Cardiopulmonary Values in Dogs with Artificial Model of Caval Syndrome in Heartworm Disease

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ABSTRACT. Cardiopulmonary values were determined in dogs with an artificial model of heartworm caval syndrome, which was produced by insertion of heartworm-like silicone tubes into the tricuspid valve orifice and right atrium. Fifteen to 25 tubes with some knots were inserted in 6 dogs (knot group), and 7 to 11 tubes (small-number group) or 29 to 37 tubes (large-number group) without a knot in 3 dogs, respectively. After tube insertion, angiographic contrast medium infused into the right ventricle regurgitated to the right atrium in all cases, and the regurgitation was the most severe in the large-number group. On electrocardiographic findings, the atrial and/or ventricular premature beat developed. The height of a- and v-wave of right atrial pressure curves elevated in all groups. The elevation in v-wave was obvious in the large-number group. The pulmonary arterial pressure tended to fall or to elevate slightly, and total pulmonary resistance increased in all groups. The right cardiac output decreased significantly in all cases. The right heart hemodynamics of the model might resemble those in spontaneous cases without disturbed pulmonary circulation.—**KEY WORDS:** artificial model, cardiopulmonary value, caval syndrome, dirofilariasis, dog.

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The clinical signs in dogs with spontaneous caval syndrome (dirofilarial hemoglobinuria) indicate severe circulatory disturbance. It has been considered that the major factor in this disturbance is the tricuspid valve dysfunction, because heartworms invariably located at the tricuspid valve orifice in dogs with this syndrome [2, 5].

The authors developed an artificial model of caval syndrome by insertion of heartworm-like silicone tubes into the tricuspid valve orifice. In this model, knotted and knot-free silicone tubes located at the tricuspid valve orifice and right atrium, and hindered mainly the valve function. The clinical signs and laboratory test results like spontaneous syndrome were reproduced in various degrees, which had been described in separate papers [8, 9], and suggested that the abnormalities might relate with the right heart hemodynamics. The present study investigates the cardiopulmonary values in dogs with artificial models of heartworm caval syndrome before and after insertion of heartworm-like silicone tubes.

MATERIALS AND METHODS

The profile of the experimental dogs, the number of live heartworms in the pulmonary arteries and the number of silicone tubes inserted are presented in Table 1. Twelve dogs, including 3 heartworm-free

and 9 heartworm-infected dogs, were used. One week or more before experiment, heartworm-infected dogs underwent surgical heartworm removal from the pulmonary arteries with a flexible alligator forceps [3]. Because several entangled worms were sometime removed on surgical treatment in dogs with spontaneous disease, silicone tubes (M-Silico, No. 00, Shin-Etsu Polymer Co. Ltd., Tokyo) with some knots were inserted surgically into the right atrium and tricuspid valve orifice in 6 dogs (knot group). Besides, 7 to 11 tubes without a knot were inserted in 3 dogs (small-number group), and 25 to 35 tubes without a knot were inserted in 3 dogs (large-number group). The measurement of cardiopulmonary values was carried out before and at 1 and 7 days after insertion. The dogs received only antibiotics after surgical treatment and cardiopulmonary measurement.

Dogs were pre-medicated with an intravenous injection of 0.05–0.1 mg/kg body weight of diazepam (Cercine Injection, Takeda Chemical Industries, Ltd., Osaka), and anesthetized with a intramuscular injection of 5 to 10 mg/kg of ketamine hydrochloride (Ktalar 50, Sankyo Co. Ltd., Tokyo). Dogs were restrained in right lateral recumbency. Electrocardiograms were recorded by bipolar standard limb lead (I, II and III) and augmented unipolar limb lead (aVR, aVL and aVF). Angiocardiography was carried out with an autoinjector of

Table 1. Profile of experimental dogs

Group	Dog No.	Age (years)	Body weight (kg)	Sex	No. of live heartworms	No. of tubes inserted
Knot	1541	3	14.5	Male	20	20
	1573	5	11.5	Female	30	25
	1579	3	8.5	Female	38	20
	1586	1.5	14.5	Male	0	15
	1593	3	10.5	Male	1	20
	1612	3	6.0	Male	20	15
Small-number	1679	2	6.5	Female	9	7
	1740	1.5	8.0	Male	0	10
	1773	4	9.0	Male	21	11
Large-number	1705	3	12.0	Male	6	37
	1739	7	11.0	Male	24	29
	1747	7	7.5	Female	0	35

contrast medium for angiography (M-500, Nemoto Kyorindo, Tokyo) and a cut-film changer (TAC-25-S, Matsuki Co. Ltd., Tokyo). The contrast medium for angiocardiology (Isopaque-440, Torii & Co. Ltd., Tokyo) was infused into the right ventricle through a catheter. The pulmonary arterial and right atrial pressures were measured with a fluid-filled catheter and pressure-transducer system, and the 0-reference was arranged so as to correspond to the mid-point of thoracic thickness at the 3rd intercostal space. For measurement of right cardiac output, a Swan-Ganz flow-directed thermodilution catheter (93-132-5F, Baxter Healthcare Corp., Irvine, U. S. A.), a thermodilution amplifier and a cardiac output computer (AH-611V and EQ-611V, Nihon Kohden, Tokyo) were used. The right cardiac output was calculated by thermodilution method. The cardiac index (right cardiac output/kg body weight of the dog), stroke volume (right cardiac output/heart rate) and total pulmonary resistance ($60 \times \text{mean pulmonary arterial pressure} \times 1,332/\text{cardiac index}$) were calculated from each parameter [10]. The data before and after tube insertion were compared by the paired t-test.

RESULTS

Figures 1 and 2 show angiocardigrams after insertion of silicone tubes in the knot and large-number groups, respectively. The contrast medium, which was infused into the right ventricle, regurgitated to the right atrium in all cases. The severity of the regurgitation varied with the individual dog, but it was the most severe in the large-number group. The right atrium enlarged considerably in almost all

Fig. 1. Angiocardiogram in a case of the knot group. Regurgitation of the contrast medium to the right atrium is recognized (arrow).

Fig. 2. Angiocardiogram in a case of the large-number group. Severe regurgitation from the right ventricle to the right atrium (arrow) is observed.

Fig. 3. Bipolar standard limb lead electrocardiogram 1 day after insertion of tubes in a case of the knot group. a) Ventricular premature beat. b) Atrial premature beat. Vertical bar indicates 1 mV.

cases, and the right ventricle also did in some cases.

On electrocardiograms, atrial and/or ventricular premature beats were recorded sporadically or continuously in almost all cases (Fig. 3). In spite of dilation of the right atrium and ventricle on radiographic findings, there were no statistically significant differences between the pre- and post-insertion levels of the mean electrical axis in the frontal plane, and amplitude of p-wave, R-wave or T-wave in all groups.

Figure 4 illustrates the right atrial pressure curve before and 7 days after insertion in a typical case of each group. Compared with the curve before insertion, the elevation of a-wave was obvious after insertion in all groups. In the large-number group, the elevation in v-wave was significantly higher than that of a-wave, and these indicated severe stenosis and regurgitation at the tricuspid valve orifice.

Table 2 indicates changes in the heart rate, right atrial and pulmonary arterial pressures and total pulmonary resistance after insertion of silicone tubes. The heart rate tended to increase after

Fig. 4. Right atrial pressure curve before and after insertion of silicone tubes.

Upper: Right atrial pressure curve. Vertical bar indicates 10 mmHg.

a) a-wave, c) c-wave, v) v-wave.

Lower: II-lead electrocardiogram. Vertical bar indicates 1 mV.

Table 2. Changes in heart rate, pulmonary arterial and right atrial pressures and total pulmonary resistance after insertion of silicone tubes

Item	Group	n	Before insertion	1 day after	7 days after
			Mean $\pm$ SD ^{a)}	Mean $\pm$ SD	Mean $\pm$ SD
Heart rate (beats/min)	Knot	6	108 $\pm$ 46 (71–192) ^{b)}	150 $\pm$ 27* (115–191)	152 $\pm$ 46 (104–240)
	Small-number	3	192 $\pm$ 25 (168–218)	196 $\pm$ 13 (184–209)	174 $\pm$ 48 (123–218)
	Large-number	3	152 $\pm$ 18 (132–168)	138 $\pm$ 17 (126–157)	160 $\pm$ 9 (154–170)
Right atrial pressure a-wave (mmHg)	Knot	6	–0.67 $\pm$ 2.87 (–5.45–2.45)	1.21 $\pm$ 2.41 (–0.55–5.78)	5.57 $\pm$ 3.11** (0.70–10.0)
	Small-number	3	1.09 $\pm$ 1.68 (0.06–3.02)	2.91 $\pm$ 1.89** (1.77–5.09)	3.52 $\pm$ 1.51 (2.55 $\pm$ 5.26)
	Large-number	3	0.42 $\pm$ 1.45 (–1.23–1.48)	7.21 $\pm$ 2.28* (5.24–9.71)	9.61 $\pm$ 5.32 (4.34–14.8)
Right atrial pressure v-wave (mmHg)	Knot	6	–1.73 $\pm$ 1.76 (–4.58–0.09)	0.73 $\pm$ 2.72* (–2.44–5.12)	2.52 $\pm$ 1.49** (0.38–4.28)
	Small-number	3	–0.21 $\pm$ 1.19 (–1.44–0.94)	1.81 $\pm$ 1.91* (0.51–4.00)	3.58 $\pm$ 2.68* (1.05–6.39)
	Large-number	3	–0.56 $\pm$ 0.86 (–1.55–0.06)	9.05 $\pm$ 5.53 (5.30–15.4)	20.83 $\pm$ 9.46* (10.8–29.6)
Mean pulmonary arterial pressure (mmHg)	Knot	6	16.2 $\pm$ 3.3 (12.1–21.0)	13.0 $\pm$ 3.5 (8.3–17.8)	13.2 $\pm$ 2.5 (11.0–17.9)
	Small-number	3	18.7 $\pm$ 4.3 (15.1–23.5)	13.4 $\pm$ 0.5 (12.9–13.9)	14.8 $\pm$ 3.9 (11.0–18.7)
	Large-number	3	13.2 $\pm$ 2.2 (11.1–15.4)	10.4 $\pm$ 1.2* (8.9–11.2)	17.3 $\pm$ 3.5 (15.0–21.3)
Total pulmonary resistance (dynes $\cdot$ sec $\cdot$ cm ^{–5} $\cdot$ kg)	Knot	6	4738 $\pm$ 1665 (1861–6641)	6195 $\pm$ 2109 (3971–8580)	5642 $\pm$ 1270 (4078–7040)
	Small-number	3	4230 $\pm$ 1193 (2854–4967)	4523 $\pm$ 1448 (2852–5412)	6002 $\pm$ 2343 (3772–8444)
	Large-number	3	3960 $\pm$ 1471 (2545–5426)	4662 $\pm$ 81 (4609–4755)	7362 $\pm$ 1602 (5849–9042)

a) Standard deviation. b) Range (minimum-maximum).

* and **: Significantly different from pre-insertion value; each asterisk indicates $p < 0.05$ and $p < 0.01$, respectively.

insertion in the knot group, but did not change significantly in the small and large-number groups. The a-wave of right atrial pressure curve elevated gradually after insertion in all groups, and the elevation was greater in the large-number group than in the knot and small-number groups. The v-wave also elevated in all groups. The height of v-wave at 7 days after insertion was near to the mean pulmonary arterial pressure in the large-number group, and indicated severe tricuspid valve dysfunction.

Although the changes were within the normal ranges, the mean pulmonary arterial pressure tended to fall 1 day after insertion not only in heartworm-infected cases but also in heartworm-free cases in all groups, and elevated slightly in some cases of the large-number group 4 weeks after insertion. The total pulmonary resistance tended to increase after insertion in all groups.

Table 3 shows the changes in right cardiac output, cardiac index and stroke volume after insertion of

Table 3. Changes in right cardiac output and its indices after insertion of silicone tubes

Item	Group	n	Before insertion	1 day after	7 days after
			Mean±SD ^{a)}	Mean±SD	Mean±SD
Right cardiac output (l/min)	Knot	6	2.74±0.77 (1.70–3.71) ^{b)}	1.78±0.31* (1.34–2.29)	1.93±0.31 (1.43–2.29)
	Small-number	3	2.80±0.50 (2.51±3.38)	1.93±0.45 (1.63±2.45)	1.52±0.11* (1.41–1.63)
	Large-number	3	2.77±0.30 (2.50–3.09)	1.79±0.35 (1.44–2.13)	1.76±0.39 (1.32–2.05)
Cardiac index (ml/min/kg)	Knot	6	258±16 (237–283)	181±66* (119–293)	209±61 (152–312)
	Small-number	3	363±75 (279–423)	259±102 (190–376)	205±28* (177–233)
	Large-number	3	288±107 (226–411)	178±25 (150–194)	175±35 (174–205)
Stroke volume (ml/beat)	Knot	6	17.6±5.4 (12.0–27.4)	11.6±1.5* (10.1–13.9)	11.9±3.1* (7.2–16.3)
	Small-number	3	15.0±4.6 (11.5–20.1)	10.0±2.8 (8.2–13.3)	9.4±3.4* (7.0–13.3)
	Large-number	3	18.3±2.3 (16.0–20.6)	13.2±3.9 (9.1–16.9)	10.9±2.1* (8.6–12.2)

a) Standard deviation. b) Range (minimum-maximum).

*: Significantly different from pre-insertion value; the asterisk indicates $p < 0.05$.

silicone tubes. In the knot group, the right cardiac output decreased significantly at 1 day after insertion of tubes, then slightly increased at 7 days. The output decreased at 1 and 7 days after insertion in the small- and large-number groups. There was no significant difference in decrease in the right cardiac output between the small- and large-number groups. The cardiac index showed almost the same change as the right cardiac output in each group. The stroke volume decreased in all groups. The stroke volume decreased significantly 1 day after insertion, and remained at a low level after 7 days in the knot group. The stroke volume decreased to a significantly lower level 7 days following insertion in the small- and large-number groups. The decrease in the cardiac output roughly correlated with a decrease in vigor and appetite of the dog.

DISCUSSION

The right heart hemodynamics in cases with spontaneous caval syndrome were characterized by low cardiac output and high right atrial pressure

(central venous pressure) [4, 6]. In all groups of the present study, although the degree was variable in the individual case, the low cardiac output and high right atrial pressure were reproduced by hindrance of tricuspid valve function. In the small-number group, the regurgitation of contrast medium to the right atrium was slight, but the elevation of a-wave in the right atrial pressure curve was noticed, and suggested that the presence of tubes at atrium-side of the tricuspid valve brought about severe stenosis. The right cardiac output was reduced because of decreased blood inflow into the right ventricle [1]. In the large-number group, on the other hand, the silicone tubes produced both severe regurgitation and stenosis at the tricuspid valve orifice, as indicated from especially high levels of v-wave and a-wave and regurgitation of contrast medium to the right atrium. The valve dysfunction in the knot group might be of intermediate degree between the small- and large-number groups. The insertion of heartworm-like silicone tubes in a different number and form could reproduce a different grade of the tricuspid valve dysfunction (i.e., venous congestion

and low cardiac output).

In the model, the low cardiac output and venous congestion tended to associate with severity of symptoms; decreases in vigor and appetite or ascites, and cardiopulmonary disturbances and symptoms were severest in the large-number group. Also, the plasma hemoglobin concentration, which suggested the severity of intravascular hemolysis, was most elevated in the large-number group, followed by the knot group [9]. Besides, among the dogs in the large-number group, the severity of clinical signs [8], intravascular hemolysis [9] and cardiopulmonary disorders changed with position and number of tubes at the tricuspid valve orifice. The severity of valve dysfunction and circulatory disorder might relate closely with number, position and knot type of silicone tubes at the tricuspid valve orifice, that is, the condition of abnormal blood-stream flow induced with tubes. These facts suggested that the derangement of hemodynamics might depend on the number, position and arrangement of heartworms at the tricuspid valve orifice also in spontaneous cases.

In many spontaneous cases with caval syndrome, pulmonary hypertension was also noticed [6]. Thromboemboli of the pulmonary arteries with dead worms, which may also reduce cardiac output and induce heartworm migration from the pulmonary arteries [7], are found in almost all spontaneous cases. Circulatory disturbance may have resulted in conjunction with tricuspid valve dysfunction and the embolization of the pulmonary arteries [6]. In our model, however, the thromboembolization including dead heartworms in the pulmonary arteries was slight or could not be found, and the pulmonary arterial pressure did not elevate or elevated only slightly after insertion of tubes. As shown in the previous study [6], the cardiopulmonary values ranged widely and pulmonary lesions were variable in dogs with spontaneous caval syndrome. The right heart hemodynamics of the model might resemble

those in spontaneous cases without disturbed pulmonary circulation, in which almost all heartworms had migrated to the right atrium and tricuspid valve orifice, and pulmonary thromboembolism were relatively mild. Further investigations are needed on a model with severe embolization of the pulmonary arteries.

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