Dear reviewer,

We wish to submit an original research article entitled, “Venous thromboembolism prophylaxis of a patient with MYH-9 related disease and COVID-19 infection” for consideration by the World Journal of Hematology. Below are our responses to your questions.

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: In this case report, a combination of platelet dysfunction and thrombocytopenia contributes to the variable increase in bleeding risk among patients with inherited platelet disorders, such as the May-Hegglin anomaly, related to MYH9. Due to the association between COVID-19 infection and an increased risk of thromboembolic events, anticoagulation in the setting of COVID-19 infection is of interest. This case study aims to provide a pragmatic, informed approach to a patient with MYH9-related disease who indicates anticoagulation. I suggested this manuscript's major revision.

The quality of language in this paper is not qualified.

Many of the sentences are hard to understand, and no correlation between the case study to explain the COVID-19 infection and an increased risk of thromboembolic events.

1. The quality of language in this paper is not qualified. Many of the sentences are hard to understand.

Response: The case report is written by a native English speaker in the United States. We recognize certain sentences were complex and long. So, we simplified the long sentences into shorter sentences.

2. No correlation between the case study to explain the COVID-19 infection and an increased risk of thromboembolic events.

Response: It is known that VTE has emerged as an important complication in critically ill patients with COVID-19. Several ongoing clinical trials evaluate the utility of anticoagulation in COVID -19 infected patients. In this review, we focused on the challenges of decision-making for starting anticoagulation in COVID-infected patients with platelet disorder due to their bleeding risk and thrombocytopenia. Therefore, we did not include a detailed discussion to explain the COVID-19 infection and an increased risk of thromboembolic events. We added a brief statement on lines 41-42. We also added more citations to support the statement.

3. It has an inconsistent format, with 11 and 12-point font sizes.

Response: We have made the font size according to the submission guideline

Q1. Suggested to provide the statistical support for the background: "Group of diseases associated with myosin heavy chain gene defects, now known as MYH9-related disease (MYH9-RD)(Lines 33-34).

Response: Statistical support is added. Line 98, added citation 8.

Q2. Any citation "Therefore, prompt initiation of anticoagulation upon hospital admission for patients with COVID-19 infection is of utmost importance to prevent thromboembolism and mortality. However, treatment decisions regarding anticoagulation for COVID-19-infected patients with MYH9-RD are challenging because of the potential increased risk of bleeding." (Lines 43-46).

Response: We made changes to the sentence to the following: "the American Society of Hematology (ASH) guideline panel suggests using prophylactic-intensity anticoagulation in patients with COVID-19–related critical illness who do not have suspected or confirmed venous

thromboembolism (VTE)." This is Line 43-45. Also added the citation for this as well, noted by 7.

So far, only one study has systematically explored the risk of VTE in patients with platelet disorders undergoing surgery. The majority of the patients with platelet disorder did not receive anticoagulation due to the concern of bleeding. Patients with thrombocytopenia or bleeding risk are not well studied in the clinical trials described in this case report. With limited data available, the decision-making is challenging.

Q3. Suggested the section "result" before " discussion."

Response: We did not have a result section. The clinical outcome and follow-up ("Follow-up and outcomes") are before the discussion section.

Q4. Although the discussion provided a lot of intervention, what is the new insight from the intervention?

Response: The new insight is that for COVID-19-infected patients, platelet disorder should not exclude them from getting anticoagulation if needed. It should be considered on case-by-case bases.

Q5. In Lines 126-139, it seems the author would like to mention that prophylactic heparin remains the agent of choice for anticoagulation in patients with severe COVID-19 infection. Can the author provide more information and details on COVID-19 management and the patient professions' correlation?

Response: The American Society of Hematology (ASH) guideline panel *suggests* using prophylactic-intensity anticoagulation in patients with COVID-19–related critical illness who do not have suspected or confirmed venous thromboembolism (VTE). Please kindly advise and clarify what the reviewer meant by “the patient professions’ correlation mean”.

Q6. Suggested Table 2 add the section of outcome/ impact of the thrombocytopenia and bleeding risk in major clinical trials.

Response: All of the main trials summarized in table 2 were reviewed and there is no published analysis of the outcome/impact of thrombocytopenia and bleeding risk. As noted in the table, thrombocytopenia to a certain degree was the exclusion criteria in all the summarized trials. The purpose of table 2 is to show that patients with thrombocytopenia and bleeding risks were excluded from clinical trials. Therefore, the outcome/ impact of thrombocytopenia and bleeding risk in major clinical trials were not studied in the trials.

Q7. Any ethical considerations with the hospital consent code or research ID can be provided?

Response: Research protocol is not required by the institution. Written consent was obtained from the patient. An informed consent statement was added in the footnote section per publishing guidelines. Line 254-255

Q8. Seems the section of the conclusion is not yet completed.

Response: A conclusion session is added and reflected in Line 171-177.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: 1.The platelet count unit should be unified as 103/uL

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1. The platelet count unit should be unified as 103/uL

Response: We changed the unit.

Q2. "It needs to be explained how long dose enoxapine prevent DVT"

The duration of optimal thromboembolism prophylaxis in Covid-19 patients remains individualized based on patient characteristics and risk factors for VTE. The major trials summarized in Table 2 all have primary endpoints within 30 days of trial enrollment and do not provide insight on extended treatment. Routine use of thromboembolism prophylaxis beyond the time of discharge for Covid-19 hospitalization is generally not advised unless risk factors are present (1). Prophylaxis for up to 45 days is suggested for patients with thromboembolism risk factors including active malignancy, decreased mobility, history of VTE, recent surgery, or trauma. (1, 2). The MICHELLE trial evaluated Covid-19 patients at elevated risk of thromboembolism at hospital discharge according to IMPROVE score and/or D-dimer. Patients treated with rivaroxaban 10 mg daily for 35 days had an improved composite outcome of venous or arterial thromboembolism and cardiovascular death at day 35 (3). Presently, randomized control clinical trials evaluating thromboprophylaxis using enoxaparin and direct oral anticoagulants (DOACs) in the post-discharge setting are ongoing (4).

1. Cuker, A, Peyvandi, F. COVID-19: Hypercoagulability. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 04, 2022.)

2. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020;75(23):2950-2973.

doi:10.1016/j.jacc.2020.04.031

3. Ramacciotti E, Barile Agati L, Calderaro D, et al. Rivaroxaban versus no anticoagulation for post-discharge thromboprophylaxis after hospitalisation for COVID-19 (MICHELLE): an open-label, multicentre, randomised, controlled trial. Lancet. 2022;399(10319):50-59. doi:10.1016/S0140-6736(21)02392-8

4. Talasaz AH, Sadeghipour P, Kakavand H, et al. Recent Randomized Trials of Antithrombotic Therapy for Patients With COVID-19: JACC State-of-the-Art Review. J Am Coll Cardiol. 2021;77(15):1903-1921. doi:10.1016/j.jacc.2021.02.035