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Correlation of Inferior Vena Cava Distensibility Index and Pulse Pressure Variation in Prediction of Fluid Responsiveness in Mechanically Ventilated Hypotensive Patients

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ORIGINAL ARTICLE

Correlation of Inferior Vena Cava Distensibility Index and Pulse Pressure Variation in Prediction of Fluid Responsiveness in Mechanically Ventilated Hypotensive Patients

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Abstract

Background: **Shocked patients require careful monitoring of intravascular volume and treatment with intravenous fluids. In the intensive care unit (ICU), patients with acute circulatory insufficiency typically benefit from fluid resuscitation.**

Objectives: **To compare the sensitivity of the pulse pressure variation (PPV) and the distensibility index of the Inferior Vena Cava (dIVC) for predicting fluid responsiveness in very ill patients who suffered shock.**

Patients and methods: **This was an interventional, cross-sectional study, that evaluated mechanically ventilated ICU patients, presented with clinical signs of shock. The study was carried out at Al-Azhar Azhar University Hospitals and conducted on 100 individuals.**

Results: **The dIVC and the PPV values fluctuated between 0.17 and 1.0 and 0.13−0.42 respectively. Using a cutoff of greater than 19.7 %, dIVC was 65.6 % sensitive, 72.4 % specific, had an AUC of 0.734, and was statistically highly significant ($P < 0.001$). PPV's sensitivity was 45.1 %, specificity was 68.5 %, AUC was 0.642, and significant ($P = 0.018$) at a threshold value of greater than 14 %.**

Conclusion: **It is important to be cautious when employing either PPV or dIVC as predictors of fluid response in shocked patients. Diagnostic performance was higher with dIVC than with PPV.**

Keywords: Cardiac output (CO), Distensibility index of the inferior vena cava, Fluid bolus (FB), Fluid resuscitation, Pulse pressure variation (PPV)

1. Introduction

In the (ICU), patients with acute circulatory insufficiency typically benefit immediately from fluid resuscitation as the first line of treatment.[1] Unfortunately, interstitial, systemic, and pulmonary edema ensues from excessive fluid treatment, which in turn reduces oxygen transport to tissues and causes hypoxia.[2,3] However, nearly half of intensive care unit patients are deemed to be fluid-responsive.[4,5] As a result, enhancing our ability to predict fluid response is urgently needed to avoid the negative clinical consequences associated with overuse of fluid therapy.[6,7]

Michard et al. showed that pulse pressure variation (PPV) is a far better predictor of fluid responsiveness than heart-filling pressure.[8] These days, PPV from an arterial cannula is typically automatically calculated and shown by hemodynamic monitors.[9]

The dIVC has been validated as a noninvasive, accurate predictor of preload response in septic cases undergoing mechanical ventilation.[10]

Therefore, this study aimed to compare the sensitivity of the PPV and the distensibility index of

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the Inferior Vena Cava (dIVC) for predicting fluid responsiveness in advance of fluid delivery in very ill patients who suffered shock.

2. Patients and methods

This was a multi-center, nonblinded, interventional, cross-sectional study performed at hospitals affiliated with Al-Azhar University in Cairo, Egypt. From August 2022 to June 2023, one hundred patients were enrolled in the research after their families gave their consent and the Research and Ethics Committee gave their stamp of approval to the endeavor. Patients between the ages of 18 and 60 who needed mechanical ventilation in the ICU and showed markers of shock (hypotension with or without evidence of hypoperfusion, such as oliguria less than 0.5 ml/kg/h and arterial lactate >2.5 mmol/l) were included in the trial. Patients were not eligible if they were spontaneously breathing, their tidal volume was less than 8 ml/kg, they had pulmonary edema, acute cardiogenic shock, and volume overload. Patients with severe valvular heart disease or arrhythmia especially atrial fibrillation or frequent ectopics, had a history of active bleeding, and individuals who have had surgery around the IVC were also excluded.

2.1. Study protocol

The baseline parameters of the chosen patients were recorded, including their age, sex, height, weight, BMI, APACHE II score, and ASA class, as well as the results of a general physical examination. SBP, DBP, and MBP, heart rate (HR), central venous pressure (CVP), and oxygen saturation (SPO_2) were measured as baseline hemodynamic variables. Intravenous titration of fentanyl starting at 0.3 mcg/kg and midazolam starting at 0.01−0.05 mg/kg were used to sedate patients during the study only.[11] Tidal volumes were set at 8 ml/kg of predicted body weight, and peak airway pressure was kept below 30 cm H_2O during volume-controlled ventilation provided by mechanical means. Atracurium, at a dose of 0.5 mg/kg, was administered as a muscle relaxant to abolish any spontaneous breathing. All of the following were regarded to be clinically significant signs of hypotension: systolic blood pressure (SBP) lower than 90 mmHg, mean arterial pressure (MAP) lower than 65 mmHg, or a drop in SBP of 20 mmHg from baseline with or without inotropes that was identified for at least 5 min. Ultrasound (UMT-200/China) with a convex probe (Mindray M5, 5−20 MHz) was utilized to measure the dIVC at baseline. M-mode was used to assess the IVC's diameter in a subcostal longitudinal segment (Fig. 1). The dIVC was determined after just one round of breathing. Distensibility index of the inferior vena cava (IVC)=(maximum diameter on inspiration − minimum diameter on expiration)/minimum diameter on expiration).[12]

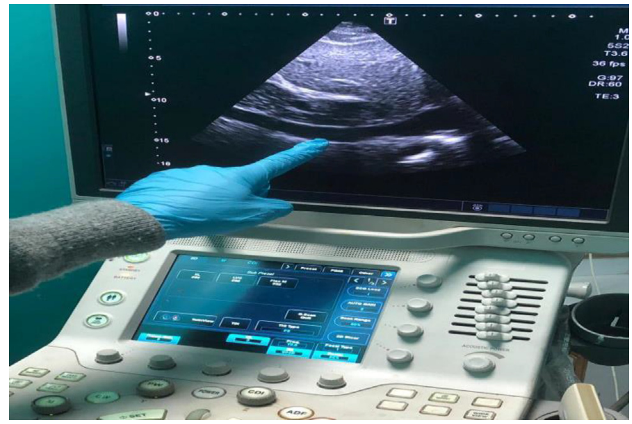

Fig. 1. Distensibility index of the Inferior Vena Cava measurement using (TTE) subcostal longitudinal view. TTE: transthoracic echocardiography

Fig. 2 shows the PPV images being presented on nihon kohden monitors connected to an artery catheter. PPV is defined as the relative variation between the highest pulse pressure (PPmax) and lowest pulse pressure (PPmin) divided by the mean of PPmax and PPmin.[13]

2.2. Cardiac output measurement[14,15]

Using transthoracic echocardiography (ACUSON X300 Ultrasound System, Premium Edition, Siemens Healthcare, Mountain View), we were able to determine the left ventricular outflow tract velocity-time integral (LVOT VTI) as well as the LVOT area (Fig. 3).

$$SV = LVOT\ CSA \times LVOT\ VTI,$$

Fig. 2. Pulse pressure variation monitoring on Nihon kohden monitor.

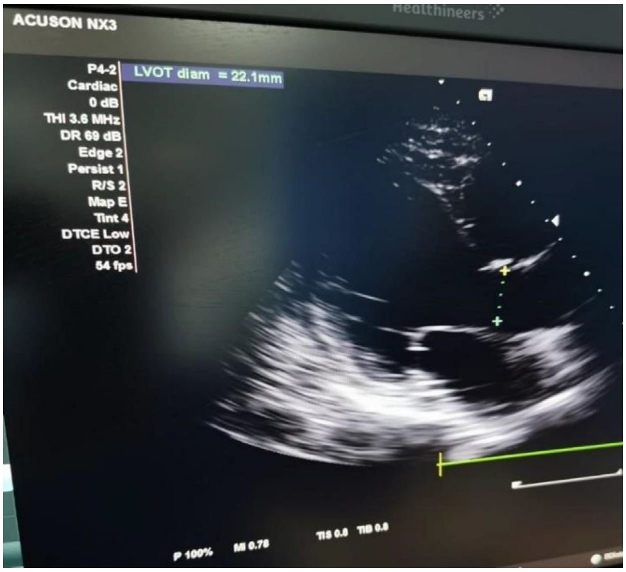

Fig. 3. Left ventricular outflow tract diameter measurement in parasternal long axis view (TTE). TTE: transthoracic echocardiography

LVOT VTI was measured in PW Doppler mode at the LVOT in an apical 5-chamber view.

LVOT CSA = 0.78 x $(\text{diameter})^2$ CO=SV × HR. Then, the cardiac index (CI) was calculated using CO, and body surface area (BSA) according to the following formula: Cl=CO/BSA ($l/min/m^2$). Patients were given a fluid challenge of 7 ml/kg Ringer's solution over 10 min.[16,17] Baseline (before fluid challenge) readings of dIVC and PPV were correlated clinically with the response to fluid challenge.

2.3. Statistical analysis

For tabulation and statistical analysis, we fed the data into Microsoft Excel 2016, SPSS 26.0, and MedCalC (19.1). For numerical parametric data, we determined the mean, standard deviation, minimum, and maximum; for numerical non-normally distributed data, we determined the median and interquartile range; and for numerical categorical data, we determined the number and percentage. For inferential analyses of quantitative variables, we employed the independent samples *t*-test where data from the two groups followed a normal distribution, and the Mann–Whitney *U* test when they did not. The ideal cutoff value for detection sensitivity and specificity was identified using receiver operating characteristic (ROC) curve analysis, and the overall efficiency of the parameter was calculated. Inferential analysis of qualitative data was performed using the χ^2 test for independent groups. A *P*-value of less trhan or equal to 0.05 was considered statistically significant, whereas anything above 0.05 was disregarded. The *P*-value of a study estimates the probability that its findings resulted from chance alone.

3. Results

Tables 1 and 2.

According to their fluid responsiveness, the patients in the research were split into two groups.[18]

(1) Responders group: 71 (71 %) patients who had ≥15 % rise in CO and
(2) Nonresponders group: 29 (29 %) patients who had less than 15 % increase in cardiac output[18] (Fig. 4).

The results of the CO measurements taken by each group are compared in Table 3. There was no statistically significant difference in CSA, VTI, CO, or CI among FB responders and nonresponders either before or after the intervention. In the responders group, there was a statistically significant rise of VTI, CO, and CI after FB compared with their values before FB ($P < 0.001$). In nonresponders group, there was a statistically significant rise of VTI, CO and CI after FB compared with their values before FB ($P < 0.001$).

Table 4 shows that maximum IVC diameter (D.max) showed statistically significant increase in nonresponders group compared with responders group before FB ($P < 0.001$) while there was significant decrease in nonresponders group matched to responders group after FB ($P = 0.003$), minimum IVC diameter (D.min) showed statistically significant increase in nonresponders group matched to responders group before FB ($P < 0.001$) while there was significant decrease in nonresponders group matched to responders group after FB ($P = 0.005$), IVC distensibility index (dIVC) showed statistically

Table 1. Distribution of studied patients regarding vital signs and hemodynamics.

Vital signs	Studied patients ($N = 100$)			
	Mean ± SD	Median	Minimum	Maximum
Hemodynamics				
Heart Rate (beats/min.)	77.80 ± 12.18	78.0	45.0	100.0
Systolic BP (mm/Hg)	85.04 ± 2.56	85.0	79.0	90.0
Diastolic BP (mm/Hg)	47.85 ± 6.73	46.0	35.0	81.0
MAP	59.00 ± 4.88	57.9	49.1	82.2
SpO_2 (%)	92.87 ± 3.03	93.0	81.0	99.0
CVP	10.38 ± 2.53	10.0	6.0	16.0
lactate	3.03 ± 1.39	3.0	1.0	8.0
PH	7.31 ± 0.05	7.31	7.19	7.41

Table 2. Vital sign and hemodynamic comparisons between the two groups.

	Responders group (No. = 71)			Non-responders group (No. = 29)			Mann-Whitney U test	
	Mean ± SD	Median	Range	Mean ± SD	Median	Range	Test value ($^{Z}_{MWU}$)	*P*-value
Heart Rate (beats/min.)	77.50 ± 12.35	78.00	45.00–100.00	78.55 ± 11.93	76.0	49.0–100.0	0.038	0.970
Systolic BP (mm/Hg)	84.92 ± 2.56	85.0	80.0–90.0	85.34 ± 2.58	85.0	79.0–90.0	0.746-	0.456
Diastolic BP (mm/Hg)	47.32 ± 7.09	45.0	35.0–81.0	49.14 ± 5.63	50.0	40.0–60.0	1.797	0.072
MAP	58.60 ± 5.16	56.8	49.1–82.2	60.00 ± 4.05	60.2	53.5–69.0	1.922	0.055
SpO_2 (%)	92.66 ± 3.20	93.0	81.0–98.0	93.38 ± 2.56	94.0	88.0–99.0	0.872	0.383
CVP	10.83 ± 2.47	10.4	6.0–16.0	9.28 ± 2.36	9.0	6.0–15.0	3.147	0.002
Lactate	3.14 ± 1.50	3.0	1.0–8.0	2.75 ± 1.03	2.5	1.4–6.0	1.271	0.204
PH	7.30 ± 0.05	7.30	7.19–7.41	7.32 ± 0.03	7.31	7.25–7.39	1.993	0.046

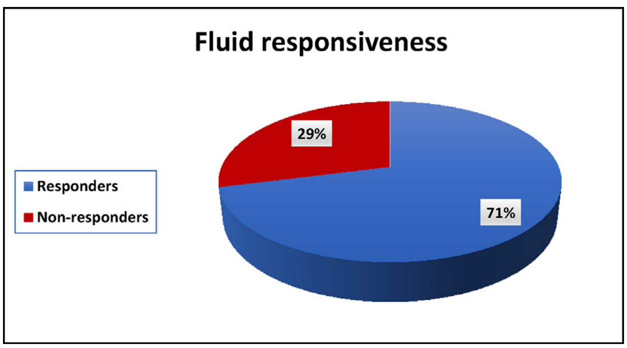

Fig. 4. Fluid responsiveness among the studied cases.

significant decline in nonresponders group compared with responders group before and after FB (*P* < 0.001, *P* < 0.001, respectively), In responders group, there was statistically significant increase of D.max and D.min after FB compared with their values before FB (*P* < 0.001) while there was statistically significant decrease of dIVC after FB compared with their values before FB (*P* < 0.001). Also in nonresponders group, there was a statistically significant rise in D.max and D.min after FB compared with their values before FB (*P* < 0.001) while there was statistically significant decrease of dIVC after FB compared with their values before FB (*P* < 0.001).

Table 5 shows comparison among the studied groups according PPV measurements. PPV before FB showed statistically significant decrease in non-responders group matched to responders group (*P* = 0.026) while no significant difference between them after FB (*P* > 0.05), In responders group, there was statistically significant decrease of PPV after FB compared with its value before FB (*P* < 0.001). In nonresponders group, there was statistically significant decrease of PPV after FB compared to its value before FB (*P* < 0.001).

Receiver operating characteristic (ROC) analysis (Table 6 and Fig. 5) was done to determine the value of dIVC, PPV, and CVP in the prediction of fluid responsiveness in mechanically ventilated hypotensive patients. dIVC had 65.6 % sensitivity and 72.4 % specificity at a threshold value of greater than 19.7 % with AUC = 0.734 and was highly significant

Table 3. Comparison between the two studied groups regarding CO measurements before and after FB.

CO measurements	Responders group (No. = 71) Mean ± SD	Nonresponders group (No. = 29) Mean ± SD	Test value	*P*-value (between groups)
CSA (cm)^2				
Before FB	3.18 ± 0.10	3.20 ± 0.11	0.874#	0.382
After FB	3.18 ± 0.10	3.20 ± 0.11	0.874#	0.382
P-value (Before Vs after FB)	1.00	1.00		
VTI (cm)				
Before FB	16.14 ± 0.83	16.29 ± 1.24	0.705*	0.482
After FB	18.75 ± 1.63	18.16 ± 1.14	1.777*	0.079
P-value (before Vs after FB)	**<0.001**	**<0.001**		
CO (L/m)				
Before FB	4.05 ± 0.63	3.82 ± 0.69	1.611*	0.110
After FB	4.61 ± 0.79	4.44 ± 0.76	0.979*	0.330
P-value (Before Vs after FB)	**<0.001**	**0.002**		
CI (L/min/m^2)				
Before FB	2.08 ± 0.30	1.93 ± 0.41	1.941*	0.052
After FB	2.43 ± 0.54	2.28 ± 0.36	1.374*	0.173
P-value (Before Vs after FB)	**<0.001**	**0.001**		

Table 4. Measurements of distensibility index of the Inferior Vena Cava (dIVC) before and after FB were compared between the two groups.

dIVC measurements	Responders group (No. = 71) Mean ± SD	Nonresponders group (No. = 29) Mean ± SD	Mann-Whitney *U* test	
			Test value	*P*-value
D.max				
Before FB	2.04 ± 0.13	2.16 ± 0.16	3.626	**<0.001**
After FB	2.21 ± 0.18	2.11 ± 0.14	2.923	**0.003**
P-value (before Vs. after FB)	**<0.001**	**<0.001**		
D.min				
Before FB	1.24 ± 0.17	1.41 ± 0.19	4.473	**<0.001**
After FB	1.58 ± 0.17	1.50 ± 0.10	2.778	**0.005**
P-value (before Vs. after FB)	**<0.001**	**<0.001**		
IVC distensibility index (%)				
Before FB	57.21 ± 18.22	28.98 ± 6.05	6.264	**<0.001**
After FB	34.80 ± 9.86	12.70 ± 4.33	8.954	**<0.001**
P-value (before Vs after FB)	**<0.001**	**<0.001**		

Table 5. Measurements of (pulse pressure variation) before and after FB were compared between the two groups.

PPV	Responders group (No. = 71)	Nonresponders group (No. = 29)	Mann-Whitney *U* test	
			Test value	*P*-value
Before FB				
Mean ± SD	26.74 ± 5.11	24.55 ± 3.96	2.228	**0.026**
Median	25.0	24.0		
Range	19.0—42.0	20.0—40.0		
After FB				
Mean ± SD	17.29 ± 2.85	17.86 ± 2.50	1.294	0.196
Median	16.0	17.0		
Range	1325.0—10.0	15.0—24.0		
P-value (before Vs after FB)	**<0.001**	**<0.001**		

Table 6. Validity (area under the curve, sensitivity, specificity) for distensibility index of the Inferior Vena Cava, pulse pressure variation and central venous pressure in prediction of fluid responsiveness in mechanically ventilated hypotensive cases.

	Best cut off	Sensitivity	Specificity	PPV	NPV	AUC	*P*-value
dIVC after FB	19.7 %	65.6 %	72.4 %	70.4 %	67.8 %	0.734	**<0.001**
PPV after FB	14	45.1 %	79.3 %	68.5 %	59.1 %	0.642	**0.018**
CVP	9	74.6 %	69 %	70.6 %	73.1 %	0.700	**0.001**

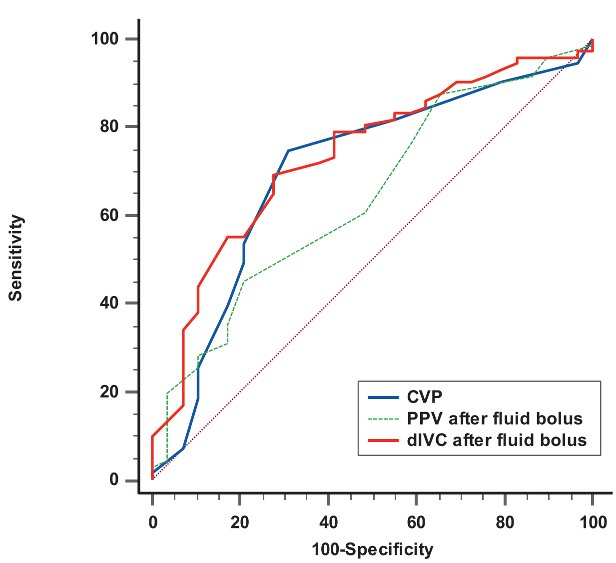

Fig. 5. A comparison of the receiver operating characteristic curves for the three approaches for predicting fluid responsiveness.

($P < 0.001$). PPV had a 45.1 % sensitivity and 68.5 % specificity at a threshold value of greater than 14 % with AUC = 0.642 and was significant ($P = 0.018$). CVP at a threshold value less than or equal to 9 mmHg had 74.6 % sensitivity and 69 % specificity, with AUC = 0.700, and was highly significant ($P = 0.001$).

4. Discussion

Comparable with the current study, El-Ghonimy et al., revealed that the response rate was 67 %.[19] Also, Kaur et al., showed that out of 67 cases, 67.2 % responded to fluid challenge.[18] However, Abdelfattah et al., showed that 21 (55.3 %) patients were fluid responder.[20] Also, Aboelnile et al., revealed that the response rate was 54.4 %.[21] While, de Oliveira et al., revealed that the response rate was 45 %.[22]

Consistent with this study, Abdelfattah et al., showed that the fluid administration resulted in significant increase in cardiac output and VTI compared to baseline in both responder and nonresponder groups, also there was no significant difference among responder and nonresponder groups at baseline and post treatment cardiac output and VTI.[19] Ait-Hamou et al., as well as de Oliveira et al., revealed that the fluid administration resulted in significant increase in VTI compared to baseline in responder but in the nonresponder this increase was nonsignificant. Also, there was no significant difference among responder and nonresponder groups at baseline and post treatment VTI.[20,23]

Regarding baseline dIVC measurements in both groups before and after FB, Abdelfattah and colleagues and de Oliveira et al., revealed that the fluid administration resulted in a significant reduction in dIVC compared to baseline in responder but in nonresponder this reduction was nonsignificant.[19,20] However, Kaur and colleagues revealed that the fluid administration resulted in improvement in dIVC, Dmax and Dmin compared with baseline but the change was statistically nonsignificant, the disagreement may be because of the difference in sample size and patients' severity. The study also showed that the basal and post dIVC was significantly higher in in the responder group.[18]

Regarding the PPV measurement before and after FB between the studied groups, Abdelfattah et al., and de Oliveira et al., revealed that the fluid administration resulted in significant reduction in PPV compared to baseline in responder but in nonresponder this reduction was nonsignificant.[19,20]

Our findings are in line with those of Aboelnile et al., who discovered that the dIVC accurately predicted fluid responsiveness with a sensitivity of 79.17 % and a specificity of 80 % at a threshold value of greater than 19.42 %. All of these findings were highly significant ($P < 0.0001$) and gave an AUC of 0.886 (0.801−0.944).[18]

On the other hand, Abdelfattah et al., indicated that a best cutoff of 10.5 (sensitivity: 76.2 %; specificity: 70.6 %) on the PPV area under the receiver operating characteristic (AUROC) curve provided a value of 78 ± 0.08. This value was derived from the data.[19]

The dIVC had an area under the receiver operating characteristic curve (AUROC) of 0.75 ± 0.07, and a cutoff value of 16.5 % was determined to be the most accurate in predicting fluid responsiveness (71.43 sensitivities, 76.5 % specificities). In addition, de Oliveira et al. found that the area under the ROC curve for dIVC was 0.84 (95 % confidence interval [CI]: 0.63−1.0), and that the ideal cut-off value for dIVC was 16 % (sensitivity: 67 % and specificity: 100 %). The best cutoff was 12.4 %, with a sensitivity of 89 % and a specificity of 100 %. The area under the ROC curve for PPV was 0.92 (95 % confidence interval [CI]: 0.76−1.0).[20]

Long et al. carried out an extensive study and meta-analysis, and they came to the conclusion that the pooled results of dIVC in patients who were receiving mechanical ventilation had an AUC of 0.79, with a sensitivity of 67 % and a specificity of 68 %. These findings are inconsistent with those that we obtained.[24]

4.1. Conclusion

These dynamic metrics, such as PPV and dIVC, have been shown to have a high positive connection with the response to fluid treatment, and this can be utilized to direct fluid therapy according to predefined cutoff boundaries. Both approaches pose minimal risk to the patient and may be done right at the bedside. It is important to utilize PPV and dIVC with caution in the context of the clinical condition together with other hemodynamic indicators, rather than as an objective for directing fluid management, in mechanically ventilated shocked patients since they are only modest predictors of fluid responsiveness. The diagnostic performance of dIVC was greater than that of PPV.

Disclosure

The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.

Authorship

All authors have a substantial contribution to the article.

Conflicts of interest

We have nothing to declare regarding conflict of interest.

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