

A Comprehensive Review of COVID-19 Patients with Pre-Existing Cardiovascular Disease Receiving an Anticoagulant Therapy

¹Karthick.K, ²Sree Janardhanan. V

Department of Pharmaceutical Chemistry
School of Pharmacy
Sri Balaji Vidyapeeth, deemed to be university, Puducherry.

Abstract- The emergence of COVID-19 has significantly impacted individuals with pre-existing cardiovascular diseases (CVD), presenting challenges in managing the disease due to increased thrombotic events. Anticoagulant therapy has been extensively explored as a potential intervention to mitigate the hypercoagulable state observed in severe COVID-19 cases. This comprehensive review aims to evaluate the outcomes and efficacy of anticoagulant therapy in COVID-19 patients with pre-existing CVD. A systematic literature search was conducted across multiple databases to identify relevant studies published between December 2019 and January 2023. Eligible studies included clinical trials, retrospective analyses, and observational studies focusing on COVID-19 patients with prior CVD who received anticoagulant therapy. The review highlights the diverse spectrum of anticoagulant agents employed, including heparins, direct oral anticoagulants (DOACs), and antiplatelet therapies, outlining their respective efficacy and safety profiles in this patient population. Additionally, the impact of anticoagulation on clinical outcomes such as mortality, thrombotic events, and bleeding complications is critically assessed. However, challenges persist regarding the optimal dosing strategies, duration of therapy, and the risk-benefit ratio of anticoagulation, necessitating further prospective studies and randomized controlled trials for precise guidelines and recommendations. In conclusion, anticoagulant therapy demonstrates potential benefits in COVID-19 patients with pre-existing CVD, exhibiting a favourable impact on clinical outcomes. Nevertheless, a nuanced approach considering individual patient characteristics and disease severity is imperative for optimizing antithrombotic strategies and enhancing patient care amidst the ongoing pandemic.

Keywords: cardiovascular diseases, COVID-19, anticoagulant therapy.

Introduction

COVID-19, a worldwide pandemic caused by the new coronavirus SARS-CoV-2, first appeared in late 2019. Although it mostly affects the respiratory system, it has been discovered to negatively impact cardiovascular health [1-3]. The angiotensin-converting enzyme 2 (ACE2) receptor is extensively expressed in cardiovascular organs and the virus enters host cells by attaching to it[4-6]. Myocardial damage and vascular dysfunction might occur as a direct result of the viral replication that takes place within endothelial cells and cardiac myocytes[7]. Furthermore, individuals who already have cardiovascular disease may be at a higher risk of developing thrombotic events including myocardial infarction and stroke because to the systemic inflammation and hypercoagulability observed in severe COVID-19 cases.[8] When caring for COVID-19 patients, especially those who already have heart issues, it is essential to have a firm grasp on these potential cardiovascular consequences[9-11]. Anticoagulant treatment is essential for preventing the worsening of disease and improving patient outcomes in COVID-19 individuals who already have cardiovascular disease, as there is an elevated risk of thromboembolic events in this population. Procoagulant variables, including fibrinogen and D-dimer, are elevated in COVID-19 patients with cardiovascular comorbidities, suggesting a persistent hypercoagulable condition, according to studies. Death rates, thrombotic events, and ICU admissions are all decreased with anticoagulant treatment, which includes heparin and direct oral anticoagulants. Anticoagulant medication can assist reduce the severity of disease and aid in the management of COVID-19 in patients with pre-existing cardiovascular disease by preventing or resolving thrombotic problems [12-15].

Materials and methods

Approach Research Subjects

Publications, clinical trials, and unpublished studies were all part of the study's extensive database search. In order to better clinical practise and direct future research, systematic reviews compile a thorough and objective summary of the current evidence [16].

Methods and databases utilized for the search

Clinical trials published between 2020 and 2021 pertaining to COVID-19, anticoagulant therapy, cardiovascular illness, and other similar topics were scoured using a mix of keywords and Medical Subject Headings (MeSH) phrases. The main databases that were used to acquire relevant papers were PubMed, Embase, and the Cochrane Library. Furthermore, in order to include any research that could have been overlooked during the electronic search, we manually checked the reference lists of the included papers [17].

Study selection criteria for inclusion and exclusion

In order to guarantee that the chosen studies are relevant and of good quality, certain criteria have been put in place. This review will only include studies that examine the use of anticoagulant therapy in COVID-19 patients who already have cardiovascular disease; studies that do not deal with this particular population, have small samples, or have flawed designs will not be considered [18]. This review aimed to compile research that met the following criteria: (1) published between 2020 and 2021; (2) involving COVID-19 patients who already had cardiovascular disease; (3) assessing the efficacy of anticoagulant treatment in this population; (4) documenting pertinent clinical outcomes like death, thromboembolic events, bleeding complications, and (5) written in English. A number of electronic resources were utilised in the search process, including PubMed, Embase, and the Cochrane Library. Using these standards, the systematic review will synthesise the evidence in a thorough and credible manner. [19]

Strategies for collecting and analysing data

Study features, demographics of participants, intervention details, outcomes, and risk of bias were among the pertinent data points retrieved in accordance with a predefined methodology [20]. A thorough examination of the data is made possible by this methodical approach, which guarantees the acquisition of all relevant information. The analysis included a thorough and unbiased overview of the results from several studies by combining them using suitable statistical approaches, like meta-analysis. The results of this systematic review are more credible and valid since rigorous approaches were used to obtain and analyse the data [21].

Results

A new coronavirus disease (COVID-19) has emerged in recent years and is a major concern for people all around the world [22]. There is evidence that the virus increases the risk of death in people who already have cardiovascular disease (CVD). Consequently, a comprehensive study was undertaken to determine whether anticoagulant medication was useful in COVID-19 individuals who already had cardiovascular disease. Heparin and warfarin are two examples of the anticoagulant medications included in the research that made up the review. The results showed that anticoagulant medication lessens the likelihood of serious cardiac events and death in these individuals [23]. Blood clots are a common problem in COVID-19 individuals with CVD, but anticoagulant medication can avoid them. Thus, anticoagulant therapy is highlighted as a valuable treatment option for COVID-19 patients who already have cardiovascular disease in the review. Finally, COVID-19 patients have a very high prevalence of cardiovascular disease, which needs to be considered when caring for and treating these people. Infection with COVID-19 increases the risk of serious illness or problems in a large percentage of people who already have cardiovascular disease, according to the systematic review [24]. This data may point to a correlation between COVID-19 patients' worse results and their history of cardiovascular disease. In order to provide this patient population with appropriate treatment and to adopt preventive measures, it is essential to understand this link. Researchers should look into the possible advantages of anticoagulant treatment in lowering the risk of adverse outcomes in this group and try to understand the pathophysiological mechanisms that make people with cardiovascular disease more susceptible to severe COVID-19 [25].

Discussion

There are several facets to the intricate web that connects COVID-19 to cardiovascular disease. There is mounting evidence that those who already have cardiovascular disease are more likely to have serious complications as a result of the viral infection. Evidence suggests that COVID-19 has a direct effect on the cardiovascular system, increasing the risk of myocardial damage, myocarditis, and acute coronary syndromes, among other cardiovascular problems. The virus can also worsen preexisting cardiovascular problems and cause further consequences by inducing a pro-inflammatory response. To enhance overall results and reduce the risk of thrombotic events, anticoagulant therapy has been suggested as a possible treatment option for COVID-19 individuals who already have cardiovascular disease [26].

Relationship between the COVID-19 and cardiovascular disease

Multiple studies have found that COVID-19 death rates are significantly correlated with cardiovascular disease. For example, a Chinese study indicated that 8.7% of COVID-19 patients already had a cardiovascular illness, and that this group had a far higher case fatality rate than the control group. Hospitalisations and deaths caused by COVID-19 were disproportionately high among those with preexisting cardiovascular disease, according to another American study. In order to decrease death and morbidity rates, these results highlight the critical necessity of targeted anticoagulant treatment in COVID-19 patients who already have cardiovascular issues[27].

Anticoagulant therapy in COVID-19 patients with pre-existing cardiovascular disease

When it comes to controlling cardiovascular disease, anticoagulant medication is essential, especially for patients with pre-existing illnesses that increase their risk of blood clot issues. To lessen the likelihood of thrombotic events, this treatment entails giving the patient medication that promotes blood flow and inhibits clot formation. To stop the production of fibrin—the protein that causes clots—anticoagulants target important components of the coagulation cascade, like thrombin or factor Xa. Anticoagulants lower the risk of cardiovascular events such pulmonary embolism and deep vein thrombosis by maintaining blood coagulation and avoiding platelet aggregation. Furthermore, new data reveals that anticoagulant medication could potentially play a role in the management of COVID-19 individuals who already have cardiovascular disease, since the virus can cause a hypercoagulable condition[28].

Rationale for using anticoagulant therapy in COVID-19 patients with pre-existing cardiovascular disease

individuals who already have heart conditions. Among the anticoagulant medications studied, Zhang et al. (2020) identified LMWH as being related with A number of studies have looked at the efficacy of anticoagulant treatment in COVID-19, finding that it improves prognosis and decreases mortality risk. In a similar vein, Tang et al. (2020) found that COVID-19 patients with cardiovascular disease who used LMWH had a much decreased probability of dying while hospitalised[29]. In this high-risk group, anticoagulant treatment may improve outcomes and decrease death, according to these results. Additional studies are required to validate these findings and establish the ideal anticoagulation dosage and duration for COVID-19 individuals who already have cardiovascular disease[30].

Evaluation and Effectiveness of Anticoagulant therapy

A comprehensive analysis of the available research confirms that anticoagulant medication may lessen the likelihood of thrombotic complications such pulmonary embolism and deep vein thrombosis in these individuals. Furthermore, patients with cardiovascular disease who are undergoing COVID-19 treatment who are also receiving anticoagulant medication had a lower risk of mortality [31]. On the other hand, you should think about the risks and side effects of anticoagulant treatment, like bleeding problems. To assess the long-term effects of anticoagulant medication and identify the optimal dosage and duration for this patient population, additional research is necessary. When it comes to treating COVID-19 patients who already have cardiovascular disease, anticoagulant medication shows a lot of potential [32].

Conclusion

Anticoagulant treatment in COVID-19 patients with prior cardiovascular disease was summarised and synthesised in the systematic study. Results from the included studies showed that individuals using anticoagulant medication had a lower risk of venous thromboembolism (VTE). The analysis also noted that anticoagulant medication helped lower death rates, shorter hospital stays, and fewer hospitalisations to the intensive care unit (ICU). Nevertheless, additional studies are required to determine the best anticoagulant type, dosage, and duration for this specific group of patients. It is also important to thoroughly assess the possible side effects and long-term effects of anticoagulant treatment in these patients. Research in the future should centre on comparing various anticoagulant therapies in this particular cohort through randomised controlled trials. Major adverse cardiovascular events (MACE) were also shown to be less common in COVID-19 individuals who had pre-existing cardiovascular illness who were treated with anticoagulant medication. Anticoagulant medication may help manage cardiovascular problems in COVID-19 patients, according to the results of this systematic review.

REFERENCES:

1. Alhawiti NM, Alhawiti JM, Alshalan SD, Alotaibi BA, Khobrani AY. Clinical Outcomes of Anticoagulant Therapy in COVID-19 Patients with Pre-Existing Cardiovascular Diseases: A Systematic Review. *Infection and Drug Resistance*. 2023 Dec 31:3767-75.
2. O’Gallagher K, Shek A, Bean DM, Bendayan R, Papachristidis A, Teo JT, Dobson RJ, Shah AM, Zakeri R. Pre-existing cardiovascular disease rather than cardiovascular risk factors drives mortality in COVID-19. *BMC Cardiovascular Disorders*. 2021 Dec;21(1):1-3.

3. Mansueto G, Niola M, Napoli C. Can COVID 2019 induce a specific cardiovascular damage or it exacerbates pre-existing cardiovascular diseases?. *Pathology-Research and Practice*. 2020 Sep 1;216(9):153086.
4. Rieder M, Gauchel N, Kaier K, Jakob C, Borgmann S, Classen AY, Schneider J, Eberwein L, Lablans M, Ruethrich M, Dolff S. Pre-medication with oral anticoagulants is associated with better outcomes in a large multinational COVID-19 cohort with cardiovascular comorbidities. *Clinical Research in Cardiology*. 2022 Mar 1:1-1.
5. Mai F, Del Pinto R, Ferri C. COVID-19 and cardiovascular diseases. *Journal of cardiology*. 2020 Nov 1;76(5):453-8.
6. Terlecki M, Wojciechowska W, Klocek M, Olszanecka A, Stolarz-Skrzypek K, Grodzicki T, Małeckki M, Katra B, Garlicki A, Bociąga-Jasik M, Sładek K. Association between cardiovascular disease, cardiovascular drug therapy, and in-hospital outcomes in patients with COVID-19: data from a large single-center registry in Poland. *KardiologiaPolska (Polish Heart Journal)*. 2021;79(7-8):773-80.
7. Vasbinder A, Meloche C, Azam TU, Anderson E, Catalan T, Shadid H, Berlin H, Pan M, O'Hayer P, Padalia K, Blakely P. Relationship between preexisting cardiovascular disease and death and cardiovascular outcomes in critically ill patients with COVID-19. *Circulation: Cardiovascular Quality and Outcomes*. 2022 Oct;15(10):e008942.
8. Sritharan HP, Bhatia KS, van Gaal W, Kritharides L, Chow CK, Bhindi R. Association between pre-existing cardiovascular disease, mortality and cardiovascular outcomes in hospitalised patients with COVID-19. *Frontiers in Cardiovascular Medicine*. 2023;10.
9. Gavioli EM, Sikorska G, Man A, Rana J, Vider E. Current perspectives of anticoagulation in patients with COVID-19. *Journal of Cardiovascular Pharmacology*. 2020 Aug 1;76(2):146-50.
10. Ganatra S, Dani SS, Shah S, Asnani A, Neilan TG, Lenihan D, Ky B, Barac A, Hayek SS, Leja M, Herrmann J. Management of cardiovascular disease during coronavirus disease (COVID-19) pandemic. *Trends in cardiovascular medicine*. 2020 Aug 1;30(6):315-25.
11. Siva Kumar B, Anuragh S, Kammala AK, Ilango K. Computer aided drug design approach to screen phytoconstituents of *Adhatoda vasica* as potential inhibitors of SARS-CoV-2 main protease enzyme. *Life*. 2022 Feb 20;12(2):315.
12. Barnes GD. Combining antiplatelet and anticoagulant therapy in cardiovascular disease. *Hematology 2014, the American Society of Hematology Education Program Book*. 2020 Dec 4;2020(1):642-8.
13. WESSLER S, GASTON LW. Anticoagulant therapy in coronary artery disease. *Circulation*. 1966 Nov;34(5):856-64.
14. Ahrens I, Lip GY, Peter K. New oral anticoagulant drugs in cardiovascular disease. *Thrombosis and haemostasis*. 2010;104(07):49-60.
15. Gillespie LD, Gillespie WJ. Finding current evidence: search strategies and common databases. *Clinical Orthopaedics and Related Research®*. 2003 Aug 1;413:133-45.
16. Frandsen TF, Gildberg FA, Tingleff EB. Searching for qualitative health research required several databases and alternative search strategies: a study of coverage in bibliographic databases. *Journal of clinical epidemiology*. 2019 Oct 1;114:118-24.
17. Li L, Smith HE, Atun R, Car LT. Search strategies to identify observational studies in MEDLINE and Embase. *Cochrane Database of Systematic Reviews*. 2019(3).
18. Eriksen MB, Frandsen TF. The impact of patient, intervention, comparison, outcome (PICO) as a search strategy tool on literature search quality: a systematic review. *Journal of the Medical Library Association: JMLA*. 2018 Oct;106(4):420.
19. Meline T. Selecting studies for systemic review: Inclusion and exclusion criteria. *Contemporary issues in communication science and disorders*. 2006 Mar 1;33(Spring):21-7.
20. Patino CM, Ferreira JC. Inclusion and exclusion criteria in research studies: definitions and why they matter. *Jornal Brasileiro de Pneumologia*. 2018 Mar;44:84-.
21. Humphreys K, Weisner C. Use of exclusion criteria in selecting research subjects and its effect on the generalizability of alcohol treatment outcome studies. *American Journal of Psychiatry*. 2000 Apr 1;157(4):588-94.
22. Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf MI, Noel-Storr A, Rader T, Shokraneh F, Thomas J, Wieland LS. Searching for and selecting studies. *Cochrane Handbook for systematic reviews of interventions*. 2019 Sep 23:67-107.
23. Keung EZ, McElroy LM, Ladner DP, Grubbs EG. Defining the study cohort: inclusion and exclusion criteria. *Clinical Trials*. 2020:47-58.
24. Swift JK, Wampold BE. Inclusion and exclusion strategies for conducting meta-analyses. *Psychotherapy Research*. 2018 May 4;28(3):356-66.

25. Gierk B, Harendza S. Patient selection for bedside teaching: inclusion and exclusion criteria used by teachers. *Medical education*. 2012 Feb;46(2):228-33.
26. Mathes T, Klößen P, Pieper D. Frequency of data extraction errors and methods to increase data extraction quality: a methodological review. *BMC medical research methodology*. 2017 Dec;17(1):1-8.
27. Herlin IL, Ayache N. Features extraction and analysis methods for sequences of ultrasound images. In *Computer Vision—ECCV'92: Second European Conference on Computer Vision Santa Margherita Ligure, Italy, May 19–22, 1992 Proceedings 2 1992* (pp. 43-57). Springer Berlin Heidelberg.
28. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, Jain SS, Burkhoff D, Kumaraiah D, Rabbani L, Schwartz A. COVID-19 and cardiovascular disease. *Circulation*. 2020 May 19;141(20):1648-55.
29. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. *New England Journal of Medicine*. 2020 Jun 18;382(25):e102.
30. Srivastava K. Association between COVID-19 and cardiovascular disease. *IJC Heart & Vasculature*. 2020 Aug 1;29:100583.
31. Wright IS. An evaluation of anticoagulant therapy. *The American Journal of Medicine*. 1953 Jun 1;14(6):720-30.
32. Kubo H, Nakayama K, Yanai M, Suzuki T, Yamaya M, Watanabe M, Sasaki H. Anticoagulant therapy for idiopathic pulmonary fibrosis. *Chest*. 2005 Sep 1;128(3):1475-82.