FIGURE LEGENDS

Fig. 1   Study protocols are shown in this scheme.

Rats were given a single subcutaneous injection of 60 mg/kg monocrotaline (MCT) or saline (Day 1). The endothelin-A receptor antagonist TA-0201 and/or the prostacyclin analogue beraprost sodium (BPS) or vehicle were administered orally once per day. Administration was initiated on the day before MCT injection (Day 0), and the administration period was 19 days (from Day 0 to Day 18). Rats were evaluated on Day 1, 7, 14, and 19 by two dimensional echocardiography. On Day 19, hemodynamics were measured, and rats were sacrificed.

The rats were divided into the following five groups: [1] normal rats administered vehicle (Control group, n=12), [2] rats with pulmonary hypertension (PH rats) administered vehicle (PH group, n=17), [3] PH rats administered oral ET-A receptor antagonist (TA-0201) (PH+TA group, n=18), [4] PH rats administered oral PGI2 analogue (beraprost sodium: BPS) (PH+BPS group, n=13), and [5] PH rats administered both TA-0201 and BPS (PH+TA+BPS group, n=18).

Fig. 2   Changes in the ratio of the short diameter (a) of left ventricle (LV) to the long diameter (b) of LV, an index of pulmonary hypertension (PH), in the parasternal short-axis view of LV by two dimensional echocardiography. The view was obtained at the level of the papillary muscle. It was evaluated on Day 1, 7, 14 and 19 after the beginning of treatment.

Open circles (O) indicate Control group (n=12)

Closed circles (●) indicate PH group (n=17)

Open squares (□) indicate PH+TA group (n=18)

Closed squares (■) indicate PH+BPS group (n=13)

Open diamonds (◇) indicate PH+TA+BPS group (n=18)

Abbreviations of group names are the same as those described in Fig. 1.

Values are mean ± S. E..

* p<0.05 vs. Control, § p<0.05 vs. PH, # p<0.05 vs. PH+TA+BPS.

¶ p<0.05 vs. baseline value of each group on Day 1.

Fig. 3   Bar graphs show right ventricular (RV) systolic pressure (A) and the ratio of RV

systolic pressure to systolic blood pressure (Pp/Ps) (B) of Control group (n=12), PH group

(n=17), PH+TA group (n=18), PH+BPS group (n=13), and PH+TA+BPS group (n=18).

Abbreviations of group names are the same as those described in Fig. 1.

Each column and bar represents the mean ± S. E..

* p<0.05 vs. Control, § p<0.05 vs. PH, # p<0.05 vs. PH+TA+BPS.

Fig. 4   Bar graphs show the ratio of right ventricular (RV) wet weight to body weight (A) and

the ratio of RV wet weight to left ventricular (LV) wet weight (B) of Control group (n=12),

PH group (n=17), PH+TA group (n=18), PH+BPS group (n=13), and PH+TA+BPS group

(n=18).

Abbreviations of group names are the same as those described in Fig. 1.

Each column and bar represents the mean ± S. E..

* p<0.05 vs. Control, § p<0.05 vs. PH, # p<0.05 vs. PH+TA+BPS.

Fig. 5   Bar graphs show the ratio of the expression level of β-myosin heavy chain (MHC)

mRNA to α-MHC m RNA in right ventricle (RV) of Control group (n=12), PH group

(n=17), PH+TA group (n=18), PH+BPS group (n=13), and PH+TA+BPS group (n=18).

Each typical example of reverse transcription (RT)- polymerase chain reaction (PCR)

products is also shown.

Abbreviations of group name of rats are same as those described in Fig. 1.

Each column and bar represents the mean ± S. E..

* p<0.05 vs. Control, § p<0.05 vs. PH, # p<0.05 vs. PH+TA+BPS.

Fig. 6   Photomicrographs of pulmonary arteries of Control group (A), PH group (B), and

PH+TA+BPS group (C). Lung histology shows a marked increase in pulmonary arterial

medial wall thickening in PH group (B). The increase of the thickening was attenuated in

PH+TA+BPS group.

Abbreviations of group names are the same as those described in Fig. 1.

Each section was stained with azan (x520).

Fig. 7   Bar graphs show the ratio of medial wall thickness to external diameter of pulmonary

arteries of rats in Control group (n=12), PH group (n=17), PH+TA group (n=18), PH+BPS

group (n=13), and PH+TA+BPS group (n=18). Pulmonary arteries with an external size of
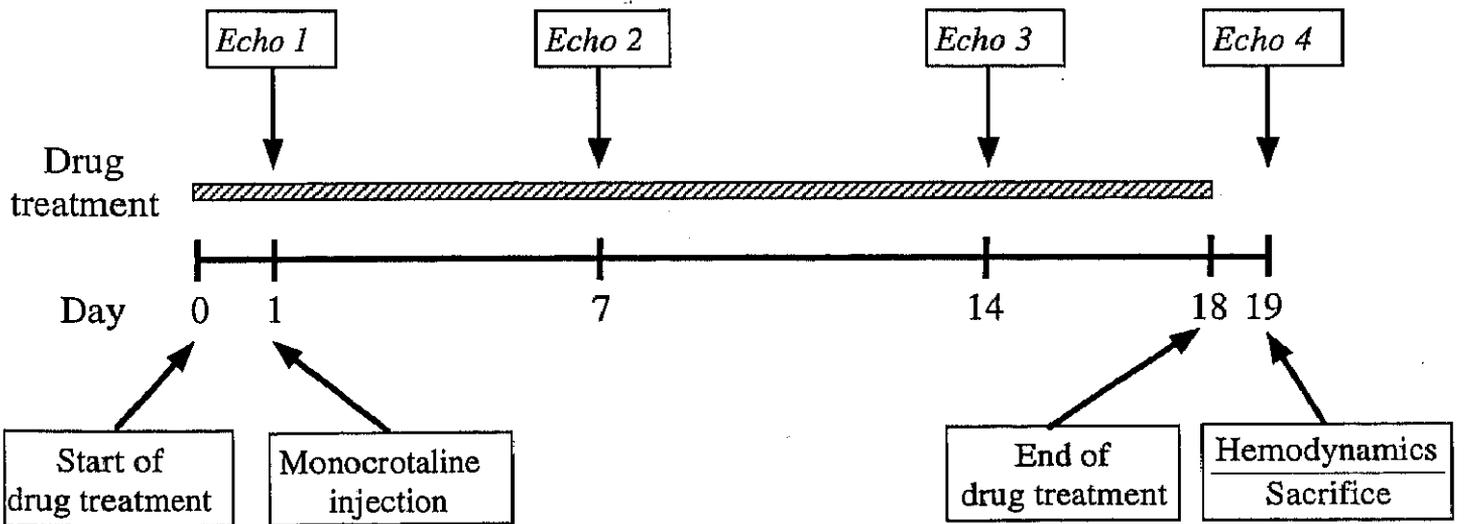
about 50 μm, were chosen.

Abbreviations of group names are the same as those described in Fig. 1.

Each column and bar represents the mean ± S. E..

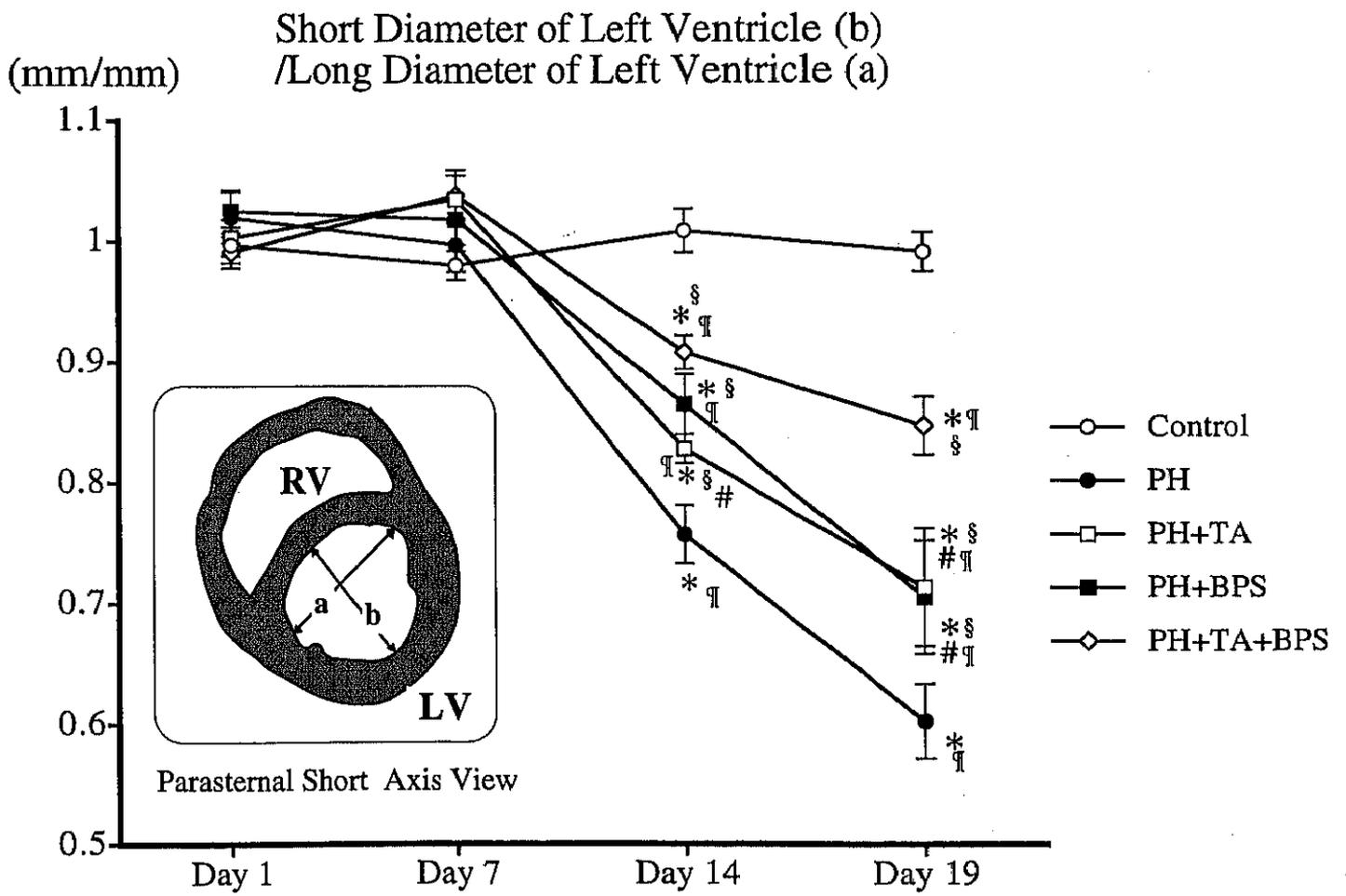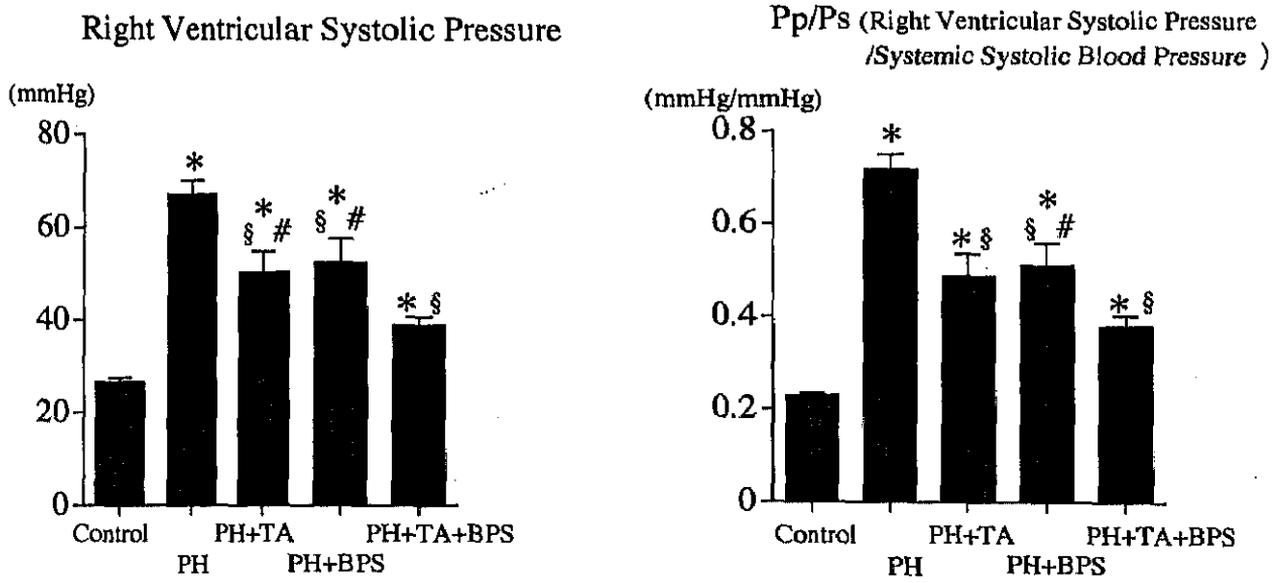* p<0.05 vs. Control, § p<0.05 vs. PH, # p<0.05 vs. PH+TA+BPS.

Ueno et. al.

Figure 1

Ueno et. al.

Figure 2
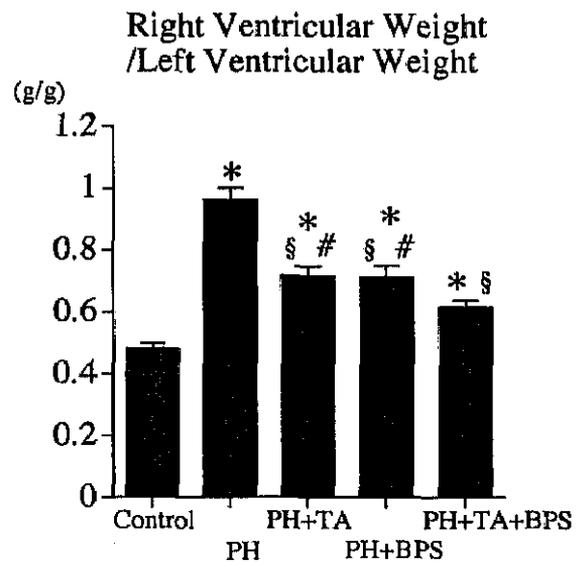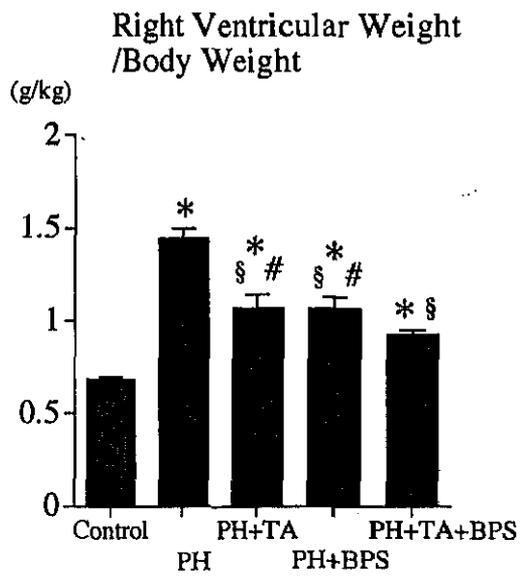
Short Diameter of Left Ventricle (b) /Long Diameter of Left Ventricle (a)

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Figure 3

Right Ventricular Systolic Pressure

(mmHg)

80 —
60 —
40 —
20 —
0 —

Control   PH+TA   PH+TA+BPS
    PH   PH+BPS

Pp/Ps (Right Ventricular Systolic Pressure /Systemic Systolic Blood Pressure)

(mmHg/mmHg)

0.8 —
0.6 —
0.4 —
0.2 —
0 —

Control   PH+TA   PH+TA+BPS
    PH   PH+BPS

Ueno et. al.

Figure 4

Right Ventricular Weight
/Body Weight

(g/kg)

Right Ventricular Weight
/Left Ventricular Weight

(g/g)

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Figure 5

Ratio of Level of Expression of
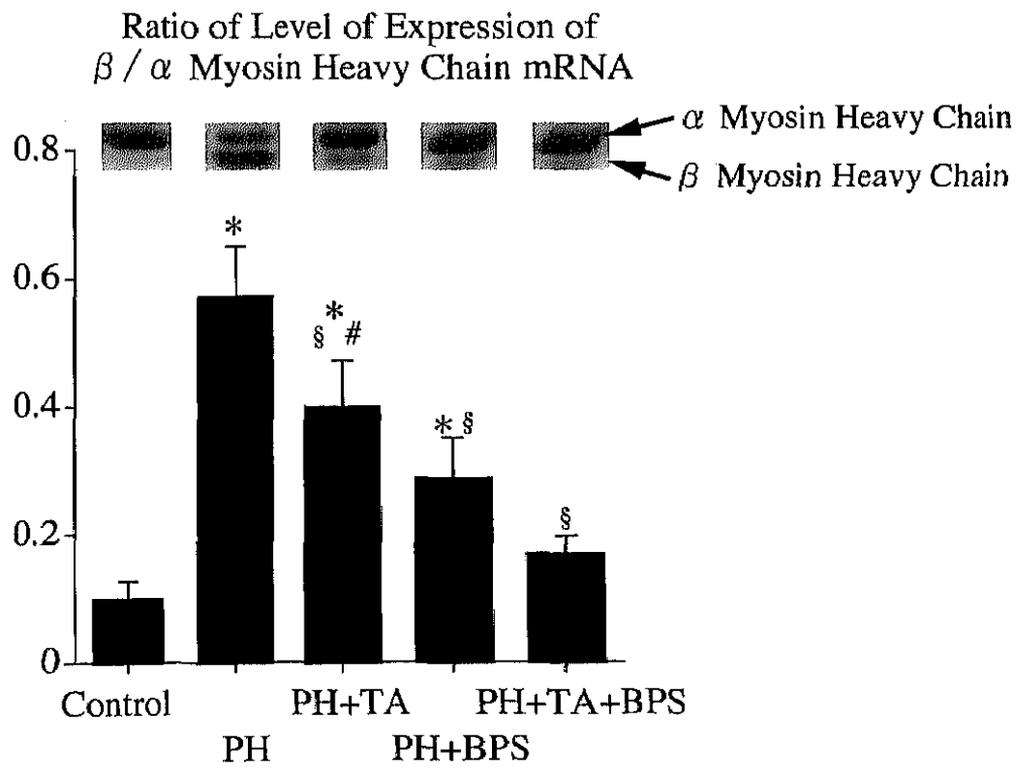β / α Myosin Heavy Chain mRNA
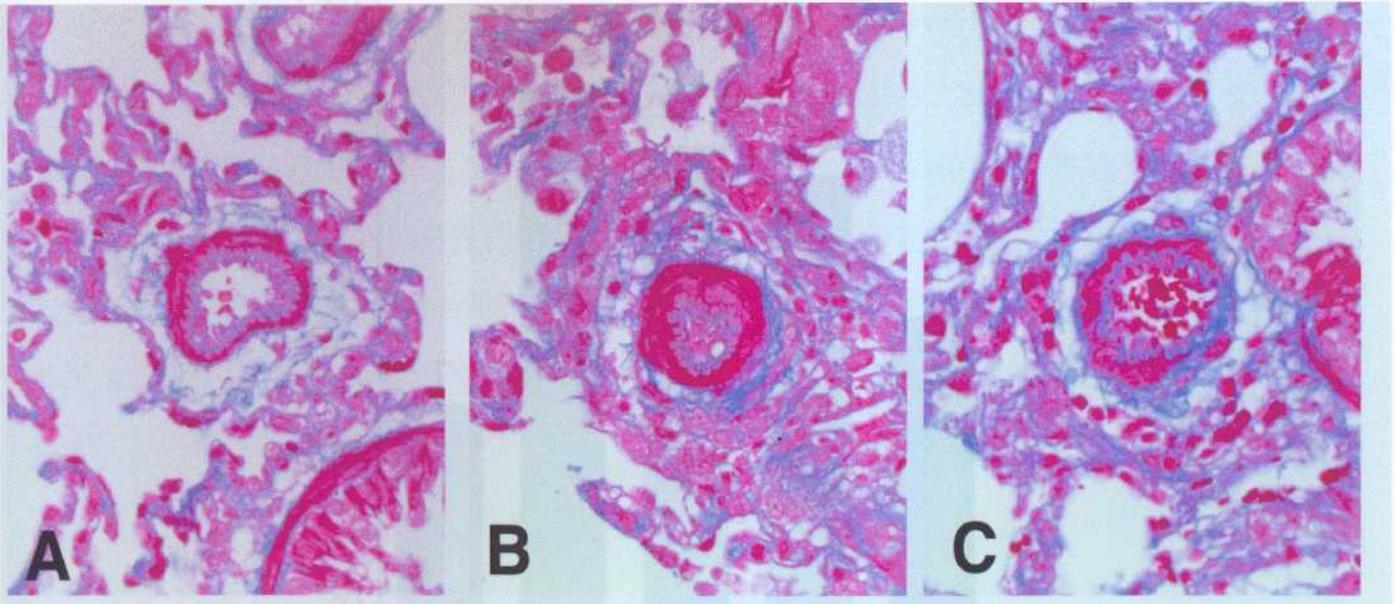
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Figure 6

AZAN x520

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Figure 7

The Ratio of Medial Wall Thickness to
External Diameter of Pulmonary Artery