ALTERATION OF PULMONARY BLOOD FLOW IN TETRALOGY OF FALLOT: PRE- AND POSTOPERATIVE STUDY WITH MACROAGGREGATES OF $^{99m}$Tc-LABELED HUMAN SERUM ALBUMIN

KAZUHIRO HASHIMOTO, M.D., *YUZURU NAKAMURA, M.D.
MICHIIKO MATSUI, M.D., HIROMI KUROSAWA, M.D.
AND TATSUTA ARAI, M.D.

The pulmonary blood distribution was examined in 17 patients with tetralogy of Fallot (TOF) pre and postoperatively with macroaggregates of $^{99m}$Tc-labeled human serum albumin. Most of the patients with TOF demonstrated an abnormal preoperative distribution pattern. The abnormalities included not only an unbalanced distribution between the right and left lungs but also a maldistribution of peripheral vessels in each lung. The Right/Left lung counts ratio and Pulmonary Peripheral Index (calculated in order to express the severity of peripheral maldistribution) correlated neither to the diameter nor the cross-sectional area of either right or left pulmonary arteries which were measured angiographically. Postoperatively, the pulmonary blood was shunted toward the developed side of the lung which further contributed to maldistribution of blood flow and unbalanced pulmonary growth. Since the patients with an unbalanced pulmonary blood distribution demonstrated a higher right ventricular pressure one year after the operation, a palliative operation facilitating the growth of the underdeveloped side of the lung might be considered as an effective procedure to precede intracardiac repair. (Jpn Clic J 56: 1992: 992–997)

Tetralogy of Fallot (TOF) is characterized by cyanosis and reduced pulmonary blood flow. Maldistribution of the pulmonary blood flow in TOF is affected by several cardiac and pulmonary anomalies such as right ventricular outflow obstruction, pulmonary stenosis, (valvular, bifurcational and/or peripheral stenosis) and pulmonary arterial growth. In order to select the proper operative procedure and take the necessary precautions, it is essential to evaluate both the pulmonary growth and the maldistribution of the pulmonary blood flow in TOF. Various methods of semiquantitative analysis of the pulmonary vasculature have been introduced for this purpose.1,2 Angiograms are often used; however, this procedure is disadvantageous when it comes to evaluating the peripheral vasculature.

The external scintillation scanning technique, following intravenous administration of $^{99m}$Tc-labeled human serum albumin ($^{99m}$Tc-MAA) macroaggregates, is an interesting approach to elucidate the pulmonary blood flow in patients with congenital heart disease.2,4 For instance, the scintigram

Key words:
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TABLE 1 RESULTS OF PULMONARY BLOOD FLOW SCINTIGRAM

<table>
<thead>
<tr>
<th></th>
<th>R U/L</th>
<th>L U/L</th>
<th>U R/L</th>
<th>L R/L</th>
<th>R/L</th>
<th>PPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>0.80±0.12</td>
<td>0.87±0.13</td>
<td>1.01±0.19</td>
<td>1.44±0.32</td>
<td>1.06±0.22</td>
<td>0.24±0.20</td>
</tr>
<tr>
<td>TOF group</td>
<td></td>
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<tr>
<td>Preop</td>
<td>0.66±0.09</td>
<td>0.74±0.17</td>
<td>1.15±0.62</td>
<td>1.24±0.57</td>
<td>1.20±0.58</td>
<td>0.85±0.25</td>
</tr>
<tr>
<td>1 month</td>
<td>0.69±0.13</td>
<td>0.80±0.13</td>
<td>1.64±1.11</td>
<td>1.82±1.16</td>
<td>1.72±1.11</td>
<td>3.21±8.01</td>
</tr>
<tr>
<td>1 year</td>
<td>0.74±0.09</td>
<td>0.82±0.18</td>
<td>1.61±1.06</td>
<td>1.91±1.73</td>
<td>1.75±1.35</td>
<td>4.79±11.54</td>
</tr>
</tbody>
</table>

R U/L: Right Upper/Lower counts ratio, L U/L: Left Upper/Lower counts ratio, U R/L: Upper Right/Left counts ratio, L R/L: Lower Right/Left counts ratio, R/L: Right/Left counts ratio, PPI: Pulmonary Peripheral Index, Preop: preoperation, 1 month: one month after the surgery, 1 year: one year after the surgery

reveals the final MAA deposition in the pulmonary vasculature, is technically simple, entails no risk and is easily applicable to a large number of patients.

Although maldistribution of the pulmonary blood flow in TOF has been mentioned in several papers, precise and extensive evaluations had not been performed. Furthermore, only a few reports are available on the postoperative alteration of the pulmonary blood flow in TOF. In this study, we describe our experience using the pulmonary blood flow scintigram in TOF. Data obtained before and after the intracardiac repair were evaluated and then compared to the data from cardiac catheterization and angiography.

MATERIAL AND METHODS

Seventeen patients with TOF were included in this study. Their ages ranged from 1 to 6 years, with an average age of 3.1±1.7 years (mean±standard deviation). All of the patients had a pulmonary blood flow scintigram with 99mTc-MAA before and after operation. Additional scintigrams were performed 1 month and 1 year after surgery. All of patients underwent intracardiac repair without preceding shunt operations. No deaths occurred during the follow-up period. Ten subjects with no intracardiac or pulmonary abnormalities, displayed normal pulmonary blood scintigrams during this period, were used as controls (an average age of 4.5±1.9 years).

To obtain the pulmonary blood flow scintigram, we placed the patient supine and intravenously injected 3 to 10 mCi 99mTc-MAA. Ketamin hydrochloride was administered as necessary. A gamma camera with a large field of view (Toshiba GCA-70A), fitted with a high sensitivity low-energy collimator, and interfaced to a VARIACUM II 64KW, was used to obtain two views of the lung scintigram. The posterior view of the pulmonary blood scintigram was used in the following analysis since the anterior view is significantly influenced by the heart location. Patients with obvious lung disorders (such as atelectasis, pneumonia, pneumothorax, pleural effusion) which might have influenced the pulmonary blood flow, were not included in this series.

Analysis

For the front scintigram image (posterior view), both lungs were divided into a upper and a lower section at the level of lung hilus. In each lung, the following counts ratios were calculated form the external counts: Upper section/Lower section (Right or Left U/L), Right Upper section/Left Upper section (Upper R/L), Right Lower/Left Lower (Lower R/L) and Right lung/Left lung (R/L). The Pulmonary Peripheral Index (PPI), which indicates the maldistribution of pulmonary blood flow in the periphery, was based on the following formula. This formula simply expresses the sum of differences from the results of counts ratios in the control group and expresses existence of the maldistribution. A value approaching one demonstrates the same distribution pattern as the control group and away from one shows the existence of maldistribution.

\[ PPI = |C_1 - R(U/L)|^2 + |C_2 - L(U/L)|^2 + |C_3 - U(R/L)|^2 + |C_4 - L(R/L)|^2 \]

(C1-4: control values, Table I)

All patients underwent cardiac catheterization before the operation. Twelve out of
17 patients underwent postoperative catheterization one year following the operation. From the right ventriculogram, the diameters of the right and left pulmonary arteries, just before branching off from the first upper branch, were measured. The right pulmonary artery/left pulmonary artery diameter ratio (RPA/LPA diameter ratio) was calculated preoperatively. The Pulmonary Artery index (PA index), which is clinically used to indicate the degree of pulmonary arterial growth, was measured by the following formula: All of the above data were expressed as a mean ± standard deviation.

Pulmonary Artery index = (diameter of right PA mm)$^2$ + (diameter of left PA mm)$^2$ * 3.14 / (4 × BSA m$^2$) (normal range: 330 ± 30 mm$^2$/BSA m$^2$)

RESULTS

A. Control group

The counts ratios from the control group are listed in Table I. The distribution of pulmonary blood flow was nearly uniform throughout the entire lung field. Only the lower Right/Left counts ratio (L R/L) demonstrated unbalanced distribution, due to the position of the heart.

B. Tetralogy of Fallot

a. Preoperation

The results of scintigram are listed in Table I. A value exceeding one standard deviation of the control mean value was considered abnormal. Seven of the 17 patients showed an abnormal R/L counts ratio. An obvious flow reduction in the right lung was
seen in 2 patients, and a flow reduction in the left lung was seen in 5 patients. Six patients displayed an abnormal PPI (Fig. 1).

The relationships between PPI and either PA index or RPA/LPA diameter ratio were as displayed in Fig. 2. No correlations were noted.

b. Postoperation

Nine out of 17 patients showed an abnormal R/L counts ratio after one month. Eight patients retained an abnormal value even after one year. All patients who had an abnormal R/L counts ratio preoperatively demonstrated a deterioration of the ratio both one month and one year after surgery (Fig. 1).

However, 8 out of 10 patients who had a normal R/L counts ratio preoperatively, showed normal PPI one month after surgery. Of these 8 patients, 3 who had an abnormal PPI preoperatively and revealed normalization of the PPI after one month, had a normal R/L counts ratio before the operation.

An abnormal PPI was observed in 7 patients after one month. Five patients were in the normal PPI range and 2 were in the abnormal PPI range before the operation.
(Fig. 1). Interestingly, all patients except one, who demonstrated an abnormal PPI after one month, displayed an abnormal R/L counts ratio preoperatively. Four patients with a normal PPI and an abnormal R/L counts ratio preoperatively, displayed an abnormal PPI after one month.

The pressure gradients between the right ventricle and the pulmonary artery were $23.1 \pm 16.2 \text{ mmHg (n=8)}$ in the group with the normal postoperative R/L counts ratio and $23.3 \pm 11.4 \text{ mmHg (n=4)}$ in the group with the abnormal postoperative R/L counts ratio. Despite similar pressure gradients between the right ventricle and the main pulmonary artery in the both groups, the right ventricular pressure was significantly higher ($p<0.01$) in the abnormal R/L counts group ($69.6 \pm 14.8$ vs $42.0 \pm 8.2 \text{ mmHg}$). The PA index from the angiogram one year following the operation was almost identical in the 2 groups ($343 \pm 57$ in the normal vs $367 \pm 131$ in the abnormal R/L counts group).

**DISCUSSION**

It is well known that patients with TOF show maldistribution of the pulmonary blood flow. This is believed to be caused by the direction of the blood flow from the RV, intracapillary thrombi, the collateral development of the bronchial arteries, the lack of congenital development of the pulmonary arteries and vasoconstriction of the pulmonary arteries.

It has been reported that the diminished flow occurs in the left lung more frequently? In this study, our subjects also displayed this phenomenon. Furthermore, since in TOF patients the scintigram indicated an abnormal PPI, the maldistribution of pulmonary blood flow resulted from abnormalities in both the central and peripheral vessels.

Since the PA index is quite accurate, it can be applied clinically to reveal pulmonary arterial growth? In addition, the PPI is thought to be even more informative concerning the periphery of the arteries. However, in this study there was no correlation between the PPI and either the PA index or the RPA/LPA diameter ratio. Therefore, neither the PA index nor the RPA/LPA diameter ratio was informative regarding the peripheral vasculature.

During the postoperative course, our main concern was whether or not the maldistribution of the pulmonary blood flow would improve. One month after intracardiac repair, a range of scintigram results, including improvement or deterioration, were observed. The preoperative value of the R/L count ratio obviously affected the results. For instance, patients with a normal preoperative R/L counts ratio showed improvements in their postoperative PPI. However, patients with an abnormal R/L counts ratio showed deterioration in both their PPI and R/L counts ratio. One year after the operation, these parameters were tested again.

Furthermore, balanced arterial growth in both lung facilitated the improvement of the peripheral blood distribution; whereas, when unbalanced arterial growth existed, the pulmonary blood tended to flow to the well-developed lung (well-grown pulmonary vasculature). This phenomenon lead to compensatory development in the well-developed lung without the appropriate development of the poorly developed lung. Therefore, the imbalanced pulmonary blood distribution further deteriorated after the operation.

Even if patients have unbalanced pulmonary arterial growth, if they have an operatively safe PA index they generally tend to do well both during and following surgery. In this study, since patients with either balanced or unbalanced pulmonary arterial growth revealed almost identical PA indexes one year following the operation, this suggested that the same degree of growth and development had occurred. However, when compared to patients with well developed arterial growth, the patients with unbalanced growth displayed a relatively high postoperative RV pressure without a significant difference in the RV-PA pressure gradient. It is therefore questionable whether or not peripheral pulmonary growth fully occurs in all cases after intracardiac repair.

Recently our policies concerning surgery on patients with TOF have changed. Candidates for intracardiac repair are becoming younger and younger. In addition, we do not usually perform a preliminary palliative operation except in severe infant cases. Facilitating the growth of the underdeveloped side of the lung by the shunt procedure, however, may have some advan-
tages. For instance, if intracardiac repair is performed after the pulmonary arterial growth has uniformly developed, there is an increased possibility of developing adequate pulmonary vasculature, uniform distribution of blood, and a low RV pressure in the long-term.

We have obtained good results with patients who first had a palliative operation and then underwent intracardiac repair after a few years when there was adequate growth of the pulmonary arteries at the shunt side. Although the underdeposition of MAA may not always express the underdevelopment of the pulmonary artery, but may be a result of intracapillary thrombi or vasoconstrictions, Yamaki et al. reported that there were no findings of intracapillary thrombi in a patient less than 4 years old. Thrombi were frequently observed in patients aged more than 5 years. The patients in this series (mostly less than 5 years old) were considered not to suffer form thrombi. Furthermore, the previous studies convinced that the increase of pulmonary flow by the shunt procedure at this age group potentially grew the underdeveloped pulmonary artery. Thus, this ordinal operative process should be considered as effective to precede intracardiac repair.

REFERENCES


