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DISTRIBUTION OF LEFT CORONARY ARTERY BRANCHES IN THE AFRICAN GREEN MONKEY

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This study of distribution of the left coronary artery (LCA) in the African green monkey (Cercopithecus aethiops sabeus) was undertaken in order to determine the coronary artery epicardial network of this terrestrial primate. Insufficient data about these characteristics of LCA is a serious obstacle for widespread use of this species for experimental purposes. A total of 55 hearts from adult monkeys of both sexes (35 females and 25 males) was examined. These hearts were divided into two groups: group A- corrosive heart specimens and group B- specimens prepared for micro dissection The blood supply of the Cercopithecus heart is obtaine through two arteries (98%), the left and right coronary artery which originated from corresponding aortic sinuses at the angles characteristic for human coronary arteries. The left coronary artery of Cercopithecus terminated by bifurcation into the ramus interventricularis arterior (RIA) and circumflex artery (RCx). It was possible, as in the human heart, to detect the short (58%) and long (42%) type of circumflex branch. In 24% of cases LCA terminated by trifurcation giving RIA, RCx and RMS (ramus marginalis sinister). RIA had greater caliber than RCx in 58% of cases, whereas both arteries were of equal caliber in 16% and RCx was larger than RIA in 25% of cases. The branch for the sinuatrial node arose from LCA in 14.5% of cases, and from RCx in 63.3%. RCx most frequently terminated (56.3%) as a posterior left ventricular branch, less frequently (38.3%) as a posterior interventricular branch, rarely (3.6%) as a posterior right ventricular branch and exceptionally (1.8%) as a left marginal branch. The results of our research clearly suggest great resemblance of the morphology of the left coronary artery distribution in humans and Cercopithecus. Therefore this terrestrial primate can be used as an adequate experimental model for functional studies of the cardiovascular system.

Key words: left coronary artery, branches, Cercopithecus aethiops sabeus

INTRODUCTION

Fundamental investigations in human and veterinary medicine are most often conducted on carefully selected experimental animals. The choice of appropriate experimental animal as the model for observation of physiological or pathophysiological mechanisms is of the greatest significance (Di Dio, 1994). The use of experimental animals in studies of coronary vascular disease is complicated for several reasons, including the limitations in morphological similarity of the vascular pattern of the model and man (Buss *et al*, 1982). Polaček and Zechmeister (1968) tried to contribute to the selection of an ideal experimental model by giving a classification of the coronary vascular pattern in different species. They classified the intramural type of vascular network in rodents as type I; type II is present in hearts with predominant epicardial distribution of the vascular network, which these authors described in small ruminants. Therefore, rats which are often used as experimental animals in studies of many functional systems, have very limited significance in studies of the cardiovascular system (Mizukami, 1994). Anatomical studies of the coronary vascular network of the rabbit, as a potentially cheap experimental animal, led to the conclusion that, in spite of some similarities, differences in the type of dominance and in irrigation zones of branches of coronary arteries, may lead to inappropriate use of the rabbit as an experimental model (Podeser *et al*, 1997). The distribution of coronary arteries in human - like primates is atypical (Chase and de Garis, 1939) and, together with their size and nutritional demands, makes these animals inappropriate as an ideal experimental model. Domestic animals (mammals) have coronary arterys morphology similar to humans, considering their position, branching and physiological role (Blagojević, 1989), but great differences can be observed in the type of dominance of coronary arteries (Sebate *et al*, 1994) as well as in the distribution of other branches of the aortic arch (Blagojević, 1989; Baptista *et al*, 1989). The majority of studies of the distribution of coronary arteries in non-human primates, have been conducted on Macaca monkeys (*Macaca fascicularis, Macaca radiata*). They indicated that these animals could be the best model for investigations of the cardiovascular system (Buss *et al*, 1982; Teofilovski *et al*, 1993; Teofilovski and Kreclović, 1998; Shimada *et al,* 1994).

Literature related to the epicardial coronary arterial pattern of *Cercopithecus aethiops* sabeus is rare, and without numerical data. Our preliminary investigations (Teofilovski *et al*, 1993 ; Nikolić *et al*, 2000) suggested a predominantly subepicardial course of the coronary arterys network, with distribution of the blood supply to particular areas of the heart being very similar to that in the human. Knowledge of the anatomy and distribution of coronary arteries in *Cercopithecus aethiops* is significant from the point of view of both comparative anatomy and experimental medicine, because it could help in the creation of an excellent experimental model.

The aim of our study was to obtain data about the vascular pattern of the left coronary artery and its branches in *Cercopithecus aethiops sabeus*, its anatomy and distribution, and to compare its characteristics with those of other (potentially

experimental) animals and of man as well. It was of interest to establish adequate base line information for using this monkey in cardiovascular research.

MATERIALS AND METHODS

Investigations of the morphology of LCA, and its branching pattern were made on 55 hearts of the Green African monkey (*Cercopithecus aethiops*). The animals used in our study originated from East Africa (Kenya, Uganda, Tanzania). Hearts were from fertile and healthy animals of both sexes (35 females and 20 males), with body weight between 2000- 2900 g.

The investigated animals were divided into 2 groups (A and B). In both groups injection of coronary arteries was performed in situ, through the aortic arch, immediately after sacrifice using Kethonal (Galenika, Beograd) overdose. Under a constant pressure of 140 mmHg the following substances were injected: Simgal (methyl metacrylate) (Galenika, Beograd) for obtaining corrosion casts (group A) and colored Latex for better visualization of blood vessels during the micro dissection (group B). After the procedures were finished, hearts were removed from the thorax and immersed in 10% formalin solution (group B), or in NaOH solution (group A).

Corrosion casts (group A) of hearts injected with Simgal were obtained after three days of liquefaction in NaOH solution. Thereafter the hearts were washed in warm water in order to remove co-liquated material and to obtain ideal plastic (acrylate) casts of the coronary arterial network. These samples were used for exact identification of coronary arteries (CA) and of their branches.

After two weeks of fixation samples from group B were micro dissected under the stereomicroscope. This way the pattern of coronary arterial network (CAM) obtained for each heart was drawn, and the corresponding morphometric data were entered into tables.

For statistical analysis we used the standard methods of descriptive statistics, measures of central tendencies and variability measures.

The terminology from human anatomy (Terminologia Anatomica) was employed, with some explanations related to the differences in Nomina Anatomica Veterinaria.

RESULTS

The hearts of Cercopithecus aethiops were most often (98,2%) vascularized by two coronary arteries – the left (LCA) and the right (RCA) (Fig 1). In one case (1.8%) we observed the origin of 3 coronary arteries from the aortic bulbus.

The left coronary artery in all cases originated from the aortic bulbus at the level of the left *sinus aortae* (Valsalve). Immediately after its origin LCA passed behind the pulmonary trunk, then between that and the left auricle. Its proximal segment in the frontal plane had a horizontal or slightly upwards direction. In the horizontal plane this segment showed variations in the posterior direction of about 10'' and in the anterior direction of about 20''. The trunk of LCA was directed anteriorly

and to the left, descending toward the left half of *sulcus coronarius*. In all observed cases LCA had a greater caliber than RCA. The average external diameter of LCA at its origin at the left *aortic sinus* was 1.65 +/- 0.39 (SD) mm, and varied between 0.6 and 2.7 mm. The trunk of LCA had an average length of 6.2 +/- 2.25 (SD) mm, with variations from 1.2 mm to 16 mm. In 41 out of 55 hearts (74.5%) LCA ended by bifurcation into two terminal branches: *ramus interventricularis anterior* (RIA) and *ramus circumflexus* (RCx). In 13 out of 55 hearts (23.6%) the trunk of LCA terminated by trifurcation giving RIA, RCx, and RMS (*ramus marginalis* sinister), which descended by the left margin of the heart (Fig 2). In 1 out of 55 hearts (1.8%) the trunk of LCA terminated by division into 4 branches.

Figure 1. Cortossion cast – left coronary artery (A), right coronary artery (B), *ramus interventricularis anterior* (C), *ramus circumflexus* (D) and *ramus coni arteriosi* (E)

Only in 8 out of the 55 investigated hearts of *Cercopithecus* (14.5%) did LCA give off a branch for vascularisation of the sinuatrial node (*ramus nodi sinuatrialis*).

Figure 2. Trifurcation of the left coronary artery – *ramus anterventricularis anterior* (A), *ramus marginalis sinister* (B), and *ramus circumflexus* (C)

Ramus interventricularis anterior (RIA) most frequently (58.1%) was the larger terminal branch of LCA, (in 32 out of 55 hearts). In 9 out 55 hearts (16.4%) both of its terminal branches were of the same caliber, and in 14 out of 55 (25%) RIA was of smaller caliber than RCx. The average value of the diameter of RIA at its origin was 1.31 +/- 0.32 (SD) mm, ranging between 0.5 mm and 2.1 mm. Descending through the anterior *interventricular sulcus* towards the heart apex, it impressed a fissure on the right heart margin and passed on to the diaphragmatic surface of the heart, where, in 18.7% of cases, it was possible to follow its epicardial path. From the epicardial segment of RIA arose the anterior left ventricular branches, anterior right ventricular branches, with often prominent vessels directed to the arterial conus, as well as numerous branches which entered the anterior part of the septum. Occasionally it was possible to follow its epicardial path only in the upper half on the sternocostal surface of the heart, where it entered the myocardium.

The circumflex artery (RCx) was present along the left half of the sulcus coronarius, and in most cases traversed the left margin of the heart (*margo obtusus*) to its diaphragmatic surface. The average external diameter of the other terminal branch of LCA i.e. RCx at its origin was 1.13 +/- 0.31 (SD) mm, and varied between 0.5 mm and 1.8 mm. In one case RCx was not a branch of LCA but RIA (Fig

3). Passing along the *sulcus coronarius* from RCx successively arose atrial (ascending) and ventricular (descending) branches. Those descending branches were named marginal branches (rami marginales), because of evident similarity in origin and distribution to human arteries. The number of marginal branches varied between 1 and 7 (average 3), supplying the myocardium on the sternocostal (anterior branches) and diaphragmatic surface (posterior ones). The marginal branch descending along the left margin of the heart was marked as ramus marginalis sinister (*ramus obtusus*). It was present in 21 out of 55 hearts (38%), but in 1 case (1.8%) it was one of the terminal branches of LCA. In 35 of 55 hearts (63.3%) we found the left nodal branch (*ramus nodi sinuatrialis*) in the first few millimeters of RCx. RCx was the single source of *ramus nodi atrioventricularis* (Fig 3) in 12 out of 55 hearts (21.6%).

RCx of the left coronary artery terminated as a posterior left ventricular branch (*ramus posterior ventriculi sinistri*) in 31 out of 55 cases (56%), as a posterior interventricular branch (*ramus interventricularis posterior*) in 21 out of 55 hearts (38%), as a right posterior ventricular artery (*ramus posterior venriculi dextri*) in 2 out of 55 (3.6%), and only exceptionally (1.8%) as a left marginal branch (*ramus obtusus s. ramus marginalis sinister*) (Fig 3).

Statistical analysis of the obtained results revealed that the observed differences between the diameters of LCA and their branches in males and females were not statistically significant.

Figure 3. Bifurcation of the left coronary artery – *ramus interventricularis anterior* (A), *ramus marginalis sinister* (B), and a branch (C) of RIA which, due to its direction, resembles *ramus circumflexus* (short type)

Figure 4. Diaphragmatic surface of the *Cercopithecus aethiops* heart – *ramus circumflexus* (A) gives off *ramus nodi atrioventricularis* (B), terminates as *ramus posterior ventriculi sinistri* (C), which is a short type of RCx

DISCUSSION

Two coronary arteries (left and right) supplied the myocardium of *Cercopithecus aethiops* in 98.2% of cases. This is similar to the findings for non-human primates such as: *Macaca radiata* (Buss *et al*, 1982), *Macaca fascicularis* (Teofilovski *et al*, 1993; Teofilovski and Krecloviċ, 1998), *Papio erxleben* (Buss *et al*, 1982; Weisse *et al*, 1976; Mandarim de Lacerda and Hureau 1986) and *Macaca fuscata* (Shimada *et al,* 1994). Two coronary arteries are most frequently found in mammaliar domestic animals (Blagojević, 1989; Weaver *et al,* 1986) and in the human heart (Hadžiselimović, 1981; James, 1961; Nikolić, 1993). Regarding variability in number of coronary arteries, we did not find data in the literature about the presence of three coronary arteries in nonhuman primates (Shimada *et al*,1994), or in dogs (Ovčina, 2002), or pigs (Weaver *et al*, 1986), or goats (Yang *et al,* 1989). We found this as an exception (in 1 out of 55), which agrees with results for the human heart, where a supernumerary third coronary artery is also a very rare finding (Mc Alpin, 1975). A third coronary artery is present with high frequency (45%) in the heart of the rat (Aikawa and Kawano, 1985).

Considering the diametar of the initial segment of the left coronary artery and of its terminal branches, no other data related to non-human primates were available, which suggests that morphometric investigations in this area are extremely rare. However, we observed certain concordance with available results for *Macaca fascicularis* (Teofilovski *et al*, 1993; Teofilovski and Krecloviċ, 1998). This

may result from the similar structure and body weight of these moneys that live under uniform conditions (for experimental animals). Morphometric data for coronary arteries in swine and goats (Weaver *et al,* 1996; Yang *et al, 1989;* Crick *et al*, 1998) are similar in that the LCA diameter was always larger than the RCA diameter, and LCA was always longer than RCA in both species.

Morphometric data in the human population are more variable (Ochsner and Mills, 1978; Nikolic, 1993), and depend on the osteomuscular structure (heart ratio), and, according to one author (Hadžiselimovic, 1981), on the type of arterial vascularisation dominance. Our findings (Nikolić, 1993) in the human population also indicate this, as the external diameter of LCA at its origin was larger than the diameter of RCA in 61.1% of cases, the same in 8.9% and smaller in 30.5%.

According to Nomina Anatomica Veterinaria the terminal branches of LCA are: *r. interventricularis paraconalis* (located in sulcus paraconalis) and *r. circumflexus* (lying along sulcus coronarius). *R. interventricularis paraconalis* is directed toward the apex cordis, crosses the right margin, passes into its posterior surface, where it is within the *sulcus subsinuosus* anastomozing with the *r. subsinuosus*, branch of RCA. The direction, branching pattern and irrigation zone of *R. interventricularis paraconalis* is remarkably similar to RIA in the human and its branches were named according to the region they irrigated. The second terminal branch of LCA is also called RCx in Nomina Veterinaria, and, according to its position and vascular area, its branch *r. collateralis proximalis* corresponded to the human *r. marginalis sinister* as we named it in this paper.

The left coronary artery most frequently terminated by bifurcation (75%), which was also noted in other non-human primates such as: *Macaca fascicularis* (Teofilovski *et al*, 1993; Teofilovski and Kreclović, 1998), Bonnet monkeys (Buss *et al*, 1982), baboon (Mandarim *et al*, 1986), Japanese monkeys (Shimada *et al*, 1994), as well as in dogs (Blagojević, 1989), swine (Weaver *et al,* 1986; Crick *et al*, 1998), goats (Yang *et al*, 1989) and the North American beaver, *Castor canadensis* (Bisaillon, 1981). There is no particular need to emphasize that bifurcation is a common type of LCA termination in the human heart (Nikolić, 1993). Comparing the RIA distribution pattern to that in the human, we observed remarkable concordance in irrigation zones. Thus, in both cases branches arose to supply blood to the anterior wall of the left ventricle, anterior wall of the right ventricle and anterior segment of the septum (Nikolić, 1993; Nikolić *et al*, 2000). RCx vascularised the anterior wall of the left ventricle, anterior wall of the left atrium, and in a high percentage, the posterior wall of the left ventricle and atrium (58%). In the remainder (42%) RCx went over the crux cordis and vascularised the posterior wall of the right atrium and ventricle. These findings were also usually observed in the human heart (Mc Alpin, 1975; Ochsner and Mills, 1978; Nikolić, 1993).

Comparative anatomical studies of left coronary artery distribution in other animals that were considered to be useful experimental models in cardiovascular research did not show the necessary similarity with human hearts. Namely, studies of the rabbit left coronary artery (carried out on 30 animals) showed the following differences: LCA was always the dominant coronary vessel; with equal frequency it terminated by bifurcation or by trifurcation; in cases when it terminated by bifurcation, it was very rarely possible to identify the blood vessel which corre-

sponded to the morphofunctional characteristics of RIA (Podeser *et al,* 1997). These findings led to the conclusion that the rabbit heart might be usefull in very limited conditions such as studies of regional ischemia. Anatomical investigations of coronary pattern of the rat showed that the rat heart, beside the left and right coronary artery (intracordem arteries), is vascularizied by other vessels (extracordem arteries), most often from the internal thoracic artery (Mizukami *et al,* 1994). This could be explained as implying a sort of "atavistic" phenomenon of the caudal coronary arteries as observed in lower vertebrates. In addition, branches of the coronary arteries of the rat usually form an intramural coronary network that is opposite to the human coronary pattern. The Syrian hamster (*Mesocricetus auratus*), which is often used as an experimental animal in research on congenital anomalies of the coronary arteries cannot be used in functional studies owing to great anatomical differences compared to the human circulation (Sans Coma *et al*, 1993) as follows: LCA most often terminates by trifurcation into RCx, RMS and RIP; RIA is not observed in a high percentage, and, even if it is present, it rarely extends to apex cordis; the course of the coronary arteries is intramyocardial.

We can conclude that the heart of the African green monkey is supplied by a left and right coronary artery in 98% of cases. They arise from corresponding aortic sinuses, at the angles characteristic for human coronary arteries. The left coronary artery more often terminated by bifurcation (75%) into anterior interventricular and circumflex branches, than by trifurcation, which is the same as in the human heart. From these major branches arose branches that formed the subepicardial vascular network, as seen in the human. The epicardial path of RIA could be traced along the diaphragmatic surface of the heart (18.7%). This artery was the source of left anterior ventricular branches, anterior septal branches and right anterior ventricular branches. RCx of this monkey had the same position and irrigation zone as RCx of the human heart. RMS was observed in a similar frequency as in the human. Termination of the LCA circumflex branch that determined the dominance of this coronary blood vessel, suggests the rare dominance of LCA, which is in accordance with results for human hearts. The left SA nodal branch arose from RCx in a high percentage (63.6%) of cases as in human heart.

Considering the complete data given above, we concluded that *Cercopithecusaethiops* might be a very useful animal model for functional studies of the cardiovascular system.

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PROUČAVANJE DISTRIBUCIJE LEVE KORONARNE ARTERIJE I NJENIH GRANA U ZELENOG AFRIČKOG MAJMUNA

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S A D R Ž A J

Proučavanja distribucije koronarnih arterija zelenog afričkog majmuna *(Cercopithecus aethiops sabeus)* sproveli smo sa ciljem da upoznamo šemu koronarne cirkulacije ovog terestrijalnog primata, obzirom da je nedovoljno poznavanje koronarne anatomije ozbiljna prepreka za njihovu veću upotrebu u eksperimentalne svrhe. Istraživanje smo izvršili na 55 srca odraslih majmuna oba pola (35 ženki i 20 mužjaka). Proučavana srca su podeljena u 2 grupe: grupa A – korozivni preparati i grupa B – preparati pripremljeni za mikrodisekciju. Koronarne arterije *Cercopithecus*-a i njihove veće grane formiraju vaskularnu mrežu na površini srca (subepikardno), odakle polazi veliki broj grana koje prodiru u miokard formirajući subendokardnu mrežu, što predstavlja distribuciju gotovo identičnu humanoj. Srce *Cercopithecus*-a najčešće vaskularizuju (98%) leva i desna koronarna arterija koje nastaju iz odgovarajućih aortnih sinusa, pod uglovima karakterističnim za humane koronarne arterije. LKA je u svim slučajevima bila većeg spoljašnjeg dijametra i završavala se najčešće bifurkacijom (75%) u prednju međukomornu granu i polukružnu granu, a ređe trifurkacijom dajući tako i levu marginalnu granu. Prednja medukomorna grana je najčešće većeg spoljašnjeg dijametra (58%),

ređe manjeg (25%), a najređe su obe grane imale identičan promer (16%). Grane za sinuatrijalni čvor poticale su iz LKA u 14,5 % slučajeva, a iz polukružne grane u 63,3% slučajeva. Polukružna grana se najčešće završavala kao zadnja leva komorna grana (56,3%), ređe kao zadnja međukomorna grana (38,3%), vrlo retko (3.6%) kao zadnja desna komorna grana, a izuzetno (1.8%) kao leva ivična arterija. Rezultati naših istraživanja nedvosmisleno govore u prilog sličnosti koronarnih šema čoveka i *Cercopithecus*-a, što čini da ovaj terestrijalni primat predstavlja zahvalan eksperimentalni model za funkcionalna istraživanja kardiovaskularnog sistema.