

COVID-19 and Coronary Stent Thrombosis: A Systematic Review of Literature

Pramod Theetha Kariyanna¹, Amog Jayarangaiah², Sushruth Das²,
Apoorva Jayarangaiah³, Ashkan Tadayoni⁴, Moro O. Salifu⁴, Isabel M. McFarlane^{4,*}

¹Division of Interventional Cardiology, Mount Sinai Heart, Icahn School of Medicine at Mount Sinai Morningside/Beth Israel Hospitals, New York City, NY-10025, U.S.A.

²Trinity School of Medicine, 925 Woodstock Road, Roswell, GA 30075, U.S.A.

³Department of Internal Medicine, Albert Einstein College of medicine/ Jacobi Medical Center, Bronx, NY 10461, U.S.A

⁴Department of Internal Medicine, State University of New York, Downstate Health Sciences University, Brooklyn, NY 11203, U.S.A.

*Corresponding author: Isabel.McFarlane@downstate.edu

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Abstract Coronavirus Disease-19 (COVID-19) is a worldwide pandemic and it has created many difficulties in providing medical care due to the various multi-organ disease manifestations caused by the virus. In this paper we explore cases of stent thrombosis which occurred in patients who were infected with COVID-19 and discuss its role in potentiating this complication through the variety of mechanisms in which it creates a prothrombotic state. Stent thrombosis is described as the thrombotic occlusion of a coronary stent. The incidence of this complication has decreased considerably (from 16% to 0.7%) since the advent of antiplatelet therapy and drug eluting stents. In this systematic review, 8 papers were found which detailed 11 patients who were infected with COVID-19 and suffered a stent thrombosis. Data from these cases were tabulated and analyzed. The ages of the patient's ranged from 49-81 years and quite interestingly the time between the time of stent placement and occurrence of stent thrombosis had great variation between patients, with some occurring within minutes of stent placement and others occurring in a stent that was placed many years ago. 91% of the patients had ST-segment elevation myocardial infarction (STEMI) for presentation of stent thrombosis and 9% had a non-ST segment myocardial infarction (NSTEMI) on presentation. Therapy mainly involved antiplatelet therapy and Percutaneous Coronary Angioplasty with new stent placement. Despite this mortality rate among the cases present was quite high at 45%, with some patients dying as a result of COVID-19 related complications. Through various literature reviews, we have found that COVID-19 contributes in creating a prothrombotic state through various inflammatory mediated mechanisms. This prothrombotic state is a major risk factor towards stent thrombosis and we recommend that physicians be aware of this potentially fatal complication in COVID-19 patients.

Keywords: COVID-19, coronary stent thrombosis, antiplatelets, percutaneous coronary intervention, acute myocardial infarction

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1. Introduction

Stent thrombosis is the thrombotic occlusion of a coronary stent. It is a complication associated with stent placement in percutaneous coronary intervention (PCI) [1]. It is an acute process that typically results in acute coronary syndrome (ACS) and has high rates of morbidity and mortality. In the early advent of PCI, stent thrombosis occurred at an incidence as high as 16% [2] in some studies, however, with the current practice of dual antiplatelet therapy, this incidence has significantly decreased to 0.7% per year [3,4]. PCI has become the

cornerstone of treatment in many cases of ACS, however, providing care in these present days can be quite difficult owing to the Coronavirus Disease-19 (COVID-19) pandemic. It has been affecting the globe for well over the past year and has changed many aspects of medical care. COVID-19 has been noted to have a broad range of complications across many organ systems, making it a challenge to provide care, especially in the realms of cardiology, given the multi-faceted problems that can arise. One notable phenomena of COVID-19 is the pro-thrombotic state rendered by a variety of physiological responses to the virus [5]. In this paper we aim to discuss how this pro-thrombotic state may have a potential role in regards to PCI and the event of stent thrombosis. We

hereby present a systematic review of acute stent thrombosis in COVID-19 patients.

2. Methods

A comprehensive computer-based literature search of English language studies was performed, using PubMed, Google Scholar, CINAHL, Cochrane CENTRAL, and Web of Science databases, to identify the relevant literature. Our search keywords included COVID-19, Coronavirus and stent thrombosis were used to determine cases of patients with COVID-19 infection who experienced stent thrombosis. This scoping study includes

articles from throughout the year 2020. Relevant cases were selected by reviewing the reference list of each article. All non-English and non-human studies were excluded. Furthermore, all meta-analysis, review articles, and abstracts were excluded from this study. Data regarding demographic information, the time from when the stent was placed and thrombosis occurred, angiogram findings, the vessel affected, type of stent used, and management methods and outcome were reviewed and analyzed.

3. Results

Table 1. Clinical characteristics of patients with COVID-19 infection and stent thrombosis

| Author/Case | Age | Time from stent placement to thrombosis | CVS Risk Factors | EKG | Vessel where stent thrombosis occurred |
|--------------------------------|-----|---|------------------|--|--|
| 2020, Lacour et al. [6] | 68 | 2 hours | DM | ST elevations in the anterior leads | Proximal LAD |
| 2020, Prieto-Lobato et al. [7] | 49 | 30 minutes | - | ST elevations in the lateral leads | Circumflex artery |
| 2020, Prieto-Lobato et al [7] | 71 | 13 years (PCI done in 2007) | - | ST elevations in inferior leads | Right coronary artery |
| 2020, Prieto-Lobato et al [7] | 86 | 2 years (PCI done in 2018) | - | ST elevations in anterior leads | LAD |
| 2020, Prieto-Lobato et al [7] | 85 | 15 years (DES placed in 2005) | - | ST elevations in anterior leads | LAD |
| 2020, Choudhary et al. [8] | 64 | 5 days | - | acute inferior STEMI. complete heart block | RCA |
| 2020, Zaher et al. [9] | 51 | Within minutes | HTN,DM | ST elevations in III, aVF, V5 and V6 | LCX |
| 2020, Hinterseer et al. [10] | 65 | 2 years | HTN, DM, HLD | ST-elevation in aVR with RBBB | LAD |
| 2020, Ayan et al. [11] | 64 | 3 days | HTN | ST segment depressions in lateral leads | Second obtuse marginal artery |
| 2020, Antuña et al. [12] | 81 | 3 months | HTN | ST-elevations in the anterior leads | LAD |
| 2020, Galleazzi et al [13] | 79 | 2 years | - | ST-elevations in the inferior leads | RCA |

HTN Hypertension DM Diabetes Mellitus HLD Hyperlipidemia.

Table 2. Management and patient outcomes of COVID-19 and stent thrombosis

| Author/Case | Anti-Platelet Therapy | Anti-coagulation Therapy | Thrombectomy | Management of stent thrombosis | Outcome |
|---|-------------------------------|--------------------------|--------------|--------------------------------|---|
| 2020, Lacour et al. [6] | ASA, Ticagrelor | Heparin | Y | PTCA | Death. Recurrent stent thrombosis 36 hrs. later. Reperfusion therapy with anticoagulation and thrombectomy failed |
| 2020, Prieto-Lobato et al. [7] (49y/o) | ASA, Ticagrelor, Tirofiban | - | - | Intra-coronary Tirofiban | Survived; Discharged 4 days later |
| 2020, Prieto-Lobato et al. [7] (71 y/o) | Tirofiban | - | Y | Tirofiban and 2 DES | Survived; Discharged without complications |
| 2020, Prieto-Lobato et al. [7] (86 y/o) | - | - | - | DES placement | Survived; Discharged 5 days later |
| 2020, Prieto-Lobato et al. [7] (85 y/o) | ASA, Prasugrel and Tirofiban | - | Y | PTCA | Survived; Discharged 10 days later |
| 2020, Choudhary et al. [8] | ASA and Plavix | - | - | - | Death: Expired before any intervention. |
| 2020, Zaher et al. [9] | ASA and Ticagrelor | Heparin | - | - | Death: Patient had died soon after thrombosis occurred |
| 2020, Hinterseer et al. [10] | ASA, Prasugrel and Tirofiban | - | - | DES placement | Death: Due to Multi-organ failure as a result of COVID-19 related complications |
| 2020, Ayan et al.[11] | ASA and Plavix | Heparin | - | DES placement | Survived; Discharged 10 days later |
| 2020, Antuña et al. [12] | ASA, Tirofiban and Ticagrelor | - | Y | PTCA | Survived; Discharged 2 days later |
| 2020, Galleazzi et al. [13] | ASA and Plavix | - | - | DES | Death. Despite successful reperfusion. Acute respiratory distress developed few hours later |

ASA Aspirin DES Drug eluting stent PTCA Percutaneous Coronary Angioplasty.

A total of 8 papers were found that featured 11 cases [6-13]. The ages of the patient's ranged from 49-81, with a mean age of 69.36. In addition, 100% of the patients were male. The prevalence of cardiovascular risk factors that were mentioned among the patients is as follows: hypertension, 36%; diabetes mellitus, 18%; and hyperlipidemia, 9%. Ten (91%) patients had ST-segment elevation myocardial infarction (STEMI) findings on electrocardiogram (EKG) while one (9%) had non ST-segment myocardial infarction (NSTEMI) as part of the presentation of stent thrombosis. Three (27%) patients suffered stent thrombosis the same day of PCI procedure, three (27%) within 90 days of PCI procedure and five (45%) sustained stent thrombosis on the PCI performed more than two years before. Management of the stent thrombosis mainly consisted of thrombectomy (36%), Percutaneous Coronary Angioplasty (PTCA) (27%) and placement of a new drug eluting stent (45%), however 2 (28%) of the patients passed away before any therapeutic interventions could be taken for the stent thrombosis. Unfortunately mortality rate in this series of cases remained high at 5 (45%) patients. All of the aforementioned information has been obtained for each patient and tabulated in [Table 1] and [Table 2].

4. Discussion

COVID-19 has a well-documented effect of precipitating thrombotic events that manifest in a large variety of ways that include DIC, thrombotic microangiopathy and venous thrombosis leading to embolic events especially in the pulmonary vasculature [14,15]. COVID-19 has also been shown to result in widespread systemic inflammation most notably through the action of neutrophils and monocytes [16]. The activation of these cells also result in a widespread release of cytokines, such as; IL-6, IL-2R, IL-10, and tumor necrosis factor α (TNF- α), all of which are well described in their function to potentiate a pro-thrombotic state [17]. In addition, COVID-19 patients display markedly increased levels of the cytokines, and this acute release of large amounts of cytokines is often referred to as a "cytokine storm". The dual clinical phenomena of widespread inflammation and thrombotic events in the setting of COVID-19 infection can be linked together through the term "immuno-thrombosis", which was coined to highlight the interwoven relationship between the immune system and the coagulation system, especially in the setting of acute infection [5]. However, besides widespread inflammation, COVID-19 has also been documented to create a pro-thrombotic environment through other means such as (1) release of tissue factor (2) the downregulation of anticoagulant mechanisms (3) NETosis (4) complement mediated and (5) viral mediated mechanisms [5].

Stent thrombosis occurrence has decreased since the advent of antiplatelet therapy and drug eluting stents [3,4]. However, the patients in these case reports were on antiplatelets medications. With these findings alongside the knowledge that COVID-19 infection creates a prothrombotic environment in the body, we can hypothesize that the risk of thrombosis may even

overpower the protective effects offered by antiplatelet therapy and modern stents. It is also interesting to note that stent thrombosis in these cases had occurred in both newly placed stents as well as stents placed several years ago (with the oldest stent being placed 15 years ago). It is worth noting that arterial thrombosis in COVID-19 is not limited to the coronary arteries; there have been reports of this occurring at various sites such as the aorta and the numerous arteries in the lower limbs that can often precipitate acute limb ischemia in many patients [18]. Lastly the biggest concern of stent thrombosis in COVID-19 patients remains the high rate of mortality. This systematic review found that 45% had died during hospitalization, and in addition to this, we must consider that a COVID-19 infection also carries its own risk of mortality, as we can see in this case review two of the patients died due to multi-organ failure and acute respiratory distress.

In the setting of COVID-19 infection and its associated prothrombotic state, providers should maintain a high index of suspicion in any COVID-19 positive patients and coronary artery disease who underwent PCI with stent placement who present with STEMI. COVID-19 has created various challenges in many fields of care. There are many reports of cardiovascular complications of COVID-19 such as COVID-19 associated myocarditis [19], ST-elevation myocardial infarction [20] and even Apical Takotsubo Cardiomyopathy [21]. To our knowledge, this is the first paper which describes yet another potential, fatal cardiovascular complication of COVID-19.

5. Limitations

This scoping study is a review of the published literature reporting an instance of stent thrombosis in the setting of COVID-19 infection, selection bias and small sample size are limiting factors. Lastly, all referenced studies were either case reports or case series without control groups to enhance the accuracy of the comparison.

6. Conclusion

Stent thrombosis is a rare complication and potentially fatal complication of PCI therapy. Its incidence has been reduced significantly with the use of anti-platelet medication. COVID-19 is a likely risk factor in inducing stent thrombosis due to its propensity to create a pro-thrombotic state. Therefore, in COVID-19 positive patients, clinical suspicion for this complication should be kept in mind for patients with distant or recent coronary stent placement who develop signs and symptoms that point to myocardial infarction.

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