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Patent foramen ovale/atrial septal defect closure and migraine: Searching the rationale for the procedure - Reply

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approximately 0.30 for LVM in the Framingham Heart Study. Analyzing data among hypertensive siblings, the HyperGEN study found that African American subjects had higher sibling correlation in LVM compared with white subjects (11) but that white subjects had a higher correlation in RWT than did African American subjects. However, no heritability was presented in their study.

Unlike most previous studies, we assessed the heritability of LVM after correction by the three most commonly used indices of body size. The estimates of heritability of LVM were not significantly affected by the type of indexing chosen, especially for model 3, with the greatest number of covariates (Table 1). This observation suggests that no single body size index appears preferable in studies on adult populations similar to ours. Adjustment for covariates other than body size, age, and gender had almost no influence on estimates of heritability in models 2 and 3.

More than 40% of our subjects were hypertensive, and 34.5% were taking antihypertensive medication. In our models, adjusting for SBP and antihypertensive medication did not appreciably influence the estimates of heritability after accounting for age, gender, weight, and height. Furthermore, excluding all participants taking antihypertensive medications had little effect on heritability estimations, although it yielded less significant \( p \) values (data not shown). Therefore, the effect of hypertension and antihypertensive medication may not be substantial in our study.

In summary, our study indicated that significant genetic factors influence the familial resemblance of LVM in the Caribbean Hispanic population. The considerable estimates of heritability provide the basis for our long-term goal of NOMAFS to map and detect genetic variants contributing to LVM and its related phenotypes.

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REFERENCES


Letters to the Editor

Patent Foramen Ovale/Atrial Septal Defect Closure and Migraine: Searching the Rationale for the Procedure

Azarbal et al. (1) studied closing patent foramen ovale (PFO) or atrial septal defect (ASD) for prophylaxis of migraine. The accompanying editorial highlights areas of caution (2). Additional concerns are: 1) Both right-to-left shunt (PFO) and left-to-right shunt (ASD) appear associated with migraine (3). 2) Closure of ASD improves left ventricular stroke volume; this physiological variable (3) might be involved in precipitating daily migraines. 3)
Following ASD closure, plasma atrial natriuretic peptide levels would decrease (3). 4) Lateralization of headaches is a characteristic feature of migraine (4). With the concept of paradoxical embolization of gas, thrombi, or vasoactive neuromediators (2), these potential precipitants are presumed to be streamed regularly through the venous system, these chemicals are usually detoxified either through ingestion, or endogenously produced. Passing either entity may permit these chemicals to enter the cerebral circulation in a high concentration and trigger the neurologic constellation that is recognized as a migraine headache. We agree with Dr. Gupta that emboli are unlikely to be the trigger of migraine headaches.

This hypothesis does not explain the mechanism of all migraine headaches. We do not understand why patients who have migraine with aura respond more frequently to PFO closure than do patients who have migraine without aura. These fascinating observations may open more avenues for research that might produce more successful therapeutic options for migraine sufferers than do current medical regimens.

With 12% of the population suffering from migraine headaches, we understand why the observations of reduction in migraine headaches following closure of interatrial shunts may generate interest and controversy. As with any new theory, the observations that support the theory come long before the randomized controlled trial that will test its validity. Our study supports the observations from other independent centers and provides a theoretical construct that "connects the dots" of rather disparate pieces of data. Let us turn the question around. How does one explain these independent observations of decreased headache following PFO closure? Placebo? This is unlikely when five independent centers all describe similar observations. Of the patients with migraine and aura, 75% had complete resolution of their headaches, with some patients followed up to three years. There is no drug or placebo that reports such a dramatic and long-lasting benefit to reduce migraine pain.

Finally, there are valid concerns with implanting a permanent device in someone’s heart, especially when the indication is not life-threatening. We should use the observations of the studies as a starting point to generate a hypothesis and then perform a randomized clinical trial that will assess the potential benefits and

**REFERENCES**