

Clinical and echocardiographic findings of patients with suspected acute pulmonary thromboembolism who underwent computed tomography pulmonary angiography

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Background: The aim of the study was to determine the correlation between clinical and echocardiographic findings and risk factors of patients with suspected acute pulmonary thromboembolism (PTE) who underwent computed tomography pulmonary angiography (CTPA). **Materials and Methods:** In this cross-sectional study, 310 hospitalized patients aged >18 years with high clinical suspicion of PTE referred to imaging center of our hospital from different wards for CTPA were enrolled. The frequency of different clinical presentations, risk factors, items of Wells' criteria, and echocardiographic findings was compared in patients with and without PTE, which have been diagnosed according to the CTPA results. **Results:** PTE was diagnosed in 53 (17.1%) of patients with suspected PTE. From clinical manifestations, tachypnea, pleuritic chest pain, and edema of lower extremities were significantly more frequent among patients with PTE ($P < 0.05$). Major surgery was the risk factor which was significantly more prevalent among patients with PTE ($P < 0.05$). Frequency of all criteria of Wells' criteria, except hemoptysis, was significantly higher in patients with PTE ($P < 0.05$). The frequency of all studied echocardiographic variables was significantly higher in patients with PTE ($P < 0.05$). **Conclusion:** It is suggested that we could use the results of this study for utilizing the diagnostic process of PTE in patients with highly clinical suspicion of PTE and providing more validated decision. Using the results of this study, we could identify high-risk patients and made appropriate risk assessment for better management of patients with suspected PTE as well as reduce the rate of unnecessary CTPA and its related adverse consequences.

Key words: Computed tomography pulmonary angiography, echocardiography, pulmonary thromboembolism, risk factor, Wells' criteria

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INTRODUCTION

Pulmonary thromboembolism (PTE) is considered as a common, devastating clinical condition with high rate of substantial morbidity and mortality.^[1] Epidemiological evidence indicated that PTE is the third most common cardiovascular disease after coronary artery disease and stroke.^[2]

Early diagnosis and proper management of the condition have resulted in reduced rate of its related

mortality.^[3] Different prediction scales and radiologic modalities have been proposed in this regard.^[4]

Recent studies have indicated that, currently, computed tomography pulmonary angiography (CTPA) is the modality of choice for diagnosis of PTE. CTPA is a fast, noninvasive, and widely available imaging technique in this field. The findings of a meta-analysis indicated that CTPA has a high sensitivity and specificity for diagnosing of PTE as well as other pulmonary and chest pathologies which could assist clinicians in differential diagnosis also. The proportion of diagnosed PTE to those with suspected PTE underwent CTPA is

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reported to range from 15.4% to 37.4% so that CTPA is used as a screening imaging method for diagnosing and risk prediction of PTE.^[5-7]

CTPA has also some limitations including lower sensitivity in visualization of subsegmental occlusions, interobserver variability in the interpretation of results, exposure to radiation, higher cost, and potentially nephrotoxic risk of contrast drugs.^[8,9]

In addition, some recent studies have indicated that CTPA is likely to be overused which could have significant medical and economic consequences.^[10,11]

Some studies have recommended using CTPA with other prediction models or other diagnostic tests for classification of highly clinically suspected patients with PTE. Although the results of mentioned studies vary according to the prediction models and methods of study, overall they support the effectiveness of using such models. Some of these studies also predict the risk of mortality in this group of patients.^[12-14]

Given the reports related to overuse of CTPA and its related side effects, it is suggested that combination use of imaging and clinical findings as well as evaluation of patients' risk factors would be more helpful for proper risk stratification for early diagnosis and treatment of PTE. Hence, the aim of this study was to determine the correlation between CTPA findings with risk factors and clinical and echocardiography findings of patients referred from different wards of our hospital with suspected acute PTE. However, our findings could provide us baseline information for rapid risk stratification in patients with suspected PTE.

MATERIALS AND METHODS

In this cross-sectional study, 310 hospitalized patients aged 18 years or older with high clinical suspicion of PTE referred to the imaging center of Al Zahra Hospital from different wards for CTPA were enrolled.

The study was conducted from September 2014 to July 2015.

The Institutional Review Board of the School of Medicine, Isfahan University of Medical Sciences, and Regional Ethics Committee approved the protocol of this study. Patients with low-quality images of CTPA were excluded from the study.

Written informed consent was obtained from all selected patients.

Using a questionnaire, the demographic characteristics (age, sex), the ward from which the patients were referred for PTE evaluation, clinical presentations (including dyspnea, tachypnea, angina, pleuritic chest pain, edema of lower extremities, cardiogenic shock, tachycardia, and syncope), results of physical examination, Wells' score, risk factors (major surgery, trauma, cord injury, respiratory distress, heart failure, renal failure, chemotherapy, oral contraceptive use), and history of cancer of the selected patients were recorded by a trained personnel according to the medical file of the patients.

Echocardiography of all participants was done by a cardiologist and findings were recorded.

Wells' score of each patient was determined based on registered information of each patient by a physician, and the patients were categorized to those high (likely) clinical probability (score >6), intermediate (2-6), low (unlikely) clinical probability (score <2) of PTE.

After data collection, the results of CTPA were verified by an expert radiologist in this field; based on CTPA results, patients with and without PTE were determined.

The frequency of different clinical presentations, risk factors, items of Wells' criteria, and echocardiographic findings was compared in patients with and without PTE which diagnosed according to the CTPA results.

Imaging method and evaluation

CTPA in selected patients was performed in supine position and craniocaudal direction during suspended inspiration. The images were performed from the lung apices to the level of the diaphragm.

For contrast enhancement, first intravenous (IV) injection of 10 ml iodinated contrast medium (SCANLUX; iopamidol, 370 mg/50 ml) at a rate of 4 ml/s was down via an IV cannula (18-gauge) into the antecubital vein (as test bolus) while density of main pulmonary artery was reached to 200 HU and residue of contrast (40 ml) was injected at the same rate. Immediately after that, 20 ml normal saline was also injected with a similar rate.^[15]

The scans were performed using a 64-MDCT scanner (LightSpeed, VCT 2007, GE Healthcare, USA).

The images were reconstructed in the axial plane in 1-mm intervals.

For a 64-slice imaging, the following protocol was used; 100-120 kVP, pitch 1.4, rotation time 0.4 s, detector width of 32 mm × 0.6 mm.

Statistical analysis

Data of participants (including demographic state, risk factors, findings of CTPA, and echocardiography) in two groups of patients (with and without PTE), based on CTPA results, were analyzed using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Quantitative (mean [standard deviation (SD)]) and qualitative (n [%]) compared in the two groups using t -test and Chi-square or Fisher's exact tests, respectively. $P < 0.05$ was considered statistically significant.

RESULTS

In this study, 310 (166 [53%] male and 144 [46%] female) patients with suspected PTE from different wards of the hospital were studied. Mean (SD) age of studied population was 56.78 (18.20) years. According to the CTPA results, PTE was diagnosed in 53 (17.1%) of patients.

From patients with diagnosed PTE, 23 (43.4%) had right main pulmonary artery PTE (with extension to lobar branches), 19 (35.8%) had left main pulmonary artery PTE (with involvement of lobar branches), and 11 (20.8%) had thromboemboli of segmental/lobar pulmonary branches.

Quality of images was considered excellent if circular region of interest within the pulmonary trunk was at a threshold of 200 HU, and quality of images was considered good if subjectively well opacification of pulmonary arteries was seen; hence, quality of images was excellent and good in 118 (38.1%) and 192 (61.9%) of patients, respectively.

Poor-quality images (including images with motion artifacts and poor-opacified pulmonary arteries) were excluded from the study.

According to the Wells' criteria, 211 (68.1%) and 99 (31.9%) were moderate and high risk for PTE.

Demographic and clinical findings of studied population with and without PTE are presented in Table 1. Mean age of patients with PTE was higher than those without ($P = 0.03$). From clinical manifestations, tachypnea (odds ratio [OR] = 2.7, confidence interval [CI] = 1.48–4.96), pleuritic chest pain (OR = 2.02, CI = 1.06–3.8), and edema of lower extremities (OR = 2.00, CI = 1.10–3.6) were significantly more frequent among patients with PTE than those without ($P < 0.05$).

Frequency of risk factors and items of Wells' criteria in studied groups is presented in Table 2. Major surgery was the risk factor which was significantly more prevalent among patients with PTE (OR = 2.3, CI = 1.25–4.2). Frequency of all items of Wells' criteria, except hemoptysis, was significantly higher in patients with PTE than those without ($P < 0.05$).

The findings of CTPA and echocardiographic variables in patients with and without PTE are presented in Table 3. The frequency of all studied echocardiographic variables was significantly higher in patients with PTE than those without ($P < 0.05$). Among the CTPA findings, wedge-shaped density was significantly higher in patients with PTE than those without (OR = 8.8, CI = 3.7–20.6).

Proportion of patients with PTE, based on CTPA results, from those who referred with suspected PTE from different wards of the hospital is presented in Figure 1.

The highest number of referrals was from emergency unit, pulmonary unit, surgery unit, Intensive Care Unit (ICU), and

Table 1: Demographic and clinical findings and risk factors of studied population with and without pulmonary thromboembolism

| Variables | Patients with PTE, $n=53$ | Patients without PTE, $n=257$ | Total patients with suspected PTE | P |
|----------------------------|---------------------------|-------------------------------|-----------------------------------|-------|
| Demographic | | | | |
| Age (years) | 61.7 (17.6) | 55.9 (18.2) | 56.78 (18.20) | 0.03 |
| Sex (%) | | | | |
| Male | 30 (56.6) | 136 (47.1) | 166 (53.54) | 0.74 |
| Female | 23 (43.4) | 121 (52.9) | 144 (46.46) | |
| Clinical presentations (%) | | | | |
| Dyspnea | 42 (79.24) | 203 (78.68) | 245 (79.3) | 0.97 |
| Tachypnea | 28 (52.83) | 75 (29.18) | 103 (33.22) | 0.001 |
| Angina | 7 (13.2) | 30 (11.67) | 37 (11.93) | 0.75 |
| Pleuritic chest pain | 18 (33.96) | 52 (20.23) | 70 (22.58) | 0.03 |
| Edema of lower extremities | 28 (52.83) | 92 (35.7) | 120 (38.70) | 0.02 |
| Cardiogenic shock | 1 (1.9) | 5 (1.9) | 6 (1.93) | 0.98 |
| Tachycardia | 11 (20.75) | 49 (19.1) | 60 (19.35) | 0.07 |
| Syncope | 0 | 2 (0.77) | 2 (0.63) | 0.99 |

PTE=Pulmonary thromboembolism

Table 2: Frequency of pulmonary thromboembolism risk factors and items of Wells' criteria in patients with and without pulmonary thromboembolism

| Variables | Patients with PTE, n=53 (%) | Patients without PTE, n=257 (%) | Total patients with suspected PTE, n=330 (%) | P |
|---|-----------------------------|---------------------------------|--|--------|
| Risk factors | | | | |
| Major surgery | 34 (64.15) | 112 (43.6) | 146 (47.1) | 0.006 |
| Trauma | 12 (22.64) | 59 (22.95) | 71 (22.90) | 0.96 |
| Cord injury | 1 (1.9) | 6 (2.33) | 7 (2.25) | 0.84 |
| Respiratory distress | 19 (35.84) | 61 (23.73) | 80 (25.80) | 0.08 |
| Heart failure | 9 (16.98) | 35 (13.6) | 44 (14.19) | 0.52 |
| Renal failure | 0 | 15 (5.83) | 15 (4.83) | 0.05 |
| Chemotherapy | 1 (1.9) | 4 (1.55) | 5 (1.61) | 0.86 |
| Oral contraceptive use | 3 (5.66) | 15 (5.83) | 18 (5.80) | 0.96 |
| History of cancer | 7 (13.2) | 27 (10.50) | 34 (10.96) | 0.57 |
| Wells' criteria | | | | |
| Clinical signs of PE | 42 (79.3) | 146 (56.80) | 188 (60.64) | 0.002 |
| Heart rate >100 beats/min | 4 (7.54) | 5 (1.94) | 9 (2.90) | 0.03 |
| History of surgery or immobilization within 4 weeks | 46 (86.79) | 166 (64.6) | 212 (68.38) | 0.002 |
| History of previous DVT or PE | 16 (30.18) | 22 (8.56) | 38 (12.25) | <0.001 |
| Active malignancy | 10 (18.86) | 25 (9.7) | 35 (11.29) | 0.03 |
| Hemoptysis | 0 | 3 (1.2) | 3 (0.96) | 0.56 |
| Alternative diagnosis less likely than PE | 40 (75.47) | 54 (21.01) | 94 (30.32) | <0.001 |

PTE=Pulmonary thromboembolism; DVT=Deep vein thrombosis, PE=Pulmonary embolism

Table 3: Echocardiographic and pulmonary computed tomography angiography findings in patients with and without pulmonary emboli

| Variables | Patients with PTE, n=53 (%) | Patients without PTE, n=257 (%) | P | OR (CI 95%) |
|---|-----------------------------|---------------------------------|--------|------------------|
| Echocardiographic findings | | | | |
| Right ventricle hypokinesia | 27 (50.94) | 32 (82.45) | <0.001 | 7.30 (3.79-14) |
| Right ventricle dilatation | 24 (45.28) | 40 (15.56) | <0.001 | 4.49 (2.3-8.4) |
| Pardoxical movement of ventricular septum | 15 (28.30) | 15 (5.83) | <0.001 | 6.3 (2.8-14) |
| Pulmonary hypertension | 33 (62.26) | 77 (29.96) | <0.001 | 3.85 (2.08-7.1) |
| McConnell sign | 3 (5.76) | 0 | 0.05 | 6.14 (4.7-7.9) |
| End diastolic diameter of right ventricle/left ventricle >0.6 | 18 (33.96) | 22 (8.56) | <0.001 | 5.49 (2.68-11.2) |
| CTPA findings | | | | |
| Pleural effusion | 17 (32.1) | 89 (34.63) | 0.72 | 0.89 (0.47-1.6) |
| Atelectasia | 17 (32.1) | 106 (41.28) | 0.21 | 0.67 (0.35-1.2) |
| Wedge-shaped density | 15 (28.3) | 11 (4.28) | <0.001 | 8.8 (3.7-20.6) |
| Ground glass opacity | 14 (26.41) | 67 (26.7) | 0.96 | 1.01 (0.52-1.9) |
| Linear opacity | 1 (1.9) | 12 (4.66) | 0.31 | 0.39 (0.5-3.08) |
| Consolidation | 10 (18.9) | 51 (19.84) | 0.87 | 0.93 (0.44-1.9) |

PTE=Pulmonary thromboembolism; CTPA=Computed tomography pulmonary angiography; OR=Odds ratio; CI=Confidence interval

obstetrics departments, in order. The proportion of positive PTE was higher in surgery (51.9%) and orthopedics (40%) wards. The rate of negative CTPA results was higher in ENT (100%) and obstetrics (96.2%) wards.

DISCUSSION

In this study, we have investigated the relation between CTPA findings and echocardiographic and clinical findings

as well as risk factors of patients with suspected PTE referred to our radiologic center. Our findings indicated that all echocardiographic variables, all items of Wells' criteria, clinical presentations such as tachypnea, pleuritic chest pain, and edema of lower extremities, risk factors such as major surgery and wedge-shaped density in CTPA are the most frequent variables which are related to the occurrence of PTE. The proportion of normal CTPA from those who referred from different wards of the hospital with clinical

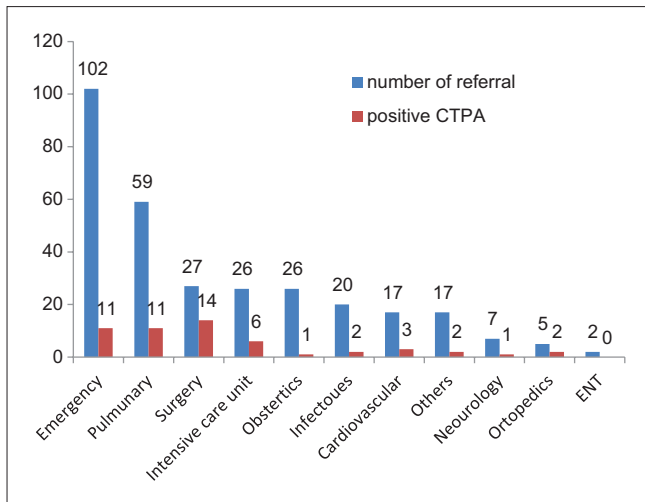


Figure 1: The number of referral and proportion of patients with positive computed tomography pulmonary angiography findings for pulmonary thromboembolism from those who referred from different wards of the hospital with high clinical suspicion of pulmonary thromboembolism

suspicion of PTE was higher in patients referred from ENT and obstetrics wards.

As mentioned, in spite of higher advantages of CTPA in the diagnosis of acute PTE, its overuse and some limitations regarding its side effects, high costs, and low sensitivity in diagnosing subsegmental clots limit its use.^[8-10]

Results of epidemiological studies indicated that though using CTPA results in increased incidence of PTE, most of the reported cases of PTE are less fetal form of PTE which has less clinical importance. These cases had not significant change in PTE-related mortality rate. Schissler *et al.* in the USA have indicated that CTPA utilization increased the rate of PTE with less severe disease form.^[16]

Some studies recommended combination use of both imaging and clinical assessment tools such as Wells' criteria for better diagnosis and management of PTE so that some recent studies developed pretest prediction models for identifying patients with low predictive risk of PTE and avoiding invasive imaging methods.^[12,13]

In the current study, we aimed to determine the association between clinical and imaging findings and related risk factors in occurrence of PTE diagnosed by CTPA. In addition, we determined the proportion of diagnosed PTE from those with suspected sign and symptoms of PTE referred for CTPA evaluation from different wards of our hospital.

In this study, the proportion rate of diagnosed PTE in patients with suspected PTE who referred for CTPA evaluation was 17.1%. The rate was similar to that reported

in previous researches. Moores *et al.* have reported that 15%–37% of patients with suspected PTE have PTE after evaluating by CTPA.^[6]

Sodhi *et al.* in India studied 50 patients with suspected PTE by CTPA, other imaging methods, and clinical and laboratory findings. They showed that 30 (60%) patients had PTE and CTPA was positive in the 29 cases of PTE. They concluded that CTPA has high sensitivity and specificity for diagnosis of PTE. In addition, it could be helpful in diagnosing other alternative clinical conditions.^[17]

In a recent study in Tehran, Iran, Molaee *et al.* evaluated patients with high clinical suspicion of PTE by CTPA, Wells' criteria, and D-dimer level. They showed that 62.2% of the patients had PTE.^[18] It seems that differences in patients' selection and diagnostic tools could explain the differences.

In this study, the higher number of referrals was from emergency unit, pulmonary unit, surgery unit, ICU, and obstetrics departments, in order. The highest rate for positive CTPA was recorded for surgery and orthopedics, and the lowest was recorded for ENT and obstetrics wards.

In a study in Turkey, Salanci *et al.* have shown that most of the inpatients referrals for CTPA were from the Internal Medicine and Surgery Departments.^[19]

In another study in New Zealand, the higher rate of CTPA referral for evaluating PTE was from emergency, general medicine, general surgery, and orthopedics, respectively. In their evaluation, 14% had positive CTPA findings for PTE.^[20]

The most important findings of our study were that although the number of referral from obstetrics and emergency departments was high, the proportion of positive CTPA was low (3.8% in obstetrics and 10.8% for emergency departments). These findings indicated that the diagnostic approach of PTE should be rereviewed in our center, especially for the mentioned two departments.

The results of a recent study in Ireland have indicated that 5% of referred pregnant women with suspicious PTE had positive CTPA findings for it.^[21] Recent studies demonstrated that using of CTPA for diagnosis of PTE in pregnant women has low yield in accordance with higher dose of radiation which could be harmful for the mothers' health, especially for breast cancer.^[22]

From demographic factors, patients with PTE were significantly older than those without. Advanced age is considered as one of the risk factors of pulmonary embolism (PE) and our results were similar to other reports.^[23,24] Results of different studies regarding sex

differences in this field were not similar.^[23,24] In this study, there was not any significant difference in sex distribution of PTE occurrence.

The most frequent clinical presentation in patients with PTE than those without was tachypnea, pleuritic chest pain, and edema of lower extremities in our study. Several studies have investigated the most frequent symptoms of PTE, which could have predictive role in its diagnosis and prognosis. The results have great variability in different studies.^[25,26] Zhang *et al.* in China have demonstrated that the clinical features of PTE are not similar in different age groups.^[27] Most of the studies in this field have reported that dyspnea, tachypnea, and chest pain are the most common clinical presentations.^[25-27]

Surgery was the most important risk factor in patients with PTE in this study, and other risk factors were similar in patients with and without PE. Similar to clinical presentations, available data regarding the most frequent risk factors of PTE have reported different results in different age groups. The most common reported risk factors were malignancy, deep vein thrombosis, and surgery.^[25-27]

In the current study, we demonstrated that patients with PTE had differences in some demographic, clinical and PE related risk factors. Akram *et al.* in the UK have compared the clinical features and radiological findings of patients with and without PTE who evaluated for suspected acute PTE. They did not find any significant difference between the studied groups.^[28]

Wells' Scoring System is considered as a clinical predictive scale for classification of PTE risk in suspicious patients and evidence indicated its reasonable accuracy.^[29] Although its utility has been demonstrated in related studies, interpretation of the Wells' criteria has interobserver variability.^[30] Some studies have also evaluated the utility of the criteria in predicting PTE in association with CTPA. There are some reports which did not support the effectiveness of the score for predicting PTE.^[31,32] Albrizio and Mizzi in Italy have studied the utility of the score in predicting of PE in terms of rate of positive CTPA. After using Wells' score, the rate of positive CTPA was reached to 27%. The rate of positive CTPA before using the score was 24%. They concluded that Wells' score had not significant effect in this regard.^[32] In our experience, we compare the frequency of different items of the score in patients with and without PTE. Our findings indicated that the frequency of all of the items, except hemoptysis, was significantly higher in patients with PTE than those without.

In our study, the presence of wedge-shaped density was significantly higher in patients with diagnosed PTE. There

was not similar study which investigated the correlation, but there evidences that wedge-shaped density has good association with the clinical outcome of PTE.^[33]

It is well established that the prognosis of patients with acute PTE and right ventricular dysfunction (RVD) is poor. Echocardiography is the recommended imaging method for evaluation of RVD and outcome of PTE, especially in hemodynamically unstable patients.^[34,35] George *et al.* have demonstrated that right ventricular (RV) strain in echocardiography could predict PE-related 30-day mortality.^[36] In addition, other studies have indicated the association between CTPA and echocardiographic findings in this group of patients. There is evidence which showed that considering the hemodynamic and clinical condition of the patients with PTE, CTPA, and echocardiography could be used instead of each other. Echocardiography is recommended as noninvasive method for evaluation of hemodynamically stable patients.^[37,38] In this study, the rate of all studied variables of echocardiography was significantly higher in patients with PTE than those without. Most of the related studies in this field mainly evaluated RV dysfunction and end diastolic diameter of right ventricle/left ventricle; whereas in this study, all echocardiography parameters were studied. Our results supported the usefulness of echocardiographic findings in diagnosis of PTE among patients with suspected clinical presentation of PTE.

The limitations of our study were lack of follow-up period for evaluation the association of the studied findings with the outcome of PTE and its related mortality rate. It is due to that our patients selected from different wards of hospital and follow-up of the patients were not favorable enough and we would have large missing data. In addition, it seems that evaluation the level of biochemical factors such as D-dimer, troponin T, N-terminal pro-B-type natriuretic peptide as well as blood gas analysis would be more helpful.^[39]

Our results could be used for better management of patients with suspected PTE and reducing the costs related to the proper diagnosis of PTE.

CONCLUSION

Our findings indicated that the proportion rate of positive CTPA results to those referred with suspicious findings of PTE was low in some of the departments of the hospital, which emphasize on revising our diagnosing protocol for PTE. On the other hand, considering the association of some risk factors and clinical, imaging, and echocardiographic findings with the results of CTPA, it is suggested that we could use the results of this study for utilizing the diagnostic process of PTE in patients with highly clinical

suspicion of PTE and providing more validated decision. Using the results of this study, we could identify high-risk patients and made appropriate risk assessment for better management of patients with suspected PTE as well as reduce the rate of unnecessary CTPA and its related adverse consequences.

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Conflicts of interest

There are no conflicts of interest.

AUTHORS' CONTRIBUTION

All author contributed to concept, design, and all stages of the work. All of them participate in preparing draft of the manuscript and approve its contents.

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