Patent Foramen Ovale: the End is in Sight

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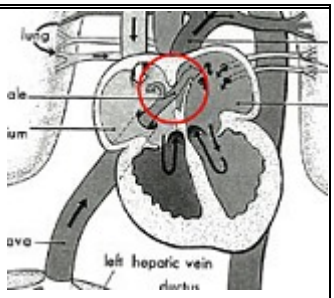
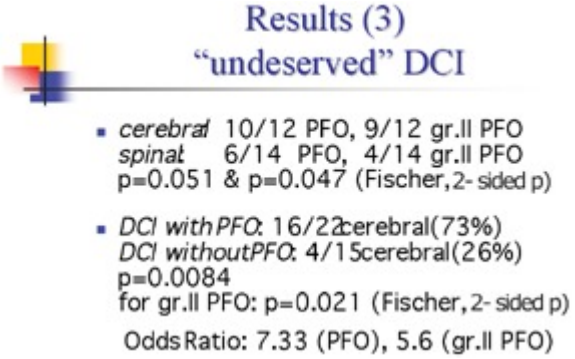
By Prof Costantino Balestra, DAN Europe Vice President Research and Education

Since 1989 with DAN America's first publication that spoke about the possible correlation between the presence of a Patent Foramen Ovale and the occurrence of decompression sickness (Moon, Camoresi et al) there has been no respite in the quest for the truth about the possibility of such a relationship. Since 1996 the research department of DAN Europe set out to investigate and respond to a serious concern at the time as a result of this alarming article: is there really an increased risk of DCS for a diver who has PFO?
The problem was not as simple as it might have seemed, because it's not enough to investigate those divers who have had history of DCS in order to see if there is a higher prevalence of PFO than in the average population. This technique is that of the retrospective study.
The problem with retrospective study is that it can't give an idea of the relative risk associated with PFO because the only population studied is that of divers who have had a history of DCS; this means that we don't know how many divers without PFO did not have accidents. This is a population bias (as scientists call it) and means that the results cannot be considered as an evaluation of the risk of DCS for those divers who have PFO.

Another possible option is to use "matched pairs", which gives a better statistical quality to the results of a retrospective population yet still does not ensure a conclusive assessment of the related risk.

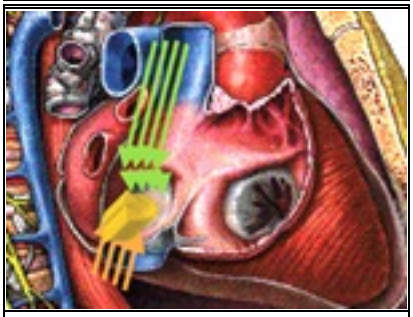


The "Matched Pairs" study



A group of 37 divers who suffered from DCS was analysed in order to see whether they had PFO by using the most effective technique: the transesophageal echocardiography. Divers were matched on the basis of criteria such as age, weight, sex, smoking habits, etc. Those who had never suffered decompression sickness underwent the same standardised echocardiography analysis . The incidence of cerebral DCS was greater among those who had PFO. This still does not mean that the presence of PFO is the cause of incidents but rather that it is a potential risk. The cause is always bubbles! Looking at the results of the other studies as Bore did in his meta-analysis we can see that the methodologies for evaluating PFO are not standardised. That is that the authors are not all in agreement on the method of application of the echocardiograph. All this does makes it difficult to obtain data that is easily comparable. We are therefore interested in the methodology and the biochemistry of the opening of the PFO.

How does the PFO open to let the bubbles pass?

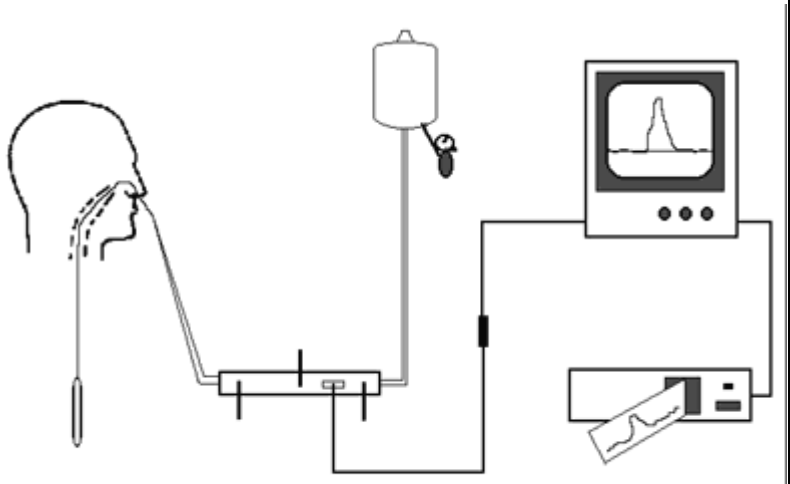


The decompression bubbles are found primarily in the veins; in the heart they are mainly found in the superior and inferior vena cava. Frequently, divers regard PFO as a hole that allows the continual passage between the right atrium and the left - the arterial part of the heart where we don't want to see bubbles (see the illustration). The flow coming from superior vena cava has to pass over a fold, providently given by Nature before touching the PFO (or the fossa Ovalis) This causes a sudden increase in the rate of the flow which meets the flow coming from the inferior vena cava and thus turbulence is caused which causes the bubbles to be TAKEN AWAY from the interatrial septum. Therefore if we understand correctly, the bubbles would not cross the Foramen Ovale in natural conditions. But then why the injections of bubbles that are made during the transesophageal echocardiogram to measure the PFO, since they pass in the left atrium? The reason is that respiratory movements are made to reverse the intracardiac flow caused by variations in the intrathoracic pressure.

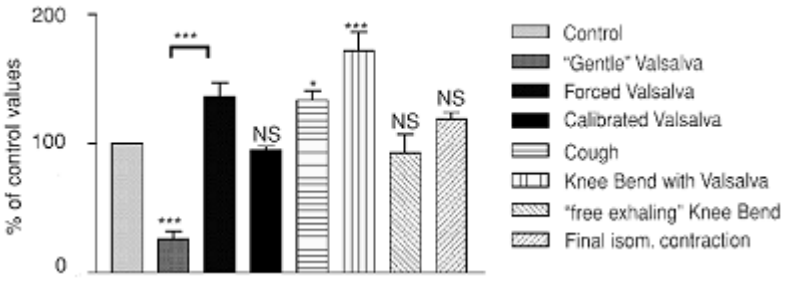
Variations in Intrathoracic Pressure

To see how the PFO opens we asked 15 volunteer divers to do a little test with a balloon catheter inserted in the oesophagus . After having asked them to use the maximum effort with the muscles of the chest, the pressure exerted on the oesophagus and hence on the thoracic cavity was measured and various manoeuvres

were carried out to increase the intrathoracic pressure.



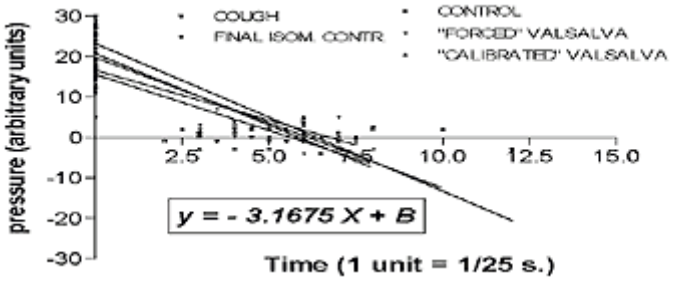
But you ask, why is the increase in pressure connected to the opening of the PFO? In fact it is not directly the increase but rather the release of pressure that opens the PFO. Lets explain. When we create a force that causes the intrathoracic pressure to rise the flow of the venous blood into the thoracic cavity is obstructed or slowed down since the blood always flows towards the lowest pressure (pressure gradient). This "blocked" blood outside of the thorax enters forcefully into the right atrium after the RELEASE of the intrathoracic pressure; the PFO opens in the direction right-left and therefore it can open during this increased flow coming from the right.



We have therefore verified that the variation of pressure is measurable and established the amount of pressure that can open the PFO. In the graph 100% equal to the pressure allows significant variations in intrathoracic pressure, the other measures are standardised methods such as the "valsalva" manoeuvre while diving to equalise the ears, a cough, an isometric chest contraction etc. One of the first measures is that of observing the pressure difference between the Valsalva manoeuvre to equalise the ears and the forced Valsalva manoeuvre. The difference is very significant and this shows that the usual diver's manoeuvre should not open the PFO. In any case you say, the problem could arise during decompression, during the ascent and hence that techniques for increasing

intrathoracic pressure do not exist. It is true however that divers have always been advised to avoid strain after diving. To see whether reaching high pressure level means having a greater release speed and thus making the person potentially more prone to the opening of the PFO, we measured it.

To measure the speed, we have to check verify the variations in pressure in a given time. This means mathematically making a regression and calculating the angular coefficient of the line.



After having measured this line, the statistical difference between their slopes can also be measured and we can find out if one speed is effectively different than the others. The results demonstrate that there are not any statistical differences between the speeds; this means that if the intrathoracic pressure is high enough, the speed of release is equal regardless of the manoeuvre. This shows that the important parameters as regards the reversal of the intracardiac flow after the release of pressure is foremost the time during which the pressure is sustained. In a few words, it is NOT so much the PRESSURE but rather the TIME that the pressure is sustained that is important. For example, divers with PFO should avoid orally-inflating the BCD on the surface or getting into the boat with full equipment to avoid prolonged strain (4 or 5 seconds). Another interesting aspect of this study is that of understanding that in published studies, the respiratory provocative manoeuvres for opening of the PFO are often too short and therefore lead to often measuring the PFO as being small because although bubbles are passed, in reality with a more prolonged manoeuvre, much more bubbles would pass and the PFO would be considered big , . This is excellent news because it demonstrates that in the population of divers there are much bigger PFO than was thought therefore that the morbidity or the risk is not as big as had been thought in view of the size of the PFO!! Now that we understand the dynamics of the opening o the PFO as well as how the bubbles pass we can turn our attention to another question: what its the prevalence of cerebral spots in divers who have PFO?

Spots on the brain and PFO

A number of years ago some studies declared the relationship between PFO and cerebral "LESIONS" . Since then others have found that there was not a direct relationship . In all of these studies, however, we encounter the same population bias that we mentioned earlier. DAN therefore asked two groups of people to sit a test of nuclear magnetic cerebral resonance imaging; 50 were divers and 50 were non-divers. All of the participants had to be under 41 years old because according to studies spontaneous lesions cerebral can occur after 45 years. The distinguishing feature was that this population was randomised; we asked 400 volunteers: 200 divers and 20 non-divers. We asked the divers to declare that they had never suffered from DCS. However, often certain accidents and cerebral incidences in particular were not declared because of benign or brief symptoms. How many of you had have felt a little dazed after a dive ...which goes away after a few minutes ... a case of badly equalised ears or a transient cerebral bubble?

To avoid this situation of poor choice of population we took the case of 1 diver in 4.

Then we made a comparison between the numbers and the size of the "spots" found among the divers and those found among the divers and non-divers.

A little more spots were detected among the divers but there was not significantly more. This is contrary to what some authors say with populations that are not randomised and without a control group. Also, to ensure accuracy in the results a particular imaging filter which allows a reliable diagnosis of the FLAIR sequence to be made was used. Another pitfall that was present was the possibility of finding naturally lacunar zones known as the Wirchow-Robin spaces and diagnosing them as "LESIONS".

The current conclusion does not demonstrate a higher prevalence of "cerebral spots" in the diving population even if they are bearers of PFO. But another question then, are these spots really of vascular origin or are they simply present without having any correlation with the arterial vascular bubbles of vascular origin that could come from the PFO? In order to certain, autopsies would have to be carried out on the bodies of divers, which poses a small ethical problem. But there is another way: fractal analysis.

Fractal analysis of cerebral images

DAN is conducting a study with the possibilities of current mathematical analysis. We have all heard of fractals but we don’t hear so much about fractal analysis. Nature has a mathematical signature of spatial distribution. This

signature is the fractal dimension when this dimension is not compatible anymore with the norm of the tissue a lesion can exist as for example in cancer, or osteoporosis problems or when the size of a spot is compatible with the size of cerebral vascularisation the spot can be considered as being of vascular origin which calls upon the strange feature of fractals: the self-similarity. This work by DAN is underway and as you can see in the references we are using the most advanced techniques of modern research.

Another question that arises with the Patent Foramen Ovale is that this anatomic situation can vary over the years or during diving activities.

Does diving open the PFO?

In Hagen's autopsy study, the prevalence of PFO in bodies was measured. It was found that the big PFO are found in older people . Is this because of age, strength or just simply a statistical accident? We wanted to answer the question of whether diving combined with the increase in pressure in the right atrium could gradually open the FO and transform it into PFO. As we have understood to ensure that the question is answered, a standardised technique for measuring the PFO is required, preferably made by the same investigators some years after the initial analysis. We conducted this research in 2002 with divers who had participated in the first phase in 1996-1997. After having found most of the participants we conducted the evaluation of PFO with the same doctors and the same doctors and the same standardised techniques of respiratory provocative manoeuvres. The results show a change in the PFO but also a case in which the PFO had closed itself spontaneously...but the person had stopped diving.

At present we cannot conclusively say that the PFO cannot be opened by diving or indeed other activities such as playing the trumpet or the saxophone.

Can we define the risk related to PFO in the pursuit of underwater activities?

Currently, the answer is NO. Since we have already understood, the risk is not in direct relation and it seems to be smaller than was thought. To give a definitive reply to the final question we need a prospective study to evaluate the relative risk of PFO. DAN has set up research in which anyone can participate and enrol in. It is a multi-centred international study to investigate PFO in divers with a method that is minimally invasive that is validated by DAN: a carotid Doppler (see the image). It is a system that is has also been adopted by NASA, thanks to DAN

Europe).

In order to be ensure statistical validity, we need at least 4000 volunteer divers to accept. See the web site and participate.

Conclusions

As you can see, arriving at a definitive conclusion to an apparently logical and simple problem is not easy and requires a lot of effort, time, dedication and volunteers...

As a scientific foundation DAN we fund these studies that are beneficial to all with a team of enthusiastic and dedicated scientists in collaboration with several universities, laboratories and hyperbaric centres. As regards the question of the risk of PFO it is clear that the risk is small and that the real risk is not PFO but rather the circulating bubble. DAN is developing the DSL system which allows the analysis of bubbles circulating in the plasma of sport divers and has already produced "bubble safe" algorithms but the research continues...