

**Basic Science** 

proCardio2022 THE GLOBAL CARDIAC

BIOMARKER FORUM

#proCardioForum

# **Executive Summary**

October 13–14, 2022 Munich, Germany

# proCardio2022



"It is remarkable to me to see the depth and insight into disease processes that we are now talking about and the interface of biomarkers with various -omics and imaging platforms, as well as translation from the hospital out to point-of-care settings.<sup>11</sup> ~ Prof James Januzzi

" proCardio is so important to me because it truly is a unique meeting that brings together so many highly specialised professionals from different fields." ~ Prof Carolyn Lam



#### proCardio 2022

The 12th International proCardio symposium, organised by Roche Diagnostics, brought together a global audience of healthcare professionals, both in-person and virtually, and included a series of insightful presentations from esteemed cardiac leaders. Held over two days, the exciting scientific program started with basic science research involving cardiac biomarkers followed by sessions across the cardiac patient journey from prevention to diagnosis through risk stratification and therapy, before concluding with the latest innovations in the field.

The Q&A sessions which followed the presentations brought about a wealth of engaging discussion among the faculty and the audience, making it a truly collaborative scientific event.

Prof. James Januzzi, MD proCardio Chair Massachusetts General Hospital,

Harvard Medical School

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Prof. Carolyn Lam, MD proCardio Co-Chair

National Heart Centre Singapore, Duke-National University of Singapore

proCardio provides a unique platform for scientific exchange between a diverse range of highly trained specialists, from cardiologists and emergency physicians to clinical chemists, from which the outcomes can further advance the field of cardiac biomarkers.



For attendees only: Click here to access the proCardio2022 On-Demand platform

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Lifecycle Leader Cardiometabolics Roche Diagnostics International

# Basic Science

Chairs:

Robert Christenson (University of Maryland School of Medicine, Maryland, USA) Gerard Pasterkamp (University Medical Center Utrecht, Netherlands)

In the first session of **proCardio 2022**, the scientific faculty presented basic science research involving the discovery and development of biomarkers in various cardiac disorders which led to fruitful discussions. Up first, **Alma Mingels** (Maastricht University, Netherlands) explored the differences between the well-known cardiac biomarkers, cardiac troponin I (cTnI) and cardiac troponin T (cTnT), including how cTnI is released earlier and at higher concentrations after myocardial injury. She also described an interesting new hypothesis of cTn release from cardiomyocytes via exophers, gathering interest from audience members who credited the importance of understanding the origin and function of biomarkers to ultimately improve clinical care.

Next, the role of proteomic biomarker profiling in heart failure was discussed by **Jasper Tromp** (National University of Singapore, Singapore), which can be used to classify patients into mutually exclusive subgroups. He highlighted how protein panels, alone and in combination with other –omics data, can enhance biomarker research by providing a better understanding of the pathophysiological role of biomarkers and disease pathways. The notion of pathway analysis for proteins as a neglected area in CV research prompted great intrigue during the discussion.

**Giuseppe Vergaro** (Fondazione Monasterio, Pisa, Italy) described pathophysiological evidence for the role of biomarkers in cardiac amyloidosis, including N-terminal pro b-type natriuretic peptide (NT-proBNP) and cTnT as key prognostic and diagnostic markers in these patients. He shared exciting data from his recent study suggesting that these markers could be used in conjunction to effectively rule out cardiac amyloidosis, which could potentially reduce unnecessary diagnostic evaluations.

#### Next, Caroline Coats (Queen Elizabeth University

Hospital, Glasgow, UK) presented the recent biomarker developments in hypertrophic cardiomyopathy, which can be used to study mechanisms of heart failure. She emphasized the exciting prospect of biomarkers to identify early disease that may be relevant to therapeutic decisions within the clinic, which could improve patient outcomes. It was agreed that integrating multiple diagnostic techniques, such as proteomics and transcriptomics, also discussed earlier by Prof Tromp, are the way of the future and provide a great opportunity for detailed clinical phenotyping of disease.





In the concluding presentation, **Peter Liu** (University of Ottawa Heart Institute, Ontario, Canada) presented exciting research suggesting that insulin like growth factor binding protein 7 (IGFBP-7) in the myocardium contributes to accelerated cardiac remodelling as well as cellular senescence and inflammation. Impressive data showing that targeting IGFBP-7 can reverse remodelling in heart failure and reduce fibrosis, thus making IGFBP-7 a potential candidate for precision medicine in heart failure, which brought about a wave of excitement. Could we be on the way to identifying subgroups of patients, e.g., older patients with enhanced senescence, who would benefit from anti-IGFBP-7 treatment? Watch this space! The session finished with an interesting discussion among the faculty and the audience regarding the impact of phenotypes on the interpretation of biomarker data, especially for non-specific markers, such as IGFBP-7. Collaboration among researchers was highlighted as being needed in order to generate large datasets for analysis to allow for greater insight – this is where the coming together of great minds at the **proCardio** event can truly advance research in the field!



# Prevention

Next up, the value of biomarkers in the prevention of future cardiovascular events was discussed. Cynthia Papendick (Royal Adelaide Hospital, South Australia) sparked a captivating debate around the pros and cons of population-wide cTn screening for cardiovascular disease. While clear guidance and further research are needed, screening programs could result in improvements in current risk scores in the general population. In her wealth of experience as an emergency department (ED) physician, many patients with detectable cTn present to the ED every day - could future events be prevented if patients are educated about their increased risk? However, the panel and audience raised concerns regarding already overcrowded EDs and discussed whether shared decision-making tools (e.g., automated risk score generators) could be implemented to facilitate these conversations.



Chairs: Shelley Zieroth (St. Boniface Hospital, Manitoba, Canada) Rudolf de Boer (Erasmus MC, Rotterdam, Netherlands)

**Flavia Kessler Borges** (McMaster University, Ontario, Canada) presented learnings from HIP ATTACK-1 trial, which analysed whether accelerated surgery would reduce mortality and major complications after hip fractures in elderly patients. Although overall trial results were neutral, a subgroup analysis showed that patients with hip fractures and elevated cTn pre-surgery had significantly lower mortality/complications. This raised the hyopthesis that this specific patient group might benefit from expedited surgery by reducing the exposure time to physiological stress associated with the hip fracture. This specifically will be analysed in the HIP ATTACK-2 trial.

The next presentation was especially timely following the recent publication of the European Society of Cardiology guidelines on cardio-oncology. **Ninian Lang** (Queen Elizabeth University Hospital, Glasgow, Scotland)

presented the evidence supporting cTn as a risk marker for anthracycline cardiotoxicity that, however, has not been particularly useful in determining the cardio-protective treatment to prescribe. The unmet need for large-scale assessments and discovery of cardio-oncology biomarkers, and perhaps multimarker panels, linking to both outcomes and how they could be used in directing which cardioprotective strategies to employ was also discussed. This interesting and developing field raised great interest from the audience and how institutions could implement cardio-oncology-specific services in routine practice was also debated.





Finally, there is high economic burden of cardiorenal complications in type 2 diabetes, mostly derived from the rate of hospitalisations. **Muthiah Vaduganathan** (Brigham and Women's Hospital, Massachusetts, USA) gave an exciting presentation on this topic including clinical trial data showing NT-proBNP-based screening in type 2 diabetes as cost-effective. He also proposed that targeted cardiorenal prevention approaches with modern therapies guided by biomarker screening could be a highly cost-effective strategy in clinical practice. This resulted in some interesting discussion topics, including the differences among guidelines, as well as the relevance of country-specific health economic data to different healthcare systems.

The concluding Q&A session also elicited an interesting deliberation on whether prevention strategies could be improved with the inclusion of sex-specific cut-offs or whether this adds a layer of complication.



## Diagnosis

Biomarkers are the foundation of improving diagnostic accuracy and precision. **Lori Daniels** (University of California, San Diego, USA) opened the session by highlighting the challenges in distinguishing between type 1 and type 2 myocardial infarction which sparked interesting debates. The isolated use of biomarkers is insufficient whereas combination with imaging may provide a more complete diagnosis, which could ultimately improve prognosis. An interesting question arose regarding the use of artificial intelligence (AI) for differentiating between type 1 and type 2 myocardial infarction however, this would be limited by the patient data available e.g., the lab tests ordered. Additionally, a key theme of differences in diagnosis and treatment practices among the sexes was also discussed.



Chairs: **Rick Body** (University of Manchester, UK) **Cynthia Papendick** (Royal Adelaide Hospital, South Australia)

Next, Nicholas Mills (University of Edinburgh, Scotland)

discussed how to differentiate patients in the observe zone with suspected ACS using high-sensitivity cTn and an evidence-based diagnostic pathway. Those with intermediate cTn levels may require further cardiac imaging and investigations, which could potentially identify those with unrecognised disease. He also touched on future statistical models which could further aid clinicians in stratifying patients based on risk, including Al-guided tools, by providing greater flexibility for healthcare systems and facilitating individualised medicine. An interesting discussion surrounding how to educate HCPs on how to successfully implement shared decision-making between cardiologists and emergency physicians took place. The ever-popular topic of multi-marker panels was also discussed, with the addition of NT-proBNP thought to be promising for differentiating causes of myocardial injury.

A thought-provoking presentation on the role of natriuretic peptides in heart failure with preserved ejection fraction with a focus on NT-proBNP was then given by **Muthiah Vaduganathan** (Brigham and Women's Hospital, Massachusetts, USA). While challenges, such as sex- and race-specific differences, do exist, he presented a wealth of compelling data from clinical trials showing how NT-proBNP can be used in risk prediction, assessing responsiveness to treatment as well as diagnosis. An interesting question from a fellow cardiologist sparked discussion about the importance of assessing the change in NT-proBNP levels, not just single measurements!



To end this session, **Jonathan Cunningham** (Brigham and Women's Hospital, Massachusetts, USA) discussed how large-scale proteomics can help identify novel proteins with causal roles in heart failure across the whole ejection fraction spectrum or even improve risk prediction. He presented his latest exciting research which led to the discovery of a novel biomarker in heart failure, SVEP1, which prompted a series of interesting questions from the audience! His thought-provoking presentation also led to questions regarding the actionability of very large multimarker panels in clinical practice – is it feasible to have a risk score with over 60 markers? Perhaps multiplex assays and auto-generated scores are the way forward! Probabilistic medicine arose as a key theme during this session and enticed some excellent exchanges between HCPs. Also, a very special guest, Chair **James Januzzi** (Massachusetts General Hospital, Massachusetts, USA), made a surprise appearance all the way from Boston for the exciting discussion, highlighting the importance of early diagnosis to improve patient outcomes and how biomarkers can help with this! Along with his co-Chair, **Carolyn Lam** (Duke-NUS Medical School, National Heart Centre Singapore) they led a provocative discussion on sex-specific cut-offs and their implementation in clinical practice.





## Risk Stratification

The concluding session of Day One of **proCardio 2022** involved four highly engaging presentations on the utility of biomarkers in risk-stratifying patients with cardiovascular diseases. **Larissa Fabritz** (University Heart and Vascular Center UKE Hamburg, Germany) opened by presenting exciting research and findings regarding novel predictive models, including biomarkers such as bone morphogenetic protein 10 (BMP-10), fibroblast growth factor 23 (FGF23), angiopoietin 2 (ANGPT2) and NT-proBNP, in new and recurrent atrial fibrillation.



Chairs: Allan Jaffe (Mayo Clinic, Minnesota, USA) Paulus Kirchhof (University Heart and Vascular Center UKE, Hamburg, Germany)

Up next, **Agneta Siegbahn** (Uppsala University, Sweden) reported on her compelling research into established and multiplex biomarkers for risk prediction in cardiovascular disease. While she concluded that the single biomarkers, NT-proBNP, cTnT and GDF-15 provided most of the essential prognostic information, multiplex analyses may identify biomarker pathophysiological pathways to better understand diseases, which may be useful for prognostication, decision support, and the individualisation of treatment. Interesting questions were raised as to whether the inclusion of the novel biomarkers highlighted by Larissa Fabritz, e.g., BMP-10, would have affected her findings – future publications and specific research was alluded to by Agneta Siegbahn. Stay tuned!

#### Stefanie Aeschbacher (University hospital Basel,

Switzerland) described her interesting research that identified a biomarker-based prediction model for heart-brain interactions in patients with cardiac arrhythmia from an analysis of the Swiss-AF study. She highlighted some of the many upcoming analyses from the Swiss-AF team including the role of BMP-10 in AF recurrence and adverse outcomes, as well as long term follow-up planned for the future.



Lastly, risk stratification of acute myocardial infarction using a single high-sensitivity cTnT sample result was discussed by **Yader Sandoval** (Minneapolis Heart Institute, Minnesota, USA). He presented supporting evidence for the established strategy for ruling out patients, i.e., those at low risk of acute myocardial infarction, before debating future research directions e.g., sex-specific differences, development of point-ofcare assays and Al-based approaches, and further research into rule-in algorithms. His impressive presentation highlighted key topics, such as the presence of sex-specific differences when using high-sensitivity cTnT for ruling out acute myocardial injury and, how patients with mild troponin elevations should be managed considering their documented increased long-term risk.



James Januzzi joined the discussion once again which focused on the development of point-of-care assays to facilitate risk stratification in primary care settings or even at home. The understanding of normal values and the ability to obtain serial measurements to monitor changes in biomarkers were also highlighted as important for prognostication. Could wearable devices and digital technologies augment continuous risk prediction?



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Chairs: Evangelos Giannitsis (Heidelberg University Hospital, Germany) Faiez Zannad (Université de Lorraine, Paris, France)

To start Day Two of **proCardio 2022**, exciting presentations on how biomarker assessment and monitoring can influence therapeutic decisions and predict treatment response were given by world-leading clinicians. **Carolyn Lam** (Duke-NUS Medical School, National Heart Centre Singapore) began by detailing individualised clinical approaches in patients with heart failure with preserved ejection fraction, a heterogeneous population with varying symptom presentations and outcomes. She also described the prominent role of co-morbidities and how machine learning approaches hold the potential to sub-phenotype such patients; however, the clinical implications for precision therapeutics have yet to be demonstrated. Having arose as a key topic of this year's proCardio, Ileana Piña (Thomas Jefferson University,

Pennsylvania, USA) gave a thought-provoking presentation, describing the inherent differences in electrophysiology by sex and how these can impact the prevalence of cardiac arrhythmias as well as the response to treatment and cardiac devices. She highlighted the inadequate representation of females across cardiovascular trials, before making pleas to future investigators to prospectively enrol women and for guideline creators to include sexspecific recommendations. Highly engaging discussions followed regarding the importance of creating equality in the management of males and females with heart failure and what clinicians can do to address these unmet needs.





Circling back to heart failure with preserved ejection fraction, **Antoni Bayes-Genis** (Hospital Universitari Germans Trias i Pujol, Barcelona, Spain) described the changing landscape, including timely and exciting clinical data on new treatments (e.g, the hot topic of SGLT2 inhibitors). The role of biomarkers, especially NT-proBNP and cTn, was also discussed including their use in predicting outcomes, discriminating risk, and potentially whether levels of biomarkers differ between treatment responders and non-responders. Future possibilities of clinical approaches conducted in primary care were postulated during the interesting discussion. Next, **Christie Ballantyne** (Baylor College of Medicine, Texas, USA) presented on the marker, lipoprotein(a) and the role it plays in cardiovascular disease before describing how lipoprotein(a) should be measured and the impact it has on current treatment and screening approaches. He also touched on the exciting prospect of targeted therapies that are currently in development.

The session was concluded by **Alexandre Mebazaa** (University Hospital Saint Louis, Paris, France) who discussed the assessment and monitoring of congestion in heart failure throughout the patient journey. He concluded with sharing the design of large randomised controlled trial, STRONG-HF, which assessed the safety and efficacy of rapid up-titration of evidence-based guideline-directed medical therapy and close follow up (physical examination, NT-proBNP) compared to usual care. Recently presented as a late breaker at the American Heart Association 2022 meeting, STRONG-HF was terminated early due to a significantly lower risk of heart failure readmission or all-cause death in the high-intensity treatment arm.





# Inn<u>ovation</u>

Chairs:

Last but certainly not least, proCardio 2022 finished with a captivating session dedicated to the latest innovations in cardiovascular research and care. Winnie Chua (University of Birmingham, UK) began by reporting on how combining biomolecule concentrations has the potential to enable early detection of disease processes and to guide stratified prevention and treatment of cardiovascular diseases. The EAST-AFNET4 study identified four patient clusters in atrial fibrillation, two dominated by inflammation markers and the others characterised by a combination of markers. She also showed how commonality analysis allows for greater understanding of the unique and shared effects of biomarkers for predicting outcomes. Excitement flowed through the audience about the possibility of a liquid cardiovascular biopsy or diagnostic in the near future!

#### David Morrow (Brigham & Women's Hospital/Harvard Medical School, Massachusetts, USA) Christopher Baugh (Brigham & Women's Hospital, Massachusetts, USA)

Next, recent advancements in the development of digital decision support tools and disease management solutions were discussed by **Rick Pleijhuis** (University Medical Center Groningen, Netherlands). He described the centralised digital platform that he co-founded, that can assist with algorithm development using standardisation and validation with anonymized institutional data. The platform can also facilitate the obtaining of CE certification and integrating approved algorithms/decision support tools in practice, contributing to patient-tailored treatment strategies. While supported by some compelling evidence, the willingness of clinicians to use such digital decision tools in real-world settings was questioned.

#### Christian Mueller (Universitat Basel, Switzerland)

debated whether the biological differences between

cTnT and cTnI, observed in the latest research, can impact the diagnostic and prognostic accuracy in cardiovascular diseases. While both have very high and comparable diagnostic accuracy when applied to the ESC 0/1hour algorithms for acute myocardial infarction, he showed that cTnT outperforms high-sensitivity cTnI when it comes to prognostication.



Women's heart health was at the forefront again with a presentation from **Emily Lau** (Massachusetts General Hospital, USA) on sex differences of biomarkers in heart failure, including discoveries from proteomic analysis. She explained how biomarkers highlight sex differences in key biological pathways (e.g., inflammation and adiposity) and echoed earlier testaments for the need for sex-specific thresholds for diagnosis and risk prediction in heart failure.



The final presentation by **Joan Montaner** (Hospital Macarena, Seville, Spain) discussed some of the latest clinical research into blood-based biomarkers, such as NT-proBNP, Ang-2, cTn, BMP-10 and FGF-23, used in the detection of atrial fibrillation among high-risk asymptomatic individuals and cryptogenic stroke patients. He concluded his presentation by showing his interesting research project that combines point-of-care testing and a smartphone application to improve the management of undetermined stroke.



#### **Overall Impressions**

Participants rated the event and topics highly

How beneficial did you find attending proCardio 2022?

How relevant were the topics presented during proCardio 2022?

Average rating (1-low, 5-high) 0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 4.89 4.81

Nearly all participants (98%) were interested in attending the next proCardio and the majority agreed that face-to-face or hybrid events are the way forward.















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