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Calibres of Aorta and Pulmonary Artery in Hypoplastic Left and Right Heart Syndromes: Effects of Abnormal Bloodflow?

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Summary. Internal diameters of the cardiac orifices and of the great vessels were determined in 9 hearts with an atresia of the left atrio-ventricular orifice and/or the aortic ostium and in 7 hearts with an atresia of the right atrio-ventricular orifice and/or pulmonary ostium. Hearts which showed a ventricular septal defect in combination with a patent aortic ostium and left hypoplasia or a pulmonary ostium and right hypoplasia were not included in the material. Twenty-four normal hearts served as a control group. The aorta was measured at 6 sites; the pulmonary trunk, the two pulmonary arteries and the ductus arteriosus were all measured at one site. The age range of the material was from birth to 16 months after birth.

Since cross-sectional areas of vessels appear more directly related to bloodflow than diameters and since absolute values of vessel calibres vary markedly with age squared values of internal diameters were expressed in normals as percentage of the sum total of the squared diameters of the pulmonary and the aortic ostium; in the hypoplasia material squared values of internal diameters were expressed as percentage of the squared value of the sole functioning ostium whether aortic or pulmonary. The aortic and pulmonary ostium showed cross-sectional areas of 222% resp. 188% of the normal value, when they functioned as sole outflow orifice. The pulmonary arteries did not evidence any deviation from the normal values neither in left, nor in right hypoplasia. The ductus arteriosus showed a supranormal value in left hypoplasia, but a normal value in right hypoplasia. Subnormal values were obtained for the pulmonary trunk in right hypoplasia, although the reduction in calibre was much more pronounced in the case of the comparable non-functioning first part of the aorta in left hypoplasia. In the latter condition the calibres of the aorta showed a grandual reduction from the descending aorta towards the ascending aorta which coincided with the direction of bloodflow in this cardiac malformation.

These findings demonstrate appropriate functional adaptations of the calibres of the great vessels to conditions of altered bloodflow. The findings also indicate that a time factor should be taken into account in further analysis of such changes in vessel calibre.

Introduction

In the syndromes of hypoplasia of the left or right heart one ventricle has little or no circulatory function and therefore the corresponding vessel whether aorta or pulmonary trunk receives blood mainly or exclusively through the ductus arteriosus. This abnormal circulatory pattern raises the question as to which

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adaptations occur in this type of cardiac malformation. It appears likely that vascular diameters and the corresponding cross-sectional areas would be of crucial interest. Nevertheless a review of the literature revealed mainly general statements and only few quantitative data on vascular calibres in these syndromes (Horley, 1955; Gittenberger-de Groot, 1972; Rudolph *et al.*, 1972). Accordingly, internal diameters of the cardiac orifices, of the ascending aorta, the aortic arch and the descending aorta, of the pulmonary trunk and its branches and of the ductus arteriosus have been measured in hearts with atresia of one atrio-ventricular orifice and/or of the aortic respectively pulmonary ostium. It was decided to focus the study on extreme cases of right or left hypoplasia and leave out cases of valvular stenosis.

It was thought that data on vascular calibres might be of value not only from a fundamental point of view, but also from a practical viewpoint in diagnostic problems in congenital cardiac malformations.

Materials and Methods

The control material consisted of 24 normal hearts from patients who died in the perinatal period or up to 16 months after birth. Hearts were considered normal on the basis of absence of cardio-vascular abnormalities during clinical examination or at autopsy. Twenty hearts from children dying within two weeks after birth formed the majority of this material. The abnormal material consisted in part of 9 hearts with an atresia of the left-ventricular orifice and/or the aortic ostium. Age range was 3 days to $6^1/_2$ weeks. The remainder of the non-normal material comprised 7 hearts with an atresia of the right atrio-ventricular orifice and/or pulmonary ostium. Age range was from 1 day to 16 months after birth. Hearts showing mitral atresia in combination with a ventricular septal defect and a patent aortic ostium were not included in the material. Hearts which showed the comparable abnormal condition on the right side were also excluded. Such hearts and those with malformations of types other than those mentioned above were occasionally used as reference material.

The measurements described below were carried out after fixation in a 4% formaldehyde solution over 24 hrs or longer and storage of varying duration in a mixture of 80% ethanol and glycerol (2:1). Seven normal hearts were measured both unfixed and after fixation and storage over at least 5 months. No trend towards recognizable increase or decrease of the measured values could be noticed.

Measurements were carried out as follows. The hearts were opened as shown in Fig. 1. In exceptional cases it was necessary to open also one or both great vessels. Probes differing 1 mm in diameter were introduced in the direction of bloodflow into the atrio-ventricular orifices, the pulmonary and aortic ostium, the aorta, the pulmonary trunk, the pulmonary arteries at their site of branching off and finally the ductus arteriosus. The measurements of the aorta were carried out at various sites. Fig. 2 shows the sites of these measurements. In the case of the ductus arteriosus it was tried to establish as accurately as possible the diameter present at death and to avoid to stretch the vessel. Even so, the measured diameters of the ductus arteriosus are probably less reliable as parameters of the *in vivo* condition than the other measurements. The error of the measurements was ascertained by repeating the measurements in 4 hearts. The standard deviations based on series of 4 measurements for each individual heart and its great vessels ranged from 20% for a diameter of 2 mm to 5% for a diameter of 15 mm.

In order to use the diameters as indicators of bloodflow the squared values of the diameters were used to compare the measurements. These squared values were expressed as a percentage of the sum total of the squared values of the diameters of the aortic and pulmonary ostia in the normal material and as percentage of the squared value of the diameter of the one functioning great vessel in the hypoplastic material. These relative surface areas were represented graphically as shown in Figs. 3 and 4. In the graphic representation of the values for the

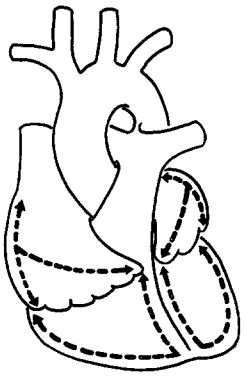

Fig. 1. Routine incisions allowing measurements of cardiac orifices and internal diameters of great vessels including their branches

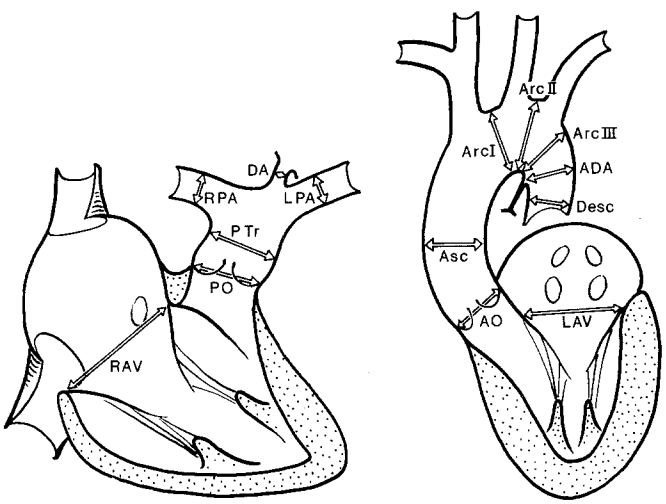

Fig. 2a and b. Sites of measurements. Abbreviations for Fig. 2a: *RAV* right atrio-ventricular ostium; *PO* pulmonary ostium; *PTr* pulmonary trunk; *LPA* left pulmonary artery; *RPA* right pulmonary artery; *DA* ductus arteriosus. Abbreviations for Fig. 2b: *LAV* left atrio-ventricular ostium; *AO* aortic ostium; *Asc* aorta ascendens; *Arc I* aortic arch between brachio-cephalic and left carotid artery; *Arc II* aortic arch between left carotid and left subclavian; *Arc III* aortic arch between left subclavian and ductus arteriosus; *ADA* aortic arch at connection with ductus arteriosus; *Desc* descending aorta at indicated site

right side of the heart and its corresponding vasculature the pulmonary trunk was included twice. This made the graph more easily comparable with that for the left side of the heart and its corresponding vessels. These graphic representations of the measurements are referred to as aorta curve and pulmonary curve.

In order to determine the effect of hypoplasia on the diameter of the sole functioning outflow vessel, aorta or pulmonary trunk, the cross-sectional areas of the aortic and pulmonary ostia, expressed per 100 cm body length were calculated in the normal and abnormal material. The absolute values showed so much age dependent variation that they were of little value in comparing the normal and hypoplastic hearts.

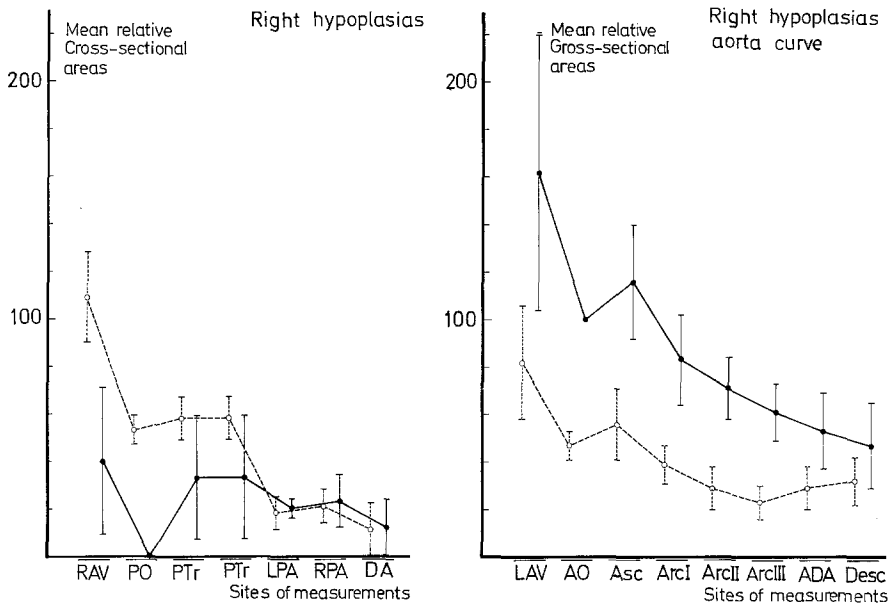

Fig. 3. Relative cross-sectional areas (mean $\pm$ standard deviation) of cardiac orifices and great vessels (see text) of 7 cases of right hypoplasia (uninterrupted line). The normal reference material of 24 normal hearts is included (interrupted line). Abbreviations see Fig. 2

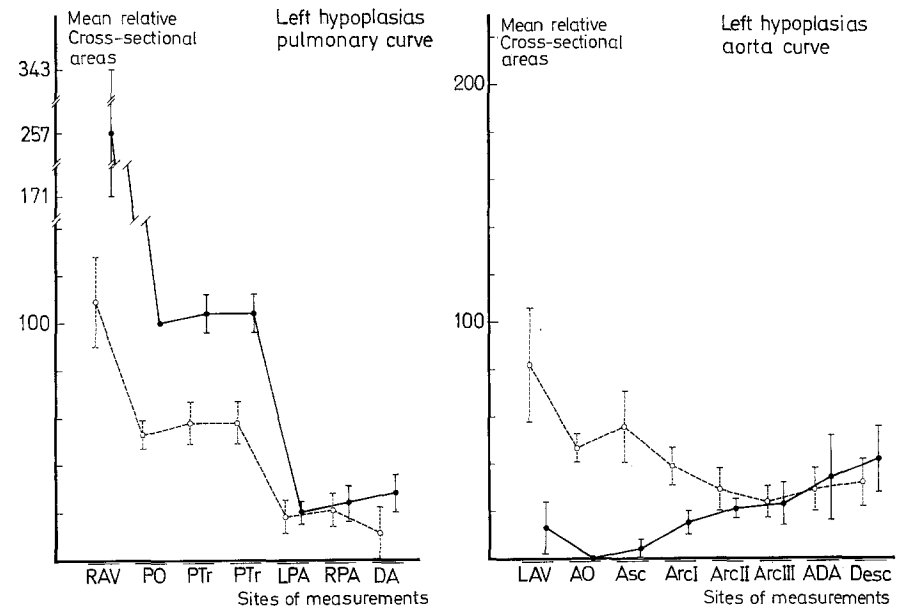

Fig. 4. Relative cross-sectional areas (mean $\pm$ standard deviation) of cardiac orifices and great vessels (see text) of 9 cases of left hypoplasia (uninterrupted line). The normal reference material of 24 normal hearts is included (interrupted line). Abbreviations see Fig. 2

Observations

Normal Hearts. Figs. 3 and 4 include the data from 24 normal hearts. Characteristic features are largely in accordance with the literature (De la Cruz *et al.*, 1960). The atrio-ventricular orifices are much larger than the pulmonary, respectively aortic ostia. Also the right atrio-ventricular orifice tends to be larger than the left one. The combined relative surface areas of the right pulmonary artery, left pulmonary artery and ductus arteriosus closely approach that of the pulmonary trunk. The aorta curve shows the well-known isthmus as a dip at Arc III, i.e. between the left subclavian artery and the connection of the ductus arteriosus with the aorta.

Hypoplastic Right Heart. Fig. 3 depicts graphically the data from 7 hearts. On the pulmonary side the most striking feature is that the functioning vessels, the pulmonary arteries and ductus arteriosus, do not show any deviation from the normal condition in their relative calibres. In the case of the pulmonary trunk a distinct but not very striking trend towards reduction of relative calibre is present. The aorta curve has a pattern which is close to normal, although of course the high values of the various points of the curve reflect the function of the aorta as the sole functioning outflow vessel. The mean cross-sectional area ($\pm$ standard deviation) of the aortic ostium was 143.4 ± 48.8 mm^2/100 cm body length, more than twice the value of 64.5 ± 29.6 mm^2 found in the normal material.

In contrast to the aorta curve of the normal material the aorta curve for the hypoplastic right heart does not show the dip at the site Arc III. This probably reflects prenatal bloodflow via the ductus arteriosus towards the pulmonary arterial system.

Hypoplastic Left Heart. The summarized data on the 9 hearts in this group are shown in Fig. 4. The pulmonary curve reflects in its left-side part the increased flow through the right ventricle and pulmonary trunk. The cross-sectional area of the pulmonary ostium was 153.6 ± 32.5 mm^2 per 100 cm body length versus a value of 81.5 ± 32.5 mm^2 in the control material. Interestingly the relative surface areas of the pulmonary arteries did not show any trend towards abnormal values. In contrast a trend towards a supranormal diameter of the ductus arteriosus was present. In this respect left hypoplasia differs from right hypoplasia. Increased diameter of the ductus arteriosus in this group may reflect that the ductus arteriosus supplies all of the greater circulation in left heart hypoplasia. The aorta curve is clearly abnormal. It shows a slope opposite to that for the normal heart.

Discussion

The condition of left or right sided cardiac hypoplasia causes changes in haemodynamic loads of the great vessels and of specific parts of these vessels. The data presented allow the general conclusion that these changes in functional load are accompanied by appropriate changes in the calibres of the vessels. The most striking example forms the aorta in left hypoplasia. This vessel demonstrates a pattern of cross-sectional areas completely different from the normal condition although it corresponds to the bloodflow which enters the aorta only at the connection with the ductus arteriosus. The calibre of the aorta in right

hypoplasia also supports the conclusion of appropriate functional changes in vessel calibres. Although the various cross-sectional areas are all well above normal the vessel shows the gradual decrease in calibre that is found also under normal conditions. The similarity of this pattern in right hypoplasia to that in the normal condition is most likely due to the unchanged direction of bloodflow in the aorta in this type of hypoplasia. On the other hand, the measurements of the aorta at the entrance of the ductus arteriosus and of the descending aorta seem to contradict the general conclusion reached above. It should be realized however that in the controls from an age group of normals as used here, the values for this section of the aorta will still reflect the prenatal pulmonary-aortic flow in the ductus arteriosus. On the other hand in right hypoplasia the opposite direction of flow is present, both pre- and postnatally.

The size of the pulmonary trunk in right sided hypoplasia does not fit the general picture of cross-sectional areas of the great vessels which corresponds to an abnormal functional load. In contrast to the first part of the aorta in left hypoplasia it shows no clear decrease in calibre which would correspond to the absence of bloodflow. This may be related to a difference in the haemodynamic conditions such as the fact that in left hypoplasia the ascending aorta remains a functioning vessel which carries blood to the coronary arteries. In contrast, the pulmonary trunk contains only stagnant blood. The well-known difference in structure of the wall of the aorta and pulmonary trunk may also play a role.

The relative calibres of the pulmonary arteries show in both groups no abnormality. On one hand this favours the supposition that lung function is maintained at a level approaching the normal one, on the other hand it is remarkable that these calibres are normal particularly since in left hypoplasia the pulmonary arteries may be subjected to an abnormal level of blood pressure. The mechanism responsible for the internal diameter of the pulmonary arteries may well be of an exceptional nature since the entire pulmonary vasculature develops with little functional load (i.e. bloodflow) since lung function is absent prenatally (Dawes *et al.*, 1953; Wagenvoort *et al.*, 1961 c).

The pathological cases discussed here have all maintained life postnatally via the shunt provided by the ductus arteriosus. One would expect therefore supranormal calibres of the ductus arteriosus. Surprisingly this seemed to be the case only in left hypoplasia. The antenatal condition may provide an explanation. Since before birth the resistance of the pulmonary arterial tree is high (Dawes *et al.*, 1953; Wagenvoort *et al.*, 1961c) there is little bloodflow through the ductus in right sided hypoplasia which may explain a relatively small calibre. A similarly reduced calibre or even lack of the ductus arteriosus is seen in tetralogy of Fallot with marked pulmonary stenosis as well as in other developmental malformations causing prenatally a diminished bloodflow through the pulmonary trunk (Powell and Hiller, 1957; Molz, 1968; Rao *et al.*, 1971). In contrast, in left hypoplasia nearly all of the bloodflow is by way of the ductus, which supplies indirectly the general circulation. This may be the cause of the relatively large ductus in the left hypoplasia material. As is rather obvious the postnatal condition appears to be the consequence of the antenatal one. Also the size of the aortic isthmus as found in early postnatal life is generally explained along the same line.

Both the fact that the aortic isthmus is still present for some time postnatally, and the difference in calibre of the ductus arteriosus in left vs. right hypoplasia, point to a time factor in the adaptation of calibres of these vessels. Studies on development of collateral circulation and data on the after-effects of cardiac surgery show this time factor (May, 1968; Bonchek *et al.*, 1973; Sunderland *et al.*, 1973).

On the other hand, the data presented allow only a limited appraisal of the degree of "plasticity" of vascular diameters. For one thing: it is unknown exactly when left and right hypoplasia develop during antenatal growth. However, the interventricular septum was usually closed in these cases of atresia of the atrio-ventricular and/or ventricular orifices (similar findings were reported by Bryan and Oppenheimer, 1969; Gittenberger-de Groot, 1972). Further, the aorta and pulmonary trunk showed three-cuspid valves (see Gittenberger-de Groot, 1972). Both findings provide an indication of the stage of development at which right or left hypoplasia may have originated. Experimental production of these syndromes reported by Harh *et al.*, 1973, may eventually allow a more accurate approach here.

A question that remains to be answered is whether alterations in vessel calibre, such as those reported here, are accompanied by histological changes in the vascular wall. In cases with grossly abnormal circulatory conditions like pulmonary hypertension such changes have been observed in the pulmonary vascular tree (Wagenvoort *et al.*, 1969a and b). Abnormalities of the coronary system also occur frequently in conditions similar to those studied by us (Bryan and Oppenheimer, 1969).

In closing, although the clinical value of the data reported here may presently be limited, comparisons of data as presented here and angiographic or echocardiographic measurements of the anatomical conditions in vivo may help in arriving at a correct diagnosis and in the assessment of the chance for surgical correction in individual patients.

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