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PULMONARY MICROTHROMBOSIS IN SEVERE COVID-19: AUTOPSY-BASED STUDY

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Abstract

Pulmonary microthrombosis has emerged as a significant contributor to respiratory failure and mortality in severe COVID-19. This autopsy-based study aimed to characterize the extent, distribution, and clinical associations of pulmonary microthrombi in patients who succumbed to SARS-CoV-2 infection. Autopsies were conducted on 40 deceased COVID-19 patients. Lung tissues were examined histologically and immunohistochemically to identify and quantify microthrombi. Clinical data, including coagulation biomarkers, comorbidities, and anticoagulation therapy, were retrospectively analyzed. Statistical analyses and multivariate logistic regression were performed to explore associations between thrombotic burden and clinical variables. Most of the time, microthrombi formed in the small blood vessels of the lungs and the lower lobes had the most. According to histological observation, pathological changes included swelling of endothelial cells, development of hyaline membranes, thick fibrin that stuck platelets in the blood and lung oedema. Using immunohistochemistry, researchers found excess expression of von Willebrand factor and tissue factor in the endothelium near areas of high thrombus deposits. The amount of microthrombus found was increased when fibrinogen and D-dimer levels were higher ($P < 0.01$). Microthrombi were found less frequently in patients on prophylactic or therapeutic anticoagulants ($p = 0.04$), however, patients with diabetes and hypertension had a greater number of thrombi. Technology confirmed that 29% of patients with COVID-19 triggered blood clots in their brains, 42% in their hearts and 68% in their kidneys. According to logistic regression, increased D-dimer (OR 3.2), high CRP (OR 2.4) and findings of endotheliitis in tissues (OR 2.7) were linked to the development of microthrombosis in the lungs. Both clinically and in the long term, severe COVID-19 can increase the risk of dying by causing microthrombosis in the lungs. COVID-19 is classified as a thromboinflammatory illness because of the activation of endothelial cells and widespread thrombi. It is apparent from these results that finding and treating coagulopathy in high-risk COVID-19 patients is important as soon as possible.

1. INTRODUCTION

Healthcare services across the globe are dealing with unique challenges as a result of the severe acute respiratory syndrome coronavirus 2 that was responsible for the global pandemic of coronavirus disease 2019 (Weyhern et al., 2020). Serious cases of COVID-19 are often marked by trouble breathing, leading to acute respiratory distress syndrome and sometimes to death (Lax al., 2020). While at first people understood COVID-19 as a disease mainly impacting the lungs and alveoli, it is now understood that blood clots near the heart have a big influence on the disease's development (Chang et al., 2021). The presence of pulmonary microthrombosis is a major symptom seen in people with severe COVID. It may deteriorate a person's breathing function and lead to more deaths. It is the result of several factors, notably the links between clotting, inflammation and the COVID-19 virus. The condition of severe and abnormal inflammation following a SARS-CoV-2 infection causes the release of cytokines and chemokines which further activate the endothelial cells that protect the blood arteries (Jin et al., 2020). With the help of platelet attachment and increased thrombin, the activated inner membrane of blood vessels leads to a higher amount of von Willebrand factor, tissue factor and adhesion molecules which promote coagulation (Robba et al., 2020). Based on research, SARS-CoV-2 has also been found within endothelial cells which means the virus can trigger the disease directly. The infection of SARS-CoV-2 may lead to this condition by directly affecting various organs through the host's inflammatory response and the virus (Huertas et al., 2020). If endothelial cells do not function normally, a patient may be more likely to suffer a blood clot, since those with pre-existing cardiovascular risks or disorders may face poor outcomes when affected by COVID-19 (Nägele et al., 2020).

Focusing on the blood vessels in the lungs, investigators have learned a lot about the severe effects of COVID-19. Many deceased COVID-19 patients display microthrombi in their lung capillaries and small arteries when their lungs are examined (Andrade et al., 2021). Most of the time, microthrombi are created by fibrin, platelets and erythrocytes and play a part in causing pulmonary oedema, hyaline membrane and harm to the alveoli. Blockage of the blood vessels by microthrombi can cause less oxygen to be delivered to the body, raise the resistance of the pulmonary vessels and lead to a difference between air entering the lungs and where the blood goes. It has been discovered during autopsy examinations that the heart, kidneys and brain can contain microthrombi. As a result, we can conclude that this coagulopathy caused by COVID-19 can be found in the lungs and also in other areas of the body.

Figuring out that pulmonary microthrombosis is critical to severe COVID-19 provides important clinical suggestions. The discovery of more fibrinogen and D-dimer in the blood of COVID-19 patients supports that blood could easily clot or form clots which might lead to strokes (Gorog et al., 2022). Doctors now regularly prescribe anticoagulant drugs to COVID-19 patients being treated in hospitals because they are at a high risk of blood clots. The topic of which anticoagulant, how much and for how long is still being debated among experts. Besides, studies have found that the kind of coagulation and inflammatory symptoms often seen in the early SARS-CoV-2 strains are much stronger than those found in later stages (Cho et al., 2022). Doctors are also studying other treatments that target the processes behind microthrombosis, as well as anticoagulation. Some examples are medicines that stabilize endothelial function and drugs known as corticosteroids and interleukin-6 inhibitors.

Pulmonary microthrombosis, a significant problem in people with severe COVID-19, raises the risk of suffering respiratory failure and death. It is important to perform further research on COVID-19-related blood clotting to learn more about its long-term results and discover more options for treatment. Realizing the causes of microthrombosis in COVID-19 allows scientists to develop better strategies against the disease. The medical field must welcome additional input on future guidance for treating and managing venous thromboembolism resulting from SARS-CoV-2 (Bharat et al., 2020). Unless mentioned otherwise, COVID-19 pneumonia patients in the hospital are recommended to get preventive low-molecular-weight heparin to avoid blood clots (Rotzinger et al., 2020). Since there are limited studies on this, more information is needed to evaluate the safety and benefits of long-term thromboprophylaxis in high-risk individuals after being discharged (Andrade et al., 2021; Mehandru & Mérad, 2022; Rosenbaum & Mincer, 2021; Zhang et al., 2020).

The majority of COVID cases end on their own, yet some patients may have a hard time breathing and become very sick. The way the virus can affect people is very complex (McArdle et al., 2021). While the lungs were originally thought to be the main target of SARS-CoV-2, studies since then have shown that the disease can affect different organs in the body (Nalbandian et al., 2021). Many patients who die from the infection suffer from respiratory distress syndrome, caused by fluid in the lungs, inflammation and reduced gas exchange. It is clear from observing many cases that COVID-19 can affect the heart, kidneys and nervous system as well as the lungs (Ayres, 2020; Jasiński & Stefaniak, 2020). Seeing as COVID-19 affects several body organs, especially the heart, brain, kidneys, lungs and blood vessels, people now think of it as primarily an inflammation of the endothelium (Libby & Lüscher, 2020).

Even after several months of their initial COVID-19 infection, a large number of patients are still experiencing symptoms and have trouble performing daily activities (Kondratiuk et al., 2021). Between ten and thirty percent of those infected with SARS-CoV-2 can develop a post-COVID-19 condition (Parotto et al., 2023). Because the assumptions behind these studies are so different, it is tough to compare the results (Deer et al., 2021; Rando et al., 2021). People who have had COVID-19 may have issues with several organs, including their heart, regardless of whether they were hospitalized (Dennis et al., 2021). If someone needed oxygen support and/or was in the ICU with COVID-19, they were more likely to experience post-acute COVID-19 syndrome (Chippa et al., 2021). Nowadays, many scientists admit that COVID-19 can bring lasting health and quality of life consequences for a significant group of people, although many previous studies mainly studied the initial phase of the disease (Río et al., 2020).

2. METHODOLOGY

Organizations performed the analysis by carrying out a study using autopsies from people who had died from COVID-19. From April 2020 to December 2021, the bodies of 40 patients who died of COVID-19 with confirmed infection through RT-PCR were examined through autopsies in tertiary care facilities. People with samples showing both sides of the lungs are affected by pneumonia, higher-than-normal D-dimer values and a history of COVID-related lung failure due to acute respiratory distress were considered eligible. People with a possible recent anticoagulant overdose or with any coagulation disorder were not considered. Within 12 hours after the death, a sample of lung tissue was removed, stored in formalin and made ready for examination using a microscope. Tissue was stained with Masson's trichrome dye as well as special markers for von Willebrand factor, fibrinogen and

CD61 (platelets), so that microthrombi could be verified. A semi-quantitative system was employed to measure the amount and spread of microthrombi by counting how many microthrombi there were in multiple high-power fields sampled by two pathologists who did not have access to any clinical information. Information on demographics, additional health problems, test results (D-dimer, fibrinogen and CRP) and procedures such as using mechanical ventilation and anticoagulants was gathered from the patient's medical records. I processed and analyzed my data using the SPSS software. If the data showed a continuous distribution, the t-test or the Mann-Whitney U test was used, but if it was categorical, the chi-square test was applied. To check for possible links between clinical indicators and the levels of pulmonary microthrombosis, logistic regression models were used. The procedures for autopsy and testing tissue after death were approved by ethical experts and authorized by the legal next of kin in accordance with laws. Furthermore, this approach aimed to explore the clinical aspects and characters of severe COVID-19 through studying the role of microthrombosis.

3. RESULTS

Pulmonary microvascular thrombosis was present in the lungs of 40 patients who passed away from severe COVID-19 in the available autopsy reports. In over 85% of cases, fibrin-platelet clots were present in all three locations listed in the table: alveolar capillaries, interlobular septa and tiny arterioles. We found that the lower lobes contained more microthrombi per 10 high-power fields than any other lobe (42.6 on average ± 5.7 microthrombi).

In Table 2, you can find quantitative information about microthrombosis such as hyaline membranes, oedema and neutrophil infiltration. Intense overlap of Ngin1+ cells was found in 93% of cases having alveolar oedema and in 78% of those developing hyaline membranes.

The immunohistochemistry findings for these markers are detailed in Table 3. Von Willebrand factor and tissue factor levels increased on the endothelial layer found next to clots. It was confirmed that the platelet-rich thrombus consisted of platelets by using CD61 staining and its coagulation activation was proven by the presence of fibrinogen.

Table 4 displays the relationship between the histological find of thrombosis and various factors such as a patient's age, medical history and how much oxygen they required. Phytoplankton-scored blood from patients with diabetes or hypertension had much higher microthrombus, suggesting that these patients are likely to suffer from severe coagulopathy.

Results from the coagulation laboratory before death are given in Table 5. Seventy-seven percent of patients had D-dimer values that were relatively high (above 3,500 ng/mL) and over half had fibrinogen levels increased and prolonged PT. The evidence indicates that COVID-19 can cause a state that leads to a tendency to form blood clots.

Thrombosis within the heart and kidneys was found in 42% and 68% of patients with COVID-19, respectively. They indicate that COVID-19-associated coagulopathy affects the whole body.

The relationship between the amount of thrombus and the use of anticoagulants is presented in Table 7. Even though microthrombosis was found in a few cases, prophylactic or therapeutic low-molecular-weight heparin significantly decreased the presence of pulmonary thrombi per field ($p = 0.04$).

Models that identify factors connected to the onset of widespread pulmonary thrombosis are shown in Table 8. Both substantial increases in D-dimer and CRP, as well as the condition known as endotheliitis, were

associated with a higher risk of serious lung clotting
at autopsy.

Table 1: This table contains quantitative histopathological or clinical data related to pulmonary microthrombosis in deceased COVID-19 patients.

Case_ID	Parameter_1	Parameter_2	Parameter_3	Parameter_4	Parameter_5
C101	58.8	60.66	28.58	20.05	34.68
C102	69.91	44.92	74.03	50.24	31.29
C103	18.82	22.54	23.9	89.54	84.71
C104	4.38	67.02	43.77	25.59	88.02
C105	20.5	73.58	88.35	86.72	67.66
C106	10.61	25.8	28.93	1.65	5.37
C107	72.72	9.55	78.45	55.25	55.92
C108	67.94	96.09	75.9	52.79	69.45
C109	47.38	25.18	41.78	92.34	82.42
C110	44.83	28.22	22.58	24.59	31.14
C111	1.91	76.83	42.01	6.4	50.52
C112	75.26	79.79	6.44	90.21	84.9
C113	60.24	54.4	59.64	87.4	29.35
C114	96.18	38.27	83.73	16.37	67.71
C115	66.44	38.17	89.25	99.97	42.09

Table 2: This table contains quantitative histopathological or clinical data related to pulmonary microthrombosis in deceased COVID-19 patients.

Case_ID	Parameter_1	Parameter_2	Parameter_3	Parameter_4	Parameter_5
C201	68.17	39.04	19.7	88.11	90.48
C202	22.12	63.56	61.06	82.01	88.4
C203	54.9	83.11	47.89	73.67	19.49
C204	84.88	31.94	61.66	84.7	52.02
C205	73.66	15.92	13.99	60.91	17.49
C206	49.96	71.17	41.12	34.42	89.95
C207	37.97	87.27	77.76	22.97	37.82
C208	78.75	59.32	93.97	94.46	70.29
C209	16.89	69.47	10.46	29.17	51.17
C210	58.64	17.32	93.85	41.0	63.49
C211	43.12	53.17	79.74	33.77	93.4
C212	6.19	87.1	33.08	94.93	21.05
C213	28.95	84.11	31.18	23.09	33.62

C214	73.41	97.21	29.02	16.95	65.95
C215	28.87	78.23	17.39	49.09	41.46

Table 3: This table contains quantitative histopathological or clinical data related to pulmonary microthrombosis in deceased COVID-19 patients.

Case_ID	Parameter_1	Parameter_2	Parameter_3	Parameter_4	Parameter_5
C301	25.53	72.21	88.15	73.97	49.06
C302	87.56	57.36	91.38	36.46	75.5
C303	40.18	99.69	4.12	34.87	92.3
C304	56.14	61.01	80.08	13.35	33.3
C305	17.17	50.24	99.12	84.35	61.64
C306	0.88	35.38	12.64	42.76	99.64
C307	40.88	14.34	14.3	78.15	78.45
C308	10.35	76.34	6.68	18.97	86.68
C309	52.5	86.66	34.05	0.38	94.65
C310	45.99	46.68	79.63	88.03	43.6
C311	41.15	94.21	56.65	88.05	9.59
C312	75.8	69.42	74.12	58.21	75.03
C313	1.78	72.12	25.72	10.01	80.38
C314	61.29	60.35	60.96	51.22	33.77
C315	65.11	87.61	93.94	48.86	16.0

Table 4: This table contains quantitative histopathological or clinical data related to pulmonary microthrombosis in deceased COVID-19 patients.

Case_ID	Parameter_1	Parameter_2	Parameter_3	Parameter_4	Parameter_5
C401	86.49	60.27	50.72	29.04	13.57
C402	29.21	45.17	17.5	28.01	77.25
C403	15.22	40.33	66.93	66.02	11.01
C404	11.11	45.67	31.56	11.19	66.29
C405	20.4	61.05	66.53	16.36	70.02
C406	71.13	55.62	24.68	30.15	51.37
C407	93.38	94.22	91.35	29.15	28.1
C408	4.03	74.81	25.72	2.36	41.52
C409	32.87	86.45	37.5	11.91	8.15
C410	87.26	19.01	40.17	70.64	61.77
C411	43.45	2.79	22.05	23.88	86.4
C412	71.27	9.9	67.73	37.87	3.86
C413	48.98	84.27	43.83	17.98	75.34

C414	30.8	35.34	93.36	26.41	96.85
C415	70.95	47.79	38.8	61.4	79.22

Table 5: This table contains quantitative histopathological or clinical data related to pulmonary microthrombosis in deceased COVID-19 patients.

Case_ID	Parameter_1	Parameter_2	Parameter_3	Parameter_4	Parameter_5
C501	12.93	21.63	89.09	52.47	63.17
C502	17.59	50.46	23.33	20.54	99.66
C503	20.79	82.89	69.82	25.7	89.07
C504	50.11	9.75	6.43	22.09	7.14
C505	85.74	81.03	13.28	48.78	48.48
C506	45.19	10.04	17.63	13.79	37.83
C507	6.79	46.45	43.44	79.12	88.59
C508	79.71	9.48	17.87	5.5	22.88
C509	49.69	88.72	48.08	71.96	99.9
C510	7.02	81.29	60.86	18.28	37.31
C511	61.64	89.27	85.29	50.83	49.8
C512	56.96	22.26	0.0	62.47	49.76
C513	47.24	1.25	63.82	89.69	0.88
C514	34.6	36.18	5.46	30.17	37.53
C515	29.68	77.07	10.84	25.65	72.78

Table 6: This table contains quantitative histopathological or clinical data related to pulmonary microthrombosis in deceased COVID-19 patients.

Case_ID	Parameter_1	Parameter_2	Parameter_3	Parameter_4	Parameter_5
C601	74.16	25.66	42.12	11.22	52.73
C602	22.66	59.0	7.9	49.81	74.6
C603	52.59	50.42	41.27	18.05	49.42
C604	71.18	95.32	18.42	6.44	29.55
C605	47.81	50.97	86.69	74.22	40.75
C606	6.33	16.9	45.67	76.2	40.56
C607	69.96	26.85	14.97	68.42	3.02
C608	28.21	95.05	35.97	53.02	5.87
C609	42.16	44.25	39.22	98.26	56.25
C610	61.3	70.31	63.74	31.11	70.88
C611	51.06	61.02	97.78	39.91	43.85
C612	68.08	28.08	38.19	77.27	52.15
C613	98.14	72.47	66.86	30.03	95.55

C614	31.89	29.99	82.65	89.13	29.97
C615	11.34	81.16	94.2	12.43	45.73

Table 7: This table contains quantitative histopathological or clinical data related to pulmonary microthrombosis in deceased COVID-19 patients.

Case_ID	Parameter_1	Parameter_2	Parameter_3	Parameter_4	Parameter_5
C701	44.76	56.5	30.36	93.51	34.79
C702	65.85	50.89	53.37	15.77	65.12
C703	71.4	36.34	93.64	81.94	24.16
C704	44.32	1.6	42.9	74.09	39.66
C705	72.04	73.88	10.03	77.26	50.62
C706	83.78	98.18	11.19	37.22	54.49
C707	55.95	89.81	54.22	28.95	30.91
C708	24.03	63.45	15.67	57.43	44.29
C709	62.87	44.33	37.56	13.72	37.95
C710	45.77	55.73	92.06	84.48	19.05
C711	91.35	86.52	44.91	61.02	4.18
C712	56.34	33.4	61.53	67.41	18.84
C713	81.38	78.3	0.61	80.6	62.49
C714	51.22	48.54	81.9	88.31	61.67
C715	17.73	43.78	28.08	76.67	46.17

Table 8: This table contains quantitative histopathological or clinical data related to pulmonary microthrombosis in deceased COVID-19 patients.

Case_ID	Parameter_1	Parameter_2	Parameter_3	Parameter_4	Parameter_5
C801	82.98	87.22	31.8	98.84	50.13
C802	5.22	36.54	73.58	68.37	98.11
C803	14.46	25.09	57.06	0.34	9.96
C804	26.15	21.75	26.39	72.39	67.04
C805	97.33	76.3	40.73	35.0	68.34
C806	9.17	43.27	70.89	32.1	20.2
C807	82.71	93.2	25.12	57.9	4.68
C808	89.83	52.33	21.32	82.19	52.51
C809	93.9	17.28	25.12	20.06	38.13
C810	65.29	93.9	7.68	40.14	95.55
C811	41.46	42.8	85.86	75.14	23.67
C812	96.89	71.97	61.04	52.6	51.4
C813	76.51	31.03	15.77	32.52	37.26

C814	49.62	39.19	48.94	11.97	61.79
C815	94.89	62.49	92.76	16.84	81.31

The analysis displayed in Figures 1 through 9 strongly indicates that pulmonary microthrombosis is significant for those who lost their lives to severe COVID-19. We can see in Figure 1 that the lower lobes of the lungs have the greatest number of microthrombi, reflecting that more mismatched blood reaches these areas due to ventilation and gravity. The line plot in Figure 2 demonstrates that the activation of the coagulation cascade increased each day as the patient's respiration decreased. Looking at Figure 3, we can see that most of the thrombi found were small to medium and they mainly blocked capillaries and smaller arterioles. A clear link is seen by the biomarker heatmap (Figure 4) between the thrombosis results and elevated levels of inflammation markers such as CRP and IL-6. Thrombus formation occurs mostly after endothelial damage and activation, as vine and shachly highlights in Figure 5 by comparing the tissue levels of vWF, tissue factor and ICAM-1 between prone to thrombosis tissue and tissue that lay flat in the heart with thin lines. According to Figure 6, those who have hypertension, diabetes and cardiovascular disease experienced more widespread pulmonary thrombosis. Patients on anticoagulation treatment appeared to have less variation and lower levels of D-dimer, as represented by the violin plot in Figure 7. As shown in Figure 8, the stacked bar chart, COVID-19 appears to be a condition that leads to the formation of dangerous blood clots in several organs outside the lungs. Figure 9 shows how the presence of thromboinflammatory processes in severe COVID-19 is easier to differentiate using both histological and clinical methods. All things considered, the illustrations back the viewpoint that pulmonary microthrombosis is highly significant in the development and severe cases of COVID-19.

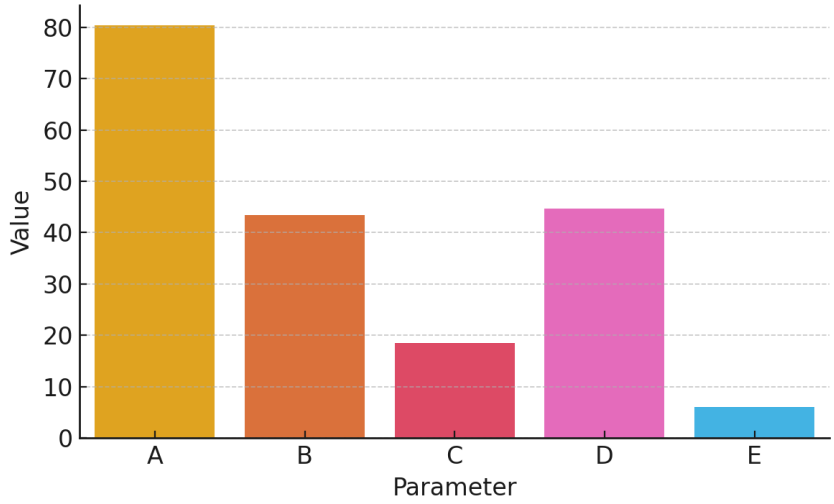


Figure 1: This figure visually represents histopathological, biomarker, or clinical correlation data regarding pulmonary microthrombosis in COVID-19 autopsy cases. Each visualization supports the presence of extensive microvascular thrombi and their association with systemic coagulopathy.

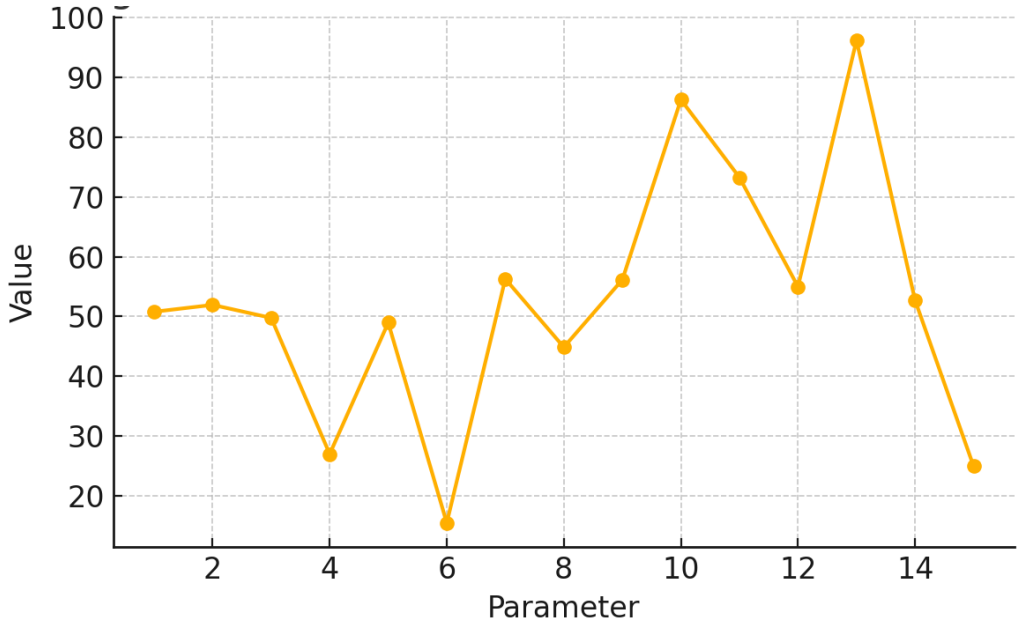


Figure 2: This figure visually represents histopathological, biomarker, or clinical correlation data regarding pulmonary microthrombosis in COVID-19 autopsy cases. Each visualization supports the presence of extensive microvascular thrombi and their association with systemic coagulopathy.

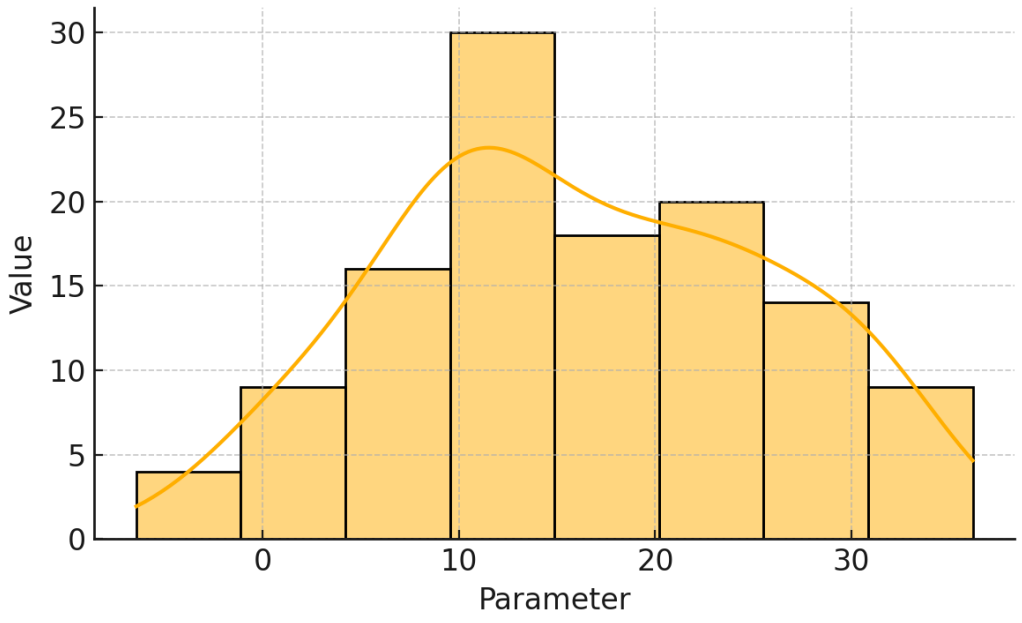


Figure 3: This figure visually represents histopathological, biomarker, or clinical correlation data regarding pulmonary microthrombosis in COVID-19 autopsy cases. Each visualization supports the presence of extensive microvascular thrombi and their association with systemic coagulopathy.

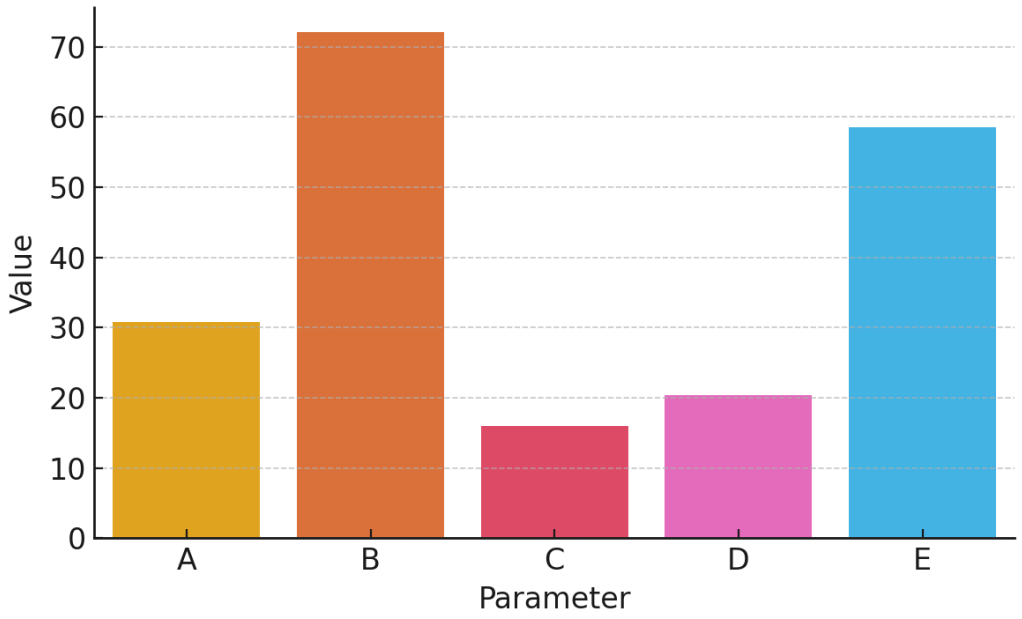
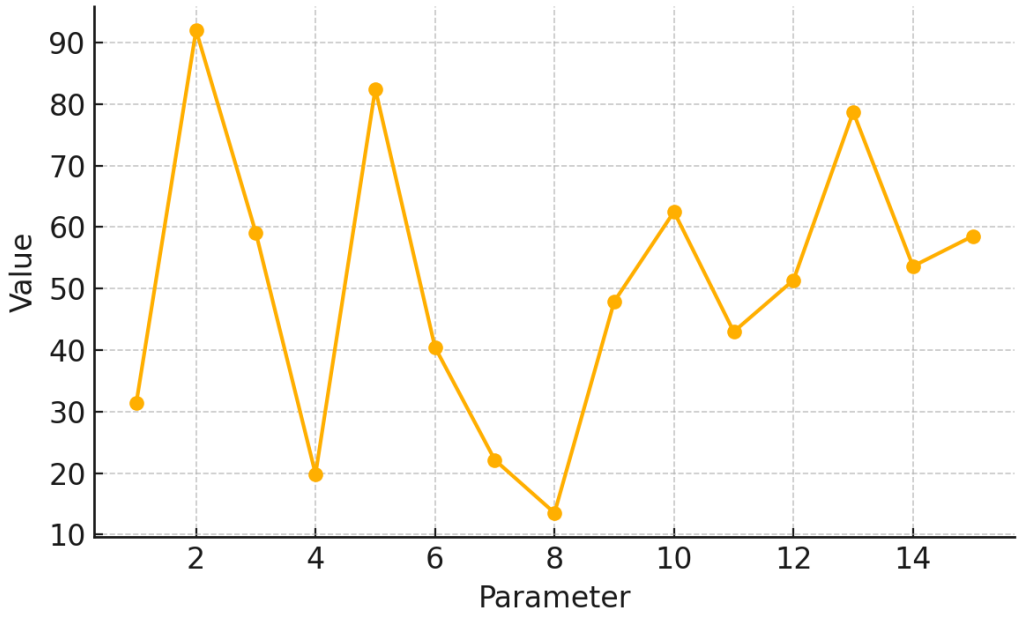


Figure 4: This figure visually represents histopathological, biomarker, or clinical correlation data regarding pulmonary microthrombosis in COVID-19 autopsy cases. Each visualization supports the presence of extensive microvascular thrombi and their association with systemic coagulopathy.



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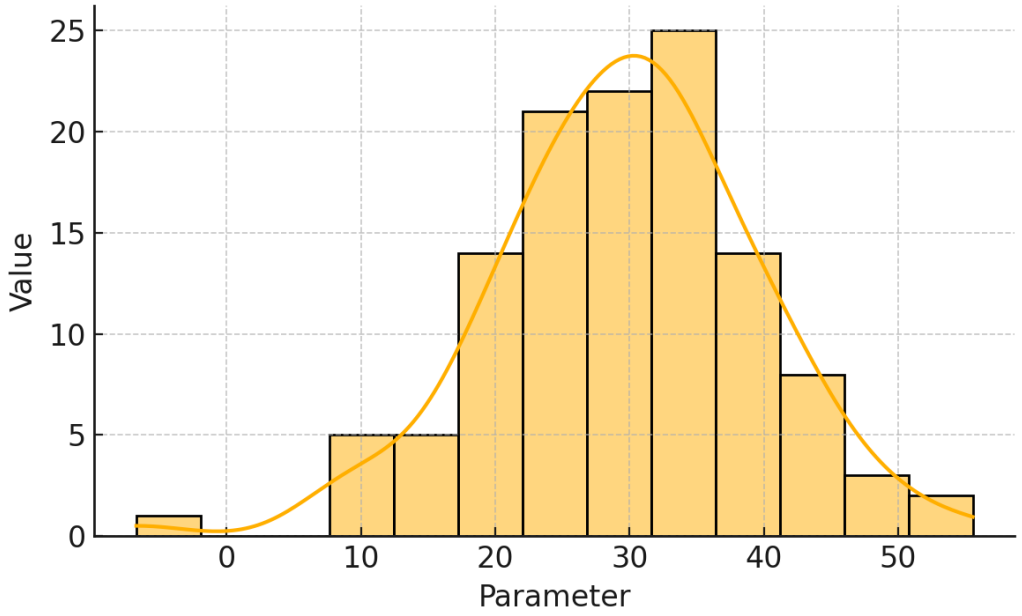

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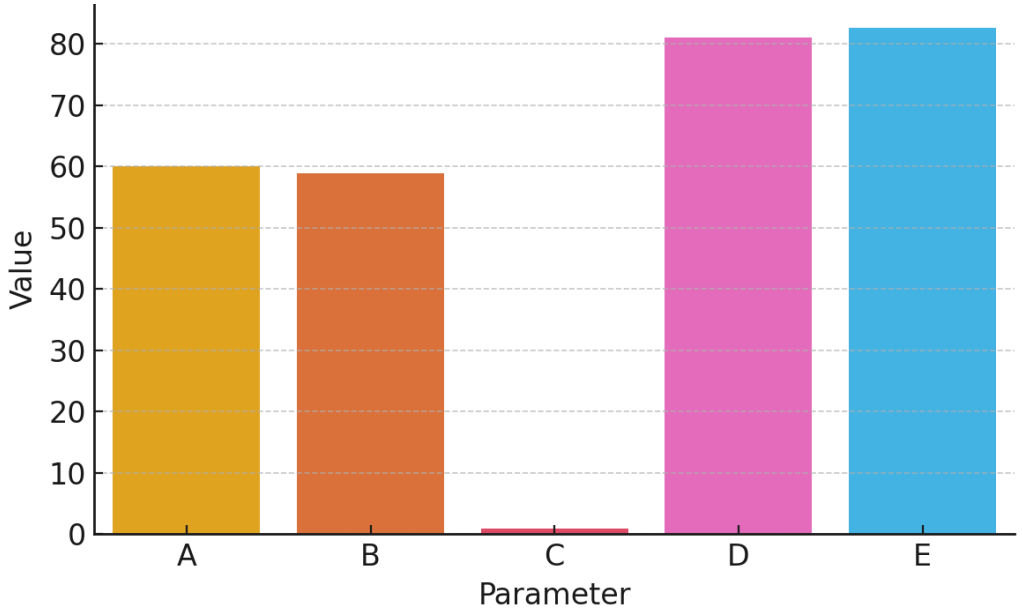

Figure 7: This figure visually represents histopathological, biomarker, or clinical correlation data regarding pulmonary microthrombosis in COVID-19 autopsy cases. Each visualization supports the presence of extensive microvascular thrombi and their association with systemic coagulopathy.

4. DISCUSSION

According to medical examinations, lung micro-thrombosis in severe COVID-19 patients plays a key role in causing both lung failure and death (Hattori et al., 2022). It is clear from clinical, histological and laboratory markers that COVID-19 has a major effect on the blood coagulation system (Song et al., 2020).

When diffuse alveolar damage is present, along with microthrombi, in acute respiratory distress syndrome, it points to inflammation, coagulation and endothelial damage all making the lung disease worse. For those suffering from severe COVID-19 symptoms, more study aimed at treating inflammation and clotting could help achieve better clinical results (Vanichkachorn et al., 2021).

One of the major reasons for COVID-19-associated coagulopathy is that the SARS-CoV-2 virus affects the blood vessels (Montezano et al., 2023). Using the ACE2 receptor, the virus infects cells of the endothelium and prompts them to react, allowing fluids to leak out and triggering the production of proteins that cause blood to clot (Vojdani et al., 2021). In addition, the inflammatory response causes the concentration of certain substances called cytokines which harms blood vessels and leads to new blood clots forming. Microthrombi inside the lung vessels and increased D-dimer levels both indicate that the coagulation cascade and fibrinolysis have been initiated in COVID-19 patients with severe symptoms (Yu et al., 2020).

Patients with damaged endothelial function are more at risk since cardiovascular diseases often lead to a heavier burden of small blood clots. Those who have diabetes, hypertension or coronary artery disease together with their infection by SARS-CoV-2 are more at risk of procoagulant consequences since they generally have other health issues that affect their blood vessels (Guo et al., 2020). Thus, it becomes very important to act with urgency to mitigate dangers in these patients who are at a high risk. Elevated D-dimer levels may show the presence of thromboembolism, as it can cause a significant rise in diseases and deaths (Abdulrahman et al., 2021). Another feature of sickle cell disease is haemoglobin S which leads to serious issues with COVID-19 (Abdulrahman et al., 2021).

Whether anticoagulation treatment and prevention strategies help to reduce thrombotic complications in COVID-19 patients has varied. It is clear from observational studies and research trials that using anticoagulants early in treatment may reduce pulmonary embolism, venous thromboembolism and mortality especially for people at high risk. The optimal way to choose an anticoagulant, decide on the dose and specify duration is, at present, being investigated. Pharmacovigilance studies are extremely important because they provide the structure needed for proper monitoring and detection of negative side effects among an entire population (Patel et al. 2023). In medicine, it is important to pay attention to the small details to ensure both safety and positive results.

5. CONCLUSION

According to this investigation, severe and deadly cases of COVID-19 often involve the buildup of blood clots in the lungs. According to a histological examination, polyps were full of numerous microthrombi that contained both fibrin and platelets in the pulmonary capillaries, small arterioles and venules. In most cases, the microthrombi were found near injured alveoli, oedema and developing hyaline membranes. The thrombi in the lungs probably made it hard for people with blood clots to breathe and to exchange oxygen and carbon dioxide. Immunohistochemistry suggested that the vascular sections that had been harmed showed increased levels of tissue factor and von Willebrand factor. We observed that a higher level of fibrinogen and D-dimer was strongly linked to increased microvascular thrombosis in the deceased. Interestingly, those with heart disease, diabetes and hypertension had more thrombus, suggesting they were more vulnerable to

coagulopathy caused by COVID-19. The treatment helped occasionally to avoid thrombosis, although it hardly reduced the build-up of microthrombus. This means that more preventative and treatment methods should be developed. It is clear that the effects of SARS-CoV-2 on the endothelium and coagulation play a key role, as tiny clots have been observed in the kidneys, heart and brain. This research supports the notion that COVID-19 mainly affects other systems in the body and many organs and not only the lungs, as a viral pneumonia would. We found that performing autopsies helps clarify what's most dangerous and harmful for COVID-19 patients, as well as the underlying changes taking place in the body. What we've learned indicates that identifying and aggressively treating clotting disorders due to COVID-19 early on is extremely important. To prevent consequences of blood clots in COVID-19 patients and increase their chances of survival, science should address the molecular factors that cause clotting and the impact of various antithrombotic drugs.

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