Thrombosis and Haemostasis 2020 Editors' Choice Papers

Christian Weber^{1,3} Anne Rigby¹ Gregory Y. H. Lip^{4,5}

¹ Institute for Cardiovascular Prevention (IPEK), LMU Munich, Munich, Germany

² German Centre for Cardiovascular Research (DZHK), partner site Munich Heart Alliance, Munich, Germany

³ Department of Biochemistry, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Centre, Maastricht, The Netherlands

⁴ Liverpool Centre for Cardiovascular Science, Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, United Kingdom

⁵ Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

Address for correspondence Gregory Y. H. Lip, MD, Liverpool Centre for Cardiovascular Science, University of Liverpool, William Henry Duncan Building, 6 West Derby Street, Liverpool L7 8TX, United Kingdom (e-mail: gregory.lip@liverpool.ac.uk).

Christian Weber, MD, Institute for Cardiovascular Prevention, LMU Munich, Pettenkoferstraße 9, 80336 Munich, Germany (e-mail: chweber@med.lmu.de).

Thromb Haemost 2021;121:109–114.

In this Editor's choice, we highlight last year's papers from *Thrombosis and Haemostasis* as well as from its open access companion journal *THOpen*, which found most resonance among our readers' community, holding promise for mechanistic understanding and improved clinical management in the fields of Thrombosis and Haemostasis. Building on the research investigations from this undoubtedly memorable year may be particularly useful to overcome the current pandemic situation. As it became apparent that coronavirus disease 2019 (COVID-19) was not merely a pulmonary disease but that thrombosis was a key element involved in its severity and complications, the thrombosis research community deployed intensive research efforts in the hope to optimize treatment and/or prophylaxis as well as to decipher the mechanisms and characteristics of COVID-19 thrombosis as rapidly as possible. Due to the urgency of the pandemic development, it was indeed not surprising that publications relating to COVID-19 received by far the most attention in 2020.

Unprecedented Research Efforts for Unprecedented Times

Early on into the pandemic, Lippi and Favaloro¹ proposed the simple D-dimer test for prognosis of COVID-19 severity in a short T&H report which received particular resonance. By using classic coagulation tests together with point-of-care methods such as whole blood thromboelastometry, Spiezia et al² further reported specific coagulation alterations, thereby identifying a state of severe hypercoagulability in COVID-19 patients with acute respiratory failure. The systematic review and meta-

analysis from Jin et al³ described the coagulation abnormalities seen in Chinese patients with COVID-19. Boscolo et al comparatively assessed the values of different coagulation tests between patients admitted to internal medicine department versus intensive care unit.⁴ Beyond this hypercoagulation state, Violi et al extensively reviewed how clotting variables behave and impact on the severity of COVID-19 along with potential antithrombotic treatment options in COVID-19.⁵ Marchandot et al proposed that haemostatic abnormalities could be used to help stage severity of COVID-19.⁶

To help thrombosis specialists, investigators, and funders, a truly multidisciplinary collaborative group of experts in disciplines including cardiovascular diseases, hematology, vascular medicine, pharmacy and pharmacology, pulmonary and critical care medicine, laboratory medicine, and health policy joined efforts to form the Global COVID-19 Thrombosis Collaborative Group. Their position paper⁷ comprehensively discussed classical anticoagulants, antiplatelet drugs, and their anti-inflammatory mechanisms and also agents that modulate inflammation and may thus help to mitigate thromboinflammation. While a panel of experts from China and Europe published a consensus statement with practical guidelines for the prevention and treatment of venous thromboembolism (VTE) associated with COVID-19,⁸ Grandmaison et al highlighted the benefits of systematic VTE screening in COVID-19 patients.⁹ A position paper from the Vas-European independent foundation reaffirmed this in angiology/vascular medicine.¹⁰

Understanding the mechanism of COVID-19 thrombosis is critical for all efforts toward defining clinical characteristics and optimizing antithrombotic treatment for COVID-19

received

December 1, 2020

accepted after revision

December 1, 2020

© 2021. Thieme. All rights reserved.
Georg Thieme Verlag KG,
Rüdigerstraße 14,
70469 Stuttgart, Germany

DOI <https://doi.org/10.1055/s-0040-1722171>.
ISSN 0340-6245.

patients. In this respect, Cattaneo et al raised an important question regarding the interpretation of thrombotic risk in COVID-19 patients, as they argued that COVID-19-related thrombosis in the lung is due to pulmonary thrombi rather than pulmonary emboli.¹¹ They further advocated for a role of von Willebrand factor and platelets in COVID-19 pathogenesis,¹² questioning the use of high-dose heparin for COVID-19 patients. Scoring well with Altmetrics, the study from Eriksson et al investigated implications of the complement system in COVID-19 pathology,¹³ identifying the mannose-binding lectin pathway as a potential target for antithrombotic treatment and diagnostic in COVID-19 thrombosis. As put forward by the review of Vaughan et al,¹⁴ obesity appears to be another crucial risk factor, which may be independently driving the heterogeneous host response and hyperinflammation driving COVID-19 and its severity. Following the hypothesis that bradykinin is involved in COVID-19 pulmonary edema, the study from Miesbach suggested that angiotensin II was elevated in COVID-19.¹⁵ In a comprehensive review, Gencer et al surveyed the mechanisms that may explain how viral entry and activation of endothelial cells by Sars-Cov-2 can give rise to a series of events including systemic inflammation, thrombosis, and microvascular dysfunction, which is particularly fatal in patients with overt cardiovascular disease.¹⁶ The review shed light on a role of the renin-angiotensin aldosterone system and its inhibitors, and the impact of antiviral and anti-inflammatory treatment options in COVID-19.

As important as it is to address the current needs for optimizing medical treatment, any given strategy will only be successful, if based on a solid foundation of understanding the underlying mechanisms.

Refining Anticoagulation Treatment Choices

Identifying and Treating Thrombosis in a Diversity of Patients

To tackle the multidimensional aspects of atrial fibrillation (AF) and the more complex treatment options available to date, a paradigm shift from classification toward a structured characterization addressing specific domains with treatment and prognostic implications has been proposed by Potpara et al, in alignment with the new 2020 European Society of Cardiology (ESC) guidelines.¹⁷ This 4S-AF scheme sums up the aspects of our initial evaluation and assessment to “characterize” the patient with AF: Stroke risk, Symptoms, Severity of AF burden, and Substrate severity. This is reflected in the new ESC AF guidelines, proposing a structured approach to integrated AF care: “A” Avoid stroke; “B” Better symptom management with patient-centered rate or rhythm control; “C” Cardiovascular risk factor and comorbidity optimisation.¹⁸

A clinical focus addressed how female sex is a stroke risk modifier rather than a risk factor per se, and cautions against ignoring the additive effect of female sex on risk, given that female AF patients tend to be suboptimally managed and often not offered oral anticoagulation for stroke prevention.¹⁹ The impact of aging and incident comorbidities on

stroke risk emphasized by Chao et al²⁰ was also cited in the new ESC guidelines to remind us that risk is dynamic, and not a static “one off” assessment.

Whether East-Asian AF patients, who may be more prone to bleeding events, should be prescribed lower warfarin international normalized ratio (INR) for stroke prevention, has been a long lasting debate. The thorough meta-analysis from Pandey et al²¹ raised concerns about this practice and suggested that a ratio of 2.0 to 3.0 should be adopted overall. Additional high-quality studies, especially prospective and randomized trials, will be necessary to define the optimal range for Asian AF patients.^{22,23}

High body weight and obese patients represent another subgroup, for whom the risks associated with anticoagulation treatment remains uncertain. The study by Martin et al was well relayed on social media, as it challenged the International Society of Thrombosis and Haemostasis guidance on routinely checking direct oral anticoagulant (DOAC) concentrations in these patients.²⁴ The results supported the growing clinical evidence on the efficacy and safety of DOACs in high body weight patients. Additional insights from an ancillary analysis on body weight from the ENGAGE-AF TIMI 48 trial show how patients with low body weight had a more fragile clinical status and poorer INR control; importantly, the pharmacokinetic/pharmacodynamic profile of edoxaban was consistent across extremes of body weight, resulting in similar efficacy compared with warfarin, while major or clinically relevant non-major bleeding were most favorable with edoxaban as compared with warfarin in low body weight patients.²⁵

In an effort toward improving the balance between benefits and risks of anticoagulation therapy, the already well-cited study by Spyropoulos et al identified elevated D-dimer levels as an indicator to predict increased bleeding risk.²⁶ Also toward this goal, the tool developed by Harenberg et al²⁷ could rapidly detect DOACs in urine and could easily be implemented in clinical routine examination of patients with suspicion of a major bleeding. As treatment efficacy as well as reliability of clinical studies rests foremost on the accuracy of the diagnostic, it is particularly important to identify those patients, who fall out of the diagnostic scope. Interestingly, several papers focused on the use of biomarkers for risk stratification in AF, and their nonspecific nature, being reflective of a sick patient or a sick heart.^{28,29} The updated systematic review on the association of antiphosphatidylserine/prothrombin antibodies with the autoimmune disorder antiphospholipid syndrome, may help identifying antiphospholipid syndrome patients otherwise negative for current tests.³⁰ The relevance of clinical conclusions also relies on the strength of the technique used. In this regard, the relevant methodological validation study by Pieters et al³¹ demonstrated the impact of different variables on maximum absorbance in plasma and should help investigators to accurately validate fibrin clot formation and structure in plasma.

Dual Pathway Therapy

In our last Editor's Choice,³² we addressed dual pathway therapy combining antiplatelet and anticoagulant therapy and mentioned the results from the randomized EDOX-APT study investigating the effects of edoxaban, the most recently approved

DOAC for AF, on patients treated with antiplatelet therapy followed by aspirin withdrawal.³³ The results showed that alternative antithrombotic treatment regimens cannot replace the selective effects of aspirin on platelet COX-1 blockade and called for caution on strategies of aspirin withdrawal in the absence of an effective alternative antithrombotic treatment. Dual antiplatelet therapy (DAPT) has to balance ischemic and bleeding risk. The progress in the field of antiplatelet therapy for acute coronary syndrome and percutaneous coronary intervention over the years including strategies to individualise DAPT intensity and duration and de-escalation of DAPT intensity were reviewed in a well-received T&H Historical Series article.³⁴ Weitz et al further elucidated the rationale of such dual pathway therapy for atherosclerotic diseases.³⁵

Thrombosis Association with Other Pathologies

The Caravaggio study, a large trial on the treatment of VTE in patients with cancer comparing apixaban with dalteparin, addressed the issue of thromboembolic complications in cancer. It was included in an updated meta-analysis of randomized controlled trials by Giustozzi et al,³⁶ which could confirm the efficacy and safety of DOACs compared with low-molecular weight heparin for the treatment of cancer-associated VTE. The meta-analysis by Cavallari et al should also reassure clinicians on the efficacy and safety of DOACs in AF patients with cancer.³⁷ An analysis of data from the United Kingdom showed as well that the use of oral anticoagulants is not associated with the incidence of cancer overall among patients with AF, although a possible association between DOACs and colorectal and pancreatic cancer may be present.³⁸

Patients suffering from renal impairment are at even higher risk of thrombosis and bleeding. In this respect, the analysis of two large studies, the MAGELLAN and MARINER trials, by Weitz et al³⁹ shed new light on dosing and safety of rivaroxaban in such patients. As successful oral anticoagulation treatment very much relies on adherence, we welcomed the efforts by Hwang et al, who reassuringly confirmed good adherence of oral anticoagulants for AF dosing regimens in real-world practice,⁴⁰ highlighting the importance of patient satisfaction in effective clinical management.^{41,42}

Aside from Anticoagulation

In some patients with AF where oral anticoagulation is unsuitable for stroke prevention, implanting left atrial appendage occlusion may represent a valid option. A balanced view on the subject was given by Ding et al in an interesting Clinical Focus article.⁴³

We also highlighted last year, new laboratory practice suitable for haemophilia A patients on the recently approved bispecific monoclonal antibody emicizumab.^{44,45} A timely review by Gelbenegger et al summarized published clinical trials and preliminary reports of promising treatment with emicizumab and discussed its clinical implications.⁴⁶ Its cost-effectiveness and budget impact were highlighted by Cortesi et al.⁴⁷ Often underestimated, the risk of major adverse limb events is unfortunately very high in patients

with peripheral artery disease. Pastori et al⁴⁸ reported a well relayed comprehensive meta-analysis to alert physicians on the positive impact of statins for this group of patients.

Underlying Mechanisms and New Targets

Inflammation, Thrombosis and Cardiovascular Implications

The link between inflammation and thrombosis is now well established and targeting inflammation represents a convincing and promising therapeutic approach to prevent thrombosis. The well-received meeting report from the third Maastricht Consensus Conference on Thrombosis⁴⁹ provided a comprehensive overview of the state-of-the-art consensus and recommendations on future challenges of thromboinflammation and cardiovascular pathologies, which may inspire new research avenues in the role of inflammatory mediators, cells, and pathways in cardiovascular disease. The implication of B lymphocytes in atherosclerosis was illustrated by a study by van der Vorst et al investigating the role of the CXCL13/CXCR5 axis on immunoglobulin M levels and atherosclerosis development.⁵⁰ As monocyte subsets are increasingly recognized as players and biomarkers of cardiovascular inflammation, the characterization of human blood monocytes by Hoffmann et al⁵¹ identifying subset-specific novel markers added a valuable contribution to our understanding of circulating monocyte heterogeneity. In a VTE mouse model of vena caval ligation, Kimball et al⁵² demonstrated the role of one specific monocyte subset, that is, the "reparative" Ly6Clo monocytes, in thrombus formation and resolution, suggesting that modulating inflammation may be a potential therapeutic strategy to prevent thrombosis.⁵³ As the first cells recruited to the site of injury, neutrophils represent another relevant immune cell subset implicated in thrombotic diseases. Stakos et al provided a well-received overview of neutrophils' ability to release neutrophil extracellular traps during thrombosis. Although their antimicrobial effects is beneficial in infectious diseases, their ability to stimulate inflammation can lead to tissue damage and thrombosis, making them novel candidates for diagnostic and therapeutic targets of thrombosis.⁵⁴ Targeting the complement system may also prove to be a successful strategy in some thrombotic conditions. In this regard, an interesting study by Gavrilaki et al⁵⁵ analyzed genetic susceptibility in patients with transplant-associated thrombotic microangiopathy, supporting the concept that complement regulatory genes play a role in severe thrombotic complications of bone marrow transplant.

Novel Diagnostic and Therapeutic Targets

In an effort to elucidate the precise mechanisms that trigger clotting in venous thrombosis, Tilburg et al⁵⁶ characterized its plasma signature in a venous thrombosis murine knockout model using mass spectrometry-based proteomics, thereby establishing a new tool to diagnose such pathologies.⁵⁷ Roka-Moiia et al elucidated the differential effects of biochemical agonists versus hemodynamic shear on platelet activation and procoagulant activity, which may have important implications in the diagnosis of thrombosis associated with cardiovascular

Fig. 1 2020 *Thrombosis and Haemostasis* articles on COVID-19 versus other diseases. (A) Percentage of articles published in *Thrombosis and Haemostasis* in 2020 relating to different diseases: Coronavirus disease 2019 (COVID-19), venous thromboembolism (VTE), atrial fibrillation (AF), haemophilia A (HA), and antiphospholipid syndrome (APS). Circle size is proportional to percentage of publications. (B) Each group was plotted according to its 2020 total number of citations (X-axis) versus Altmetrics score (Y-axis).

devices.⁵⁸ Albeit the anticoagulation properties of diverse sea cucumber species had already been identified, attempts had failed to isolate its oligosaccharides. Zhou et al⁵⁹ achieved this goal, allowing them to comprehensively characterize their individual structures in relation to biological activities. Promising antithrombotic candidates could be identified that exhibited anticoagulation effects without the undesirable stimulatory effects on factor XII and platelet aggregation.

Not unexpectedly, studies that investigated COVID-19 represented a significant amount of publications at T&H last year. Manuscripts on COVID-19 accounted for 17% of articles published in 2020. As a comparison, manuscripts on VTE and AF represented 14 and 6%, respectively (►Fig. 1). Not only did COVID-19 studies represent a substantial publication volume but they also ranked top in terms of citations and Altmetrics (►Fig. 1). Simultaneously, we have been thriving not to neglect diversity and quality throughout the fields of cardiovascular biology and medicine. We are more than ever looking forward to this New Year by your side and hope it will bring its very much needed share of new scientific insights.

Conflict of Interest

G.Y.H.L. reports consultancy and speaker fees from Bayer, Bayer/Janssen, BMS/Pfizer, Biotronik, Medtronic, Boehringer Ingelheim, Microlife, Roche and Daiichi-Sankyo outside the submitted work. No fees received personally.

Acknowledgment

We very much thank Dr. Johan Duchêne for elaborating the figure. Images: Centers for Disease Control and Prevention, Servier Medical Art and Pixel perfect from Flaticon.com.

References

- Lippi G, Favaloro EJ. D-dimer is associated with severity of coronavirus disease 2019: a pooled analysis. *Thromb Haemost* 2020;120(05):876–878
- Spiezia L, Boscolo A, Poletto F, et al. COVID-19-related severe hypercoagulability in patients admitted to intensive care unit for acute respiratory failure. *Thromb Haemost* 2020;120(06):998–1000
- Jin S, Jin Y, Xu B, Hong J, Yang X. Prevalence and impact of coagulation dysfunction in COVID-19 in China: a meta-analysis. *Thromb Haemost* 2020;120(11):1524–1535
- Boscolo A, Spiezia L, Correale C, et al. Different hypercoagulable profiles in patients with COVID-19 admitted to the internal medicine ward and the intensive care unit. *Thromb Haemost* 2020;120(10):1474–1477
- Violi F, Pastori D, Cangemi R, Pignatelli P, Loffredo L. Hypercoagulation and antithrombotic treatment in coronavirus 2019: a new challenge. *Thromb Haemost* 2020;120(06):949–956
- Marchandot B, Trimaille A, Curtiaud A, et al. Staging severity of COVID-19 according to hemostatic abnormalities (CAHA score). *Thromb Haemost* 2020;120(12):1716–1719
- Bikdeli B, Madhavan MV, Gupta A, et al; Global COVID-19 Thrombosis Collaborative Group. Pharmacological agents targeting thromboinflammation in COVID-19: review and implications for future research. *Thromb Haemost* 2020;120(07):1004–1024
- Zhai Z, Li C, Chen Y, et al; Prevention Treatment of VTE Associated with COVID-19 Infection Consensus Statement Group. Prevention and treatment of venous thromboembolism associated with coronavirus disease 2019 infection: a consensus statement before guidelines. *Thromb Haemost* 2020;120(06):937–948
- Grandmaison G, Andrey A, Périard D, et al. Systematic screening for venous thromboembolic events in COVID-19 pneumonia. *TH Open* 2020;4(02):e113–e115
- Gerotziafas GT, Catalano M, Colgan MP, et al; Scientific Reviewer Committee. Guidance for the management of patients with vascular disease or cardiovascular risk factors and COVID-19: position paper from VAS-European Independent Foundation in Angiology/Vascular Medicine. *Thromb Haemost* 2020;120(12):1597–1628
- Cattaneo M, Bertinato EM, Bircocchi S, et al. Pulmonary embolism or pulmonary thrombosis in COVID-19? Is the recommendation to use high-dose heparin for thromboprophylaxis justified?. *Thromb Haemost* 2020;120(08):1230–1232
- Morici N, Bottiroli M, Fumagalli R, Marini C, Cattaneo M. Role of von Willebrand factor and ADAMTS-13 in the pathogenesis of thrombi in SARS-CoV-2 infection: time to rethink. *Thromb Haemost* 2020;120(09):1339–1342
- Eriksson O, Hultström M, Persson B, et al. Mannose-binding lectin is associated with thrombosis and coagulopathy in critically ill COVID-19 patients. *Thromb Haemost* 2020;120(12):1720–1724
- Vaughan CJ, Cronin H, Ryan PM, Caplice NM. Obesity and COVID-19: a Virchow's triad for the 21st century. *Thromb Haemost* 2020;120(11):1590–1593

- 15 Miesbach W. Pathological role of angiotensin II in severe COVID-19. *TH Open* 2020;4(02):e138–e144
- 16 Gencer S, Lacy M, Atzler D, van der Vorst EPC, Döring Y, Weber C. Immunoinflammatory, thrombohaemostatic, and cardiovascular mechanisms in COVID-19. *Thromb Haemost* 2020
- 17 Potpara TS, Lip GYH, Blomstrom-Lundqvist C, et al. The 4S-AF Scheme (Stroke Risk; Symptoms; Severity of Burden; Substrate): a novel approach to in-depth characterization (rather than classification) of atrial fibrillation. *Thromb Haemost* 2020. Doi: 10.1055/s-0040-1716408
- 18 Yoon M, Yang PS, Jang E, et al. Improved population-based clinical outcomes of patients with atrial fibrillation by compliance with the simple ABC (Atrial Fibrillation Better Care) pathway for integrated care management: a nationwide cohort study. *Thromb Haemost* 2019;119(10):1695–1703
- 19 Nielsen PB, Overvad TF. Female sex as a risk modifier for stroke risk in atrial fibrillation: using CHA2DS2-VASc versus CHA2DS2-Va for stroke risk stratification in atrial fibrillation: a note of caution. *Thromb Haemost* 2020;120(06):894–898
- 20 Chao TF, Liao JN, Tuan TC, et al. Incident co-morbidities in patients with atrial fibrillation initially with a CHA2DS2-VASc score of 0 (males) or 1 (females): implications for reassessment of stroke risk in initially 'low-risk' patients. *Thromb Haemost* 2019;119(07):1162–1170
- 21 Pandey AK, Xu K, Zhang L, et al. Lower versus standard INR targets in atrial fibrillation: a systematic review and meta-analysis of randomized controlled trials. *Thromb Haemost* 2020;120(03):484–494
- 22 Chao T-F, Guo Y. Should we adopt a standard international normalized ratio range of 2.0 to 3.0 for Asian patients with atrial fibrillation? An appeal for evidence-based management, not eminence-based recommendations. *Thromb Haemost* 2020;120(03):366–368
- 23 Kim HK, Tantry US, Smith SC, et al. The East Asian paradox: an updated position statement on the challenges to the current antithrombotic strategy in patients with cardiovascular disease. *Thromb Haemost* 2020. Doi: 10.1055/s-0040-1718729
- 24 Martin AC, Thomas W, Mahir Z, et al. Direct oral anticoagulant concentrations in obese and high body weight patients: a cohort study. *Thromb Haemost* 2020
- 25 Boriani G, Ruff CT, Kuder JF, et al. Edoxaban versus warfarin in patients with atrial fibrillation at the extremes of body weight: an analysis from the ENGAGE AF-TIMI 48 trial. *Thromb Haemost* 2020
- 26 Spyropoulos AC, Lipardi C, Xu J, et al. Modified IMPROVE VTE risk score and elevated D-dimer identify a high venous thromboembolism risk in acutely ill medical population for extended thromboprophylaxis. *TH Open* 2020;4(01):e59–e65
- 27 Harenberg J, Beyer-Westendorf J, Crowther M, et al; Working Group Members. Accuracy of a rapid diagnostic test for the presence of direct oral factor Xa or thrombin inhibitors in urine—a multicenter trial. *Thromb Haemost* 2020;120(01):132–140
- 28 Camelo-Castillo A, Rivera-Caravaca JM, Marín F, Vicente V, Lip GYH, Roldán V. Predicting adverse events beyond stroke and bleeding with the ABC-stroke and ABC-bleeding scores in patients with atrial fibrillation: the Murcia AF project. *Thromb Haemost* 2020;120(08):1200–1207
- 29 Esteve-Pastor MA, Roldán V, Rivera-Caravaca JM, Ramírez-Macías I, Lip GYH, Marín F. The use of biomarkers in clinical management guidelines: a critical appraisal. *Thromb Haemost* 2019;119(12):1901–1919
- 30 Radin M, Foddai SG, Cecchi I, et al. Antiphosphatidylserine/prothrombin antibodies: an update on their association with clinical manifestations of antiphospholipid syndrome. *Thromb Haemost* 2020;120(04):592–598
- 31 Pieters M, Guthold M, Nunes C, et al. Interpretation and validation of maximum absorbance data obtained from turbidimetry analysis of plasma clots. *Thromb Haemost* 2020;120(01):44–54
- 32 Weber C, Rigby A, Lip GYH. Thrombosis and Haemostasis 2019 Editor's Choice Papers. *Thromb Haemost* 2020;120(01):184–190
- 33 Franchi F, Rollini F, Garcia E, et al. Effects of edoxaban on the cellular and protein phase of coagulation in patients with coronary artery disease on dual antiplatelet therapy with aspirin and clopidogrel: results of the EDOX-APT study. *Thromb Haemost* 2020;120(01):83–93
- 34 Gorog DA, Geisler T. Platelet inhibition in acute coronary syndrome and percutaneous coronary intervention: insights from the past and present. *Thromb Haemost* 2020;120(04):565–578
- 35 Weitz JI, Angiolillo DJ, Geisler T, Heitmeier S. Dual pathway inhibition for vascular protection in patients with atherosclerotic disease: rationale and review of the evidence. *Thromb Haemost* 2020;120(08):1147–1158
- 36 Giustozzi M, Agnelli G, Del Toro-Cervera J, et al. Direct oral anticoagulants for the treatment of acute venous thromboembolism associated with cancer: a systematic review and meta-analysis. *Thromb Haemost* 2020;120(07):1128–1136
- 37 Cavallari I, Verolino G, Romano S, Patti G. Efficacy and safety of nonvitamin K oral anticoagulants in patients with atrial fibrillation and cancer: a study-level meta-analysis. *Thromb Haemost* 2020;120(02):314–321
- 38 Abrahami D, Renoux C, Yin H, Fournier JP, Azoulay L. The association between oral anticoagulants and cancer incidence among individuals with nonvalvular atrial fibrillation. *Thromb Haemost* 2020;120(10):1384–1394
- 39 Weitz JI, Raskob GE, Spyropoulos AC, et al. Thromboprophylaxis with rivaroxaban in acutely ill medical patients with renal impairment: insights from the MAGELLAN and MARINER trials. *Thromb Haemost* 2020;120(03):515–524
- 40 Hwang J, Han S, Bae H-J, et al. NOAC adherence of patients with atrial fibrillation in the real world: dosing frequency matters? *Thromb Haemost* 2020;120(02):306–313
- 41 Proietti M, Lane DA. The compelling issue of nonvitamin K antagonist oral anticoagulant adherence in atrial fibrillation patients: a systematic need for new strategies. *Thromb Haemost* 2020;120(03):369–371
- 42 Ivany E, Lane DA. Patient satisfaction: a key component in increasing treatment adherence and persistence. *Thromb Haemost* 2020. Doi: 10.1055/s-0040-1718734
- 43 Ding WY, Mandrolia J, Gupta D. Left atrial appendage occlusion: past, present and future. *Thromb Haemost* 2020;120(11):1484–1491
- 44 Adamkewicz JI, Chen DC, Paz-Priel I. Effects and interferences of emicizumab, a humanised bispecific antibody mimicking activated factor VIII cofactor function, on coagulation assays. *Thromb Haemost* 2019;119(07):1084–1093
- 45 Müller J, Pekrul I, Pötzsch B, Berning B, Oldenburg J, Spannagl M. Laboratory monitoring in emicizumab-treated persons with hemophilia A. *Thromb Haemost* 2019;119(09):1384–1393
- 46 Gelbenegger G, Schoergenhofer C, Knoebl P, Jilma B. Bridging the missing link with emicizumab: a bispecific antibody for treatment of hemophilia A. *Thromb Haemost* 2020;120(10):1357–1370
- 47 Cortesi PA, Castaman G, Trifirò G, et al. Cost-effectiveness and budget impact of emicizumab prophylaxis in haemophilia A patients with inhibitors. *Thromb Haemost* 2020;120(02):216–228
- 48 Pastori D, Farcomeni A, Milanese A, et al. Statins and major adverse limb events in patients with peripheral artery disease: a systematic review and meta-analysis. *Thromb Haemost* 2020;120(05):866–875
- 49 d'Alessandro E, Becker C, Bergmeier W, et al; Scientific Reviewer Committee. Thrombo-inflammation in cardiovascular disease: an expert consensus document from the Third Maastricht Consensus Conference on Thrombosis. *Thromb Haemost* 2020;120(04):538–564
- 50 van der Vorst EPC, Daissormont I, Aslani M, et al. Interruption of the CXCL13/CXCR5 chemokine axis enhances plasma IgM levels

- and attenuates atherosclerosis development. *Thromb Haemost* 2020;120(02):344–347
- 51 Hoffmann J, Fišer K, Liebetrau C, et al. High-content immunophenotyping and hierarchical clustering reveal sources of heterogeneity and new surface markers of human blood monocyte subsets. *Thromb Haemost* 2020;120(01):141–155
 - 52 Kimball AS, Obi AT, Luke CE, et al. Ly6C^{Lo} monocyte/macrophages are essential for thrombus resolution in a murine model of venous thrombosis. *Thromb Haemost* 2020;120(02):289–299
 - 53 Knopp T, Karbach S, Wenzel P. Myeloid cells to the rescue: improving thrombus resolution. *Thromb Haemost* 2020;120(02):197–198
 - 54 Stakos D, Skendros P, Konstantinides S, Ritis K. Traps N' clots: NET-mediated thrombosis and related diseases. *Thromb Haemost* 2020;120(03):373–383
 - 55 Gavriilaki E, Touloumenidou T, Sakellari I, et al. Pretransplant genetic susceptibility: clinical relevance in transplant-associated thrombotic microangiopathy. *Thromb Haemost* 2020;120(04):638–646
 - 56 Tilburg J, Michaud SA, Maracle CX, et al. Plasma protein signatures of a murine venous thrombosis model and *Slc44a2* knockout mice using quantitative-targeted proteomics. *Thromb Haemost* 2020;120(03):423–436
 - 57 Scheller I, Nieswandt B. Novel approaches to unravel risk factors and mechanisms of venous thrombosis. *Thromb Haemost* 2020;120(03):372
 - 58 Roka-Moiia Y, Walk R, Palomares DE, et al. Platelet activation via shear stress exposure induces a differing pattern of biomarkers of activation versus biochemical agonists. *Thromb Haemost* 2020;120(05):776–792
 - 59 Zhou L, Gao N, Sun H, et al. Effects of native fucosylated glycosaminoglycan, its depolymerized derivatives on intrinsic factor Xase, coagulation, thrombosis, and hemorrhagic risk. *Thromb Haemost* 2020;120(04):607–619