Appendacide! Alas, poor auricle...

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Auricles have fallen on hard times! The ones on our heads were fingered by the Association of periOperative Registered Nurses (AORN) as an important source of surgical site infections: “*Although there is no conclusive evidence [italics added]...team members should cover their heads, hair and ears...*”¹ This revelation reached the Joint Commission on Accreditation of Healthcare Organizations, triggering jihad against exposed ears in hospitals hoping to remain accredited. As a consequence, surgeons now fuss daily to avoid flashing ear while fitting loops and headlights over bouffant head-coverings. AORN’s oracle? A single 2004 report on culture swabs obtained from 20 operating room (OR) personnel.²

Although better supported by something approaching evidence, a similar kind of inferential conflation of association with cause-and-effect threatens the left auricle of the heart with extinction. Did you know that it is “Our most lethal human attachment”?³ Not the dominant hand, mind you, not that midline assault weapon that men carry, but the left atrial appendage (LAA)! The purpose of this commentary, although provoked by a specific publication that I will get to eventually, is to raise 1 lonely hand against this universally popular belief system. Table 1 summarizes the 8 pillars of this orthodoxy, in 2 columns according to the breadth of the crusade they purport to justify.

Not unlike AORN, authors riffing on the lethality of the LAA almost invariably emphasize a review article by Blackshear and Odell⁴ that summarized 23 studies published between 1948 and 1994, designed to look for evidence of LAA thrombus in patients with atrial fibrillation (AF). Ascertainment depended on autopsy, observation in an operating room, or transesophageal echocardiogram (TEE). Approximately two-thirds of the data were obtained by TEE. The authors assure us this is not a problem, because TEE is “100% sensitive and 99% specific.” Does any test in medicine, based on qualitative interpretation of images by human eyeballs, have that level of accuracy? Blackshear and Odell⁴ cite Manning et al⁵ to support this claim: TEE identified left atrial thrombus in 14 of 231 patients, confirmed during surgery in 12 patients (86%). Sounds to

Off with their heads!

Central Message

Left atrial appendage occlusion is driven by appealing but marginally substantiated theory and should not be applied indiscriminately.

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me like TEE found false-positive left atrial thrombus in 14% of patients. But I quibble. Perfectly accurate or not, indeed 91% of the nonrheumatic group had thrombus that was “isolated to, or originated in” the LAA. However, Blackshear and Odell⁴ did not correlate presence of thrombus with stroke. A suggestive association, certainly, but not proof of cause and effect. Many authors citing their work imply otherwise: “...approximately 90% of strokes originate from the LAA...” is a recent example from JAMA.⁶

A statement like, “90% of strokes originate from the LAA”⁶ is the kind of inferential leap that supports the 8 pillars. Leaps of faith reinforce belief, and belief breeds confirmation bias. When I see a bunch of young men loitering on a street corner, my prejudices may lead me to assume they have already robbed my house, or soon will. Yet the single thing I know, based purely on the observable facts, is that they are not actively engaged in robbing my house. The 8 pillars require belief that the LAA is a sluggish cul-de-sac in which undesirables loiter before invariably running off to trash the brain. If the LAA is to be targeted for eradication, as if on a par with smallpox or polio, it seems reasonable to require very strong proof of concept.

Has LAA thrombus ever been caught in the act of embolizing? A limitation is that the evidence is derived entirely from echocardiography (divination of shadows by human eyeballs). Be that as it may, a 3-paragraph report from Madrid, Spain,⁷ shows tantalizing images of a smooth, spherical object caught at “the precise

TABLE 1. The 8 pillars of appendacism

LAAO in patients with AF	LAAO in everyone
I. Stroke is bad	V. The LAA is a useless vestigial organ
II. AF increases stroke risk	VI. We have harmless methods for occluding the LAA
III. AF is very prevalent	VII. The best methods utilize commercial devices
IV. Some AF patients have LAA clot	VIII. Enthusiasm for LAAO signifies a cutting-edge practitioner

LAAO, Left atrial appendage occlusion; AF, atrial fibrillation; LAA, left atrial appendage.

moment” when it exited the LAA, and the patient was found to have a splenic infarct (timing in relation to the precise moment is unspecified). Forgive me for swerving from published anecdotes to personal observation, but I have directly inspected a reasonable number of LAAs during the past 34 years. During the 1980s, treating previous-generation rheumatics, adherent, laminated thrombus in the appendage and the atrium was not infrequent. Since then, for reasons I cannot explain, years go by between sightings. On the rare occasions that I do see thrombus in the left atrium or LAA it is always at least loosely adherent to the endocardium, and is never spherical. A 2015 case report⁸ claims to document embolization of an appendage cast during transcatheter aortic valve replacement, ultimately captured by aspiration in the aortic sinus. In addition to the usual intracardiac manipulations necessary for transcatheter aortic valve replacement, in this case the guidewire repeatedly crossed the mitral valve into the left atrium. Perhaps this example is not strong proof of concept in noninvasive settings that are far more common, even if this case report strongly suggests that a thrombus departed the appendage. Other so-called proof tends to be suggestive but circumstantial, as in a 2-paragraph report from Australia⁹ that claimed simultaneous presence of LAA thrombus and left anterior descending artery thrombus as proof of embolization.

Supplicants of the 8 pillars will argue that I have no reasonable alternative hypothesis. It is fair to ask. Is it possible that the LAA is a holding pen for clot, particularly when the propulsive force provided by atrial systole is absent? Might sequestration even be among its functions? Perhaps clots that form in the main cavity of the left atrium are more dangerous than those that form in the LAA holding pen, and more dangerous than clots that form in the left atrium and become sequestered in the LAA. Among the patients described by Blackshear and Odell⁴ who had LAA thrombus ascertained by direct observation (at autopsy or in an operating room), 73% also had left atrial thrombus.

When TEE was the source, only 14% had left atrial thrombus. Might TEE shadow-divination excel at detecting comparatively harmless sequestered shadows in the LAA while missing those in the left atrium? Mechanistically, this would be an important distinction because there is no nifty device or procedure to sell for treating left atrial thrombus. If my alternative hypothesis is true, would the existing literature show that stroke is increased by LAA occlusion (LAAO)? Not necessarily, if LAA thrombus is primarily a marker for more dangerous thrombus somewhere else, which would also help explain why benefits of LAAO have been quantitatively slight and not easily demonstrated—more on that to follow.

It would be irresponsible of me to undermine the pillars of appendacism by suggesting that the LAA might be relatively harmless, or even useful. However, there is some evidence that the LAA is not entirely useless. Like its right atrial counterpart, it is known to contain high concentrations of atrial natriuretic factor,¹⁰ which might play a role in regulation of intravascular volume. It has also been shown to be more compliant than the body of the left atrium, such that it makes a disproportionate contribution to overall left atrial compliance.¹¹ In experiments in which the LAA was amputated, overall left atrial compliance was markedly decreased, which could contribute to transmission of elevated pressures to the lungs, exacerbating congestive symptoms.^{12,13} Lower left atrial compliance might also promote AF,¹² an interesting concept to which I will return. To be sure, these investigations predate recognition that the LAA is “our most lethal human attachment,”³ and laboratory interest in LAA function has waned.

Relief is in sight—I have finally arrived at what stimulated this heretical commentary! Yao and colleagues¹⁴ recently conducted an exhaustive strip-mining operation of a large administrative database that relied on diagnosis and procedure codes as proxy measures. A total of 75,782 patients who underwent cardiac surgery over an 8.25-year period ending in 2017 were studied. Of these, 25,721 patients had pre-existing AF, and 4,374 had LAAO. Enter propensity-score matching, stage left, with multiple sensitivity analyses in train. A total of 8,590 matched pairs were generated. I wonder why the mean follow-up was only 2.1 years when the study period was 4-fold longer. My statistical consultants could not explain that nuance, but they assure me that the overall analysis was very capably done. The principle finding that slaps mortar on the 8 pillars is that LAAO was associated with a reduced risk of stroke (1.14 vs 1.59 events per 100 person-years; hazard ratio, 0.73; 95% confidence interval, 0.56-0.96; $P = .03$). A proportionally similar benefit was seen for mortality. The interaction term between AF and LAA occlusion was not significant, which is reassuring. These results are similar to those reported a few months earlier by Friedman and colleagues,⁶ who strip-mined a smaller administrative

database (10,524 patients), used a different adjustment methodology, and lumped ischemic stroke with thromboembolism. I will be considered churlish for arguing that only under statistical waterboarding are such miniscule differences revealed (0.45 strokes per 100 person-years in Yao and colleagues¹⁴), and that association does not show cause and effect. Nonetheless, this statistically respectable contribution from Yao and colleagues¹⁴ definitely props up the spinal-reflex use of LAAO in patients with AF that is becoming de facto standard of care.

Game, set, and match to occlusion devices? Not so fast. It is important to note in Yao and colleagues¹⁴ the risk of stroke was not different in patients with LAAO who did not have prior AF, and the frequency of postoperative AF in those patients was 27.7% versus 20.2% events per 100 person-years (hazard ratio, 1.46; 95% confidence interval, 1.22-1.73; $P < .001$). In other words, LAAO in patients without pre-existing AF may be both inefficacious and harmful. This relationship has been reported previously. Melduni and colleagues¹⁵ propensity-matched 461 pairs from 10,633 patients undergoing cardiac surgery and found that the frequency of early postoperative AF was 31.9% without LAAO and 68.6% with LAAO ($P < .001$). This outcome may support clinical relevance of the compliance changes following LAAO observed in animal studies and discussed above.^{12,13}

I will return to where I started and raise a lonely hand against hammers looking for nails. Procedures should aspire to be grounded on fact more than theory. It is not enough to believe, simply because we have a neat little device for doing so, that we should eliminate a body part that associates with undesirables. I grant there is reasonable conjecture behind LAAO in patients with persistent AF. But as long as we still have a few LAAs running loose in their vanishing habitat, I feel compelled to speak out against indiscriminate LAAO. That practice gives free rein to the unholy trinity of drive-by surgeons eager to perform procedures, interventional cardiologists eager to own structural heart disease, and manufacturers eager to sell devices to both parties. To be fair, this fad seems to be driven disproportionately by surgeons,¹⁶ and to their credit, cardiologists are publishing evidence that LAAO is not entirely harmless.^{17,18} Even overlooking the paucity of evidence supporting indiscriminate LAAO, where is the logical limit to that approach? Should we place an occluding device in every patient undergoing diagnostic catheterization? Should LAAO be part of every left lobectomy? Every esophageal resection? Every transthoracic exposure of the spine? Every emergency room thoracotomy? How about a 2-for-1 at the time of circumcision? Silly of me to get so carried away—until you consider the procedure and device profits (going to the unholy trinity) and costs (paid by everyone else)

associated with treating the fear of an uncommon complication of a highly prevalent condition. We should do the necessary randomized trials, but I fear the 8 pillars have ensured that sufficient equipoise no longer exists. Meanwhile, as illustrated by Yao and colleagues,¹⁴ even when we slice, dice, propensity, then turbocharge with the power of large numbers, in the search for truth we only have 7 maids with 7 mops.

*The Walrus and the Carpenter
Were walking close at hand;
They wept like anything to see
Such quantities of sand:
"If this were only cleared away,"
They said, "it would be grand!"*

*"If 7 maids with 7 mops
Swept it for half a year.
Do you suppose," the Walrus said,
"That they could get it clear?"
"I doubt it," said the Carpenter,
And shed a bitter tear.*

—Lewis Carroll, *Through the Looking-Glass*

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