Closing the Ventricular Septal Defect Because You Can: Evidence-Averse Care?

"What this patient needs is a doctor."—Eugene A. Stead, Jr, MD

A central tenet of evidence-based care is that data show the consequences of therapy to be preferable to the natural history of the disease. Translated, this means that before we insert a surgical knife or other foreign-body into a child's heart, we must require evidence that treatment outcomes are preferable to the defect's natural history. Of course, ventricular septal defect (VSD) closure is warranted for an infant with a large VSD and congestive failure or pulmonary hypertension; the unkind natural history of a large VSD is known with certainty. However, what treatment, if any, is best for the child with a moderate VSD and left ventricular (LV) volume overload, but who has no symptoms or pulmonary hypertension? Should we close that VSD because we can? Are there data to support that course of action?

In this issue of *The Journal*, Kleinman et al[1] provide valuable natural history data to help answer these questions and to inform our future therapeutic decisions. They observed 70 children with a moderate VSD (mean age at inclusion, 4.9 years), most of which were perimembranous in type, for an average of 7.3 years. All children had an initial LV end-diastolic (LVED) Z-score exceeding +1, and none had congestive heart failure, pulmonary artery hypertension, or an associated defect (eg, subaortic stenosis or aortic cusp prolapse) that might require surgery. In the group of 70 children, substantial improvement in LVED Z-scores was documented with serial follow-up echocardiograms. Of more interest are the data reported in the subgroup of 33 children whose initial LVED Z-scores exceeded +2. During a 7.8-year follow-up period, the mean LVED Z-score for these children decreased from +3.0 to +1.2, a spontaneous 60% improvement. Indices of LV systolic and diastolic function remained normal in every child during the follow-up period. The authors conclude that children with a pressure-restrictive VSD and LV volume overload who have no symptoms should be observed conservatively and don't require intervention unless serial studies document an increasing LVED Z-score with time (which is uncommon).

LV	Left ventricular
LVED	Left ventricular end-diastolic
VSD	Ventricular septal defect

These natural history data could not have arrived at a better time. Soon, transcatheter VSD closure devices will become widely available in the United States, and interventional cardiologists will benefit from data to help guide their therapeutic decisions. A review of the published VSD device trials suggests that cardiologists badly need guidance right now. The Table summarizes pertinent clinical data from all 11 English-language publications reporting transcatheter closure of a perimembranous VSD in ≥10 patients. In these series, the majority of patients had a closure device implanted to treat a small-moderate, pressure-restrictive VSD; most patients were treated for a Qp/Qs ratio <2 (the traditional definition of a small shunt). Few patients in these reports had symptoms, congestive heart failure, or pulmonary hypertension, which would have provided conventional clinical indications for VSD closure. Presumably these device implants occurred with the scrutiny and approval of local investigational review boards or their equivalent, but it is difficult to understand what the justification was for closing the smaller defects.

Transcatheter VSD closure devices promise an exciting, revolutionary approach to the treatment of patients with a clinically important VSD. Defects can be closed without a sternotomy, without the need for cardiopulmonary bypass, and with a relatively short recovery time and hospital length of stay. However, transcatheter VSD closure procedures do carry some risks. The reports cited in the Table describe an assortment of adverse events, including device embolization, heart block, aortic valve insufficiency, injury to the tricuspid valve, and transient hemolysis. It is essential, therefore, that cardiologists carefully weigh the procedural risks against the known natural history of an untreated VSD. In children with a pressure-restrictive VSD who have no symptoms, the data support thoughtful follow-up and withholding of intervention in most cases. Before the report by Kleinman et al,[1] one might have described

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Table. All English-language publications reporting transcatheter closure of a perimembranous ventricular septal defect in 10 or more patients

Year	Author	N	Age range (years)	Qp/Qs Shunt		
				Median	Mean	Range
2006	Fu[2]	35	1-54	1.8	*	1-4
2006	Pinto[3]	20	5-21	*	1.7	*
2005	Anil[4]	26	3-23	2.0	1.9	1.2-3.0
2005	Carminati[5]	87	0.5-64.0	*	2.1	1.3-4.0
2005	Pawelec-Wojtalik[6]	11	0.8-18.0	1.6	1.7	1.5-2.3
2004	Pedra[7]	10	6-32	1.9	2.2	1.5-5.0
2003	Arora[8]	91	3-33	2.0	2.1	1.4-3.2
2003	Bass[9]	27	1.3-32.0	*	1.6	*
2003	Thanopoulos[10]	10	1.5-12.0	2.0	1.9	1.5-2.4
1999	Kalra[11]	28	5.5-33.0	1.6	1.7	1.4-2.6
1994	Rigby[12]	13	0.1-16.0	4.2	*	all >3.0

N, Number of subjects; *Qp/Qs,* pulmonary to systemic flow ratio.
*Data not available in publication.

transcatheter intervention for a moderate perimembranous VSD as evidence-deficient care. Going forward, it is imperative that the care we provide not become evidence-averse.

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Minimal Risk, Yet Again

The determination that research risks are sufficiently low to justify the exposure of children to such risks absent the prospect of direct benefit is a central component of the additional protections afforded children who are to be enrolled in research.[1,2] The risks of research interventions or procedures lacking a prospect of direct benefit must be restricted to either minimal risk (for all children) or a minor increase over minimal risk (for children with a disease or condition). This restriction on research risk applies to either an entire protocol or to those components of a protocol that lack the prospect of direct benefit, such as the collection of blood for pharmacokinetic sampling or basic research involving tissue specimens. In addition, research that presents no more than minimal risk becomes eligible for such procedural effi-

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