Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 CORRESPONDENCE

Management of perioperative thromboprophylaxis for surgery following COVID-19: an expert-panel survey

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Editor—COVID-19 is associated with a high incidence of thrombotic events, up to 50% of critical care patients.[1] Whether or how long this risk extends post-discharge remains controversial. A recent registry showed an incidence of major thromboembolic events of 7.13% in a mean follow up of 92 days. In this registry, continuing anticoagulant therapy, mostly at prophylactic dosages, reduced the risk.[2] Although there has been broad discussion about the pathophysiology, the duration of the procoagulant state, and the optimal anticoagulant drug and dosing regimens, consensus is currently lacking. Different thromboprophylaxis schemes have been proposed for both hospitalised and post-discharge patients, and several trials are ongoing to evaluate the best anticoagulant treatments.[3–7] Nevertheless, these trials and recommendations do not include surgical patients and perioperative thromboprophylaxis is still a subject to be clarified.

Perioperative venous thromboembolism (VTE) risk is known and can be scored,[8] but there is doubt whether COVID-19-related hypercoagulability and endotheliopathy implies a new VTE risk, a risk factor that is not included in the previously validated scales. Therefore, clarifying existing protocols to guide optimal timing for scheduling surgery, the importance of biomarker normalisation or increased dose and thromboprophylaxis extension is needed for management and follow-up of these patients. In view of the paucity of high-quality evidence coupled with demand from clinicians to provide practical guidance that will inform best practices, we performed a survey with the objective of defining an appropriate strategy for perioperative thromboprophylaxis for patients who have had COVID-19 and now require surgery.

A multidisciplinary group with expertise in perioperative care and thromboembolism was convened to assess 16 questions by selecting one of five options: strong agreement; slight agreement; no agreement or disagreement; slight disagreement; or strong disagreement (see Supplementary material). For analysis, 'agreement' was defined as >70% of respondents selecting a strong or slight agreement option, and 'disagreement' was defined as >70% of respondents selecting a strong or slight disagreement option. An uncertain response was defined as >70% of respondents selecting the no agreement or disagreement option. A modified Delphi approach was used, following the recommendations of the European Society of Anaesthesiology and Intensive Care (ESAIC). The group facilitators modified and revised the questions according to the advice of survey participants and the ESAIC methodologist (A. Afshari).

A multidisciplinary group of 28 clinicians (see Supplementary material) who mostly had treated COVID-19 patients and had been involved in collaborative efforts for COVID-19 protocols voted (Table 1), with agreement on 5/16 questions (71.4–85.7% of strong or slight agreement).

Amongst all questions, results highlight the 'increased thromboembolic risk for at least 1 month from the time of polymerase chain reaction (PCR) normalisation/neutralisation' and 'higher thromboembolic risk in patients with moderate or severe COVID-19 infection'. Consequently, 'non-oncologic elective surgery should be deferred for at least 1

Table 1 Survey questions and results. CRP, C-reactive protein; PCR, polymerase chain reaction; VTE, venous thromboembolism. n(%): number of answers (% over 28 clinicians); %: sum of answers of agreements (strong+slight)/no agreement or disagreement/disagreements (strong+slight)/no opinion.

	Strong agreement	Slight agreement	No agreement or disagreement	Slight disagreement	Strong disagreement	No opinion
	Agreement		Unsure	Disagreement		
1. Patients after COVID-19 have an increased thromboembolic risk for at least ONE month from the time of PCR normalisation/neutralisation						
n (%)	16 (57.1)	4 (14.3)	5 (17.9)	2 (7.1)	1 (3.6)	0 (0)
%	71.4		17.9	10.7		0
2. Patients after COVID-19 have an increased thromboembolic risk for at least THREE months from the time of PCR normalisation/neutralisation						
n (%)	6 (21.4)	8 (28.6)	5 (17.9)	5 (17.9)	3 (10.7)	1 (3.6)
%	50.0		17.9	28.6		3.6
3. Patients after COVID-19 have an increased thromboembolic risk for at least SIX months from the time of PCR normalisation/neutralisation						
n (%)	1 (3.6)	4 (14.3)	9 (32.1)	2 (7.1)	7 (25.0)	5 (17.9)
%	20.9		32.1	32.1		17.9
4. Patients with moderate or severe COVID-19 experience a higher thromboembolic risk						
n (%)	22 (78.6)	2 (7.1)	2 (7.1)	0 (0)	1 (3.6)	1 (3.6)
%	85.7		7.1	3.6		3.6
5. Because of thromboembolic risk after COVID-19, non-oncologic elective surgery should be deferred for at least ONE month from the time of PCR normalisation/neutralisation, if no contraindications are present						
n (%)	16 (57.1)	6 (21.4)	1 (3.6)	3 (10.7)	2 (7.1)	0 (0)
%	78.5		3.6	17.8		0
6. Because of thromboembolic risk after COVID-19, non-oncologic elective surgery should be deferred for at least THREE months from the time of PCR normalisation/neutralisation, if no contraindications are present						
n (%)	4 (14.3)	7 (25.0)	3 (10.7)	4 (14.3)	8 (28.6)	2 (7.1)
%	39.3		10.7	42.9		7.1
7. Because of thromboembolic risk after COVID-19, non-oncologic elective surgery should be deferred for at least SIX months from the time of PCR normalisation/neutralisation, if no contraindications are present						
n (%)	0 (0)	2 (7.1)	6 (21.4)	6 (21.4)	12 (42.9)	2 (7.1)
%	7.1		21.4	64.3		7.1
8. Because of thromboembolic risk after COVID-19, non-oncologic elective surgery should NOT be deferred after PCR normalisation/neutralisation						
n (%)	3 (10.7)	2 (7.1)	4 (14.3)	8 (18.6)	9 (32.1)	2 (7.1)
%	17.8		14.3	50.7		7.1
9. A preoperative assessment of patients with prior or ongoing COVID-19 should include D-dimer measurement for VTE risk stratification						
n (%)	14 (50)	4 (14.3)	1 (3.6)	3 (10.7)	6 (21.4)	0 (0)
%	64.3		3.6	32.1		0
10. A preoperative D-dimer level higher than 1000 ng ml^{-1} preoperatively implies a higher thrombotic risk						
n (%)	7 (25.0)	12 (42.9)	3 (10.7)	3 (10.7)	2 (7.1)	1 (3.6)
%	67.9		10.7	17.8		3.6
11. Would you consider other markers such as interleukin-6, ferritin, or CRP to evaluate the inflammatory status in the preoperative exam?						
n (%)	4 (14.3)	9 (32.1)	3 (10.7)	3 (10.7)	7 (25.0)	2 (7.1)
%	46.4		10.7	35.7		7.1
12. Unless contraindicated, all patients after COVID-19 should receive pharmacological thromboprophylaxis postoperatively, when a surgery is performed during the first 6 months post-PCR normalisation/neutralisation						
n (%)	13 (46.4)	4 (14.3)	3 (10.7)	3 (10.7)	3 (10.7)	2 (7.1)
%	60.7		10.7	21.4		7.1
13. Hospitalised patients with COVID-19 who were receiving anticoagulant therapy with a direct oral anticoagulant or vitamin K antagonist should be switched to low-molecular-weight heparin						
n (%)	16 (57.1)	3 (10.7)	5 (17.9)	3 (10.7)	0 (0)	1 (3.6)
%	67.8		17.9	10.7		3.6
14. If a surgery is performed when the patient is at higher thromboembolic risk after COVID-19, the pharmacological thromboprophylaxis (low-molecular-weight heparin) dose should be increased over standard prophylaxis to an intermediate dose (100 IU kg^{-1} day^{-1})						
n (%)	10 (35.7)	10 (35.7)	4 (14.3)	1 (3.6)	3 (10.7)	0 (0)
%	71.4		14.3	14.3		0
15. If a surgery is performed when the patient is at higher thromboembolic risk after COVID-19, the pharmacological thromboprophylaxis duration should be increased with a factor of 1.5						
n (%)	10 (35.7)	7 (25.0)	5 (17.9)	1 (3.6)	4 (14.3)	1 (3.6)
%	60.7		17.9	17.9		3.6
16. When a surgery is performed during the period of higher thromboembolic risk after COVID-19, mechanical thromboprophylaxis (intermittent pneumatic compression) should be used in addition to pharmacological thromboprophylaxis up to resuming ambulation, if not contraindicated						
n (%)	16 (57.1)	5 (17.9)	4 (14.3)	1 (3.6)	2 (7.1)	0 (0)
%	75.0		14.3	10.7		0

month from the time of PCR normalisation/neutralisation', but if it is not possible and the surgical procedure 'is performed when the patient is at higher thromboembolic risk after experiencing COVID-19, pharmacological thromboprophylaxis dosing should be increased over standard prophylaxis to an intermediate dose (100 IU kg^{-1} day^{-1} of low-molecular-weight heparin)'. Finally, mechanical thromboprophylaxis (intermittent pneumatic compression) could be an option for increasing the thromboprophylaxis, being used in addition to pharmacological thromboprophylaxis up to ambulation.

The objective of this survey was to assess an appropriate strategy for perioperative thromboprophylaxis for patients who have had COVID-19 and subsequently required surgery. However, in light of limited evidence, the aim was not to reach a full consensus but to shed light on current practices. Expert opinions are based on both perceived and potential future benefits given clinical models or known management protocols. If they are summarised through a survey, they have value to implement individual practices and highlight unmet questions for future research.

Although current data show that the rate of post-discharge thrombotic events in COVID-19 patients seems lower than those observed during hospitalisation, the duration of the higher thrombotic risk period after COVID-19 is uncertain. Our survey suggests that it could last about 1 month instead of 3–6 months after PCR normalisation. Similar recommendations can be found in recent papers suggesting a 7-week minimum delay for elective surgery from the beginning of symptoms, although thrombotic events were not specifically considered in the outcomes.[9]

In order to help determine the thrombotic risk period, biomarkers have been proposed (D-dimer, interleukin-6, C-reactive protein, ferritin), but no one biomarker has been deemed important in determining the optimal timing of surgery after COVID-19. As such, there was agreement that there is no need for routine evaluation before scheduling surgery. Viscoelastic assays have been proposed to assess the COVID-19 hypercoagulable state.[10] Although the amplitude parameters could be associated with a hypercoagulable profile, their usefulness in this setting is still unknown.

This survey has some limitations. The main one is the very nature of the study, as a survey will never provide strong evidence. Besides, the methodological development does not adhere to a standard Delphi-type consensus, but assesses the initial responses of the experts. Moreover, expert panel selection is subject to bias and perhaps the same survey among another set of experts would reach different conclusions. However, the experts involved all have considerable expertise in the topic such that their opinion can be considered reliable.

In conclusion, as COVID-19 is associated with a prothrombotic state that may persist after PCR normalisation, the expert panel suggests deferring non-oncologic surgery for at least 1 month from a negative PCR test, considering that current thromboprophylaxis protocols are to be applied. If surgery is performed during this first month, an increase up to intermediate low molecular weight dosing is proposed, adding mechanical devices up to resumption of ambulation if possible. Biomarkers are not helpful, so purely clinical evolution after COVID-19 is considered by the experts to determine the optimal time for scheduling surgery.

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Declarations of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2021.06.041.

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