$	−5.9 (−8.7 to −3.1)	10.4	94.4 (88.3 to 100)
CKD-EPI$_{Cys}$	−9.5 (−13.0 to −6.0)	13.2	75.9 (64.5 to 87.3)
CKD-EPI$_{Cr\text{-}Cys\,2021}$	−4.1 (−7.1 to −1.1)	11.4	87.0 (78.1 to 96.0)
FAS$_{combi}$	−5.2 (−8.6 to −1.8)	12.7†	83.3 (73.4 to 93.3)†
Validation population 3 ($n = 60$)			
MMB-eGFR	7.4 (3.2 to 11.5)	16.3	75.0 (64.0 to 86.0)
Mean MMB-eGFR/CKD-EPI$_{Cys}$	3.2 (0.1 to 6.2)	12.1	86.7 (78.1 to 95.3)
CKD-EPI$_{Cys}$	−1.0 (−6.2 to 4.2)	20.5	61.7 (49.4 to 74.0)
CKD-EPI$_{Cr\text{-}Cys\,2021}$	3.8 (0.4 to 7.1)	13.3	81.7 (71.9 to 91.5)
FAS$_{combi}$	3.3 (0.5 to 6.2)	11.3*	78.3 (67.9 to 88.8)

Conclusion

- It is difficult to predict muscular mass
- Including MMB could be of interest in some patients
- This is an “opportunistic” equation

THANK YOU FOR YOUR ATTENTION