ESC European Society of Cardiology

European Heart Journal: Acute Cardiovascular Care (2021) **10**, 1084–1085
doi:10.1093/ehjacc/zuab088

BIOMARKER SPOTLIGHT

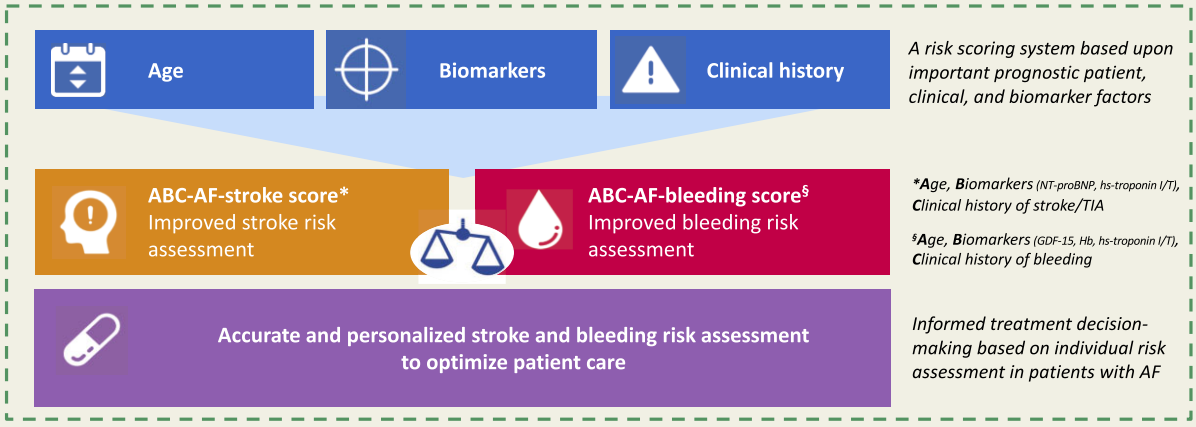
Biomarker-based risk scores in atrial fibrillation

Ziad Hijazi [1,2]*, Nicholas L. Mills[3], and Christian Mueller [4]; on behalf of the Study Group on Biomarkers of the ESC Association for Acute Cardiovascular Care

[1]Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden; [2]Deptartment of Medical Sciences, Cardiology, Uppsala University, Uppsala, Sweden; [3]British Heart Foundation and Usher Institute, Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, UK; and [4]Department of Cardiology and Cardiovascular Research Institute Basel, University Hospital Basel, University of Basel, Basel, Switzerland

Online publish-ahead-of-print 26 October 2021

Graphical Abstract



Atrial fibrillation (AF) is a common arrhythmia that poses a significant burden to the global healthcare system as it increases the risk of stroke, death, and other cardiovascular complications.[1] International guidelines for the management of patients with AF recommend a structured risk assessment in order to decide whether oral anticoagulant therapy should be prescribed, mainly by the use of the CHA_2DS_2-VASc score.[1] However, under- and overuse of evidence based preventive therapies remains common. As such, the need for better risk prediction tools for stroke and major bleeding events have been identified among the key knowledge-gaps in AF. Plasma biomarkers capture broad underlying information on general health, disease severity, and even undiagnosed cardiovascular illness.[2] In patients with AF, N-terminal pro-B-type natriuretic peptide (NT-proBNP) is strongly associated with the risk of stroke, growth differentiation factor 15 (GDF-15) with the risk of major bleeding, and high-sensitivity cardiac troponin I and T with both outcomes.[2] The prognostic information captured by these biomarkers often greatly exceeds that of anthropometric data or binary information on comorbidities. Based on these findings, biomarker-based risk scores have been developed in patients with AF in order to improve the risk assessment of stroke and major bleeding events.

These ABC-AF-stroke[3] and ABC-AF-bleeding[4] risk scores (Age, Biomarkers and Clinical history) have shown superior performance in regards to discrimination and calibration, when compared with the traditional risk scores in AF based on clinical variables, such as the CHA_2DS_2-VASc and HAS-BLED scores. Several large-scale studies have confirmed these results and thus the use of biomarkers for refining the risk assessment of patients with AF have been incorporated into the European Society of Cardiology guidelines (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Atrial-Fibrillation-Management). Recently, the usefulness of the ABC-AF risk scores were further expanded into the clinically relevant setting of broad AF populations without oral anticoagulant treatment.[5] Additionally, insights have recently also been gained into the dynamic nature of these risk biomarkers including the biomarker-based ABC-AF risk scores. For instance, data points to the stability of the prognostic information gained

* Corresponding author. Email: ziad.hijazi@ucr.uu.se

from the ABC-AF risk scores during a short-to-intermediate time-period, whereas for longer time periods, an annual reassessment may further refine the risk prediction.[6] These results provide additional information of value from both scientific and clinical perspective. Altogether, current data show that clinical risk scores in AF are limited by modest discrimination and calibration, and that the ABC-AF risk scores are validated, well calibrated, and provide better risk prediction than CHA_2DS_2-VASc and HAS-BLED (graphical abstract). Thus, the ABC-AF risk scores serves as new useful tools for improved risk stratification and decision support in patients with AF (web calculator available at: https://www.ucr.uu.se/en/services/abc-risk-calculators).

Other members of the Study Group on Biomarkers of the ESC Association for Acute Cardiovascular Care include:
Evangelos Giannitsis[1], Allan S. Jaffe[2], Kurt Huber[3], Johannes Mair[4], Louise Cullen[5], Ola Hammarsten[6], Martin Möckel[7], Konstantin Krychtiuk[8], Kristian Thygesen[9], and Bertil Lindahl[10]
[1]Department of Cardiology, University Heidelberg, Heidelberg, Germany;
[2]Mayo Clinic and Medical School, Rochester, MN, USA;
[3]Department of Medicine, Cardiology and Intensive Care Medicine, Wilhelminen Hospital, and Sigmund Freud University, Medical School, Vienna, Austria;
[4]Department of Internal Medicine III—Cardiology and Angiology, Medical University Innsbruck, Innsbruck, Austria;
[5]Emergency and Trauma Centre, Royal Brisbane and Women's Hospital, University of Queensland, Herston, QLD, Australia;
[6]Department of Clinical Chemistry and Transfusion Medicine, University of Gothenburg, Gothenburg, Sweden;
[7]Division of Emergency Medicine, Charité-Universitätsmedizin Berlin, Berlin, Germany;
[8]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria;
[9]Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; and
[10]Department of Medical Sciences, Uppsala University, Uppsala, Sweden

Funding

Z.H. is supported by a research grant from the Swedish Society for Medical Research (S17-0133), the Swedish Heart-Lung Foundation (20200722), and Uppsala University Hospital, Sweden. N.L.M. is supported by a Research Excellence Award (RE/18/5/34216), Programme Grant (RG/20/10/34966), and a Chair Award (CH/F/21/90010) from the British Heart Foundation.

Conflict of interest: Z.H. reports lecture and consulting honoraria from Boehringer Ingelheim, Bristol-Myers Squibb, Pfizer, and Roche Diagnostics. N.L.M. reports research grants awarded to the University of Edinburgh from Abbott Diagnostics and Siemens Healthineers outside the submitted work, and honoraria from Abbott Diagnostics, Siemens Healthineers, Roche Diagnostics and LumiraDx. C.M. has received research support from the Swiss National Science Foundation, the Swiss Heart Foundation, the KTI, the University Hospital Basel, the University of Basel; Abbott, Beckman Coulter, Brahms, Idorsia, Novartis, Ortho Diagnostics, Quidel, Roche, Siemens, Singulex, Sphingotec outside the submitted work, as well as speaker honoraria/consulting honoraria from Amgen, Astra Zeneca, Bayer, Boehringer Ingelheim, BMS, Novartis, Osler, Roche, and Sanofi, all paid to the institution. All other coauthors had no conflicts to report.

References

1. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C, Boriani G, Castella M, Dan GA, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau JP, Lettino M, Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021;**42**:373–498.
2. Hijazi Z, Oldgren J, Siegbahn A, Wallentin L. Application of biomarkers for risk stratification in patients with atrial fibrillation. *Clin Chem* 2017;**63**:152–164.
3. Hijazi Z, Lindback J, Alexander JH, Hanna M, Held C, Hylek EM, Lopes RD, Oldgren J, Siegbahn A, Stewart RA, White HD, Granger CB, Wallentin L. The ABC (age, biomarkers, clinical history) stroke risk score: a biomarker-based risk score for predicting stroke in atrial fibrillation. *Eur Heart J* 2016;**37**:1582–1590.
4. Hijazi Z, Oldgren J, Lindback J, Alexander JH, Connolly SJ, Eikelboom JW, Ezekowitz MD, Held C, Hylek EM, Lopes RD, Siegbahn A, Yusuf S, Granger CB, Wallentin L. The novel biomarker-based ABC (age, biomarkers, clinical history)-bleeding risk score for patients with atrial fibrillation: a derivation and validation study. *Lancet* 2016;**387**:2302–2311.
5. Benz AP, Hijazi Z, Lindback J, Connolly SJ, Eikelboom JW, Oldgren J, Siegbahn A, Wallentin L. Biomarker-based risk prediction with the ABC-AF scores in patients with atrial fibrillation not receiving oral anticoagulation. *Circulation* 2021;**143**:1863–1873.
6. Oyama K, Giugliano RP, Berg DD, Ruff CT, Jarolim P, Tang M, Murphy SA, Lanz HJ, Grosso MA, Antman EM, Braunwald E, Morrow DA. Serial assessment of biomarkers and the risk of stroke or systemic embolism and bleeding in patients with atrial fibrillation in the ENGAGE AF-TIMI 48 trial. *Eur Heart J* 2021;**42**:1698–1706.