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Coronary artery distribution in *Macaca fascicularis* (Cynomolgus)

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Summary

The studies were performed using stereomicroscopic dissection, and light microscopy examination on hearts of healthy and fertile non-human primates (*Macaca fascicularis*) of both sexes. The results indicate that the anatomy of the coronary arteries offers points of similarity as well as departure from humans. The blood supply to the hearts was by left (LCA) and right (RCA) coronary arteries. The LCA averaged 1.78 ± 0.29 (SD) mm (range 1.40–2.40 mm) in external diameter at its origin, and 4.34 ± 1.29 (SD) mm (range 1.8–6.5 mm) in length. It usually terminated by dividing into a left anterior descending artery (LAD) and the circumflex branch (CXA). The CXA branch coursed along the left part of the atrioventricular groove and gave off a varying number of branches to the left ventricle and atrium along its course. It averaged 1.14 ± 0.30 (SD) mm (range 0.70–1.70 mm) in external diameter at its origin. The LAD averaged 1.28 ± 0.25 (SD) mm (range 0.90 ± 1.80 mm) in external diameter at its origin. In 73% cases the LAD continued over the apex to course dorsally in the posterior interventricular groove, and gave off a varying number of diagonal and septal branches. The RCA arose from the right aortic sinus and coursed along the right part of the atrioventricular groove and averaged 0.94 ± 0.15 (SD) mm (range 0.70–1.20 mm) in external diameter at its origin. The posterior descending coronary artery (PDCA) arose from the LCA in 55% of the cases, and from the RCA in 45%. Myocardial bridges (MB) were present in 54% of the hearts and over the LCA branches exclusively. The average length of all MB was 5.68 ± 3.31(SD) mm (range 2.4–11.5 mm). The coronary arteries of *Macaca fascicularis* are medium sized muscular arteries with well developed tunics intima, media and adventitia, and so resemble human arteries more closely than the dog. Therefore, we suggest this primate species might be a useful model for physiological studies on the coronary circulation.

Keywords Coronary arteries; *Macaca fascicularis*; myocardial bridges; heart coronary circulation; sinuatrial node artery; anatomy

The use of non-human primates as experimental models for coronary vascular disease in humans has been hampered, besides other factors, by the limited availability of any detailed anatomy of the vessels (Buss *et al.* 1982, Teofilovski-Parapid *et al.* 1988, Van Nie & Vincent 1989). The extrapolation of data on experimental coronary vascular physiology obtained from dogs to humans is inappropriate because of the species differences in aspects such as coronary artery anatomy and heart size in relation to body weight (Bruyneel & Opie 1972). Furthermore, there are physiological studies which emphasize the value of non-human primates as a model for coronary research (Vatner *et al.* 1971, Weisse *et al.* 1976, Crozatier *et al.* 1978, Bellinger *et al.* 1988). The aim of this study was to describe the coronary artery distribution in *Macaca fascicularis* which is

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an experimental primate of suitable size, modest needs and available. Our data will be compared with similar investigations on human coronary arteries (Banchi 1904, Mouchet 1933, Schlesinger 1938, James 1961, Polaček 1961, Mc Alpin 1975, Soto *et al.* 1976, Ochsner & Mills 1978, Lambić 1980, Hadziselimović 1981, DiDio & Rodrigues 1983, Ishii *et al.* 1986, Bezerra *et al.* 1987, Baptista *et al.* 1989).

Materials and methods

Animals

The investigations were carried on 11 *Macaca fascicularis* non-human primates (six females and five males) all wild imported in 1988. The country of origin of the population was Indonesia but the precise location was unknown. Animals spent at least 6 weeks in captivity before euthanasia (all non-human primates upon arrival at our laboratory are placed in quarantine for 6 weeks). They were all healthy and with body weights between 2000 and 3800 g, and their mean age, based on dentition, was 4–5 years.

Husbandry and feeding

The animal room was maintained at 25 ± 2°C with 60 ± 10% relative humidity with a fresh air supply. There was no artificial lighting, and the daylight was 14 h (from 05:00 h to 19:00 h at the time of the experiment). All animals were adults and kept in groups of two in cages 1.00 m wide, 1.00 m deep and 1.00 m high. They were fed once a day with a special commercial diet (SDS—Essex, UK) supplemented with fresh bananas and apples. Automatic watering was available.

Methods

Animals were anaesthetized with ketamine (RALATEK—Hemofarm, YU) in a dose of 15 mg/kg and exsanguinated. Their hearts were immediately perfused *in situ* at 18 kPa pressure with 10% formalin; the inferior vena cava was incised for run off. When the outflow appeared to be free of blood the inferior vena cava was clamped to reduce flow, and coloured latex or a warmed ink-gelatine mixture was injected. The latter was prepared by diluting 10 g of gelatin powder in 50 ml of boiling water, and a few drops of black ink are added. The hearts were then removed and immersion fixed for a week in 10% formalin before being dissected using a stereomicroscope (9 latex-injected specimens) or processed for light microscopy (2 ink-gelatine injected specimens).

Epicardiotomy was performed using a stereomicroscope, followed by removal of the periadventitial adipose tissue to expose the external surface of the myocardium and the arteries and their branches. The vessels were traced, identified, measured, drawn and photographed. The stereomicroscopic examination included measuring the external diameter at the beginning of the left and right coronary arteries, the circumflex branch of the left coronary artery and the anterior descending coronary artery, as well as the length of the left coronary artery. The results are presented in Tables 1 and 2.

For the microscopic examination two hearts with coronary arteries injected by ink-gelatine mixture were cut transversely in 5 mm wide blocks. The blocks underwent routine processing for light microscopy and were stained with hematoxylin and eosin and van Gieson.

Results

In all cases the blood supply to the *Macaca fascicularis* hearts was provided by two coronary arteries, left and right. The LCA arose from the left aortic sinus at about the level of the valve cusp, and averaged 1.78 mm in external diameter at its origin, and averaged 4.34 mm in length. In 9 out of 11 hearts (82%), the LCA bifurcated into the LAD artery and the CXA. In 2 out of 11 hearts (18%), the LCA formed a trifurcation and the middle branch was the left marginal (Fig 1).

The CXA branch coursed along the atrioventricular groove under the left atrial appendage and gave off a varying number of branches to the left ventricle and atrium along its course. Usually, the CXA continued as a final branch to descend between the ventricles as the dominant left posterior descending coronary artery of a dominant left arterial system. In two hearts it did not reach the crux, and in one heart it terminated beyond

Table 1 Morphometric data on *Macaca fascicularis* left coronary artery

	LCA			CXA					LAD			DA			OBTUS	
Case No.	Length[1] (mm)	Diameter[2] (mm)	Termination	Diameter[3] (mm)	Termination	Ramus margin	MB	MB: length (mm)	Diameter[4] (mm)	MB	MB: length (mm)	No.	MB	MB: length (mm)	Present	MB
13	5.10	2.40	B	1.70	PDCA	4	-	-	1.70	-	-	2	-	-	-	-
14	4.30	2.00	B	1.30	PDCA	4	-	-	1.40	1	2.40	2	-	-	-	-
15	5.20	1.90	B	1.50	PDCA	5	1	2.80	1.80	-	-	1	-	-	-	-
16	4.80	2.10	B	1.40	PDCA	6	1	2.70	1.30	1	3.10	2	1	11.5	Y	-
17	2.80	1.70	T	1.10	PDCA	3	-	-	1.20	1	0.90	2	-	-	Y	-
18	5.40	1.80	B	1.70	LPVA	5	-	-	1.20	-	-	5	-	-	-	-
19	6.50	1.70	B	1.30	PDCA	7	-	-	1.20	-	-	5	1	9.80	-	-
20	1.80	1.40	B	0.80	RPVA	6	-	-	1.20	1	5.90	5	-	-	-	-
21	2.90	1.70	B	1.00	LPVA	6	-	-	1.10	-	-	3	-	-	-	-
22	4.30	1.40	B	0.80	PDCA	8	-	-	1.10	-	-	1	-	-	-	-
23	4.60	1.50	T	0.70	LPVA	4	-	-	0.90	-	-	1	-	-	Y	-

[1]$\bar{x} = 4.34$; SD = 1.29; [2]$\bar{x} = 1.78$; SD = 0.29; [3]$\bar{x} = 1.14$; SD = 0.30; [4]$\bar{x} = 1.28$; SD = 0.25. LCA, L = left coronary artery; B = bifurcation; T = trifurcation; CXA = circumflex branch of LCA; PDCA = posterior descending coronary artery; LPVA = left posterior ventricular artery; RPVA = right posterior ventricular artery; i.m. = intramural; LAD = left anterior descending artery; DA = diagonal artery; OBTUS = left marginal artery; RCA, R = right coronary artery; MB = myocardial bridge; Y = yes

Table 2 Morphometric data on *Macaca fascicularis* right coronary artery

	RCA			PDCA		
Case No.	Diameter[1] (mm)	MB	MB: length (mm)	From	MB	MB: length (mm)
13	1.20	-	-	L	-	-
14	1.00	-	-	L	-	-
15	0.90	-	-	L	i.m.	-
16	1.10	-	-	L	-	-
17	1.00	-	-	L	-	-
18	1.10	-	-	R	i.m.	-
19	0.80	-	-	L+R	-	-
20	0.70	-	-	L	i.m.	-
21	0.80	-	-	R	-	-
22	0.80	-	-	L+R	-	-
23	0.90	-	-	R	-	-

[1] $\bar{x} = 0.94$; SD = 0.15. See Table 1 for other abbreviations

the crux as one of the posterior branches of the right ventricle. The CXA averaged 1.14 mm in external diameter at its origin.

The LAD averaged 1.28 mm in external diameter at its origin and coursed downward in the anterior interventricular groove, usually embedded in fat and, in four hearts, in muscle too. The LAD generally (73%) continued over the apex to course dorsally in the posterior interventricular groove, and in 3 hearts (27%) it terminated in the anterior interventricular groove near the apex. As it coursed toward the apex it gave off a varying number of diagonal branches that supplied the left ventricle, and septal branches which pierced directly into the ventricular septum.

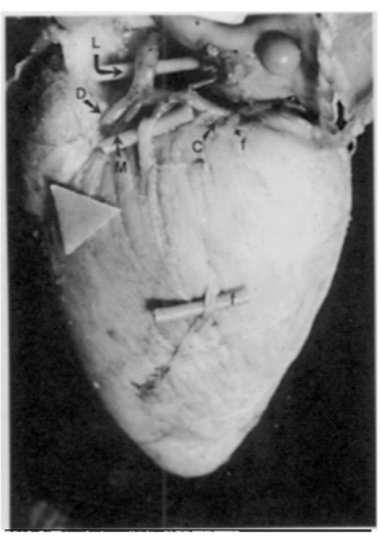

Fig 1 The left coronary artery (L) of *Macaca fascicularis* heart terminates by trifurcation into the left anterior descending artery (D), the left marginal artery (M), and the circumflex branch (C). Myocardial bridges over left anterior descending artery (arrow head) and fourth marginal branch (f-f)

Variable degrees of muscular overbridging, i.e. overlying bands of myocardium, of the LAD were observed in 4 out of 11 animals (see Fig 1). Muscular bridges (MB) were also observed over the diagonal arteries (2 MB) and over the marginal branch (1 MB) (Table 1) and were always single. The incidence of myocardial bridges in our series of *Macaca fascicularis* hearts was 54%. The average length of all myocardial bridges was 5.68 ± 3.31 (SD) mm (range 2.4–11.5 mm).

The RCA arose from the right aortic sinus. It coursed along the right part of the atrioventricular groove in a bed of epicardial fat. The RCA averaged 0.94 mm in external diameter at its origin. In the majority of the cases (6 out of 11, i.e. 55%), the RCA terminated before the crux cordis as one of the right posterior ventricular branches, while in the remaining five hearts (45%), it terminated as the right posterior descending artery (PDCA). The sinuatrial node and conus arteries often arose within the first few millimeters of the RCA. The RCA gave off numerous branches to the right atrium and right ventricle.

In our series, no myocardial bridges were present either over the RCA or over its branches. However, in 3 out of 11 hearts (27%), the PDCA (as a terminal branch of the RCA) was completely intramural.

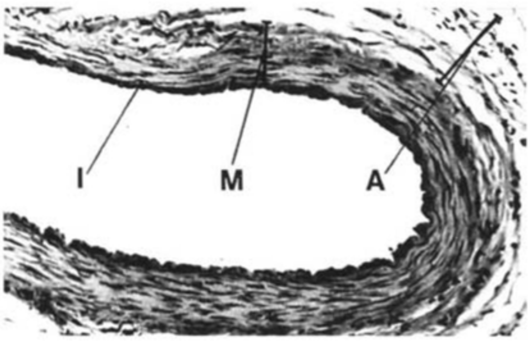

Fig 2 Cross section of the epicardial segment of *Macaca fascicularis* left coronary artery. The wall structure of the vessel has the normal morphology: tunica intima (I), tunica media (M) and tunica adventitia (A). HE × 160

The source of arterial supply to the sinuatrial node was specifically noted. In 5 out of 11 hearts (46%), the sinuatrial node was supplied by the left and right sinuatrial arteries. In four hearts (36%) we could trace only the left sinuatrial artery arising from the circumflex branch of the LCA and in two hearts (18%) the right one exclusively.

The coronary arteries of *Macaca fascicularis* are medium sized muscular arteries with well developed tunicae intima, media and adventitia (Fig 2). The intima is characterized by an endothelial cell lining and a thin subendothelial layer. It is separated from the tunica media by a dense internal elastic lamina. The tunica media is composed of a few concentric layers of smooth muscle cells with interposed elastic fibres. Nearby, in the adventitia, the elastic fibres are localized mainly in thin external elastic lamina. Finally, the most superficial layer of the coronary artery wall—the tunica adventitia, consists of a thin layer of connective tissue containing elastic and nerve fibres.

Discussion

These results indicate that the anatomy of *Macaca fascicularis* coronary arteries offers points of similarity as well as departure from that in humans. In all cases the blood supply of *Macaca fascicularis* heart was provided only by two coronary arteries. The human heart is also most frequently supplied exclusively by the left and right coronary arteries (Banchi 1904, Ochsner & Mills 1978). It is similar to the heart of *Macaca radiata* (Buss *et al.* 1982) and the baboon (*Papio cynocephalus*) (Vatner *et al.* 1974, Weise *et al.* 1976, Crozatier *et al.* 1978).

In our series, the left coronary artery more frequently terminated in a bifurcation rather than a trifurcation (18%), similar to humans (James 1961), and in less than 1 per 2000 coronary cineangiograms, the left coronary artery forms a quadrifurcation (Ochsner & Mills 1978). Bonnet monkeys (*Macaca radiata*) in the study of Buss *et al.* were generally found to have two major branches, the LAD and CXA with a third large arterial branch arising from the root of one of those primary branches. The same has been reported in African green monkey (*Cercopithecus aethiops*) hearts (Teofilovski-Parapid *et al.* 1988).

In 45% of our series, the RCA was the origin of the PDCA, and in the remaining 55% of hearts, the origin of the PDCA was from the LCA. The RCA in humans serves as the origin for the PDCA in 50% to 84% of cases (Mouchet 1933, Schlesinger 1938, Lambić 1980, DiDio & Rodrigues 1983, Baptista *et al.* 1989). In any event, the origin of PDCA in *Macaca fascicularis* resembles the human more closely than the dog in which the PDCA almost invariably arises from the LCA (James 1961).

The blood supply to the sinuatrial node in *Macaca fascicularis* was more consistent than in humans. The right sinuatrial node artery was present in 36% of the cases whereas, according to James (1961) and Soto *et al.* (1976), the SA nodal artery in human hearts originates from the proximal RCA in 48% to 60% of the cases. Also, in human hearts (James 1961, Mc Alpin 1975) the sinuatrial node artery arose from the LCA in 46% and 52% of the cases, respectively.

The reported incidence (54%) of myocardial bridging phenomenon in *Macaca fascicularis* hearts is important for comparative anatomy studies as well as for physiological studies. It can be compared with the incidence of myocardial bridges reported in human hearts which ranged from 36% up to 85.7% (Polaček 1961, Hadziselimović 1981, Ishii *et al.* 1986, Bezerra *et al.* 1987).

Myocardial bridging phenomenon has also been reported in *Cercopithecus aethiops* (Teofilovski-Parapid *et al.* 1988) and *Macaca radiata* (Van Nie & Vincent 1989). On the other hand, the frequent presence of myocardial bridges, specially over the LAD, must be functional in angiographic and physiological studies. Thus, in cases with MB, if the radiograph is taken during ventricular systole, the contraction of MB may give the appearance of severe vascular narrowing or total occlusion. Additionally, implantation of flow transducers on the LAD would be more difficult.

Although our results indicate that the anatomy of *Macaca fascicularis* coronary arteries offers points of similarity as well as departure in humans, it resembles that of humans more closely than the dog. Therefore, we suggest that further studies be made on its haemodynamics to determine whether this is a suitable model for the study of coronary artery physiology.

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