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REVIEW ARTICLE

Kinetic estimated glomerular filtration rate (KEGFR) as predictor of dialytic acute kidney injury: a systematic review

Cinética do ritmo de filtração glomerular estimado (KERFG) como preditor de lesão renal aguda dialítica: uma revisão sistemática

Cristiano Araújo Costa[1,2].

João Paulo Pereira Cunha[1].

Samuel Teixeira Rios[1].

José Ronaldo Vasconcelos da Graça[1].

Cláudia Maria Costa de Oliveira[3].

1 Universidade Federal do Ceará (UFC), Sobral, Ceará, Brasil.

2 Hospital Universitário Walter Cantídio (HUWC), Fortaleza, Ceará, Brasil.

3 Universidade Christus, Fortaleza, Ceará, Brasil.

ABSTRACT

Objective: To analyze the use of the kinetic estimated glomerular filtration rate (KeGFR) model as an early predictor of dialysis acute kidney injury (AKI). **Methods:** This is a literature review, where authors analyzed the use of the KeGFR model to predict dialysis AKI earlier. **Results:** Patients with reduced KeGFR were more likely to have more comorbidities and were more severe patients. The lower the KeGFR, the greater the risk of death. This was also observed in the need for Renal Replacement Therapy, ICU admission and hospital admission. The agreement between the severity of AKI and the worst KeGFR achieved is controversial in the literature evaluated. **Conclusion:** We suggest that the AKI classification systems and the KeGFR model be used together for decision making and to obtain additional information, such as severity and prognosis.

Keywords: Acute kidney injury. Patient Acuity. Mortality.

RESUMO

Objetivo: Analisar o uso do modelo de cinética do ritmo de filtração glomerular estimado (KeRFG) como preditor precoce de lesão renal aguda (LRA) dialítica. **Metodologia:** Trata-se de uma revisão de literatura, onde autores analisaram o uso do modelo de KeRFG para prever de forma mais precoce a LRA dialítica. **Resultados:** Os pacientes com KeRFG reduzida eram mais propensos a ter mais comorbidades e eram pacientes mais graves. Quanto menor o KeRFG, maior foi o risco de morte. Isso também foi observado na necessidade de Terapia de Substituição Renal, internação na UTI e internação hospitalar. A concordância entre a gravidade da LRA e o pior KeRFG alcançado é controversa na literatura avaliada. **Conclusão:** Sugerimos que os sistemas de classificação de LRA e o modelo KeRFG sejam utilizados de forma conjunta para tomada de decisão e para obtenção de informações adicionais, como gravidade e prognóstico.

Palavras-chave: Lesão renal aguda. Gravidade do Paciente. Mortalidade.

Autor correspondente: Cristiano Araújo Costa, Universidade Federal do Ceará, Campus Sobral, Rua Comandante Maurocélio Rocha Ponte, 100, Derby, Sobral, Ceará, Brasil. CEP: 62042-280. Telefone: +55 88 3611-8000. E-mail: cristiano@stacasa.com.br.
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INTRODUCTION

Acute kidney injury (AKI) represents a serious health problem worldwide, as it is related to high mortality and high risks of progression to chronic kidney disease (CKD).[1] This condition is defined as a sudden loss of glomerular function, determined by an increase in serum creatinine levels and/or a reduction in urine output (oliguria).[2]

In recent years, several diagnostic criteria for AKI have been developed based on changes in serum creatine (SCr) and diuresis values, including RIFLE (Risk, Injury, Failure, Loss of renal function, and End-stage Kidney Disease), the Acute Kidney Injury Network (AKIN) and Kidney Disease Improving Global Outcomes (KDIGO). The latter is the most recent and currently used definition.[2] However, although such tools have come from many collective efforts and have been proven through research, they have some flaws in diagnosing AKI early. In this way, it causes a delay in decision-making, directly influencing the patient's prognosis.[3]

In most situations, the glomerular filtration rate (GFR) is the best measure of kidney function. Serum creatinine, on the other hand, does not reflect changes in GFR in real time if it is changing rapidly. In the early stages of AKI, given that there is not enough time for plasma creatinine to accumulate, SCr levels overestimate the real GFR. As demonstrated by Chen in 2013, patients with AKI show a tendency to decrease creatinine excretion, allowing this substance to accumulate in the body.[4] However, in the AKI recovery phase there is a tendency for greater creatinine excretion.

While clinical parameters such as urine output, increased creatinine concentration, and fluid balance can be used at the bedside to inform us about the patient's clinical picture, a dynamic formula to help estimate rapidly changing GFR would be a useful tool to our diagnostic arsenal.

The model proposed by Chen (2013) incorporates the principles of mass balance (generation, distribution, excretion) together with an "elapsed time" factor to consider a GFR at each SCr value, as long as the time elapsed since the last value be known.

Kinetic estimated glomerular filtration rate (KeGFR) is a mathematical tool derived from creatinine clearance calculated from two SCr equations at different time points,[4] showing the advantage of not requiring any additional tests beyond those routinely requested in patients with acute illnesses. It is relatively easy to calculate and theoretically reflects dynamic changes in kidney function.

In view of the above, the objective of this study was to analyze the use of the kinetic estimated glomerular filtration rate (KeGFR) as an early predictor of acute kidney injury (AKI), with the hypothesis that the KeGFR can predict dialytic AKI earlier compared to current classification models, such as KDIGO, reducing possible errors or failures of this scoring system, in addition to improving the prognosis of these patients.

METHODS

This study is a literature review, where the authors analyzed the use of the kinetic estimated glomerular filtration rate (KeGFR) to predict dialytic AKI earlier. The bibliographic research was carried out in the main international databases, including PudMed, MEDLINE, LILACS, Scielo and BVS.

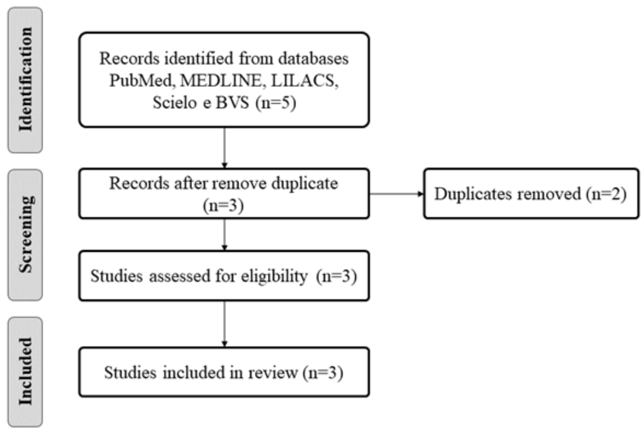
To carry out the search, we used as descriptors acute kidney injury AND severity AND mortality AND kinetic estimated glomerular filtration rate OR KeGFR.

The search was based on reviewing the title and summary of the articles. The inclusion criteria were observational studies (case reports, case series, cross-sectional, case control and cohort studies) that used the KeGFR model applied to AKI. We used works published until July 2023, without language restrictions. The exclusion criteria were comments, editorials, letters, reviews, or articles with only the abstract or title available.

RESULTS

Our search found 5 publications, of which two were duplicated and were excluded. After determining eligibility through titles and abstracts, three articles remained for full-text review, in the end, all were eligible for the study (Figure 1).

Figure 1. Article search flow.



In the study conducted by Oliveira et al. in 2017, patients with reduced KeGFR during the first 7 days of ICU admission were more likely to have more comorbidities (except arterial hypertension), more diagnosed with sepsis and were more seriously ill patients.[5]

On the other hand, according to the study carried out by Dumnicka et al. (2022), regardless of age, sex and pre-existing comorbidities, a lower KeGFR value was significantly associated with AKI.[6]

Regarding mortality from AKI, Oliveira et al. (2017) found that the lower it was the worst KeGFR achieved in the first 7 days of hospital admission, the greater it was the risk of death, rising from 7.0% in patients with KeRFG > 70 ml/min/1.73m^2, to 27.8% in patients with KeGFR < 30 ml/min/1.73m^2.[5] This association was also observed in other outcomes evaluated, such as the need for Renal Replacement Therapy (RRT), ICU admission and hospital admission. Mortality increased to 40% when stage 3 AKI and KeGFR < 30 ml/min/1.73 m^2 were present (Table 1).

In the study by Latha et al. (2020), which evaluated children admitted to the ICU, the comparison of hospital mortality between patients with AKI and those without AKI showed no significant difference, when stratified by KDIGO or KeGFR.[7]

There was not a good agreement between the severity of AKI and the worst KeGFR achieved, since many patients with AKI were identified according to the KDIGO classification (stages 1, 2 and 3), but maintained KeRFG above 70 ml/min /1.73 m^2.[5] On the other hand, several patients achieved KeGFR < 45 ml/min/1.73 m^2 but did not have AKI or only had KDIGO stage 1 AKI.

In contrast, using the same KeGFR model, 73.3% of patients were detected as having AKI, and those who did not have AKI by KDIGO were 9% of them, considering worst KeGFR on a daily basis.[7] As a result, Latha et al. (2020) found a good agreement between the worst KeGFR achieved and the AKI staging using the KDIGO criteria (p = < 0.001) (Table 2).

Still in the same study carried out by Latha et al. (2020), it was observed that 81.3% of group-I (> 70 ml/min), 56% of group-II (45 - 70 ml/min), 77.8% of group-III (30 - 45 ml/min) and 90% of group-IV (< 30 ml/min) stratified by KeGFR were classified as stage 0 (no AKI), stage 1, stage 2 and stage 3 AKI by KDIGO criteria, respectively. However, other results did not show statistical significance regarding AKI staging using the KDIGO criteria and the KeGFR model.[7]

Regarding the need for RRT, this rate was almost 44% when patients had KDIGO stage 3 and worst KeRFG < 30 ml/min/1.73 m^2.[5] In the group of patients with KDIGO stage 3 and a worse KeGFR > 30 ml/min/1.73 m^2 or a worse KeGFR < 30 ml/min/1.73 m^2 and KDIGO stage 1 or 2, the RRT rate was not higher than 10%.

Table 1. Outcomes for all patients according to maximum AKI severity and worst achieved KeGFR.[5]

	Worst achieved KeGFR during ICU stay				
KDIGO stage urine and SCr- based	>70mL/min	45-70mL/min	30-45mL/min	<30mL/min	Total
No AKI	2764	841	143	174	3922
Dead (%)	4,1	6,4	6,3	12,1	5,0
RRT (%)	0,3	0,4	-	0,6	0,3
Stage 1	2322	1124	304	246	3996
Dead (%)	4,0	9,5	9,5	15,0	6,6
RRT (%)	0,5	1,4	1,6	1,6	0,9
Stage 2	1689	1169	457	511	3826
Dead (%)	14,3	16,1	19,9	22,1	16,5
RRT (%)	0,4	0,4	6,3	4,3	1,6
Stage 3	314	286	208	732	1540
Dead (%)	16,5	25,5	24,5	40,0	30,4
RRT (%)	6,4	7,3	10,6	44,0	25,0
Total	7089	3420	1112	1663	13284
Dead (%)	7,0	12,2	16,2	27,8	11,8
RRT (%)	0,7	1,3	4,6	21,0	3,7

Note: AKI: acute kidney injury; ICU: intensive care unit; KDIGO: Kidney Disease Improving Global Outcomes; KeGFR: kinetic estimated glomerular filtration rate; RRT: renal replacement therapy; SCr: serum creatinine.

Table 2. KDIGO criteria and KeGFR to the diagnosis of AKI.[7]

		AKI by KDIGO criteria	
		AKI – Yes	AKI – No
AKI by KeGFR method	AKI – Yes	40 (93%)	4 (23.5%)
	AKI – No	3 (7%)	13 (76.5%)
Total		43	17

Note: AKI: Acute Kidney Injury; KDIGO: Kidney Disease Improving Global Outcomes; KeGFR: Kinetic estimated Glomerular Filtration Rate.

DISCUSSION

In this study, the objective was to evaluate the performance of KeGFR by searching current literature for information on the severity, mortality and detection of dialysis AKI using this model in relation to current AKI staging systems.

According to what was found in the literature, KeGFR does not seem to be a method to replace current AKI classification systems, but it can help with additional information about prognosis in patients affected by this entity.[5] Thus, both the LRA and KeGFR classification systems appear to be complementary in predicting outcomes. With this, we do not aim to replace the LRA classification with the KeGFR model, but we believe that both can be used together.

Although significant advances have been made in recent years, several questions still remain when evaluating patients with AKI. The results of our search demonstrate several important findings. First, we found in the study by Oliveira et al. (2017) a discordance between the severity of AKI and the worst KeGFR achieved by finding that several patients had stage 3 AKI according to KDIGO but maintained KeGFR greater than 70 ml/min/1.73 m^2, that is, the normal kidney function.[5]

This can be explained by a slow increase in SCr over the days, as the KeGFR model takes into account the evolution time of the LRA, and the longer this time, the less influence it will have on the decrease in the KeGFR value.[5] On the other hand, the study by Latha et al. (2020) was able to find a good agreement between KDIGO and KeGFR staging in pediatric patients.[7]

Regarding mortality, it was possible to notice that a gradual reduction in KeGFR results in an increase in the risk of death at each stage of AKI.[5] In this sense, to correctly quantify AKI in critically ill patients, we must take into account not only the degree of increase in SCr, but also the speed at which this increase occurs.

A study by Seelhammer et al. (2016), which involved 4,022 post-cardiac surgery patients, found that the KeGFR model had good discrimination in predicting AKI and operative mortality.[8] The study by Dumnicka et al (2022) also found this association between the KeGFR model and mortality from AKI.[6]

However, in the study conducted by Latha et al. (2020) it was not possible to find a significant correlation between the development of AKI (both by KDIGO and KeGFR models) and mortality.[7] This same finding was seen in a retrospective study involving 107 ICU patients, which found that there was no significant association between the KeGFR model and 30-day mortality.[9]

Furthermore, the LRA classification systems and the KeGFR model can be used in a complementary way to predict the need for RRT. We can take as an example the result found in the study by Oliveira et. al (2017), in which almost 45% of patients with stage 3 AKI and KeGFR < 30 ml/min/1.73 m^2 required RRT compared to less than 10% of patients with stage 3 AKI but with reduced KeGFR less severe, and less than 5% of patients with KeRFG < 30 ml/min/1.73 m^2, but only stage 1 or 2 AKI.[5]

In agreement with this finding, a study involving 107 patients with acute illnesses analyzed the relationship between the KeGFR model and the need for RRT.[10] They were able to demonstrate a good association between the KeGFR model and the need for RRT, by identifying 16 patients who needed RRT earlier.

As a limitation of our study, we can mention the number of studies currently available in the literature. Taking as a basis only 3 studies that evaluated the KeGFR model in relation to mortality and AKI severity does not give us much reliable information to use in the general population. Therefore, more studies are needed on this new method in the most diverse populations. In this way, we aim to add more information to the literature, supporting decision-making regarding this entity that is so present in clinical practice.

CONCLUSION

In view of the above, we suggest that the AKI classification systems and the KeGFR model be used together for decision making and to obtain additional information, such as severity and prognosis. It was observed that there is good agreement between the KeGFR model and the KDIGO criteria in identifying the severity of AKI in children, although the same was not found in the adult population. On the other hand, it was possible to find that the gradual reduction in KeGFR results in an increase in the risk of death at each stage of AKI.

Finally, more research is needed, such as multicenter studies, targeting population sample size to validate the results of these studies and also to explore the association of the KeGFR model with clinical outcomes.

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