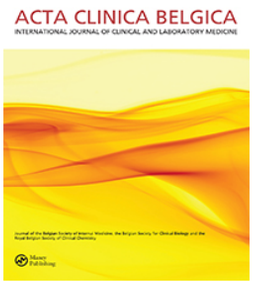
Taylor & Francis
Taylor & Francis Group



Acta Clinica Belgica
International Journal of Clinical and Laboratory Medicine

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/yacb20

Belgian clinical guidance on anticoagulation management in hospitalised and ambulatory patients with COVID-19

Thomas Vanassche , Christelle Orlando , Kristel Vandenbosch , Alain Gadisseur , Cédric Hermans , Kristin Jochmans , Jean-Marc Minon , Serge Motte , Harlinde Peperstraete , Pierre Péters , Muriel Sprynger , Patrizio Lancellotti , Isabelle Dehaene , Patrick Emonts , Christophe Vandenbriele , Peter Verhamme & Cécile Oury

To cite this article: Thomas Vanassche , Christelle Orlando , Kristel Vandenbosch , Alain Gadisseur , Cédric Hermans , Kristin Jochmans , Jean-Marc Minon , Serge Motte , Harlinde Peperstraete , Pierre Péters , Muriel Sprynger , Patrizio Lancellotti , Isabelle Dehaene , Patrick Emonts , Christophe Vandenbriele , Peter Verhamme & Cécile Oury (2020): Belgian clinical guidance on anticoagulation management in hospitalised and ambulatory patients with COVID-19, Acta Clinica Belgica, DOI: 10.1080/17843286.2020.1829252

To link to this article: https://doi.org/10.1080/17843286.2020.1829252

ACTA CLINICA BELGICA
https://doi.org/10.1080/17843286.2020.1829252

Taylor & Francis
Taylor & Francis Group

Belgian clinical guidance on anticoagulation management in hospitalised and ambulatory patients with COVID-19

Thomas Vanassche[a], Christelle Orlando[b], Kristel Vandenbosch[c], Alain Gadisseur[d], Cédric Hermans[e], Kristin Jochmans[b], Jean-Marc Minon[f], Serge Motte[g], Harlinde Peperstraete[h], Pierre Péters[c], Muriel Sprynger[i], Patrizio Lancellotti[i], Isabelle Dehaene[j], Patrick Emonts[k], Christophe Vandenbriele[a], Peter Verhamme[a] and Cécile Oury[l]

[a]Department of Cardiovascular Sciences, University of Leuven, Leuven, Belgium; [b]Department of Haematology, Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel, Brussels, Belgium; [c]Department of Laboratory Haematology, CHU University Hospital of Liège, Liège, Belgium; [d]Department of Haematology, Antwerp University Hospital, Antwerp, Belgium; [e]Department of Haematology, Cliniques Universitaires St-Luc, Brussels, Belgium; [f]Department of Laboratory Medicine, Thrombosis-haemostasis and Transfusion Unit, CHR Citadelle, Liège, Belgium; [g]Department of Vascular Diseases, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium; [h]Department of Cardiac Intensive Care, Ghent University Hospital, Ghent, Belgium; [i]Department of Cardiology, CHU University Hospital of Liège, Liège, Belgium; [j]Vlaamse Vereniging voor Obstetrie en Gynaecologie, Universitair Ziekenhuis Gent, Ghent, Belgium; [k]Groupement des Gynécologues Obstétriciens de Langue Française de Belgique, CHU University Hospital of Liège; [l]Laboratory of Cardiology, GIGA Institute, University of Liège, Liège, Belgium

ABSTRACT

Objectives: COVID-19 predisposes patients to thrombotic disease. The aim of this guidance document is to provide Belgian health-care workers with recommendations on anticoagulation management in COVID-19 positive patients.

Methods: These recommendations were based on current knowledge and a limited level of evidence.

Results: We formulated recommendations for the prophylaxis and treatment of COVID-related venous thromboembolism in ambulatory and hospitalised patients, as well as recommendations for the use of antithrombotic drugs in patients with prior indication for anticoagulation who develop COVID-19.

Conclusions: These recommendations represent an easy-to-use practical guidance that can be implemented in every Belgian hospital and be used by primary care physicians and gynaecologists. Of note, they are likely to evolve with increased knowledge of the disease and availability of data from ongoing clinical trials.

KEYWORDS
Practice guideline; primary health care; COVID-19

1. Background and challenges

COVID-19, a viral respiratory illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1], may predispose patients to thrombotic disease, both in the venous and arterial circulation, due to excessive inflammation, platelet activation, endothelial dysfunction, and stasis [2–4]. Indirect effects of infection, e.g. severe inflammatory response, critical illness, and traditional risk factors may also contribute to risk for thrombotic disease/events [3]. In addition, many patients receiving antithrombotic therapy may develop COVID-19, which can have implications for choice, dosing, and laboratory monitoring of antithrombotic therapy [3].

Venous thromboembolism (VTE) has been reported in 25% to 69% of patients with severe COVID-19 in the intensive care unit, and is associated with poor prognosis/morbidity and mortality [5–10]. A French study showed an increased rate of CT-scan detected pulmonary embolism in ICU COVID-19 patients compared to the usual rate encountered in critically ill non-COVID -19 patients [11]. Laboratory findings indicate that markers of coagulopathy, including elevated D-dimers and prolonged prothrombin time, are linked to more severe disease and a higher mortality [2,12–15]. Several case series also describe an increased risk of arterial thrombosis and of microvascular organ damage, including pulmonary intravascular coagulation [16] as well as widespread pulmonary thrombosis [17]. Furthermore, a non-randomized study showed a lower mortality in COVID-19 patients who used thromboprophylaxis as compared to patients who did not receive antithrombotic therapy, particularly in patients with elevated D-dimers [18]. Another retrospective study indicated that the use of therapeutic anticoagulation was associated with lower in-hospital mortality [19], but neither the indication for anticoagulation nor the type of treatment was described.

The American Society of Hematology and the International Society for Thrombosis and Hemostasis recommended to institute venous thromboembolism

CONTACT Cécile Oury cecile.oury@uliege.be Laboratory of Cardiology, GIGA-Cardiovascular Sciences, University of Liège, Liège 4000, Belgium; Thomas Vanassche thomas.vanassche@kuleuven.be Centrum voor Moleculaire en Vasculaire Biologie, UZ Herestraat 49, Leuven 3000, Belgium

prophylaxis measures for patients at risk [3,20]. Nevertheless, the choice and dose of thromboprophylaxis remain controversial [21–23].

Low molecular weight heparin (LMWH) is the recommended therapy for pharmacological thromboprophylaxis in critically ill patients, with the exception of patients with severe renal dysfunction (for whom unfractionated heparin could be considered based on a careful risk/benefit assessment) and patients with a history of heparin-induced thrombocytopenia [24,25]. In the latter, fondaparinux is an alternative drug for the prevention or treatment of thrombosis, although it is not reimbursed for hospitalised patients in Belgium. Several experimental antivirals used to treat COVID-19 may increase plasma levels of direct oral anticoagulant (DOAC) because of P-glycoprotein inhibition and/or competition, inhibition or induction of CYP3A4-dependent pathways [26]. Therefore, parenteral LMWH is the preferred agent for thromboprophylaxis [26]. Although interim guidelines agree on the choice of thromboprophylaxis, the optimal anticoagulant dose in COVID-19 in patients is unknown; intermediate- or full-dose regimens rather than prophylactic doses have been suggested but higher doses also cause more bleeding [3,27].

Furthermore, given the high incidence of VTE even despite thromboprophylaxis [9], a clear strategy for the treatment of newly diagnosed VTE in the context of COVID-19 is required. Finally, the optimal management of patients who require therapeutic anticoagulation because of a pre-existing indication (atrial fibrillation, mechanical heart valves, history of VTE) is unknown.

Algorithms for the management of coagulopathy in COVID-19 patients have been produced in order to provide answers to urgent clinical needs across the world [28]. Due to local specificities, it is however mandatory that every country or area formulates recommendations that easily apply to the regional health-care setting.

2. Methods

These guidelines were developed by a Belgian Working Group gathering members of the Belgian Society on Thrombosis and Haemostasis council belonging to Belgian University Hospitals, general practitioners and gynaecologists, in collaboration with the Belgian Health Care Knowledge Center (KCE, https://kce.fgov.be) and Sciensano. The recommendations were based on published reports (MEDLINE PubMed) and local experience, in accordance with most recent guidance from Scientific and Standardization Committee Communication of the International Society on Thrombosis and Haemostasis [20] and the American anticoagulation forum [29]. Given the time-sensitive nature of the challenges encountered during COVID-19 pandemia, the majority of existing data are based on retrospective and often single-center small studies. There are no published or completed prospective cohort studies or randomized controlled trials. This has important implications for the recommendations presented herein, which mainly rely on limited level of evidence and are likely to evolve with knowledge of COVID-19 pathophysiology and availability of data from ongoing clinical trials.

3. Recommendations

We formulated recommendations, including schematic algorithms, on anticoagulation management in hospitalised COVID-19 patients and after discharge (Figure 1), and on anticoagulation management in non-hospitalised COVID-19 patients (Figure 2).

Recommendations for anticoagulation management during pregnancy and post-partum period in COVID-19 positive women were also included.

3.1. Anticoagulation management in hospitalised COVID-19 patients and after discharge

3.1.1. General consideration

The guidelines apply to most patients. However, in patients at high risk of bleeding (e.g., platelet count < $50x10^3$/µl, recent major bleeding, dialysis or frail elderly patients), we recommend that the risks and benefits of thromboprophylaxis should be weighed on an individual basis.

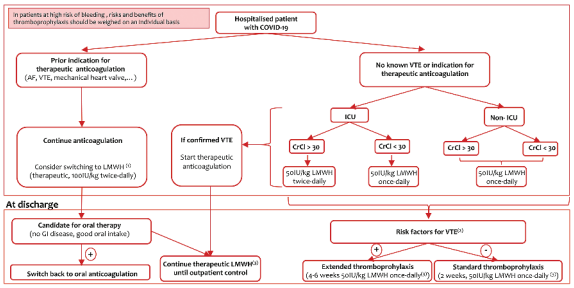


Figure 1. Anticoagulation management in hospitalised COVID-19 patients and after discharge.

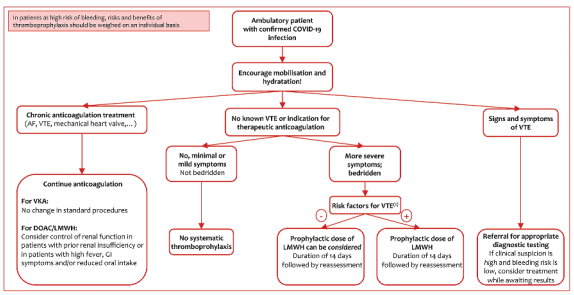


Figure 2. Anticoagulation management in non-hospitalised COVID-19.

3.1.2. At admission

We emphasize the importance of a low threshold of clinical suspicion of VTE at diagnosis and during the whole duration of the hospitalisation period.

We highly recommend that patients with a prior indication for anticoagulation (e.g., atrial fibrillation, VTE, mechanical heart valve) should continue to receive anticoagulation. We recommend switching to LMWH instead of oral anticoagulation (vitamin K antagonist or DOAC) in the following cases: severely ill patients, patients with gastro-intestinal problems, planned invasive procedures, patients with unstable INRs and/or presence of potential drug–drug interactions, including antivirals and immunomodulatory investigational therapies [26,30].

We recommend administering prophylactic anticoagulation of LMWH in patients who have no prior indication for anticoagulation and no VTE at admission.

3.1.3. Anticoagulation regimen in patients with a prior indication for anticoagulation

For hospitalised patients with an established indication for therapeutic anticoagulation (e.g., atrial fibrillation, VTE, mechanical heart valve), we recommend continuation of anticoagulation in therapeutic doses.

If oral anticoagulation is switched to parenteral treatment, we recommend a therapeutic dose of LMWH of 100 anti-Xa IU/kg twice-daily (i.e. 1 mg/kg enoxaparin twice-daily) in patients with a high risk of thrombotic complications (mechanical heart valves, recent VTE, high-risk thrombophilia, or atrial fibrillation [31]). In patients with a lower risk of thrombotic complications (secondary prevention of VTE without high-risk thrombophilia), we suggest using either LMWH therapeutic dose or high intermediate dose of LMWH based on the severity of the disease and of the bleeding risk. The dose should be adjusted to renal function. In patients with Cockroft (CrCl) <30 ml/min, we recommend dose-adjusted therapeutic LMWH or tinzaparin, while patients with CrCl <15 ml/min should receive unfractionated heparin with appropriate monitoring (anti-Xa monitoring may be preferred over aPTT monitoring in critically ill patients) or adjusted LMWH with careful monitoring of anti-Xa, taking into account local expertise and experience.

3.1.4. Anticoagulation regimen for thromboprophylaxis in hospitalised patients with COVID-19

For patients who are not in intensive care unit (ICU), we recommend a weight-adjusted LMWH prophylactic dose with a minimum of 50 anti-Xa IU/kg once-daily, irrespective of renal function. Several studies indeed suggest that a standard fixed VTE prophylaxis dose may not be appropriate in patients at extremes of weight [32].

For ICU patients, we recommend a high-prophylactic anticoagulation regimen with 50 anti-Xa IU/kg twice-daily for patients with CrCl >30 mL/min. For patients with CrCl <30 mL/min, we suggest to use a reduced dose of 50 anti-Xa IU/kg once-daily. In the case of severe renal dysfunction (CrCl <15 mL/min), we suggest the use of unfractionated heparin or anti-Xa monitoring. This recommendation is based on several reports of case series indicating VTE incidence reaching up to 27% in critically ill COVID-19 patients with pneumonia, despite standard-dose thromboprophylaxis [5,6,9], and on preliminary clinical data suggesting that either use of prophylactic or intermediate dose of LMWH in patients with high SIC (sepsis-associated coagulopathy) score (≥4) or high D-dimers (>6 times ULN) was associated with better prognosis [18].

Notwithstanding, a recent study highlights that major bleeding rates may be higher than initially thought (5.6% in critically ill patients), while VTE rate was far lower (7.6% in critically ill patients), therefore suggesting that empiric intensifying of anticoagulation in these patients should be pursued with caution [33]. The potential benefit of intensified anticoagulation needs to be evaluated in ongoing randomized clinical trials [34]***. Therefore, we recommend that therapeutic anticoagulation is restricted to patients with prior indication for therapeutic anticoagulation or patients with confirmed VTE. Therapeutic anticoagulation in patients with COVID-19 might be associated with improved outcomes in selected very severely ill patients, especially patients under mechanical ventilation, but this has to be put in balance with bleeding risks. Hence, we recommend to restrict the use of therapeutic anticoagulation in patients without clear indication to clinical trial protocols.

3.1.5. Anticoagulation regimen for the treatment of COVID-19-related VTE

For COVID-19 patients who develop VTE during hospitalisation, we recommend treatment with therapeutic doses of LMWH (100 anti-Xa IU/kg twice-daily). In patients with CrCl <30 ml/min, dose-adjusted therapeutic LMWH or tinzaparin should be considered. In patients with CrCl <15 ml/min, we recommend the use of unfractionated heparin or anti-Xa monitoring.

3.1.6. D-dimer

We do not recommend to routinely adapt the anticoagulation regimen based on D-dimer levels. Indeed, elevated D-dimers levels are a common finding in COVID-19 [30,35], which correlates with inflammation; they appear to be useful markers of poor overall outcome [2,12,13].

However, clinical suspicion, guided by clinical signs and symptoms, changing cardiopulmonary status, and, possibly, abruptly changing D-dimer levels should be used to guide the decision to rule out or in VTE with validated algorithms [36].

3.1.7. Screening for VTE

Systematic screening for VTE in COVID-19 positive patients is not recommended but there should be an increased awareness for VTE during hospitalisation (e.g., look for clinical signs like swollen leg, hypoxemia non-proportionate to the respiratory status, acute right ventricle failure or dilation, catheter issues).

There should be a low threshold to perform imaging whenever VTE is suspected. When strongly suspected, we suggest therapeutic anticoagulation especially in the ICU when it is not possible to obtain confirmation by imaging.

3.1.8. Anti-Xa monitoring

We do not recommend performing systematic monitoring of LMWH. It is however suggested to perform an anti-Xa assay when there is a suspicion of accumulation of LMWH (and thus increased risk of bleeding) in the following circumstances: patients with extreme body weight (BMI< 18 or BMI >30 kg/m2) or renal insufficiency or in patients with a bleeding diathesis.

3.1.9. Anticoagulation management at discharge

We recommend to routinely evaluate the need for anticoagulation after discharge.

In patients with a prior/established indication for anticoagulation, we recommend switching back to the initial oral anticoagulation medication and regimen unless oral therapy is not feasible, e.g. due to drug–drug interaction issues [26].

In patients who developed VTE during the hospitalization period, we recommend continuing therapeutic LMWH until outpatient control. Switching to oral therapy, i.e. DOAC, can be considered in selected patients who are in good general condition and no longer have symptoms of COVID-19. The duration of therapeutic anticoagulation should be at least 3 months.

In patients without a prior indication for therapeutic anticoagulation who received thromboprophylaxis during hospitalisation, a 2-week standard post-discharge LMWH thromboprophylaxis (50 anti-Xa IU/kg once-daily) should be considered. If additional risk factors for VTE are present (e.g., ICU stay, known thrombophilia, obesity, high-dose estrogen use, immobilization, heart failure, respiratory failure, age >70 years, active cancer, personal or familial history of VTE and/or major surgery in the last 3 months) we suggest extended thromboprophylaxis for 4 to 6 weeks after discharge. Continuation of thromboprophylaxis should be discussed according to risk-benefit balance (mobility/bleeding risk and other risk factors).

In order to limit contacts with health-care workers when the patients are back home, it can be considered to switch LMWH to a DOAC if the patient is eligible and needs continued anticoagulation, has good oral intake and good renal function. If this is not possible, self-administration should be encouraged.

3.2. Anticoagulation management in non-hospitalised COVID-19 patients

3.2.1. General considerations

The following guidelines apply to most non-hospitalised patients. However, in patients at high risk of bleeding (e.g., platelet count < $50x10^3$/µl, recent major bleeding, dialysis or frail elderly patients), we recommend that the risks and benefits of thromboprophylaxis should be weighed on an individual basis.

Whenever possible, mobilisation should be encouraged to reduce the risk of VTE. In any case, we recommend being aware of signs and symptoms of VTE. In the case of suspected VTE, the patient should be referred for appropriate diagnostic testing. While awaiting results of diagnostic testing, initiation of therapeutic anticoagulation can be considered if clinical suspicion is high and bleeding risk is low. If LMWH administration is needed at home, self-administration is encouraged in order to avoid contact with health-care workers.

3.2.2. Patients in need of long-term anticoagulation

In patients treated with vitamin K-antagonist therapy, we recommend against changing the standard of care, as long as the patient has good oral intake and stable INRs.

In patients under chronic DOAC or LMWH therapy, control of renal function should be considered in patients with prior renal impairment or in patients with high fever, gastrointestinal symptoms and/or reduced intake.

3.2.3. Patients without known VTE or any other indication for long-term anticoagulation

In COVID-19 positive patients who are asymptomatic or mildly symptomatic, we recommend against prophylactic anticoagulation in the ambulatory setting.

In COVID-19 patients who are severely ill and who are immobilised (bedridden), we recommend LMWH prophylaxis when additional risk factors for VTE are present: known thrombophilia, personal or familial history of VTE, obesity, pregnancy, heart failure, respiratory failure age >70 years, active cancer and/or major surgery in the last 3 months. If patients do not have additional risk factors for VTE, LMWH prophylaxis can be considered.

The optimal duration for prophylaxis in non-hospitalised patients (if no chronic anticoagulation is required) is unknown, but we propose a 14-day treatment. Thereafter, the need for extended thromboprophylaxis should be reassessed.

3.3. Anticoagulation management during pregnancy and post-partum period in COVID-19 positive women

In pregnant women with confirmed COVID-19 but without severe symptoms, we recommend against thromboprophylaxis if not otherwise indicated.

In pregnant women with severe symptoms (e.g., high fever, immobilisation), we recommend thromboprophylaxis.

For hospitalised, asymptomatic COVID-19 positive pregnant women, we recommend a standard obstetric thromboprophylactic risk assessment (based on current recommendations [37]). This assessment should be repeated if necessary.

For hospitalised, symptomatic COVID-19 positive pregnant women, we recommend starting thromboprophylaxis (unless contraindicated).

If VTE is confirmed, we recommend continuing anticoagulant treatment (LMWH) for 6 to 8 weeks during postpartum with a minimal duration of 3 months [37].

We recommend VTE prophylaxis in postpartum women with COVID-19, based on individual risk assessment. In the absence of risk factors requiring antepartum prophylaxis, we do not recommend postpartum prophylaxis in asymptomatic or mildly symptomatic patients with uncomplicated delivery and no obstetric indication for postpartum VTE prophylaxis. If antepartum prophylaxis was given because of COVID-19, we recommend continuing prophylaxis for at least 14 days. After 14 days, the need for anticoagulation should be reassessed according to risk-benefit balance (severity of COVID infection and other risk factors).

Acknowledgments

We are grateful to Dr Vicky Jespers (KCE) and Geert Musch (Federal Agency for Medicines and Health Products) who contributed to the guideline development. C.O. is Research Director at the National Funds for Scientific Research, Belgium.

Disclosure statement

The authors report no declarations of interest.

ORCID

Thomas Vanassche http://orcid.org/0000-0002-7404-8918
Christelle Orlando http://orcid.org/0000-0003-2163-8778
Harlinde Peperstraete http://orcid.org/0000-0001-5435-1752
Muriel Sprynger http://orcid.org/0000-0003-4358-0183
Isabelle Dehaene http://orcid.org/0000-0002-4826-6946
Cécile Oury http://orcid.org/0000-0002-7561-0132

Dissemination

The guideline is available at https://www.bsth.be/professionals, https://COVID-19.sciensano.be/fr/COVID-19-procedures, and https://kce.fgov.be/fr/COVID-19-contributions-du-kce.

References

[1] Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020;579(7798):265–269.
[2] Huang* C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497–506.
[3] Bikdeli B, M V M, 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.
[4] Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708–1720.
[5] Klok FA, Kruip MJHA, NJM VDM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145–147.
[6] Cui S, Chen S, Li X, et al. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J Thromb Haemost. 2020;18(6):1421–1424.
[7] Llitjos J-F, Leclerc M, Chochois C, et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost. 2020;18(7):1743–1746.
[8] Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of venous thromboembolism in hospitalised patients with COVID-19. J Thromb Haemost. 2020;18(8):1995–2002.
[9] Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020;46(6):1089–1098.
[10] Wichmann D, Sperhake J-P, Lütgehetmann M, et al. Autopsy findings and venous thromboembolism in patients with COVID-19. Ann Intern Med. 2020;173(4):268–277.
[11] Leonard-Lorant I, Delabranche X, Severac F, et al. Acute pulmonary embolism in COVID-19 patients on CT angiography and relationship to D-dimer levels. Radiology. 2020;296(3):E189–E191.
[12] Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844–847.
[13] Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–1062.
[14] Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Hematological findings and complications of COVID-19. Am J Hematol. 2020;95(7):834–847.
[15] Giusti B, Gori AM, Alessi M, et al. Sars-CoV-2 induced coagulopathy and prognosis in hospitalised patients:

a snapshot from Italy. Thromb Haemost. 2020;120 (8):1233–1236.
[16] McGonagle D, O'Donnell JS, Sharif K, et al. Immune mechanisms of pulmonary intravascular coagulopathy in COVID-19 pneumonia. Lancet Rheumatol. 2020;2(8): e460–e461.
[17] Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in COVID-19. N Engl J Med. 2020;383 (2):120–128.
[18] Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020;18(5):1094–1099.
[19] Paranjpe I, Fuster V, Lala A, et al. Association of treatment dose anticoagulation with in-hospital survival among hospitalised patients with COVID-19. J Am Coll Cardiol. 2020;76(1):122–124.
[20] Spyropoulos AC, Levy JH, Ageno W, et al. Scientific and standardization committee communication: clinical guidance on the diagnosis, prevention and treatment of venous thromboembolism in hospitalised patients with COVID-19. J Thromb Haemost. 2020;18(8):1859–1865.
[21] Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood. 2020;135 (23):2033–2040.
[22] Shang Y, Pan C, Yang X, et al. Management of critically ill patients with COVID-19 in ICU: statement from front-line intensive care experts in Wuhan, China. Ann Intensive Care. 2020;10(1):73.
[23] Bikdeli B, Madhavan MV, Gupta A, et al. Pharmacological agents targeting thromboinflammation in COVID-19: review and implications for future research. Thromb Haemost. 2020;120(7):1004–1024.
[24] Levi M, Thachil J, Iba T, et al. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol. 2020;7(6):e438–e440.
[25] Wada H, Thachil J, Di Nisio M, et al. Guidance for diagnosis and treatment of disseminated intravascular coagulation from harmonization of the recommendations from three guidelines. J Thromb Haemost. 2013;11 (4):761–767.
[26] Testa S, Prandoni P, Paoletti O, et al. Direct oral anticoagulant plasma levels' striking increase in severe COVID-19 respiratory syndrome patients treated with antiviral agents: the Cremona experience. J Thromb Haemost. 2020;18(6):1320–1323.
[27] Thachil J. The versatile heparin in COVID-19. J Thromb Haemost. 2020;18(5):1020–1022.
[28] Atallah B, Mallah SI, AlMahmeed W. Anticoagulation in COVID-19. Eur Hear. 2020;6(4):260–261.
[29] Barnes GD, Burnett A, Allen A, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. J Thromb Thrombolysis. 2020;50(1):72–81.
[30] Driggin E, M V M, Bikdeli B, et al. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. J Am Coll Cardiol. 2020;75 (18):2352–2371.
[31] Kirchhof P, Benussi S, Kotecha D, et al. ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016;37 (38):2893–2962.
[32] Sebaaly J, Covert K. Enoxaparin dosing at extremes of weight: literature review and dosing recommendations. Ann Pharmacother. 2018;52 (9):898–909.
[33] Al-Samkari H, Karp Leaf RS, Dzik WH, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. Blood. 2020;136(4):489-500.
[34] Yu B, Li X, Chen J, et al. Evaluation of variation in D-dimer levels among COVID-19 and bacterial pneumonia: a retrospective analysis. J Thromb Thrombolysis. 2020;50:548–557.
[35] Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 2020;18 (5):1023–1026.
[36] Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with European Respiratory Society (ERS). Eur Heart J. 2020;41(4):543–603.
[37] Wiegers HMG, Middeldorp S. Contemporary best practice in the management of pulmonary embolism during pregnancy. Ther Adv Respir Dis. 2020;14:1753466620914222.