News and Views From the Literature

Patent Foramen Ovale

Incidental Patent Foramen Ovale During Cardiothoracic Surgery: To Repair or Not to Repair?

Reviewed by Quynh A. Truong, MD, MPH,[1] Ana C. Garrido-Castro,[1] Christopher P. Cannon, MD, FACC[2]

[1]Cardiac MR-PET-CT Program, Division of Cardiology and Department of Radiology, Massachusetts General Hospital, Boston, MA
[2]TIMI Study Group, Cardiovascular Division, Brigham and Women's Hospital, Boston, MA

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Prevalence and Repair of Intraoperatively Diagnosed Patent Foramen Ovale and Association With Perioperative Outcomes and Long-Term Survival

Krasuski RA, Hart SA, Allen D, et al.

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Due to the increasing use of transesophageal echocardiography (TEE) in cardiac surgical operations, there has been an increment in incidental detection of patent foramen ovale (PFO) over the past decade. Although the presence of both PFO and atrial septal aneurysm places patients with prior ischemic stroke at substantial risk for recurrent stroke despite medical therapy with aspirin, those with isolated PFO are not at higher risk for recurrent strokes.[1] In addition, there are no completed randomized clinical trials to determine the optimal treatment of incidental PFO, especially those found intraoperatively. Thus, Krasuski and colleagues sought to determine the prevalence of intraoperatively diagnosed PFO and its association to perioperative outcomes and long-term mortality.[2]

In this single-center retrospective study conducted by the Cleveland Clinic (Cleveland, OH), the authors reviewed 41,578 cardiothoracic (CT) surgeries performed from 1995 to 2006. Of these CT surgeries, 14,165 (34%) had available pre- and postoperative TEE. A total of 1073 were excluded from the study; 1046 were due to preoperatively diagnosed PFO or atrial septal defect (ASD) and 27 were due to postoperative ASD with no preoperative ASD (presumed surgical iatrogenic). The remaining 13,092 had no history of PFO or ASD, of which 3236 (25%) were only coronary artery bypass grafts (CABG), 3679 (28%) were only valve procedures, 2312 (18%) were CABG plus valve procedures, 553 (4%) were CABG

plus another procedure (coronary and carotid endarterectomy, ventricular aneurysm repair, and other unclassified procedures), 1594 (12%) were valve plus other, 893 (7%) were CABG plus valve plus other, and 825 (8%) were other procedures only. Of these 13,092 CT surgeries, 2277 (17%) were intraoperatively diagnosed with PFO (1638 not repaired, 639 repaired).

A set of predictors of stroke was established including previous stroke or transient ischemic attack (TIA), atrial septal aneurysm, aortic arch atheroma, left atrial dilation, and atrial fibrillation, along with other comorbidities considered potential confounders such as hypertension, diabetes mellitus, smoking, myocardial infarction (MI), peripheral vascular disease, carotid artery disease, chronic obstructive pulmonary disease, and renal disease. Primary outcome was measured as postoperative stroke and all-cause hospital death; secondary outcomes included length of stay from surgery to discharge, length of stay in intensive care units (ICU), and total cardiopulmonary bypass time. Surgical complications such as MI, bleeding, renal failure, septicemia, and circulatory arrest were also considered.

Baseline demographics and risk factors were similar between patients with (n = 2277) and without (n = 10,815) intraoperative PFO, with the exception that patients with PFO were more likely to be older (63.5 ± 13 years vs 62.9 ± 13 years; $P = .03$), have atrial septal aneurysm (5% vs 1%; $P < .001$), were less likely to have left atrial dilation (54% vs 57%; $P < .006$), and had no differences in comorbidities. Of the patients with incidentally diagnosed PFO, 639 (28%) were surgically repaired; 97% of these repairs were surgical closures. Patients who underwent repair (n = 639) were more likely to be women (42% vs 33%; $P < .001$), at a younger age (61.1 ± 14 years vs 64.4 ± 13 years; $P < .001$), undergoing mitral or tricuspid valve surgery (51% vs 32%; $P < .001$), with history of prior TIA or stroke (16% vs 10%; $P < .001$), left atrial dilation (61% vs 51%; $P < .001$), or atrial fibrillation (13% vs 10%; $P = .03$), and had fewer comorbidities (including hypertension, smoking, MI, peripheral vascular disease, and carotid artery disease) than patients who were not repaired (n = 1638). Three surgeons had a greater tendency to repair than the other 10.

The authors used a propensity score with greedy matching technique[3-5] to adjust for differences between patients with intraoperatively diagnosed PFO (n = 2265) and those without PFO (n = 2265), as well as for those who were repaired (n = 603) and those who where not (n = 603), in their analyses of the intraoperative and postoperative outcomes. In comparing patients with or without PFO, the only difference was the amount of time spent on cardiopulmonary bypass (110 ± 46.4 min vs 104 ± 41 min; $P = .001$), with no differences in the primary outcome of stroke or hospital death; secondary outcome of length of stay or ICU stay; or surgical complications, such as MI, bleeding, renal failure, septicemia, and circulatory arrest. When comparing propensity-matched patients with repaired versus unrepaired PFO, patients with repaired PFO had a 2.47-fold increase in odds of having postoperative stroke than those who were unrepaired (2.8% vs 1.2%; $P = .04$), with a trend toward longer time on cardiopulmonary bypass (107 ± 45 min vs 104 ± 45.6 min; $P = .08$). However, there were no differences in hospital death, hospital length of stay, ICU length of stay, or surgical complications. For long-term 10-year survival rates with a median of 5.7 years follow-up, in unadjusted analyses, there was a trend toward better survival rate in patients without PFO than those with PFO (63% vs 60%; log-rank $P = .06$) and improved survival in those with PFO repair than those who were unrepaired (66% vs 59%; log-rank $P = .03$). However, after propensity matching, there was no difference in survival among those with or without PFO (60% vs 65%; log-rank $P = .40$) or those who underwent PFO repair compared with those without repair (67% vs 63%; log-rank $P = .12$).

The authors concluded that the prevalence of incidental PFO was 17% of CT surgery patients. The finding that patients with incidental PFO had no difference in prior stroke or TIA and short-term perioperative and long-term outcomes than patients without PFO suggests that asymptomatic PFOs are benign events among the population. In addition, it seems that surgical closure of incidental PFO may increase the risk of postoperative stroke, although there is no long-term difference in survival among patients with repaired incidental PFO when compared with those with PFO that are not repaired.

Several topics are noteworthy of discussion with regard to this study. The epidemiologic aspect of this Cleveland Clinic study includes the fact that the cohort does not reflect the true prevalence of PFO in the population, due to the exclusion criteria. If previous ASD or PFO diagnosis is included, the prevalence rises from 17% to 23.5%, the equivalent to prior autopsy studies.[2] In addition, the authors specify that they cannot assure that PFOs were accurately looked for with TEE or that full TEE studies were acquired. Moreover, perioperative antiplatelet and anticoagulant therapies were not evaluated in this study, which would have been interesting to control for, given the finding of increase risk of postoperative strokes in patients who had PFO repaired.

Currently, there is general agreement that PFO should always be closed if the procedure has a high risk of perioperative hypoxemia (eg, left ventricular assist device, heart transplant) and procedures with atriotomy, such as mitral or tricuspid valve surgery; however, no common criteria for indication of direct closure of incidental PFO have been established among surgeons.[6] In this study, surgeons were more likely to repair if patients were female, younger in age, were undergoing mitral or tricuspid valve surgery, had history of prior TIA or stroke, had left atrial dilation, or had fewer comorbidities, including smoking, hypertension, MI, peripheral vascular disease, and carotid disease. However, the intraoperative decision to repair PFO did not seem to be influenced by the presence of septal aneurysm or atrial fibrillation, 2 features commonly associated with TIA or strokes. This may be influenced by the American Heart Association/American Stroke Association and American College of Cardiology Foundation recommendation that PFO closure may be considered for recurrent strokes after failed optimal medical therapy and that there are insufficient data to endorse PFO closure in asymptomatic PFO patients and even PFO patients with a first stroke.[7] Interestingly, 3 of 13 surgeons in this study showed a greater tendency to repair than the other 10, thereby supporting the lack of unanimity among CT surgeons and their views on the management of intraoperatively diagnosed PFO.

Proponents for not repairing incidental PFO may elect not to repair because the population with PFO is mostly asymptomatic. In contrast, if a PFO is incidentally diagnosed and left unrepaired, intraoperative problems such as oxygen desaturation secondary to the development of right-to-left shunt can appear (ie, when the heart is elevated to expose the posterior branches of the coronary arteries).[6] Other complications that may arise if PFO remain untreated include platypnea-orthodeoxia syndrome, high altitude pulmonary edema, decompression sickness, intraoperative and postoperative hypoxemia, and migraine headache with aura.[8] Even a rare case report of a thrombus entrapped across a PFO that continuously produced pulmonary and systemic thromboemboli has been described.[9] Therefore, attention should not be exclusively drawn toward the advantages or disadvantages of repairing PFO for stroke prevention but also toward evasion of these other complications.

Due to the small number of events, propensity scores were used to compare outcomes between 2 cohorts that are matched with multiple exposures or covariates. However, if 2 groups to be matched do not have a substantial overlap, then error may be introduced. If the worst cases of the treated group are compared with the best cases of the untreated group, the resulting regression may favor the untreated group. When trying to increase the number of exact matches, researchers may exclude cases that do not match at both ends, consequently resulting in loss of data. Therefore, although propensity scores are a close approximation to randomization, significant hidden bias may remain because this method only corrects for observed variables.

PFO incidental diagnosis during cardiac surgery is increasingly common due to the intraoperative use of TEE. Agreement on criteria for indication of surgical closure of incidental PFO has not been established among surgeons. Although no randomized clinical trials have concluded, results suggest that there is no additional benefit in short-term perioperative outcomes or in long-term survival rates in patients with repaired incidental PFO compared with those with PFO that were not surgically intervened. Even more, Krasuski and colleagues report a possible increased risk of perioperative stroke after repairing PFO. However, these studies do present several limitations that should be considered when analyzing the results, and therefore they encourage the need to complete randomized clinical trials to reach more reliable conclusions. Moreover, although it may not be unreasonable to use short-term postoperative antiplatelets and anticoagulants in patients who have had incidental PFO repaired to reduce the increased risk of perioperative stroke, data remain limited with no current guidelines to support such use and the risk-benefit ratio of bleeding needs to be accounted for on an individual basis. Given the risk of bleeding and no increased risk for perioperative stroke, short-term postoperative antiplatelets or anticoagulants specifically for primary stroke prevention are not recommended for patients with unrepaired isolated PFO or for unrepaired PFO with an interatrial septal aneurysm. Because PFO is considered a benign entity, the use of lifelong antiplatelets and anticoagulants in asymptomatic PFO patients whether repaired, unrepaired, or unrepaired with interatrial septal aneurysm for primary prevention, is not warranted. ■

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