

# Highlights from 2022 in *EHJ Open*

**Magnus Bäck** <sup>1,2,3,\*</sup>, **Maciej Banach**<sup>4</sup>, **Frieder Braunschweig**<sup>1,2</sup>,  
**Salvatore De Rosa** <sup>5</sup>, **Alessia Gimelli**<sup>6</sup>, **Thomas Kahan** <sup>7,8</sup>,  
**Daniel FJ. Ketelhuth**<sup>9</sup>, **Patrizio Lancellotti** <sup>10</sup>, **Susanna C. Larsson**<sup>11,12</sup>,  
**Linda Mellbin**<sup>1,2</sup>, **Edit Nagy**<sup>1,2</sup>, **Gianluigi Savarese**<sup>1,2</sup>, **Karolina Szummer**<sup>1,13</sup>,  
and **Denis Wahl** <sup>3</sup>, European Heart Journal Open Section Editors

<sup>1</sup>Department of Cardiology, Heart and Vascular Center, Karolinska University Hospital, 17177 Stockholm, Sweden; <sup>2</sup>Department of Medicine Solna, Karolinska Institutet, 17177 Stockholm, Sweden; <sup>3</sup>Nancy University Hospital, University of Lorraine and INSERM U1116, 54511 Nancy, France; <sup>4</sup>Department of Preventive Cardiology and Lipidology, Medical University of Lodz and Polish Mother's Memorial Hospital Research Institute, Lodz, Poland; <sup>5</sup>Division of Cardiology, Department of Medical and Surgical Sciences, Magna Graecia University of Catanzaro, Catanzaro, Italy; <sup>6</sup>Cardiovascular and Imaging Departments, Fondazione Toscana Gabriele Monasterio, Pisa, Italy; <sup>7</sup>Department of Cardiology, Danderyd University Hospital, Stockholm, Sweden; <sup>8</sup>Department of Clinical Sciences, Danderyd Hospital, Karolinska Institutet, Stockholm, Sweden; <sup>9</sup>Department of Molecular Medicine, University of Southern Denmark, Odense, Denmark; <sup>10</sup>GIGA Cardiovascular Sciences, University of Liège Hospital, Centre Hospitalier Universitaire Sart Tilman, Liège, Belgium; <sup>11</sup>Unit of Cardiovascular and Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; <sup>12</sup>Department of Surgical Sciences, Uppsala University, Uppsala, Sweden; and <sup>13</sup>Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden

Online publish-ahead-of-print 20 December 2022

In this editorial, the section editors are looking back at 2022 by summarizing a few of the many highlights in the *EHJ Open* content. All publications in *EHJ Open* are indexed in PubMed and PubMed Central (PMC), which will facilitate our mission to promote open and interactive cardiology for an accelerated and global sharing of science to fight cardiovascular disease.

Randomized controlled trials (RCTs) have been published in *EHJ Open* since the start of the journal.<sup>1,2</sup> A RCT in patients with signs of mild hypertensive heart disease<sup>3</sup> published in the section on Hypertension (Section and Deputy Editor Thomas Kahan) in 2022 examined the effects of curcumin, a polyphenol compound derived from the herb turmeric with anti-inflammatory and anti-oxidant effects, and animal experimental evidence suggesting effects to reduce the development of hypertensive heart disease. The study showed that treatment with curcumin for 24 weeks reduced plasma brain natriuretic peptide levels, as compared to placebo, while diastolic function (by echocardiography) was unchanged.<sup>3</sup> Whether curcumin may offer an opportunity to prevent the transition from hypertension to heart failure with preserved function requires further study.

In Arrhythmia and Electrophysiology (Section and Deputy Editor Frieder Braunschweig), atrial fibrillation screening<sup>4</sup> is highlighted through the meta-analysis by McIntyre *et al.*<sup>5</sup> which showed a modest relative stroke risk reduction of 0.91 (0.84–0.99) in a total of 35 836 participants. However, the heterogenous populations as well as varying screening intervention and stroke outcome definition limited the conclusions and prompted for further studies.<sup>5</sup> Comparing quarterly vs. annual electrocardiogram (ECG) screening for Atrial Fibrillation in elderly Chinese by an Automated ECG system in Community Health centres (AF-CATCH), Zhang *et al.*<sup>6</sup> reported that a change in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $\geq 2$  was associated with a significantly elevated risk of incident atrial fibrillation and suggested that regular re-

assessments of cardiovascular risk factors in the elderly may improve atrial fibrillation detection.

Coronary Artery Disease (Section and Deputy Editor Maciej Banach) as well as Interventional Cardiology and Cardiac Surgery (Section and Social Media Editor Salvatore De Rosa) highlight sex-differences, which was one of the subjects also marking the previous year with *EHJ Open*.<sup>7</sup> A comparison within four European registries revealed sex-related differences in ST-elevation myocardial infarction (STEMI).<sup>8</sup> Women underwent angiography, PCI, and echocardiography to a lesser extent than men and also received less guideline-recommended post-STEMI therapies.<sup>8</sup> Along the same line, novel data from the nationwide Japanese Percutaneous Coronary Intervention (J-PCI) registry highlighted how a significantly lower proportion of women were treated with preoperative mechanical circulatory support compared to intraprocedural use.<sup>9</sup>

The section for Epidemiology and Prevention (Section Editor: Karolina Szummer) spans a broad area of topics exploring associations between cardiovascular outcomes and markers including gastrointestinal factors, behaviours such as anger,<sup>10</sup> and differences between trial and real-world populations. A highlight in 2022 was achievements of primary prevention targets in individuals with high risk of cardiovascular disease,<sup>11</sup> accompanied by an editorial.<sup>12</sup> This study, although being descriptive, points to areas where implementation of treatments may alter future outcomes. We look forward to a follow-up in a decade or so, when the effects of intensified primary prevention will further have decreased cardiovascular disease incidence.

Vascular stiffness is a marker of subclinical disease affected by cardiovascular risk factors as well as Cardiovascular Genetics (Section Editor Susanna C Larsson), which was highlighted by a study of genetic variations within the fatty acid desaturase (FADS) loci.<sup>13</sup> Since FADS is

The opinions expressed in this article are not necessarily those of the Editors of the *European Heart Journal Open* or of the European Society of Cardiology.

\* Corresponding author: Tel: +46 8 123 70 000, Email: [magnus.back@ki.se](mailto:magnus.back@ki.se)

© The Author(s) 2022. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

involved in the metabolism of omega-3 polyunsaturated fatty acid (PUFA), the study investigated the relation between dietary omega-3 PUFA intake and vascular stiffness in relation to FADS genetic variations. A possible interpretation of the results is that the FADS genetic risk factor for vascular stiffness potentially can be neutralized by a high omega-3 PUFA intake. Since the carriers of the protective genotype had less benefit of omega-3 PUFA dietary intake for vascular stiffness, the findings raise the notion of a possible personalized medicine approach for identifying responders and non-responders to omega-3 PUFA-based cardiovascular prevention.<sup>13</sup>

Adult congenital heart disease (ACHD; *Section Editor Edit Nagy*) highlights a nationwide population-based study by Omann *et al.*<sup>14</sup> which analyses the impact of maternal preeclampsia on neurodevelopmental disorders in children born with congenital heart disease. The study assessed whether the maternal-fetal environment further contributes to neurodevelopmental disorders in children born with congenital heart disease (CHD) as opposed to compromised fetal circulation and oxygenation being the main trigger. The main finding is that maternal preeclampsia increases the risk of behavioural diagnoses such as attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders compared to those children born with CHD not exposed to preeclampsia. In addition, CHD and pre-eclampsia may act synergistically and potentiate this effect. These findings are novel and deserve attention with a great impact on further maternal and offspring complications. The section of ACHD welcomes articles in the field of broad spectrum of ACHD including studies with imaging and interventional character.

Current single-cell technologies in atherosclerosis are opening up new opportunities and clinical implications.<sup>15</sup> In *Translational Basic Science* (*Section Editor Daniel F.J. Ketelhuth*), we learned from Slenders *et al.*,<sup>16</sup> about the power of multi-omics, using a single-cell transcriptomics-driven workflow rooted into human large-scale genetic studies, to identify putative candidate genes as well as affected cells associated with cardiovascular traits. *EHJ Open* readers also had the chance to better understand the intriguing event of immune thrombotic thrombocytopenia (TIT) triggered by adenoviral vector-based severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination, its major clinical consequences, and potential mechanisms that could be exploited for preventing and treating it.<sup>17</sup> This year, *Vascular Medicine* (*Section Editor Denis Wahl*) highlights the pre-TIT syndrome for which Salih *et al.*<sup>18</sup> offer a clinical pathway for early recognition and treatment to prevent thrombotic complications of COVID-19 vaccination. It has also been pointed out by Noyé and Lecompte<sup>19</sup> that there are other thrombosis and thrombocytopenia syndromes, e.g. heparin-induced thrombocytopenia and antiphospholipid syndrome, which encompass a range of pathogenic processes of which some overlap with TIT.

Autoimmune connective tissue diseases (CTDs) are associated with valvular heart disease (VHD; *Section Editor: Patrizio Lancellotti*). In particular, anti-phospholipid antibody positivity without systemic manifestations is more prevalent in aortic stenosis patients compared with matched healthy controls.<sup>20</sup> In terms of aortic stenosis management, Gad *et al.*<sup>21</sup> reported that outcomes for patients with CTD after aortic valve replacement (AVR) followed in the American Nationwide Readmissions Database were not inferior compared to their non-CTD counterparts. Tricuspid regurgitation (TR) is a prevalent VHD associated with high morbidity and mortality when severe, which is highlighted by the causal relation of TR for heart failure outcomes in a mediation analysis of echocardiographic predictors by Hakuno *et al.*<sup>22</sup> There are in addition few treatment options for TR, and often, the management is done late in the evolution of the disease when the patient already presents major comorbidities while the type of treatment depends essentially on the operative risk. Hochstadt *et al.*<sup>23</sup> provided a new scoring system to stratify the risk of patients with significant TR treated conservatively. The interest and the limitations of this new score were discussed by Donal *et al.*<sup>24</sup>

*Vascular and Cardiac Imaging* (*Section Editor Alessia Gimelli*) highlights that coronary-specific quantification of myocardial deformation by strain echocardiography may disclose the culprit vessel in patients with non-ST-segment elevation acute coronary syndrome,<sup>25</sup> which was accompanied by a linked publication of an example of these diagnostic approaches in an *EHJ-Case Reports* article.<sup>26</sup> In addition to the widely studied left ventricular strain post myocardial infarction (MI), echocardiographic evaluation of atrial function may bring additional value to risk prediction following acute MI.<sup>27</sup> Myocardial deformation is in fact a topic, which has spanned over several *EHJ Open* sections in 2022, including prognostic value in congenital aortic stenosis<sup>28</sup> and in patients with severe aortic stenosis undergoing AVR.<sup>29</sup>

Myocardial deformation characterization is also an important approach in *Heart Failure* (*Section Editor Gianluigi Savarese*). The implications of the latter were shown in *Special Populations* (*Section Editor Linda Mellbin*) relating to cardio-oncology. In the latter context, serial changes of layer-specific myocardial function according to chemotherapy regimen in patients with breast cancer identified the endocardial layer as the most vulnerable to chemotherapy-induced myocardial damage.<sup>30</sup> Villarraga and Herrman made the analogy of chemotherapy cardiotoxicity to the differentiation of MI into endocardial, transmural, or of another kind.<sup>31</sup>

Although we only highlighted some articles in this editorial, we encourage you to explore the full content of *EHJ Open*, which is freely available by Open Access. We also want to thank all of the authors for their contributions to the journal and welcome your future submissions to *EHJ Open*.

## Acknowledgements

The editorial work of *EHJ Open* would not be possible without the efforts of the associate editors, editorial board members, and reviewers. The *EHJ Open* editorial board members can be found at <https://academic.oup.com/ehjopen/pages/editorial-board>, and the reviewers will be acknowledged in the first issue of 2023.

**Conflict of interest:** None declared.

## References

- Cremer PC, Sheng CC, Sahoo D, Dugar S, Prada RA, Wang TKM, Hassan OKA, Hernandez-Montfort J, Wolinsky DA, Culver DA, Rajendram P, Duggal A, Brennan DM, Wolski KE, Lincoff AM, Nissen SE, Menon V. Double-blind randomized proof-of-concept trial of canakinumab in patients with COVID-19 associated cardiac injury and heightened inflammation. *Eur Heart J Open* 2021;1:oeab002.
- Bartholomew CL, Muhlestein JB, May HT, Le VT, Galenko O, Garrett KD, Brunner C, Hopkins RO, Carlquist JF, Knowlton KU, Anderson JL, Bailey BW, Horne BD. Randomized controlled trial of once-per-week intermittent fasting for health improvement: the WONDERFUL trial. *Eur Heart J Open* 2021;1:oeab026.
- Funamoto M, Sunagawa Y, Katanasaka Y, Kato T, Funada J, Ajiro Y, Komiyama M, Akao M, Yasoda A, Yamakage H, Satoh-Asahara N, Wada H, Ikeda Y, Morimoto T, Hasegawa K. Effects of high-absorption curcumin for the prevention of hypertensive heart disease: a double-blind, placebo-controlled, randomized clinical study. *Eur Heart J Open* 2022;2:oeac057.
- Svennberg E, Braunschweig F. Screening for atrial fibrillation: less is more? *Eur Heart J Open* 2021;1:oeab038.
- McIntyre WF, Diederichsen SZ, Freedman B, Schnabel RB, Svennberg E, Healey JS. Screening for atrial fibrillation to prevent stroke: a meta-analysis. *Eur Heart J Open* 2022;2:oeac044.
- Zhang W, Chen Y, Hu LX, Xia JH, Ye XF, Cheng YB, Wang Y, Guo QH, Li Y, Lowres N, Freedman B, Wang JG; AF-CATCH Investigators and Coordinators. Changes in the CHA(2)DS(2)-VAS(C) score as a predictor of incident atrial fibrillation in older Chinese individuals: the AF-CATCH study. *Eur Heart J Open* 2022;2:oeac046.
- Huded CP, Kumar A, Kassis N, Johnson MJ, Kravitz K, Brown A, Shanahan M, Trentanelli K, Reed GW, Menon V, Krishnaswamy A, Ellis SG, Kralovic DM, Meldon SW, Kapadia SR, Khot UN. Five years of a comprehensive ST-elevation myocardial infarction protocol and its association with sex disparities. *Eur Heart J Open* 2021;1:oeab011.
- Hellgren T, Blondal M, Jortveit J, Ferenci T, Faxen J, Lewinter C, Eha J, Loiveke P, Marandi T, Ainla T, Saar A, Veldre G, Andreka P, Halvorsen S, Janosi A, Edfors R. Sex-related differences in the management and outcomes of patients hospitalized with

- ST-elevation myocardial infarction: a comparison within four European myocardial infarction registries. *Eur Heart J Open* 2022;**2**:oeac042.
9. Muramatsu T, Inohara T, Kohsaka S, Yamaji K, Ishii H, Shinke T, Toriya T, Yoshiki Y, Ozaki Y, Ando H, Amano T, Nakamura M, Ikari Y. Mechanical circulatory support devices for elective percutaneous coronary interventions: novel insights from the Japanese nationwide J-PCI registry. *Eur Heart J Open* 2022;**2**:oeac041.
  10. Titova OE, Baron JA, Michaelsson K, Larsson SC. Anger frequency and risk of cardiovascular morbidity and mortality. *Eur Heart J Open* 2022;**2**:oeac050.
  11. Hagen AN, Ariansen I, Hanssen TA, Lappégard KT, Eggen AE, Lochen ML, Njolstad I, Wilsgaard T, Hopstock LA. Achievements of primary prevention targets in individuals with high risk of cardiovascular disease: an 8-year follow-up of the tromso study. *Eur Heart J Open* 2022;**2**:oeac061.
  12. De Backer G. Prevention of cardiovascular disease: are we successful? *Eur Heart J Open* 2022;**2**:oeac062.
  13. Bäck M, Xhaard C, Rouget R, Thuillier Q, Plunde O, Larsson SC, Gierd N, Ferreira JP, Boivin JM, Bozec E, Merckle L, Zannad F, Hoge A, Guillaume M, Dandine-Roulland C, Floch EL, Bacq-Daïan D, Deleuze JF, Van den Berghe L, Nazare JA, Laville M, Branlant C, Behm-Ansmant I, Wagner S, Rossignol P. Fatty acid desaturase genetic variations and dietary omega-3 fatty acid intake associate with arterial stiffness. *Eur Heart J Open* 2022;**2**:oeac016.
  14. Omann C, Nyboe C, Kristensen R, Ernst A, Ramlau-Hansen CH, Rask C, Tabor A, Gaynor JW, Hjortdal VE. Pre-eclampsia is associated with increased neurodevelopmental disorders in children with congenital heart disease. *Eur Heart J Open* 2022;**2**:oeac027.
  15. de Winther MPJ, Bäck M, Evans P, Gomez D, Goncalves I, Jorgensen HF, Koenen RR, Lutgens E, Norata GD, Osto E, Dib L, Simons M, Stellos K, Yla-Herttuala S, Winkels H, Bochaton-Piallat ML, Monaco C. Translational opportunities of single-cell biology in atherosclerosis. *Eur Heart J* 2022;ehac686. doi:10.1093/eurheartj/ehac686.
  16. Slenders L, Landsmeer LPL, Cui K, Depuydt MAC, Verwer M, Mekke J, Timmerman N, van den Dungen NAM, Kuiper J, de Winther MPJ, Prange KHM, Ma WF, Miller CL, Aherrahrou R, Civelek M, de Borst GJ, de Kleijn DPV, Asselbergs FW, den Ruijter HM, Boltjes A, Pasterkamp G, van der Laan SW, Mokry M. Intersecting single-cell transcriptomics and genome-wide association studies identifies crucial cell populations and candidate genes for atherosclerosis. *Eur Heart J Open* 2022;**2**:oeab043. doi:10.1093/ehjopen/oeab043.
  17. Marchandot B, Curtiaud A, Trimaille A, Sattler L, Grunebaum L, Morel O. Vaccine-induced immune thrombotic thrombocytopenia: current evidence, potential mechanisms, clinical implications, and future directions. *Eur Heart J Open* 2021;**1**:oeab014.
  18. Salih F, Kohler S, Schonborn L, Thiele T, Greinacher A, Endres M. Early recognition and treatment of pre-VITT syndrome after adenoviral vector-based SARS-CoV-2 vaccination may prevent from thrombotic complications: review of published cases and clinical pathway. *Eur Heart J Open* 2022;**2**:oeac036.
  19. Noyé M, Lecompte T, Wahl D. Vaccination-induced thrombocytopenia and thrombosis (VITT) and pre-VITT: Do not miss (or misdiagnose) the new member of the thrombotic thrombocytopenias family. *Eur Heart J Open* 2022;**2**:oeac036. doi:10.1093/ehjopen/oeac056.
  20. Plunde O, Svenungsson E, Ferrannini G, Franco-Cereceda A, Bäck M. Antiphospholipid antibodies in patients with calcific aortic valve stenosis. *Rheumatology (Oxford)* 2022;keac466. doi:10.1093/rheumatology/keac466.
  21. Gad MM, Lichtman D, Saad AM, Isogai T, Bansal A, Abdallah MS, Roselli E, Chatterjee S, Reed GW, Kapadia SR, Menon V, Wassif H. Autoimmune connective tissue diseases and aortic valve replacement outcomes: a population-based study. *Eur Heart J Open* 2022;**2**:oeac024.
  22. Hakuno D, Fukae T, Takahashi M, Sueyoshi K. Causal relation of tricuspid regurgitation for heart failure outcomes: a mediation analysis of echocardiographic predictors. *Eur Heart J Open* 2021;**1**:oeab027.
  23. Hochstadt A, Maor E, Ghantous E, Merdler I, Granot Y, Rubinshtein R, Banai S, Segev A, Kuperstein R, Topilsky Y. A validated score to predict one-year and long-term mortality in patients with significant tricuspid regurgitation. *Eur Heart J Open* 2022;**2**:oeac067.
  24. Donal E, Lancellotti P. A new score to stratify the risk in tricuspid regurgitation: the icing on the cake. *Eur Heart J Open* 2022;**2**:oeac068.
  25. Guaricci AI, Chiarello G, Gherbesi E, Fusini L, Soldato N, Siena P, Ursi R, Ruggieri R, Guglielmo M, Muscogiuri G, Baggiano A, Rabbat MG, Memeo R, Lepera M, Favale S, Pontone G. Coronary-specific quantification of myocardial deformation by strain echocardiography may disclose the culprit vessel in patients with non-ST-segment elevation acute coronary syndrome. *Eur Heart J Open* 2022;**2**:oeac010.
  26. Guaricci AI, Soldato N, Chiarello G, Pontone G. Territorial longitudinal strain discloses the culprit vessel in a patient with non-ST-segment elevation acute coronary syndrome. *Eur Heart J Case Rep* 2022;**6**:ytac097.
  27. Backhaus SJ, Rosel SF, Stiermaier T, Schmidt-Rimpler J, Evertz R, Schulz A, Lange T, Kowallick JT, Kutty S, Bigalke B, Gutberlet M, Hasenfuss G, Thiele H, Eitel I, Schuster A. Left-atrial long-axis shortening allows effective quantification of atrial function and optimized risk prediction following acute myocardial infarction. *Eur Heart J Open* 2022;**2**:oeac053.
  28. Mutluer FO, Bowen DJ, van Grootel RWJ, Kardys I, Roos-Hesselink JW, van den Bosch AE. Prognostic value of left atrial strain in patients with congenital aortic stenosis. *Eur Heart J Open* 2022;**2**:oeac023.
  29. Bi X, Yeung DF, Thaden JJ, Nhola LF, Schaff HV, Pislaru SV, Pelliikka PA, Pochettino A, Greason KL, Nkomo VT, Villarraga HR. Characterization of myocardial mechanics and its prognostic significance in patients with severe aortic stenosis undergoing aortic valve replacement. *Eur Heart J Open* 2022;**2**:oeac074. doi:10.1093/ehjopen/oeac074.
  30. Kim MN, Kim SR, Kim HD, Cho DH, Jung SP, Park KH, Park SM. Serial changes of layer-specific myocardial function according to chemotherapy regimen in patients with breast cancer. *Eur Heart J Open* 2022;**2**:oeac008.
  31. Villarraga H, Herrmann J. Cardiotoxicity assessment in breast cancer patients: is it straining? *Eur Heart J Open* 2022;**2**:oeac020.