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Incidence and Outcomes of Positive Bubble Contrast Study Results After Transcatheter Closure of a Patent Foramen Ovale

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ABSTRACT

OBJECTIVES The aim of this study was to assess the incidence of persistently positive results on agitated saline contrast injection after patent foramen ovale (PFO) closure, the underlying mechanism, and management.

BACKGROUND Transcatheter intervention to close a PFO is reasonable in highly selected patients younger than 60 years, after a thorough cardioneurological investigation following a cryptogenic stroke, particularly in the presence of thromboembolic disease or in patients at high risk for venous thrombosis. The U.S. Food and Drug Administration approved the Amplatzer PFO Occluder in October 2016 for such an indication. Confirmation of PFO closure is usually verified by an agitated saline contrast injection during an echocardiographic examination. The appearance of bubbles in the left atrium raises the concern of incomplete closure or other sources of shunting.

METHODS The medical records and echocardiograms of patients who were treated with transcatheter closure of a PFO for cryptogenic stroke were reviewed.

RESULTS From January 1998 through December 2015, 880 patients were taken to the catheter laboratory for PFO closure, of whom 568 patients, 320 men (56.3%), underwent transcatheter closure of a PFO using an Amplatzer PFO Occluder, at a mean age of 48.1 ± 12.9 years. The incidence of right-to-left shunting (RLS) was 19.5% at a mean of 4 months' follow-up, which reduced to 8.4% at 11 ± 2 months. Sources of RLS were identified in 10 (1.8%); pulmonary arteriovenous malformation (n = 4) was the most common etiology, followed by leak through the device (n = 3). All patients with additional sources of RLS were treated percutaneously. At 2-year follow-up, 16 patients (2.8%) persisted with only mildly positive results on agitated saline contrast injection, without an apparent additional source of shunting.

CONCLUSIONS Coexistence of a PFO and an additional lesion responsible for RLS is uncommon, but not rare; the majority are amenable to transcatheter or surgical intervention. (J Am Coll Cardiol Intv 2018;11:1095–104)

Patent foramen ovale (PFO) is the most common interatrial communication and is presumed responsible for a proportion of cryptogenic strokes through paradoxical embolization, especially in young patients (1). Meta-analysis of randomized trials has provided different conclusions with respect to the value of PFO closure in this population (2). Recently published results from the intention-to-treat analysis

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ABBREVIATIONS AND ACRONYMS

ASCI = agitated saline contrast injection

CS = coronary sinus

CT = computed tomography

HHT = hereditary hemorrhagic telangiectasia

PAVM = pulmonary arteriovenous malformation

PFO = patent foramen ovale

PSLVC = persistent left-sided superior vena cava

RLS = right-to-left shunting

TC = transcatheter closure

TEE = transesophageal echocardiography

TTE = transthoracic echocardiography

of the RESPECT (Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment) trial have shown that long-term follow-up in a highly selected group of patients with cryptogenic stroke, transcatheter closure (TC) of PFO reduced the rate of recurrent cryptogenic but not all-cause stroke compared with medical therapy (3). The results of the REDUCE trial, a controlled, open-label, randomized trial of 664 patients 18 to 59 years of age with cryptogenic stroke randomly assigned to PFO closure with the Gore septal occluder and antiplatelet therapy versus antiplatelet therapy alone, met its primary endpoint with a 76.6% reduction in stroke over an average of 3.4 years of follow-up. That study also showed a reduction in new brain infarcts by core laboratory interpretation of baseline versus 2-year magnetic resonance imaging from 11.3% in the control group to 5.7% in the device arm (4). The CLOSE (Closure of Patent Foramen Ovale, Oral Anticoagulants or Antiplatelet Therapy to Prevent Stroke Recurrence) trial randomized 524 patients to oral anticoagulation, PFO closure, or antiplatelet therapy. All patients had either atrial septal aneurysms or significantly positive results on bubble study. The study met its primary endpoint, demonstrating that PFO closure plus antiplatelet therapy reduced the risk for stroke recurrence compared with antiplatelet therapy alone. Anticoagulants did not significantly reduce the risk for recurrent stroke compared with antiplatelet therapy (5). The U.S. Food and Drug Administration approved the Amplatzer PFO Occluder (St. Jude Medical, St. Paul, Minnesota) in October 2016.

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Atrial-level defects are not the sole source of paradoxical emboli. Pulmonary arteriovenous malformations (PAVMs), venous abnormalities including persistent left-sided superior vena cava (PLSVC) to the left atrium, or an unroofed coronary sinus (CS) may also cause paradoxical embolization. Coexistence of a PFO and another anomaly, both of which may result in right-to-left shunting (RLS), is uncommon, and prevalence is unknown. Successful closure of a PFO is confirmed by agitated saline contrast injection (ASCI) during an echocardiographic examination in follow-up. The appearance of bubbles in the left atrium raises the concern of incomplete closure or other sources of shunting. Our PFO closure experience involved multiple devices, some of which are of historical interest at this time; this report focuses on the results of the cohort treated with the Amplatzer PFO Occluder. We sought to assess the incidence of persistently positive ASCI after PFO closure, the underlying mechanism, and subsequent management.

METHODS

PATIENTS. We reviewed our institutional database of patients who underwent transcatheter PFO closure, primarily for cryptogenic stroke, between January 1998 and December 2015. PFO closure to treat the platypnea-orthodeoxia syndrome was not included. After the procedure, patients were reviewed in the outpatient clinic at 2 to 3 months and yearly and investigated using transthoracic echocardiography (TTE) with ASCI, both at rest and after a Valsalva maneuver. Results of the bubble study were defined as mild, moderate, or strongly positive if 3 to 9, 10 to 30, or >30 bubbles appeared in the left atrium, as described previously (3). The shunt was thought to be at the atrial level if bubbles appeared in the left atrium within 3 heartbeats after opacifying the right atrium, whereas bubbles appearing late were suggestive of an extracardiac communication.

INVESTIGATIONS. A diagnosis of cryptogenic stroke was made only after excluding known secondary causes. Patients with cryptogenic stroke were reviewed by a neurologist and underwent magnetic resonance imaging, magnetic resonance angiography, computed tomography (CT), or computed tomographic angiography of the brain if necessary; TTE or transesophageal echocardiography (TEE); thrombophilia work-up; and ambulatory cardiac rhythm monitoring. Since evidence supporting up to 4 weeks of cardiac monitoring has emerged, we have changed our practice from 48 h to 2 to 4 weeks of Holter monitoring (4,6).

PROCEDURE. TC of PFOs was performed under fluoroscopy, local anesthesia, and appropriate use of intravenous sedation, as previously described (5). Intracardiac echocardiography was available as a standby if issues arose during the procedure or if TEE suggested potential challenges (e.g., coexistent atrial septal defect). One hundred units per kilogram of intravenous unfractionated heparin was administered, adjusted to an activated coagulation time of >250 s, and prophylactic antibiotics were administered to each patient. Device positioning and adequacy of closure was assessed using right atrial angiography.

FOLLOW-UP. Patients were investigated using TTE with ASCI at the time of follow-up, 2 to 3 months after