

ORIGINAL ARTICLE

Incidence of intracardiac thrombi in times of Covid 19

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Objective. To find the relationship in patients with a history of COVID 19, with the increased presentation of intracardiac thrombi. **Material.** This is an observational, cross-sectional, retrospective study, with review of cases in electronic and physical files, starting in March 2020, and ending in May 2022, including patients with intracardiac thrombi during the COVID 19 pandemic, in our institution. Descriptive data were reported as percentages, ranges, and means. **Results.** A total of 12 patients, with age range between 20 to 46 years, mean of 34.5 years, of which 6 women (50%) and 6 men (50%). As background, 6 patients presented symptomatic COVID 19 and positive test (50%), none vaccinated prior to the onset of symptoms. Chronic kidney disease was identified in 9 patients (75%), 8 with a Mahurkar catheter; 7 required removal of the Mahurkar catheter during surgery. Of the remaining 25% (n=3), 1 female patient presented HELLP syndrome, episodes of deep vein thrombosis and pulmonary thromboembolism; another female presented thrombi attached to the dual-chamber pacemaker requiring removal, without bacterial growth in the culture, and another only with a history of diabetes mellitus. All presented intracardiac thrombus were at the level of the right atrium. **Conclusions.** There is a strong relationship between the history of COVID 19 and the presentation of intracardiac thrombi, as well as an increased incidence in patients with risk factors, mainly chronic kidney disease present in 75% of cases with the presence of a Mahurkar catheter.

Key words: Chronic kidney disease; COVID 19; Intracardiac thrombus; Mahurkar catheter, Post-covid thrombi.

Objetivo. Buscar la relación en pacientes con antecedente COVID 19, con el aumento de presentación de trombos intracardíacos. **Material.** Este es un estudio observacional, transversal, retrospectivo, con revisión de casos en expediente electrónico y físico, con fecha de inicio en Marzo del 2020, y conclusión Mayo 2022, incluyéndose pacientes con trombos intracardíacos durante la pandemia del COVID 19, del centro médico del Bajío León, Guanajuato, México. Los datos descriptivos fueron reportados como porcentaje, rangos y medias. **Resultados.** Un total de 12 pacientes, con un rango de edad de 20 hasta 46 años, con una media de: 34.5 años, de los cuales 6 mujeres (50%) y 6 hombres (50%). Como antecedente 6 pacientes presentaron COVID 19 sintomático y prueba positiva (50%), ninguno estaba vacunado previo al inicio de los síntomas. Se identificó insuficiencia renal crónica (IRC) en 9 pacientes (75%), 8 con catéter mahurkar; 7 requirieron el retiro del catéter Mahurkar durante la cirugía. Del 25% restante (n=3), 1 paciente femenino presentó síndrome de HELLP, episodios de trombosis venosa profunda y tromboembolia pulmonar; otra paciente presentó trombos adosados al marcapasos bicameral requiriendo su retiro, sin crecimiento bacteriano en el cultivo, y otra solo con antecedente de diabetes mellitus. Todos presentaron trombo intracardíaco a nivel de la aurícula derecha. **Conclusiones.** Existe una fuerte relación entre el antecedente de COVID 19 y la presentación de trombos intracardíacos, así como aumento de incidencia en pacientes con factores de riesgo, principalmente enfermedad renal crónica presente en el 75% de los casos con presencia de catéter Mahurkar.

Palabras clave: Insuficiencia renal crónica; COVID 19; Trombo intracardíaco; Catéter Mahurkar; Trombo pos-covid

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On January 3, 2020, scientists from the National Institute for Viral Disease Control and Prevention identified the first complete genome of the new coronavirus (2019-nCoV) in samples of bronchoalve-

olar lavage fluid from a patient in Wuhan, China [1]. The coronavirus is a positive-stranded RNA virus belonging to the order nidovirales, family coronaviridae, and subfamily orthocoronavirinae [2]. The disease caused by the new 2019 coronavirus has posed an unprecedented problem in global health systems. The incubation period is between 2 to 14 days, with an average of 5 days. The most frequent symptom is fever, also observing dry cough, dyspnea, headache, fatigue, anorexia, myalgia, arthralgia [3]. Although originally believed to be a syndrome characterized by acute lung injury, respiratory failure, and death, it is now apparent that severe COVID 19 disease is further characterized by exuberant cytokine elevation, endothelial inflammation, microvascular thrombosis, and vascular multiorgan failure [4].

COVID-19-associated coagulopathy can cause various thromboembolic complications, especially in critically ill patients, bearing in mind Virchow's triad with endothelial injury, stasis, and a hypercoagulable state. Endothelial injury is secondary to the direct invasion of endothelial cells by SARS Cov 2, these cells have a high number of angiotensin-converting enzyme II receptors, the site through which the virus enters [5]. There is release of cytokines such as interleukin 6, acute phase reactants, and activation of alternate pathways of complement, which leads to further endothelial injury [6]. Stasis is due to immobilization of patients, especially those critically ill. In patients with COVID-19, the virus has been shown to have the ability to trigger a cycle of inflammation and thrombosis through angiotensin-converting enzyme 2 receptors located on the surface of the alveoli. Angiotensin-converting enzyme 2 is expressed in the alveolar epithelium of the lung, enterocytes of the small intestine, and vascular endothelium [7.]

Although the mechanism of coagulopathy has not been precisely established, it is known that viral infections induce a systemic inflammatory response accompanied by a cytokine storm, which causes an alteration in the balance between procoagulant and anticoagulant mechanisms, causing endothelial dysfunction, elevation of von Willebrand factor and tissue factor, platelet stimulation, and alterations in fibrinolysis, culminating in the generation of fibrin at the vascular level [8].

The hallmark of COVID-19 is the presence of platelet and fibrin thrombi of small vessels and megakaryocytes in all major organs including the heart, lungs, kidneys, liver, and mesenteric fat [9]. Right heart thrombosis is rare and life-threatening, with a reported mortality rate of almost 100% if left untreated [10]. The European Echocardiography Working Group classified right atrial thrombi into 3 groups; type A, thrombus in transit, characterized by being large, freely moving and originating from the deep venous system; type B, thrombus in situ, small clots attached to atrial wall or intracardiac device; and type C, mobile thrombi in situ, which have a stalk and a thin zone that attaches to the atrial wall, similar to atrial myxoma [11].

The risk of embolization and prognosis are variable according to the type. Mortality of type A thrombi is 28% to 44% [12]. Although the prevalence of type B thrombi is unknown,

they have better outcomes than type A thrombi [13]. The use of thrombolytic agents in type B thrombi has been previously advised because they can dissolve the adherent area and promote distal embolism of these organized thrombi [14]. In contrast to type A thrombi, favorable hospital survival was reported when treated with thrombolytics [15]. Thrombolytics can save lives in patients with acute pulmonary embolism complicated by a type A thrombus. Because distal spread of type A thrombi occurs early, thrombolytics are a mainstay of treatment, particularly in centers without immediate access to heart surgery [16].

Treatment decreases mortality three to four times. Treatment options include anticoagulation, thrombolysis, and surgical thrombectomy/embolectomy [17]. Meta-analyses have reported that thrombolytic and surgical options have better outcomes. However, there is no definitive treatment algorithm to follow [18].

Therefore, the objective of the study is to verify if there is a statistically significant relationship in the development of intracardiac thrombi in times of the COVID 19 pandemic, in patients with a history of contagion, and to identify which are the risk factors in patients favoring to occur more frequently.

MATERIAL

This is an observational, cross-sectional, retrospective study, with review of cases through electronic and physical files, taking March 2020 as the start date, and May 2022 as the end date, in which included patients diagnosed with intracardiac thrombi during the COVID 19 pandemic, who were operated on by the cardiothoracic surgery department of the Centro Médico del Bajío UMAE T1 León, Guanajuato, México.

The following data collection variables were included: age, gender, weight, height, body surface area, cardiopulmonary bypass time, aortic clamping time, use of blood components, blood group, history of COVID 19, history of COVID 19 vaccination, chronic renal failure, echocardiographic findings, use of mahurkar catheter, germ isolated in thrombus culture, macroscopic findings of surgery. All our information was collected from our physical and digital archive; descriptive data was reported as percentages, ranges, and means.

RESULTS

A total of 12 patients, diagnosed with intracardiac thrombosis, all older than 18 years, who underwent surgery, with an age range of 20 to 46 years, with a mean of: 34.5 years, of which 6 were women (50 %) and 6 were men (50%), weight from 53 kg to 93 kg, with a mean of 67.15 kg, with a body surface area calculated with the Mosteller formula with results from 1.52 to 2.07, with a mean of 1.72 m².

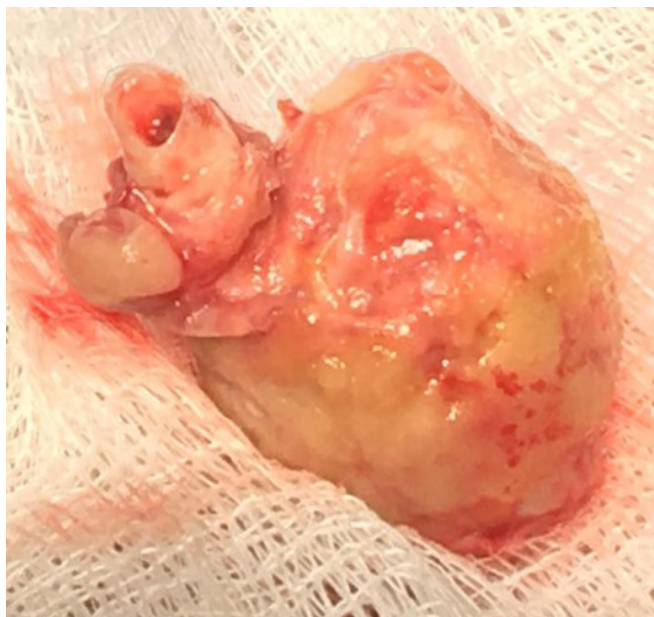


Figure 1. Intraatrial right thrombus in a patient with a Mahurkar catheter.

As background, 6 patients had a history of symptomatic COVID 19 and with a positive test (50%), of which none had been vaccinated prior to the onset of symptoms. Chronic kidney disease was identified in 9 patients (75%), 8 had a mahurkar catheter; 7 patients required removal of the mahur-

kar catheter during surgery due to intracardiac thrombi; 2 patients reported bacterial growth: E. Coli and S. Epidermis. Of the remaining 25% (n=3), 1 female patient presented with HELLP syndrome, episodes of deep vein thrombosis, and pulmonary embolism; another female presented thrombi attached to the dual-chamber pacemaker at the level of the right atrium, requiring its removal, without bacterial growth in the culture, and another only with a history of diabetes mellitus. All cases of the patients presented intracardiac thrombus at the level of the right atrium (Fig. 1).

In the preoperative echocardiogram, measurements of intracardiac thrombi ranging from 16 x 16 mm to 49 x 33 mm were found. Regarding the most common location of the thrombus, it was observed in the lateral wall of the right atrium (RA) in 33% (n=4), of mixed type in 33% (n=4), of which 2 included inferior vena cava (IVC) and right atrium, and 2 compromised sinus venosus and right atrium, in the superior vena cava (SVC) in 16.6% (n=2), near the ostium of the coronary sinus venosus 8.3% (n=1), followed by inferior vena cava 8.3% (n=1) (Fig. 2).

During operation, cardiopulmonary bypass was from 19 to 63 minutes (mean, 30.8 minutes; the aortic-cross clamping ranged from 20 to 55 min (mean 37.6 minutes). Only 1 patient required tricuspid valve repair with a ring. The intraoperative bleeding was between 120 and 1300 mL (mean 503 mL). Red blood cells transfusion was from 2 to 6 red blood cell packages (mean, 3.08). Fresh frozen plasma transfusion was from 0 to 5 (mean, 2.92). Platelet apheresis transfusion

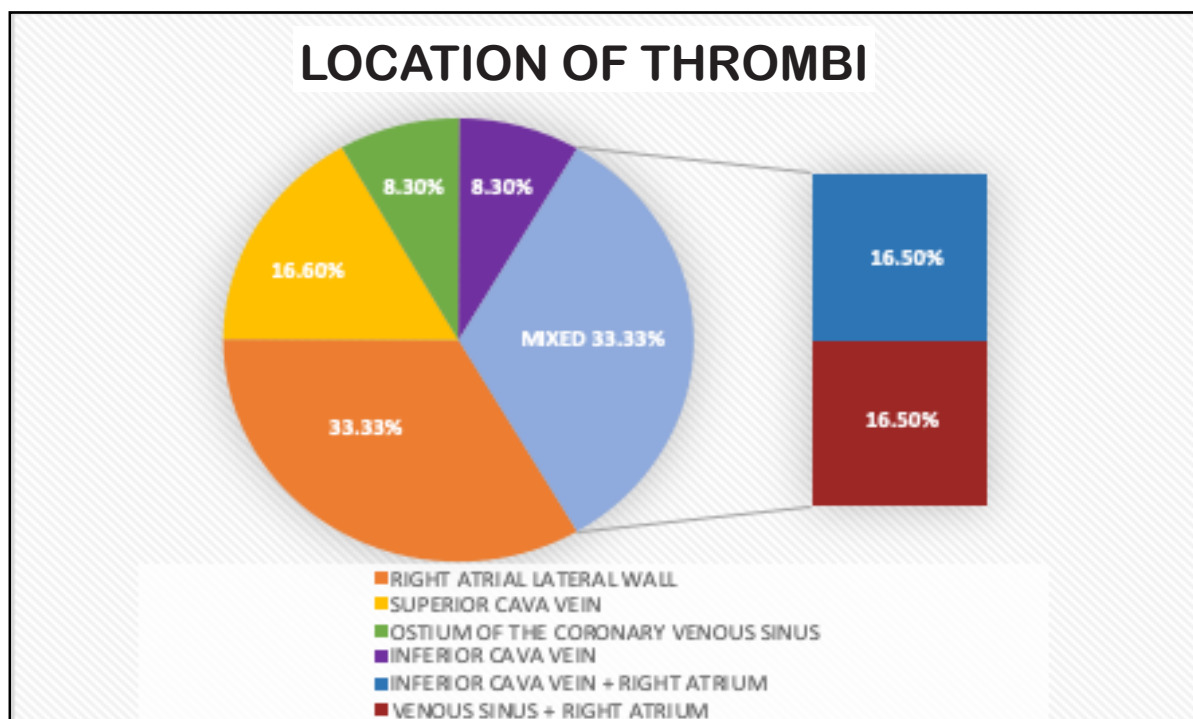


Figure 2. Distribution and location of intracardiac thrombi

was from 0 to 2 (mean, 0.92). Related to blood group, group B+ was found in 33% (n=4), group A+ in 33% (n=4), O+ in 25% (n=3) and AB- in 8% (n=1) of the 12 patients. Hospital mortality was 0% (Table 1).

DISCUSSION

Intracardiac thrombi are generally diagnosed after episodes of persistent fever, with a history of hypercoagulable states, dyspnea, and general condition, which make the patient come to the emergency room for evaluation, with the arrival of times due to COVID 19 pandemic, an increase in cases was observed, which required surgical thrombectomy.

A literature association has been identified between the spread of COVID 19, with the development of hypercoagulation states; Our largest number of patients with intracavitary thrombosis occurred in renal patients, and could be caused by the handling of devices such as mahurkar-type catheters. However, when combined with the proinflammatory state of COVID 19, we have observed that the incidence increases.

According to the classification of the European echocardiography working group mentioned above, type B, thrombus in situ, which is related to intracardiac devices (in our study population, the use of a mahurkar catheter), the mechanism of thrombus formation associated with catheters is secondary to repeated mechanical trauma to the atrial wall caused by movement of the catheter tip secondary to movement of the heart, this causes endothelial damage, causes activation of the coagulation cascade, platelet aggregation, and thrombus formation at the point of contact, this added to the state of hypercoagulation secondary to COVID 19 infection, makes it more likely to develop intracardiac thrombi.

In the study reported by Anthi et al, a transesophageal echocardiogram shows a thrombus in the right atrium in a patient admitted to the ICU after infection by COVID 19, being managed only with therapeutic dose anticoagulation, after treatment the echocardiogram transesophageal did not reveal signs of residual thrombus in the right atrium and the patient had a significant improvement, however the size of the thrombus is not reported in the article, but an adequate response to anticoagulant treatment is observed [19].

In a series by Tran et al. they reported a failure rate with anticoagulation and thrombolysis of 27.3% and 33.3%, respectively. In addition, 42.9% of these patients required surgical thrombectomy as primary or rescue treatment. The authors emphasize the thrombectomy as first-line therapy in patients with a thrombus greater than 2 cm or the presence of infection/sepsis [20]. By contrast, Stavroulopoulos et al. recommend anticoagulation as first-line therapy and surgery reserved for thrombus larger than 6 cm or after failure in alternative therapies. The mortality in the surgical thrombectomy group was lower when compared to the anticoagulation group (13% vs 16.2%) with an average size of surgically approached thrombus of 3.5 cm [21].

Table 1. Preoperative/intraoperative characteristics

Variable	Value
Cases (n)	12
Age (years)	34.5
Gender (male:female in %)	50:50
Weight (kg)	67.15
Body surface area (m ²)	1.72
COVID19 + (%)	50
Vaccines applied prior to infection (%)	0
Chronic kidney disease (%)	75
Cardiopulmonary bypass (minutes)	30.8
Aortic clamping time (minutes)	37.6
Intraoperative bleeding (mL)	503
Intraoperative erythrocyte packages	3.08
Intraoperative fresh frozen plasmas	2.92
Intraoperative platelet apheresis	0.92
Blood group B+ (%)	30
Blood group A+ (%)	30
Blood group O+ (%)	25
Blood group AB- (%)	8

In the study by Hamid et al., 3 cases of intracardiac thrombi in children after COVID 19 infection were reported, considering these findings as unexpected due to not having a history of heart disease or coagulopathy. In all 3 cases, large thrombi were reported in left cavities, contrarily to what was observed in our investigation in which all patients presented it in the right cavity [22].

In conclusion, we observed that the use of devices that require vascular access to the right atrium (catheters or pacemaker electrodes) was the main risk factor for developing a thrombus in the right atrium, associated with persistent chronic disease and/or a state of hypercoagulability like COVID 19. During the course of the pandemic, we observed an increase in the incidence of cases with thrombus in the right atrium, in patients with a history of COVID 19 and pre-existing chronic disease. Due to the lack of diagnostic scrutiny at the beginning of the pandemic, and due to ignorance of the clinic as well as complications secondary to COVID 19, it was difficult to have a previous diagnostic test. A+ and B+ groups were found as predominant blood groups, and one case of negative group. In our study, the main risk factor for developing a thrombus in the right atrium was chronic kidney disease in renal replacement therapy with hemodialysis and Mahurkar catheter carriers. In non-renal patients, it was the female gender with a history of diabetes mellitus, pacemaker lead and/or history of hypercoagulable states (HELLP Syndrome).

In the absence of evidence-based guidelines for the management of right atrial thrombi, the treatment should be individualized for each patient, based on thrombus type, size, location, hemodynamic status, presence or absence of associated pulmonary emboli, and associated infection. We rec-

ommend a close surveillance in patients with chronic kidney disease, performing screening to identify intracardiac thrombi in all patients with the use of devices that require vascular access to the right atrium for renal replacement therapy.

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