Should we close small ventricular septal defects?

"I have often said that the sole cause of man's unhappiness is that he does not know how to sit quietly in his room."

As we race each other to close increasingly smaller holes in the catheterization laboratory, we would do well to remember these wise words of Blaise Pascal, a French mathematician, and philosopher who laid the foundation for the modern theory of probability. In this editorial, we aim to look at the existing evidence surrounding the closure of the isolated small ventricular septal defect (VSD), which is typically perimembranous in position in an attempt to rationalize our management strategy in this controversial group of patients. This editorial will not address the issue of aortic valve prolapse, which we believe is a separate subset requiring special consideration.

There remains a great deal of controversy regarding what constitutes a "small" VSD with some authors defining a small VSD as one with a significant gradient across the defect and others using arbitrary VSD size cutoffs.[1] Many operators typically allow their decision-making regarding the need for VSD closure to be guided by the secondary effect of left heart volume loading.

WHAT IS THE PROBABILITY OF SPONTANEOUS CLOSURE OF THE ISOLATED SMALL VENTRICULAR SEPTAL DEFECT?

Reports on the natural history of isolated small VSDs have been published as early as the 1970s with a spontaneous closure rate of 75% in a small cohort of 50 infants followed up for up to 10.5 years.[2] Two further cohort studies (n = 222 and n = 124) of patients with isolated small VSDs followed up for a mean duration of 12 months showed a spontaneous closure rate of 34% at 1 year of age.[3,4] This rate was higher (45%) in patients detected at birth.[3] The proportion of muscular defects that underwent spontaneous closure was higher than perimembranous defects.[3,4] In the cohort of 124 infants, the incidence of spontaneous closure was found to increase to 67% at 5 years of age.[4] A retrospective review of 882 patients with isolated VSD of which 77% were asymptomatic, small defects showed that 40% of the small defects closed spontaneously during a mean follow-up of 9.5 years.[5]

Serial annual evaluation of 106 older children with isolated VSD from a mean age of 8.6 years to a mean age of 16.6 years showed spontaneous closure of the defect in 24 children and a significant decrease in mean defect diameter from 5.3 to 2.7 mm indicating that there remains a significant chance of spontaneous closure and decrease in defect size even into adolescence.[6]

There is a substantial body of evidence that suggests a significant rate of spontaneous closure and further restriction of small VSDs, which extends into late childhood and early adolescence. This would favor delaying closure of small VSDs till adolescence or early adulthood (if the pulmonary artery pressures are within normal limits) giving the patient the best chance of spontaneous closure and an opportunity to participate in the decision-making regarding whether they would like to have their small VSD closed.

WHAT IS THE COURSE AND SIGNIFICANCE OF LEFT VENTRICULAR DILATATION IN PATIENTS WITH A SMALL VENTRICULAR SEPTAL DEFECT?

Small VSDs are generally considered "significant" warranting closure if they are associated with left heart volume loading. There are several important practical considerations related to the estimation of left heart volume loading that need to be emphasized. First, how do we define left ventricular (LV) volume loading in our routine clinical practice? Ideally, we should use body surface area (BSA) adjusted LV dimension charts or Z-scores to determine if the LV is volume loaded rather than a subjective visual assessment or non-BSA adjusted cutoff for LV dimension. Second, how do we determine whether LV dilation is a reflection of a "previously" large shunt that is improving or an indication of sustained and/or increasing left heart volume loading at the time of assessment? The only way to perhaps determine this would be to obtain serial measurements over time accounting for changes in BSA.

The study by Baumgartner's group[7] looking at 229 patients who presented in the GUCH clinic with a small VSD that was thought to not require closure during childhood found most of them to have a normal (89%) or borderline LV dimension implying that perhaps the LV dilation noted during childhood would improve and normalize during adulthood. Another study published in 2010 included 220 patients aged 16 years or over with a restrictive perimembranous VSD and showed an increase in the ejection fraction and decrease in the LV end systolic dimension over a median study period of 6 years.[8]

A recent study by Karonis *et al.* that looked at 231 patients aged ≥16 years with an isolated VSD reported increased LV dimension (in 21%) and decreased LV function (in 6%) in a proportion of these patients.[9] In this study, only 164 of the 231 patients were included in the final echo assessment raising the possibility of selection bias and overestimation of the problem. However, the study does raise concerns regarding the long-term outcome of patients with a small VSD. Large registry studies of patients with small VSDs have consistently shown low mortality, excellent quality of life and functional status raising into question the significance of left heart dilatation on the long-term outcome of these patients.[10-12]

Most available evidence suggests that there is a tendency for left heart dilation to improve with time in patients with small restrictive VSDs. Furthermore, there is no clear evidence in literature linking left heart dilation with adverse clinical outcomes like death or hospitalization in this group of patients. Although some studies have shown a higher incidence of sudden death and serious arrhythmia in patients with small VSDs[12] this has not been borne out in other large population-based registries. Furthermore, there is no existing literature that clearly demonstrates that closing the VSD eliminates this risk of arrhythmia and/or sudden death. Larger, prospective studies are needed to ascertain the clinical impact of left heart volume loading on outcomes and the threshold for intervention in this group of patients.

WHAT IS THE INCIDENCE OF INFECTIVE ENDOCARDITIS IN PATIENTS WITH ISOLATED VENTRICULAR SEPTAL DEFECT?

One of the important reasons cited for closing even hemodynamically insignificant VSDs is the risk of infective endocarditis. In a retrospective series of 882 patients with isolated VSD, five patients (0.5%) developed infective endocarditis.[5] Baumgartner's group ($n = 229$) reported an incidence of infective endocarditis of 1.8% in patients aged 16 years and over which is similar to the data presented by the Belgian registry on Adult Congenital Heart Disease.[11] A large registry cohort of 3495 children from Norway with an isolated VSD showed a low incidence of infective endocarditis of 0.9% (0.1 per 1000 person-years).[10] The Swedish registry of 779 patients with VSDs showed an overall incidence of infective endocarditis of 2% (1.7–2.7/1000 patient-years in unoperated patients) which although low was higher than normal population.[13] Somewhat different is the data published by the Karonis group which reported an incidence of 23% which seems exceptionally high and out of keeping with the rest of the published literature.[9] This study, however, is not population based and refers to a preselected group of patients attending the GUCH service.

In addition to reports of infective endocarditis in untreated VSDs, there are several case reports of infective endocarditis following both surgical and transcatheter closure of VSDs.[14-17] A study of 125 patients with isolated VSD who were followed up for a mean of 15 years showed no statistical difference in the incidence of bacterial endocarditis between the untreated patients (4.3%) and those that were surgically closed (2.7%) although the sample size of the study was small.[18] The Swedish registry data also showed an incidence of endocarditis of 1.2% in patients who had undergone surgery for VSD versus an overall incidence of 2% in the entire group. All of these patients, however, had additional aortic valve issues (1 bicuspid aortic valve, 2 postaortic valve replacement) and required reoperation.[13] Even if there is a benefit in terms of reduced incidence of endocarditis, it would be important to determine the number needed to treat, i.e., how many small VSDs will need to be closed to prevent a single episode of endocarditis? Given the higher complication rate during and following device closure of VSD (as compared to a patent arterial duct), does this benefit outweigh the incremental risk?

Closing a VSD, therefore, does not seem to abolish the risk of endocarditis, which is anyway quite low in a population setting. Perhaps advice regarding dental hygiene would have a greater impact in reducing infective endocarditis than device closure.

IS IT JUSTIFIABLE TO CLOSE A SMALL VENTRICULAR SEPTAL DEFECT SIMPLY BECAUSE A CARDIAC MURMUR WOULD COME IN THE WAY OF PROSPECTIVE EMPLOYMENT?

Problems in seeking employment particularly in the military services due to a cardiac murmur are sometimes cited as a reason to device close otherwise small, insignificant VSDs. Published literature reveals a significant incidence of arrhythmia following VSD device closure requiring long-term follow-up and sometimes re-intervention.[19,20] Furthermore, complications such as late aortic cusp perforation and worsening aortic regurgitation [Video 1] have been variously reported making regular follow-up mandatory for these patients.[21] In comparison, an isolated, small, restrictive VSD may carry less morbidity and require less stringent follow-up.[10]

Are we not replacing one disease with another by closing a small VSD with no clinical indication for device closure apart from a murmur? We may eliminate the murmur but in fact accentuate the need for long-term monitoring with the possibility of needing repeat interventions to deal with iatrogenic complications.

WHO FOOTS THE BILL?

The cost implications of carrying out procedures without clearly proven benefit must also be borne in mind. Not only resource-limited countries like India but also so-called advanced western societies are demanding more efficient utilization of limited health-care resources. The economic impact of admission for cardiac procedures on the average Indian family is significant[22] and families often raise money for procedures by selling assets or taking loans, which further weakens their economic standing. As a nation, we are yet to achieve our Millennium Development Goals in several states, and it is essential that central and state governmental healthcare funding is utilized judiciously bearing in mind the overall health and well-being of the nation.

With the unregulated and widespread use of transcatheter intervention to close small, restrictive mainly perimembranous VSDs we enter unchartered territory, which is unsubstantiated by clinical evidence. Published literature is filled with several reports of complications of device closure of VSDs, yet most papers conclude that the risks and complications are within acceptable limits. If a procedure is performed without clear indication, no risk however small is acceptable. "Primum nonnocere" or "first, do no harm" has been famously attributed to being a part of the Hippocratic Oath but although it was written by Hippocrates (in a slightly different form) it forms part of a different work called "Of the Epidemic." It is, however, a reminder that we need robust research to help us understand better the balance of risk and benefit for the treatments that we recommend to our patients.

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