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Diameter of coronary arteries in 36 species of mammalian from mouse to giraffe

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Summary

Systematic quantitative investigations were performed in the coronary arteries of 102 hearts of 36 mammal species with an overall more than tenthousandfold difference of their heart weight. After postmortem coronary angiography with a filling pressure of 100 mm Hg x-rays were taken, and the widest diameters of the coronary artery stems were determined. We found a nearly linear correlation between diameter of a standardized coronary artery and virtual diameter of heart, but the increase in diameter of coronary arteries exceeded somewhat that of the diameter of heart especially for heart weights surmounting 100 g. Perhaps relative enlargement of coronary arteries in the bigger hearts contributes to the prevention of large increase of blood flow velocity.

Key words: coronary artery diameter, heart weight, coronary blood flow

Introduction

The size of coronary arteries has been investigated systematically only in the adult human. Recently we examined a larger number of human coronary arteries ranging from infancy to old age for the evaluation of growth of coronary arteries under physiologic and pathologic conditions (Hort et al.). We found good correlation between the post-natal growth of the diameter of coronary arteries and the virtual diameter of the heart (calculated from the cubic root of heart weight) under physiologic conditions and even in pathologic heart enlargement. Coronary artery diameter tended to show a little more enlargement than heart diameter. To confirm these findings, it was thought that a larger number of mammalian species would display a wider range of heart mass than the human heart under physiologic and pathologic conditions. Such investigations have not, to our knowledge, been done before, and should provide a better explanation for the correlation of size of heart and coronary arteries. Distribution of arteries supplying the heart muscle have been described in different species (e.g., rat, guinea pig, dog, pig, horse, monkey, deer, sheep, elephant (Ahmed et al.; Bishop et al.; Gościcka et al.; Habermehl; Hadžiselimović et al.; Hoffmann; McNamara et al.; Rawlings; Sostman et al.); systematic studies on the size of arteries have mostly been performed within one species, as in the whale heart (Truex et al.).

Material

We investigated 102 hearts of mostly adult mammals of 36 domestic and exotic species. For the contribution of the hearts of animals which had died in preserves or zoos, we owe acknowledgment to

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Dr. Manz from the Veterinarian Research Institute in Frankfurt/Main. Other hearts were obtained from slaughterhouses or research institutes, where experiments on other organs had been done.

The range of fresh weight of the hearts was 0.2 g (mouse) to 3700 g (horse). Single species and numbers are shown in table 1.

Methods

Post-mortem arteriograms of coronary arteries were done a few hours to a maximum of 3 days after death of the animals. Filling pressure was 100 mm Hg. For this reason, a cannula was fixed in each coronary artery, only in very small hearts (from the mouse to the hamster) were arteriograms performed by injection directly into the aorta. Contrast dye was a 5:2 mixture of barium sulphate (Micropaque®) and 25 % gelatine at a temperature of 40 °C, injected after irrigation of coronary arteries by saline with constant pressure over 10 to 15 minutes. This mixture only enters small arteries and arterioles, but not capillaries. Afterwards, refrigeration at 4 °C jelled the contrast medium-gelatine mixture. X-ray was performed before fixation in formaline in different projections (anterior-posterior [= A-p] and lateral). In addition, an x-ray was taken of the basal slice of the heart with a thickness of about ⅛ to ⅒ of the long axis of the ventricular part of the heart. Distance from x-ray tube to film was 117 cm. Pictures were taken with 100 kV voltage.

The widest diameter of coronary artery stems was measured on the x-ray film with a 7-fold magnifying glass with indicating lines of ⅒ mm. Measurements were taken at the proximal part of the stem of the right coronary artery as well as the left descending and left surrounding artery. Distribution of coronary arteries in 4 species (mouse, hamster, muskrat and rabbit) varied from the others, as there was an additional, large septal coronary artery. The stem of the left descending artery was taken from the A-p x-ray; right artery and left surrounding artery were investigated on the separated heart basis.

In large hearts there was a magnification of arteries on the x-ray due to distance from the film. Correction of data was necessary to reduce arteries to natural size. No correction was necessary if the distance of arteries from the x-ray films was less than 1.2 cm, as in those cases magnification would have been less than 1 %. In several very small hearts, coronary artery size was controlled by direct measurements of the separated arteries. Differences between both measurements did not exceed 0.025 mm in very small arteries. In large arteries, data of x-ray measurements and measurements on the arteries themselves were identical. Reading errors are minimal (Hort et al.). The cross section area of the coronary arteries was calculated from the diameter (under the assumption that the cross-sectional area was circular).

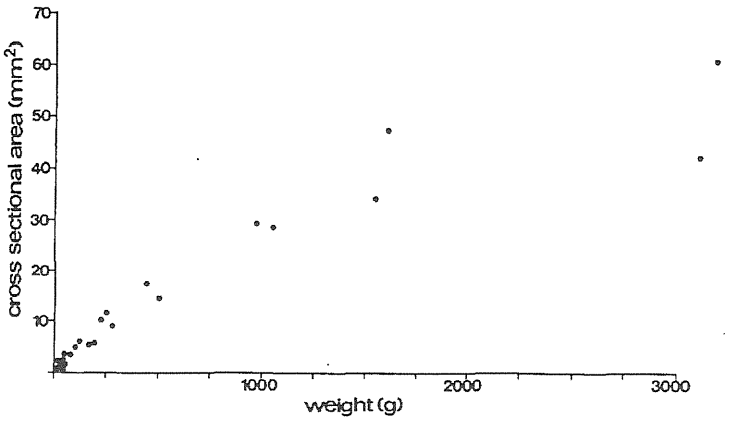

Fig. 1. Correlation between cross-sectional area of coronary arteries and weight of the ventricular part of hearts from 36 different species. In small animal species some measurements are nearly identical. Therefore the number of dots in the left part is smaller than the number of species investigated.

Table 1. Weight of ventricular part, virtual diameter of ventricular part mass, diameter of standardized coronary artery and cross-sectional area of standardized coronary artery of 36 animal species (mean values). The English, German and scientific names of the different species are given.

Species	Number	Weight of the ventricular part (wvp)	Virtual heart diameter $= (\sqrt[3]{wvp}$	Diameter of standardized coronary artery (mm)	Cross-sectional area of standardized coronary artery $\pi \cdot \left(\frac{d}{2}\right)^2$ [mm²]
mouse/Maus (Mus musculus)	2	0.15 ± 0.0	0.53 ± 0.0	0.16 ± 0.0	0.02 ± 0.0
squirrel/Eichhörnchen (Sciurus vulgaris)	3	0.80 ± 0.30	0.92 ± 0.12	0.38 ± 0.08	0.12 ± 0.05
marmosez/Weißpinsel-ohräffchen (Callithrix jacchus)	1	0.80	0.93	0.51	0.21
guinea-pig/Meerschweinchen (Cavia aperea porcellus)	10	1.04 ± 0.25	1.00 ± 0.09	0.45 ± 0.07	0.16 ± 0.05
hamster/Feldhamster (Cricetus cricetus	7	1.29 ± 0.37	1.08 ± 0.11	0.43 ± 0.07	0.15 ± 0.05
European gray rabbit/Wildkaninchen (Oryctolagus cuniculus)	2	2.05 ± 1.63	1.22 ± 0.36	0.51 ± 0.02	0.22 ± 0.02
musk-rat/Bisamratte (Ondatra zibethica)	2	1.83 ± 0.53	1.22 ± 0.12	0.51 ± 0.02	0.20 ± 0.01
prairie-dog/Präriehund (Cynomys Ludovicianus)	1	2.0	1.26	0.60	0.28
hedgehog/Igel (Erinaceus europeus)	2	2.40 ± 0.0	1.34 ± 0.0	0.59 ± 0.13	0.28 ± 0.12
aotes/Nachtaffe (Aotes trivirgatus)	1	3.80	1.56	0.73	0.42
Tragulus javanicus	1	4.70	1.68	0.92	0.67
skunk/Skunk (Mephitis mephitis)	1	5.85	1.80	1.02	0.82
mink/Nerz (Mustela lutreola)	2	6.90 ± 3.39	1.88 ± 0.32	0.73 ± 0.17	0.44 ± 0.20
rabbit/Kaninchen (Oryctolagus cuniculus domestica)	11	6.65 ± 0.81	1.88 ± 0.08	0.99 ± 0.06	0.77 ± 0.10
pine marten/Marder (Martes martes)	5	7.71 ± 2.22	1.96 ± 0.19	0.65 ± 0.12	0.34 ± 0.13
uakari/Uakari (Cacajao rubicundus)	1	15.3	2.48	1.14	1.02
chimpanzee/Schimpanse (Pan troglodytes)	1	17.8	2.61	1.17	1.08

scientific names of the different species are given.

Species	Number	Weight of the ventricular part (wvp)	Virtual heart diameter $= (\sqrt[3]{wvp}$	Diameter of standardized coronary artery (mm)	Cross-sectional area of standardized coronary artery $\pi \cdot \left(\frac{d}{2}\right)^2$ [mm²]
bush-dog/Waldhund (Speothos venaticus)	1	20.4	2.73	1.09	0.93
raccoon/Waschbär (Procyon lotor)	3	25.5 ± 5.18	2.94 ± 0.21	1.17 ± 0.09	1.08 ± 0.16
red fox/Fuchs (Vulpes vulpes)	5	37.2 ± 5.08	3.33 ± 0.15	1.48 ± 0.22	1.76 ± 0.51
badger/Dachs (Meles meles)	1	54.4	3.79	1.83	2.64
guerza/Guereza (Colobus abyssinicus)	1	80.0	4.31	2.08	3.39
fallow buck/Damwild (Dama dama)	1	123.0	4.97	2.89	6.56
wart-hog/Warzenschwein (Phacochoerus aethiopicus)	2	161.5 ± 87.0	5.35 ± 1.01	3.02 ± 0.75	7.38 ± 3.57
roe/Reh (Capreolus capreolus)	6	162.9 ± 40.3	5.42 ± 0.43	2.64 ± 0.34	5.54 ± 1.48
dog/Hund (Canis lupus familiaris)	12	193.3 ± 31.9	5.77 ± 0.31	2.79 ± 0.29	6.19 ± 1.34
pig/Schwein (Sus scrofa domestica)	5	254.7 ± 33.3	6.33 ± 0.28	3.89 ± 0.15	11.90 ± 0.93
sea-lion/Seelöwe (Zalophus californianus)	1	273.0	6.49	3.37	8.90
guanaco/Guanako (Lama guanicoë)	1	438.0	7.59	4.71	17.43
duiker/Gelbrücken-Ducker (Cephalophus sylvicultor)	1	499.0	7.93	4.29	14.43
okapi/Okapi (Okapia johnstoni)	1	982.0	9.94	6.15	29.71
polar bear/Eisbär (Ursus maritimus)	1	1060.0	10.20	6.11	29.34
kodiak bear/Kodiakbär (Ursus arctos middendorfi)	1	1570.0	11.62	6.43	32.49
cow/Rind (Bos primigenius taurus)	3	1615.0 ± 60.6	11.73 ± 0.15	7.81 ± 0.21	47.96 ± 2.60
giraffe/Giraffe (Giraffa camelopardalis)	1	3120.0	14.61	7.44	43.46
horse/Pferd (Equus przewalskii caballus)	2	3195.0 ± 148.5	14.73 ± 0.23	8.91 ± 0.11	62.33 ± 1.60

Table 2. Quotient of the standardized coronary artery diameter and virtual heart diameter by groups of different heart weights.

Weight groups	n	Mean values
1: 0– 1 g	11	0.415 ± 0.085
2: 1– 10 g	39	0.453 ± 0.081
3: 10– 100 g	15	0.437 ± 0.060
4: 100–1000 g	29	0.527 ± 0.068
5: > 1000 g	8	0.609 ± 0.058

Total heart weight was measured on fresh hearts; weight of ventricular part was determined in fixed hearts (4 % formaline for 2-3 weeks) after removal of the atrial part.

Taking variations of coronary arteries into consideration, we calculated a standard coronary artery for every species. This is the average of the 3 (or 4) measured coronary arteries. We used the arithmetic mean value, because maximum error was 2 % compared to the diameter calculated from the cross-sectional areas of the single coronary arteries.

Results

Figure 1 shows the correlation between cross-sectional area of coronary arteries and heart weight. In the group of small hearts, there is a high rise of cross-sectional area with augmentation of heart weight. In larger hearts, this increase is less. This means that the relative cross-sectional area of coronary arteries reduced with increasing growth.

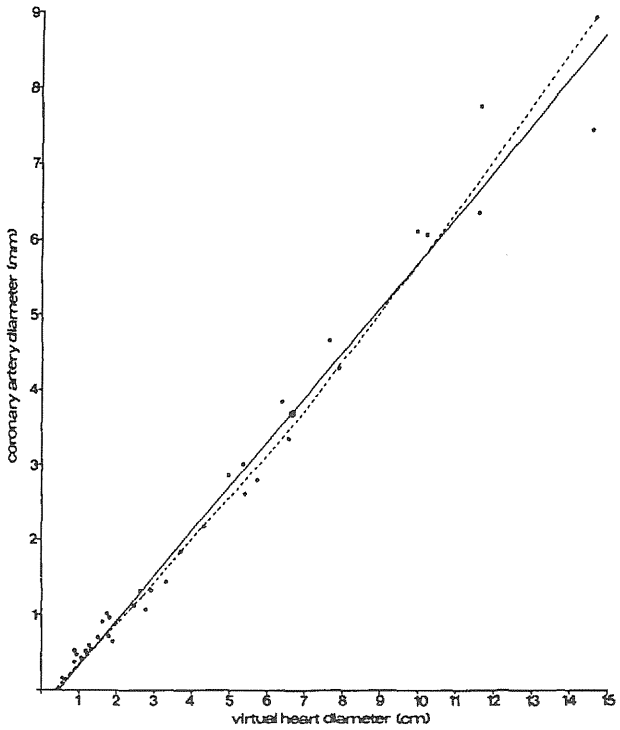

Fig. 2. Correlation between coronary artery diameter and virtual heart diameter (calculated as the cubic root of ventricular part weight) of 36 animal species and human hearts (big dot). For further explanation see text.

There is a nearly linear correlation between coronary artery diameter and virtual heart diameter, which was calculated as the cubic root of the weight of both ventricular walls. Mean values of different species are shown in table 1 and figure 2. The correlation may be approximately expressed by the function $y = -0.262 + 0.600 \times$ (see the unbroken line in fig. 2). The correlation coefficient is extremely high ($r = 0.990$). Average value of the adult

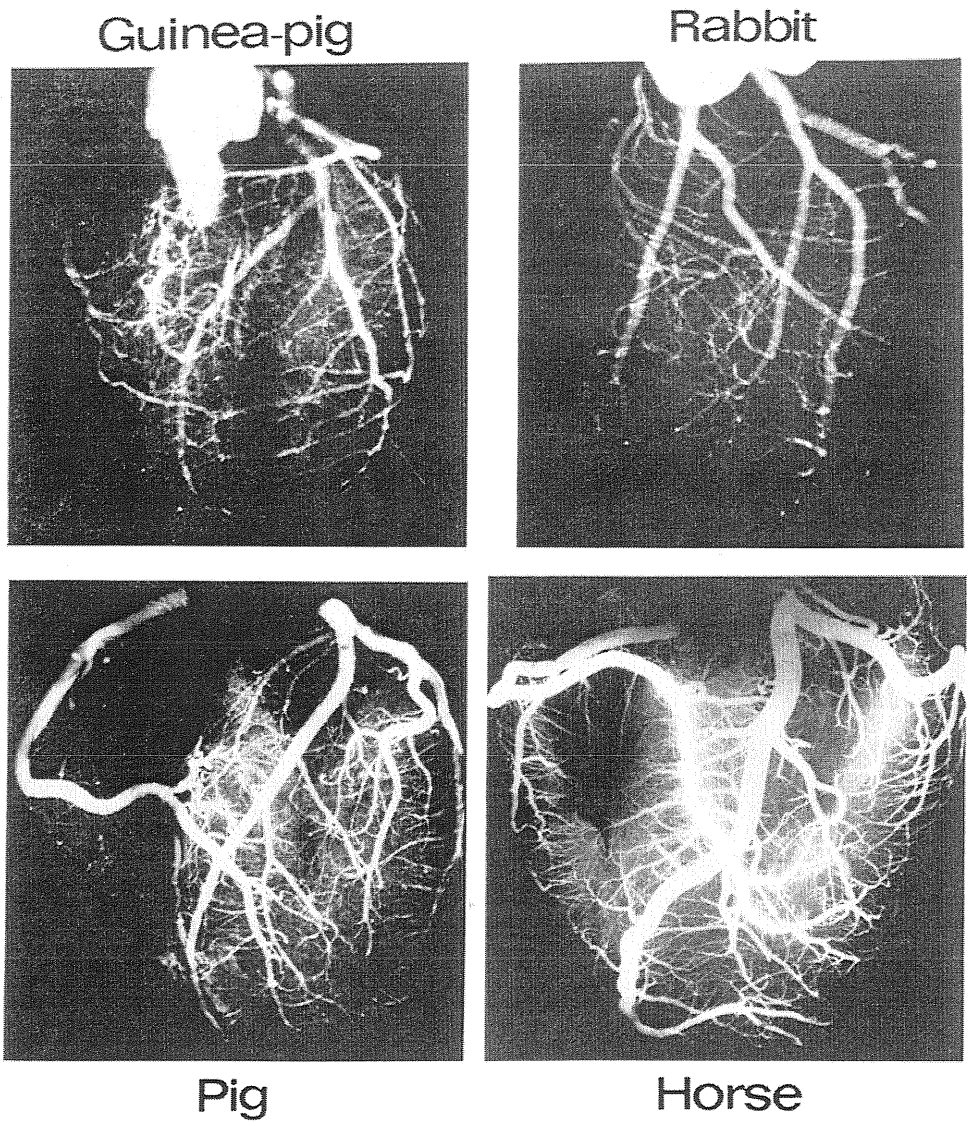

Fig. 3. Coronary angiograms of guinea-pig, rabbit, pig and horse heart equalized by magnification or reduction.

human heart is shown as a big dot in figure 2. This value was found in an earlier investigation (Hort et al.), which correlates well with our findings in different mammalian species.

On the other hand, coronary artery diameter displays a somewhat higher increase with augmentation of heart muscle mass than virtual heart diameter especially for heart weights surmounting 100 g. This means that coronary arteries demonstrate a somewhat positive allometric growth. Therefore no exact linear correlation between coronary artery diameter and virtual heart diameter exists. This correlation can be better described by the formula $y = -0.153 + 0.518x + 0.007x^2$ (see the broken line in fig. 2) than by the linear function $y = -0.262 + 0.600x$. But the differences are very small.

Table 2 shows the quotient of the standardized coronary artery diameter and virtual heart diameter by broups of several ranges of heart weight. Differences of mean values between group 5 and all other groups as well as between group 4 and all other groups are statistically significant ($p < 0.05$), but no significant differences could be found between the first three groups.

Relative increase in diameter of coronary arteries with augmentation of heart weight is shown in figure 3, too. Arteriograms of the coronary arteries of a guinea-pig, rabbit, pig and horse heart were equalized by magnification or diminution.

Discussion

We found a nearly linear correlation of coronary artery diameter and virtual heart diameter in 36 mammalian species with an overall more than tenthousandfold difference of their heart weight. This correlates with the findings obtained in human hearts from newborn to adults with and without hypertrophy (Hort et al.; Hutchins et al.), in which the closest correlation was found between coronary artery diameter and virtual heart diameter. The cross-sectional area of coronary arteries was relatively diminished with the increase of heart weight. This does not mean that coronary blood supply becomes more and more reduced in larger hearts, as a correlation of different arteries is the second exponent of length in comparison to heart weight, which is the third exponent. This is the reason why we correlated data of equal dimension, namely diameter of coronary arteries and virtual heart diameter from the cubic root of heart weight. We found a somewhat steeper increase of coronary artery diameter in comparison to virtual heart diameter. The same trend was found in the human heart (Hort et al.).

This seems surprising, as we expected the contrary. We assumed a relatively larger diameter of coronary arteries in very small hearts because of increased blood flow resistance.

Blood flow (volume/time in a vessel (i) is proportional to pressure gradient ΔP and reverse proportional to resistance (W);

$$i = \frac{\Delta P}{W}.$$

Resistance is described by the equation:

$$W = \frac{8 \cdot \eta \cdot l}{\pi \cdot r^4}.$$

From this correlation, the following can be drawn (if r is proportional to l)

$$i \sim r^3$$

If the diameter of an artery supplying an organ would increase equally with the diameter of an organ, blood volume flow per time would be proportional to organ mass in case of constant other conditions. In a very simplified example this can be illustrated by comparing a

heart of 1 g weight with a heart of 1000 g, which would need a 1000-fold blood flow (volume/time). The larger heart can be imagined as a 10-fold magnification of the smaller heart. The heart diameter would be 10 times bigger and diameter of coronary artery and length of coronary arteries the same. With constant pulse rate, and, if the big hearts were to get the same amount of blood per unit of weight and time from its coronary arteries, blood flow velocity would be 10 times faster than in the coronary arteries of the small heart. Perhaps there are 2 mechanisms to avoid such a high flow velocity: reduction of pulse rate and relative enlargement of arterial diameters. Pulse rate is diminished in mammalians with increasing body weight due to the reduced metabolic rate (e.g., the mouse has a pulse rate of about 600/min, horse and cow have a pulse rate of about 40/min). But it is difficult to evaluate the influence of pulse rate on the flow velocity because of the differences in systolic and diastolic flow in the coronary arteries. The other reason is relative enlargement of diameter of coronary arteries, which implies reduction of flow velocity. For example, with duplication of arterial diameter, flow velocity is reduced to ¼ if volume/time is constant.

We suppose that relative enlargement of coronary artery diameter with increasing heart diameter could contribute to the reduction of differences in flow velocity in small and big hearts, which should be expected in case of constant pulse rate and harmonic growth of coronary arteries.

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