Pulmonary hypertension after ventriculoatrial shunt implantation

Clinical article

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Object. Ventriculoatrial (VA) shunts inserted for the treatment of hydrocephalus are known to be a risk factor for pulmonary hypertension. The aim of this study was to evaluate the incidence of pulmonary hypertension among adult patients with VA shunts.

Methods. All patients who had received a VA shunt at one of two institutions between 1985 and 2000 were invited for a cardiopulmonary evaluation. The investigation included a thorough history taking, clinical examination, echocardiography, and pulmonary function testing including diffusing capacity of the lung for carbon monoxide (DLCO). Pulmonary hypertension was defined as systolic pulmonary artery pressure > 35 mm Hg at rest.

Results. The study group consisted of 86 patients, of whom 38 (44%) could be examined. The patients’ mean age was 47.1 ± 18.4 years; the median interval between shunt insertion and cardiopulmonary evaluation was 15 years (range 5–20 years). Of the 38 patients, 20 (53%) had Doppler velocity profiles of tricuspid regurgitation that were adequate for the estimation of pulmonary artery systolic pressure. Doppler-defined pulmonary hypertension was observed in 3 patients (8%), 2 of whom underwent right heart catheterization. Chronic thromboembolic pulmonary hypertension was confirmed in both patients, and medical therapy, including anticoagulation, was started. The VA shunt was removed in both cases and replaced with a different type of device. Pulmonary function tests revealed a restrictive pattern in 15% and typical obstructive findings in 9% of patients. In 30% of patients the DLCO was less than 80% of predicted, and blood gas analysis showed hypoxemia in 6% of patients. No significant differences in pulmonary function tests were noted between the patients with and without echocardiographic evidence of pulmonary hypertension. However, patients with pulmonary hypertension had significantly lower DLCO values.

Conclusions. The authors detected pulmonary hypertension by using Doppler echocardiography in a significant proportion of patients with VA shunts. It is therefore recommended that practitioners perform regular echocardiography and pulmonary function tests, including single-breath DLCO in these patients to screen for pulmonary hypertension to prevent hazardous late cardiopulmonary complications. (DOI: 10.3171/2010.6.JNS091541)

KEY WORDS • pulmonary hypertension • ventriculoatrial shunt • pulmonary thromboembolism

Pulmonary hypertension has been reported as a severe complication of VA shunt insertion in the treatment of hydrocephalus. Pulmonary hypertension is characterized by a progressive increase in pulmonary vascular resistance, which may lead to right ventricular failure and premature death. The main symptoms are increasing dyspnea, fatigue, weakness, angina, syncope, and abdominal distension. The relative rarity of the condition in the general population and long delay between shunt insertion and development of respiratory symptoms can result in delayed or misdiagnosis.

The pathogenetic process that causes pulmonary hypertension after shunt insertion is unclear. Several mechanisms, such as shunt infection causing persistent activation of clotting factors (with recurrent thromboembolism), or a reaction of the pulmonary endothelium to some contents of CSF, for example brain thromboplastin, have been proposed.
Nowadays, ventriculoperitoneal shunts are used in preference to VA shunts for hydrocephalus. However, clinicians continue to see patients (now mainly adults) who received VA shunts in the past. The prevalence of pulmonary hypertension in adults with VA shunts has not been determined. Although earlier studies in children showed thromboembolism in 50–100% of cases, and it has been estimated that the prevalence of pulmonary hypertension is 0.03 to 0.3 per 1000 patients, similar population studies have not been performed in adults.

The present study was therefore designed to assess the frequency of pulmonary hypertension in adults with VA shunts who were recruited from two large neurosurgical centers.

Methods

All patients who had undergone VA shunt insertion at the Departments of Neurosurgery at the University Medical Center Hamburg-Eppendorf and Medical University of Lübeck between 1985 and 2000 were invited for a cardio-pulmonary evaluation. This assessment included a complete history, physical examination, transthoracic echocardiography, pulmonary function testing including DLCO and measurement of arterial blood gases. Patients with a history of pulmonary hypertension associated with other factors (such as cardiac disease, pulmonary disease, collagen vascular disease, pulmonary venoocclusive disease, deep venous thrombosis, liver disease, HIV infection, intravenous drug or appetite suppressant use, or a family history of pulmonary hypertension) were excluded.

Each patient gave informed consent to participate in the study, which was approved by the ethics committee of the chamber of physicians in Hamburg, Germany.

Echocardiography Studies

An experienced operator (S.K.) performed all the echocardiography studies, using a Vivid 3 expert ultrasound machine (General Electric Medical Systems) with 2.5- and 3.5-MHz transducers. A complete 2D, M-mode, Doppler echocardiogram was obtained for each patient. Tricuspid regurgitation was characterized as mild, moderate, or severe by qualitative assessment by using Doppler color flow imaging. To estimate the right-ventricular-to-right-atrial systolic pressure gradient, the modified Bernoulli equation \[4 \times (\text{tricuspid systolic jet})^2\] was used.

The PASP was quantified by adding the Bernoulli-derived pressure gradient to the estimated mean right atrial pressure. The mean right atrial pressure was calculated according to the degree of collapse of the inferior vena cava. Pulmonary hypertension was defined as a PASP of \(>35\) mm Hg at rest.

Right heart catheterization was performed using standard techniques on patients with Doppler-estimated pulmonary hypertension if they consented to this procedure.

Pulmonary Function Testing

Pulmonary function studies were performed according to recommended guidelines, with a body plethysmograph (Jaeger GmbH). The DLCO was assessed using a spirometry (Jaeger GmbH) and the single-breath method, with the patient in a seated position. Values below 80% of predicted were considered pathological.

Statistical Analysis

All data were analyzed with Statistica version 6.0 software (StatSoft, Inc.). Data are presented as the mean ± SD for data that were normally distributed or as the median (range) for data that were outside the normal distribution.

Results

Between January 1985 and the end of December 2000, a total of 86 patients were hospitalized for VA shunt insertion at the 2 participating institutions (47 in Hamburg-Eppendorf and 39 in Lübeck). Of these patients, 27 (31.4%) had died, 9 (10.5%) refused to participate, 6 (7%) could not be located, 5 (5.8%) were excluded due to poor general condition, and 1 (1.2%) was excluded due to categorization in chronic obstructive pulmonary disease. Global Initiative for Chronic Obstructive Lung Disease (the so-called GOLD scale) Class III, which could cause pulmonary hypertension (Fig. 1).

Characteristics of the Patients Included in the Study

Table 1 shows the characteristics of the final study group, which consisted of 38 patients.

There were 17 men (44.7%) and 21 women (55.3%). The mean age was 47.1 ± 18.4 years (range 16–78 years). The median interval from shunt insertion to cardiopulmonary evaluation was 15 years (range 5–20 years). In 26 of the 38 patients, one or more revisions of the shunt had been necessary.

Results of Echocardiography

In 21 patients (55%), the distal end of the VA shunt was seen in the right atrium. Of the 38 study patients, 20 (53%) had Doppler velocity profiles of tricuspid regurgitation that were adequate for the estimation of PASP (Fig. 2). Doppler-defined pulmonary hypertension occurred in 3 patients (8%).

In these 3 patients, the median interval between VA shunt placement and the diagnosis of pulmonary hypertension was 9 years (range 5–20 years). All 3 patients were symptomatic, with dyspnea ranging from New York Heart Association functional Class I to Class III. Two of the 3 patients underwent right heart catheterization. Pulmonary hypertension was confirmed in both cases, based on mean pulmonary artery pressures of 51 and 35 mm Hg. Further diagnostic tests revealed CTEPH in both patients, and medical therapy, including anticoagulation, was started. The VA shunt was removed in both cases and replaced with a different type of shunt. The third patient was a 29-year-old woman who had received a VA shunt 5 years earlier. Echocardiography showed a systolic pulmonary artery pressure of 38 mm Hg, with minimal tricuspid regurgitation. However, the patient was categorized in New York Heart Association Class I, had no signs of heart failure, and refused further diagnostic tests (such as right heart catheterization) or removal of the VA shunt.
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Pulmonary Function Tests

The results of the pulmonary function tests are shown in Table 2. In 5 (15%) of 33 patients a restrictive pattern was found. This deficit was mild in 4 (12%) and moderate in 1 (3%) of 33; there were no severe alterations. Three (9%) of 33 patients had typical obstructive findings (all mild). In 8 (30%) of 27 patients, the DLCO was less than 80% of predicted, and blood gas analysis showed hypoxemia in 2 (6%) of 34 patients.

Lung function tests could not be performed in 5 patients due to their severe disability, and DLCO measurement was not possible in a further 6 patients because they were unable to hold their breath for 10 seconds.

No significant differences in pulmonary function were noted between the patients with and without echocardiographic evidence of pulmonary hypertension. However, patients with pulmonary hypertension had significantly lower DLCO values (61.2%).

Discussion

Pulmonary hypertension can be a major complication after VA shunt insertion.9 We report on 38 adult patients with VA shunts who were screened for pulmonary hypertension. We found that 8% of our patients had elevated PASPs, with no other cause of pulmonary hypertension. To our knowledge, this is the largest cohort of adult patients with VA shunts who have been comprehensively evaluated with clinical evaluation, serial echocardiography, and lung function testing. Only a few reports regarding screening of patients with VA shunts to assess for pulmonary hypertension or pulmonary thromboem-
bolism have been published previously, and these focus mainly on children.

Sperling and colleagues\textsuperscript{18} used electrocardiography and chest x-rays to evaluate 30 asymptomatic children who had received VA shunts (follow-up period 5–78 months). Among them, 2 had pulmonary hypertension. Nugent et al.\textsuperscript{14} performed angiocardiography in 11 children with VA shunts, and demonstrated thrombosis or embolism in 6. One article\textsuperscript{1} described 21 patients with VA shunts (mainly children) who were screened with perfusion scans. Perfusion defects were found in 3 asymptomatic children, and it was concluded that the perfusion scan is a safe and simple procedure in patients with shunts. Finally, Sleigh et al.\textsuperscript{17} prospectively studied 20 asymptomatic patients (mean age 9 years) with VA shunts by clinical examination, electrocardiography, chest x-ray, and echocardiography, and found no evidence of pulmonary hypertension.

Although researchers agree that a VA shunt presents an independent risk factor for the development of pulmonary hypertension,\textsuperscript{2} there is little consistency between studies regarding the prevalence of pulmonary hypertension in patients with VA shunts. Various screening techniques to detect pulmonary hypertension or pulmonary embolism have been suggested. Current guidelines recommend Doppler echocardiography,\textsuperscript{11} which allows non-invasive estimation of PASP. The sensitivity and specificity of Doppler echocardiography is 0.79–1 and 0.68–0.98, respectively, for detecting pulmonary hypertension.\textsuperscript{16}

Pulmonary hypertension in patients with VA shunts is classified as CTEPH,\textsuperscript{8} which was found in 2 of our 3 patients with pulmonary hypertension on echocardiography. Pulmonary function testing in these patients, performed to evaluate the individual’s dyspnea, is often within normal limits. However, the majority of patients have a reduction in the single-breath DLCO, which is a sensitive indicator of chronic recurrent pulmonary emboli.\textsuperscript{59} Accordingly, patients with pulmonary hypertension in our study had significantly lower DLCO values than did patients without pulmonary hypertension.

Lack of awareness of the possible association between progressive dyspnea and the development of pulmonary hypertension in a patient with a VA shunt may result in delayed diagnosis. It is noteworthy that the median interval between VA shunt placement and diagnosis of pulmonary hypertension in our 3 cases was 9 years.

There are limitations to our study. First, only 38 (44%) of the initial 86 patients who had undergone VA shunt insertion at the 2 institutions during the study period could be examined. Second, 1 of the 3 patients with echocardiographic evidence of pulmonary hypertension refused right heart catheterization, which is the gold standard for diagnosing pulmonary hypertension. This may have led to an overestimation of pulmonary hypertension in our study group, because echocardiography can overestimate the pulmonary artery pressure compared with catheterization.\textsuperscript{6} On the other hand, we cannot exclude the possibility that the high mortality level in the study group (27 of 86 patients) might be due at least in part to unrecognized pulmonary hypertension.

Although the process of microembolization commonly affecting patients with VA shunts appears to be intermittent and mild, these individuals often develop

\begin{table}
\centering
\caption{Results of blood gas and pulmonary function tests*}
\begin{tabular}{lcc}
\hline
Parameter & No. of Patients & Value (mean ± SD) \\
\hline
blood gases & & \\
\text{PaO}_2, \text{mm Hg} & 34 & 82 ± 9.9 \\
\text{PCO}_2, \text{mm Hg} & 34 & 37 ± 3.8 \\
\text{pH} & 34 & 7.43 ± 0.022 \\
pulmonary function tests (% of predicted) & & \\
\text{TLC} & 33 & 97 ± 18 \\
\text{VC} & 33 & 82 ± 18 \\
\text{FEV}_1 & 33 & 85 ± 21 \\
\text{FEV}_1/\text{VC} & 33 & 106 ± 15 \\
\text{DLCO} & 27 & 92 ± 17 \\
\hline
\end{tabular}
\footnotesize
* \text{FEV}_1 = \text{forced expiratory volume in 1 second; TLC = total lung capacity; VC = vital capacity.}
\end{table}
severe pulmonary hypertension. Once pulmonary hypertension has been diagnosed, the prognosis is serious and often life threatening, even with immediate removal of the shunt and adequate therapy, and may end in lung or heart-lung transplantation. In a large population of untreated patients with pulmonary hypertension, the median survival rate was only 2.8 years.

Serious complications of pulmonary hypertension in patients with VA shunts have led to the development of guidelines for follow-up in our institution, including echocardiography and pulmonary function tests with single-breath DLCO every 12 months. This follow-up should be lifelong. Once a diagnosis of pulmonary hypertension has been made, treatment involves immediate shunt removal, replacement with a different type of shunt, and medical therapy including anticoagulation. Currently, prostanooids, endothelin receptor antagonists, and phosphodiesterase-5 inhibitors are the main treatments.

Conclusions

We found that 8% of adult patients who had received VA shunts at our institutions had pulmonary hypertension according to the results of echocardiography studies. This was due to CTEPH, and could occur decades after shunt insertion. Therefore, patients with VA shunts should be screened with regular clinical reviews that include echocardiography and pulmonary function tests, including single-breath DLCO for early detection of pulmonary hypertension. Clinicians should consider this complication in any patient with a VA shunt who develops respiratory symptoms.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Kluge, Regelsberger, Kehler, Meyer. Acquisition of data: Kluge, Baumann, Gliemroth, Koziej, Meyer. Analysis and interpretation of data: Kluge, Koziej, Meyer. Drafting the article: Kluge, Regelsberger, Klose. Critically revising the article: Kluge, Kehler, Meyer. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Kluge, Koziej, Meyer. Administrative/technical/material support: Kluge, Kehler, Gliemroth, Meyer. Study supervision: Kluge, Klose.

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Manuscript submitted October 14, 2009.
Accepted June 2, 2010.
Please include this information when citing this paper: published online July 2, 2010; DOI: 10.3171/2010.6.JNS091541
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