Published in: Nature Reviews Nephrology (2025), vol. 21, n°5, pp. 285-286
DOI: 10.1038/s41581-025-00947-0
Status: Postprint (Author's version)

A DIFFICULT PATH TO POINT-OF-CARE MEASUREMENT OF GLOMERULAR FILTRATION RATE

Pierre Delanaye
Department of Nephrology, Dialysis, Transplantation, CHU Sart Tilman, University of Liège, Liège, Belgium.

Richard J. Glassock
Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA.

Abstract

Transdermal detection of fluorescent markers has potential to provide point-of-care measurement of glomerular filtration rate. However, validation of proposed approaches and confirmation of their clinical utility should be required ahead of their adoption in the clinic.

In clinical practice, glomerular filtration rate (GFR) is typically estimated (eGFR) using creatinine-based equations, sometimes complemented with cystatin C measurements[1]. It is crucial to recall that all eGFR equations provide approximations, with varying bias, precision and accuracy relative to measured GFR (mGFR). The literature often states that an eGFR equation is sufficiently accurate if it falls within 30% of mGFR in 75% of cases — an accuracy parameter known as the P30. However, this statement, first proposed in the 2002 KDOQI guidelines[2], implies that an equation that yields values within 30% of mGFR in three out of four patients is clinically acceptable. Fortunately, most modern eGFR equations achieve 80–85% accuracy in general populations, although their performance varies widely across specific patient groups[1,3]. Regardless, a 30% margin of error remains a substantial concern. For example, if a true GFR is 30 ml/min/1.73 m^2 or 100 ml/min/1.73 m^2, an eGFR of 21–39 ml/min/1.73 m^2 or 70–130 ml/min/1.73 m^2, respectively, is considered acceptable[3]. Given this large imprecision and weak accuracy, direct mGFR determination remains clinically relevant[3]. New findings may represent a step towards the use of fluorescent markers for the transdermal measurement of GFR; however, external validation and confirmation of the accuracy of such an approach is necessary before their adoption in the clinical setting.

Two critical questions arise regarding the measurement of GFR: when and how it should be measured. The 'when' question defies an easy answer. Measuring GFR might be useful when eGFR is particularly unreliable or in situations in which precise values are clinically essential. Although several publications have discussed indications for mGFR[4,5], recommendations remain largely based on 'expert opinion', as no prospective study has shown a clinical benefit of using mGFR instead of eGFR.

At first glance, the question of how to measure GFR seems easier to address. However, substantial changes in available mGFR methodologies have occurred in the past few years. Notably, the number of available reference methods has declined. For example, the classic urinary inulin clearance test is no longer widely available. Two widely used GFR biomarkers, iothalamate in the USA and ^{51}Cr-EDTA in

Published in: Nature Reviews Nephrology (2025), vol. 21, n°5, pp. 285-286
DOI: 10.1038/s41581-025-00947-0
Status: Postprint (Author's version)

Europe, are also no longer broadly available. ^{99}Tc-DTPA remains available but has limitations inherent to isotopic methods. Moreover, the use of ^{99}Tc-DTPA for dynamic imaging (the Gates method) is fraught with serious errors of bias and precision. Currently, non-radioactive iohexol plasma clearance is the most commonly used reference method for GFR measurement. It offers several advantages over other approaches: ease of use, relative affordability and standardization. However, drawbacks to its use include limited validation for iohexol urinary clearance, unsuitability for patients with contrast medium allergies, and a lengthy procedure (up to 7–10 h in patients with chronic kidney disease (CKD))[6].

Given the paucity of methodologies available for measuring GFR, it is encouraging that a new generation of fluorescently labelled markers has emerged, which enable direct, real-time GFR measurement. The 372 Da tracer relmapirazin (also known as MB-102) is the most advanced of these. Relmapirazin exhibits ideal characteristics for a GFR marker, including hydrophilicity, stability, minimal protein binding and exclusive filtration without tubular secretion. Moreover, it has successfully passed all required toxicity evaluations in humans[5,7,8]. A pivotal phase II study published in 2024 compared relmapirazin with iohexol plasma clearance in 120 patients, including 68 patients with stable CKD. Serial measurements of relmapirazin and iohexol in blood (by ultra-performance liquid chromatography and liquid chromatography–tandem mass spectrometry, respectively) after their intravenous administration revealed that the two biomarkers exhibited comparable plasma pharmacokinetics and the same classical two-compartment model characterized by two curves: an initial curve with rapid decline corresponding to the distribution of markers into the body and a second curve with a slow slope corresponding to the elimination of the markers by the kidneys. Although GFR was measured in only 104 patients owing to dosing, sampling and analytical errors, regression analysis between the two methods showed a slope of 0.994, suggesting good agreement between relmapirazin and iohexol values. Bland–Altman analysis revealed a negligible bias of –0.7 ml/min, with 95% of values falling within +5.6 and –7.0 ml/min. Concordance within 10% and 30% (that is, the percentage of mGFR by relmapirazin being within ±10% or ±30% of mGFR as measured by iohexol) was remarkable at 95% and 100%, respectively[7].

Although that study provided proof of principle for the use of relmapirazin as a reliable GFR marker, it primarily validated its use in plasma clearance measurements rather than the transdermal detection method for which it was developed. Researchers have now taken the next step of assessing whether relmapirazin could be used for continuous, point-of-care GFR measurement via a transdermal detection system. This approach was evaluated in another phase II study in patients with varying GFRs and skin tones[8], using a transdermal detector, which is a small device that contains two LED sources and two silicon detectors that are adhesively placed on the manubrium. When excited by LED light, relmapirazin emits a fluorescent signal that is detected. The phase II study continuously recorded fluorescence for 12 h after injection of relmapirazin. Blood samples were also taken at 14 time points 5–720 min after injection to measure plasma relmapirazin concentrations. The goal was to compare GFR obtained by relmapirazin clearance with blood measurement (GFR_{RMP}) with that of GFR obtained by transdermal fluorescence (GFR_{TF}). The participants were apparently the same as those who participated in the original (above-described) phase II study. Of the 104 haemodynamically stable patients with GFR_{RMP} values, GFR_{TF} measurements were obtained from only 74 owing to adhesion issues with the detector, which equates to a 30% failure rate. The researchers found that relmapirazin

Published in: Nature Reviews Nephrology (2025), vol. 21, n°5, pp. 285-286
DOI: 10.1038/s41581-025-00947-0
Status: Postprint (Author's version)

transdermal fluorescence signals also followed a classical two-compartment pharmacokinetics model in both healthy participants and in those with CKD. To obtain GFR_{TF}, the fluorescence clearance rate (FCR; that is, the decrease in fluorescence signal over time) was measured for each patient in the phase corresponding to the second compartment and compared to GFR_{RMP}. The slope observed between FCR and GFR_{RMP} was then used to derive a conversion algorithm (which differed according to skin colour) from which a GFR_{TF} value was deducted. Bland–Altman analysis revealed a bias of 1.8 ml/min/1.73 m^2, but with wide limits of agreement (–19.4 to +17.5 ml/min), a concern that is not thoroughly discussed in the manuscript. Crucially, no internal validation of the conversion algorithm was performed. Furthermore, GFR_{TF} was not compared to iohexol-based GFR measurements, raising additional concerns regarding its accuracy. In our opinion, the methodology used to calculate FCR is also unclear[8].

These two studies highlight the potential of relmapirazin and transdermal measurement for real-time, point-of-care GFR measurement. Both studies were conducted by researchers affiliated with MediBeacon, a company that is developing relmapirazin and its transdermal detector for the measurement of GFR[7,8]. On the basis of the above-described findings, the MediBeacon Transdermal GFR System (with relmapirazin now named Lumitrace) received Food and Drug Administration approval in the USA for GFR assessment. However, external validations by independent research groups are anticipated and necessary. Another crucial need will be the identification of clinical scenarios in which point-of-care GFR measurement provides tangible benefits. In comparison to current mGFR methods, the major added value of the transdermal GFR determination is a relatively rapid, point-of-care result. In settings such as kidney donor evaluations or oncology (with the inherent use of nephrotoxic drugs)[4], accuracy is more important than immediacy, making iohexol plasma clearance preferable[6]. However, patients in the intensive care unit or post-surgery could represent a promising target population for transdermal GFR monitoring, although their fundamental instability represents a formidable challenge. Future studies must not only demonstrate accuracy of these results but also show that using such technology has positive implications for the care and, ideally, for the outcomes of the patients.

References

1. Delanaye, P. et al. Diagnostic standard: assessing glomerular filtration rate. Nephrol. Dial. Transplant. 39, 1088–1096 (2024).

2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am. J. Kidney Dis. 39 (Suppl. 1), S1–S266 (2002).

3. Delanaye, P. & Mariat, C. The applicability of eGFR equations to different populations. Nat. Rev. Nephrol. 9, 513–522 (2013).

4. Ebert, N. et al. Assessment of kidney function: clinical indications for measured GFR. Clin. Kidney J. 14, 1861–1870 (2021).

5. Tuttle, M. & Levey, A. S. Relmapirazin, a new exogenous filtration marker, and more widespread use of measured GFR. Kidney Int. 106, 562–565 (2024).

Published in: Nature Reviews Nephrology (2025), vol. 21, n°5, pp. 285-286
DOI: 10.1038/s41581-025-00947-0
Status: Postprint (Author's version)

6. Ebert, N. et al. Iohexol plasma clearance measurement protocol standardization for adults: a consensus paper of the European Kidney Function Consortium. Kidney Int. 106, 583–596 (2024).

7. Dorshow, R. B., Debreczeny, M. P., Goldstein, S. L. & Shieh, J. J. Clinical validation of the novel fluorescent glomerular filtration rate tracer agent relmapirazin (MB-102). Kidney Int. 106, 679–687 (2024).

8. Dorshow, R. B., Debreczeny, M. P. & Goldstein, S. L. Glomerular filtration rate measurement utilizing transdermal detection methodology. J. Am. Soc. Nephrol. https://doi.org/10.1681/ASN.0000000639 (2025).

Competing interests

P.D. is a consultant for Nephrolyx. R.J.G. declares no competing interests.