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Thyroid Storm Patients With Elevated Brain Natriuretic Peptide Levels and Associated Left Ventricular Dilatation May Require Percutaneous Mechanical Support

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OBJECTIVES: To determine the characteristics of thyroid storm patients with acute decompensated heart failure who should be candidates for temporary percutaneous mechanical circulatory support in addition to beta-blocker treatment to prevent cardiogenic shock.

DESIGN: A single-center, retrospective review of treatment details and data collected from electronic medical records.

SETTING: Thyrotoxicosis complicated with acute decompensated heart failure.

PATIENTS: Eight consecutive patients who were admitted to our hospital for acute decompensated heart failure with thyroid storm between December 2011 and August 2020 were retrospectively reviewed. Of the eight patients, four were treated with percutaneous mechanical circulatory support.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Compared with thyroid storm patients who did not require percutaneous mechanical circulatory support, those who did had a significantly higher initial plasma brain natriuretic peptide level (1,231 [911–3,387] vs 447 pg/mL [243–653 pg/mL], respectively; $p = 0.015$), as well as a significantly larger left ventricular end-diastolic diameter (56 [54–63] vs 48 mm [38–48 mm], respectively; $p = 0.029$) and end-systolic diameter (50 [49–58] vs 28 mm [28–30 mm], respectively; $p = 0.029$) on echocardiogram. In terms of thyroid storm severity, the Burch-Wartofsky score was higher in patients with percutaneous mechanical circulatory support than in those without, although the difference was not significant. All patients survived this index admission.

CONCLUSIONS: In thyroid storm patients, the presence of a high brain natriuretic peptide level, "left ventricular dilatation," or both may necessitate hemodynamic assessment to determine the indication of percutaneous mechanical circulatory support before beta-blocker administration.

KEY WORDS: acute decompensated heart failure; brain natriuretic peptide; echocardiogram; percutaneous mechanical circulatory support; thyroid storm

Thyroid storm (TS), an endocrine crisis that occurs in 1–5% of patients hospitalized for thyrotoxicosis, has a high mortality rate of 8–25% and usually requires emergency treatment (1, 2). It may be precipitated by an acute event such as thyroid or nonthyroid surgery, trauma, infection, an acute iodine load, or parturition. In addition to specific antithyroid therapy, supportive therapy in an ICU and recognition and treatment of any precipitating factors are essential. Although beta-blockers are used as a first-line treatment for TS, there are reports of patients with TS

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who developed cardiogenic shock after administration of beta-blockers (3, 4). Temporary percutaneous mechanical circulatory support (p-MCS) is useful to stabilize hemodynamics, especially in TS patients who are hemodynamically compromised (5). We sought to determine the clinical characteristics of TS patients who require p-MCS in addition to beta-blockers.

METHODS

Between July 1999 and August 2020, 30 patients (13 males) were admitted to our hospital with a diagnosis of hyperthyroidism, Basedow disease, or thyroid crisis complicated with acute decompensated heart failure (ADHF). Eight consecutive patients whose electronic medical records could be retrospectively evaluated in detail were enrolled. This study was approved by the National Cerebral and Cardiovascular Center Institutional Review Board for Clinical Research (M29-156-3). All patients were diagnosed with TS based on the following Akamizu criteria (6). Briefly, patients with evidence of thyrotoxicosis (elevated free tri-iodothyronine and/or free thyroxine levels) as a prerequisite and either of the following criteria were regarded as definite TS cases: 1) at least one CNS manifestation (Japan Coma Scale score ≥ 1 or Glasgow Coma Scale score ≤ 14) plus one of the following findings: fever (≥ 38°C), tachycardia (≥ 130 beats/min), severe manifestations of ADHF (pulmonary edema, cardiogenic shock, New York Heart Association class IV, or Killip class ≥ III), or gastrointestinal/hepatic manifestations (nausea, vomiting, diarrhea, bilirubin > 3 mg/dL, or prothrombin time-international normalized ratio > 1.5) or 2) three or more of the findings listed in (1), excluding CNS manifestations. Patients with evidence for thyrotoxicosis who had two of the findings mentioned in (1) (i.e., fever, tachycardia, ADHF, or gastrointestinal/hepatic manifestations), excluding CNS manifestations, were regarded as suspected TS cases. All patients were also assessed using the Burch-Wartofsky score (BWS) for TS severity (7). Patients were divided into two groups, namely the p-MCS and non–p-MCS groups, based on whether or not they underwent temporary p-MCS. Data are reported as frequency and percentage for qualitative variables and as median and interquartile range (IQR) for quantitative variables. Group means were compared using the permutation test. All analyses were conducted using R Version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria). A p value of less than 0.05 was considered statistically significant.

RESULTS

Three of the eight patients (37.5%) were male, and the median age was 59 years (IQR, 46–84 yr) (**Table 1**). All patients survived this index admission. Four patients were treated with p-MCS; three of these received treatment with only an intra-aortic balloon pump (IABP), whereas the fourth underwent IABP implantation and venoarterial extracorporeal membrane oxygenation (Table 1). The median duration of hospitalization was 33 days (26–89 d) in the overall study group, 92 days (74–152 d) in the p-MCS group, and 25 days (21–28 d) in the non–p-MCS group. At admission, there were significant differences between the two groups in the initial brain natriuretic peptide (BNP) level (1,231 [911–3,387] vs 447 pg/mL [243–653 pg/mL], respectively; $p = 0.015$), as well as the left ventricular end-diastolic diameter (56 [54–63] vs 48 mm [38–48 mm], respectively; $p = 0.029$) and left ventricular end-systolic diameter (50 [49–58] vs 28 mm [28–30 mm], respectively; $p = 0.029$). Although the BWS was higher in the p-MCS group than in the non–p-MCS group, there was no significant difference between the two groups (90 [88–90] vs 73 [45–58], respectively; $p = 0.057$) (**Fig. 1*A*–*D***). Among typical symptoms of hyperthyroidism, CNS symptoms and gastrointestinal/hepatic dysfunction occurred more frequently in the p-MCS group than in the non–p-MCS group (**Fig. 1*E***).

Notably, three of four patients in the p-MCS group had underlying heart disease, as follows (**Table 2**): Patient No. 5 had been diagnosed with dilated cardiomyopathy before the onset of TS. Patient No. 6 had concomitant TS and giant cell fulminant myocarditis (GCM); thus, steroidal pulse therapy and immunosuppressive therapy were performed simultaneously for GCM. Patient No. 7 had a medical history of percutaneous coronary intervention, coronary artery bypass grafting, and mitral valve replacement for angina pectoris and mitral regurgitation. She was also diagnosed with severe aortic stenosis at the index admission for

TABLE 1.
Summary of Clinical Variables at Admission

	Non–p-MCS Group				p-MCS Group			
Patient no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Age and gender	72 yr, male	78 yr, female	67 yr, male	51 yr, female	51 yr, male	50 yr, female	84 yr, female	46 yr, female
p-MCS, type	None	None	None	None	IABP	IABP	IABP	venoarterial extracorporeal membrane oxygenation and IABP
Continuous renal replacement therapy	None	None	None	Plasma exchange	None	None	Continuous hemodiafiltration	Plasma exchange
Underlying diseases/ comorbidities	Basedow disease	Basedow disease	None	Chronic thyroiditis	Dilated cardiomyopathy	Giant cell fulminant myocarditis	Post-percutaneous coronary intervention, coronary artery bypass grafting, and mitral valve replacement, and severe aortic stenosis	Basedow disease
Systolic/ diastolic BP at admission (mm Hg)	120/70	127/50	175/128	101/87	NA	90/65	97/48	181/131
Heart rate at admission (beats/min)	142	92	138	190	NA	135	155	191
Free tri-iodothyronine (pg/mL)	7.8	> 32.6	9.5	4.7	7.1	12.3	22.8	25.5
Free thyroxine (ng/dL)	3.3	> 7.7	4.2	7.7	3.6	> 7.7	> 7.7	6.8
Thyroid-stimulating hormone (μIU/mL)	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	0.01	< 0.01
Lactate level at admission (mmol/L)	NA	NA	1.7	5.8	1.3	3.9	4.0	11
Brain natriuretic peptide level at admission (pg/mL)	307	221	588	675	890	4,020	1,487	974
Left ventricular ejection fraction at admission (%)	58	72	57	20	14	20	20	20

(*Continued*)

TABLE 1. (*Continued*).
Summary of Clinical Variables at Admission

Patient no.	Non–p-MCS Group				p-MCS Group			
	1	2	3	4	5	6	7	8
p-MCS support duration (d)	NA	NA	NA	NA	30	7	10	10
Systolic BP at p-MCS induction (mm Hg)	NA	NA	NA	NA	122	85	113	73
Diastolic BP at p-MCS induction (mm Hg)	NA	NA	NA	NA	83	72	93	56
Heart rate at p-MCS induction (beats/min)	NA	NA	NA	NA	119	138	150	186
Lactate level at p-MCS induction (mmol/L)	NA	NA	NA	NA	NA	34	4.3	13.2
Mixed venous oxygen saturation at p-MCS induction (%)	NA	NA	NA	NA	23.5	61.9	39.9	53.7
Burch-Wartofsky score	45	70	45	80	90	80	90	90
Akamizu criteria	TS2	TS1	TS2	TS1	TS1	TS1	TS1	TS1
In-hospital outcome	Alive	Alive	Alive	Alive	Alive	Alive	Alive	Alive
Hospitalization duration (d)	21	28	21	29	315	98	86	37

BP = blood pressure, IABP = intra-aortic balloon pump, NA = not available, p-MCS = percutaneous mechanical circulatory support, TS = thyroid storm.

TS and finally underwent transcatheter aortic valve implantation after being weaned from IABP treatment.

DISCUSSION

This is the first report to identify the clinical characteristics of TS patients that were associated with an increased likelihood of undergoing p-MCS. Because cardiogenic shock is correlated with increased mortality in TS patients (2), the proper timing of mechanical circulatory support for TS is important. Notably, three of four patients in the p-MCS group had underlying heart disease. Even in TS patients without heart disease, excessive and longstanding exposure to thyroid hormone could reduce myocardial contractility reserve and lead to left ventricular dysfunction (8). Cardiovascular conditions may significantly reduce hemodynamic supply in the context of excessive energy demands caused by thyroid hormone oversecretion. These patients are therefore susceptible to cardiac decompensation, multiple organ failure, and shock and may require p-MCS. Thus, a higher BNP level and the presence of "left ventricular (LV) dilatation" could indicate a higher degree of hemodynamic decompensation and may be markers of the need for p-MCS in TS patients.

Beta-blockers are a traditional first-line treatment for managing the sympathoadrenal activation of TS and inhibiting the conversion of thyroxin to tri-iodothyronine (4). Because the thyroid-induced

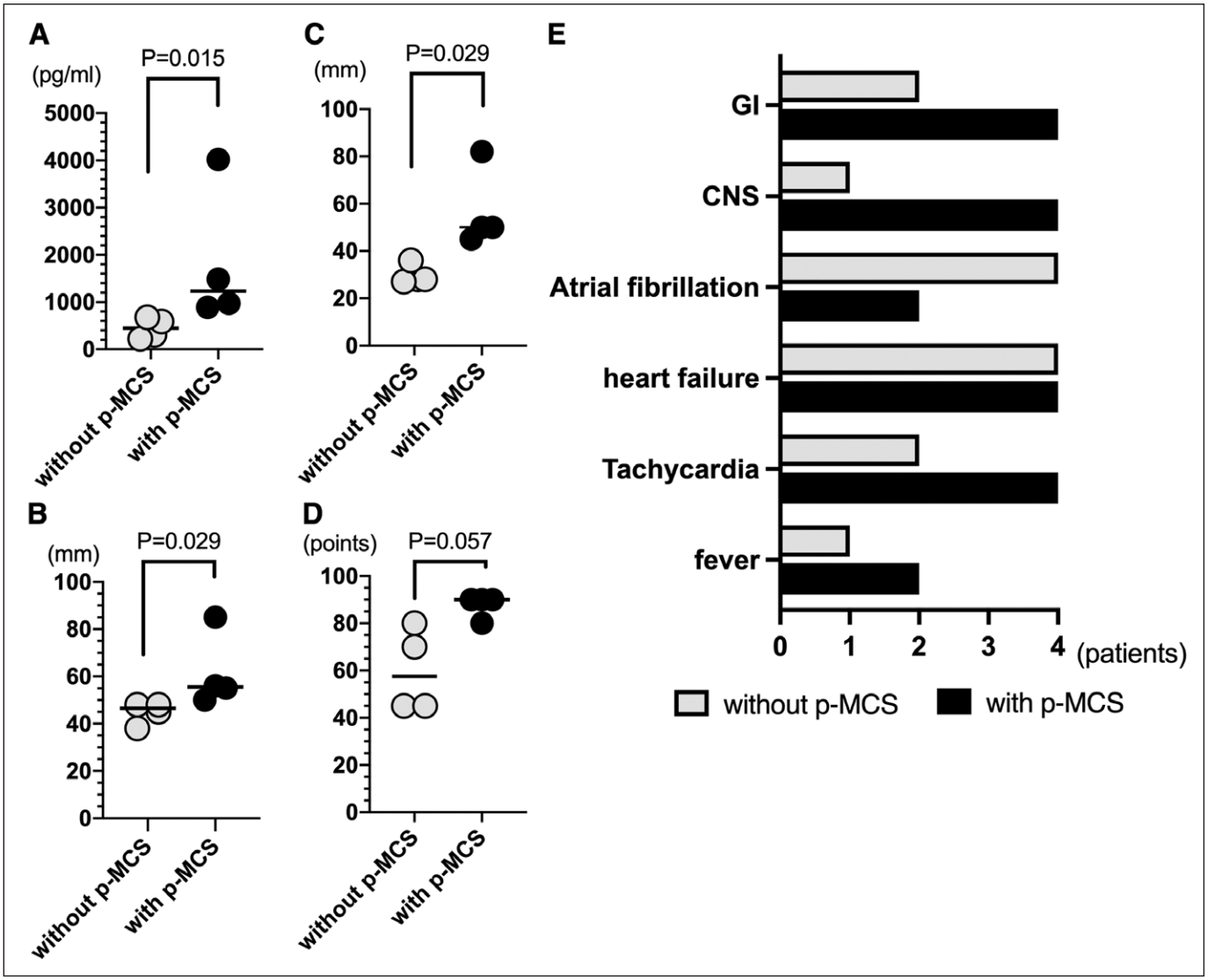

Figure 1. Comparison of patients with and without percutaneous mechanical circulatory support (p-MCS) in terms of brain natriuretic peptide (BNP) level at admission, echocardiographic variables at admission, the Burch-Wartofsky score (BWS), and clinical signs. **A**, BNP level, **B**, left ventricular end-diastolic diameter, **C**, left ventricular end-systolic diameter, **D**, BWS, and **E**, number of patients with each traditional sign and symptom of thyroid storm. GI = gastrointestinal.

hyperadrenergic state plays a compensatory role in maintaining cardiac output (CO) in patients with hyperthyroidism and low-output cardiac failure, the negative inotropic effect of beta-blockers could hamper this effect and cause a significant fall in CO and consequent hemodynamic instability (4). However, it is often difficult to determine whether tachycardia is caused by high CO secondary to hyperthyroidism or by compensation for low-output cardiac failure. Our findings suggest that TS patients with a high BNP level, "LV dilatation," or multiple organ failure should undergo hemodynamic assessment and mixed venous oxygen saturation measurement via pulmonary artery flotation catheter and bedside echocardiogram before beta-blocker administration. Further studies with larger numbers of patients are needed to clarify these issues.

CONCLUSIONS

In TS patients, the presence of a high BNP level, "LV dilatation," or both may necessitate hemodynamic assessment to determine the indication of p-MCS before beta-blocker administration.

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TABLE 2.
Treatments for Thyroid Storm and Underlying Heart Diseases and Variables at Discharge

	Non–p-MCS Group				p-MCS Group			
Patient no.	1	2	3	4	5	6	7	8
Beta-blockers	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Antithyroid drugs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Inorganic iodide	Yes	Yes	Yes	Yes	None	Yes	Yes	Yes
Thyroidectomy	None	None	None	None	None	None	None	None
Corticosteroids	None	None	None	Yes	Yes	Yes	None	Yes
Catecholamine	None	None	None	None	Yes	Yes	Yes	None
Plasma exchange	None	None	None	Yes	None	None	None	Yes
Coronary angiography	None	None	Yes	None	None	Yes	Yes	Yes
Treatment for underlying heart disease during index hospitalization	–	–	–	–	Ventricular assist device implantation	Corticosteroids, cyclosporine	Transcatheter aortic valve implantation	–
Brain natriuretic peptide level at discharge (pg/mL)	314	459	131	129	138	22	1,209	76
Left ventricular ejection fraction at discharge (%)	NA	60	38	48	15	60	18	51
Left ventricular end-diastolic diameter at discharge (mm)	NA	42	42	44	90	43	55	53
Left ventricular end-systolic diameter at discharge (mm)	NA	30	34	34	85	27	50	39

NA = not applicable, p-MCS = percutaneous mechanical circulatory support.
Dashes indicate no additional special treatments for underlying heart disease.

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