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Utilizing point-of-care lactate testing for rapid prediction of clinical outcomes in patients with acute gastrointestinal bleeding in the emergency department

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ABSTRACT

Objectives: We aimed to rapidly predict the prognosis of patients who present to the emergency department (ED) with acute gastrointestinal bleeding (AGIB) using point-of-care (POC) lactate testing.

Methods: This single-center retrospective observational study included 327 patients (survival group, 287; non-survival group, 40) who presented to the ED with AGIB between March 2021 and February 2022. We compared POC-measured lactate levels with laboratory-measured lactate levels using Pearson's correlation. Multivariate logistic regression analysis was used to identify early predictors of in-hospital mortality and correlated clinical outcomes. Receiver operating characteristic (ROC) curves were used to determine the optimal cutoff for POC-measured lactate levels for predicting in-hospital mortality, and the ROC curves for POC-measured lactate levels and AIMS65 scores were compared using the DeLong test.

Results: POC-measured lactate levels strongly correlated with laboratory-measured lactate levels $(R^2 = 0.82)$. Patients in the non-survival group had higher POC-measured lactate levels than did those in the survival group (2.6 mmol/L vs. 1.4 mmol/L, p *<* 0.001). POC-measured lactate level, age, systolic blood pressure, heart rate, and malignancy were identified as early predictors of inhospital mortality (adjusted odds ratio [aOR] for POC-measured lactate levels: 1.15; 95 % confidence interval [CI] 1.02–1.30). The optimal POC-measured lactate level cutoff was 3.2 mmol/L. Areas under the ROC curves for POC-measured lactate level and the AIMS65 score were 0.70 and 0.73, respectively, showing statistical compatibility. Higher POC-measured lactate levels correlated with ICU admission, blood transfusion, and mechanical ventilation (aOR: 1.16, 95 % CI 1.05–1.27; 1.16, 1.04–1.30; and 1.31, 1.13–1.53, respectively]. Further, the hyperlactatemia subgroup (POC-measured lactate level \geq 3.2 mmol/L) exhibited a lower survival probability in the Kaplan–Meier survival analysis (p *<* 0.01).

Conclusions: Our study shows that rapidly obtainable POC-measured lactate levels are valuable for predicting critical outcomes in AGIB patients and should be considered an early prognostic indicator for in-hospital mortality in the ED.

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1. Introduction

Acute gastrointestinal bleeding (AGIB) poses a significant public health problem, affecting approximately 288 in 100,000 individuals who visit the emergency department (ED) annually, and is associated with a crude mortality rate of 2.9 per 100,000 individuals [\[1](#page-8-0)]. Patients who present to the ED with AGIB range from having mild symptoms to life-threatening conditions [\[2\]](#page-8-0). Early identification of critically ill patients is important in AGIB cases because early detection of high- and low-risk patients can significantly influence the initial management strategies as well as the patient outcomes [3–[5\]](#page-8-0).

Various prognostic prediction methods have been developed to facilitate risk stratification of patients with AGIB, including the AIMS65, Glasgow–Blatchford, and Rockall scores [\[6](#page-8-0)–8]. However, implementing these methods is contingent upon the complete reporting of essential risk factors, including international normalized ratio; albumin, blood urea nitrogen, and hemoglobin levels; and endoscopic examination results. This time-consuming process impedes the practical application of these conventional methods in ED settings as well as the early identification of critically ill patients.

In the ED context, lactate has garnered significant attention owing to its capability to predict mortality $[9-12]$ $[9-12]$. Hyperlactatemia is associated with increased mortality in conditions such as sepsis and trauma $[13,14]$ $[13,14]$ $[13,14]$. In a retrospective cohort study, hyperlactatemia observed in the ED was not only associated with infection and trauma but also with cardiac and gastrointestinal diseases [[15\]](#page-8-0). Moreover, higher lactate levels are associated with higher in-hospital mortality rates and can be an independent predictor of in-hospital mortality in patients with AGIB who visit the ED $[16-18]$ $[16-18]$. Therefore, lactate level has emerged as a potentially valuable prognostic indicator for patients with AGIB in the ED.

Point-of-care (POC) testing refers to diagnostic testing conducted near the patient, allowing for prompt test results. A retrospective observational study has revealed that implementing POC testing significantly reduced the test turnaround time and ED length of stay [\[19](#page-9-0)]. POC-measured lactate level is a rapidly obtainable blood parameter that can be valuable for promptly stratifying the risk for sepsis [[20,21\]](#page-9-0). However, little is known regarding the association between POC-measured lactate levels and the prognosis of patients with AGIB. Therefore, in this study, we aimed to investigate the usefulness of POC-measured lactate levels in patients with AGIB in an ED setting.

2. Materials and methods

2.1. Study design and participants

This single-center retrospective observational study was conducted at an urban university-affiliated hospital with an annual ED census of approximately 40,000 individuals. Patients were enrolled through a comprehensive electronic medical records review, focusing on those with chief complaints of hematochezia, melena, and hematemesis recorded between March 1, 2021, and February 28, 2022. Patients who met the following criteria were excluded: (1) transfer cases with an unknown prognosis, (2) an age under 19 years, and (3) not having undergone POC lactate testing. Subsequently, the included participants were stratified into survival and nonsurvival groups based on their in-hospital mortality outcomes.

2.2. Measurements

Vital signs, sex, age, level of consciousness, personal medical history, and POC-measured lactate levels, regarded as variables that emergency physicians could access without delay, were recorded. Vital signs, including systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR), were recorded during triage. Personal medical history was acquired from the patients or their accompanying guardians, including a history of diabetes mellitus, hypertension, any malignancies, cardiovascular disease (such as stroke, coronary artery disease, and pulmonary thromboembolism), and liver disease (such as hepatitis, liver cirrhosis, fatty liver, and liver cancer). Heavy alcohol consumption was defined as the consumption of more than 4 glasses per day or 14 glasses per week for men, and more than 3 glasses per day or 7 glasses per week for women.

In the ED, arterial blood samples were drawn and POC lactate testing was performed immediately using a GEM Premier 3500 (Instrumentation Laboratory, Bedford, MA, USA). Simultaneously, venous blood samples were obtained for laboratory analyses of blood chemistry and complete blood counts. In-hospital mortality was recorded during hospitalization, regardless of the cause of death.

2.3. Outcomes

The primary outcome was in-hospital mortality among patients presenting with AGIB at the ED. The secondary outcomes were admission to the intensive care unit (ICU), blood transfusion requirements, and the need for mechanical ventilation.

2.4. Statistical analysis

The baseline characteristics of the study population are described as median (interquartile range [IQR]) for continuous variables and numbers (percentages) for categorical variables. Independent *t*-tests, chi-square tests, and Fisher's exact tests were used to assess the statistical differences between the two groups, as appropriate.

A Pearson product-moment correlation test was used to evaluate the reliability of POC-measured lactate levels and their correlation

with laboratory-measured lactate levels. Multivariate logistic regression analysis employing backward stepwise variable selection was conducted to identify independent outcome predictors. Adjusted odds ratios (aOR) with 95 % confidence intervals (CI) were calculated for rapidly obtainable variables. The receiver operating characteristic (ROC) curve and Youden index were used to determine the optimal cutoff for POC-measured lactate levels for predicting in-hospital mortality. The DeLong test was used to compare the ROC curves of POC-measured lactate levels and AIMS65 scores to further assess the prognostic performance of POC-measured lactate levels. The survival rates were compared between patients with and without hyperlactatemia using Kaplan–Meier survival analysis. Statistical significance was set at p *<* 0.05, and statistical analyses were performed using R software (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria) and IBM SPSS Statistics (version 22.0; IBM Corp., Armonk, NY, USA).

2.5. Ethics declarations

This study was reviewed and approved by the Institutional Review Board (IRB) of the Catholic Kwandong University International St. Mary's Hospital, with the approval number: IS23RISI0038, dated July 13, 2023. The IRB determined that written informed consent is not required due to the study's minimal risk, strong privacy protections, significant public benefit, and impracticality of obtaining consent.

3. Results

3.1. Basic demographic and clinical characteristics of the participants

Overall, 419 patients with AGIB presented at the ED during the study period. We excluded 18 transfer cases with an unknown prognosis and 3 patients younger than 19 years of age. Additionally, 71 patients who did not undergo POC lactate testing were excluded. Finally, 327 patients were included in the study (Fig. 1).

The median age of the study population was 61 years (IQR, 47–74 years), and there were 124 women (37.9 %). A total of 300 patients (91.7 %) were alert upon arrival at the ED. The median SBP, DBP, and HR were 117 mm Hg (IQR, 100–133 mm Hg), 70 mm Hg (IQR, 56–83 mm Hg), and 93 bpm (IQR, 77–110 bpm), respectively. The median POC-measured lactate level was 1.5 mmol/L (IQR, 0.9–2.8 mmol/L), and the median hemoglobin level was 10.5 g/L (IQR, 8.2–13.2 g/L). Of the included patients, 82 (25.0 %) were admitted to the ICU and 165 (50.4 %) required blood transfusions. Mechanical ventilation was administered to 14 patients (4.2 %), and 40 patients (12.2 %) died during hospitalization. [Table 1](#page-3-0) presents the detailed demographic and clinical characteristics of the study participants.

3.2. Correlation between POC- and laboratory-measured lactate levels

Pearson's product-moment correlation test revealed a correlation coefficient (R) between POC-measured and laboratory-measured lactate levels of 0.907 (95 % CI: 0.870–0.933, p < 0.001). The coefficient of determination (R²) was 0.822 ([Fig. 2\)](#page-3-0).

3.3. Primary outcome: in-hospital mortality

Based on the ROC curve analysis and the Youden index, the optimal cutoff for POC-measured lactate level for predicting in-hospital mortality was 3.2 mmol/L, yielding 47 % sensitivity and 81 % specificity. The area under the ROC curve (AUROC) for predicting in-hospital mortality was 0.70 for POC-measured lactate level and 0.73 for the AIMS65 score [\(Fig. 3](#page-4-0)). A comparison of the two ROC curves

Fig. 1. Flowchart of participant selection. Abbreviation: POC, point-of-care.

Table 1

Basic demographic characteristics of the patients presenting to the emergency department with acute gastrointestinal bleeding.

Continuous variables are described as median (interquartile range).

Categorical variables are described as numbers (percentages).

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; POC, point-of-care; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ICU, intensive care unit.

Fig. 2. Pearson's product-moment correlation test between POC-measured and laboratory-measured lactate levels. Abbreviation: POC, pointof-care.

Fig. 3. Comparison of the area under the receiver operating characteristic curve for in-hospital mortality between POC-measured lactate levels and the AIMS65 score. Abbreviation: POC, point-of-care.

using the DeLong test revealed no significant difference in their ability to predict in-hospital mortality ($p = 0.43$).

In the multivariate logistic regression analysis with backward stepwise variable selection, the independent in-hospital mortality predictors among patients with AGIB included POC-measured lactate level, age, SBP, HR, and medical history of malignancy. POCmeasured lactate level exhibited an aOR of 1.15 (95 % CI: 1.02-1.30) for predicting in-hospital mortality in patients with AGIB (Fig. 4).

3.4. Secondary outcomes: ICU admission, blood transfusion, and mechanical ventilation

An elevated POC-measured lactate level positively correlated with ICU admission (aOR: 1.15 [95 % CI, 1.05–1.27]) and the requirements for blood transfusion (aOR: 1.16 [95 % CI, 1.04–1.31]) and mechanical ventilation (aOR: 1.30 [95 % CI, 1.11–1.53]) [\(Table 2](#page-5-0)).

3.5. Subgroup analysis based on optimal cutoff for POC-measured lactate level

Based on the optimal cutoff for POC-measured lactate level, 73 patients (22.3 %) were classified into the hyperlactatemia group (POC-measured lactate level ≥3.2 mmol/L) and 254 (77.6 %) into the non-hyperlactatemia group (POC-measured lactate level *<*3.2 mmol/L) ([Table 3](#page-5-0)). Compared with the non-hyperlactatemia subgroup, the hyperlactatemia subgroup more frequently presented to the ED with hematemesis as chief complaint (65.7 % vs. 22.8 %, p *<* 0.001) and had a lower rate of alertness upon arrival (80.8 % vs. 94.8 %, p *<* 0.001). Additionally, this group exhibited hemodynamic instability, which was reflected in parameters such as SBP, DBP,

Fig. 4. Risk factors for in-hospital mortality of patients who present to the emergency department with acute gastrointestinal bleeding. Abbreviation: POC, point-of-care.

Table 2

Multivariate logistic regression analysis results of the secondary outcomes.

The multivariate logistic regression model was adjusted for age (continuous), systolic blood pressure, heart rate, and a personal medical history of malignancy.

Abbreviation: ICU, intensive care unit.

Table 3

Comparison between patients with acute gastrointestinal bleeding with and without hyperlactatemia.

Continuous variables are described as median (interquartile range).

Categorical variables are described as numbers (percentages).

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; POC, point-of-care; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ICU, intensive care unit.

and HR. A higher proportion of patients in this subgroup had a history of liver disease (46.5 % vs. 15.7 %, p *<* 0.001) and engaged in heavy alcohol consumption (42.4 % vs. 15.3 %, p *<* 0.001). The in-hospital mortality rate was significantly higher in the hyperlactatemia group than in the non-hyperlactatemia group (26.0 % vs. 8.2 %, p *<* 0.01). The hyperlactatemia group had a significantly higher ICU admission rate (46.5 % vs. 18.8 %, p *<* 0.001), blood transfusion rate (78.0 % vs. 42.5 %, p *<* 0.001), and need for mechanical ventilation (13.6 % vs. 1.5 %, p *<* 0.001) than the non-hyperlactatemia group did. Furthermore, the Kaplan–Meier survival analysis demonstrated significantly lower survival rates in the hyperlactatemia group than in the non-hyperlactatemia group [\(Fig. 5](#page-6-0)).

4. Discussion

To our knowledge, this study is the first to investigate the prognostic value of POC-measured lactate levels in patients with AGIB who present to the ED. We found that the POC-measured lactate level strongly correlated with the traditional laboratory-measured serum lactate level. Additionally, with each 1 mmol/L increase in POC-measured lactate level, there was a 1.15-fold increase in the odds of in-hospital mortality. Similarly, POC-measured lactate level demonstrated the ability to predict ICU admission and the requirement for blood transfusion and mechanical ventilation.

The importance of these findings lies in the rapid availability of POC-measured lactate levels. The expedited access to these test

Group + Non-hyperlactatemia + Hyperlactatemia

Fig. 5. Kaplan–Meier survival analysis of the non-hyperlactatemia and hyperlactatemia groups.

results allows ED physicians to make faster, more informed clinical decisions, which is vital for improved patient outcomes and has the potential to transform standard care practices. For instance, early recognition of elevated lactate levels can prompt more aggressive resuscitation efforts, such as the initiation of fluid therapy, blood transfusions, and inotropic support to stabilize the patient's hemodynamic status. A rapid response is particularly critical in patients with AGIB, where delayed intervention can lead to worsening tissue hypoxia, organ failure, and ultimately a higher mortality rate. Moreover, the use of POC lactate testing allows for the dynamic monitoring of a patient's condition. As treatment progresses, repeated lactate measurements can provide real-time feedback on the effectiveness of interventions, allowing physicians to adjust their management strategies promptly.

Despite the absence of prior studies exploring the correlation between POC-measured lactate levels and in-hospital mortality among patients with AGIB in an ED setting, our findings are consistent with those of investigations examining the association between laboratory-measured lactate levels and mortality in patients with AGIB. In a retrospective study of 1644 patients with AGIB in the ED, the optimal cutoff for laboratory-measured lactate levels to predict in-hospital mortality was 4.0 mmol/L [\[17](#page-9-0)]. Patients in whom this level was surpassed exhibited a 6.4 times higher risk of in-hospital mortality (95 % CI: 3.3–12.4). Berger et al. included 366 patients with AGIB in the ED and reported consistent results [\[16\]](#page-9-0), concluding that laboratory-measured lactate level is an independent in-hospital mortality predictor (odds ratio [OR]: 1.32, 95 % CI 1.11–1.57), with an optimal cutoff of 2.75 mmol/L. A recent study by Kahraman et al. demonstrated that elevated lactate levels significantly correlated with increased mortality, with an AUROC of 0.714 for its predictive performance [[18\]](#page-9-0). Furthermore, a prospective study showed that patients with AGIB with elevated lactate levels experienced significantly longer hospital stays (7.38 vs. 3.96 days), higher ICU admission rates (95 % vs. 67 %), more frequent blood transfusions (98 % vs. 72 %), and higher mortality rates (9 % vs. 3 %) than did those with normal lactate levels [[22\]](#page-9-0). Similarly, another prospective study found that elevated lactate levels were significantly associated with higher in-hospital mortality (OR: 1.39, 95 % CI 1.22–1.58, p *<* 0.001) and ICU admission (OR: 1.33, 95 % CI 1.19–1.5, p *<* 0.001) rates [[23](#page-9-0)]. Notably, the optimal cutoff values and ORs varied slightly among studies. This variability is potentially attributable to heterogeneity in the study designs, such as including confounding factors in the logistic regression analysis model as well as the inclusion and exclusion criteria. However, the overarching result consistently highlights the positive association between hyperlactatemia and in-hospital mortality among patients with AGIB in the ED setting.

Understanding lactate metabolism may provide valuable insights into the association between hyperlactatemia and adverse clinical outcomes in patients with AGIB. Whether attributed to generalized hypoxia or microcirculatory dysfunction, tissue hypoxia can cause impaired mitochondrial oxidation and result in the excessive production or insufficient utilization of lactate [\[24,25](#page-9-0)]. Furthermore, aerobic glycolysis, an efficient adenosine triphosphate (ATP) generation method used under stressful conditions, can contribute to hyperlactatemia. This is due to the association of lactate production with increased Na^+K^+ -ATPase activity stimulated by elevated epinephrine levels in stress-inducing conditions, including sepsis, trauma, cardiogenic shock, and hemorrhagic shock [[26\]](#page-9-0). The hyperlactatemia in patients with AGIB may be due to circulatory dysfunction or aerobic glycolysis. Moreover, the liver is responsible for up to 70 % of lactate clearance, and hyperlactatemia is exacerbated by chronic liver disease [\[27](#page-9-0)]. We found significantly higher aspartate aminotransferase levels in the hyperlactatemia group than in the non-hyperlactatemia group, with a higher prevalence of personal medical histories involving liver disease and heavy alcohol consumption, which may indicate diminished lactate clearance.

Herein, the AUROC for in-hospital mortality was 0.70, indicating moderate predictive performance. Additionally, the ROC curve for POC-measured lactate levels demonstrated comparable performance to that of the AIMS65 score. Berger et al. incorporated laboratory-measured lactate levels into the AIMS65, Glasgow–Blatchford, and Rockall scores [\[16](#page-9-0)]. This integration resulted in a statistically improved predictive value, particularly for the Glasgow–Blatchford score and post-endoscopic Rockall score. However, we opted not to combine POC-measured lactate levels with conventional methods in our study because such a combination would not mitigate the time-consuming nature of the conventional methods. Our primary focus was the early detection of critically ill patients to enhance outcomes through the use of rapidly obtainable variables as independent in-hospital mortality predictors in patients with AGIB, including age, SBP, HR, and a personal medical history of malignancy. This outcome highlights the importance of considering rapidly obtainable variables, as they may play crucial roles when evaluating patients with AGIB in the ED. Future studies should

identify additional rapidly obtainable variables that were not considered in our investigation for a more accurate prognostic prediction and improved outcomes.

Several stress factors may serve as key prognostic determinants in patients with AGIB. We found a significant difference in the median age of the patients in the survival group versus those in the non-survival group (59 vs. 67 years). Ageing is associated with a decline in gastrointestinal function and adaptive capacity, which is influenced by multiple factors such as the intestinal microbiota, immune function degradation, physiological decline, host-specific variations, and the impact of comorbidities and medications [[28\]](#page-9-0). These deteriorations can intensify the severity of bleeding episodes and compromise physiological compensatory mechanisms. Furthermore, while the administration of enteral nutrition, proton pump inhibitors, or histamine-2 receptor antagonists can reduce the risk of upper gastrointestinal bleeding, conditions such as coagulopathy, shock, and chronic liver disease can act as significant stress factors [[29,30\]](#page-9-0). These stress factors underscore the importance of considering them in the prognosis of AGIB patients, as they can exacerbate bleeding severity and diminish the effectiveness of physiological compensatory mechanisms, ultimately impacting overall survival outcomes.

Our study has some limitations. First, we used a retrospective design and conducted the study at a single center. This may have limited the generalizability of our findings to other settings and introduced selection bias. Second, a comparison between POCmeasured lactate levels and other widely utilized prognostic markers, such as hemodynamic parameters or established scoring systems, in predicting outcomes in AGIB patients was not thoroughly conducted. Third, including patients with both upper and lower AGIB when comparing POC-measured lactate levels and AIMS65 scores may be considered inappropriate because the AIMS65 was originally developed for upper AGIB [\[8\]](#page-8-0). However, a subsequent study has revealed that the AIMS65 is the most reliable in-hospital mortality predictor in patients with lower AGIB [\[31](#page-9-0)]. Additionally, determining the bleeding site is often inaccurate in the ED setting, and the bleeding source in patients presenting with lower AGIB may be in the upper gastrointestinal tract [[32,33\]](#page-9-0). Consequently, a notable finding of our study is that POC-measured lactate level has a prognostic performance comparable to that of the AIMS65, irrespective of whether the AGIB occurs in the upper or lower gastrointestinal tract. Fourth, acquiring the necessary equipment to perform POC lactate testing demands a significant financial investment, which may limit accessibility in some settings. Fifth, POC-measured lactate level was found to have moderate performance in terms of prognosis prediction. This suggests that while lactate levels can provide valuable insights, they should not be used in isolation for clinical decision-making. Emergency physicians should interpret POC-measured lactate levels within the broader context of the patient's history, physical examination findings, and other clinical indicators. This comprehensive approach can help mitigate the limitations of relying solely on lactate levels for prognostic predictions and enhance the overall quality of patient care.

The integration of POC lactate testing into the initial assessment and management of patients with AGIB presents a promising avenue for enhancing early decision-making and optimizing resource allocation in the ED setting. Future studies should focus on developing early risk stratification algorithms and customizing standard treatments for high-risk populations, such as older patients and those with hyperlactatemia. Future studies should also explore strategies such as fluid resuscitation, transfusion, mechanical ventilation, and the use of inotropic support when guided by POC-measured lactate levels. Additionally, research should focus on establishing lactate level thresholds that not only predict mortality but also indicate the urgency for intervention. The effectiveness of the interventions can subsequently be evaluated by comparing lactate clearance rates between groups in which lactate levels were normalized versus groups in which the levels were not normalized. To confirm these observations and advocate for the inclusion of POC-measured lactate level in clinical practice, prospective randomized controlled trials with large sample sizes are necessary.

5. Conclusions

Our findings underscore the rapid availability of POC-measured lactate levels and their accuracy in predicting critical clinical outcomes in patients with AGIB in the ED. POC-measured lactate levels should be considered as an early predictor of in-hospital mortality in this patient population. However, further research is required to elucidate the implications of these findings and to establish guidelines for the safe application of POC lactate testing. A prospective, multicenter study involving a larger cohort is essential to validate these results, understand the underlying mechanisms, and further clarify the role of POC-measured lactate levels in clinical practice.

Abbreviations

Ethical statement

This study was reviewed and approved by the Institutional Review Board of the Catholic Kwandong University International St. Mary's Hospital, with the approval number: IS23RISI0038, dated July 13, 2023. The IRB determined that written informed consent is not required due to the study's minimal risk, strong privacy protections, significant public benefit, and impracticality of obtaining consent.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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CRediT authorship contribution statement

Minsu Cha: Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Jongsu Park:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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