Responses of cardiac natriuretic peptides after paroxysmal supraventricular tachycardia: ANP surges faster than BNP and CNP

Jen-Yuan Kuo,1,4 An-Mei Wang,2 Sheng-Hsiung Chang,1,3 Chung-Lieh Hung,1,3,4 Chun-Yen Chen,1,4 Bing-Fu Shih,2 and Hung-I Yeh1,3,4

1Division of Cardiology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan; 2Department of Nuclear Medicine, Mackay Memorial Hospital, Taipei, Taiwan; 3Mackay Medicine, Nursing, and Management College, Taipei, Taiwan; and 4Mackay Medical College, Taipei, Taiwan

Submitted 24 August 2015; accepted in final form 15 January 2016

Atrial natriuretic peptide (ANP) secretion increases after 30 min of paroxysmal supraventricular tachycardia: ANP surges faster than BNP and CNP. Am J Physiol Heart Circ Physiol 310: H725–H731, 2016. First published January 22, 2016; doi:10.1152/ajpheart.00668.2015.—Atrial natriuretic peptide (ANP) secretion increases after 30 min of paroxysmal supraventricular tachycardia (PSVT). Whether this phenomenon also applies to brain or C-type natriuretic peptides (BNP or CNP) remains unknown. Blood samples of 18 patients (41 ± 11 yr old; 4 men) with symptomatic PSVT and normal left ventricular systolic function (ejection fraction 65 ± 6%) were collected from the coronary sinus (CS) and the femoral artery (FA) before and 30 min after the induction, and 30 min after the termination of PSVT. The results showed that the ANP levels rose steeply after the PSVT and then reduced at 30 min after the termination (baseline vs. post-PSVT vs. posttermination: CS: 34.0 ± 29.6 vs. 74.1 ± 42.3 vs. 46.1 ± 32.9; FA: 5.9 ± 3.2 vs. 28.2 ± 20.7 vs. 10.0 ± 4.6 pg/ml; all P < 0.05). In contrast, compared with ANP, the increases of BNP and CNP in CS after the PSVT were less sharp, but continued to rise after the termination of tachycardia (BNP, 10.2 ± 6.4 vs. 11.3 ± 7.1 vs. 11.8 ± 7.9; CNP, 4.5 ± 1.2 vs. 4.9 ± 1.4 vs. 5.0 ± 1.4 pg/ml; all P < 0.05). The rise of BNP and CNP in FA was similarly less sharp after the PSVT and remained stationary after the termination. PSVT exerted differential effects on cardiac natriuretic peptide levels. ANP increased greater after a 30-min induced PSVT, but dropped faster after termination of PSVT, compared with BNP and CNP.

ANP; BNP; CNP; natriuretic peptide; paroxysmal supraventricular tachycardia

NEW & NOTEWORTHY

This research article showed for the first time that paroxysmal supraventricular tachycardia (PSVT) exerted differential effects on cardiac natriuretic peptides levels. Atrial natriuretic peptide increased greater after a 30-min induced PSVT, but dropped faster after termination of PSVT, compared with brain and C-type natriuretic peptide.

Atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and C-type natriuretic peptide (CNP) are a family of structurally related peptides that participate in the integrated control of renal and cardiovascular function. ANP is a 28-amino acid peptide that is secreted from the atria and possesses natriuretic, vasoactive, and rennin-inhibiting actions (4, 6). BNP, also found in the heart, is a 32-amino acid peptide that shares structural and biological similarity to ANP (15). CNP, a vasorelaxant with a half-life of 2.6 min, is a 22-amino acid peptide that was first isolated from the porcine brain in 1990 (21). Although it shares structural and physiological properties with ANP and BNP, it appears to be secreted predominantly from the vascular endothelium (22, 25). In ventricular tissue, immunohistochemical staining confirmed the presence of all three peptides in normal hearts and was markedly enhanced in those with congestive heart failure (9, 26).

Some studies have shown a marked increase of ANP secretion after paroxysmal supraventricular tachycardia (PSVT) sustains for 30 min (11, 24). Whether this phenomenon also occurs for BNP and CNP is unknown. Our laboratory previously found that the myocardium regularly produced or released CNP in patients with normal left ventricular (LV) systolic function. Brief periods of rapid right atrial (RA) pacing (with pacing cycle lengths starting from 750 ms, in 50-ms decrement, to a minimum of 400 ms, each for 2 min and rest for 2 min) or PSVT (sustained <2 min) did not change the production and/or release (13). The aim of this study was to compare the response of the three peptides against a 30-min induced PSVT.

METHODS

Consecutive patients with clinically documented, symptomatic PSVT were referred to this laboratory for electrophysiological study (EPS) and radio-frequency (RF) ablation. The patients with age between 20 and 60 yr old and relatively healthy were enrolled into the study. The patients who had chronic obstructive lung disease, abnormal renal function, impaired LV systolic function, previous myocardial infarction, or coronary artery disease, which may affect endothelial function, were excluded from the study. Routine coronary angiography was performed in patients who were older than 45 yr old. Twelve-lead electrocardiogram, treadmill exercise test, myocardial perfusion scan, and/or coronary angiography were used to exclude coronary artery disease, if necessary. Ethical approval was granted by the Institute Review Board of our hospital. All patients had signed written consent forms.

Electrophysiological test and RF ablation. EPS was performed while the patient was fasting and not sedated. All antiarrhythmic medications were discontinued for at least five half-lives before study, and anti-diabetic agents were held on the day of study. Details of the EPS have been described previously (12). In brief, the diagnostic portion of the EPS included the following: 1) measurement of the electrical properties of the atrium, atrioventricular node, ventricle, and accessory pathways; 2) induction of supraventricular tachycardia by programmed atrial and ventricular burst pacing or extrastimuli; and 3) determination of the mechanism of tachycardia. If tachycardia could not be induced in the baseline state, isoproterenol (1–4 μg/min iv) was infused to facilitate its induction. Atrioventricular nodal reentrant tachycardia, atrial tachycardia, and arteriovenous reentrant tachy-
cardia (AVRT) were diagnosed and differentiated from each other by previously described criteria.

A 7F quadrupolar electrode catheter with a 4-mm distal electrode and a thermistor-embedded tip (Daig, Bard, or EP Technologies) was used for ablation. RF energy was delivered from a generator (EPT 1000). The maximal preset temperature was 70°C in every patient with AVRT, or 60°C in patients with atrial tachycardia or atrioventricular nodal reentrant tachycardia. The ablation techniques used in various types of tachycardias have been described previously (12).

Collection of blood sample and measurement of natriuretic peptides. Six samples, 2 ml each, were collected from each patient. First, blood samples were collected from the coronary sinus (CS) and the femoral artery (FA) immediately after four multipolar electrode catheters (Response CSL and Livewire, St. Jude Medical, Daig Division, Minnetonka, MN) were positioned in the CS, the RA, the His-bundle area, and the right ventricle (RV) under fluoroscopy. The location of the CS mapping catheter in CS was confirmed by direct contrast medium injection via the catheter. Second, PSVT was induced and allowed to continue for 30 min, while the RA, RV, and His mapping catheters were withdrawn to the inferior vena cava in the meantime for safety reasons. Then PSVT was terminated by ventricular- or atrial rapid pacing immediately, and blood samples were collected from the CS and the FA. Third, blood samples were collected from the CS and the FA at 30 min after the termination of PSVT. Heart rate, blood pressure, and RA pressure were recorded before PSVT, 30 min after the induction of PSVT, and 30 min after the termination of PSVT.

Details of the quantification of plasma natriuretic peptides in this laboratory have been described previously (8, 13). In brief, blood samples were collected into chilled test tubes containing ethylene diamine tetraacetic acid and aprotinin (0.6 trypsin inhibitor unit/ml blood; Phoenix Pharmaceuticals). Samples were immediately centrifuged and plasma stored at −80°C until measurement. The plasma levels of natriuretic peptides were determined by a blinded operator (A.-M. Wang) using radioimmunoassay method with commercially available kits (Phoenix Pharmaceuticals), conducted according to the manufacturer’s manual. The intra-assay coefficient of variation was 7.5% for ANP, 6.5% for BNP, and 6.9% for CNP. The lower limit of detection was 1 pg/ml.

Determination of LV function by echocardiography. Cardiac function was evaluated using echocardiography. An ejection fraction of LV > 50% without regional wall motion abnormality was considered as normal LV systolic function. The LV ejection fraction was measured by (LV diastolic volume − LV systolic volume)/LV diastolic volume.

Statistical analysis. Quantitative data were expressed as means ± SD. Parametric data were compared by ANOVA or t-test, and categorical data were analyzed by the χ² test with Yates’ correction or Fisher’s exact test. P < 0.05 was considered statistically significant.

RESULTS

Eighteen patients (4 men and 14 women, mean age 41 ± 11 yr old) were enrolled into the study. The baseline characteristics of patients are listed in Table 1. Two had diabetes mellitus

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Type of PSVT</th>
<th>LVEF (%)</th>
<th>Cr (mg/dl)</th>
<th>BMI (kg/m²)</th>
<th>B-BP (mmHg)</th>
<th>B-HR (beats/min)</th>
<th>BSCL (ms)</th>
<th>PSVT-HR (beats/min)</th>
<th>TCL (ms)</th>
<th>B-HR</th>
<th>PSD</th>
<th>HTN</th>
<th>CAD/Angina</th>
<th>LVEF</th>
<th>DM</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>27</td>
<td>AVNRT</td>
<td>59</td>
<td>0.7</td>
<td>20.64</td>
<td>94/55</td>
<td>88</td>
<td>68</td>
<td>190</td>
<td>315</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>51</td>
<td>AVNRT</td>
<td>79</td>
<td>0.6</td>
<td>20.7</td>
<td>140/98</td>
<td>98</td>
<td>612</td>
<td>209</td>
<td>287</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil, Fludiazepam</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>19</td>
<td>OAVRT</td>
<td>70</td>
<td>0.8</td>
<td>25.35</td>
<td>120/70</td>
<td>72</td>
<td>833</td>
<td>139</td>
<td>431</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>24</td>
<td>OAVRT</td>
<td>68</td>
<td>0.8</td>
<td>16.12</td>
<td>111/67</td>
<td>72</td>
<td>833</td>
<td>156</td>
<td>384</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>52</td>
<td>AVNRT</td>
<td>62</td>
<td>0.6</td>
<td>21.64</td>
<td>100/60</td>
<td>82</td>
<td>732</td>
<td>188</td>
<td>320</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil, Fludiazepam</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>42</td>
<td>OAVRT</td>
<td>71</td>
<td>0.8</td>
<td>21.31</td>
<td>110/70</td>
<td>80</td>
<td>750</td>
<td>149</td>
<td>403</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>42</td>
<td>OAVRT</td>
<td>67</td>
<td>0.8</td>
<td>18.33</td>
<td>130/70</td>
<td>94</td>
<td>638</td>
<td>219</td>
<td>274</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>46</td>
<td>AVNRT</td>
<td>64</td>
<td>0.7</td>
<td>31.64</td>
<td>116/73</td>
<td>97</td>
<td>619</td>
<td>125</td>
<td>480</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil, Fludiazepam</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>26</td>
<td>AVNRT</td>
<td>66</td>
<td>0.5</td>
<td>18.93</td>
<td>99/53</td>
<td>85</td>
<td>706</td>
<td>233</td>
<td>257</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>39</td>
<td>OAVRT</td>
<td>65</td>
<td>0.6</td>
<td>25.28</td>
<td>133/70</td>
<td>66</td>
<td>909</td>
<td>149</td>
<td>402</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>Verapamil, Nateglinide, Metformin</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>42</td>
<td>AVNRT</td>
<td>55</td>
<td>0.9</td>
<td>27.22</td>
<td>118/70</td>
<td>85</td>
<td>706</td>
<td>209</td>
<td>287</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil, Fludiazepam</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>50</td>
<td>AVNRT</td>
<td>59</td>
<td>0.7</td>
<td>24.08</td>
<td>137/90</td>
<td>78</td>
<td>769</td>
<td>199</td>
<td>302</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>Verapamil, Fludiazepam, Propafenone, Gilmepride</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>52</td>
<td>AVNRT</td>
<td>66</td>
<td>0.8</td>
<td>26.71</td>
<td>120/70</td>
<td>84</td>
<td>714</td>
<td>178</td>
<td>337</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>Verapamil, Atenolol, Perindopril</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>48</td>
<td>AVNRT</td>
<td>64</td>
<td>0.6</td>
<td>27.51</td>
<td>122/60</td>
<td>66</td>
<td>909</td>
<td>166</td>
<td>362</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>Verapamil, Fludiazepam, Metformin, Gilmepride</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>41</td>
<td>AVNRT</td>
<td>73</td>
<td>0.7</td>
<td>22.48</td>
<td>110/70</td>
<td>78</td>
<td>769</td>
<td>155</td>
<td>386</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>42</td>
<td>OAVRT</td>
<td>57</td>
<td>0.8</td>
<td>20.2</td>
<td>113/68</td>
<td>84</td>
<td>714</td>
<td>141</td>
<td>426</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>17</td>
<td>F</td>
<td>42</td>
<td>AVNRT</td>
<td>66</td>
<td>0.7</td>
<td>19.76</td>
<td>98/67</td>
<td>82</td>
<td>732</td>
<td>120</td>
<td>502</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Verapamil</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>58</td>
<td>OAVRT</td>
<td>60</td>
<td>1.2</td>
<td>28.66</td>
<td>110/66</td>
<td>62</td>
<td>968</td>
<td>148</td>
<td>406</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>Verapamil</td>
</tr>
</tbody>
</table>

PSVT, paroxysmal supraventricular tachycardia; LVEF, left ventricular ejection fraction; Cr, serum creatinine; BMI, body mass index; B-BP, baseline blood pressure; B-HR, baseline heart rate; BSCL, baseline sinus cycle length; PSVT-HR, heart rate of paroxysmal supraventricular tachycardia; TCL, tachycardia cycle length; HF, heart failure; HTN, hypertension; CAD, coronary artery disease; LVEF, left ventricular hypertrophy; DM, diabetes mellitus; F, female; M, male; AVNRT, atrioventricular reentrant tachycardia; OAVRT, orthodromic atrioventricular reciprocating tachycardia. +, Disease present in subject; −, disease not present in subject.

AJP-Heart Circ Physiol • doi:10.1152/ajpheart.00668.2015 • www.ajpheart.org
with well-controlled blood sugar, two had hypertension with well-controlled blood pressure, and one had mild LV hypertrophy. Twelve-lead electrocardiogram of all the patients showed no myocardial ischemia. No patient had angina symptoms. Routine coronary angiography was performed in seven patients who were older than 45 yr old. No patient had chronic obstructive lung disease, previous myocardial infarction, coronary artery disease, or angina. No patient underwent study within 1 wk of the last PSVT. All patients had normal renal function (serum creatinine 0.7 ± 0.2 mg/dl) and LV systolic function (LV ejection fraction 65 ± 6%). All of the 18 patients had successful RF ablation for their PSVT and did not have recurrence during a 2-yr follow-up. Two additional patients were excluded from analysis because they did not complete the blood test due to no inducible PSVT in the electrophysiological laboratory.

The ANP levels at 30 min after the induction of PSVT were significantly higher than those before the induction of PSVT (CS, 74.1 ± 42.3 vs. 34.0 ± 29.6; FA, 28.2 ± 20.7 vs. 5.9 ± 3.24 pg/ml; both P < 0.001). The ANP levels at 30 min after the termination of PSVT were also significantly higher than those before the induction (CS, 46.1 ± 32.9 vs. 34.0 ± 29.6; FA, 10.0 ± 4.6 vs. 5.9 ± 3.24 pg/ml; both P < 0.05). Moreover, the ANP levels at 30 min after the induction of tachycardia were significantly higher than those at 30 min after the termination of PSVT (CS, 74.1 ± 42.3 vs. 46.1 ± 32.9, P < 0.05; FA, 28.2 ± 20.7 vs. 10.0 ± 4.6 pg/ml, P < 0.001) (Fig. 1). The BNP levels at 30 min after the induction of PSVT were significantly higher than those before the induction of PSVT (CS, 11.3 ± 7.1 vs. 10.2 ± 6.4; FA, 9.6 ± 6 vs. 8.7 ± 5.6 pg/ml; both P < 0.05). The BNP levels in CS at 30 min after the termination of PSVT were also significantly higher than those before the induction of PSVT (11.8 ± 7.9 vs. 10.2 ± 6.4 pg/ml; P < 0.05). However, there was no significant difference between baseline and 30 min after the termination of PSVT in FA (9.1 ± 6.3 vs. 8.7 ± 5.6 pg/ml; P = 0.29). There was also no significant difference between the BNP levels at 30 min after the induction of PSVT and those at 30 min after the termination (Fig. 2). The CNP levels at 30 min after the induction of PSVT were significantly higher than those before the induction of PSVT (CS, 4.9 ± 1.4 vs. 4.5 ± 1.2; FA, 4.3 ± 1.1 vs. 3.9 ± 0.9 pg/ml; both P < 0.005). The CNP levels in CS at 30 min after the termination of PSVT were also significantly higher than those before the induction of PSVT (5 ± 1.4 vs. 4.5 ± 1.2 pg/ml; P = 0.005). However, there was no significant difference between baseline and 30 min after the termination of PSVT in FA (4.1 ± 0.9 vs. 3.9 ± 0.9 pg/ml; P = 0.07). There was also no significant difference between the CNP levels at 30 min after the induction of PSVT and those at 30 min after the termination (Fig. 3). In 150 of 162 (92.6%) pairs of natriuretic peptide values, the natriuretic peptide levels in the CS were higher than those in the FA. The ANP, BNP, and CNP levels in the CS at each time point were significantly higher than those in the FA (Fig. 4, all P < 0.001). However, the transcardiac net production or release of natriuretic peptides did not correlate with the heart rate, tachycardia rate, RA pressure, or blood pressure.

The mean RA pressure at 30 min after the induction of PSVT was significantly higher than that before the induction of PSVT (6 ± 4 vs. 4 ± 2 mmHg; P < 0.01) (Fig. 5). However, the change did not correlate with any of the natriuretic peptide levels (all P > 0.05). Baseline heart rate, tachycardia rate, or blood pressure also did not correlate with the natriuretic peptide levels.

**DISCUSSION**

**Major findings.** This study showed that ANP, BNP, and CNP levels in the CS at baseline and each time point after PSVT were significantly higher than those in the FA in individuals with PSVT and normal LV systolic function, indicating that, in the body, the heart is a major source of natriuretic peptides, including ANP, BNP, and CNP, at rest and post-PSVT. In addition, sustained PSVT for 30 min could enhance the heart to release ANP, BNP, and CNP. The increase of ANP to PSVT was to a greater degree but dropped faster, compared with BNP and CNP.

**Previous reports regarding production or release of natriuretic peptides during PSVT.** Several previous studies showed that induction or spontaneous initiation of PSVT resulted in a
marked elevation of plasma ANP levels (11, 17, 20, 23, 24). However, the effects of PSVT on the ANP levels remained discrepant. Tsai et al. (24) showed that, immediately after the induction of PSVT, plasma ANP levels began to increase, peaked at 32 min (734% increment on average), and then gradually decreased in five patients. The ANP levels significantly increased at 15 and 30 min after the induction of PSVT, and 5 min after the termination of PSVT, compared with those of control, but showed no significant increase at 5 min after the induction of PSVT, or 15 or 30 min after the termination of PSVT (24). Kojima et al. (11) found that plasma ANP levels in 10 patients with PSVT significant increased from 37 pg/ml during the control period to 110 pg/ml at 30 min, 160 pg/ml at 60 min after the induction of PSVT, and to 90 pg/ml at 30 min after the termination of PSVT (11). Anderson et al. (1) showed that induction of AVRT in three patients produced an acute and marked rise in plasma ANP concentrations, which returned to normal at 30 min after restoration of the sinus rhythm. In those studies, the PSVT was allowed to sustain for 10.5, 30, and 42 min, respectively. In the present study, we found that the plasma ANP levels significantly increased at 30 min after the induction of PSVT, compared with those before PSVT. The ANP levels significantly fell at 30 min after the termination of PSVT, but were still significantly higher than those before PSVT. These findings were consistent with Kojima and coworker’s findings (11). However, the response of the ANP to PSVT in FA was greater in this study (+378 vs. +197%). In the study of Tsai et al. (24), the ANP levels at 30 min after termination of PSVT remained higher than those of control, but showed no significant difference. Small patient numbers (N = 5) might be one of the reasons. Taken together, with more patients and a strict protocol, the present study unequivocally showed that the release of ANP continued for at least 30 min after termination of PSVT.
Mechanisms of myocardial production or release of natriuretic peptides during PSVT.

In a rat study, Dietz (7) showed that an increase in blood volume resulted in the release of ANP via atrial stretch. Lang et al. (14) also demonstrated that increased atrial stretch or ventricular stretch, such as volume overload, led to increased secretion of ANP in atria and BNP in ventricles, respectively. Increases in ANP were also found during both pacing-stimulated and spontaneously PSVT in the study of Nicklas et al. (16). They speculated that the stimulus to ANP secretion during PSVT appears to be related to the rise in RA pressure rather than to the increase in heart rate. However, several studies showed that a significant positive correlation was found between plasma ANP levels and mean pulmonary capillary wedge pressure, while the correlation between plasma ANP levels and mean RA pressure was not significant (19, 24). In the present study, we found that there was no significant linear correlation between RA pressure and ANP levels, although the mean RA pressure at 30 min after the induction of PSVT was significantly higher than that before PSVT, and ANP levels did increase in the CS and FA. This might imply that the left atrial pressure plays a more important role than the RA pressure in the production or release of ANP. However, the underlying mechanism remains unclear. Different effects of RA and left atrial stretch by volume or pressure overload might partially explain the different results. Further studies are required to elucidate these issues.

The mechanisms regulating myocardial production or release of BNP and CNP in arrhythmias or tachycardias remain unclear. Kalra et al. (10) suggested that elevated ventricular filling pressure may contribute to the increased production of CNP in patients with congestive heart failure. Borgeson et al. (2) showed that acute intravascular volume overload in dogs resulted in the expected increase in RA pressure, pulmonary capillary wedge pressure, plasma ANP, and urinary CNP, but no change in plasma BNP and CNP levels. Rademaker et al. (18) found that acute ventricular pacing for 1.5 h in sheep increased plasma ANP and BNP levels by 8.6- and 3.6-fold, respectively, whereas chronic ventricular pacing for 4 days increased ANP and BNP by 7.8- and 9-fold, respectively. There was no study investigating whether a 30-min induced PSVT in patients could affect the production or release of BNP or CNP in the past. In the present study, we showed that plasma BNP and CNP levels significantly increased after 30 min of PSVT and remained raised at 30 min after the termination of PSVT. Enough loading of ventricular and/or atrial stretch during PSVT might enhance the release of BNP and CNP. Previously, our laboratory demonstrated that brief periods of rapid atrial pacing, short-term PSVT (<2 min), routine EPS, or RF ablation procedure did not increase the production or release of CNP (13). The different baseline CNP values might be due to different clinical characteristics, such as LV ejection fraction, age, and baseline heart rate between these two groups. The different changes of CNP values in CS and FA might be due to different duration of PSVT. However, how long PSVT
is necessary to enhance the release of BNP and CNP remains unknown. The half-life of BNP was longer than that of ANP or CNP. This might partially explain why BNP remained raised, while ANP fell at 30 min after the termination of PSVT in the CS. However, it could not explain why CNP also remained raised at 30 min after the termination of PSVT. There might be other factors affecting the production or release of CNP. Another possible explanation was that the start of production or release of BNP and CNP could last longer than that of ANP after the stimulation of 30-min PSVT. Again, further studies are required to elucidate the underlying mechanism.

Study limitations. This study has several limitations. First, the sample size of the study is small. If more patients could be enrolled into the study, there would be more power to draw the current conclusion. However, it is the largest patient group to test the effects of PSVT on cardiac natriuretic peptide levels in the literature so far. Second, we might suspect that the length and the frequency of previous PSVT could affect the production of natriuretic peptide at baseline or the response to the PSVT. In this study, the length of previous PSVT ranged from several-decade minutes to several hours, and the frequency of previous PSVT ranged from several times a month to several times a year in these patients. These might have a chance to affect the production of natriuretic peptide at baseline, although we did not know how much the influence was. However, no patient underwent study within 1 wk of the last PSVT. We speculated that the influence might be tiny. Third, to record heart rate, blood pressure, and urine amount, and to check the plasma renin activity, serum aldosterone level, and urine sodium value may help to understand the pathophysiology of myocardial release and/or production of natriuretic peptides. However, in this study, we only recorded blood pressure and heart rate and found that they did not correlate with any of the natriuretic peptide levels. Fourth, to measure RA pressure, pulmonary arterial pressure, ventricular pressure, and pulmonary capillary wedge pressure of patients may help to understand the mechanisms of the increment of natriuretic peptides after an induced PSVT sustaining for 30 min. However, because it was not the routine procedure during the mapping and ablation of PSVT, we did not attempt to measure all of them. In this study, we only recorded RA pressure and found that they did not correlate with any of the natriuretic peptide levels.

Fifth, RF ablation may have its own acute and chronic effects on natriuretic peptides. Previously, our laboratory found that the production or release of CNP did not change at the end of EPS and/or RF ablation (13). In the literature, only two previous studies investigated the effect of RF ablation on plasma natriuretic peptide in patients with PSVT. One study showed increment of plasma BNP level 3 and 24 h after RF ablation, but no increment of plasma BNP level 30 min after RF ablation (5). The other study showed that levels of NT-pro-BNP were significantly higher before RF ablation compared with day 1 and day 120 after RF ablation. However, that study had no data regarding the level of natriuretic peptide within 3 h after RF ablation (3). The blood samples were collected within 30 min after RF ablation in all of our patients. Whether plasma levels of ANP or CNP would increase 30 min after RF ablation remained unknown before.

Clinical implications. To assay the plasma levels of ANP, BNP, and CNP might have diagnostic significance for differentiating PSVT from non-PSVT palpitations. Other more serious cardiac diseases, such as congestive heart failure, resulting from different cardiac etiologies, have more atrial and/or ventricular pressure or volume overload. Whether differential responses of ANP, BNP, and CNP have more values of diagnosis or evaluation of treatment or not deserve further investigation.

Conclusions. PSVT exerted differential effects on cardiac natriuretic peptide levels in persons with PSVT and normal LV systolic function. ANP increased greater after a 30-min induced PSVT, but dropped faster after termination of PSVT, compared with BNP and CNP.

ACKNOWLEDGMENTS

We thank Hsin-Yu Chiu for the assistance of data collection, and Nikida Huang for the assistance of figure preparation.

GRANTS

This study was supported by Grant MMH-9585 from the Department of Medical Research, MacKay Memorial Hospital, Taipei, Taiwan.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


REFERENCES


