Abnormal distribution of pulmonary blood flow after the Glenn shunt or Fontan procedure: risk of development of arteriovenous fistulae

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ABSTRACT Since the Fontan procedure results in low pulsatile pulmonary blood flow similar to that seen in patients with a Glenn shunt, it may also be associated with abnormal distribution of flow to the lower lung lobes and with the development of pulmonary arteriovenous fistulae (PAVF). In 12 patients 0.8 to 4.5 years after Fontan procedure and in 20 patients 0.2 to 18 years after receipt of Glenn shunts we assessed ventilation (with Tc-99mXe) and perfusion (after a peripheral injection of Tc-99m macroaggregated albumin) to compare upper to lower lobe distribution of blood flow with that in a control group. The presence of PAVF was assessed by radionuclide activity in kidneys and the brain and by a two-dimensional echocardiographic contrast study. A decreased upper/lower lobe perfusion ratio was noted in 13 of 20 patients with Glenn shunts (65%) and correlated with the time after surgery (p < .05). Despite the shorter follow-up period, two of 12 (16%) patients who had undergone the Fontan procedure also had a decreased upper/lower lobe perfusion ratio, and one of these developed right heart failure. Brain and kidney radionuclide counts above control values were observed in all patients with Glenn shunts and in 11 of 12 patients who had the Fontan operation. However, in only five of 20 (25%) patients with Glenn shunts were PAVF confirmed by the two-dimensional echocardiographic contrast study. Three of the five patients with PAVF had Glenn shunts of long duration. While only two of five patients with PAVF had a decreased upper/lower lobe perfusion ratio at the time of the study, this abnormality may have been present in the other three at an earlier stage. Our data suggest that a decreased ratio of upper/lower lobe perfusion may be one of several factors associated with the development of PAVF after a Glenn shunt. Also, longer follow-up of patients who have had a Fontan procedure will be necessary to determine whether they are also a group at risk.


THE FONTAN procedure,1 which establishes a right atrial–to–pulmonary arterial (RA-PA) communication, and its modification, which incorporates the right ventricle (RA-RV communication), result in low pulsatile pulmonary blood flow. This hemodynamic state is similar to the one observed after creation of a Glenn shunt (superior vena cava–to–pulmonary arterial anastomosis).2 It is well established that the Glenn shunt favors distribution of pulmonary flow to the lower lobe1 and that with increasing duration of shunt time, pulmonary arteriovenous fistulae (PAVF) can occur in the same area.4 Whether these PAVF result from the low pulsatile pulmonary blood flow or from the maldistribution of flow or are associated with other factors such as pulmonary hypertension in the unshunted lung5 is still unclear. If indeed low pulsatile pulmonary flow leads to maldistribution and the potential to develop PAVF, then patients who have had Fontan’s procedure represent a group at risk.

We therefore performed ventilation/perfusion lung scans to determine the distribution of pulmonary blood flow in patients after the Fontan procedure (RA-PA and RA-RV). We assessed the presence of PAVF by the scintigraphic appearance of Tc-99m macroaggregated albumin (MAA) in the brain and kidneys after a peripheral intravenous injection and by twodimensional echocardiographic contrast studies. Our findings were compared with those obtained in patients with Glenn shunts and in normal subjects.

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Methods

Patient population. We reviewed the records of the cardiac patients who received a Glenn shunt or underwent Fontan procedure between June 1965 and August 1983 at the Hospital for Sick Children, Toronto. Twenty-nine patients were available and consented to participate in our study. In 20, a Glenn shunt had been created; three of these patients and nine others had undergone Fontan procedure. Of those 12 with a Fontan procedure, six had RA-RV and six RA-PA communication. This represents a random group of 22% of all patients in whom these procedures had been performed. The age range was similar in the Fontan and Glenn groups (table 1), but the duration after surgery was shorter in the Fontan (0.08 to 4.5 years, mean 2.4) than in the Glenn group (0.02 to 18 years, mean 8.8). Six volunteers from 28 to 32 years old served as normal control subjects. All studies were carried out after approval of the protocol and the method of obtaining informed consent by our Clinical Investigation Committee.

Radionuclide assessment. The ventilation/perfusion lung scan was performed with a Picker gamma camera (Dynamacamera 4/15) interfaced to a Medical Data System® computer. Ventilation was assessed from a posterior view of the lungs, with the patient in the sitting position, with $^{133}$Xe as the radionuclide tracer. The patient breathed until equilibrium, then washout of the substance was allowed. For assessment of perfusion, the patient and camera position remained unchanged. In control subjects and in those with a Glenn shunt or Fontan procedure only, a dose of 0.05 mCi/kg (1.85 MBq) of $^{99m}$Tc-MAA was injected in an arm vein. In patients who had undergone a Fontan procedure and had a previous Glenn shunt, half the dose was injected in a leg vein for determination of perfusion of the left lung supplied by the Fontan anastomosis, and the other half dose was injected in an arm vein to image perfusion of the right lung supplied by the Glenn shunt. After each injection, the camera was also positioned over the opposite lung and over the kidneys and brain to detect radionuclide activity at these sites. The $^{133}$Xe ventilation study was used to determine the height of the lung on the scintigram and from this, the lung was divided into three equidistant segments from base to apex. Radionuclide perfusion counts ($^{99m}$Tc-MAA) were measured in each of these regions. An upper-to-lower lobe perfusion ratio was then calculated.

The presence of right-to-left shunting was detected by the appearance of $^{99m}$Tc-MAA in the kidneys and brain and contralateral lung of patients with Glenn shunts. These large radionuclide particles (10 to 50 μm) should otherwise lodge and remain in the capillaries of the lung. For control subjects and patients who underwent a Fontan procedure, we calculated the ratio of brain + kidney counts/right and left lung counts; for patients with a Glenn shunt, brain + kidney + left lung counts/right lung counts was calculated. (For the one patient with a left-sided Glenn shunt, the lung counts were reversed.) For patients who had Fontan procedure and a previous Glenn shunt, we used the following formula: brain + kidney + right lung counts/left lung counts for the Fontan (peripheral leg injection) and brain + kidney + left lung counts/right lung counts for the Glenn (peripheral arm injection). Since the arm injection was given after the leg injection, the residual counts from the latter were subtracted before counting the ratio for the former.

Echocardiographic contrast study. A two-dimensional contrast study was performed the same day as the radionuclide scan. The heart was visualized in the precordial four-chamber view. Ten milliliters of normal saline mixed with approximately

<p>| TABLE 1 |</p>
<table>
<thead>
<tr>
<th>Clinical details on patients studied</th>
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<tr>
<td>Group</td>
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<td>Glenn</td>
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<td>Fontan</td>
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<td>RA-PA</td>
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<td></td>
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<tr>
<td>Fontan</td>
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<tr>
<td>RA-RV</td>
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<td>Control</td>
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TGA = transposition of the great arteries; RVOT = right ventricular outflow tract; DORV = double-outlet right ventricle; IVC = inferior vena cava; RPA = right pulmonary artery.

³Also included in the Glenn shunt group.
5 ml of CO₂ was injected through the same peripheral intravenous site used for the radionuclide tracer. Normally, after a right-sided injection, the echo quality of the bolus is lost in the passage through the pulmonary capillary bed and therefore no “bubbles” should be observed in the left heart. In patients with a Glenn shunt bubbles observed in the pulmonary veins and left atrium suggest the presence of PAVF, and bubbles in the right atrium indicate the presence of a systemic venous collateral. In patients who had undergone the Fontan procedure, the contrast bolus was followed from its first appearance in the right atrium. After disappearance of the bolus in the lung, attention was directed to the pulmonary veins and left atrium to identify any return suggestive of PAVF. In the patients with a Glenn shunt who had also undergone a Fontan procedure, separate injections in an arm and leg vein were performed.

Cardiac catheterization study. During the period of this study cardiac catheterization was carried out in nine patients in whom it was clinically indicated; six had Glenn shunts and three a Fontan procedure (all RA-RV communication). Angiographic findings were correlated with features of PAVF suggested by the radionuclide scan and by the two-dimensional echocardiographic contrast study.

Analysis of data. Multiple linear regression analysis was used to correlate distribution of pulmonary blood flow (upper/lower lobe ratio) as well as radionuclide and two-dimensional echocardiographic contrast evidence of PAVF with age at surgery and time after surgery in patients with a Glenn shunt or who had undergone Fontan procedure (RA-PA and/or RA-RV communication). A p value < .05 was considered indicative of a significant difference.

Results

Ventilation. In all control subjects and patients, the scintigraphic appearance of homogeneous distribution of 133Xe through both lung fields suggested normal ventilation.

Distribution of pulmonary perfusion. In control subjects the upper/lower lobe radionuclide count perfusion ratio was 0.07 to 0.29 in the right lung and 0.10 to 0.28 in the left. Four of five patients with Glenn shunts whose upper/lower lobe perfusion ratios fell within this “normal” range had received the shunts less than 4 years before, whereas 12 of 13 patients with a decreased ratio were studied at a later time postoperatively (p < .05) (figures 1 and 2). In the remaining two Glenn patients the upper/lower lobe perfusion ratio was increased: one had surgery less than 4 years before, the other more than 4 years before the study. There was no correlation between upper/lower lobe perfusion ratio and the age at which the Glenn shunt was received nor was there any correlation with the presence, type, or duration of a previous surgically created systemic-to-pulmonary arterial shunt. In one patient with a Glenn shunt and a decreased upper/lower lobe perfusion ratio (0.005), the creation of an axillary-to-pulmonary arterial fistula resulted in an increase of the ratio to 0.51.

Eight of 12 patients who had undergone the Fontan procedure had a normal upper/lower lobe perfusion ratio. All were studied less than 4 years after surgery. Two patients had a decreased ratio; one with a RA-RV communication was studied 4.5 years after repair and the other, with a RA-PA communication, only 1 year later. The latter patient developed severe congestive heart failure, perhaps as a result of pulmonary vasoconstriction secondary to ventilation/perfusion mismatch. An increased ratio of upper/lower lobe perfusion was observed in the remaining two patients (both RA-RV) (figure 3). One of us (G. T.) independently scored the patients in the RA-RV Fontan group as to size of the right ventricle and pulmonary valve. We could not correlate these features with either an increased or a decreased upper/lower lobe perfusion ratio. We could not detect any influence on the ratio in the left lung after the Fontan operation if a previous Glenn shunt had been created in the right lung. Of three patients who had undergone both procedures, all had decreased ratios in the right (Glenn) lung, but only one had a decreased ratio in the left lung; the other two were normal.

Radionuclide detection of right-to-left shunt. In control subjects the ratio of brain + kidney/right + left lung radionuclide counts ranged from 0.003 to 0.005. In all patients with a Glenn shunt or who had Fontan procedure the ratio was higher (0.02 to 1.30). In eight of 20 patients in the Glenn group and in 11 of 12 of those in...
the Fontan group, the ratio was 0.03 to 0.06, but in the others it was 0.07 to 1.30.

Detection of PAVF with radionuclide scanning and two-dimensional echocardiographic contrast. In no patient with a radionuclide shunt ratio of less than 0.07 did an echocardiographic contrast bolus appear in the right atrium (Fontan group) or in the pulmonary veins or left atrium (Fontan and Fontan group), suggesting that the degree of right-to-left shunting was trivial. Of 12 Glenn patients with a shunt ratio of 0.07 or greater, the echocardiographic contrast study confirmed the presence of PAVF in five and identified systemic venous collaterals in four (figures 4 and 5). Two of the remaining three patients with Glenn shunts had anatomic characteristics that could explain the discrepancy between the positive radionuclide results and the negative echocardiographic contrast study. In one, an end-to-side Glenn shunt had been performed so the right pulmonary artery was in continuity with the left, and in the other, an anomalous pulmonary vein was draining into an innominate vein. Hence there was a high brain + kidney + left lung/right lung count but echocardiographic contrast bubbles did not appear in the left atrium. The third patient did not undergo cardiac catheterization to clarify the reason for the discrepancy between the two noninvasive studies, but we believe the bolus of contrast in the echocardiographic study was inadequately injected. In the one patient in the

**FIGURE 3.** Left. Radionuclide lung scan from a patient with decreased flow to the upper lobes after Fontan procedure (RA-PA). Right. Patient with increased flow to the upper lobes after Fontan procedure (RA-RV). Incidentally noted are increased counts in the kidneys, suggesting some right-to-left shunting.
Fontan group with a radionuclide ratio of greater than 0.07, right-to-left shunting at the atrial level was observed on two-dimensional echocardiogram.

Cardiac catheterization study and PAVF. In two of the six patients with Glenn shunts who underwent cardiac catheterization there were findings consistent with PAVF on both the radionuclide scan and the two-dimensional echocardiogram. In one patient, PAVF were confirmed, but in the other, they were not apparent angiographically. However, since pulmonary venous saturations were not obtained, we could not exclude the presence of small communications in the latter patient. The positive catheterization study was obtained in the patient with the highest radionuclide shunt ratio (1.3), while the negative study was obtained in the patient with a much lower value (0.08). In the patient with the positive catheterization study, the PAVF were embolized; on subsequent radionuclide study, the shunt ratio had decreased from 1.3 to 0.43 (figure 6).

Cardiac catheterization confirmed the presence of systemic venous collaterals in two patients. The absence of venous collaterals as well as PAVF was confirmed in another and, in the remaining patient, the anatomic source of right-to-left shunting was identified as an anomalous pulmonary vein. The absence of venous collaterals or PAVF was also confirmed in the three patients in the Fontan group that underwent cardiac catheterization.

Duration of Glenn shunt, distribution of pulmonary blood flow, and PAVF. Three of the five patients with PAVF had Glenn shunts of long duration (13 to 16 years). Two of these had decreased ratios of upper/lower lobe perfusion: radionuclide ratios were 0.07 and 0.08. The third patient had an increased upper/lower lobe perfusion ratio, probably because severe right-to-left shunting through PAVF (radionuclide ratio = 1.3) caused impaired trapping of radionuclide material in the lower lobe. Two patients with PAVF and Glenn shunts of only 2 to 4 years duration had normal upper/lower lobe perfusion ratios. Both were severely cyanotic and in both, perfusion to the left lung was decreased. In one patient this was due to a thrombosed left pulmonary artery, in the other, to an obstructed left Blalock-Taussig shunt. Both conditions favor distribution of flow to the right lung and may have accelerated the formation of PAVF. Only one of these patients, however, had more severe right-to-
left shunting (radionuclide ratio of 0.28), and presumably less trapping of radionuclide material, than the patients with decreased upper/lower lobe perfusion ratios (table 2).

**Discussion**

**Methodology.** Abnormal distribution of pulmonary blood flow in patients with Glenn shunts has been described qualitatively, but its quantification and relationship to development of PAVF has not been determined. Moreover, we are aware of comparisons in only four patients who have had Fontan’s procedure after placement of a Glenn shunt and these are all qualitative descriptions. The pulmonary blood flow was reported to be evenly distributed in the left (Fontan) lung, whereas the right lung had the characteristic maldistribution observed with a Glenn shunt. The time after surgery at which the patients were studied was not mentioned. Our study is the first to quantify distribution of pulmonary blood flow in right and left lungs in

**TABLE 2**

Results in patients in the Glenn group

<table>
<thead>
<tr>
<th>Ratio of upper/lower lobe perfusion</th>
<th>Radionuclide data on left-to-right shunting</th>
<th>2D echo data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥0.07&lt;sup&gt;a&lt;/sup&gt; Value in PAVF pt(s)</td>
<td>PAVF Venous collateral</td>
</tr>
<tr>
<td>&gt;0.28 (increased)</td>
<td>n=2 1.3</td>
<td>1 0</td>
</tr>
<tr>
<td>≥0.07, ≤0.28 (normal)</td>
<td>n=5 0.08, 0.23</td>
<td>2 0</td>
</tr>
<tr>
<td>&lt;0.07 (decreased)</td>
<td>n=13 0.07, 0.08</td>
<td>2 4</td>
</tr>
<tr>
<td>Total (%)</td>
<td>n=20 (100) 12 (60)</td>
<td>5 (25) 4 (20)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Brain + kidney + left lung/right lung.

<sup>b</sup>Includes two patients with other anatomic sources of right-to-left shunting.
patients after placement of a Glenn shunt and after the Fontan procedure, to combine the use of radionuclide scans and two-dimensional echocardiographic contrast studies to detect right-to-left shunting, and to determine the source of this shunting.

Our method of assessing radionuclide distribution of pulmonary flow differs from that described by Friedman et al. and accounts for the lower values for upper/lower lobe perfusion ratio we obtained. We used $^{133}$Xe to measure the lung height, whereas they took this measurement from the perfusion study. Use of our method is advantageous in patients in whom there is impaired segmental perfusion that may make determination of lung boundaries inaccurate. The nature of the radionuclide studies required that our control volunteers be young adults. The mean age of our patients was 15 years. Previous investigations suggest that children of normal height who are more than 10 years of age should have the same distribution of perfusion as adults. Younger children may be expected to have more flow to the apeces. Since the latter constituted 18% of our group (five patients) we may have underinterpreted as normal a decreased upper/lower lobe perfusion ratio in three patients in the Glenn and one patient in the Fontan group and overinterpreted as high a normal value in another patient with a Glenn shunt. This, however, could not be determined with certainty.

Detection of PAVF by radionuclide scanning in patients with other conditions, as well as in patients with Glenn shunt, has depended largely on a qualitative assessment. In a quantitative study by Glenn et al., the presence of PAVF was inferred by decreased uptake of $^{99m}$Te-MAA in the right lung. Our method has the added advantage of quantifying the distribution of isotopes in peripheral organs and should therefore be more sensitive.

The echocardiographic contrast method used also had advantages over the one described previously in patients with this condition. A greater contrast was added by the use of CO$_2$ and use of the two-dimensional rather than the M mode echocardiographic approach allowed simultaneous visualization of all four cardiac chamber and pulmonary veins, as well as easier differentiation of venous collateral vessels from PAVF.

Abnormal distribution of perfusion. Our findings are in agreement with those of Boruchow et al., who observed increased perfusion to the lower lung lobes, the amount of which correlated with duration after placement of a Glenn shunt. In our study, the increase was observed consistently when the patient was studied 4 years or more after surgery. These changes occur because there is any clinical evidence of shunt failure, which is uncommon until 10 years after surgery. The exact cause of the maldistribution is unknown and, while it most likely results from the inability of low pulsatile pulmonary blood flow to counteract the effect of gravity, it is difficult to understand why it takes years to become manifest. Presumably the upper lobe vessels constrict and the lower ones dilate to accommodate the preferential direction of flow. A change in distribution of perfusion may not be readily apparent on a lung scan until the vessels become altered structurally and the discrepancy is more severe. The only patient in the Fontan group who had undergone surgery more than 4 years before this study had preferential flow to lower lung lobes. He was asymptomatic but had a RA-RV communication. The other patient developed preferential flow to the lower lobes only 1 year after surgery along with concomitant right-sided congestive heart failure. He also had a RA-PA communication, so we can speculate that since he lacked the ancillary pump a right ventricular chamber might provide, he could tolerate less well the pulmonary vasoconstriction that may have resulted from ventilation/perfusion mismatch. Alternatively, other factors that contributed to congestive heart failure might also have resulted in a decreased ratio of upper/lower lobe perfusion. This seems unlikely since right-sided congestion, particularly if associated with a rise in pulmonary arterial pressure, would tend to favor distribution toward the upper lung.

We cannot readily explain the fact that two patients who had undergone Fontan procedure (RA-RV) had increased flow to the upper lung lobes. They could not be distinguished from the others with respect to age, duration after surgery, nature of previous palliative procedures, or anatomic or hemodynamic characteristics.

PAVF and abnormal distribution of flow. The 25% incidence of PAVF in patients with Glenn shunts that we observed is similar to that previously reported. Increased perfusion to lower lung lobes was only present in two of five patients with PAVF, and both of these had had Glenn shunts for more than 13 years. The two patients in whom PAVF were associated with normal perfusion were studied only 2 and 4 years after surgery, respectively. Both were symptomatic and each had an anatomic abnormality causing decreased perfusion to the left lung. In these patients it is possible that there was diversion of flow from the lower extremities to the superior vena cava (via the ayzygous vein) and this accelerated the formation of PAVF. In patients with severe right-to-left shunting through PAVF, less
trapping of radiopharmaceutical material in the lower lobes may result in a normal or increased ratio of upper/lower lobe perfusion. Thus, the formation of PAVF may result from several interrelated factors that could include an abnormally increased distribution of flow to the lower lobes, increased time after surgery, and decreased perfusion or increased resistance in the contralateral lung. Degree of hypoxemia or polycythemia may be additional contributing factors, but this could not be determined from our small series.

**Clinical implications.** We do not know why patients who had undergone Fontan procedure or had received a Glenn shunt had higher radionuclide counts in peripheral organs when compared with control subjects. Perhaps it is a feature common to other patients after thoracotomy or perhaps it is low pulsatile pulmonary blood flow that induces the formation of small arteriovenous communications. We speculate that with increasing time after surgery and in response to preferential distribution of pulmonary flow to lower lung lobes, these communications, regardless of their cause, may enlarge to form true fistulae. There is no experimental basis for this speculation, but studies of the response of the microcirculation to nonpulsatile flow are certainly feasible and could be carried out.

The radionuclide scan indicated the presence of a right-to-left shunt and the two-dimensional echocardiographic contrast study localized the site of shunting in almost every patient. In two patients there was an anatomic reason for the apparent right-to-left shunt that was clarified by results of cardiac catheterization. In one patient there was still a discrepancy but the bolus of contrast material may have been inadequately injected or visualized. PAVF may be missed by catheterization studies unless, as suggested by Glenn et al., \(^\text{12, 18}\) selective pulmonary venous saturations and angiograms are obtained, but this may not always be technically feasible.

On the basis of our findings we propose that when a surgical procedure such as creation of an auxiliary arteriovenous fistula or a Fontan operation is being considered in patients with a Glenn shunt, radionuclide scan and two-dimensional echocardiographic contrast studies should be performed and analyzed, according to the method presented, as part of the preoperative evaluation. If, on the basis of these studies, PAVF are suspected, cardiac catheterization should be directed at localizing them and evaluating their hemodynamic significance. Embolization may be of great benefit in selective cases.\(^\text{21}\)

Patients who have undergone the Fontan procedure may be at risk for the development of PAVF. All patients in this group in our series had at least trivial right-to-left shunting identified on their radionuclide scans (as did all Glenn patients), and two demonstrated maldistribution of flow. It is possible that when the length of the follow-up period for patients who have had a Fontan procedure reaches that for patients with a Glenn shunt, a similar incidence of fistulae will be found. If maldistribution of flow causes hypoxic pulmonary vasoconstriction resulting from ventilation perfusion mismatch it may be poorly tolerated in post-Fontan patients, particularly those with RA-PA communications, who lack whatever contribution to cardiac output the small right ventricle may provide.\(^\text{20}\)

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