HF Biomarkers in Clinical Practice

時間: 115 年 5 月 31 日(星期日) 13:30-16:30
地點: 張榮發基金會國際會議中心 7F 703 會議室 (台北市中正區中山南路 11 號)

13:30 Opening Remarks..... **李貽恒**

Chair: 林宗憲

13:35 Introduction: Classification and Types of HF Biomarkers — Pathological and Molecular Basis ....**洪崇烈**

Chair: 林宗憲

14:05 The Application of HF Diagnosis: Workflow and Cutoffs (Acute vs. Chronic HF, HFrEF vs. HFpEF, High risk population: CKD, Diabetes, HTN, CAD, and AF) .....**徐千舜**

Chair: 謝宜璋

14:35 Biomarkers in Guiding Clinical Management of HF (Evidences and Meta-analysis)..... **張鴻猷**

Chair: 王俊傑

15:05 Biomarkers Monitoring during HF Treatment.....**張瑋婷**

Chair: 王俊傑

15:35 Prognostic Utilization of Biomarkers in HF.....**吳卓鍇**

16:05 Discussion..... **林文雄**

16:25 Closing Remarks ....**林文雄**

Dr HUNG CURRICULUM VITAE

Basic Data

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Education:

MD. (Medical College, National Taiwan University, Taipei, Taiwan)
MSc. (College of Public Health, National Taiwan University, Taipei, Taiwan)
PhD. (Institute of Clinical Medicine, National Yang Ming Chiao Tung University)

Research Interest and Expertise

- Heart failure
- Echocardiography
- Cardiovascular Imaging
- Molecular biology in ALDH2 knock-in alcohol and high-fat diet mice model

Deputy Editor/Associate Editor (SCI Journals)

- JACC: Asia (AE)
- International Journal of Gerontology (Deputy Editors-in-Chief)
- JCDD
- Diagnostics (Board)
- Frontiers in Cardiovascular Medicine: Guest Editor

Major Grants as PI (National Science and Technology Council [NSTC]/Ministry of Science and Technology [MOST])

1. MOST: The Role of Aldehyde Dehydrogenase 2 Polymorphism in Electromechanical Disturbances of Alcoholic Cardiomyopathy. (MOST 103-2314-B-195-006-MY3; 20140801~20170731)
2. MOST: The Therapy Mechanisms of Aldehyde Dehydrogenase Enhancer in Aldehyde Dehydrogenase 2 Polymorphism Alcoholic Cardiomyopathy. (MOST 106-2314-B-195-008-MY2; 20170801~20190731) (108-2314-B-195 -018 -MY2)
3. NSTC: Establishment of Artificial Intelligence based Platform for Cardiac Imaging-Genetics Research in Heart Failure (112-2314-B-715-008-MY3)
4. Participated in more than 20 NSTC/MOST programs as Co-PI

個 人 簡 歷 (*Curriculum Vitae*)

姓名：徐千彝　**Chien-Yi Hsu, MD, PhD, FESC, FAPSC**

學歷：

1. 國立陽明大學醫學士
2. 國立陽明大學臨床醫學研究所博士

現職：

1. 臺北醫學大學附設醫院心臟內科專任主治醫師
2. 臺北醫學大學附設醫院研究部副主任
3. 臺北醫學大學附設醫院心臟內科心臟衰竭組主任
4. 臺北醫學大學專任副教授
5. 教育部部定副教授 (副字第 151134 號)
6. 台灣動脈硬化暨血管病醫學會 TSAVD 理事(第十屆)
7. 中華民國血脂及動脈硬化學會 TSLA 副秘書長(第十一屆)
8. 台灣心肌梗塞學會 TAMIS 副秘書長(第二屆)，國際委員會主任委員(第二屆)
9. 臺灣介入性心臟血管醫學會 TSCI 研究暨登錄委員會委員(第十一屆)
10. 歐洲心臟學會會士 (FESC, Fellow of European Society of Cardiology)
11. 亞太心臟學會會士 (FAPSC, Fellow of Asian Pacific Society of Cardiology)
12. 國際腫瘤心臟學會會員 (Member of International Cardio-Oncology Society, ICOS)
13. 亞太心血管研究聯盟 Asia-Pacific Cardiovascular Research (ASPIRE) Network 指導委員會委員
    (Steering Committee Member)

經歷：

1. 台北榮民總醫院內科部住院醫師、住院總醫師、內科部主治醫師
2. 台北榮民總醫院玉里分院心臟內科主治醫師
3. 台北榮民總醫院心臟內科特約醫師
4. 國立陽明大學內科學系兼任講師
5. 美國加州大學聖地牙哥分校 (UCSD) 短期進修醫師
6. 史瓦帝尼王國 (Kingdom of Eswatini) 王室醫療團醫師 (2018, 2025)
7. 臺北醫學大學附設醫院特等病房主任、君蔚國際病房主任
8. 中華民國心臟學會 TSOC 青年工作小組主任委員(第二十八屆)
9. 台灣高血壓學會 THS 理事(第八屆、第九屆)，台灣高血壓學會 THS 學術委員會委員(第八屆)， 教育委員會執行秘書(第八屆)，教育委員會委員(第七屆、第八屆、第九屆)
10. 台灣心肌梗塞學會 TAMIS 學術委員會委員(第一屆)
11. 臺灣介入性心臟血管醫學會 TSCI 編輯暨登錄委員(第九屆) 、研究暨登錄委員會委員(第十屆)， 公共醫療政策委員會委員 (第十屆)
12. 內科專科醫師甄審委員會資格審查小組委員 (2021, 2022, 2023, 2024)

Curriculum Vitae

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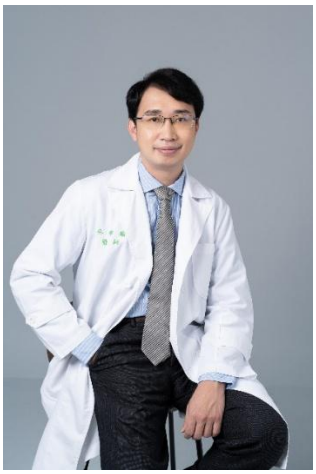
Education and Experience

2000/9 – 2007/6 Department of Medicine, National Cheng Kung University, Tainan, Taiwan
Doctor of Medicine, 2007
2013/9 – 2014/8 Brigham and Women's Hospital, Harvard University, MA, USA
Research Fellow, Cardiac Muscle Research Laboratory
2019/8 – 2023/06 Graduate Institute of Clinical Medicine, National Cheng Kung University, Taiwan
PhD
2023/07Visiting Scholar with certificate of Precisional Medicine in St. Edmund Hall, Oxford (OXCEP)

Professional Experience

2014/8-	**Chi-Mei Medical Center, Tainan, Taiwan** *Attending physician*, Department of Cardiology
2017/8-	**Chi-Mei Medical Center, Tainan, Taiwan** *Director and Principal Investigator*, Circulation Lab
2023/8-	**Chi-Mei Medical Center, Tainan, Taiwan** *Director*, Cardio-Oncology Center
2017/8-202/7	**Southern Taiwan University of Science and Technology, Taiwan** *Assistant Professor*, Department of Biotechnology
2020/08-	**Southern Taiwan University of Science and Technology, Taiwan** *Associate Professor*, Department of Biotechnology
2023/08	**National Sun Yat-sen University, Taiwan** *Associate Professor*, Department of Clinical Medicine
2014/8-	**Chi-Mei Medical Center, Tainan, Taiwan** *Principal Investigator or Co-PI* of more than 30 clinical trials



Curriculum Vitae

Dr. Cho-Kai Wu
Professor in Cardiology
Department of Internal Medicine
National Taiwan University Hospital

Introducing Dr. Cho-Kai Wu

Dr. Cho-Kai Wu is a cardiologist at National Taiwan University Hospital and professor of College of Medicine, NTU. Cho-Kai Wu's main research topics include the heart failure with preserved ejection fraction and basic molecular mechanism of cardiac diastolic dysfunction. He has also assisted in applying information technology to cardiovascular care and formulating biological models to understand the pathophysiology of cardiovascular diseases. He is currently a participant in an Academia Sinica grant using the translational approach towards both clinical and molecular aspects of heart failure with preserved systolic function.

After he finished his cardiology training program in National Taiwan University Hospital, he got his master and PhD degree after 2013 in the field of clinical medicine. He also did his post-doc training in Stanford University from 2018 to 2019. His latest works also revealed a new pathophysiological explanation of the role of immunoinflammatory system over the development of heart failure with preserved ejection fraction. His achievements were published in more than 100 SCI papers in recent years as first or corresponding authors including Journal of the American College of Cardiology, European Journal of Heart Failure, Critical Care Medicine, Journal of Internal Medicine, JACC Asia, JACC advances, JACC Intervention and European Radiology.

Education Background

2018/12~2019/12 Visiting scholar in cardiovascular institute, Stanford University

2009~2013 PhD degree in Graduate Institute of Clinical Medicine National Taiwan University

2005-2007 Master degree in Graduate Institute of Clinical Medicine National Taiwan University

1995-2002 Bachelor degree in National Taiwan University School of Medicine

Classification and Types of HF Biomarkers – Pathological and Molecular Basis

洪崇烈醫師
(台北馬偕心臟內科)

Natriuretic peptides, particularly NT-proBNP, are well-established markers in HF for diagnosis, risk stratification, and monitoring1. Pathophysiologically, NT-proBNP reflects myocardial wall stress and is elevated in both left-sided and right-sided HF, including pulmonary arterial hypertension (PAH) and valvular heart disease (VHD)1-3. Several studies, including Val-HeFT, PARADIGM-HF and EMPEROR-Reduced, demonstrated that reductions in NT-proBNP levels correlate with improved outcomes in patients with HFrEF (heart failure with reduced ejection fraction)4-6. Notably, NT-proBNP <1000 pg/mL emerged as a favorable threshold across studies5, 6. Serial measurements provide more prognostic value than isolated readings7. A recent study by Fuery et al. showed that NT-proBNP trajectories can predict adverse events months in advance7. This highlights its potential in dynamic risk reclassification and tailoring individualized care.

While early meta-analyses suggested that NT-proBNP-guided therapy might reduce mortality and HF hospitalization, definitive RCTs have yielded mixed results[8, 9]. The pivotal GUIDE-IT trial compared NT-proBNP–guided therapy (target <1000 pg/mL) to usual care in patients with chronic HFrEF[10]. Despite equivalent follow-up schedules and protocol-driven GDMT titration, the trial failed to show a significant improvement in clinical outcomes with biomarker-guided management[10]. Post-hoc analyses identified several barriers, including clinician reluctance to up-titrate medication despite elevated NT-proBNP and suboptimal therapy delivery[10]. Moreover, many patients never achieved the biomarker target, pointing to gaps between theoretical frameworks and real-world implementation[10, 11]. Conversely, secondary analyses of GUIDE-IT reaffirmed the prognostic importance of reaching NT-proBNP <1000 pg/mL, which was associated with reduced mortality and hospitalization[11]. This dichotomy suggests that while NT-proBNP is a valid risk marker, using it as a titration target may be insufficient unless therapeutic intensification is simultaneously optimized[11].

Recognizing limitations in prior studies, the STRONG-HF trial tested a more intensive intervention as rapid GDMT titration combined with close follow-up and biomarker monitoring in patients with acute HF[12]. This multicenter RCT randomized patients at discharge to either usual care or high-intensity care, where NT-proBNP and safety labs were checked at weeks 1, 2, 3, and 6 to guide therapy[12]. The results were compelling. At 180 days, high-intensity care reduced the composite of all-cause death or HF readmission by 34% (absolute risk reduction 8.1%, NNT = 12)[12]. Importantly, this strategy was safe, with no increase in serious adverse events. NT-proBNP changes

early post-discharge were predictive of future events, further supporting its role as a monitoring tool rather than a sole therapeutic target[12, 13]. Notably, patients in the high-intensity arm were more likely to achieve full or at least half of the recommended doses of ACEi/ARB/ARNi, β-blockers, and MRAs[13]. These findings suggest that effective implementation of NT-proBNP–guided therapy depends not only on biomarker interpretation but also on structured care pathways and aggressive therapy up-titration[14].

HF BIOMARKERS IN CLINICAL PRACTICE

The Application of HF Diagnosis: Workflow and Cutoffs

(Acute vs. Chronic HF, HFrEF vs. HFpEF, High-Risk Populations: CKD, Diabetes, HTN, CAD, and AF)

Chien-Yi Hsu, MD, PhD
Taipei Heart Institute; Taipei Medical University Hospital

Heart failure (HF) diagnosis requires a systematic and clinically integrated approach, particularly in the context of heterogeneous presentations and overlapping comorbidities. Biomarkers, especially natriuretic peptides such as BNP and NT-proBNP, have become central to contemporary diagnostic workflows and provide objective, rapid assessment in both acute and chronic settings. In patients presenting with acute dyspnea, NT-proBNP functions as a highly sensitive rule-out tool at a threshold below 300 pg/mL, while age-adjusted rule-in cutoffs of 450, 900, and 1800 pg/mL improve diagnostic accuracy and reduce indeterminate grey zone cases. In non-acute settings, lower thresholds including BNP ≥35 pg/mL or NT-proBNP ≥125 pg/mL are recommended to trigger further evaluation, most commonly with echocardiography.

A structured workflow that integrates clinical history, physical examination, electrocardiography, imaging, and biomarker assessment is essential for confirming HF and guiding etiologic evaluation. The diagnosis of heart failure with reduced ejection fraction (HFrEF) is usually straightforward once systolic dysfunction is documented. In contrast, heart failure with preserved ejection fraction (HFpEF) requires a more comprehensive approach that combines symptoms, preserved left ventricular ejection fraction, elevated natriuretic peptides, and objective evidence of structural or functional abnormalities. Biomarker thresholds must always be interpreted within the clinical context. For example, higher NT-proBNP cutoffs are required in patients with atrial fibrillation due to baseline elevation.

In high-risk populations such as chronic kidney disease, diabetes, hypertension, coronary artery disease, and atrial fibrillation, biomarker interpretation requires additional consideration. Renal dysfunction is associated with elevated natriuretic peptide levels, and adjusted cutoffs, such as increasing thresholds in advanced CKD, may improve diagnostic specificity. On the other hand, obesity is associated with lower circulating peptide levels and may lead to under-recognition of HF. Importantly, elevated natriuretic peptide levels in these populations should not be dismissed as false positives but instead should be recognized as markers of increased cardiovascular risk and worse prognosis.

Clinical timing and indications for NT-proBNP measurement are essential for optimizing HF care across the disease trajectory. Measurement at hospital admission provides important information for initial risk stratification. Assessment during the peri-discharge phase helps guide discharge planning and refine prognostic evaluation. Reassessment at approximately six months after discharge supports treatment optimization and ongoing risk stratification. In patients with chronic HF, periodic

monitoring every 6 to 12 months is recommended to guide therapy, with additional testing indicated whenever symptoms worsen or clinical status changes. Furthermore, NT-proBNP screening can be considered in high-risk individuals with comorbid conditions such as type 2 diabetes, chronic kidney disease, persistent angina in coronary artery disease, pulmonary hypertension, resistant hypertension, or atrial fibrillation, in order to facilitate early detection and initiation of targeted therapy.

Beyond natriuretic peptides, additional biomarkers including cardiac troponins, CA125, and renal markers such as cystatin C provide complementary insights into myocardial injury, congestion, and cardiorenal interactions. A multi-biomarker strategy, when incorporated into a standardized diagnostic workflow, improves diagnostic precision and supports early detection, risk stratification, and personalized management. As HF increasingly reflects a complex cardiovascular, kidney, and metabolic continuum, appropriate application of biomarker-guided workflows is essential to improve clinical outcomes.

Biomarkers Monitoring during HF Treatment

奇美醫院 心臟內科 張瑋婷

Biomarkers are integral to contemporary heart failure (HF) management, with N-terminal pro–B-type natriuretic peptide (NT-proBNP) serving as the most established marker for diagnosis, risk stratification, and treatment monitoring. Evidence from major trials demonstrates that reductions in NT-proBNP correlate with improved outcomes, and serial measurements provide greater prognostic value than single assessments, enabling early detection of clinical deterioration. However, the role of NT-proBNP in guiding therapy remains debated. While earlier studies suggested benefit, the GUIDE-IT trial showed no significant improvement in outcomes with biomarker-guided therapy compared to usual care, largely due to clinical inertia and suboptimal implementation of guideline-directed medical therapy (GDMT). Notably, achieving lower NT-proBNP levels remained associated with better prognosis, underscoring the gap between biomarker insight and therapeutic action. Also, the STRONG-HF trial provided a paradigm shift by integrating intensive GDMT up-titration with frequent biomarker monitoring, demonstrating significant reductions in mortality and HF readmissions. In this context, NT-proBNP functions best as a dynamic monitoring tool rather than a fixed treatment target, guiding therapy within a structured care framework.

In this consensus, I will summarize the role of NT-proBNP as a robust biomarker for HF management while multidisciplinary care pathways are also crucial rather than isolated use as a treatment target.