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Renal Artery Thrombosis Associated with COVID-19: A Systematic Review

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Abstract: Arterial thromboembolism associated with COVID-19 is a rare complication in the renal arteries and, when present, can lead to severe conditions. The aim of this study is to understand renal artery thrombosis associated with acute or previous SARS-CoV-2 infection. This review was conducted according to PRISMA guidelines and registered with PROSPERO. Articles were searched in the following databases: MEDLINE, LILACS, PubMed, and SciELO. The exclusion criteria included patients with risk factors for thrombosis. A total of 139 studies were found, of which thirteen met the pre-established criteria. The review emphasizes that this complication is more prevalent during infection and is more common in young male patients, with a predilection for the left renal artery. In these cases, no benefit was identified from thromboprophylaxis after a COVID-19 diagnosis. The clinical presentation was marked by sudden lower back pain, and occasionally fever, nausea, and oliguria. Contrast-enhanced computed tomography was sufficient to make the diagnosis. There was a preference for conservative treatment, and a cycle of therapeutic anticoagulation was also performed after hospital discharge. Information regarding renal function impairment is more related to acute manifestations, revealing limited knowledge of long-term consequences.

Keywords: Thrombosis; Thromboembolism; Renal artery; Hypercoagulability; COVID-19.

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1. Introduction

In 2020, the World Health Organization (WHO) declared the SARS-CoV-2 pandemic, with its first cases reported in Wuhan, a city in China's Hubei province, which became the center of an initially unexplained outbreak. The disease is primarily transmitted through infectious person-to-person contact via inhalation of aerosolized viral particles [1, 2]. This pathogen belongs to the Coronaviridae family, with a positive-sense single-stranded RNA genome and is found in humans and other mammals [3, 4].

SARS-CoV-2 infection generally leads to asymptomatic or mild symptoms, but it is notable for the diversity of potentially severe clinical complications it can cause, including Acute Respiratory Distress Syndrome (ARDS), myocarditis, Acute Kidney Injury (AKI), multiple organ failure, and shock. Coagulopathy in the form of arterial and venous thromboembolism is considered one of the most severe complications of the disease. This event is rare in the renal arteries and, when present, can result in conditions ranging from electrolyte disturbance episodes to more severe scenarios like acute kidney injury and renal infarction [5-7].

It is evident that this infection leads to endothelial dysfunction caused by an inflammatory response to the virus [1, 3]. This situation, combined with the host's inflammatory defense reactions, can predispose to thrombotic disease in both venous and arte-

rial circulation due to excessive inflammation, platelet activation, endothelial dysfunction, and stasis [1]. One possible explanation for such thrombotic events and the involvement of multiple organs relates to the fact that SARS-CoV-2 generally invades human cells through binding with the angiotensin-converting enzyme 2 (ACE2). This binding to ACE2, along with viral replication, seems to contribute to the infiltration of inflammatory cells, endothelial apoptosis, and pro-thrombotic microvascular events [1, 2, 8, 9].

ACE2 is highly expressed in the kidneys, making these organs possible targets. The kidney is considered the second most affected organ, surpassed only by the lungs [10, 11, 4]. Although the clinical presentation of renal artery thrombosis (RAT) is associated with low back pain, renal hypertension, and acute kidney injury, it can also present with nonspecific symptoms. Thus, its diagnosis was initially incidental and underestimated [12]. Therefore, the relationship between this infection and the development of a hypercoagulable state, represented by microvascular and macrovascular thromboembolic events, is evident. The objective of this systematic review is to contribute to a less addressed topic, highlighting RAT associated with COVID-19, including its clinical presentation, diagnosis, treatment, and complications.

2. Material and Methods

2.1 Databases and Search Strategy

This quantitative systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist and is registered with PROSPERO (CRD42024511370). The review was guided by the following research question, using the PICo strategy: renal artery thrombosis associated with acute or previous SARS-CoV-2 infection, including its clinical presentation, diagnosis, treatment, and complications. The selection of articles took place in April and May 2024. At this stage, Portuguese terms were chosen through the Health Sciences Descriptors (DeCs), and English terms through the Medical Subject Headings (MeSH), used in the following databases: Medical Literature Analysis and Retrieval System Online (MEDLINE) via the Virtual Health Library (BVS), Latin American and Caribbean Health Sciences Literature (LILACS) via BVS, PubMed, and Scientific Electronic Library Online (SciELO).

The following DeCS were used in the aforementioned databases: "trombose"; "tromboembolismo"; "artéria renal"; "obstrução da artéria renal"; "COVID-19," including the new coronavirus SARS-CoV-2 and "infarto renal." The last term is not included in DeCS/MeSH but is widely used in the databases included in this work. These words were linked to the operator "OR" and combined using the expression "AND," in Portuguese and their respective translations in English.

2.2 Inclusion and Exclusion Criteria

Primary studies in patients diagnosed with RAT associated with acute or previous SARS-CoV-2 infection were included, with no age or sex restriction, and articles described in Portuguese and English. Excluded were systematic reviews, articles that were not free and full-text, and studies in patients with the following risk factors for thrombosis: thrombophilias, systemic arterial hypertension, diabetes mellitus, kidney disease, active neoplasia, smoking, use of contraceptives and/or hormone therapy with estrogen, and obesity.

2.3 Study Selection

Initially, a search strategy was developed, followed by two independent reviewers conducting their searches. Articles were selected first by title, then by abstract, and finally by full text, following the inclusion and exclusion criteria. In cases of discrepancies between the researchers, a third reviewer was requested.

2.4 Risk of Bias Assessment

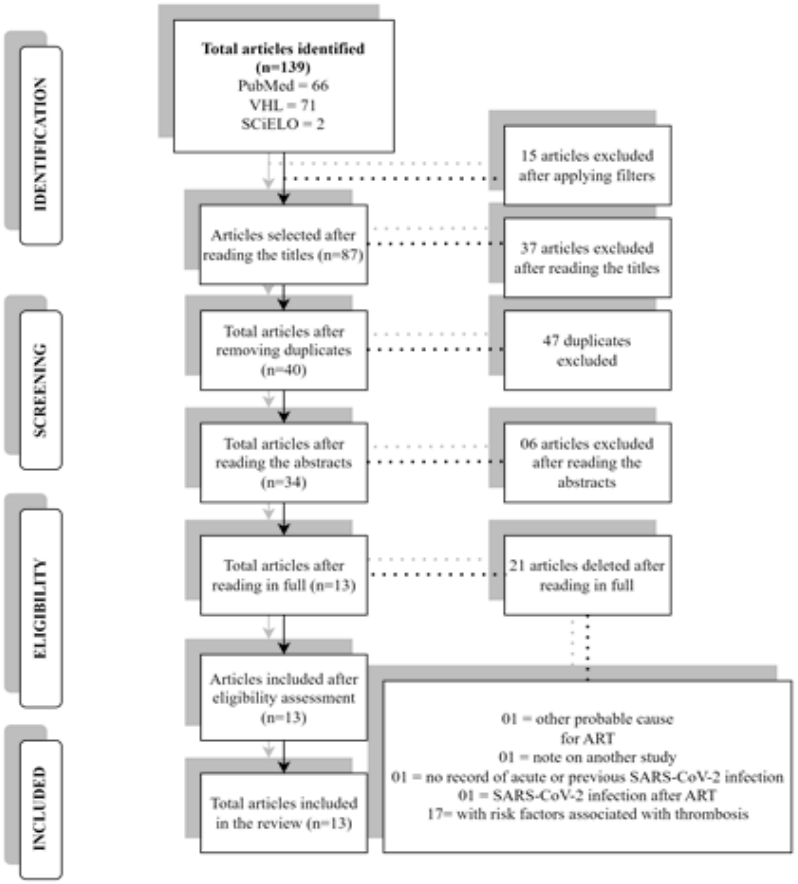
Two authors independently assessed the risk of bias for each included study using the Joanna Briggs Institute's critical appraisal tools [13], where the quality of the primary studies used in the review was assessed. This tool for case reports and case series contains a scale with eight items that helped determine the potential for bias in the design, conduct, and analysis of each study.

3. Results

3.1 Study Characteristics and Risk of Bias

A total of 139 articles were identified through a bibliographic search, leaving 124 after applying the filters "full-text and free articles" and "no systematic reviews." Titles were then read, and 87 works were selected. Forty-seven duplicates were manually removed, leaving 40 articles for abstract reading. After reading the abstracts, six of these articles were excluded, leaving 34 works for full-text reading. With the full-text reading, 21 articles were excluded, thus, 13 studies were included for eligibility assessment. There was an 80% agreement between the two reviewers on the selected articles. A third reviewer served as a tiebreaker. Finally, 13 articles were included, with a total of 14 patients (Figure 1).

Figure 1. Schematic representation of the synthesis and analysis of the results.



An assessment of the quality of individual articles is detailed in Table 1. The quality assessment results revealed that four studies scored 8/8 points on the JBI Critical Appraisal Tool and ten scored 7/8 points. The average JBI score for all included studies was 7.28. A score of seven or higher indicates that the studies have high methodological quality.

Table 1. Quality Assessment of Included Studies According to the JBI Critical Appraisal Tool.

Reference	1	2	3	4	5	6	7	8	Overall Evaluation: Include/Exclude/Seek more information
[14]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
[15]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[16]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[17]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[18]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[19]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
[21]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
[22]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[23]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[24]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[25]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[26]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
[27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include

Note: 1. Were the patient's demographic characteristics clearly described? 2. Was the patient's history clearly described and presented in a timeline? 3. Was the patient's current clinical condition at presentation clearly described? 4. Were the diagnostic tests or assessment methods and results clearly described? 5. Were the treatment intervention(s) or procedure(s) clearly described? 6. Was the post-intervention clinical course clearly described? 7. Were adverse events (harms) or unexpected events identified and reported? 8. Does the case report provide take-away lessons?

Table 2 demonstrates the characteristics of the articles selected for the study, based on their title, author, year of publication, indexed journals, country, and sample size. It also includes the following patient data: sex, age, previous pathologies, COVID-19 test, and thromboprophylaxis after COVID-19 diagnosis.

3.2 Patient Characteristics

Of the 14 cases of RAT, 13 patients (92.8%) were male and 1 patient (7.1%) was female. Twelve adult patients with an average age of 42.1 years were included, with only 2 pediatric cases reported, 1 male patient aged 13 months and 1 female patient aged 12 months (Table 2). The patients were from India (n = 4), Italy (n = 1), Netherlands (n = 1), Chile (n = 1), USA (n = 2), Argentina (n = 1), Kosovo (n = 1), Greece (n = 1), Saudi Arabia (n = 1), and Brazil (n = 1).

Table 2. Characteristics of Included Studies and Patient Data.

Reference	Age/Sex/Sample	Previous Pathologies/COVID-19 Test	Thromboprophylaxis Post COVID-19 Diagnosis
[14]	71 years; M; 1	No; RT-PCR +	LMWH
[15]	58 years; M; 2	OSA; RT-PCR +	LMWH

[16]	37 years; M; 1	Ureteral stents; RT-PCR +, IgG -	No
[17]	25 years; M; 1	No; RT-PCR +	No
[18]	37 years; M; 1	No; RT-PCR +	No
[19]	62 years; M; 1	No; RT-PCR +	LMWH
[20]	50 years; M; 1	No; RT-PCR -, IgG +	No
[21]	43 years; M; 1	HT, non-functioning adrenal adenoma; RT-PCR +	No
[22]	62 years; M; 1	No; RT-PCR +	No
[23]	64 years; M; 1	No; RT-PCR +	LMWH
[24]	50 years; M; 1	No; RT-PCR +	LMWH
[25]	31 years; M; 1	HT, dyslipidemia; RT-PCR +	No
[26]	13 months, M and 12 months, F; 2	No; RT-PCR -, IgG +	No

Note: M - male; F - female; LMWH – low molecular weight heparin; OSA - Obstructive Sleep Apnea Syndrome; AS - Aortic Valve Stenosis; HT – hypothyroidism; RT-PCR - Reverse Transcription Polymerase Chain Reaction; IgG - Immunoglobulin G antibodies.

Eleven patients were diagnosed with RAT during acute SARS-CoV-2 infection, and three were diagnosed after this infection. The three patients who tested negative for the Reverse Transcription Polymerase Chain Reaction (RT-PCR) test underwent serological testing, all of which were positive for IgG (Table 2). In seven studies, COVID-19 vaccination status was not recorded. In the remaining studies, only two patients had been vaccinated, both with the Pfizer-BioNTech vaccine. After the infection diagnosis, five patients began prophylactic anticoagulation with low molecular weight heparin (LMWH) (Table 2).

3.3 Medical History

Regarding personal pathological history, cases of obstructive sleep apnea (n=1), ureteral stents (n=1), moderate aortic valve stenosis (n=1), and hypothyroidism and dyslipidemia (n=1) were reported. Ten patients had no significant medical history. During hospitalization, in patients without personal pathological history, diagnoses included left ventricular hypertrophy (n=1), severe systolic dysfunction (n=1), and atherosclerotic plaque in the abdominal aorta (n=1) (Table 2).

3.4 Clinical Presentation and Diagnostic Approach

Among the symptoms most associated with RAT, lower back pain (n=11), fever (n=9), and oliguria (n=2) were observed. In nine reports, it was not specified whether patients presented with oliguria and/or hematuria (Table 3). The most commonly used imaging tests to diagnose RAT were abdominal angiography (n=10) and abdominal computed tomography (n=4).

In most patients, left renal infarction (n=10) was observed. There were also reports of right renal infarction (n=1), bilateral renal infarction (n=1), left renal artery thrombosis (n=1), and right renal artery thrombosis (n=1). In three of these cases, thrombosis and/or infarctions were also diagnosed in other areas, with thoracic aorta artery thrombosis, splenic vein and artery thrombosis, and splenic infarction (n=1), intestinal ischemia (n=1), and ascending aorta artery thrombosis (n=1) observed (Table 3).

Table 3. Clinical Presentation, Affected Kidney, and Other Sites of Thrombosis and/or Infarction.

Reference	Clinical Presentation Associated with RAT	Affected Kidney	Other Sites of Thrombosis/Infarction
[14]	Lower back pain	LRI	Thrombus in the ascending aorta artery
[15]	Lower back pain, fever, and oliguria	LRI	Intestinal ischemia
[16]	Lower back pain	BRI	None
[17]	Lower back pain, fever	LRI	None
[18]	Lower back pain, fever	LRI	None
[19]	Fever, oliguria	LRI	None
[20]	Lower back pain	LRI	None
[21]	Lower back pain, fever	LRI	None
[22]	Lower back pain, fever	LRI	None
[23]	Lower back pain, fever	LRI	Thrombosis in the thoracic aorta; thrombosis in the splenic vein and artery; splenic infarction
[24]	Lower back pain	RRI	None
[25]	Lower back pain	LRI	None
[26]	NR	Complete occlusion of the LRA	None
[27]	NR	Complete occlusion of the proximal ostial segment of the RRA	None

Note: SR - Not Reported; LRI – Left Renal Infarction; BRI - Bilateral Renal Infarction; LRA - Left Renal Artery; RRA - Right Renal Artery.

In the admission laboratory tests, at least one inflammatory marker was elevated, including C-reactive protein (n=14); lactate dehydrogenase (n=11); D-dimer (n=5); and fibrinogen (n=5). Regarding creatinine levels, 2 reports did not have recorded creatinine values in the admission tests. In the remaining cases, 10 patients did not have a significant increase (Table 4). Only 2 patients had creatinine levels above laboratory parameters. In 8 cases, tests for antiphospholipid antibodies were performed, all of which were negative.

Table 4. Admission Laboratory Tests of Patients with RAT Associated with COVID-19.

Reference	CRP	Ferritin	LDH	D-dimer	PT/INR	Factor I	Antiphospholipid Antibody	Creatinine
[14]	111 mg/dL	636 ng/mL	424 u/L	317 ng/mL	SR	SR	SR	0.72 mg/dL
[15]	33.4 mg/dL	SR	686 u/L	SR	SR	SR	SR	0.89 mg/dL

[16]	9.482 mg/dL	1,990 ng/mL	366 u/L	226 ng/mL	13.3/1.2	505 mg/dL	Negative	0.9 mg/dL
[17]	91.45 mg/dL	Normal	725 u/L	502 ng/dL	Normal	495 g/L	Negative	0.78 mg/dL
[18]	SR	SR	SR	SR	SR	SR	Negative	SR
[19]	36 mg/dL	SR	786 u/L	SR	SR	SR	Negative	1.3 mg/dL
[20]	4.3 mg/dL	SR	SR	142 ng/mL	SR	SR	SR	1.2 mg/dL
[21]	127.6 mg/L	SR	462 u/L	<150 µg/L	SR/1.12	681.2 mg/dL	Negative	75 µmol/L
[22]	331.53 mg/dL	SR	751 u/L	>1,000 ng/mL	14.2 s/SR	SR	SR	0.94 mg/dL
[23]	19.9 mg/dL	SR	551 u/L	0.57 mg/L	SR	SR	Negative	SR
[24]	Positive	1,361 mg/mL	685 u/L	270 ng/mL	SR	574 mg/dL	SR	0.6 mg/dL
[25]	19.60 mg/L	471.7 µg/L	1,210 u/L	0.80 mg/L	16.5s/1.3	SR	Negative	72 µmol/L
[26]	0.3 mg/L	39.4 mg/mL	SR	SR	SR	SR	SR	0.5 mg/dL
[27]	8.2 mg/dL	SR	SR	SR	SR	SR	SR	0.3 mg/d

Note: SR - Not Reported.

3.5 Treatment and Long-Term Complications

The treatments selected for RAT varied, but the most common approach was through anticoagulants, with LMWH being the most used (n=12), followed by oral anticoagulants (n=7), antiplatelet agents (n=6), unfractionated heparin (n=1), intrarenal tirofiban (n=1), and regional anticoagulation with citrate (n=1). Nine patients used more than one anticoagulation regimen. Some patients also underwent percutaneous thrombectomy and percutaneous angioplasty with and without stent placement. One patient underwent an unsuccessful thrombectomy, requiring an angioplasty with stent insertion. Renal replacement therapy was performed in 2 cases (Table 5).

Regarding renal function, 10 reports did not specify the renal function status of patients after hospital discharge. In the remaining cases, 3 patients recovered renal function after the RAT episode. After discharge, a therapeutic anticoagulation cycle was performed in nine cases. Five patients used oral anticoagulants, one received dual antiplatelet therapy, and three used an oral anticoagulant combined with an antiplatelet agent (Table 5).

Table 5. Treatments Used for RAT, Post-RAT Renal Function, and Post-Discharge Treatment.

Reference	RAT Treatment	Post-RAT Renal Function	Post-Discharge Treatment
[14]	Heparin, clopidogrel, apixaban	Improved RF	Apixaban, clopidogrel, home oxygen therapy
[15]	Nadroparin, hemofiltration, regional anticoagulation with citrate	SR	SR

[16]	LMWH, apixaban	SR	Apixaban
[17]	Dalteparin, rivaroxaban	SR	Rivaroxaban
[18]	LMWH, warfarin	SR	SR
[19]	LMWH, hemodiafiltration	SR	SR
[20]	ASA, UFH, thrombectomy, intrarenal tirofiban, stent angioplasty	Improved RF	ASA, clopidogrel
[21]	LMWH	Improved RF	LMWH
[22]	LMWH	SR	Dabigatran
[23]	LMWH, ASA, fondaparinux	SR	Amoxicillin, ASA, fondaparinux
[24]	Renal angioplasty, ASA, clopidogrel, LMWH	SR	Anticoagulation
[25]	LMWH, warfarin	SR	Warfarin
[26]	Renal angioplasty	SR	Carvedilol, enalapril
[27]	Renal angioplasty	SR	Amlodipine, metoprolol, enalapril

Note: SR – Not Reported; RF – Renal Function; RAT – Renal Artery Thrombosis.

4. Discussion

The hypercoagulability triggered by SARS-CoV-2 infection can affect both venous and arterial systems. This virus can infect cells through the angiotensin-converting enzyme 2 (ACE2) receptors, which are highly expressed in the lungs, heart, vascular endothelium, kidneys, and intestines. As a result, it can lead to widespread endothelial inflammation, microvascular pro-thrombotic effects, and endothelial cell apoptosis [24, 25]. According to Mancini et al. [21], the state of systemic hyperinflammation can eventually lead to a "cytokine storm syndrome," contributing to the development of intravascular coagulopathies. Mavraganis et al. [23] note that the infection can impair renal function through the direct effect of the pathogen on renal tubular and endothelial cells and by indirect damage from cytokine release, as well as potential hypoperfusion due to restrictive fluid strategies.

In this review, only patients without risk factors for thrombosis were included. There was a predominance of cases in male patients, with an average age of 42.29 years. Jana et al. [16] state that most records of RAT associated with COVID-19 are in patients who already had comorbidities or underlying factors that would increase their risk. Sethi, Mehta, and Mahajan [19] report that renal infarction is rare, with an incidence of 0.1% to 1.4%. These authors list male gender, diabetes, chronic kidney disease, pre-existing hypertension, peripheral arterial disease, hyperlipidemia, and smoking as risk factors. Gentili et al. [24] report that the primary trigger is thromboembolism, through emboli originating from the heart or aorta, usually in patients with atrial fibrillation. Mavraganis et al. [23] also add excessive venous stasis due to immobilization and platelet activation in hospitalized patients as predisposing factors.

Unilateral thromboses, predominantly in the left renal artery, and bilateral cases were reported. Three cases of RAT were associated with other areas of thrombosis and infarction. Mukherjee et al. [14] reported a case of RAT in a 71-year-old patient without pre-existing comorbidities. On the ninth day of hospitalization, the patient began to experience acute pain in the left iliac fossa and flank associated with nausea. A computed tomography (CT) scan of the abdomen revealed areas of infarction in the posterior middle pole of the left kidney, as well as a thrombus in the ascending aorta. It was hypothe-

sized that the patient developed severe COVID-19 pneumonia, which induced a pro-thrombotic state, resulting in thrombosis of the ascending aorta that may have embolized to the renal artery, or it could have been due to isolated renal artery thrombosis.

Post et al. [15] also report a case of RAT concomitant with another site of thrombosis, involving a 58-year-old patient with obstructive sleep apnea, presenting with a history of abdominal pain and increasing dyspnea for two weeks. During hospitalization, the patient was intubated, developed oliguria, deteriorating renal function, and elevated inflammatory markers. On the tenth day of hospitalization, the patient presented with a distended abdomen and absence of bowel sounds. An abdominal CT suggested intestinal ischemia and revealed multiple renal infarctions.

It is evident that acute SARS-CoV-2 infection is associated with a hypercoagulable state; however, cases of patients developing RAT long-term have also been recorded. The endothelial injury that occurs during the infection can trigger the thrombotic cascade, which can later culminate in thrombosis [20]. Some studies describe that the inflammatory cascade and associated thrombosis risk remain elevated for many weeks after the infection [21].

In this review, three cases of RAT after acute infection were described. Two of these cases were reported by Mishra et al. [26]. In this report, one patient was a 13-month-old male with no prior disease history, diagnosed with complete occlusion of the left renal artery. The other case was a 12-month-old female with no prior pathologies, with a case of complete occlusion of the right renal artery. Both reports had negative RT-PCR and positive immunoglobulin G (IgG) antibodies.

According to the guidelines proposed by the Anticoagulation Forum, the American College of Cardiology, and the International Society on Thrombosis and Haemostasis, a standard prophylaxis regimen is recommended for hospitalized and non-severely ill patients. For critically ill patients, higher doses are indicated. This regimen may include enoxaparin or unfractionated heparin [14]. Post-diagnosis COVID-19 thromboprophylaxis was performed in older patients or those with significantly elevated inflammatory markers. Despite the use of prophylactic doses of low molecular weight heparin (LMWH) as per the cited guidelines, no evident benefit was seen.

From the included reports, the clinical presentation was mainly marked by abdominal and/or flank pain and occasionally by fever and oliguria. Jain et al. [22] mention that such symptoms may also be associated with nausea, vomiting, hematuria, and proteinuria. Due to the rarity of this complication and its nonspecific clinical presentation, many patients progressed to more severe conditions. One of the reports that well describes these clinical manifestations was by Farias et al. [18], presenting a 37-year-old patient with a history of nausea, vomiting, fever, and sudden lower back pain for three days. On physical examination, the patient presented a positive Giordano sign, and an abdominal CT revealed left renal artery thrombosis.

SARS-CoV-2 infection triggers a significant inflammatory response, releasing inflammatory mediators, activating the endothelium and hemostatic systems. This manifests with a prominent elevation of D-dimer and fibrin/fibrinogen degradation products [14]. Other inflammatory markers that are elevated in a large proportion of patients include lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, and interleukin-6 [24]. Elevated D-dimer, prolonged prothrombin time, thrombocytopenia, and presence of fibrin degradation products portend a poor prognosis in COVID-19 patients [16]. Creatinine was also a frequently requested laboratory test at hospital admission. In most reports, its elevation was recorded only during the hospitalization period, with the progression of deteriorating renal function.

Unlike what was seen in severe infection, patients with a mild to moderate RAT condition did not show many elevated inflammatory markers, with the most altered tests being CRP and LDH. This can be seen in the report by Murray et al. [17], which recorded a case of a 25-year-old male with no prior disease history and/or risk factors for RAT. His

admission laboratory tests showed elevated LDH and CRP, with slight elevations in D-dimer and fibrinogen.

According to Mukherjee et al. [14], imaging exams play a fundamental role in diagnosing RAT, with conventional renal angiography being the gold standard. However, contrast-enhanced abdominal CT was the imaging modality of choice in most cases. One disadvantage of this exam is the difficulty in visualizing microvascular thrombi. Renal ultrasound is an exam that generally can detect any changes in organ size or corticomedullary differentiation, with lower sensitivity for RAT diagnosis.

The treatment for RAT was based on conservative therapy using anticoagulants, mainly low molecular weight heparin. It was also done through oral anticoagulants, antiplatelet agents, and unfractionated heparin. Murray et al. [17] state that patients with severe COVID-19 may have pseudo-heparin resistance due to significant systemic inflammation, requiring high doses to achieve therapeutic levels. In four cases, an anticoagulant was combined with an antiplatelet agent. Mancini et al. [21] suggest through their report that there may be greater therapeutic benefit in adding antiplatelet therapy to isolated anticoagulation. They also state that this is consistent with the theory of platelet activation associated with the pathogenesis of thromboembolic complications in COVID-19.

In addition to conservative management, there were reports of percutaneous thrombectomy and percutaneous angioplasty with and without stent placement. Some factors can affect the treatment outcome, such as ischemia time, collateral flow, and pre-existing kidney disease. Angioplasty is considered a safe treatment, aiming to restore artery patency, even in prolonged ischemia [24].

Only three reports described the patients' renal function post-RAT. In these three cases, patients regained much of their renal function days to weeks after diagnosis. Understanding the mechanism of persistence of the hypercoagulable state after the acute phase resolution is essential for proper long-term thromboprophylaxis management. Jana et al. [16] explain that prolonged anticoagulation duration can help prevent thrombus formation as a long-term disease sequel. Post-discharge clinical follow-up is essential to assess organ viability, allocate the correct anticoagulant, and other treatment strategies [23]. Generally, after hospital discharge, a therapeutic anticoagulation cycle of 45 to 90 days is recommended, depending on the individual risk for each patient [14].

One of the main factors related to a good prognosis for these patients was the early diagnosis of the pathology. This initially proved to be one of the challenges faced during the pandemic, given the logistical challenges of using CT in mechanically ventilated patients and the potential risks of administering contrast agents in individuals with acute kidney injury (AKI) [15]. A late diagnosis of RAT was more associated with deteriorating renal function and the need for a more invasive therapeutic approach. Allocating an anticoagulant treatment regimen with an appropriate dose for the severity of the disease can improve prognosis, alleviate symptoms, reduce mortality rates, and decrease the risk of renal function impairment, which can remain as a long-term sequela of the infection [23].

4. Conclusions

RAT associated with SARS-CoV-2 infection correlates with an intense inflammatory state, described by elevated inflammatory markers. Most cases occurred during the acute phase of the disease, mainly in young male patients. The left kidney was the most affected, representing a finding that is still not well understood. Post-diagnosis COVID-19 thromboprophylaxis was chosen in individuals of older age or with significantly elevated inflammatory markers. Despite this, no benefit was seen with the isolated use of prophylactic dose LMWH.

Contrast-enhanced abdominal CT was sufficient and essential for diagnosis. Treatment with LMWH, oral anticoagulants, and/or antiplatelet agents is beneficial in these patients. A post-hospital discharge therapeutic anticoagulation cycle is recommended.

Renal function impairment may remain as a long-term sequela of the infection; however, more data are available on acute manifestations, evidencing limited knowledge of long-term consequences. This could change through randomized and case-control studies.

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