Diagnostic Yield and Model Prediction Using Wearable Patch Device in HFpEF

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Abstract. Heart failure (HF) is a prevalent global health issue projected to escalate, notably in aging populations. The study aimed to identify predictive markers for Heart Failure with preserved Ejection Fraction (HFpEF). We scrutinized vital parameters like age, BMI, eGFR, and comorbidities like atrial fibrillation, coronary artery disease (CAD), diabetes mellites (DM). Evaluating phonocardiogram indicators—third heart sound(S3) and Systolic Dysfunction Index (SDI)—our logistic regression revealed age (≥ 65years), BMI (≥ 25 kg/m²), eGFR (<60 mL/min/1.73m²), CAD, DM, S3 intensity ≥5, and SDI ≥5 as HFpEF predictors, with AUC = 0.816 ($p < .001$). ROC diagnosis curve showed that the sensitivity, specificity and Youden's index J of the model were 0.755, 0.673 and 0.838, respectively. Nonetheless, further exploration is crucial to delineate the clinical applicability and constraints of these markers.

Keywords. HFpEF, Wearable, Model, Prognostic

1. Introduction

Heart failure, a global health crisis affecting over 64 million people worldwide, is projected to increase by 46% in the United States by 2030, primarily due to an aging population [11]. In Taiwan, an estimated 700,000 individuals suffer from heart failure, yet only 240,000 receive medical attention, signifying a substantial undiagnosed population [2;10;17]. The European Society of Cardiology's 2021 guidelines categorize heart failure into two based on left ventricular ejection fraction (LVEF) heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). HFpEF accounts for nearly half of heart failure cases when LVEF exceeds 50% [9]. Early diagnosis and timely intervention show promise in halting heart failure progression [4]. Phonocardiography, an advanced non-invasive diagnostic tool, analyzes heart sounds and murmurs to provide crucial diagnostic data. It simplifies examinations compared to traditional methods and serves as an effective screening tool for identifying HFrEF [14;15;20]. Parameters from phonocardiography, like the systolic dysfunction

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index (SDI) and the third heart sound (S3), effectively identify HFrEF patients, aiding in rapid diagnosis and risk stratification [18;19]. Studies suggest that phonocardiography can monitor post-myocardial infarction cardiac function swiftly [21]. Optimizing post-discharge heart failure treatment using phonocardiography parameters, such as maintaining electromechanical activation time (EMAT)< 15% and S3 intensity < 5, may reduce rehospitalization rates within a year and improve patient outcomes [13]. However, limited research exists on using phonocardiography to diagnose HFpEF. Recent studies propose that phonocardiography could be comparable to NT-proBNP in evaluating HFpEF patients [8]. This study aims to evaluate the efficacy of phonocardiography parameters in predicting the model for heart failure with preserved ejection fraction (HFpEF).

Methods

This retrospective study covered 2016-2022 with 1735 participants. Patients with LVEF >50% were categorized into HFpEF or non-HFpEF groups: 1402 (80.8%) non-HFpEF, 333 (19.2%) HFpEF. 238 participants had Acoustic Cardiographic reports showing Atrial Fibrillation (AF). Data collected included demographics, medical histories, and Dispatch Electrocardiogram and Phonocardiogram recordings. Acoustic Cardiographic raw data underwent computerized analysis for heart sounds and Systolic Time Intervals (STIs). Variables comprised PR interval, QT interval, QTc interval, QRS duration, EMAT, LVST, S3, S4 intensity, and SDI (0-10, >5 indicating systolic dysfunction with elevated filling pressures) [19]. Results were presented as mean and standard deviations for continuous variables and frequency/proportions for categorical variables. Student's t-test compared normally distributed data between groups. Receiver Operating Characteristic (ROC) curves assessed AUC, sensitivity, and specificity.

Results

A total of 1735 participants, with an average age of 60.9±14.6 years and 1017 females (58.6%), demonstrated significant differences between the two groups across various factors, including hypertension, CAD, AF, DM, and Hyperlipidemia in Table 1. HFpEF risks listed in Table 2: increased risk with age (10-year intervals), higher BMI (every 5 kg/m²), and increased eGFR (10-unit increase, resulting in 32% lower HFpEF risk). Significant escalations in HFpEF risk were noted with atrial fibrillation, coronary artery disease, diabetes mellitus, S3≥5, and SDI ≥5 in Acoustic Cardiographic findings.

Further analysis involved transforming age, BMI, and eGFR into binary variables (Age ≥ 65 years: 1/0, BMI ≥ 25 kg/m²: 1/0, eGFR < 60 mL/min/1.73m2: 1/0). Logistic regression, after this transformation with logarithmic adjustments while maintaining other independent variables unchanged, revealed in Table 3.The risk assessment model was established as the probability of HFpEF, Π= exp { -3.066 + (AGE ≥65 years * 0.382) + (BMI ≥25 kg/m²* 0.465) + (eGFR< 60 mL/min/1.73m2 * 1.677) + (CAD* 0.511) + (DM* 0.386) + (Acoustic Cardiographic show AF * 2.246) + (Third heart sound (≥5)* 0.937) + (SDI (≥5) * 1.042) /1+ exp (-3.066 + (AGE ≥65 years * 0.382) + (BMI ≥25 kg/m² * 0.465) + (eGFR< 60 mL/min/1.73m2* 1.677) + (CAD* 0.511) + (DM* 0.386) + (Acoustic Cardiographic show AF * 2.246) + (Third heart sound (≥5)* 0.937) + (SDI (≥5) * 1.042))}. ROC diagnosis curve of the new model is shown in Figure 1, with AUC = 0.816 ($p < .001$). ROC diagnosis curve showed that the sensitivity, specificity and

Youden's index J of the model were 0.755, 0.673 and 0.838, respectively, which suggested that the new model was of good diagnostic value.

Table 1 Demography

	Total (n=1735)		**non HFpEF(n=1402)**		**HFpEF(n=333)**		**P value**
Female	1017	58.6%	847	60.4%	170	51.1%	<0.001*
Age (mean, SD)	60.9	14.6	59.1	14.0	68.2	14.4	<0.001*
BMI (mean, SD)	25.9	9	25.6	8.8	27.5	7.8	<0.001*
Systolic pressure (mean, SD)	131.8	20.8	131.6	20.0	132.9	24.0	0.303
EF % (mean, SD)	64.8	6.3	65.5	6.0	61.6	6.7	< 0.001
Hypertension (n, %)	954	55.0%	737	52.6%	217	65.2%	<0.001*
Coronary heart disease (n, %)	543	31.3%	391	27.90%	152	45.6%	<0.001*
Diabetes mellitus (n, %)	406	23.4%	278	19.80%	128	38.4%	<0.001*
Hyperlipidemia (n, %)	672	38.7%	530	37.80%	142	42.6%	0.103

Table 2 Multiple logistic regression results relating the factors of HFpEF

Variable	B	SE	Odds	95% CI	P value
Age (per 10 years +)	0.171	0.062	1.186	1.051 -1.34	0.006*
BMI (per 5kg/m2 +)	0.370	0.074	1.447	1.253 -1.672	0.000*
eGFR (per 10 units +)	-0.310	0.032	0.733	0.689 -0.78	0.000*
CAD	0.416	0.15	1.517	1.131 -2.033	0.005*
DM	0.339	0.16	1.404	1.026 -1.92	0.034*
Acoustic Cardiographic show AF	2.139	0.306	8.495	4.664 -15.474	0.000*
EMATc (%) >12%	0.338	0.158	1.402	1.028 -1.912	0.033*
Third heart sound (≥5)	1.140	0.372	3.128	1.508 -6.491	0.002*
SDI (≥5)	0.731	0.235	2.077	1.311 -3.291	0.002*
Constant	-2.925	0.722	0.054		0.000

Table 3 Multiple logistic regression results relating the factors of HFpEF to reclassifications of Age, BMI and eGFR

Variable (yes=1)	B	SE	Odds	95% CI	P value
Age ≥ 65 years	0.382	0.157	1.465	1.078-1.992	0.015*
BMI ≥ 25 kg/m2	0.465	0.155	1.592	1.176 - 2.155	0.003*
eGFR< 60 mL/min/1.73m2	1.677	0.159	5.351	3.919 -7.304	0.000*
CAD	0.511	0.148	1.666	1.246 -2.228	0.001*
DM	0.386	0.158	1.471	1.079 -2.005	0.015*
Acoustic Cardiographic show AF	2.246	0.295	9.446	5.302 -16.830	0.000*
Third heart sound (≥5)	0.937	0.340	2.553	1.311 -4.972	0.006*
SDI (≥5)	1.042	0.221	2.836	1.839 -4.373	0.000*
Constant	-3.066	0.169	0.047		0.000

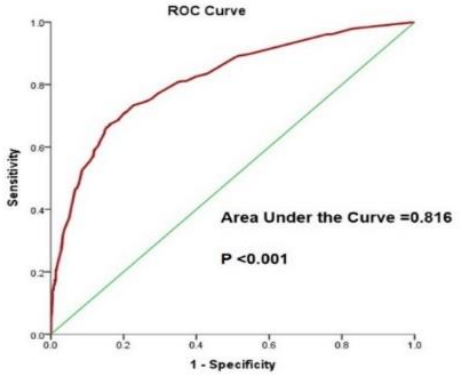

Figure 1. ROC curve for the risk assessment model of HFpEF

Discussion

Our investigation aimed to establish a predictive framework delineating the risk factors associated with HFpEF. We focused on crucial parameters such as age, BMI, eGFR, and concurrent conditions like AF, CAD, and DM. Additionally, we examined significant phonocardiogram markers, particularly S3 and SDI. Employing logistic regression, we identified specific determinants predictive of HFpEF: age over 65 years, BMI above 24 kg/m², eGFR less than 60 mL/min/1.73m², CAD and DM, as well as the acoustic cardiography parameters S3 and SDI. These variables emerged as significant predictors for HFpEF in our analysis.

In a cohort study investigating risk factors influencing various types of heart failure, significant associations were found between atrial fibrillation, obesity, pulmonary hypertension, and valvular disease, and the development of HFpEF. [7] Another study has identified risk factors for HFpEF, including BMI, hypertension, DM, and renal dysfunction [3]. Moreover, aging and obesity are well-established risk factors common to HFpEF [16], which further supports our research.

S3 in heart disease patients signals a critical condition[5]. Acoustic cardiography might aid diagnosing HFpEF, especially with inconclusive BNP levels[6;8]. Non-invasive S3 shows promise and prognostic value. Our study linked S3 with HFpEF onset (OR=2.6, 95% CI 1.3-5.0). However, EMATc changes weren't directly linked to LVEF changes in ADHF[12]. EMATc wasn't predictive in our study.

Acoustic Cardiographic is a non-invasive, cost-effective method showing promise in early heart failure detection in primary care. Studies highlight S3, EMAT, and SDI as key predictors for adverse cardiac events and distinguishing between heart failure types. SDI, with an AUC exceeding 0.81 and good sensitivity/specificity at an SDI threshold of >5.43, holds potential as a diagnostic tool. Further research is needed to understand their full clinical applicability and limitations.[1;19]

Retrospective analysis links S3, SDI to HFpEF onset, yet inherent biases may exist. Unaccounted factors could alter these links; more varied research is needed. Prospective, multi-center studies with broader samples are vital for refining predictive frameworks in clinical practice.

Conclusions

Our current study provides valuable insights into HFpEF prediction using wearable phonocardiography parameters, addressing the clinical limitations of accurate and diagnostic strategies for HFpEF. Our data support the implementation of such device in remote and underserved areas for those subjects manifesting high risk for HFpEF, ensuring improved access to early screening and better management in such patient population.

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References

[1] New auscultation: can we detect heart failure by auscultation ?, Journal of Community Medicine and Public Health Reports (2022).

[2] N. Ang, C. Chandramouli, K. Yiu, C. Lawson, and J. Tromp, Heart Failure and Multimorbidity in Asia, Curr Heart Fail Rep 20 (2023), 24-32.

[3] F.F. Gong, M.V. Jelinek, J.M. Castro, J.M. Coller, M. McGrady, U. Boffa, L. Shiel, D. Liew, R. Wolfe, S. Stewart, A.J. Owen, H. Krum, C.M. Reid, D.L. Prior, and D.J. Campbell, Risk factors for incident heart failure with preserved or reduced ejection fraction, and valvular heart failure, in a community-based cohort, Open Heart 5 (2018), e000782.

[4] P.A. Heidenreich, B. Bozkurt, D. Aguilar, L.A. Allen, J.J. Byun, M.M. Colvin, A. Deswal, M.H. Drazner, S.M. Dunlay, L.R. Evers, J.C. Fang, S.E. Fedson, G.C. Fonarow, S.S. Hayek, A.F. Hernandez, P. Khazanie, M.M. Kittleson, C.S. Lee, M.S. Link, C.A. Milano, L.C. Nnacheta, A.T. Sandhu, L.W. Stevenson, O. Vardeny, A.R. Vest, and C.W. Yancy, 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines, Circulation 145 (2022), e876-e894.

[5] M. Johnston, S.P. Collins, and A.B. Storrow, The third heart sound for diagnosis of acute heart failure, Curr Heart Fail Rep 4 (2007), 164-168.

[6] D.L. Kosmicki, S.P. Collins, M.C. Kontos, M. Zuber, P. Kipfer, C. Attenhofer Jost, and A.D. Michaels, Noninvasive prediction of left ventricular systolic dysfunction in patients with clinically suspected heart failure using acoustic cardiography, Congest Heart Fail 16 (2010), 249-253.

[7] M.P. Lee, R.J. Glynn, S. Schneeweiss, K.J. Lin, E. Patorno, J. Barberio, R. Levin, T. Evers, S.V. Wang, and R.J. Desai, Risk Factors for Heart Failure with Preserved or Reduced Ejection Fraction Among Medicare Beneficiaries: Application of Competing Risks Analysis and Gradient Boosted Model, Clin Epidemiol 12 (2020), 607-616.

[8] H. Luo, J. Weerts, A. Bekkers, A. Achten, S. Lievens, K. Smeets, V. van Empel, T. Delhaas, and F.W. Prinzen, Association between phonocardiography and echocardiography in heart failure patients with preserved ejection fraction, Eur Heart J Digit Health 4 (2023), 4-11.

[9] T.A. McDonagh, M. Metra, M. Adamo, R.S. Gardner, A. Baumbach, M. Bohm, H. Burri, J. Butler, J. Celutkiene, O. Chioncel, J.G.F. Cleland, A.J.S. Coats, M.G. Crespo-Leiro, D. Farmakis, M. Gilard, S. Heymans, A.W. Hoes, T. Jaarsma, E.A. Jankowska, M. Lainscak, C.S.P. Lam, A.R. Lyon, J.J.V. McMurray, A. Mebazaa, R. Mindham, C. Muneretto, M. Francesco Piepoli, S. Price, G.M.C. Rosano, F. Ruschitzka, A. Kathrine Skibelund, and E.S.C.S.D. Group, 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, Eur Heart J 42 (2021), 3599-3726.

[10] E.B. Reyes, J.W. Ha, I. Firdaus, A.M. Ghazi, A. Phrommintikul, D. Sim, Q.N. Vu, C.W. Siu, W.H. Yin, and M.R. Cowie, Heart failure across Asia: Same healthcare burden but differences in organization of care, Int J Cardiol 223 (2016), 163-167.

[11] B. Shahim, C.J. Kapelios, G. Savarese, and L.H. Lund, Global Public Health Burden of Heart Failure: An Updated Review, Card Fail Rev 9 (2023), e11.

[12] J. Shitara, T. Kasai, N. Murata, N. Yamakawa, S. Yatsu, A. Murata, H. Matsumoto, T. Kato, S. Suda, Y. Matsue, R. Naito, M. Hiki, and H. Daida, Temporal changes of cardiac acoustic biomarkers and cardiac function in acute decompensated heart failure, ESC Heart Fail 8 (2021), 4037-4047.

[13] S.H. Sung, C.J. Huang, H.M. Cheng, W.M. Huang, W.C. Yu, and C.H. Chen, Effect of Acoustic Cardiography-guided Management on 1-year Outcomes in Patients With Acute Heart Failure, J Card Fail 26 (2020), 142-150.

[14] M.E. Tavel, Cardiac auscultation: a glorious past--and it does have a future!, Circulation 113 (2006), 1255-1259.

[15] M. Tokodi and A. Kovács, Reviving the origins: acoustic biomarkers of heart failure with preserved ejection fraction, European Heart Journal - Digital Health 4 (2022), 1-3.

[16] B. Upadhya and D.W. Kitzman, Heart failure with preserved ejection fraction: New approaches to diagnosis and management, Clin Cardiol 43 (2020), 145-155.

[17] C.C. Wang, C.K. Wu, M.L. Tsai, C.M. Lee, W.C. Huang, H.H. Chou, J.L. Huang, N.H. Chi, H.W. Yen, B.H. Tzeng, W.T. Chang, H.Y. Chang, C.H. Wang, Y.Y. Lu, J.P. Tsai, C.H. Su, W.J. Cherng, W.H. Yin, C.T. Tsai, Y.W. Wu, J.L. Lin, and J.J. Hwang, 2019 Focused Update of the Guidelines of the Taiwan Society of Cardiology for the Diagnosis and Treatment of Heart Failure, Acta Cardiol Sin 35 (2019), 244-283.

[18] S. Wang, F. Fang, M. Liu, Y.Y. Lam, J. Wang, Q. Shang, J.P. Sun, J.E. Sanderson, and C.M. Yu, Rapid bedside identification of high-risk population in heart failure with reduced ejection fraction by acoustic cardiography, Int J Cardiol 168 (2013), 1881-1886.

[19] S. Wang, Y.Y. Lam, M. Liu, F. Fang, J. Wang, Q. Shang, J.P. Sun, J.E. Sanderson, and C.M. Yu, Acoustic cardiography helps to identify heart failure and its phenotypes, Int J Cardiol 167 (2013), 681-686