Original Article

Prediction of Mortality by using Red Blood Cell Distribution Width in Patients with Sepsis and Septic Shock admitted in an Intensive Care Unit of a Tertiary Care Hospital in Bangladesh

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Abstract:

Background: *Sepsis and septic shock progress rapidly, but early and accurate risk stratification can help prevent poor outcomes. Previous studies have shown that red blood cell distribution width (RDW), which reflects variation in cell size, plays a potential role in assessing disease severity.*

Aims: *To identify the relationship with the outcome in adult Bangladeshi patients with sepsis admitted in ICU.*

Methods: *This prospective observational study was conducted in the Department of Critical Care Medicine, BIRDEM, over six months. A total of 63 patients with severe sepsis and septic shock were enrolled based on predefined inclusion and exclusion criteria. Patient demographics, comorbidities, laboratory parameters including RDW, and SOFA scores were evaluated and analyzed.*

Results: *The mean age of patients was 50.3 ± 13.5 years with a female-to-male ratio of 1.5:1. Mean RDW was 15.5 ± 1.0% at admission, 14.8 ± 1.6% on day 4, and 13.9 ± 2.2% on day 7. Elevated RDW on day 4 and day 7 was significantly higher in non-survivors ($p < 0.05$), being 15.2 and 10.0 times more frequent, respectively. RDW (%) also showed a positive correlation with SOFA score ($r = 0.478$, $p = 0.010$).*

Conclusions: *This study found that elevated RDW on the 4th and 7th days was significantly associated with ICU mortality in patients with sepsis and septic shock.*

Keywords: *Biomarker, ICU, Mortality Prediction, Prognosis, Red Blood Cell Distribution Width, RDW, Sepsis, Septic Shock, SOFA score.*

Introduction

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] It is a major global health problem with an incidence of 300-1000 cases per 100,000 people annually and is one of the leading causes of hospital mortality.[2] Septic shock, characterized by persistent hypotension despite adequate fluid resuscitation, carries an even higher mortality risk of 40-50%.[3-4] Globally, an estimated 48.9 million sepsis cases and 11 million related deaths were reported, accounting for nearly 19.7% of all deaths.[5] Early recognition and timely intervention are essential, as each hour of delay in appropriate antimicrobial therapy decreases survival by 7.6%, while prompt management can prevent up to 84% of sepsis-related deaths.[6]

Several scoring systems, including the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA), are currently used to assess prognosis in sepsis.[2] However, these systems have limitations in early recognition and are not always feasible in resource-limited settings.[7] Thus, there is an increasing need for simple, cost-effective, and reliable biomarkers to predict outcomes in septic patients.

Red blood cell distribution width (RDW) is an inexpensive and routinely available hematological parameter that reflects the variability in erythrocyte size.[8] It is calculated as the standard deviation of the mean corpuscular volume divided by the mean corpuscular volume, multiplied by 100, with normal values ranging from 11-15%. Elevated RDW can result from iron, vitamin B12, or folate deficiencies, hemolysis, or inflammation.[9-10] Proinflammatory cytokines in sepsis alter erythropoiesis and red blood cell deformability, leading to increased RDW.[11] Recent studies have identified RDW as an independent predictor of poor outcomes in sepsis and as a potential prognostic marker for mortality, including 28-day mortality.[4,12-13] Serial RDW measurements within the first 72 hours of hospitalization have also been linked to disease severity and mortality.[8]

In resource-limited countries like Bangladesh, where sepsis

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and septic shock remain major causes of ICU mortality, an affordable and readily available prognostic biomarker is crucial. Therefore, this study aimed to determine whether an increase in red blood cell distribution width from baseline could predict mortality in patients with sepsis and septic shock admitted to the intensive care unit of a tertiary care hospital in Bangladesh.

Methods

This longitudinal study was conducted in the Department of Critical Care Medicine, BIRDEM General Hospital, Dhaka, Bangladesh, from 1st April 2021 to 30th September 2021. Ethical approval was obtained from the Institutional Review Board (IRB) of BIRDEM General Hospital prior to commencement of the study. Informed written consent was obtained from each participant or their legal guardian after a thorough explanation of the study objectives, procedures, and potential risks. The participants were assured of confidentiality, and all information collected was used solely for academic and research purposes. For data analysis, all patient identities were kept anonymous.

Patients aged 18 years or older who were admitted to the Intensive Care Unit (ICU) with clinical features of sepsis and septic shock, or who developed these features after ICU admission, were consecutively enrolled in the study based on inclusion and exclusion criteria. Patients with known chronic liver disease, renal disease, thyroid disorders, pre-existing anemia, hematological disorders, autoimmune diseases, malignancy, chronic heart failure, cardiogenic or hemorrhagic shock, polytrauma, pregnancy, or those readmitted to the ICU during the same hospitalization episode, as well as those who had received blood or Fresh Frozen Plasma (FFP) transfusions, were excluded.

A total of 63 patients were included. Sepsis was defined as life-threatening organ dysfunction resulting from a dysregulated host response to infection,[1] while septic shock was defined as sepsis with persistent hypotension despite adequate fluid resuscitation.[3] Clinical history, including comorbidities such as diabetes mellitus, hypertension, ischemic heart disease, chronic kidney disease, asthma, and chronic obstructive pulmonary disease, was documented. A detailed clinical examination was performed at ICU admission, and findings such as heart rate, respiratory rate, systolic and diastolic blood pressure, and temperature were recorded.

Relevant laboratory investigations-including serum hemoglobin, total white blood cell count, platelet count, serum creatinine, serum bilirubin, red blood cell distribution width (RDW), and oxygen saturation were carried out. The Glasgow Coma Scale (GCS) and Sequential Organ Failure Assessment (SOFA) scores were calculated and recorded for each patient. Therapeutic interventions, such as antibiotic administration, fluid resuscitation, vasoactive drug use, and mechanical ventilation, were also documented. Patients were followed up at ICU admission, on the 4th day, and on the 7th day. Outcomes were measured in terms of survival or mortality until discharge or transfer from the ICU. Patients who survived and were discharged or transferred to a general ward were categorized as survivors, while those who died during ICU stay were classified as non-survivors.

Operational Definitions:

Critically ill patients: Patients requiring /likely to require endotracheal intubation and invasive mechanical ventilator support. Patients requiring support of two or more organ system (e.g. inotropes and hemofiltration). Patients with chronic impairment of one or more organ systems (e.g. COPD or severe ischemic heart disease) who require support for acute reversible failure of another organ.

Sepsis: Acute change in total sequential / sepsis related organ failure assessment (SOFA) score >2 points secondary to infection.

Septic shock: Persisting hypotension requiring vasopressors to maintain MAP >65 mmHg despite adequate fluid resuscitation and lactate level >2 mmol/lit.

Statistical analysis:

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). A descriptive analysis was performed for all collected data. Mean values were calculated for continuous variables, while categorical variables were presented as frequencies and percentages. Descriptive statistics were used to summarize patient characteristics. The Chi-square test was applied to compare qualitative variables, and the independent Student's t-test was used for quantitative variables. Patient outcomes were compared according to the levels of red cell distribution width (RDW). The optimal cutoff value of RDW was determined using the Receiver Operating Characteristic (ROC) curve. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated. A p-value of less than 0.05 was considered statistically significant.

Results:

The mean age of the study participants was 50.3 ± 13.5 years, with most patients belonging to the 46-60 year age group 26(41.3%), followed by 30-45 years 14(22.2%), >60 years 15(23.8%), and 18-29 years 8(12.7%). Females constituted the majority 38(60.3%) compared to males 25(39.7%). The most common primary source of infection was pulmonary 21(33.3%), followed by urinary tract 19(30.2%), skin and soft tissue 12(19%), gastrointestinal 4(6.3%), neurological 3(4.8%), intravascular catheter 2(3.2%), and blood infections 2(3.2%). Among comorbid conditions, hypertension 45(71.4%), diabetes mellitus 43(68.3%), and bronchial asthma 32(50.8%) were predominant, followed by heart disease 12(19%) and chronic kidney disease 11(17.5%). The mean ± SD of clinical parameters were heart rate 100.6 ± 12.6 beats/min, respiratory rate 26.7 ± 8.2 breaths/min, systolic blood pressure 105.7 ± 18.2 mm Hg, diastolic blood pressure 65.2 ± 14 mm Hg, mean arterial pressure 66.2 ± 12.2 mm Hg, and temperature 37.1 ± 1.2 °C.

At Day 1, the mean ± SD values of the investigated parameters were hemoglobin 11.3 ± 1.2 g/dL, total WBC 13563.5 ± 3675.9 cells/mm³, platelet count 143333.33 ± 46904.2 cells/mm³, serum creatinine 2.1 ± 0.6 mg/dL, and serum bilirubin 2.3 ± 1.4 mg/dL. The mean RDW was 15.5 ± 1.0%, SpO_2 81.4 ± 17.5%, GCS 9.5 ± 2.8, and SOFA score 10.1 ± 2.3. The individual SOFA components were respiratory 1.9 ± 0.9, coagulation 0.6 ± 0.8, liver 1.6 ± 0.7, cardiovascular 2.1 ± 0.8, CNS 2.4 ± 0.9, and renal 1.5 ± 0.6.

At Day 4, the mean ± SD values of the investigations were hemoglobin 11.3 ± 1.2 g/dL, total WBC 15912.7 ± 3609.5 per mm³, platelet count 143492.1 ± 40247.6 per mm³, serum creatinine 2.1 ± 0.6 mg/dL, and serum bilirubin 2.2 ± 1.1 mg/dL. The mean RDW was 14.8 ± 1.6%, SpO_2 83.2 ± 14.4%, and GCS 9.5 ± 3.1.

At Day 7, the mean ± SD values were hemoglobin 11.4 ± 1.2 g/dL, total WBC 14095.2 ± 3956.3 per mm³, platelet count 170238.1 ± 120226.4 per mm³, serum creatinine 2.2 ± 0.6 mg/dL, and serum bilirubin 2.3 ± 1.5 mg/dL. The mean RDW was 13.9 ± 2.2%, SpO_2 85.2 ± 13.2%, GCS 9.7 ± 3.9, and SOFA score 9.8 ± 2.5. The SOFA components were respiratory 1.8 ± 0.8, coagulation 0.7 ± 0.7, liver 1.6 ± 0.7, cardiovascular 2.0 ± 0.8, CNS 2.1 ± 1.1, and renal 1.5 ± 0.6.

Among the patients, 63.5% had sepsis and 36.5% had septic shock (fig 1). Among all the ICU patients, 23.8% died and 76.2% patients survived (fig 2). Advanced age, increased SOFA score and increased RDW (%) were significantly associated with mortality (table I). Increased RDW (%) at day 4 and at day 7 were significantly associated with mortality in both sepsis and septic patients (table II).

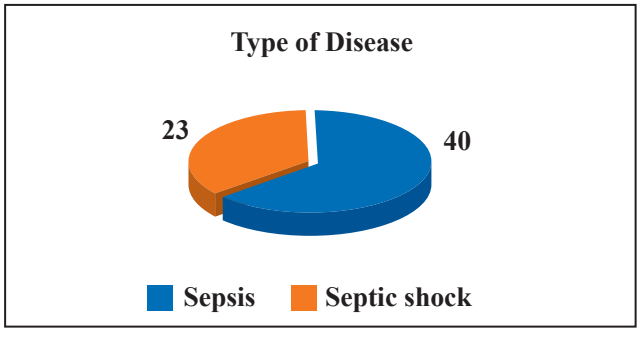


Figure 1: Distribution of the patients according to Disease (N=63)

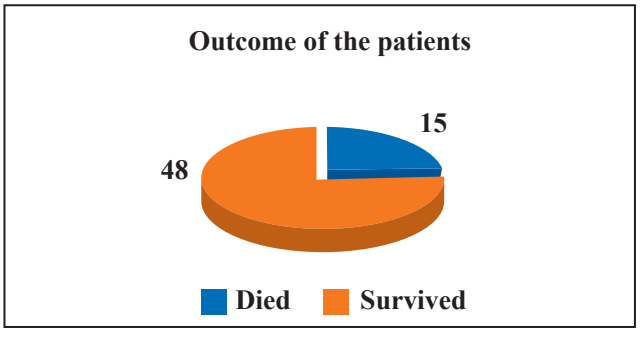


Figure 2: Distribution of the patients by Outcome of the patients (N=63)

Table I: Factors associated with poor outcome of the patients (N=63)

Factors	Died (n=15)	Survived (n=48)	P value
Age (mean±SD)	58.5±12.8	47.7±12.8	0.006*
Gender (n%)			
Male	6 (40)	19 (39.6)	
Female	9 (60)	29 (60.4)	0.603**
SOFA at 7th (mean±SD)	11.5±2.6	9.3±2.3	0.003*
RDW (%) at 7th day (mean±SD)	16.2±2.5	13.2±1.6	<0.01*
Septic shock present (n%)	3 (20)	20 (41.7)	0.111***
Diabetes mellitus	10 (66.7)	11 (22.9)	0.558**
Hypertension	12 (80)	33 (68.8)	0.311**
Bronchial asthma	7 (46.7)	25 (52.1)	0.472**
Chronic kidney disease	1 (6.7)	10 (20.8)	0.196***
Heart disease	3 (20)	9 (18.8)	0.590***

P value was determined by *Independent sample t test, **Chi-square test and ***Fisher Exact test.

Table II: Association of Disease severity with poor outcome of the patients (N=63)

Disease severity	Died (mean±SD)	Survived (mean±SD)	P value*
Sepsis	**(n=12)**	**(n=28)**	
RDW (%) at day 1	15.7±0.9	15.8±0.8	0.706
RDW (%) at day 4	16.3±1.8	14.4±1.3	0.001
RDW (%) at 7th day	15.8±2.6	13.4±1.5	0.001
Septic shock	**(n=3)**	**(n=20)**	
RDW (%) at day 1	16.3±1.5	15.1±1.0	0.082
RDW (%) at day 4	17.1±1.0	14.1±1.2	0.001
RDW (%) at 7th day	17.9±0.5	13.1±1.7	<0.01

*P value was determined by Independent sample t test.

Table III: Risk factor analysis of poor outcome of sepsis patients by Univariate logistic regression (N=63)

Risk Factors	Odds ratio	95% CI	P value*
Age	0.921	0.863-0.981	0.011
Gender (Female)	0.983	0.301-3.211	0.977
SOFA at 7th day	0.695	0.535-0.907	0.007
RDW (%) at 7th day	0.540	0.394-0.741	<0.01*

*p value was determined by Univariate logistic regression.

Univariate logistic regression shows that age, SOFA score and RDW (%) were significantly associated risk factors for mortality in ICU patients (table III). Multivariate logistic regression shows that only RDW (%) was significantly associated risk factors for mortality in ICU patients (table IV).

Table IV: Risk factor analysis of poor outcome of sepsis patients by Multivariate logistic regression (N=63)

Risk Factors	Odds ratio	95% CI	P value*
Age	0.921	0.863-0.981	0.265
Gender (Female)	0.983	0.301-3.211	0.775
SOFA at 7th day	1.492	0.958-2.325	0.415
RDW (%) at 7th day	0.540	0.394-0.741	0.011

*p value was determined by Multivariate logistic regression.

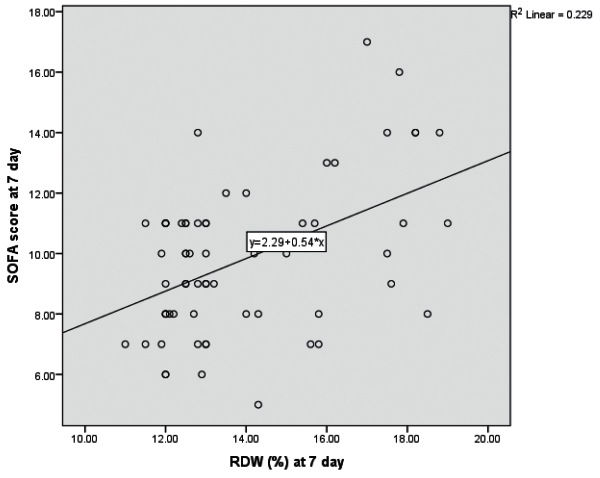


Figure 3: Scatter plot showing a significant positive Pearson correlation (r = 0.478, p=0.010) between SOFA score and RDW (%) after 7 days among ICU patients (N=63)

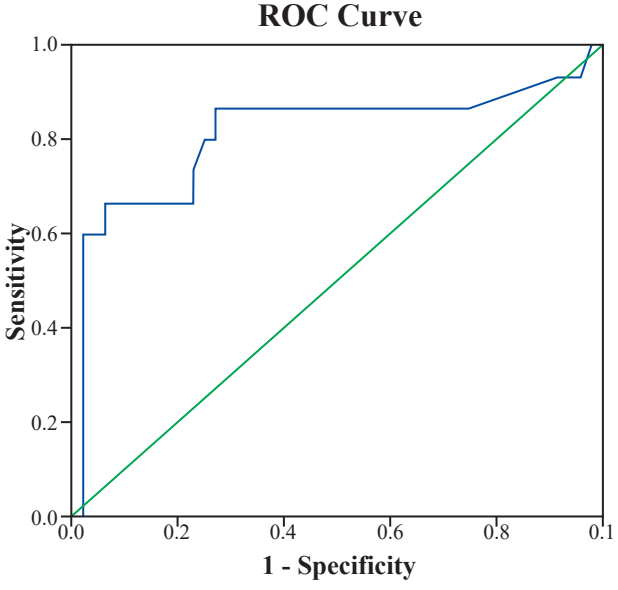


Figure 4: ROC analysis showing RDW (%) level in prediction of poor ICU outcome (N=63)

ROC analysis found highly significant cut-off value of RDW (%) ≥14 in the prediction of poor outcome of ICU patients with sensitivity (80%), specificity (75%), positive predictive value (50%), negative predictive value (92.3%), and overall accuracy (76.2%) (fig 4). A cut off value of RDW (%) ≥14 in the prediction of poor outcome of ICU patients showed sensitivity, specificity, positive predictive value, negative predictive value and accuracy was 80%, 75%, 50%, 92.3% and 76.2% accordingly (fig 5). Significant difference was found between dead and survived patients regarding RDW (%) Day 4 and Day 7. In survived group RDW (%) significantly decreases from the Day 1 (table V). A significant difference was found between dead and survived group regarding RDW level at Day 4 and Day 7 (table VI).

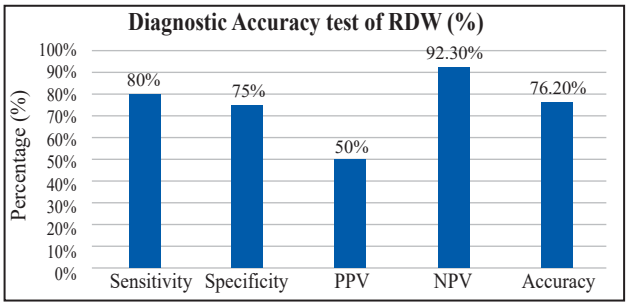


Figure 5: Diagnostic accuracy test of RDW (%) in the prediction of poor outcome of ICU patients (N=63)

Table V: Association of RDW (%) with outcome of the patients (N=63)

RDW (%)	Death Mean±SD	Survival Mean±SD	P value*
Day 1	15.8±1.0	15.5±1.0	0.294
Day 4	16.4±1.7	14.3±1.2$	<0.01
Day 7	16.2±2.5	13.2±1.6$#	<0.01

P value was determined by *Independent sample t test and Repeated measure ANOVA test.

$ denotes significant difference between Day 1 vs Day 4 and Day 7 in survived group.

# denotes significant difference between Day 4 vs Day 7 in survived group.

Table VI: Association of elevated RDW (%) with the outcome (N=63)

RDW (%)	Death n (%)	Survival n (%)	OR (95%CI)	P value*
Day 1				
Elevated	8 (53.3)	22 (45.8)	-	0.416
Normal	7 (46.7)	26 (54.2)		
Day 4				
Elevated	12 (80)	10 (20.8)	15.2(3.6-64.4)	<0.01
Normal	3 (20)	38 (79.2)		
Day 7				
Elevated	10 (66.7)	8 (16.7)	10.0(2.7-37.2)	<0.01
Normal	5 (33.3)	40 (83.3)		

*P value was determined by Chi-square test. Percentage expressed in column.

Discussion

Sepsis is a life-threatening condition resulting from the body's abnormal response to infection, with outcomes ranging from mild illness to fatal organ failure. Early identification of patients at high risk of mortality is crucial for effective management. Although several prognostic markers exist, many are complex and not readily available in resource-limited hospital settings. Therefore, identifying a simple, cost-effective, and reliable predictor is essential to improve outcomes. Previous studies have demonstrated an association between red blood cell distribution width (RDW) and mortality in sepsis.[14-15] The present study aimed to evaluate whether dynamic changes in RDW could predict mortality among patients with sepsis and septic shock admitted to the intensive care unit of a tertiary care hospital in Bangladesh.

In this study, the ICU mortality rate was 23.8%, which closely aligns with the findings of Kim et al[16] who reported a mortality rate of 24.6%. Similarly, Foy et al[17] observed a 17.0% mortality rate among sepsis patients, while Ghimire et al[2] reported 27.02% deaths among 148 sepsis cases.

This study showed that advanced age and female predominance were found to be significantly associated with higher mortality ($p < 0.01$). Ghimire et al[2] reported a mean age of 51.29 years, with females being more common (59.5%) than males (40.5%), and mortality significantly higher among older patients ($p < 0.01$). Similarly, Li et al[18] observed that mortality rates were notably greater in elderly and female patients.

An increasing SOFA score was found to be significantly associated with higher mortality, and RDW (%) showed a positive correlation with the SOFA score. Similar associations between elevated RDW and higher SOFA scores were also reported in previous studies.[16,18]

Binary logistic regression identified age, SOFA score, and RDW (%) as significant predictors of mortality among ICU patients with sepsis, but multivariate analysis revealed that only RDW remained an independent predictor. An RDW cut-off ≥14% demonstrated strong prognostic accuracy (AUC = 0.814, 95% CI = 0.658-0.970, $p < 0.01$) with 80% sensitivity and 75% specificity. Elevated RDW reflects anisocytosis caused by inflammation, oxidative stress, and impaired erythropoiesis is common in sepsis which may explain its strong association with mortality.

Supporting evidence shows similar findings: RDW alone significantly predicted mortality in sepsis with cut-off 15.05% (73% sensitivity, 60% specificity);[2] higher RDW was linked to all-cause mortality[19] and increased hospital deaths when > 14.5%.[18] Ellahony et al[14] reported RDW ≥ 16.35% (AUC = 0.751, $p < 0.01$) as a reliable threshold. Martin et al[15] further confirmed RDW as an independent prognostic factor in sepsis. In Bangladesh, A. Q. Huda et al[20] demonstrated that combining RDW with APACHE II improved predictive accuracy (r = 0.915) versus APACHE II alone. Thus, RDW provides significant prognostic value in predicting mortality among septic and septic shock patients, and when integrated with SOFA scores, it can enhance the accuracy of early outcome prediction in ICU settings.

In this study, elevated RDW (%) on day 4 and day 7 was significantly associated with mortality. This finding aligns with Martin et al[15], who reported significantly higher RDW among non-survivors ($p < 0.003$), and is consistent with previous studies,[16,18] which also found elevated RDW levels in deceased patients compared to survivors.

Some similarities and differences were observed compared to previous studies, which may be attributed to variations in patient selection, clinical condition, and socio-economic factors. However, this study has notable strengths, including the use of more recent data and the application of updated inclusion criteria incorporating the SOFA score based on the latest definition of sepsis an approach seldom adopted in earlier research.

Limitations: This single-center study with a small sample size may limit generalizability. RDW could have been influenced by unmeasured factors like iron, folate, or vitamin B12 deficiency, and survival analysis assumed discharged patients remained alive after ICU discharge.

Conclusion: This study demonstrated that RDW is a valuable predictor of ICU mortality in sepsis and septic shock, with prognostic value beyond SOFA scores. While further research is needed to clarify the underlying mechanisms, these findings support using RDW to help identify critically ill patients at higher risk of death.

Recommendations: RDW should be routinely assessed in ICU patients with sepsis and septic shock to identify high-risk cases. Those with elevated RDW and SOFA scores need closer monitoring. Larger multicenter studies with longer follow-up are recommended.

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