REVIEW

Intraoperative Echocardiography in Valvular Heart Disease: An Evidence-Based Appraisal

Hector I. Michelena, MD; Martin D. Abel, MD; Rakesh M. Suri, MD, PhD;
William K. Freeman, MD; Roger L. Click, MD, PhD; Thoralf M. Sundt, MD;
Hartzell V. Schaff, MD; and Maurice Enriquez-Sarano, MD

Intraoperative (IO) transesophageal echocardiography (TEE) is widely used for assessing the results of valvular heart disease (VHD) surgery. Epiaortic ultrasonography (EAU) has been recommended for prevention of perioperative strokes. To what extent does high-quality evidence justify the widespread use of these imaging modalities? In March 2009, we searched MEDLINE (PubMed and OVID interfaces) and EMBASE for studies published in English using database-specific controlled vocabulary describing the concepts of IOTEE, cardiac surgery, VHD, and EAU. We found no randomized trials or studies with control groups assessing the impact of IOTEE in VHD surgery. Pooled analysis of 8 observational studies including 15,540 patients showed an average incidence of 11% for prebypass surgical changes and 4% for second pump runs, suggesting that patients undergoing VHD surgery may benefit significantly from IOTEE, particularly from postcardiopulmonary bypass IOTEE in aortic repair and mitral repair and replacement, but less so in isolated aortic replacement. Further available indirect evidence was satisfactory in the test accuracy and surgical quality control aspects, with low complication rates for IOTEE. The data supporting EAU included 12,687 patients in 2 prospective randomized studies and 4 nonrandomized, controlled studies, producing inconsistent outcome-related results. Despite low-quality scientific evidence supporting IOTEE in VHD surgery, we conclude that indirect evidence supporting its use is satisfactory and suggests that IOTEE may offer considerable benefit in valvular repairs and mitral replacements. The value of IOTEE in isolated aortic valve replacement remains less clear. Evidence supporting EAU is scientifically more robust but conflicting. These findings have important clinical policy and research implications.

Mayo Clin Proc. 2010;85(7):646-655

AR = aortic regurgitation; AVR = aortic valve replacement; CPB = cardiopulmonary bypass; EAU = epiaortic ultrasonography; IO = intraoperative; LVOT = left ventricular outflow tract; MR = mitral regurgitation; OR = operating room; PFO = patent foramen ovale; TEE = transesophageal echocardiography; TR = tricuspid regurgitation; TTE = transthoracic echocardiography; VHD = valvular heart disease

Significant valvular heart disease (VHD) affects 13% of patients aged 75 years or older, has a national prevalence of 2.5%,[1] and is primarily due to mitral regurgitation (MR).

Intraoperative (IO) transesophageal echocardiography (TEE) is widely used to monitor patients undergoing VHD surgery. Landmark practice guidelines for the implementation of IOTEE[2-4] recommend its use in VHD surgery.

The incidence of perioperative stroke in cardiac surgery has been estimated to range between 1% to 2% (Society of Thoracic Surgeons, 2007) and 4% to 5%.[5] Intraoperative TEE is superior to surgical palpation in detecting atheromas[6,7]; however, epiaortic ultrasonography (EAU) is more sensitive than IOTEE and has been recommended recently for use in patients at risk for stroke.[8]

Given the expansion in the use of these technologies, we sought to review the literature to determine the extent to which high-quality scientific evidence justifies their use.

METHODS

REVIEW QUESTION

To what extent do IOTEE and EAU improve outcomes in patients undergoing VHD surgery?

ELIGIBILITY CRITERIA

Randomized trials of test management using IOTEE or EAU and consecutive case series of IOTEE or EAU reporting patient-important outcomes were eligible. In their absence, observational, nonconsecutive series and case reports became eligible. To ensure that observational studies reflected mature learning curves associated with IOTEE, we chose arbitrarily to limit studies to those describing experience with more than 100 patients.

SEARCH STRATEGY

In March 2009, we searched MEDLINE (PubMed and OVID interfaces) and EMBASE for studies published in English using database-specific controlled vocabulary describing the concepts of IOTEE, cardiac surgery, VHD, and EAU (Table 1).

DATA ANALYSIS

For each study, we noted methodological quality, surgical indications, change in the surgery planned, rate of second

pump run, morbidity and mortality, and complications from imaging. We contacted the authors of one study to clarify its methodological characteristics.[9]

For pooled analysis of IOTEE impact in VHD surgery, we chose studies reporting actual alterations in surgical (not medical) management, in which a single valve was addressed or in which a valve-by-valve breakdown of results was provided. For EAU in stroke prevention, we chose available randomized trials and nonrandomized controlled studies.

RESULTS

SEARCH FINDINGS

Duplicates, reviews, commentaries, congenital and pediatric heart disease articles, and studies related to commercial valve brands or specific surgical techniques were eliminated. Of the remaining articles, 8 were appropriate for pooled analysis of the surgical impact of IOTEE in VHD[9-16] (Table 2) and 6 for analysis of EAU impact on stroke prevention[17-22] (Table 3). Five additional observational studies of the impact of IOTEE[23-27] and 1 additional EAU study[28] were eligible. The remaining studies related to test accuracy,[29-43] IOTEE-related outcomes,[44-47] surgical quality control by IOTEE,[48-54] IOTEE safety reports,[55,56] and case reports.[57-60]

One impact-related study[61] not identified by the search was reported for its academic value. To enhance comprehensiveness, 9 additional studies were reported for test accuracy,[62-70] 2 for surgical quality control,[71,72] and 1 for IOTEE safety.[73]

METHODOLOGICAL QUALITY OF INCLUDED STUDIES

The 8 IOTEE surgical impact studies included for pooled analysis were observational without control groups or consecutive patients (Table 2). Patients were chosen on the basis of probe availability[13]; presence of images both before and after cardiopulmonary bypass (CPB),[15,16] as indicated by the attending anesthesiologist and surgeon[9,11,12,14]; and availability of preoperative and follow-up echocardiograms.[10]

Studies of the IOTEE/EAU impact on stroke prevention included 2 available prospective randomized trials,[17,19] 2 observational retrospective studies of nonconsecutive patients,[18,20] and 2 observational prospective studies of consecutive patients[21,22] (Table 3). Studies of IOTEE-related outcomes included consecutive patients and control groups.[44-46]

SURGICAL ALTERATIONS PROMPTED BY IOTEE IN VHD SURGERY

The surgical impact of IOTEE in mixed cardiac surgical populations has been evaluated in more than 35,000 pa-

TABLE 1. **Literature Search Strategy**

PubMed (1980-2009)
  Core journals, human studies, all publication types, English language
  Search terms: *transesophageal echocardiography*, *intraoperative*, and *cardiac*
  Human studies, all publication types, English language
  Search terms: *epiaortic ultrasound* and *intraoperative*

OVID-MEDLINE (1950-2009) and EMBASE (1988 to 2009)
  All publication types, human adults, English language
  Search terms: *TEE*, *intraoperative*, *heart valve surgery*, *outcome*, *heart valve diseases*, *aortic valve insufficiency*, *aortic valve stenosis*, *heart valve prolapse*, *mitral valve insufficiency*, *mitral valve stenosis*, *tricuspid valve insufficiency*, *tricuspid valve stenosis*, *heart valve prosthesis*, *cardiac surgical procedures*, and *heart valve prosthesis implantation*

tients.[9-16,23-27,61] Of these patients, the impact of IOTEE in VHD surgery can be analyzed in 15,540 patients from 8 major observational reports.[9-16] Changes in the planned surgical procedure related to pre-CPB IOTEE evaluation ranged from 6% to 29%, with a pooled average of 11% (Table 2). Second pump runs prompted by post-CPB IOTEE ranged from 0% to 7%, with a pooled average of 4% (Table 2). The most common pre-CPB finding that resulted in alterations to the surgical procedure was the presence of a patent foramen ovale (PFO). Other pre-CPB IOTEE surgery-altering findings were unsuspected MR, aortic atheroma, intracardiac thrombus, endocarditis complications, left ventricular outflow tract (LVOT) obstruction, and aortic homograft sizing.[11,14] Post-CPB alterations (second pump runs) were related to residual valvular abnormalities (Table 2).

The 1996 American Society of Anesthesiologists IOTEE guidelines were prospectively tested in 851 patients undergoing cardiac surgery,[61] and surgical alterations were necessary in 17% of patients undergoing class I surgical procedures (includes valve repairs) and in 4% of patients undergoing class II surgical procedures (includes valve replacements) ($P<.001$).

In a mixed cardiac surgery population of 203 consecutive patients, the incidence of second pump runs was 2.5%[24] (vs 4.0% in our VHD pooled analysis). Similarly, the most recent report in a mixed cardiac surgery population showed a second pump run incidence of 2.2% (vs 4.0% in our VHD pooled analysis) in 12,566 nonconsecutive patients.[12] This report was also consistent with others showing an IOTEE-prompted incidence of graft revisions of 0.8% to 1.0% in isolated revascularization surgery.[12,13,27]

DIAGNOSTIC ACCURACY OF IOTEE IN VHD AND RELATED OUTCOMES

Mitral Valve. The evaluation of MR severity with pre-CPB IOTEE was 95% to 97% accurate compared with find-

TABLE 2. **Studies Addressing the Specific Impact of IOTEE in VHD Surgery**[a]

Reference	Design	Year	No. of patients	Valve surgery (%)	Pre-CPB impact[b] (%)	Post-CPB findings	Second pump run (%)
Sheikh et al[16]	Prospective Nonconsecutive	1985-1988	154	Mitral surgery (60) (repair [26]) Aortic surgery (40) (repair [11])	9	Residual regurgitation	6.0 All mitral surgery
Grimm & Stewart[9]	Retrospective Nonconsecutive	1984-1996	4066	Mitral repair (75) Aortic repair (12) Tricuspid repair (13)	NS	Inadequate repair Residual regurgitation	7.0 Total 5.0 Mitral 1.8 Aortic[c] 0.2 Tricuspid
Mishra et al[13]	Prospective Nonconsecutive	1993-1997	1356	Mitral (62) (repair or MVR) AVR (38)	13	Inadequate repair	2.0 All mitral repair
Click et al[11]	Prospective Nonconsecutive	1993-1997	2369	Mitral repair (36) MVR (18) AVR (30) Aortic repair (5) Other (11)	14	Inadequate repair Perivalvular leak LVOT obstruction	2.0 All mitral repair
Nowrangi et al[14]	Retrospective Nonconsecutive	1993-1996	383	AVR for aortic stenosis (100)	7	New RWMA	0.0
Shapira et al[15]	Retrospective Nonconsecutive	1999-2003	352	MVR (47) AVR (43) TVR (10)	29	Perivalvular leak Immobilized leaflet Coronary obstruction	4.0 Total 2.0 MVR 1.7 AVR 0.3 TVR
Bajzer et al[10]	Prospective Nonconsecutive	1990s	335	Tricuspid surgery (100) (repair or replacement)	6	Failed repair	4.0
Eltzschig et al[12]	Retrospective Nonconsecutive	1990-2005	6525	MVR or repair (28) AVR or repair (25) Both (6) CABG + aortic (21) CABG + mitral (20)	9	Inadequate mitral or aortic repair/ replacement New RWMA	3.0 Total 1.2 MVR or repair 0.6 AVR or repair 0.2 Both 0.3 CABG + aortic 0.7 CABG + mitral
Summary		1984-2005	15,540	Mitral surgery (56) Aortic surgery (36) Tricuspid surgery (8)	11 (n=11,474)	Abnormal valve result most common	4.0

[a] AVR = aortic valve replacement; CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass; IOTEE = intraoperative transesophageal echocardiography; LVOT = left ventricular outflow tract; MVR = mitral valve replacement; NS = not specified; RWMA = regional wall motion abnormality; TVR = tricuspid valve replacement; VHD = valvular heart disease.
[b] Pre-CPB findings that altered the planned surgery.
[c] This represented 14% of all aortic repairs, compared with 7% of all mitral repairs requiring a second pump run.

ings on preoperative transthoracic echocardiography (TTE) for flail leaflets.[30] In a large study of patients with a predominantly degenerative MR mechanism, the exact severity agreement between preoperative TTE and pre-CPB IOTEE was 64%.[64] However, when mixed MR mechanisms were studied, the correlation between preoperative TTE and pre-CPB IOTEE was weaker (r=0.40), with an exact agreement of 54%.[41] The post-CPB severity of residual MR by IOTEE after mitral repair for degenerative MR correlates fairly well (r=0.66-0.71) with early and late postoperative TTE evaluations.[42] Agreement between a pre-CPB, IOTEE-identified dysfunction mechanism and actual operative findings is excellent for both mitral and aortic valve disease.[31,63,64]

Surprisingly, one study showed that a TTE-defined MR mechanism in 279 patients had a 97% accuracy in predicting mitral valve repair and a 91% agreement with surgical visualization of specific prolapsed segments (no different than pre-CPB IOTEE).[39] Importantly, quantification methods by TTE have been validated for TEE,[43,65,70] and additional TEE severity-estimation parameters have emerged (ie, pulmonary vein systolic flow reversal in MR).[38] Mitral regurgitation may be sensitive to anesthesia-induced hemodynamic conditions, leading to underestimation of severity,[30,36] particularly in patients with ischemic MR[29]; however, administration of intravenous phenylephrine[67] and volume to restore physiologic conditions may allow appropriate evaluation of severity.[35] In patients undergoing mitral valve repair with concomitant tricuspid regurgitation (TR), we have found that the severity of TR is also significantly underestimated under anesthesia conditions (Figure, submitted data).

TABLE 3. **Studies Addressing the Specific Impact of IOTEE/EAU on Stroke Prevention**[a]

Reference	Design	Year	No. of patients	No. of patients in randomization or control group	Type of operation	Outcome measured	Results
Murkin[19]	Prospective Randomized	2003	191	90 Ao palpation 101 EAU	CABG	Quantification of MCA emboli by insonation	47 vs 29 embolic counts (*P*<.05)
Djaiani et al[17]	Prospective Randomized	2008	113	58 Ao palpation 55 EAU	CABG	Pre-CPB changes[b] TCD emboli NIH Stroke Scale In-hospital mortality	Pre-CPB change 12% vs 29% (*P*=.02) Embolic counts (*P*=.46) Stroke (*P*=.51) Death (*P*=.95)
Trehan et al[21]	Prospective Nonconsecutive	1993-1997	3660	104 With mobile atheroma by IOTEE 3556 Control group	CABG	Pre-CPB changes[b] Perioperative stroke	Pre-CPB change in 104 patients with mobile atheroma Perioperative stroke <1% in both groups
Gold et al[18]	Prospective Consecutive	1996-2003	500	500 Ao palpation, IOTEE, EAU-guided Ao manipulation Control = NYS CABG Registry	CABG	Perioperative stroke In-hospital mortality	Perioperative stroke 0% (control group not reported) Mortality rate 0% vs 2% (*P*<.001)
Zingone et al[22]	Prospective Consecutive	2000-2004	2172	366 Ao palpation 1116 Selective EAU 690 Routine EAU	Mixed	Pre-CPB changes[b] Perioperative stroke	Pre-CPB change 24% vs 16% vs 0.5% (*P*<.001) Perioperative stroke 2.2% vs 0.5% vs 0.6% (*P*=.02)
Rosenberger et al[20]	Retrospective Nonconsecutive	1996-2006	6051	6051 IOTEE and EAU Control group = 9105 remaining cardiac surgery patients for the time period	CABG 59% CABG-valvular 20% MVR and/or AVR 15% Other 6%	Pre-CPB changes[b] Perioperative stroke	Total pre-CPB change 4.1% Isolated MVR 1.4% CABG and valvular 6.7% Stroke CABG 1.4% vs 1.6% (*P*<.05) Stroke CABG-valvular 3.2% vs 4.2% (*P*<.05)

[a] Ao = aorta; AVR = aortic valve replacement; CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass ; EAU = epiaortic ultrasonography; IOTEE = intraoperative transesophageal echocardiography; MCA = middle cerebral artery; MVR = mitral valve surgery; NIH = National Institutes of Health; NYS = New York State; TCD = transcranial Doppler.
[b] Change in cannulation site, switch to off-pump procedure, avoidance of cross-clamp or change cross-clamp location, aortic arch atherectomy, and aorta repair.

Aortic Valve. In aortic stenosis, TTE is the criterion standard for severity quantification by virtue of the multiple continuous-wave Doppler interrogation sites that prevent underestimation of severity. Planimetry of aortic valve area by 2-dimensional TEE has produced conflicting accuracy results.[62,66] The correlation for aortic regurgitation (AR) severity is fair (*r*=0.70), with 59% exact agreement with TTE.[41] Assessment of cusp mobility and jet direction during pre-CPB IOTEE is highly accurate in defining the AR mechanism,[63] and aortic valve repair is highly dependent on post-CPB IOTEE for surgical success.[9,12]

Perivalvular Leaks. The correlation between periprosthetic leaks described by post-CPB IOTEE and direct surgical observation is excellent.[69] Nevertheless, post-CPB perivalvular leaks tend to be mild in the aortic and mitral

positions[40] and resolve over time in more than 50% of cases, with a benign clinical course at late follow-up for most.[45]

Outcomes. Observational data in patients with moderate residual valve dysfunction determined by post-CPB IOTEE (aortic or mitral valve replacement) suggest that these patients have more postoperative complications and a higher mortality rate compared with those with a satisfactory valve surgery result.[16] In patients with ischemic heart disease who are undergoing surgical revascularization (mitral valve surgery patients excluded), identification of even mild residual MR by IOTEE is associated with a worse clinical prognosis.[46] In patients with degenerative MR, postrepair residual 1+ or 2+ MR as determined by post-CPB IOTEE is related to an increased rate of reopera-
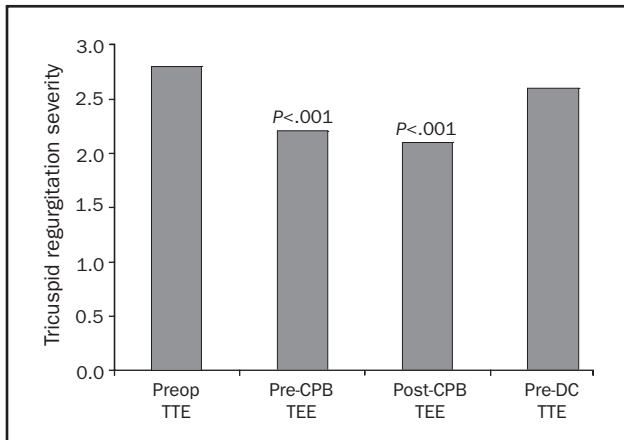
FIGURE. Tricuspid regurgitation severity (1+ to 4+) by preoperative (Preop) transthoracic echocardiography (TTE), by intraoperative transesophageal echocardiography (TEE) before and after cardiopulmonary bypass (CPB), and predischarge (pre-DC) TTE in 115 patients with more than mild tricuspid regurgitation undergoing mitral valve repair for mitral regurgitation. Severity under general anesthesia (both pre-CPB and post-CPB) was significantly less than both preoperative and pre-DC levels (P<.001 in all).

tions,[44] and the mere use of post-CPB IOTEE decreases the rate of reoperations.[47] Intraoperative TEE has been touted as cost-effective because it avoids the high costs of reoperation at follow-up.[33,37]

SURGICAL QUALITY CONTROL BY IOTEE IN VHD SURGERY

In cardiac surgery requiring CPB, more than mild AR may preclude antegrade cardioplegia administration and require further strategies for myocardial protection.[52]

Aortic Valve. Intraoperative TEE is highly accurate in predicting annular size,[53] potentially reducing CPB time by 10 to 30 minutes of thaw time when homografts are used. Recently, attention has been focused on the impact of patient-prosthesis mismatch in the aortic position,[74] significant mismatch being an independent predictor of long-term mortality. Small calcified annuli (<2 cm) may require annular debridement and/or pericardial patch aortic enlargement to insert an adequately sized prosthesis. After CPB, LVOT subvalvular obstruction may increase the prosthetic aortic mean gradient and may decrease blood pressure,[49] requiring concomitant myectomy with aortic valve replacement (AVR). Calcific aortic stenosis is related to ascending aorta atheroma, especially if concomitant coronary disease is present,[54,75] necessitating imaging to potentially guide aorta manipulation.

Mitral Valve. In degenerative MR, repairing instead of replacing the valve conveys a survival benefit.[76] Probability of repair is substantial when leaflet tissue is abundant[32] and annular calcification is not severe. Severe annular calcification predisposes to perivalvular leaks after replacement. In

patients with extensive Barlow bileaflet mitral valve disease, it is critical to prioritize scallops requiring intervention, a task accomplished by IOTEE. After repair, the left ventricle is insufflated with saline to visually assess mitral valve integrity. In Barlow disease with dilated ventricle and annulus, it is often difficult to fully insufflate the leaflets to assess coaptation in a static and flaccid heart. It is only after CPB under physiologic loading conditions that mitral valve competence is confirmed by IOTEE. Residual commissural jets are very difficult to assess by methods other than IOTEE. A cause of persistent MR and hemodynamic embarrassment is LVOT obstruction due to systolic anterior motion, which has been described in 1% to 9% of mitral valve repairs.[34,50,51] Failure to medically eliminate systolic anterior motion of the mitral valve apparatus in the post-CPB period often necessitates a second pump run for correction. Pre-CPB IOTEE may be predictive of systolic anterior motion at the pre-CPB stage,[68,77] potentially modifying the surgeon's repair approach.

In minimally invasive mitral valve repair, pre-CPB IOTEE verifies the cardioplegia catheter in the coronary sinus, the venous cannula position across the right atrium, and the arterial cannula in the descending thoracic aorta.[48] After mitral valve replacement, mechanical leaflets may be "stuck" to residual subvalvular tissue,[58,59] with resultant obstruction or regurgitation. After mitral annuloplasty, severe AR caused by left coronary cusp retraction has been reported.[57] Damage to the circumflex artery after mitral valve repair has been described.[60] These conditions are recognized by post-CPB IOTEE.

Mitral abnormalities prompting additional mitral surgery are found in 7% of patients[26] on pre-CPB IOTEE during septal myectomy for obstructive hypertrophic cardiomyopathy. In up to 7% of patients, post-CPB IOTEE detects new findings, potentially requiring a second pump run.

Tricuspid Valve. Despite repair, recurrence of significant TR is not uncommon and may be predicted by IOTEE. Tricuspid annulus dilatation,[71] amount of leaflet tethering,[72] and significant residual regurgitation after repair are predictors of recurrence and have correction potential before the patient leaves the operating room (OR); however, IOTEE underestimates TR severity (Figure).

SAFETY OF IOTEE

Studies including more than 25,000 patients undergoing TEE and IOTEE demonstrate a complication rate of 0.2% or less and a mortality rate of less than 0.1%.[11,13,23,55,73] However, a recent retrospective study of 859 cardiac surgery patients found an incidence of major gastrointestinal complications of 1.2%, mostly gastric tears and perforations,[56] occurring late (after >24 hours). However, inexperienced echocardiographers performed those procedures,

limiting the applicability of the results to experienced centers. In 22,179 patients undergoing IOTEE from 1991 to 2007 at Mayo Clinic in Rochester, MN, 7 esophageal perforations (0.032%) occurred, 3 (0.014%; 43% of perforations) of which were fatal (unpublished data). Therefore, the complication risk of IOTEE in experienced hands is very low, but the mortality associated with complications is considerable. Available data suggest that perforations tend to occur in older patients with poor-quality echocardiographic images and tend to involve the lower esophagus, gastroesophageal junction, and cardias. Whether avoiding low-esophageal and gastric imaging prevents perforations remains unknown.

INTRAOPERATIVE TEE AND EAU IN STROKE PREVENTION DURING CARDIAC SURGERY

When compared with direct palpation and IOTEE, EAU has been found to have a better sensitivity and specificity for atheroma detection than IOTEE.[28] The incidence of stroke may be reduced with the use of pre-CPB IOTEE[18] and IOTEE- and EAU-guided aortic cannulation to minimize handling of the aorta. Randomly compared with surgical palpation alone, EAU is associated with a decrease in perioperative stroke markers[19] (Table 3). However, a prospective series of elderly patients undergoing coronary revascularization randomized to EAU-guided aortic cannulation or cannulation guided by IOTEE and aortic palpation showed no differences in stroke incidence between the groups, despite significantly higher alteration of the cannulation procedure prompted by EAU.[17] Although EAU has a higher sensitivity for atheromas than IOTEE, these findings suggest that adding EAU to IOTEE may have little clinical impact (Table 3). A recent retrospective study of 6051 nonconsecutive patients undergoing EAU for cardiac surgery without a formal control population revealed an impact of EAU in surgical decision making of 4% and a decreased stroke rate compared with patients not receiving EAU during the same period[20] (Table 3). Another study in patients with severe atheroma showed no difference in stroke rates despite substantial IOTEE-prompted changes in aorta manipulation in patients with severe atheroma.[21] Zingone et al[22] showed that selective and routine use of EAU decreased stroke rates in a large number of patients; however, the comparison was made with aortic palpation and not IOTEE (Table 3).

DISCUSSION

Our review found low-quality evidence supporting the use of IOTEE for VHD surgery. We found no randomized trial of test management that clearly established the value of IOTEE and its impact on patient-important outcomes.

However, a body of indirect evidence supports IOTEE in VHD and has been explored in this review. Because aortic atheroma evaluation cannot be excluded from the echocardiographic assessment of patients undergoing valvular surgery, we have also analyzed EAU. Evidence supporting EAU was scientifically more robust but contradictory.

Most recommendations about diagnostic testing rely on an implicit 2-step process to assess how the accuracy of a test indirectly changes patient-important outcomes.[78]

The first step involves comparing the new test to a reference test to determine accuracy. The accuracy of IOTEE for both severity estimation and mechanism identification must be assessed. Transthoracic echocardiography has been used to validate IOTEE findings, with overall favorable comparative results in regurgitant lesions; however, an important caveat is that MR and TR are underestimated. Mechanistically, IOTEE shows excellent performance compared with operative findings. Furthermore, real-time 3-dimensional IOTEE, which is superior to 2-dimensional TEE for identification of native mitral valve regurgitation mechanisms,[79] is currently available and can be performed expeditiously in the OR. Three-dimensional TEE also provides additional information on the anatomy of dehiscence of mitral prosthetic rings and valves.[80] However, patient-important outcomes have not been tested for this technology. Interestingly, preoperative TTE is also highly accurate for determination of mechanisms in MR. Also, for aortic stenosis, the most accurate evaluation is achieved by TTE. Thus, a high value must be placed on preoperative TTE in VHD. Furthermore, several of the pre-CPB surgical quality control aspects can readily be evaluated by preoperative TTE; for example, the presence of AR can be established for cardioplegia planning and the prevention of patient-prosthesis mismatch. These advantages of preoperative TTE and the uncertain clinical benefit of correcting mild residual valvular abnormalities with a second pump run raises the following question: Should all patients with VHD undergo IOTEE, a technique that increases costs and whose complications are minimal but potentially life-threatening? The indirect evidence evaluated suggests that both pre-CPB and post-CPB IOTEE are relevant for valvular repairs and that post-CPB IOTEE is relevant for mitral replacements and hypertrophic cardiomyopathy surgery. Isolated AVRs appear to benefit the least from IOTEE (Table 2), except in the case of homograft sizing.

The second step is to assess the relevance of test accuracy as a surrogate to patient-important outcomes (eg, the consequences of being correctly or incorrectly classified as having or not having a disease).[78] Judgments must be transparent. In an effort to be transparent, we note that the overall impact of IOTEE in VHD could be significantly

lower than our pooled analysis suggests if all consecutive patients had been included in the studies. Furthermore, due to their observational nature, these reports may be biased by false-positive results that may prompt unnecessary second pump runs. The incidence, cost, and morbidity and mortality of unnecessary second pump runs have not been studied and could eliminate any savings prompted by true-positive results or incur additional costs. False-negative results also limit cost-effectiveness and incur future morbidity and mortality. False-negative results seem particularly important in the evaluation of MR, TR, and aortic stenosis severities by IOTEE.

The available relationships between post-CPB IOTEE findings and outcomes are limited and observational. Regarding the relationship between residual MR and adverse clinical outcomes, the latter are thought to be prevented by IOTEE detection and immediate correction; however, we found no prospective, randomized trial determining whether a second pump run to correct less than moderate MR has any positive clinical impact in ischemic or degenerative MR. Also, immediate and effective correction of post-CPB abnormalities requires appropriate communication between echocardiographer and surgeon regarding the anatomic location of residual valvular abnormalities, an issue that we find recurrent in our practice and that remains unstudied in the literature.

A definitive answer to our research question, akin to one on the effectiveness of a therapy, would require direct evidence (randomized trials) regarding the impact of IOTEE and EAU in VHD surgery. In the absence of direct evidence, the diagnostic advantages afforded by IOTEE and EAU provide only indirect evidence of their effectiveness. Nevertheless, improvement in patient-important outcomes can be inferred from the results of nonrandomized trials of test accuracy, provided that effective treatment for the abnormalities detected by that test is available and that test-related adverse effects (ie, IOTEE-related complications) can be reduced.[81] Case reports may offer lower-quality evidence of efficacy that could be considered of higher quality if the effect of IOTEE is considered large (eg, it obviously prevented severe morbidity or obviated the need for emergent reoperation in a patient). These conditions are obviously met by IOTEE in VHD, particularly post-CPB IOTEE. The available literature on the surgical impact of IOTEE suggests that the incidence of IOTEE-prompted second pump runs is greater for VHD surgery than for other cardiac surgeries. Mitral valve repair is the leading cause of second pump runs (Table 2), and aortic valve repair is the most common single-valve procedure requiring a second pump run (Table 2). Mitral replacements are subject to a number of uncommon but real complications that are detectable by post-CPB IOTEE

and are immediately correctable. Interestingly, the need for second pump runs has decreased from the earliest series to the most current (Table 2), likely reflecting superior prostheses and improved surgical repair techniques. Even this lower second pump rate continues to be significantly higher than the complication rate of IOTEE.

Evidence is lacking as to whether correction of PFO, the most common surgery-altering finding on pre-CPB, has any impact on prevention of stroke, and a call to completion of randomized trials has been issued.[82] Moreover, in a recent retrospective study of 2277 cardiac surgery patients with incidental pre-CPB IOTEE-diagnosed PFO, patients with repaired PFO were surprisingly twice as prone to develop postoperative stroke as patients with unrepaired PFO (P=.04).[83]

Despite conflicting data on clinical outcomes and acknowledging potential limitations of EAU (possible contamination of the sterile field, need for more expensive equipment and training), recent guidelines advocate the use of EAU[8] in patients considered to be at high risk for stroke. Whether EAU adds clinical benefit beyond that afforded by IOTEE alone for prevention of stroke remains as yet unanswered.

LIMITATIONS

Our review is limited by the scope of the search strategy (limited to the English language), the high risk of bias in the available evidence (selective reporting of nonconsecutive patients may have overestimated the usefulness of the procedure), and the lack of randomized trials of diagnostic management. Our appraisal raises more questions than it answers. Nonetheless, these questions have the potential of improving institutional quality-control measures and stimulating further scientific exploration of the issues raised.

Given the lower prevalence of pulmonary valve disease in adults, we have not addressed this valve.

IMPLICATIONS FOR CLINICAL POLICY AND RESEARCH

In VHD surgery, available indirect evidence favors the use of IOTEE, placing a high value on avoiding reoperation and a low value on avoiding second pump runs, the very low rate of complications in experienced hands, and the potential incremental costs. Research efforts must concentrate on improving the accuracy of the technique and preventing its related complications. One strategy must be enforcement of guidelines for training in IOTEE, with advanced training of all operators.[84] To prevent false-negative results, preoperative TTE should be performed and reviewed for MR, TR, and aortic stenosis, such that operative indica-

tions are secured by TTE before the patient reaches the OR. To prevent false-positive results, all available specific and supportive echocardiographic signs of regurgitation should be explored before deciding on second pump runs.[85] The ability of the echocardiographer and the surgeon to communicate effectively regarding the residual defect location should be studied and developed.

Randomized studies should be undertaken to address the clinical impact of correcting MR down to a trivial level or abolishing it completely with a second pump run for both ischemic and degenerative scenarios.

Randomized studies addressing the clinical value of IOTEE in isolated AVR could be valuable; however, this would require an alternative technique for exploration of aortic atheroma, such as preoperative computed tomography.

A randomized trial comparing IOTEE with EAU in the prevention of perioperative stroke is critical. Comparison with preoperative computed tomography as an alternative technique seems appropriate.

Studies addressing the sensitivity and specificity of IOTEE for detection of significant TR and maneuvers to improve its accuracy should be conducted. At this juncture, reliance on preoperative TTE is critical.

Closure of incidental PFOs is recommended in patients at high risk of hypoxemia (those with a left ventricular assist device or those undergoing heart transplant)[86] but remains controversial in all other situations.

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