Research Article

Correlation of D-dimer Measurement Values Using Quantum Dots Fluorescence Immunochromatographic Assay and Latex-Enhanced Immunoturbidimetric Assay

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Keywords

D-dimer, fluorescence immunochromatography, latex-enhanced immunoturbidimetric assay

Abstract

Introduction: D-dimer, a fibrin degradation product, is widely used in the diagnosis of thrombotic disorders and in clinical decision-making. Quantum dots (QDs) fluorescence immunochromatography has emerged as a rapid method for detecting protein biomarkers; however, comparative data with the established latex-enhanced immunoturbidimetric assay remain limited.

Methods: A laboratory-based method comparison study was conducted using 80 consecutively collected plasma samples from patients at Dr. Soetomo General Academic Hospital, Surabaya. D-dimer levels were measured using a QDs fluorescence immunochromatography assay (QD-S2000, Vazyme, China) and a latex-enhanced immunoturbidimetric assay (Sysmex CS-2500, Sysmex Corporation, Japan). Correlation and agreement between methods were assessed using Spearman correlation analysis and Bland–Altman plots.

Results: Among the 80 samples (60% female, 40% male), a very strong correlation was observed between the two methods (Spearman $r = 0.951$, $p < 0.001$). Bland–Altman analysis demonstrated good agreement, with most data points falling within the 95% limits of agreement. Although the QDs fluorescence immunochromatography method consistently produced higher absolute D-dimer values, both assays showed comparable trends across the measurement range.

Conclusion: QDs fluorescence immunochromatography and the latex-enhanced immunoturbidimetric assay demonstrated strong correlation and acceptable agreement in D-dimer measurement. Despite yielding higher absolute values, the QDs-based method showed consistent performance, supporting its potential as a reliable and rapid alternative for clinical D-dimer assessment.

Introduction

During the hemostatic process, fibrin clots are formed through activation of the coagulation cascade in response to vascular injury, followed by clot degradation via the fibrinolytic system. D-dimer is a specific degradation product generated when cross-linked fibrin is cleaved by plasmin. Structurally, D-dimer consists of two fibrin D domains covalently linked by factor XIII during clot formation. This unique molecular structure forms a specific epitope that can be recognized by monoclonal antibodies, making D-dimer a useful biomarker for detecting activation of coagulation and fibrinolysis pathways [1–4].

For nearly three decades, D-dimer testing has been widely used in the initial evaluation of suspected venous thromboembolism, including deep vein thrombosis (DVT) and pulmonary embolism (PE), as well as in the assessment of disseminated intravascular coagulation (DIC) [5]. Due to its high analytical sensitivity, D-dimer testing is primarily applied as a rule-out tool in appropriate clinical settings [6,8].

Since the COVID-19 pandemic, the demand for D-dimer testing has increased substantially in many healthcare facilities. At Dr. Soetomo General Academic Hospital, Surabaya, the number of D-dimer examinations rose markedly during 2020–2021, highlighting the growing reliance on laboratory-based coagulation markers in routine clinical practice. This increase underscores the importance of understanding the analytical characteristics and comparability of different D-dimer assay methods.

Various methods are available for D-dimer measurement, including enzyme immunoassays, latex-enhanced immunoturbidimetric assays, and immunochromatographic techniques, which may be performed manually, semi-automatically, or on fully automated platforms. Enzyme-linked immunosorbent assay (ELISA) methods have historically been used as reference procedures in analytical evaluations of D-dimer assays [9]. Latex-enhanced immunoturbidimetric assays are widely implemented in clinical laboratories due to their automation compatibility and suitability for high-throughput testing [6,10]. These assays are based on the agglutination of antibody-coated particles, producing increased turbidity proportional to the D-dimer concentration, which is measured photometrically [6,8,11].

As a rapid and cost-effective alternative, immunochromatographic or lateral flow immunoassays (LFIA) have been developed [12,13]. Conventional LFIA methods, however, may suffer from limited signal intensity, particularly when using organic fluorescent dyes that are prone to photobleaching [12]. To address these limitations, quantum dot (QD)-based labeling technologies have been introduced. Quantum dots are semiconductor nanocrystals with favorable optical properties, including high fluorescence intensity, resistance to photobleaching, tunable emission spectra, and high absorption coefficients [14–16].

The Vazyme QD-S2000 is an automated immunoassay analyzer that applies quantum dots fluorescence immunochromatography for quantitative D-dimer measurement. This system employs a double-antibody sandwich principle, in which D-dimer in the sample binds to a quantum dot–conjugated anti–D-dimer antibody and is subsequently captured by an immobilized monoclonal antibody on a nitrocellulose membrane. The emitted fluorescence signal is then detected and quantified by the instrument [14,17].

The aim of this study was to evaluate the analytical agreement between D-dimer measurements obtained using a latex-enhanced immunoturbidimetric assay on the Sysmex CS-2500 analyzer and a quantum dots fluorescence immunochromatographic assay using the Vazyme QD-S2000 system.

Materials and methods

Study Population and Sampling

The study population comprised inpatients and outpatients at Dr. Soetomo General Academic Hospital, Surabaya, who underwent D-dimer testing between September and November 2022. Clinical suspicion was defined as physician-indicated testing based on symptoms suggestive of thromboembolic events, such as unexplained dyspnea, chest pain, or limb swelling. Risk factors included conditions associated with coagulation abnormalities, such as age >60 years, prolonged immobility, active malignancy, recent surgery, pregnancy, or prior venous thromboembolism.

Inclusion criteria consisted of patients for whom D-dimer testing was clinically indicated, with venous blood collected into 3 mL sodium citrate tubes and processed within 8 hours. Only plasma samples without visible hemolysis, icterus, or lipemia were included. Samples that did not meet these criteria were excluded. A consecutive sampling strategy was applied, enrolling all eligible specimens obtained during the study period. The source population included patients attending both inpatient and outpatient services at Dr. Soetomo General Academic Hospital.

The sample size was considered adequate for a preliminary method comparison study and is consistent with the Clinical and Laboratory Standards Institute (CLSI) EP09-A3 guideline, which recommends the use of 40–100 patient samples for method comparison and bias estimation.

Sample Collection and Handling

Venous blood samples (3 mL) were collected into sodium citrate tubes (BD Vacutainer®, Becton Dickinson, Franklin Lakes, NJ, USA) using standard aseptic technique, in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines for specimen collection and handling (CLSI GP41-A7). Samples were gently inverted immediately after collection to ensure proper anticoagulant mixing.

Citrate plasma was obtained by centrifugation at 3000 rpm for 10 minutes at room temperature within 2 hours of sample collection. Plasma aliquots were transferred into polypropylene cryovials and stored at - 80 °C until analysis.

Samples were stored for a maximum of three months before testing. Although repeated freeze–thaw cycles were avoided, minimal unavoidable freeze–thaw exposure related to sample handling cannot be entirely excluded and is acknowledged as a potential source of analytical variability.

Laboratory Methods

Plasma D-dimer concentrations were measured using two analytical platforms: a Quantum Dots Fluorescence Immunochromatography assay (Vazyme QD-S2000, Nanjing Vazyme Medical Technology Co., Ltd., China; QD-D-Dimer Kit, Cat. No. QD2001-DD) and a Latex-Enhanced Immunoturbidimetric Assay (Sysmex CS-2500, Siemens Healthcare Diagnostics Inc., USA; Innovance® D-dimer, Cat. No. OQGN14). Both assays were performed strictly according to the manufacturers' instructions.

For analytical classification purposes, a D-dimer concentration ≥0.5 mg/L FEU was defined as abnormal and <0.5 mg/L FEU as normal for both platforms. This fixed cut-off was applied to ensure methodological comparability between assays. Although age-adjusted thresholds have been proposed in clinical practice, they were not applied in this analytical comparison study.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA), and a two-sided p-value <0.05 was considered statistically significant. The Kolmogorov–Smirnov test was applied to assess the normality of continuous D-dimer data. Since the values were not normally distributed, comparisons of paired results obtained from the two analytical platforms were conducted using the Wilcoxon signed-rank test, which is appropriate for related nonparametric data. To evaluate the strength and direction of association between the two methods, Spearman's rank correlation coefficient was employed, as it does not assume linearity or normal distribution. Agreement between assays was further explored using the Bland–Altman method, which allows identification of systematic bias across measurement ranges. For categorical comparisons, D-dimer results were classified as normal or abnormal based on the manufacturer-defined cut-off, and concordance was assessed using cross-tabulation and Cohen's kappa coefficient to quantify inter-method agreement beyond chance. Additionally, the Chi-square test was used to examine associations between categorical classifications; Fisher's exact test was substituted where expected frequencies were less than five. This combination of statistical approaches ensured robust evaluation of distribution, correlation, agreement, and categorical associations between the two D-dimer assays.

Laboratory Procedure

All plasma specimens were analyzed using both assay platforms. The Quantum Dots Fluorescence Immunochromatography assay (Vazyme QD-S2000) is based on a double-antibody sandwich immunoassay with quantum dot-conjugated antibodies for fluorescence detection. The Latex-Enhanced Immunoturbidimetric Assay (Sysmex CS-2500) measures photometric changes resulting from antigen-antibody-mediated latex particle agglutination.

Both analyzers were calibrated in accordance with the manufacturer's recommendations before analysis. Internal quality control was performed daily at two concentration levels using manufacturer-provided control materials. Analytical runs were accepted or rejected based on internal quality control performance; no individual patient results were selectively excluded.

All laboratory procedures were conducted in compliance with Clinical and Laboratory Standards Institute (CLSI) guidelines for method comparison and internal quality control (CLSI EP09-A3 and EP15-A3).

This study received ethical approval from the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (Reference No. 0513/KEPK/X/2022), and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants or their legal guardians before sample collection.

Results and discussion

Results

A total of 80 samples were analyzed, including 32 samples from male patients (40%) and 48 from female patients (60%). The mean age of participants was 41 years (range: 1–78 years) (Table 1).

Table 1: Patient Characteristics.

No.	Variable	Count
1	Age (years) Mean (Min-Max)	41 (1-78)
2	Gender Male Female	32 (40%) 48 (60%)

The Kolmogorov–Smirnov test indicated that D-dimer values obtained from both analytical platforms were not normally distributed ($p<0.05$). Therefore, paired comparisons were performed using the Wilcoxon signed-rank test. A statistically significant difference was observed between D-dimer concentrations measured by the two methods ($p < 0.001$), with higher median values obtained using the Vazyme QD-S2000 compared to the Sysmex CS-2500 (Table 2).

Table 2: Comparison of D-dimer levels between Vazyme QD-S2000 and Sysmex CS2500 (Wilcoxon signed-rank test).

	Median (Range) mg/L FEU	p-value
Vazyme QD-S2000	0.72 (0.17–13.94)	<0.001*
Sysmex CS-2500	0.49 (0.08–11.51)	

* $p < 0.001$ (Wilcoxon signed-rank test), significantly different p-value < 0.05

Table 2 summarizes the comparison of D-dimer values measured by Vazyme QD-S2000 and Sysmex CS2500. The Wilcoxon signed-rank test revealed a statistically significant difference between the two methods ($p < 0.001$). The median D-dimer level measured with Vazyme (0.72 mg/L FEU) was consistently higher than that measured with Sysmex (0.49 mg/L FEU). The Kolmogorov–Smirnov test yielded a p-value < 0.05 for the overall sample, indicating that D-dimer data from both methods did not follow a normal distribution. Subsequent comparison using the Wilcoxon signed-rank test across all samples and subgroups yielded a p-value < 0.001, confirming a significant difference between D-dimer values obtained from Vazyme and Sysmex.

Figure 1: Correlation of D-Dimer levels using Quantum Dots immunofluorescence chromatography and turbidimetric immunoassay (Spearman r = 0.951, $p<0.05$).

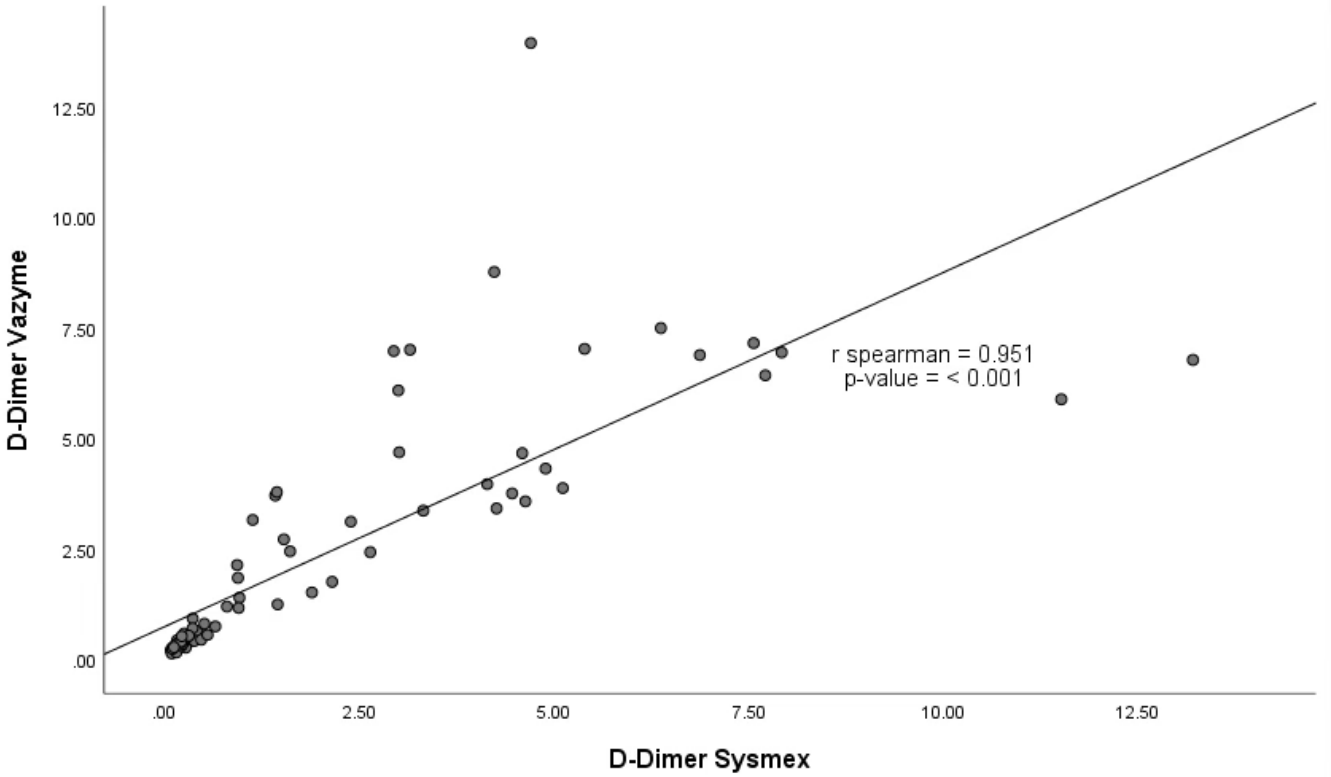
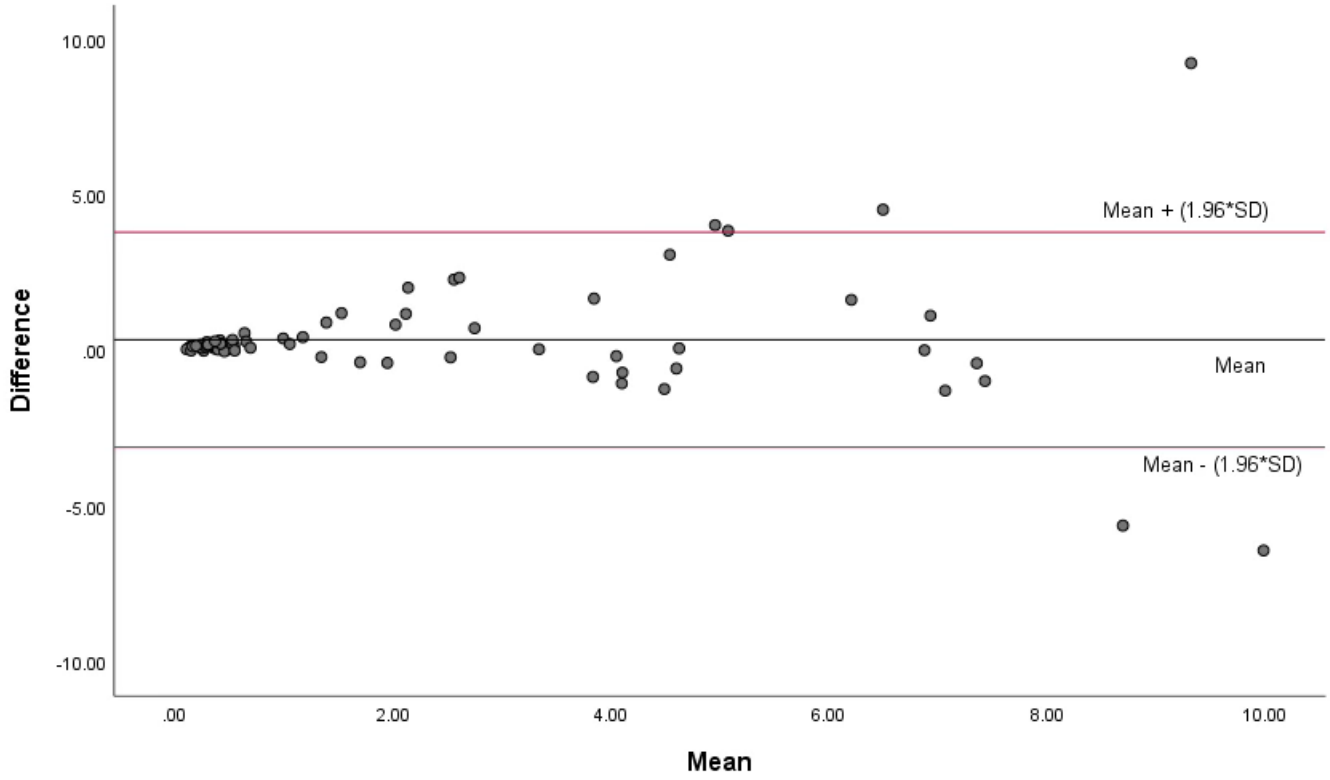


Figure 2: Bland-Altman Plot comparing Quantum Dots immunofluorescence chromatography and latex immunoturbidimetric assay.



Cross-tabulation analysis confirmed concordance between both instruments (Table 3), with a Kappa coefficient of 0.700 indicating good agreement in classifying results.

Table 3: Cross-tabulation of D-dimer results between Vazyme QD-S2000 and Sysmex CS2500.

D-Dimer Vazyme	D-Dimer Sysmex		Total n (%)
	Normal n (%)	Abnormal n (%)	
Normal	28 (35%)	0 (0%)	28 (35%)
Abnormal	12 (15%)	40 (50%)	52 (65%)
Kappa	0,7		
p-value	< 0.001		

Spearman correlation analysis demonstrated a strong positive association between D-dimer measurements obtained from the two platforms ($r = 0.951$, $p < 0.001$) (Figure 1).

Agreement between the two methods was further assessed using Bland–Altman analysis (Figure 2). The analysis demonstrated a positive mean bias of 2.44 mg/L FEU, indicating that the Vazyme QD-S2000 systematically yielded higher D-dimer values compared to the Sysmex CS-2500. The 95% limits of agreement ranged from –11.53 to 16.40 mg/L FEU, with most data points falling within these limits. Categorical agreement was evaluated by classifying results as normal or abnormal based on a cut-off value of 0.5 mg/L FEU. Cross-tabulation analysis showed concordance between the two methods in 68 of 80 samples (85%). Cohen's kappa coefficient was 0.700 ($p < 0.001$), indicating good categorical agreement (Table 3).

Discussion

This study demonstrated a statistically significant difference in D-dimer concentrations measured by the Vazyme QD-S2000 and Sysmex CS-2500 analyzers, with consistently higher values observed using the quantum dot–based immunochromatographic method. Despite this difference, Spearman correlation analysis showed a strong positive association between the two platforms ($r = 0.951$; $p < 0.001$),

indicating that relative changes in D-dimer levels were preserved across both methods.

Bland - Altman analysis revealed a systematic positive bias of 2.44 mg/L FEU, with relatively wide 95% limits of agreement ranging from –11.53 to 16.40 mg/L FEU. Although most measurements lay within the limits of agreement, the magnitude of dispersion, particularly at higher D-dimer concentrations, suggests that the two methods are not directly interchangeable without method-specific considerations.

Categorical agreement analysis based on a fixed cut-off of 0.5 mg/L FEU yielded a Cohen's kappa coefficient of 0.700, reflecting good agreement beyond chance. Importantly, all discordant results were attributable to samples classified as abnormal by the Vazyme assay but normal by the Sysmex assay. This pattern further supports the presence of a systematic positive bias rather than random misclassification [18–20].

Inter-assay variability in D-dimer measurement has been widely reported and is influenced by both biological and analytical factors. Biological variation includes intra-individual and inter-individual variability, while analytical variation arises from differences in assay design, antibody specificity, reagent composition, calibration traceability, and analytical principles employed by different platforms [6,18]. These factors contribute to the limited comparability of D-dimer results obtained using different immunoassays.

The lack of harmonization among D-dimer assays remains a major challenge in laboratory medicine. Differences in antibody specificity and analytical commutability mean that results generated by one platform cannot be directly extrapolated to another [19,20]. Consequently, D-dimer assays should be interpreted within the context of their respective analytical characteristics, and method-specific validation is required prior to clinical implementation [18-21].

Several limitations of this study should be acknowledged. First, this was a single-center study with a relatively limited sample size, which may restrict the generalizability of the findings to other clinical settings or populations. Second, a reference method such as enzyme-linked immunosorbent assay (ELISA) was not included; therefore, this study focused on inter-method comparison rather than analytical accuracy against a gold standard. Third, although samples were stored under controlled conditions and repeated freeze–thaw cycles were avoided, the potential impact of sample storage duration on D-dimer stability cannot be entirely excluded. Finally, clinical outcomes were not assessed, and thus the implications of inter-assay bias on diagnostic or prognostic decision-making were beyond the scope of this study

Overall, the findings of this study indicate that while the Vazyme QD-S2000 and Sysmex CS-2500 assays demonstrate strong correlation and acceptable categorical agreement, the presence of systematic bias precludes their interchangeable use. Awareness of assay-specific behavior is therefore essential when interpreting D-dimer results, particularly near clinical decision thresholds.

Conclusions

This study demonstrated a statistically significant difference in median D-dimer concentrations between the quantum dots fluorescence immunochromatography assay (Vazyme QD-S2000) and the latex-enhanced immunoturbidimetric assay (Sysmex CS-2500), with the Vazyme platform consistently yielding higher values. Despite this difference, a strong positive correlation was observed between the two methods (Spearman r = 0.951), indicating that relative changes in D-dimer levels were preserved across both analytical platforms.

Categorical analysis based on a fixed cut-off value of 0.5 mg/L FEU showed good agreement, with a Cohen's kappa coefficient of 0.700. However, all discordant classifications were attributable to higher D-dimer values measured by the Vazyme assay, reflecting a systematic positive bias rather than random disagreement.

Bland–Altman analysis further confirmed the presence of systematic bias, indicating that the two methods are not directly interchangeable. The observed mean bias of 2.44 mg/L FEU with wide limits of agreement further supports that these two assays should not be used interchangeably, particularly in samples with markedly elevated D-dimer levels. These findings highlight the importance of method-specific interpretation when comparing D-dimer results obtained from different analytical platforms, particularly near clinical decision thresholds.

In conclusion, while the Vazyme QD-S2000 and Sysmex CS-2500 assays demonstrate strong correlation and acceptable categorical agreement, the observed systematic bias precludes their interchangeable use. Awareness of assay-specific analytical characteristics is therefore essential for accurate interpretation of D-dimer measurements in laboratory practice.

Author contributions

Conceptualization, A.A. and P.B.N.; methodology, F.R.M.; validation, A.A.; formal analysis, A.A.; investigation, A.A. and F.R.M.; writing - original draft preparation, A.A.; writing - review and editing, A.A. and P.B.N.; supervision, P.B.N. All authors have read and agreed to the published version of the manuscript.

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Ethics statement

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (approval number: 0513/KEPK/X/2022).

Conflict of interest

The authors declare no conflict of interest.

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