The University of Osaka
Institutional Knowledge Archive

Title	Prognostic Impact of Echocardiographic Diastolic Dysfunction on Outcomes in Patients With Heart Failure With Preserved Ejection Fraction — Insights From the PURSUIT-HFpEF Registry —
Author(s)	Oeun, Bolrathanak
Citation	大阪大学, 2022, 博士論文
Version Type	
URL	https://hdl.handle.net/11094/87866
rights	
Note	やむを得ない事由があると学位審査研究科が承認したため、全文に代えてその内容の要約を公開しています。全文のご利用をご希望の場合は、大阪大学の博士論文についてをご参照ください。

The University of Osaka Institutional Knowledge Archive : OUKA

https://ir.library.osaka-u.ac.jp/

The University of Osaka

[Format-P02]

論　文　内　容　の　要　旨
Synopsis of Thesis

氏　名 Name	Bolrathanak OEUN
論文題名 Title	Prognostic Impact of Echocardiographic Diastolic Dysfunction on Outcomes in Patients With Heart Failure With Preserved Ejection Fraction — Insights From the PURSUIT-HFpEF Registry — (心臓超音波検査による拡張機能障害が、収縮機能が保持された心不全患者の転帰に及ぼす予後への影響：PURSUIT-HFpEFレジストリからの洞察)

論文内容の要旨

〔目　的(Purpose)〕

Heart failure (HF) with preserved ejection fraction (HFpEF) is an increasing type of HF in which left ventricular (LV) systolic function is preserved. No effective therapy for HFpEF has yet been established, due to the complex and heterogeneous pathophysiology of HFpEF. It is, therefore, important to identify high-risk features of HFpEF patients which can be the targets of the treatment. LV diastolic dysfunction, characterized by impaired LV relaxation and increased LV stiffness, has been presumed as important pathophysiology of HFpEF. Nonetheless, the prognostic impact of diastolic dysfunction remains controversial, especially in HFpEF patients presenting with atrial fibrillation (AF), a frequent comorbidity of HFpEF. This may be due to the absence of any single reliable index for the assessment of diastolic function. The evaluation of diastolic function in patients with AF is challenging due to irregular heartbeats, loss of atrial contraction, and variability of flow velocity. Recently, the American Society of Echocardiography (ASE)—2016 updated the algorithms for the evaluation of LV diastolic function by echocardiography, one of which is applicable even in patients with AF. In this study, we aimed to clarify the impact of diastolic dysfunction on prognosis in patients with HFpEF, including those with AF, using this algorithm.

〔方法ならびに成績(Methods/Results)〕

Methods: We studied patients registered in the PURSUIT-HFpEF registry, a prospective multicenter observational study of patients with HFpEF. The registry enrolled patients with HFpEF who were hospitalized due to acute decompensated HF based on the Framingham HF diagnostic criteria and fulfilled the following two criteria on admission: (1) Left ventricular ejection fraction ≥ 50% by transthoracic echocardiography; (2) N-terminal pro B-type natriuretic peptide (NT-proBNP) ≥ 400 pg/mL. Echocardiographic data at discharge were used to classify patients into three groups according to the 2016 ASE recommendations for the evaluation of diastolic function: normal diastolic function (ND), indeterminate (ID), and diastolic dysfunction (DD). The primary endpoint was a composite of all-cause death or HF rehospitalization. The secondary endpoints were each endpoint. Baseline patient characteristics were compared among the three groups. Kaplan-Meier survival analyses with log-rank test were constructed. Multivariable Cox proportional hazards regression analyses were performed to investigate the impact of DD and ID on prognosis, using ND with a hazard ratio of 1.00 as the reference.

Results: This study included 863 patients with HFpEF (321 patients concomitantly had AF). The median age of the study population was 83 years (interquartile range: 77, 87), and 479 patients (55.5%) were female. 196 patients (22.7%) were classified with ND, 253 patients (29.3%) with ID and 414 patients (48.0%) with DD. Patients with DD were significantly older, more likely female, higher body mass index, higher NT-proBNP, lower hemoglobin, and lower estimated glomerular filtration rate than those with ND or ID. The primary endpoint occurred more frequently in patients with DD than those with ND [incidence rate (IR): 38.5 vs. 17.8 per 100 person-year, log-rank P < 0.001) or those with ID (IR: 38.5 vs. 25.7 per 100 person-year, log-rank P = 0.007). Patients with DD had a significantly higher event rate of all-cause mortality (IR: 15.1 vs. 7.2 per 100 person-year, log-rank P = 0.003) and HF rehospitalization (IR: 26.4 vs. 11.3 per 100 person-year, log-rank P < 0.001) than those with ND. Multivariable Cox regression analyses revealed that DD (HR: 1.57, 95% CI: 1.06-2.32, P = 0.024) was independently associated with the composite endpoint, whereas ID (HR: 1.28, 95% CI: 0.84-1.95, P = 0.255) was not. DD was associated with the composite endpoint both in patients with AF (HR: 2.25, 95% CI: 1.29-3.94. P = 0.004) and without AF (HR: 1.80, 95% CI: 1.16-2.80, P = 0.009).

〔総　括(Conclusion)〕

Patients with HFpEF, including those with AF, presenting with left ventricular diastolic dysfunction assessed with the 2016 ASE recommendations had worse clinical outcomes than those with normal diastolic function. Diastolic dysfunction may be considered a prognostic marker in patients with HFpEF regardless of the presence of AF.

論文審査の結果の要旨及び担当者

（申請者氏名）OEUN BOLRATHANAK

		（職）	氏　　名
論文審査担当者	主　査	大阪大学教授	坂田 泰史
	副　査	大阪大学教授	藤野 裕士
	副　査	大阪大学教授	宮川 繁

論文審査の結果の要旨

左室収縮機能が保持された心不全(HFpEF)は、左室拡張機能障害が病態の主因を成していると考えられているが、心エコー図法にて評価される左室拡張機能障害の存在と予後との関連は明らかではなく、特に心房細動合併例も含めたHFpEF患者における関連は不明であった。本研究では、大阪大学を中心とする多施設共同HFpEF観察研究データを使用して検討を行った。863人の研究対象者（年齢中央値：83歳、女性55.5%）を、米国心エコー検査学会が発表したアルゴリズムを用いて拡張機能障害、不定、正常拡張機能の3群に分類したところ、拡張機能障害群では正常拡張機能群と比較して、全死亡および心不全再入院からなる複合エンドポイントのリスクが有意に高く、拡張機能障害の存在は種々の交絡因子で調整後も独立して予後不良と関連していた。本研究は左室拡張障害の存在が心房細動も含むHFpEF患者の予後不良と関連していることを初めて見出したものであり、学位に値するものと認める。