

## Rapid Shallow Breathing Index as a Predictor of Ventilatory Support Necessity in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Mohammed Moustafa Megahed, Tamer Nabil Habib, Eman Dwidar\*

Critical Care Medicine Department, Faculty of Medicine, Alexandria University, Alexandria,  
Egypt

\*Corresponding author e-mail: Emydwidar@hotmail.com

### ABSTRACT

**Introduction:** Patients with chronic obstructive pulmonary disease (COPD) are frequently admitted to intensive care unit because of respiratory failure which often necessitates mechanical ventilation.

**Objectives:** To evaluate the role of rapid shallow breathing index as a predictor of ventilatory support necessity in patients with acute exacerbation of chronic obstructive pulmonary disease.

**Methods:** The study was conducted on 80 patients admitted to Critical Care Medicine Department and Chest Diseases Department, at the Alexandria Main University Hospital with acute exacerbation of COPD. All patients were subjected on admission to complete history taking, complete physical examination and Laboratory investigations. Vital signs and rapid shallow breathing index (ratio determined by respiratory rate divided by spontaneous tidal volume in liters) were measured using ventilator model Neumovent GraphNet on admission and every 30 minutes for 2 hours.

**Results:** The RSBI cutoff value that discriminated best between the need for noninvasive ventilation and invasive mechanical ventilation using the Receiver Operating Characteristic (ROC) was  $> 241$  breath/minute/Liter that yielded a sensitivity of 88.33 % and a specificity of 100 % for determining the need for invasive mechanical ventilation.

**Conclusion:** Rapid Shallow Breathing Index is a good predictor of ventilatory support necessity in patients with acute exacerbation of COPD.

**Keywords:** Rapid shallow breathing index, Ventilatory support, COPD

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## INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and co-morbidities contribute to the overall severity in individual patients. <sup>(1)</sup>

COPD is a leading cause of morbidity and mortality worldwide and results in an economic and social burden that is substantial and increasing <sup>(2,3)</sup>. COPD prevalence, morbidity and mortality vary across countries and across different groups within countries. Often the prevalence of COPD is often directly related to the prevalence of tobacco smoking, although in many countries, outdoor, occupational and indoor pollution are major risk factors. <sup>(4)</sup>

The characteristic symptoms of COPD are chronic and progressive dyspnea, cough and sputum production that can be variable from day to day. <sup>(5,6)</sup> Acute exacerbation of COPD is defined as an acute event characterized by worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in regular medication in a patient with underlying COPD. <sup>(7-9)</sup>

Management of acute exacerbation of COPD (AECOPD) includes conventional treatments (Supplemental oxygen, bronchodilators, corticosteroids and antibiotics) ventilatory support if needed and treating the cause of disease exacerbation.

## AIM OF THE WORK

The aim of the work is to evaluate the role of rapid shallow breathing index as a predictor of ventilatory support necessity in patients with acute exacerbation of chronic obstructive pulmonary disease.

## METHODS

### Participants

This prospective study was conducted on 80 patients admitted to Critical Care Medicine Department and Chest Diseases Department, at the Alexandria Main University Hospital with acute exacerbation of COPD. The study was approved by the medical ethics committee of Alexandria faculty of Medicine. An informed consent from patients' next of kin was taken before enrollment to the study.

### Inclusion criteria

1. Patients of both genders.
2. Patients above 40 years old, as COPD is common after the age of 40.
3. Patients with the diagnosis of AECOPD which is an event in the natural course of the disease characterized by: <sup>(1)</sup>
  - a. Change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations and may warrant a change in regular medication in a patient with underlying COPD. <sup>(7,8)</sup>
  - b. Onset of new physical signs as cyanosis and peripheral edema.
  - c. Failure to respond to initial medical treatment.

### Exclusion criteria

1. Patients with respiratory arrest.
2. Patients with hemodynamic instability.
3. Uncooperative patients.
4. Facial abnormalities.
5. Pregnant females.

All patients were subjected on admission to complete history taking, complete physical examination and Laboratory investigations. During the first two hours of admission the following parameters were monitored every thirty minutes: Vital signs, Glasgow coma score (GCS), arterial blood gases (ABG) and Rapid shallow breathing index (RSBI), a ratio determined by respiratory rate divided by spontaneous tidal volume in liters. Acute Physiology and Chronic Health Evaluation (APACHE II) score was calculated for all patients. Patients were classified into two

groups of requiring non invasive mechanical ventilation (group A) and requiring invasive mechanical ventilation (group B).

### Statistical Analysis<sup>(10)</sup>

Data were analyzed using SPSS software package version 18.0 (SPSS, Chicago, IL, USA). Quantitative data were expressed using range, mean, standard deviation and median while Qualitative data were expressed in frequency and percent. Qualitative data were analyzed using Chi-square test also exact tests such as Fisher exact was applied to compare the two groups. Normally distributed quantitative data were analyzed using student t-test while quantitative data that were not normally distributed was analyzed using Mann Whitney test for comparing the two groups. In addition, ROC was used to determine sensitivity of different variables in predicting mechanical ventilation requirement. p value equal or less than 0.05 was considered significant.

## RESULTS

There were 13 females (26%) and 37 males (74%) in group A, while in group B, there was 10 females (33.3%) and 20 males (66.7%). There was no significant difference between the two groups as regards sex and regarding the age of studied patients, it ranged from 41–72 years with a mean of  $52.30 \pm 7.88$  years in group A, and 45-87 years with a mean of  $61.93 \pm 9.59$  years in group B, showing a significant difference between the two groups.

As regards to the symptoms of acute exacerbation, all patients of group A suffered the four cardinal symptoms except for 12 patients (24%) didn't experience an increase in the purulence of the sputum, while in group B, all patients suffered the four cardinal symptoms except for 6 patients (20%) didn't experience an increase in the purulence of the sputum. There was no significant difference between the two groups as regards symptoms of exacerbation of COPD.

As regards to the precipitating factors of AECOPD, most patients were precipitated by chest infection except for 10 patients (20%) in group A and 5 patients (16.7%) in group B where the precipitating factors were smoke inhalation and air pollution.

The mean APACHE II score was  $11.68 \pm 2.47$  in group A, while the mean in group B was  $25.03 \pm 4.35$ . There was a significant difference between the two groups as regards the APACHE II score. APACHE II score was significantly higher in group B (Table 1).

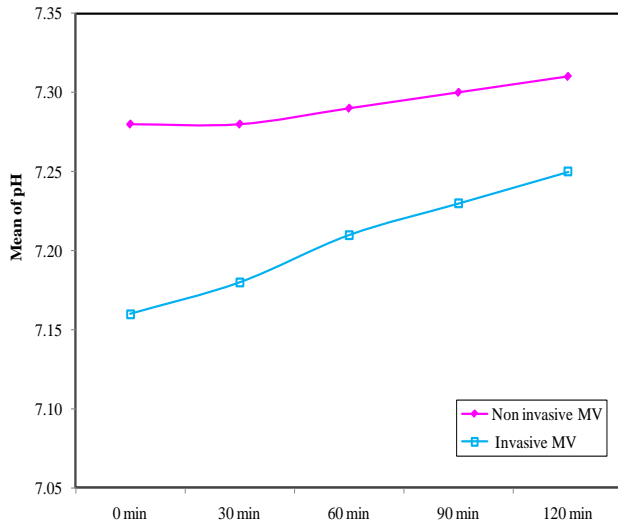
**Table (1): Comparison between two studied groups according to APACHE II score**

	Non invasive MV (n = 50)	Invasive MV (n = 30)	t	p
<b>APACHE II score</b>				
Min. – Max.	7.0 – 20.0	18.0 – 39.0		
Mean $\pm$ SD.	$11.68 \pm 2.47$	$25.03 \pm 4.35$	17.538*	<0.001*
Median	11.0	25.0		

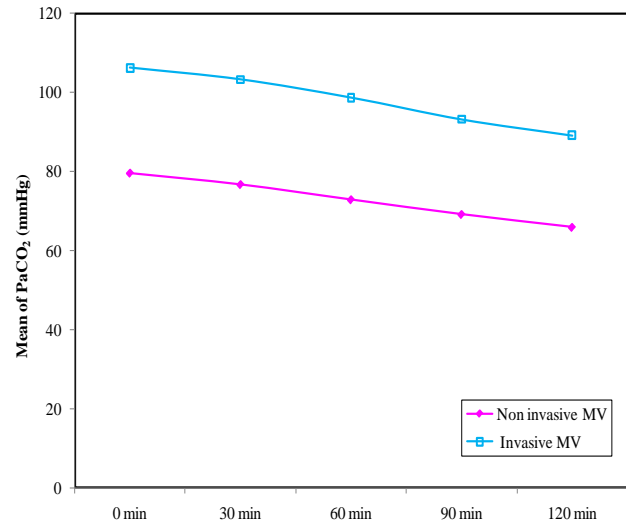
t: Student t-test    \*: Statistically significant at  $p \leq 0.05$     MV: Mechanical ventilation

As regards vital signs measured in the five stages (on admission and every 30 minutes for 2 hours), heart rate on admission and respiratory rate in each stage were significantly higher in the group requiring invasive mechanical ventilation. When comparing respiratory rate values at 30, 60, 90 and 120 minutes with respiratory rate on admission, they showed a statistically significant difference in both groups and when comparing the repeated measures of heart rate with admission, only values at 90 and 120 minutes showed a statistically significant difference in group A, and values at 60, 90 and 120 minutes showed a statistically significant difference in group B.

As regards admission ABG, the mean pH was  $7.28 \pm 0.02$  in group A, while it was  $7.16 \pm 0.09$  in group B (Figure 1 & 2). Findings of ABG in patients requiring NIV were considerably better than group B. There was only a significant difference between the two groups regarding pH and arterial carbon dioxide tension ( $\text{PaCO}_2$ ). When comparing pH and  $\text{PaCO}_2$  values at 30, 60, 90 and 120 minutes with pH and  $\text{PaCO}_2$  on admission, they showed a statistically significant difference in both groups.



**Figure (1): Comparison between the two studied groups according to pH.**



**Figure (2): Comparison between the two studied groups according to PaCO<sub>2</sub>.**

GCS assessment in the five stages, it was significantly better in group requiring noninvasive mechanical ventilation. When comparing GCS at 30, 60, 90 and 120 minutes with GCS on admission, it showed a statistically significant difference in both groups.

As regards to the routine laboratory investigations for the two groups, there were no significant difference between the two groups as regard hematocrit, white blood count (WBC), sodium, potassium, creatinine, blood urea nitrogen (BUN), C reactive protein (CRP) and D-dimer. There was only a significant difference between the two groups regarding platelets.

As regard tidal volume (Table 2) and minute volume measured in the five stages, we found a significant difference between the two groups, it was worse in group requiring invasive mechanical ventilation.

Table (2): Comparison between two studied groups according to tidal volume

Tidal Volume (liter)	0 min	30 min	60 min	90 min	120 min
<b>Non invasive MV(n=50)</b>					
Min. – Max.	0.12 – 0.24	0.12 – 0.24	0.12 – 0.26	0.13 – 0.26	0.15 – 0.27
Mean ± SD.	0.17 ± 0.03	0.18 ± 0.03	0.19 ± 0.03	0.20 ± 0.03	0.21 ± 0.03
Median	0.16	0.17	0.19	0.20	0.22
<b>p<sub>1</sub></b>		<0.001*	<0.001*	<0.001*	<0.001*
<b>Invasive MV (n=30)</b>					
Min. – Max.	0.08 – 0.20	0.09 – 0.22	0.09 – 0.22	0.10 – 0.24	0.10 – 0.26
Mean ± SD.	0.15 ± 0.03	0.13 ± 0.04	0.14 ± 0.04	0.15 ± 0.04	0.16 ± 0.05
Median	0.12	0.12	0.13	0.14	0.15
<b>p<sub>1</sub></b>		<0.001*	<0.001*	<0.001*	<0.001*
<b>t</b>	6.531*	6.179*	6.419*	6.157*	5.721*
<b>p</b>	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

t: Student t-test    p<sub>1</sub>: Stands for (adjusted Bonferroni) p-value for ANOVA with repeated measures for comparison between 0min with each other period    \*: Statistically significant at p ≤ 0.05    MV: Mechanical ventilation

As regards RSBI measured in the five stages, there was a significant difference between the two groups. RSBI was higher in group B and when comparing RSBI values at 30, 60, 90 and 120 minutes with RSBI on admission, they showed a statistically significant difference in both groups. The mean RSBI on admission was  $189.42 \pm 29.83$  in group A, while the mean was  $356.63 \pm 118.49$  in group B (Table 3). The RSBI cutoff value that discriminated best between the need for NIV and the need for invasive mechanical ventilation was  $> 241$  breath/minute/Liter that yielded a sensitivity of 88.33 % and a specificity of 100 % for determining the need for invasive mechanical ventilation with 100 % positive predictive value and 90.9 % negative predictive value (Figure 3).

Table (3): Comparison between two studied groups according to rapid shallow breathing index

RSBI (Breath/minute/Liter)	0 min	30 min	60 min	90 min	120 min
<b>Non invasive MV(n=50)</b>					
Min. – Max.	130.0 – 241.0	115.0 – 233.0	106.0 – 291.0	92.0 – 170.0	88.0 – 151.0
Mean ± SD.	189.42 ± 29.83	168.86 ± 27.90	144.25 ± 28.83	125.06 ± 17.16	115.16 ± 13.39
Median	187.50	166.0	141.50	124.0	109.0
<b>p<sub>1</sub></b>		<0.001*	<0.001*	<0.001*	<0.001*
<b>Invasive MV (n=30)</b>					
Min. – Max.	157.0 – 687.0	138.0 – 555.0	130.0 – 500.0	125.0 – 450.0	107.0 – 346.0
Mean ± SD.	356.63 ± 118.49	303.47 ± 106.49	258.30 ± 96.86	228.93 ± 85.40	146.79 ± 58.46
Median	342.50	303.0	244.50	210.0	116.0
<b>p<sub>1</sub></b>		<0.001*	<0.001*	<0.001*	<0.001*
<b>t</b>	7.587*	6.785*	6.284*	6.583*	6.875*
<b>p</b>	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

t: Student t-test    p<sub>1</sub>: Stands for (adjusted Bonferroni) p-value for ANOVA with repeated measures for comparison between 0min with each other period    \*: Statistically significant at p ≤ 0.05    MV: Mechanical ventilation  
 RSBI: rapid shallow breathing index

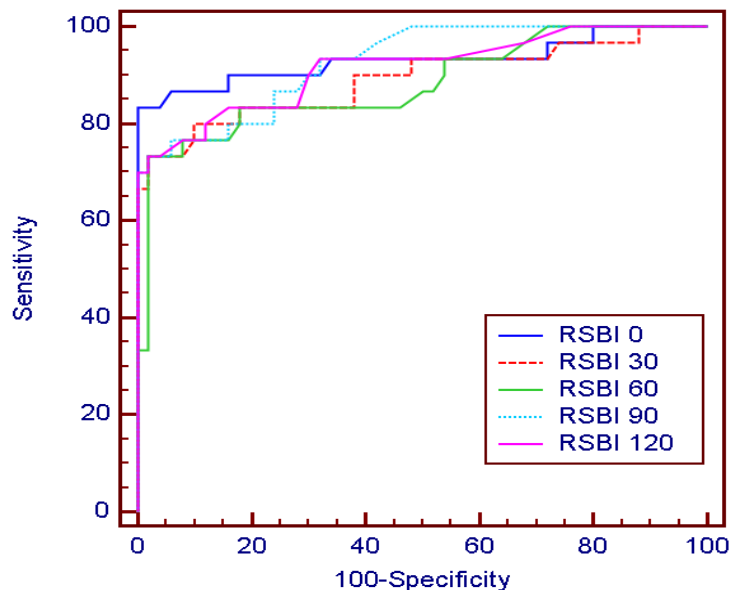


Figure (3): ROC curve for Rapid Shallow Breathing Index.



In non invasively ventilated group, total intensive care unit (ICU) stay days ranged from 2-11 days with a mean of  $4 \pm 1.77$  days, while in invasively ventilated group, total ICU stay days ranged from 3-15 days with a mean of  $7.17 \pm 2.97$  days, revealing 3.17 days difference in favor of non invasively ventilated group. Total days of mechanical ventilation in group A ranged from 1-8 days with a mean of  $2.36 \pm 1.32$  days while in group B, they ranged from 2-15 days with a mean of  $5.33 \pm 3.18$  days, revealing 2.97 days difference in favor of group A. Among group A, there was no deaths while in group B, there were 4 deaths (13.3 %). There was a significant difference between the two groups as regards outcome measures. Complications of mechanical ventilation were significantly higher in group requiring invasive mechanical ventilation as regards atelectrauma, ventilator associated pneumonia (VAP) and barotrauma, 13 patients (43.3 %), 21 patients (70 %) and 5 patients (16.7 %), respectively while only one patient was complicated with barotrauma in group A. As regards complications of bed ridden; deep vein thrombosis (DVT) and bed sore; only a significant difference was noted as regards bed sore complication between the two groups, 10 patients (33.3 %) in group B and 5 patients (10 %) in group A. Only one patient (2 %) was complicated with DVT in group A while 3 patients (10 %) were complicated with DVT in group B.

## DISCUSSION

Evidence justifying the role of RSBI in mechanically ventilated patients is yet to be fully demonstrated, although RSBI has been tested in many situations such as weaning of mechanically ventilated patients, postcardiac surgery patients and acute respiratory failure. In addition, it was compared with many predictive indices.

To determine indications of mechanical ventilation, different criteria have been stated most of them necessitate ABG analysis for definite indication of mechanical ventilation requirement. <sup>(11)</sup> Very few studies has been carried out to eliminate invasive interventions for determining ventilatory needs including Crawford's study <sup>(12)</sup> in which different parameters have been studied such as: RSBI, pH, Lactate, minute volume ( $\dot{V}_E$ ), Carbon Dioxide production ( $VCO_2$ ), End-Tidal  $CO_2$  ( $ETCO_2$ ) and APACHE II criterion.

In the current study using the Receiver Operating Characteristic (ROC), the RSBI on admission evaluated sensitivity ratio was 83.33 % and specificity value was 100 %. In the

subsequent four stages, the evaluated sensitivity ratios were 73.33 % and specificity values were 98 %. Cutoff points in the five stages were more than 241, 223, 188, 164 and 147, respectively was associated with high sensitivity and specificity for determining the need for invasive ventilation. RSBI more than 241 was associated with the highest sensitivity and specificity for determining the need for invasive ventilation. RSBI less than or equal to 241, 223, 188, 164 and 147, respectively was associated with high sensitivity and specificity for determining the need for non invasive ventilation (NIV). RSBI less than or equal to 241 was associated with the highest sensitivity and specificity for determining the need for non invasive ventilation.

In agreement with our study as regards predictive ability of RSBI for necessity of mechanical ventilation, Hassan Soleimanpour et al. <sup>(13)</sup> tested the hypothesis that RSBI could predict necessity of non invasive ventilation in chronic obstructive pulmonary disease exacerbation. The study was conducted on 98 patients. Patients were divided into two groups of requiring non-invasive ventilation (group I) and not requiring non-invasive ventilation (group II). Using Logistic Regression statistical tests to evaluate the predictive value of RSBI variable for non-invasive ventilation necessity revealed that RSBI prior to treatment, an hour and two hours subsequent to treatment, in addition to possessing high diagnostic sensitivity in patients requiring NIV, has also a significant predictive ability on admission in patients requiring NIV. As at each measured stage, evaluated sensitivity ratios were 94.8 %, 92.8 % , 97.7 % and specificity values were 94.8 %, 92.8 % and 97.7 %, respectively and values for cutoff point were more or equal to 110, 105 and 107, respectively.

In a similar study, Crawford et al. <sup>(12)</sup> conducted a blinded, observational cohort trial. The threshold value for RSBI that discriminated best between no NIV and the need for NIV was determined in 61 patients. Thirty-five patients who did not require ventilatory support had a mean RSBI of 105, and 26 patients with NIV had a mean RSBI of 222. A receiver-operating-characteristic curve was constructed, a RSBI > 120 yielded a sensitivity of 0.81 and a specificity of 0.74 for determining the need for NIV. Authors concluded that a RSBI of 120 or greater may be a predictor of when NIV support should be considered.

In the study, the mean APACHE II score was  $11.68 \pm 2.47$  in group A, while the mean APACHE score in group B was  $25.03 \pm 4.35$ . APACHE score was higher in group requiring invasive mechanical ventilation. There was a significant difference between the two groups ( $p < 0.001$ ).

The Putinati study<sup>(14)</sup> was conducted on a group of 59 COPD patients admitted with acute respiratory failure (ARF) and a high APACHE II score. High APACHE II score was predictive of failure of NIV and the need for intubation, a result in accordance with Confalonieri et al.<sup>(15)</sup> and Lin et al.<sup>(16)</sup>. However, in the study of Lin<sup>(16)</sup>, RSBI failed to be considered as a good predicting factor of successful NIV intervention in patients with acute ARF. With similar results, Youshida et al.<sup>(17)</sup>, observed that patients in need of intubation had significantly higher APACHE II scores and lower arterial pH, as APACHE II score higher than 17 and respiratory rate above 25 breath per minute after receiving NIV for an hour were introduced as independent determinants of requiring intubation.

In our study we found a significant difference in admission level of acidosis and hypercapnia between patients enrolled in the study and also a significant difference was noted after initiation of mechanical ventilation either with NIV or invasive mechanical ventilation. The mean pH was  $7.28 \pm 0.02$  in non invasively ventilated group, while it was  $7.16 \pm 0.09$  in invasively ventilated group. Mechanical ventilation was effective to improve pH and  $PCO_2$  level.

In Putinati et al. study<sup>(14)</sup>, they found a significant difference in admission level of acidosis and hypercapnia between patients successfully ventilated with NIV and those who failed with NIV. NIV was effective in reducing  $PaCO_2$  levels and improving pH in both groups of patients, a result in accordance with the findings of Brochard, Meduri, Ambrosino and Wysocki.<sup>(18-21)</sup>

In our study, total days of ICU stay and total days of mechanical ventilation were much lower in NIV group. The hospital stay and total days of mechanical ventilation were significantly shortened by noninvasive ventilation and these findings can be explained by absence of sedation and shorter weaning time, a result in accordance with the findings of previous studies by Brochard and Fernandez.<sup>(22,23)</sup>

We found that mortality was significantly reduced with the use of noninvasive ventilation. This approach, as compared with invasive mechanical ventilation, was associated with fewer complications, many of which are specifically linked with invasive mechanical ventilation and are believed to have an effect on mortality. Among group B, 21 patients (70%) were complicated by ventilator associated pneumonia (VAP). Among group A, there was no deaths while in group B, there were 4 cases (13.3%). The organisms isolated by minibal cultures for those 4 cases were *pseudomonas aeruginosa* (3 cases) and *acinetobacter baumannii* (1 case).

In a large randomized controlled trial by Brochard <sup>(18)</sup> comparing NIV with a standard ICU approach where endotracheal intubation was performed after failure of medical treatment, the use of NIV was shown to reduce complications, length of stay in the ICU, and mortality. The in-hospital mortality, however, was also significantly reduced by NIV from 20% to 10% according to the study by Plant and colleagues. <sup>(24)</sup>

In a study performed by Bott and coworkers <sup>(25)</sup>, a reduction in mortality was suggested when treatment with NIV was compared with medical treatment alone, but only a few patients received endotracheal intubation after failure of the medical treatment.

In contrast to our study, Vitacca <sup>(26)</sup> compared between patients treated with NIV and invasive mechanical ventilation. NIV has shown a reduction in intubation rate, but no difference in hospital mortality, a result in accordance with findings of Martin et al. <sup>(27)</sup>

According to Fagon et al., Stevens et al. and Bryan et al. <sup>(28-30)</sup> Pneumonia due to pseudomonas or acinetobacter species is usually associated with a high mortality rate; this rate is frequently > 70% and is significantly higher than those among patients with pneumonia due to other microorganisms.

## CONCLUSION

Rapid Shallow Breathing Index is a good predictor of ventilatory support necessity in patients with acute exacerbation of COPD.

## STATEMENT OF INTEREST

No conflict of interest.

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