

Associate Editor and Reviewer: 1		
Reviewer comments	Authors' response	Changes made
This paper is of interest to the PGMJ but please could you resubmit with attention to the points of the reviewers. The review article summarizes available data on the mechanisms, prophylaxis and therapy of COVID-19 associated venous thromboembolism, which is a hot topic of paramount clinical importance during the pandemic.	We would like to thank the reviewer for appreciating the potential significance of this review article. We did our best to revise the manuscript in a more organized way as suggested by the reviewer.	We have incorporated the changes as suggested by the reviewer in the revised manuscript.
The first part presenting the anticoagulant agents and guidelines for the management of VTE contains several imprecise data and mistakes listed below.	We are extremely thankful to the reviewer for pointing out those important issues regarding the revision of our article.	We have thoroughly revised our manuscript as advised by the reviewer.
Regarding the key issues of this review, tables 3 and 4 are of great value and are well designed.	We would like to thank the reviewer for appreciating the potential significance of table 3 and 4.	-----
The authors need to clarify the recommended doses of LMWH. They claimed that " Weight and Renal function based intermediate dose (e.g. 1mg/kg Enoxaparin SC 12hrly in a 70 kg adult with normal renal function)." and then "Therapeutic dose (Enoxaparin 1mg/kg 12hrly SC" According all guidelines and product characteristics, a prophylactic dose of enoxaparin is 40 mg SC or 0.5 mg/ kg body weight. The same daily dose 1 mg/kg enoxaparin bid cannot be both intermediate and therapeutic dose; it is a therapeutic dose.	Agreed. We have modified our statement regarding the prophylactic, intermediate and therapeutic dosing of enoxaparin. We have mentioned the recommended doses of LMWH in accordance to the BTS Guidance on Venous Thromboembolic Disease in patients with COVID-19. (Updated 8 th February, 2021) and the product information available at https://www.medicines.org.uk/emc/medicine/10054 .	The changes have been incorporated in the revised manuscript and highlighted in yellow. (Page 17 and 18-marked copy)

<p>Little attention has been paid on a predictive value of elevated D-dimer, though this issue has been mentioned.</p>	<p>Agreed. We have discussed this issue in a more detail in our revised manuscript under the heading ‘Anticoagulants in COVID-The present consensus’. We have mentioned the importance of D-dimer in investigating a possible acute VTE/PE. We have also highlighted that, although a high D-dimer level is a proven poor prognostic factor, it should not guide anticoagulant dosage or escalation.</p>	<p>The changes have been incorporated in the revised manuscript. (Page 16 and 17- marked copy)</p>
<p>Please state clearly whether or not any scoring systems implemented in routine hospital practice to assess VTE risk on admission should be used in hospitalized COVID-19 patients.</p>	<p>We are again grateful to the reviewer for mentioning this point. There is no separate scoring system to assess VTE risk on admission specific to COVID-19. But all patients hospitalized with COVID-19 should be thoroughly assessed for VTE risk as in other hospitalized patients.</p>	<p>We have mentioned this information under the heading ‘Anticoagulants in COVID-The present consensus’. (Page 16-marked copy)</p>
<p>Regarding duration of thromboprophylaxis following discharge, how long should it be administered? In several centers at least 2 weeks of prophylaxis is recommended in high-risk patients post-discharge given increased risk of VTE within the first month. The authors provided suggestions regarding the identification of such patients however, they should address the issue of duration; should D-dimer levels be measured after 2 weeks?, if further elevated e.g. 1500 ng/ml, should LMWH be continued or not?</p>	<p>We are extremely grateful to the reviewer for pointing out this issue. In fact, at least 2 weeks of prophylaxis is recommended in high-risk patients post-discharge given increased risk of VTE within the first month in several centers. We have discussed the issue of duration of thromboprophylaxis in a more detail in our revised manuscript. There is no mention of routine measurement of D-dimer during post-discharge follow-up in any of the guidelines.</p>	<p>We have added those information under the heading ‘Post discharge prophylaxis in covid-19’ of our revised manuscript. (Page 18, 19, 20- marked copy).</p>

	ACC suggested extended thromboprophylaxis with LMWH or DOACs for a maximum period of 45 in case of high risk for VTE such as, D-dimer level of more than 2 times ULN.	
Minor comments p. 4 l. 18-22 The statement "Purified heparin, including unfractionated heparin (UFH) and low molecular weight heparin (LMWH), inactivate thrombin by binding to antithrombin and producing a surface change." requires modification; LMWH are indirect inhibitors of FXa (2-4:11) as compared to inhibition of thrombin and heparins increase the antithrombin mediated inhibition of those proteins.	Agreed	We have modified our statement as-‘Purified heparin, including unfractionated heparin (UFH) and low molecular weight heparin (LMWH), act by promoting formation of an intermediate protease-heparin-antithrombin complex which facilitates inhibition of thrombin and activated factor X.’ We have also replaced the previous reference with a new one [Ref no-7] in support of our statement.
p. 4 l. 35 VKA were the first oral anticoagulants; heparins are also anticoagulant agents!	We are extremely grateful to the reviewer for pointing out this issue as well.	We have modified our statement as-‘Historically, Vitamin K antagonists such as warfarin (dicoumarol) and other coumarin derivatives were one of the earliest anticoagulants to be approved for clinical use.’

<p>p. 5. l. 1 idarucizumab and andexanet alfa are approved in the European Union, and the first one is widely available in Europe and used as shown in several observational studies. Please correct the sentence.</p>	<p>Agreed.</p>	<p>We have modified our statement as-‘While Idarucizumab and andexanet alfa are two such drugs approved for use in the US as well as EU, other reversal agents are under development.’</p>
<p>p. 5 l. 9 the current guidelines recommend using the term antithrombin, not antithrombin III (there are no antithrombin I, II or IV).</p>	<p>Agreed.</p>	<p>We have made changes in the revised manuscript as suggested by the reviewer.</p>
<p>p. 5 l. 27 the term multivariate etiologies should be replaced by multifactorial.</p>	<p>Agreed.</p>	<p>The term ‘multivariate etiologies’ has been replaced by ‘multifactorial etiologies’.</p>
<p>p. 5 ref 24 the comment on the 2019 ESC guidelines refers solely to high-risk acute PE (5% of all PE cases); this statement must be rephrased or removed. The key issue is clinical risk assessment (3 main categories).</p>	<p>We would like to thank the reviewer again for pointing out the issue.</p>	<p>We have revised our statement as suggested by the reviewer.</p>
<p>p. 5 l. 52 apixaban is also approved and used in acute PE.</p>	<p>Agreed</p>	<p>We have revised our statement as suggested by the reviewer.</p>
<p>While presenting studies, ie ref 30 the authors should use the name of the first author followed by et al or and co-workers.</p>	<p>Agreed.</p>	<p>We have made necessary changes as suggested by the reviewer.</p>

Table 2, units must be provided for each parameter. In this table percentage difference not change has been shown.	We would like to thank the reviewer again for pointing out the issue.	We have made changes as suggested in the revised manuscript.
p. 16 l. 27 randomized controlled trial, not control	Agreed.	Correction has been made.
Other changes	Reference no 7, 25, 58 and 59 have been replaced with four new references to better explain our statements.	

The changes incorporated in the revised manuscript have been highlighted in yellow.