論　文　内　容　要　旨

Clinical Features of Tachycardia-Induced Cardiomyopathy in Patients with Atrial Fibrillation

（心房細動患者における頻脈誘発性心筋症の臨床的特徴についての検討）

Internal Medicine, in press.

主指導教員：中野　由紀子教授
（医系科学研究科　循環器内科学）
副指導教員：北川　知郎講師
（医系科学研究科　循環器内科学）
副指導教員：東　幸仁教授
（原爆放射線医科学研究所　再生医療開発）

魚谷　悠希未

（医系科学研究科　医歯薬学専攻）

Background

Atrial fibrillation (AF) is a common cause of tachycardia-induced cardiomyopathy (TIC), which is a nonischemic and reversible cardiomyopathy triggered by arrhythmia. Although the mechanism by which TIC develops in patients with AF has yet to be completely reported and TIC can only be diagnosed through cardiac function recovery after controlling tachycardia via rate or rhythm control. Early and appropriate treatment of TIC can dramatically improve cardiac function. Therefore, early identification of people who are susceptible to TIC is critical in providing early therapeutic intervention to affected patients in order to prevent further progression of heart failure. In this study, we investigated the clinical features of AF patients with TIC.

Methods

A total of 1,087 patients with AF underwent RFCA at Hiroshima University Hospital between November 2009 and September 2016. Of these, the remaining 722 patients were then divided into the TIC group (n = 82), defined as those with an initial left ventricular ejection fraction (LVEF) of ≤40% and a >20% recovery of LVEF after successful AF ablation, and the control group (n = 640), defined as those with an initial LVEF of >40%. We compared the clinical characteristics between the TIC and control groups.

Results

The proportions of type 2 diabetes (30.5% vs. 14.7%), renal dysfunction (34.2% vs. 23.8%), hypertension (67.1% vs. 54.8%), and persistent AF (62.2% vs. 32.2%) were significantly higher in the TIC group (n = 82) than in the control group (n = 640). A multivariable analysis revealed that the existence of persistent AF (odds ratio [OR], 3.19; 95% confidence interval [CI], 1.94–5.24; p <0.001), renal dysfunction (OR, 1.87; 95% CI, 1.06–3.32; p = 0.034), and type 2 diabetes (OR, 2.30; 95% CI, 1.31–4.05; p = 0.005) but not hypertension was significantly associated with TIC. Among the electrophysiological study parameters, the AVNERP (303 ± 72 ms vs. 332 ± 86 ms; p = 0.017) was significantly shorter in the TIC group than in the control group. According to a Holter ECG, the mean heart rate was significantly higher in the TIC group (N = 76) than in the control group (N = 612) (83.2 ± 18.6 bpm vs. 73.9 ± 15.2 bpm, p <0.001). There was no significant difference in the length of sinus rhythm maintenance or rate of AF recurrence between the groups.

Discussion

In this study, we investigated the clinical characteristics of AF patients with TIC compared with those without TIC. Our results demonstrated that persistent AF, type 2 diabetes, and

renal dysfunction were significantly associated with TIC. A short AVNERP in electrophysiological studies was also a hallmark of TIC.

The true incidence of TIC is not well recognized in clinical practice, it has been reported that 8%-28% of patients with focal/ectopic atrial tachycardia and 9%-34% with ventricular tachycardia develop TIC. Although the mechanisms underlying the association between AF and TIC are not fully understood, the previous study reported that rapid and sustained atrial pacing cause heart failure with a low cardiac output. In animal models, persistent tachycardia increased the severity of heart failure with a cell-typical phenotype of heart failure. That is, persistent tachycardia first causes remodeling of the extraventricular matrix, followed by contractile dysfunction due to cellular remodeling, and finally severe contractile dysfunction due to abnormal Ca2+ handling. In addition, heart rate irregularity, sympathetic dysregulation, and loss of atrial contraction during AF have been considered significant triggers of TIC. Consistent with previous reports, the present study found that persistent AF was associated with TIC. Prolonged exposure to heart rate irregularity and loss of atrial contraction may be responsible for the development of TIC in persistent AF rather than in paroxysmal AF.

Our findings showed that, among the electrophysiological study parameters, a shorter AVNERP increased the susceptibility to TIC. The atrioventricular nodal conduction capacity is a crucial determinant of heart rate during AF. Therefore, a shorter AVNERP may promote higher heart rates in patients with AF, leading to the development of TIC.

The most notable finding of this study was that type 2 diabetes was significantly associated with TIC. The close and complex relationship between type 2 diabetes and AF has been well documented. First, type 2 diabetes is known to be a significant risk factor for AF. Furthermore, several studies have reported that patients with AF and type 2 diabetes had increased mortality compared to those without type 2 diabetes. Our findings suggested that patients with AF and type 2 diabetes were more susceptible to TIC than AF patients without type 2 diates, possibly explaining the increased mortality in patients with AF complicated by diabetes. Patients with TIC showed an improvement in the left ventricular function after recovery of sinus rhythm via catheter ablation or pharmacological treatment. Therefore, early therapeutic interventions in TIC cases may help improve the prognosis of patients with AF with type 2 diabetes. However, patients with impaired glucose metabolism had higher rates of AF recurrence than those without. It has been reported that recurrence of tachycardia decreases the left ventricular function and promotes the development of heart failure, increasing the risk of cardiac death. Patients with AF complicated by diabetes should be especially aware of the risk of recurrence after AF ablation. Further investigations are needed concerning the prognosis of patients with type 2 diabetes and

TIC.

In this study, renal dysfunction was also associated with TIC. Renal dysfunction increases the risk of AF, while AF increases the risk of developing CKD, resulting in frequent comorbidity of the two conditions. It is well known that renal dysfunction is involved in the development of cardiac remodeling and dysfunction. Coexistence of CKD and AF may enhance hemodynamic overload, leading to the onset of TIC.

Conclusions

In the present study, we showed that type 2 diabetes and renal dysfunction were associated with TIC in AF patients. Persistent AF and shorter AVNERP may be involved with the development of TIC. The results of this study can serve as a starting point from which effective therapeutic strategies can be established.