Haemodynamic Quantification of Different Provocation Manoeuvres by Simultaneous Measurement of Right and Left Atrial Pressure: Implications for the Echocardiographic Detection of Persistent Foramen Ovale

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Aims: Persistent foramen ovale (PFO) is found in 9.2–32% of echocardiographic examinations. The gold standard for the detection of a PFO is transoesophageal echocardiography (TEE) and the mostly used provocation test is the Valsalva manoeuvre. The aim of our study was to evaluate the effectiveness of the Valsalva manoeuvre compared to other provocation tests by simultaneous haemodynamic measurements of the right and left atrial pressure.

Methods: Fifty patients underwent Swan-Ganz catheterization. Right atrial pressure and pulmonal capillary wedge pressure, which corresponds to the left atrial pressure, were measured simultaneously. The following manoeuvres were compared: the Valsalva manoeuvre, coughing, deep inspiration and expiration pressures of 20 mmHg, 40 mmHg and 60 mmHg. The main objective of our study was to compare the occurrence of pressure gradients (right atrial pressure > left atrial pressure). For further quantification mean gradients, time duration of pressure overlap, as well as products of mean gradients and overlap time were analysed.

Results: During the Valsalva manoeuvre a significant pressure gradient could be observed in 84% of the patients, followed by an expiration pressure of 60 mmHg (82%), inspiration (78%), expiration pressure of 40 mmHg (76%), coughing (75%) and an expiration pressure of 20 mmHg (62%). Comparing the mean gradients and the products of mean gradients and overlap time duration during the different manoeuvres, we could detect the significantly best results with the Valsalva manoeuvre.

Conclusions: The Valsalva manoeuvre might be the most effective test to provoke a right-to-left atrial shunt for the detection of a PFO during echocardiographic examinations.

Key Words: persistent foramen ovale; haemodynamic; echocardiography.

Introduction

Transoesophageal echocardiography (TEE) has gained widespread acceptance as part of the diagnostic evaluation of patients with cerebral ischaemia. Numerous studies have demonstrated the value of TEE for the detection of a patent foramen ovale (PFO) as a possible cardiac cause of cerebral ischaemia[1-6]. The incidence of a PFO is reported to be higher in patients with unexplained cerebral ischaemia than in patients with pre-existing cardiac or cerebrovascular risk factors, such as atrial fibrillation, hypertension or carotid artery...
stenosis. The clinical decision to anticoagulate a patient with unexplained cerebral ischaemia and a documented PFO is made by grading the PFO by contrast TEE. Patients with larger shunts (more than 20 microbubbles of contrast passing between the atria within three cardiac cycles) should be anticoagulated, while patients with smaller shunts are recommended to be followed conservatively. In view of this treatment approach, a more detailed approach for quantification of the exact degree of the interatrial shunt seems to be necessary to guide this important therapeutic decision. Different manoeuvres have been used to provoke a right-to-left shunt during contrast TEE, and are discussed controversially. All of these studies were done during TEE procedures without invasive haemodynamic control.

The aim of this study was to evaluate the most effective manoeuvre to provoke a right-to-left pressure gradient using simultaneous invasive measurements of the right and left atrial pressure.

**Methods**

**Patients**

This prospective clinical study consisted of 50 consecutive patients (32 male and 18 female; range 25–80 years). All patients underwent diagnostic left and right heart catheterization. The indications were as follows: (i) coronary heart disease; (ii) dyspnoea of unknown cause; (iii) reduced left ventricular function; and (iv) valvular heart disease. Informed written consent for heart catheterization and participation in the study was obtained from all patients. The study protocol was approved by the appropriate institutional ethical committee.

Exclusion criteria were: (i) elevated pulmonary capillary wedge pressure (PCWP) (mean pressure >12 mmHg); (ii) elevated right atrial pressure (RAP) (mean pressure >10 mmHg); (iii) strong sedation; (iv) dementia; (v) critically ill patients.

An additional group of five patients was investigated with and without simultaneous transoesophageal echocardiography (TEE). The Valsalva manoeuvre and coughing as provocation manoeuvres were tested in these patients for the detection of a right-to-left shunt.

**Catheterization**

For right heart catheterization, 7 French Swan-Ganz catheters (Baxter, Irvine, CA, U.S.A.) were positioned in a pulmonary capillary wedge position. Two transducer systems were attached to the proximal and distal port of the catheter. RAP and PCWP, which corresponds to left atrial pressure, were measured simultaneously. The pressure curves were recorded digitally and on paper (Siemens Cathecor). Additionally, continuous electrocardiographic recording and measurement of heart frequency were performed. A slight sedation with 3 mg Diazepam i.v. was performed by all patients before the procedure.

**Provocation Manoeuvres**

Simultaneous measurement of PCWP and RAP was done during the following provocation tests: the Valsalva manoeuvre, coughing, deep inspiration and defined expiration pressures of 20 mmHg, 40 mmHg and 60 mmHg. To perform the defined expiration tests a modified pressometer using a mouthpiece providing a extra large scale was applied. The patients were requested to perform each manoeuvre twice and the best of the two pressure diagrams was analysed.

**Analysis of Pressure Gradients**

The pressure diagrams of PCWP and RAP were analysed regarding the pressure gradient. The occurrence of RAP elevation above PCWP before, during and at the end of each manoeuvre were evaluated. For quantification the mean gradients, the time of the pressure overlap, and the product of mean gradients and overlap time were analysed.

**Statistical Analysis**

All data were expressed as mean values ± SD and compared by the Wilcoxon sign-rank test. A P-value of less than 0·05 was considered to be statistically significant. The occurrence of pressure gradients were compared using the McNemar test.

**Results**

To evaluate the most effective manoeuvre the occurrence of pressure gradients (RAP>PCWP), the mean gradients, and the products of mean gradients and overlap time were compared.

**Occurrence of Pressure Gradients (RAP>PCWP)**

During Valsalva manoeuvre a pressure gradient could be observed in 84%, followed by an expiration pressure of 60 mmHg (82%), inspiration (78%), an expiration pressure of 40 mmHg (76%), coughing (75%), and an expiration pressure of 20 mmHg (62%) (Fig. 1). The Valsalva manoeuvre was significantly better than the expiration test using a pressure of 20 mmHg (P<0·001).

**Mean Gradients**

Using the different manoeuvres the following mean gradients were documented: with the Valsalva
manoeuvre the mean gradient was $8.8 \pm 6.8$ mmHg. coughing caused a mean gradient of $6.4 \pm 3.6$ mmHg, an expiration pressure of 60 mmHg induced a mean gradient $6.1 \pm 4.4$ mmHg, an expiration pressure of 40 mmHg a mean gradient of $6.1 \pm 4.6$ mmHg, expiration pressure of 20 mmHg a mean gradient of $5.8 \pm 2.9$ mmHg and inspiration a mean gradient of $5.8 \pm 3.6$ mmHg. Comparing the manoeuvres by pairs, the significantly best results were documented using the Valsalva manoeuvre compared to coughing ($P=0.01$), an expiration pressure of 20 mmHg ($P=0.027$), an expiration pressure of 40 mmHg ($P=0.013$) and an expiration pressure of 60 mmHg ($P=0.043$) (Wilcoxon-sign-rank-test) (Fig. 2).

**Product of Mean Gradients and Manoeuvre Time**

The calculation of the product of mean gradients and manoeuvre time gave the following results: Valsalva manoeuvre $28.0 \pm 41$ mmHg . sec, expiration pressure of 60 mmHg $12.0 \pm 20.5$ mmHg . sec, inspiration $10.7 \pm 10.3$ mmHg, expiration pressure of 40 mmHg $10.4 \pm 14.4$ mmHg . sec, expiration pressure of 20 mmHg $8.9 \pm 11.0$ mmHg . sec and coughing $5.5 \pm 4.7$ mmHg . sec. Significant differences were found between the Valsalva manoeuvre and coughing ($P<0.001$), the Valsalva manoeuvre and expiration pressure of 20 mmHg ($P=0.007$) and between the Valsalva manoeuvre and expiration pressure of 40 mmHg ($P=0.028$). Significant differences between the Valsalva manoeuvre and expiration pressure of 60 mmHg and between the Valsalva manoeuvre and deep inspiration were not observed (Wilcoxon-sign-rank-test) (Fig. 3).

**Measurements With and Without Simultaneous TEE**

**Occurrence of pressure gradients**

During the Valsalva manoeuvre a pressure gradient without a simultaneous TEE examination could be observed in all five patients, and in four patients with simultaneous TEE examination, respectively. Coughing caused a pressure gradient in four patients without TEE and in three patients with TEE examination.

**Mean gradients**

The mean gradients during the Valsalva manoeuvre were: $12.1 \pm 3.1$ mmHg (without TEE), $7.8 \pm 5.8$ mmHg (with TEE). Coughing caused a mean gradient of $7.2 \pm 3.8$ mmHg (without TEE) and $6.1 \pm 3.1$ mmHg (with TEE).

**Product of mean gradients and manoeuvre time**

Using the Valsalva manoeuvre the product of mean gradients and manoeuvre time was calculated as $34.2 \pm 28$ mmHg . sec (without TEE) and as $21.0 \pm 25$ mmHg . sec (with TEE). The product of mean gradients and manoeuvre time during coughing were $6.8 \pm 2.2$ mmHg . sec (without TEE) and $5.7 \pm 2.8$ mmHg . sec (with TEE).

**Discussion**

About 20% of stroke patients are believed to have experienced cardiac embolism$^{[19]}$. Several studies have
shown that the incidence of a PFO is increased in patients with an otherwise unexplained cerebral ischaemia\textsuperscript{6–11}. Likewise, it was shown that a severe contrast shunting from the right to the left atrium during TEE and a wide opening of the PFO during provocation manoeuvres could be identified as a cause of paradoxical embolism\textsuperscript{10,14,19}. In clinical routine practice, different manoeuvres are used to provoke contrast shunting during TEE examinations. The reliability and overall value of these different manoeuvres are controversially discussed\textsuperscript{15–17}. However, the optimal mode of provocation testing to induce interatrial shunting which can be subsequently detected by contrast echocardiography has not been sufficiently investigated. To evaluate the most effective manoeuvre for provocation of a sufficient right to left atrial gradient, we compared different procedures using invasive haemodynamic measurements.

The essential result of our study is that the Valsalva manoeuvre as well as an expiration pressure of 60 mmHg are more effective for provocation of a right to left atrial shunt than cough, deep inspiration or expiration pressures of 20 mmHg and 40 mmHg.

The results are in accordance with the findings of Zanette \textit{et al.}, who compared the timing of contrast agent injection and the incidence of right to left atrial shunting during Valsalva manoeuvre and cough under transcranial doppler (TCD) control\textsuperscript{16}. Zanette \textit{et al.} concluded that the Valsalva manoeuvre with injection of a contrast agent before the provocation test is more effective than cough. On the other hand, Stoddard \textit{et al.} declared the cough test superior to the Valsalva manoeuvre for detection of a PFO during contrast TEE\textsuperscript{15}. A possible explanation for these controversial results might be that patients under sedation perform the cough test easier than a Valsalva manoeuvre, which is also in accordance with Dubourg \textit{et al.}, who demonstrated a higher sensitivity for the cough test as compared to the Valsalva manoeuvre to induce a right-to-left shunt\textsuperscript{17}.

The value of an optimal performance of the Valsalva manoeuvre with provocation of high intrathoracic

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\textbf{Figure 4.} Example of Valsalva manoeuvre.

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pressures was demonstrated by Droste et al. in 1999. In this study, TEE and TCD were compared for the detection of a right to left shunt during the Valsalva manoeuvre, standardized Valsalva manoeuvre and coughing. The best results were obtained using the Valsalva manoeuvre\[20\]. Further investigations showed, however, due to the better co-operation of patients without sedation, that TCD could identify minimal shunts missed by TEE\[21,22\]. The results of our study in five additional patients are in accordance with these observations. Patients with strong sedation during TEE examination were limited to perform the Valsalva manoeuvre or coughing adequately, as compared to these without simultaneous TEE examination and sedation.

Another promising method for the detection of right to left atrial shunts is transthoracic contrast echocardiography using second harmonic imaging. Second harmonic imaging is a new modality that enhances the visualization of echocardiographic contrast agents. In contrast to examinations using fundamental imaging, preliminary results suggest that this new technique has nearly the same sensitivity as TEE\[23\].

The haemodynamic pressure diagrams of our study showed an increase of RAP and PCWP at the beginning of the Valsalva manoeuvre, which is caused by an increase of intrathoracic pressure. During maximal pressure the curves showed a plateau and the RAP was nearly equal or slightly higher than PCWP. When the valsalva strain was released, the venous blood reflux to the heart caused a relevant increase of RAP compared to PCWP. These findings are comparable to former physiological studies (Fig. 4)\[24,25\]. At this interval the Valsalva manoeuvre showed the highest product of mean gradient and overlap time and was significantly better for provocation of a right-to-left shunt as compared with the other investigated provocation tests.

The cough test causes a lower incidence of RAP to PCWP gradients and a significantly lower product of mean gradient and overlap time than the Valsalva manoeuvre. The diagrams showed a short and sharp increase of RAP and PCWP. If an elevation of RAP over PCWP could be observed, the overlap time was short and the mean gradient was lower compared to the Valsalva manoeuvre.

The frequency of right-to-left pressure gradients and the mean gradients during deep inspiration were significantly less than during the Valsalva manoeuvre. A significant difference between deep inspiration compared to cough could not be observed.

The other tested provocation manoeuvres of expiration pressures of 20 mmHg and 40 mmHg showed highly significant lower products of mean gradients and overlap time, and only a minor occurrence of right-to-left pressure gradients. These results suggest that the Valsalva manoeuvre, when performed under optimal conditions with patients who could perform the manoeuvre adequately, is the most sensitive method for detection of right-to-left atrial shunting via a patent foramen ovale.

Limitations of the Study

The study was performed in the Catheter Laboratory under optimal conditions. Only slightly sedated patients, who could perform the different provocation manoeuvres accurately, were included. A TEE to simulate routine conditions of TEE examinations was not simultaneously performed in the majority of patients. During TEE examinations the patients are often heavily sedated and are not able to perform the provocation manoeuvres accurately. These difficulties were confirmed in the group of patients who underwent diagnostic heart catheterization and TEE examination simultaneously. However, in these patients also the Valsalva manoeuvre was the most effective manoeuvre for provocation of a right-to-left atrial pressure gradient.

Conclusion

From these haemodynamic results, we conclude that the Valsalva manoeuvre is the most effective provocation procedure for the induction of a right-to-left pressure gradient, detection and the exact grading of a PFO during echocardiographic examinations.

References


