Echocardiography: Systolic and Diastolic Function

impact of dapagliflozin on left ventricular diastolic function in diabetic patients with heart failure complicating cardiovascular risk factors

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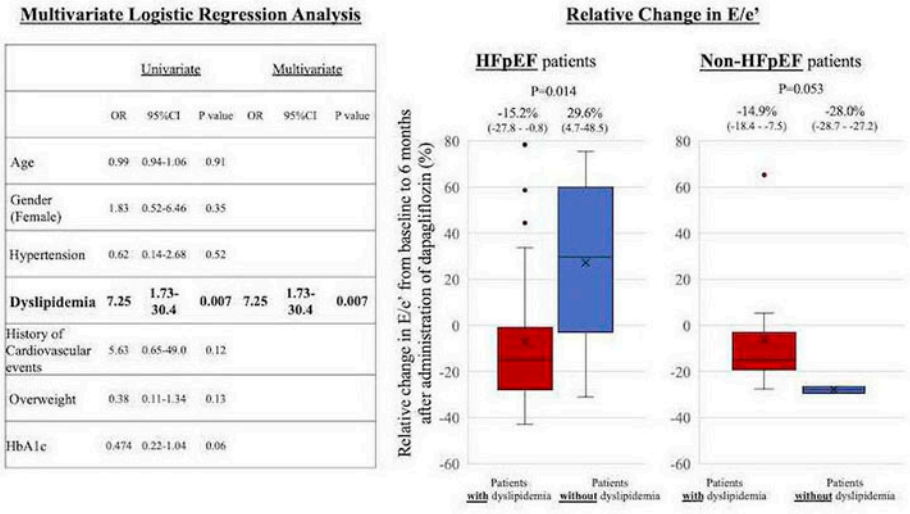
Background: Type 2 diabetes mellitus (T2DM) is a well-known risk factor for heart failure (HF), even in patients without a structural heart disease or a symptom of HF. Diabetes-related cardiomyopathy is presented as an left ventricular (LV) diastolic dysfunction, which, like cardiovascular disease, is a contributor of the development of HF in both patients with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HFpEF). Furthermore, comorbid factors other than T2DM also have been identified as high risk factors for of progression to HF. Dapagliflozin is a sodium glucose cotransporter type 2 (SGLT2) inhibitor, and represents a new class of anti-hyperglycemic agents for T2DM. A result from a recent large clinical trial showed that dapagliflozin reduced risk of worsening HF or death from cardiovascular causes for patients with HFrEF compared to those who received a placebo, regardless of the presence or absence of T2DM. However, the effect of SGLT2 inhibitors on LV diastolic function in T2DM patients with HF who had cardiovascular risk factors other than T2DM remains uncertain.

Purpose: Our purpose was to investigate the impact of dapagliflozin on LV diastolic function in T2DM patients with stable HF complicating cardiovascular risk factors.

Methods: We analyzed data from our previous prospective multicenter study, which investigate the effect of dapagliflozin on LV diastolic function of 53 T2DM patients with stable HF at five institutions in Japan. Patients who had been taking at least one antidiabetic drugs other than SGLT2 inhibitor started the administration of dapagliflozin. Cardiovascular risk factors other than T2DM was determined as age, gender, hypertension, dyslipidemia, history of cardiovascular events and overweight.

Results: E/e′ significantly decreased from 9.3 to 8.5 cm/s 6 months after administration of dapagliflozin (p = 0.020) as previously described. Multivariate logistic regression analysis showed that dyslipidemia was the only independent determinant of an improvement of E/e' among cardiovascular risk factors. Furthermore, relative changes in E/e' from baseline to 6 months after administration of dapagliflozin seen in HFpEF patients with dyslipidemia were significantly larger than those in HFpEF patients without dyslipidemia (-15.2% vs. 29.6%, p = 0.014), but such a difference was not observed in non-HFpEF patients. In addition, relative changes in high-density lipoprotein cholesterol (HDL-C) from baseline to 6 months after administration of dapagliflozin had significant correlation with those in E/e' (r=-0.300, p = 0.038). However, such correlations were not observed in low-density lipoprotein cholesterol (LDL-C) and triglyceride (r = 0.05, p = 0.72 and r = 0.05, p = 0.73). Conclusion: Dapagliflozin was more beneficial effect on LV diastolic function for T2DM patients with stable HF, especially those with complicating dyslipidemia. Our findings may thus offer a new insight into the management of T2DM patients with HF.

Abstract Figure.



Multivariate Logistic Regression Analysis

	Univariate			Multivariate		
	OR	95%CI	P value	OR	95%CI	P value
Age	0.99	0.94-1.06	0.91			
Gender (Female)	1.83	0.52-6.46	0.35			
Hypertension	0.62	0.14-2.68	0.52			
Dyslipidemia	**7.25**	**1.73-30.4**	**0.007**	**7.25**	**1.73-30.4**	**0.007**
History of Cardiovascular events	5.63	0.65-49.0	0.12			
Overweight	0.38	0.11-1.34	0.13			
HbA1c	0.474	0.22-1.04	0.06			