Significance of Lung Biopsy in Determining Surgical Indication in Cases of Congenital Cardiac Anomalies with Pulmonary Hypertension

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YAMAKI, S. Significance of Lung Biopsy in Determining Surgical Indication in Cases of Congenital Cardiac Anomalies with Pulmonary Hypertension. Tohoku J. exp. Med., 1982, 137 (1), 33-39 —— Correlation between the grade of pulmonary arterial change and pulmonary arterial pressure was studied in 60 patients with congenital cardiac anomalies associated with pulmonary hypertension. Of the 60, 45 specimens of pulmonary arteries were obtained by autopsy and 15 by biopsy. Pulmonary arterial pressure was correlated with the products of the medial thickness and intimal lesions of small pulmonary arteries both in the autopsy and in the biopsy specimens. Also, medial thickness and intimal lesions were independently correlated to the pulmonary arterial pressure. However, the regression equation was not identical among the kinds of diseases, although significant correlation was found between the degree of intimal lesions and pulmonary arterial pressure. Medial hypertrophy was reversible after corrective surgery, but intimal lesions were irreversible except for cellular proliferation. Therefore, to determine the indication for corrective surgery, it should be emphasized that intimal change of the small pulmonary arteries should be carefully evaluated. Since the degree of intimal lesions is not accurately diagnosed from hemodynamic parameters alone, diagnosis of intimal lesions by lung biopsy is indispensable to determine the possibility of corrective surgery in the congenital heart disease with severe pulmonary hypertension. —— —— lung biopsy; pulmonary hypertension; pulmonary arterial change; index of pulmonary vascular disease

Lung biopsy to examine the severity of pulmonary vascular disease seems to be useful for the determination of indication for total correction in cases of congenital heart disease in which severe pulmonary hypertension is revealed by the hemodynamic study. The opinion has often been expressed, however, that the histopathological findings on pulmonary arteries are not necessarily in agreement with the hemodynamic findings. Indeed, there are some cases of ventricular septal defect (VSD) in which pulmonary arterial pressure is extremely high, but the intimal alteration of small pulmonary arteries is only slight, and also some cases of complete transposition of the great arteries (TGA) in which progressing occlusive alterations of pulmonary blood vessels are apparent by lung biopsy, although pulmonary arterial pressure is not elevated markedly.

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In order to clarify the reason for the lack of agreement between histopathological and hemodynamic findings, I have attempted to investigate comparatively the degree of pulmonary arterial changes and the pulmonary arterial pressure in autopsy and biopsy cases. This paper reports the results of investigation and discusses the significance of lung biopsy in determining the indication for corrective surgery.

**Materials and Methods**

Materials for the histopathological study included biopsy lung tissue from 15 cases and autopsy lung tissue from 45 cases of congenital heart disease or primary pulmonary hypertension (PPH) in which pulmonary arterial pressure had been measured; ages ranged from 6 months to 52 years. The cases of heart disease consisted of 24 cases of simple cardiac anomalies (SCA) such as VSD and patent ductus arteriosus, 23 cases of TGA and 13 cases of PPH. In each autopsy case, about 30 samples of lung were randomly excised from formalin-fixed specimens of both lungs. The biopsy samples were step-sectioned at intervals of 50 µm, producing 10 to 100 slices per case. Elastica-Masson staining was used.

The degree of medial hypertrophy of small pulmonary arteries was determined using Suwa's method (Suwa and Takahashi 1971; Yamaki and Tezuka 1976; Yamaki and Horiuchi 1979) and expressed as the thickness of the media, 100 µm in radius of small pulmonary arteries (DR=100µm). The severity of intimal alteration of pulmonary arteries was determined according to the index of pulmonary vascular disease (IPVD) reported previously (Yamaki and Tezuka 1976, 1979; Yamaki et al. 1980; Yamaki and Wagenvoort 1981).

**Results and Discussion**

*Correlation between the pulmonary arterial change and pulmonary arterial pressure*

Since the pulmonary arterial change consisted of medial hypertrophy and intimal lesions, the thickness of the media (DR=100µm) and the severity of intimal alteration (IPVD) were determined in all autopsy cases. Multiplying DR=100µm by IPVD, a score for the total pulmonary vascular alteration was obtained in each case, and the correlation of the score with pulmonary arterial pressure, an indicator of the pulmonary hypertension, was examined. A strictly linear correlation between the two parameters was found on a semilogarithmic coordinate system (r=0.89, p<0.001) (Fig. 1). The regression equation was unchanged regardless of the kind of heart diseases, such as SCA, TGA and PPH. This fact indicates that the pulmonary arterial pressure can be estimated from the sum total of the two histopathological parameters, DR=100µm and IPVD, regardless of the nature of the heart disease.

Comparison of the value DR=100µm × IPVD to the pulmonary arterial pressure in the biopsy cases again showed a significant correlation with a linear regression identical to that in the autopsy cases (p<0.001) (Fig. 2). This indicates that the distinction between biopsy and autopsy cases is not necessary to the study on the correlation of histopathological changes of pulmonary arteries to pulmonary arterial pressure.

Next, the two histopathological factors, DR=100µm and IPVD, were studied separately in relation to the pulmonary arterial pressure. DR=100µm was correlated
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Positively with pulmonary arterial pressure (SCA $r=0.90$, $p<0.001$; TGA $r=0.92$, $p<0.001$; PPH $r=0.78$, $p<0.001$), and two regression lines were obtained depending upon the type of heart diseases (Fig. 3); one for the cases of SCA (VSD type) and the other for the cases of TGA and PPH (TGA type). As illustrated in Fig. 3, they were parallel to each other, but the former was situated significantly

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**Fig. 1.** Correlation between the pulmonary arterial peak pressure and the product of medial thickness ($D_{R-100\mu m}$) and intimal lesions (IPVD) in the small pulmonary arteries of simple cardiac anomalies (SCA), complete transposition of the great arteries (TGA) and primary pulmonary hypertension (PPH).

**Fig. 2.** Correlation between the pulmonary arterial peak pressure and the product of medial thickness ($D_{R-100\mu m}$) and intimal lesions (IPVD) in the small pulmonary arteries of biopsy and autopsy cases.
upper than the latter \( (p<0.001) \). IPVD also correlated positively with pulmonary arterial pressure \( (\text{SCA} \ r=0.64, \ p<0.01; \ \text{TGA} \ r=0.72, \ p<0.01; \ \text{PPH} \ r=0.71, \ p<0.05) \) and again two significantly different, parallel regression lines \( (p<0.001) \) were obtained; i.e. TGA type and VSD type (Fig. 4). The result indicates that, under the same pulmonary arterial pressure, the intimal alteration of small pulmonary arteries is milder in VSD type diseases than in TGA type diseases.

**Significance of lung biopsy in determining the indication for corrective surgery**

As stated above, the pulmonary arterial pressure measured by cardiac catheterization correlated well with the total histopathological alteration of pulmonary arteries expressed as the product of \( D_{R=100\text{m}} \) and IPVD. Each of the
two histopathological parameters was also correlated independently with the level of pulmonary arterial pressure.

It has previously been reported that the thickness of the media of the intrarenal arteries increases in response to high intra-arterial blood pressure (Suwa and Takahashi 1971). Therefore, it is considered that the thickness of the media of small pulmonary arteries in patients with pulmonary hypertension decreases after pulmonary arterial pressure has been lowered by surgical treatment. Fig. 5 shows the histological findings of pulmonary arteries obtained by lung biopsy 10 years after total correction of VSD. The patient had severe pulmonary hypertension (pulmonary arterial pressure 106/60 (89) mmHg, and the pulmonary-systemic

![Figure 5](image-url)

**Fig. 5.** Transverse sections of small pulmonary arteries obtained by lung biopsy 10 years after total correction of ventricular septal defect with pulmonary hypertension. a: Small pulmonary artery showing marked hypertrophy of the media and complete occlusion of the lumen due to fibroelastic proliferation of the intima. b: Small pulmonary artery without medial hypertrophy.
resistance ratio 0.92) and was operated on at the age of 6. Fig. 5a shows a small pulmonary artery with marked hypertrophy of the media. This hypertrophy was thought to have developed in the preoperative period, because the lumen of this vessel was completely occluded by intimal fibrous proliferation. In this case, however, the great majority of small pulmonary arteries had a nearly normal media, as shown in Fig. 5b. This finding suggests that the medial hypertrophy disappeared after the pulmonary arterial pressure had been lowered by the total correction of VSD. Thus, the medial hypertrophy seems to be reversible. In contrast, as previously reported (Wagenvoort and Wagenvoort 1977), intimal lesions except for cellular proliferation are probably irreversible, no postoperative improvement being brought about.

Consequently, for determining the indication for total correction by means of lung biopsy, the primary consideration should be the degree of intimal lesions. In the cases of congenital heart disease with marked medial hypertrophy, but slight intimal lesions, the hypertrophy of the media will gradually disappear after the corrective surgery. Prognosis of such a case is good. However, in cases of progressed, irreversible changes of the intima, the pulmonary arterial pressure may not decrease over a long period postoperatively, but may even increase (Rosengart et al. 1975; Yamaki and Horiuchi 1979). Consequently, total correction is not recommended in such a case.

We have previously reported the histological findings of lung tissue from survivors and autopsy cases following surgery for TGA (Yamaki et al. 1980). It was then found that when an IVPD of less than 2.2 was obtained total correction was indicated.

It is apparent that the degree of intimal lesions, an important factor for the determination of the indication for total correction, cannot be accurately estimated from hemodynamic parameters. Lung biopsy is, therefore, indispensable for exploring the possibility of corrective surgery in the cases of congenital heart disease with severe pulmonary hypertension.

Nonetheless, the total correction is generally thought to be indicated in cases of VSD type, such as SCA, in which a low regression line of IPVD (as in Fig. 3) is obtained, and even pulmonary hypertension is revealed. We would stress that the total correction is not indicated in cases of TGA type with a high regression line of IPVD, even if the pulmonary hypertension is relatively mild.

References

