Impact of Appropriate Use Criteria for Transthoracic Echocardiography in Valvular Heart Disease on Clinical Outcomes

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Background: The association between appropriate use criteria for transthoracic echocardiography (TTE) and clinical outcomes is unknown for patients with valvular heart disease (VHD). The aim of this study was to identify the association of TTE appropriateness with downstream cardiac tests and clinical outcomes in patients with VHD over 365 days.

Methods: A subset of 2,297 patients with VHD across six Ontario academic hospitals was selected from the Echo WISELY (Will Inappropriate Scenarios for Echocardiography Lessen Significantly) trial and linked to administrative databases. Each patient's index TTE was classified as "rarely appropriate" (rA) versus "appropriate" (comprising "appropriate" and "may be appropriate" TTE according to the 2011 appropriate use criteria). Overall, 431 of 452 patients with rA TTE were matched 1:1 with patients with appropriate TTE using propensity scores to account for measured confounding.

Results: Matched patients with rA TTE were less likely to undergo repeat TTE (relative risk, 0.46; 95% CI, 0.33–0.66) or cardiac catheterization (relative risk, 0.27; 95% CI, 0.16–0.47) at 90 days compared with patients with appropriate TTE. rA TTE was significantly associated with a decreased hazard of aortic valve intervention (hazard ratio, 0.40; 95% CI, 0.14–0.42), all-cause hospitalization (hazard ratio, 0.44; 95% CI, 0.34–0.57), and death (hazard ratio, 0.31; 95% CI, 0.15–0.66) over 365 days of follow-up.

Conclusions: Patients with appropriate TTE for VHD were more likely to undergo subsequent cardiac testing within 90 days and valve intervention within 1 year than those with a rA TTE. The 2011 appropriate use criteria for TTE have important clinical implications for outcomes in patient with VHD. (J Am Soc Echocardiogr 2020;33:1481-9.)

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Transthoracic echocardiography (TTE) is an important imaging modality for evaluating cardiac conditions and undertaking clinical decision-making.[1] To address concerns regarding increased cardiac utilization and quality assurance, appropriate use criteria (AUC) were developed and have been broadly integrated into quality improvement efforts.[1-5] Prior research has demonstrated that TTE ordered for appropriate indications was more likely to show significant abnormalities compared with rarely appropriate (rA) TTE.[6,7] In TTE ordered for valvular heart disease (VHD), appropriate indications were more likely to yield significant abnormalities

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Abbreviations

AUC = Appropriate use criteria

Echo WISELY = Will Inappropriate Scenarios for Echocardiography Lessen Significantly

HR = Hazard ratio

rA = Rarely appropriate

RR = Relative risk

TTE = Transthoracic echocardiography

VHD = Valvular heart disease

who underwent rA TTE.

compared with rA indications.[5] It remains unclear whether appropriate TTE is more likely to change clinical decision-making or lead to future interventions. In fact, prior work suggests that even TTE ordered for appropriate indications did not change clinical decision-making, although that was a single-center study.[8]

The aim of this study was to determine if TTE ordered for appropriate indications in patients with VHD leads to differences in clinical decision-making compared with patients

METHODS

Study Design and Setting

This study was a secondary analysis of patients from the Echo WISELY (Will Inappropriate Scenarios for Echocardiography Lessen Significantly) trial. Specifically, we investigated patients with known or suspected VHD living in Ontario, Canada, who underwent TTE ordered by a cardiologist participating in the Echo WISELY trial between December 1, 2014, and October 31, 2016. Echo WISELY was a prospective, international, multicenter, investigator-blinded randomized controlled trial whose aim was to reduce the ordering of inappropriate TTE.[9] Participating physicians from eight academic hospitals (seven in Ontario and one in Massachusetts) were randomized 1:1 to receive either an educational intervention, including audit and feedback, or no intervention (control group; ClinicalTrials.gov identifier NCT02038101).[9] The full study protocol and main results have been published.[9,10]

The research team catalogued all transthoracic echocardiographic examinations ordered by participating physicians in the main trial database.[9] On the basis of the clinical indication, they classified each study according to the 2011 AUC and used 2013 AUC nomenclature to define appropriateness categories (i.e., "appropriate," "may be appropriate," or "rarely appropriate").[1-3,9] A second database, the Echo WISELY TTE registry, was maintained in parallel with the Echo WISELY trial database. For the seven Ontario-based sites, CorHealth Ontario captured findings of the examinations ordered by participating physicians. Both the Echo WISELY trial database and the TTE registry were linked, encoded, and analyzed at ICES with the following administrative claims databases: (1) the Registered Persons Database, which contains sociodemographic information on patients with Ontario health cards; (2) the ICES Physician Database, which records sex, date of birth, date of medical school graduation, location of medical school, and specialty for physicians in Ontario; (3) the Ontario Health Insurance Plan database of billing claims submitted for health care services covered by the Ontario government and rendered to patients with Ontario health card numbers; (4) the Discharge Abstract Database, which captures administrative, clinical, and demographic information on hospital discharges and day surgical procedure in Ontario; (5) the National Ambulatory Care Reporting System database, which captures information on hospital- and community-based ambulatory care (including day surgery and emergency department visits); (6) the CorHealth Cardiac Registry, which contains information on patient history of cardiovascular disease and invasive cardiac procedures performed in the province of Ontario; and disease-specific registries for (7) chronic obstructive pulmonary disease, (8) hypertension, and (9) diabetes.

The use of administrative claims data was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a research ethics board. The use of Echo WISELY trial and associated TTE registry data for this study was approved by the research ethics boards of all participating sites.

Participant Characteristics

Patients in Ontario with TTE ordered for VHD-related indications were included if their examinations could be linked with provincial administrative claims data. Starting with all transthoracic echocardiographic studies with AUC classifications ($n = 14,607$ by 153 unique physicians), any studies ordered at the lone US site were excluded, because they could not be linked to provincial databases. All examinations from one Ontario site were excluded because of data quality issues (consistent with the main trial analysis).[9] This resulted in a total of 10,081 studies ordered across six unique hospitals (Figure 1). The pool of eligible studies was further restricted by removing (1) tests ordered by general practitioners to focus on cardiologist ordering patterns who were the majority of ordering physicians and (2) studies that could not be linked to the ICES Physician Database because of a missing identifier. Last, we restricted the analysis to TTE ordered for AUC indications for VHD (i.e., AUC indications 34–56).[3]

Overall, 2,728 of 2,825 transthoracic echocardiographic examinations (96.6%) from the main trial database could be linked with the Echo WISELY TTE registry, of which 2,650 were ordered for Ontario residents with valid provincial health card numbers, aged 18 to 105 years, not living in long-term care homes, and with complete sociodemographic information (i.e., age, sex, and postal code). For patients with multiple examinations, we only selected patients' index examination (i.e., earliest by date), resulting in 2,297 eligible study patients.

Exposure

The primary exposure of interest was whether a patient's index TTE was classified as rA according to the 2011 AUC. The reference (or unexposed) group, defined as "appropriate," comprised patients whose index TTE was classified as "appropriate" or "may be appropriate." Combining both classifications into a single unexposed group of patients was performed because both of these classifications could result in changes in clinical decision-making, and there was also sparsity of observed patients with a "may be appropriate" TTE (defined by only two AUC indications, 44 and 45). Patients in the reference group are hereafter collectively referred to as having undergone appropriate TTE.

Outcomes

Health Care Services Utilization. Dichotomous study outcomes, all capturing whether a patient underwent a given diagnostic test or therapeutic procedure within 90 days after index TTE, included (1) cardiac stress testing, (2) repeat TTE, and (3) cardiac catheterization. Alternatively, we also captured whether patients underwent repeat TTE within 180 days after index TTE.

HIGHLIGHTS

- rA TTE does not yield novel information that alters patient care.
- AUC for TTE can affect clinical outcomes and subsequent cardiac testing in VHD.
- Appropriate TTE was associated with changes in clinical decision-making.
- Appropriate TTE affects rate of hospitalization, mortality, and valve intervention.

We assessed the following count-based outcomes over 90 days per patient: (1) the frequency of visits to a general practitioner, cardiologist, or cardiac surgeon; (2) the frequency of repeat visits to the same cardiologist who ordered their index TTE; and (3) the frequency of visits to a cardiologist or cardiac surgeon. The frequency of emergency department visits over 365 days of follow-up (excluding index TTE date) was also captured.

Clinical Outcomes. Time-to-event outcomes included death (all-cause) and several nonfatal outcomes—hospitalization (all-cause), hospitalization for cardiovascular disease, and valve intervention—assessed over 365 days of follow-up. Only aortic valve surgical or percutaneous interventions were included and modeled in the analysis, as no corresponding events for mitral, tricuspid, or pulmonary interventions were observed among patients with rA TTE. Supplemental Table 1 provides full definitions for study outcomes.

Covariates

Several patient sociodemographic characteristics were captured at baseline: age (in years, treated as continuous), sex, rurality,

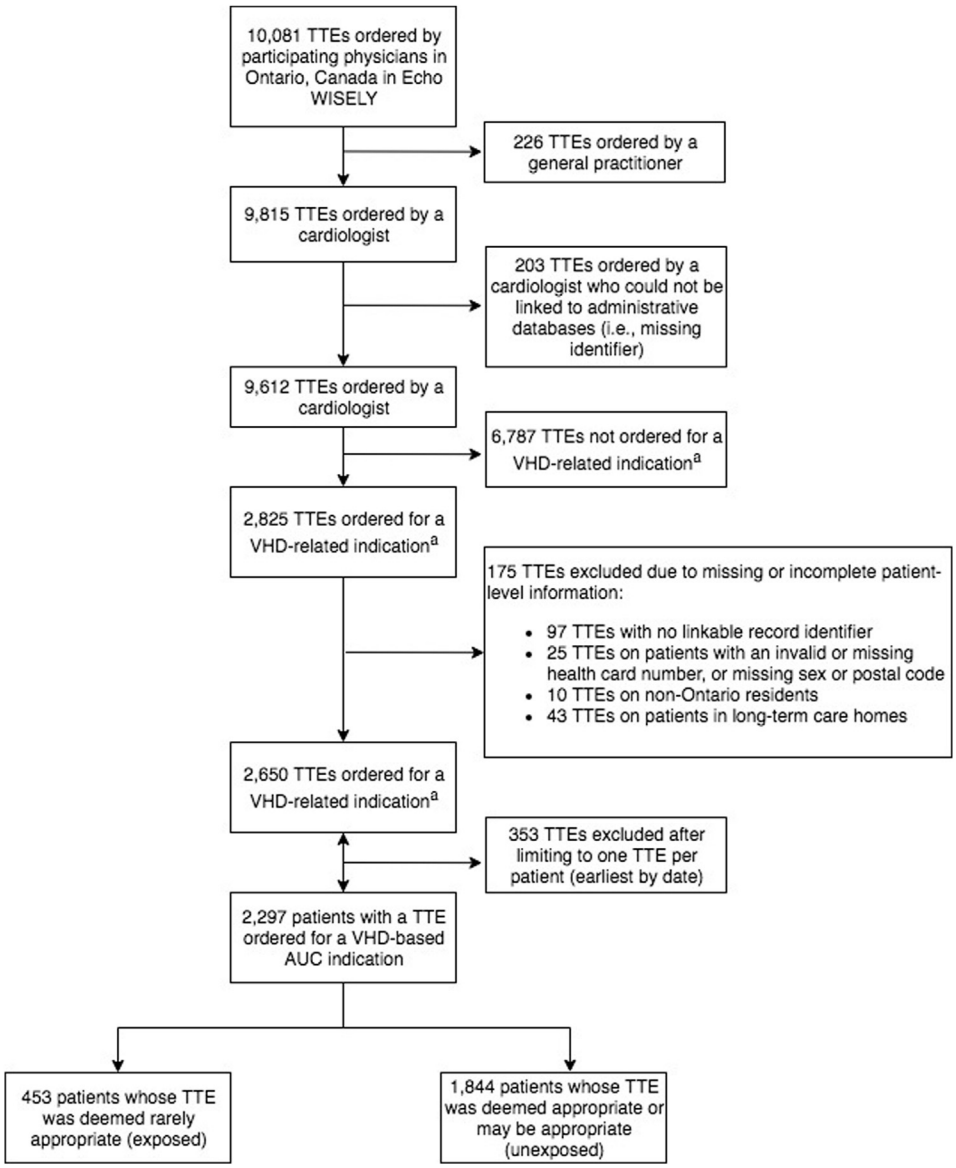

Figure 1 Flow of participants. Selection of participants into unmatched and matched study samples on the basis of the inclusion and exclusion criteria. [a]VHD-related indication considered to be an AUC indication numbered 34 to 56.

Table 1 Distribution of patient and physician characteristics at baseline TTE for VHD-related indication both before and after matching on the logit of patients' propensity scores

Characteristic	Unmatched sample (*N* = 2,297)			Matched sample (*N* = 862)		
	TTE appropriateness*			TTE appropriateness*		
	rA (*n* = 453)	Appropriate (*n* = 1,844)	*d* (%)	rA (*n* = 431)	Appropriate (*n* = 431)	*d* (%)
Patient						
Age, y	74.9 ± 12.9	71.8 ± 14.9	0.23	74.9 ± 12.9	75.6 ± 12.4	0.05
Sex, male	263 (58.1)	969 (52.5)	0.11	250 (58.0)	250 (58.0)	0.00
TTE reason: routine surveillance†	>447 (>98.0)	1,714 (93.0)	0.25–0.35	>425 (NA)	>425 (NA)	<0.08
Live in rural area	36 (7.9)	136 (7.4)	0.02	35 (8.1)	38 (8.8)	0.03
Income quintile						
1 (lowest)	98 (21.6)	391 (21.2)	0.01	89 (20.6)	89 (20.6)	0.00
2	69 (15.2)	368 (20.0)	0.12	65 (15.1)	65 (15.1)	0.00
3	95 (21.0)	344 (18.7)	0.06	92 (21.3)	92 (21.3)	0.00
4	71 (15.7)	293 (15.9)	0.01	65 (15.1)	65 (15.1)	0.00
5 (highest)	120 (26.5)	448 (24.3)	0.05	120 (27.8)	120 (27.8)	0.00
Prior conditions						
Acute myocardial infarction	30 (6.6)	73 (4.0)	0.12	24 (5.6)	32 (7.4)	0.08
Heart failure	100 (22.1)	354 (19.2)	0.07	96 (22.3)	88 (20.4)	0.05
Endocarditis	12 (2.6)	51 (2.8)	0.01	12 (2.8)	11 (2.6)	0.01
Rheumatic fever	≤6 (NA)	≤6 (NA)	<0.08	≤6 (NA)	≤6 (NA)	<0.08
Coronary revascularization	89 (19.6)	150 (8.1)	0.34	74 (17.2)	80 (18.6)	0.04
Renal disease	56 (12.4)	169 (9.2)	0.10	53 (12.3)	54 (12.5)	0.01
Stroke	42 (9.3)	102 (5.5)	0.14	38 (8.8)	48 (11.1)	0.08
PVD	46 (10.2)	123 (6.7)	0.13	41 (9.5)	36 (8.4)	0.04
COPD	109 (24.1)	436 (23.6)	0.01	101 (23.4)	103 (23.9)	0.01
Hyperlipidemia	364 (80.4)	1,258 (68.2)	0.28	344 (79.8)	353 (81.9)	0.05
Diabetes	186 (41.1)	592 (32.1)	0.19	170 (39.4)	168 (39.0)	0.01
Hypertension	380 (83.9)	1,446 (78.4)	0.14	361 (83.8)	365 (84.7)	0.03
TTE ordering physician						
Years since graduation	29.0 ± 11.8	30.2 ± 12.2	0.10	29.2 ± 11.8	29.3 ± 11.6	0.01
Sex, male	400 (88.3)	1,677 (90.9)	0.09	387 (89.8)	387 (89.8)	0.00
International medical graduate	14 (3.1)	101 (5.5)	0.12	13 (3.0)	11 (2.6)	0.03

COPD, Chronic obstructive pulmonary disease; *d*, standardized difference; *NA*, not available; *PVD*, peripheral vascular disease.

Data are expressed as mean ± SD or as number (percentage). For cells with observed frequencies >0 but <6, numbers were suppressed (reported as "≤6" and percentages as "NA") per ICES guidelines. Similarly, those cells that are within 0 to 6 of the total (approaching 100%) were also suppressed (">" or "NA") to prevent calculation of observed frequencies of "≤6." In either case, the standardized difference was also suppressed to prevent back-calculation of cell totals. In addition to matching on the logit of the propensity score, patients were hard-matched on patient sex, income quintile, and physician sex.

*TTE appropriateness defined according to indication and 2011 AUC as either rA or appropriate (which combines TTE classified as "appropriate" or "may be appropriate").

†Reference group: TTE reason diagnostic (i.e., TTE ordered to detect previously undiagnosed condition).

health region (i.e., Local Health Integration Network), and neighborhood income quintile (derived from postal code).[11] We identified whether patients had histories (i.e., billing claims in the past 3 years coded with relevant ICD-10-Canada diagnostic codes or Canadian Classification of Health Interventions procedure codes) of myocardial infarction, heart failure, coronary revascularization, renal dysfunction, stroke, and peripheral vascular disease. We also captured whether patients had histories of endocarditis, rheumatic fever or rheumatic heart disease, chronic obstructive pulmonary disease, hyperlipidemia, diabetes, and hypertension. The full definitions used to identify prior comorbidities and procedures are available in Supplemental Table 2. We recorded several baseline characteristics for the cardiologist who ordered a given patient's index TTE, including sex, years since medical school graduation, and international medical graduate status. Last, we used the recorded 2011 AUC indication to create a variable indicating whether a patient's index TTE was ordered for "surveillance" (including reevaluation or postoperative surveillance) of known VHD versus "diagnosis" (including initial evaluation) of suspected VHD (see Supplemental Table 3).

Table 2 Relative association between appropriateness of index TTE and risk or rate of health care utilization outcomes at 90, 180, and 365 days on the basis of 431 matched pairs of patients with VHD

Outcome	Follow-up time (days)	Exposure (appropriateness of TTE)	Risk ratio	95% CI*
Dichotomous				
Cardiac stress test	90	rA	0.94	0.50–1.80
		A	Reference	Reference
Repeat TTE		rA	0.46	0.33–0.66
		A	Reference	Reference
Cardiac catheterization		rA	0.27	0.16–0.47
		A	Reference	Reference
Repeat TTE	180	rA	0.78	0.64–0.93
		A	Reference	Reference
Count-based			Rate ratio	
Physician visit†,‡	90	rA	0.57	0.48–0.69
		A	Reference	Reference
Repeat cardiologist visit‡		rA	0.53	0.40–0.71
		A	Reference	Reference
Cardiologist or cardiac surgeon visit‡		rA	0.33	0.22–0.50
		A	Reference	Reference
ED visit	365	rA	0.65	0.51–0.83
		A	Reference	Reference

A, Appropriate (classified as "appropriate" or "may be appropriate" according to the 2011 AUC); *ED*, emergency department.
*Variance estimation accounted for matched nature of sample.
†Composite of visits made to general practitioner (or family physician), cardiologist, or cardiac surgeon.
‡Only counted a maximum of one visit per unique physician per day.

Statistical Analysis

Propensity score matching was used to reduce or eliminate baseline imbalances in measured confounders between patients undergoing rA TTE (exposed) and those undergoing appropriate TTE (unexposed) before estimating associations between our study exposure and outcomes.[12] We estimated patients' propensity scores (i.e., their probability of exposure conditional on observed baseline characteristics) using logistic regression to regress an indicator of rA TTE exposure on fixed effects for all covariates listed in the preceding section and a random effect for cardiologist to account for correlation among patients with TTE ordered by the same cardiologist.[12] Following propensity score estimation, patients with rA TTE were matched 1:1 with those with appropriate TTE on the logit of the propensity score using greedy nearest neighbor matching (without replacement) with calipers of width equal to 0.2 times the SD of the logit of the propensity score.[12]

In both the unmatched and matched samples, standardized differences were used to compare the distribution (mean or prevalence) of baseline covariates between patients with rA and appropriate TTE. A standardized difference ≥ 0.10 in absolute value was taken to suggest a potentially meaningful imbalance in the corresponding characteristic between exposure groups at baseline.[12,13] In the event of one or more standardized differences' suggesting baseline imbalance, the propensity score model was iteratively modified by hard matching on problematic categorical covariates and/or including nonlinear terms for problematic continuous covariates.[12]

For dichotomous outcomes, the McNemar test for correlated proportions was used to compare the marginal probability of the event of interest between patients with rA and appropriate TTE in the matched sample. Marginal exposure-outcome associations are presented as risk ratios with corresponding 95% CIs estimated using Wald methods to account for correlation within matched pairs.

Multiple regression analyses were undertaken to independently analyze count-based and time-to-event outcomes. Each count-based outcome was regressed on an indicator of exposure status using negative binomial regression in the matched sample. Resulting exposure-outcome associations are presented as rate ratios with 95% CIs. The incidence of death over 1 year of follow-up was compared between matched rA and matched appropriate TTE subjects using a stratified log-rank test to account for clustering within matched pairs.[14] The association between exposure and all-cause mortality was expressed as a hazard ratio (HR) with 95% CI obtained from a marginal Cox proportional-hazards regression including an indicator variable for exposure status.[14] For nonfatal time-to-event outcomes, all-cause mortality was treated as a competing risk; thus, participants who died during follow-up and before the occurrence of a nonfatal outcome of interest were censored at their time of death.[15] Because Kaplan-Meier estimates of incidence are biased upward in the presence of competing risks, we instead estimated cumulative incidence functions per nonfatal outcome (accounting for death as a competing risk) within each exposure group in the matched sample.[16,17] The equality of cumulative incidence functions between exposure groups was assessed using a Wald test for an indicator of exposure included in a marginal subdistribution hazard (Fine-Gray) regression model on the basis of the matched sample.[17,18] The relative effect of exposure on each nonfatal outcome, accounting for death as a competing risk, was estimated as an HR with 95% CI using marginal cause-specific hazards regression with an indicator variable denoting exposure status

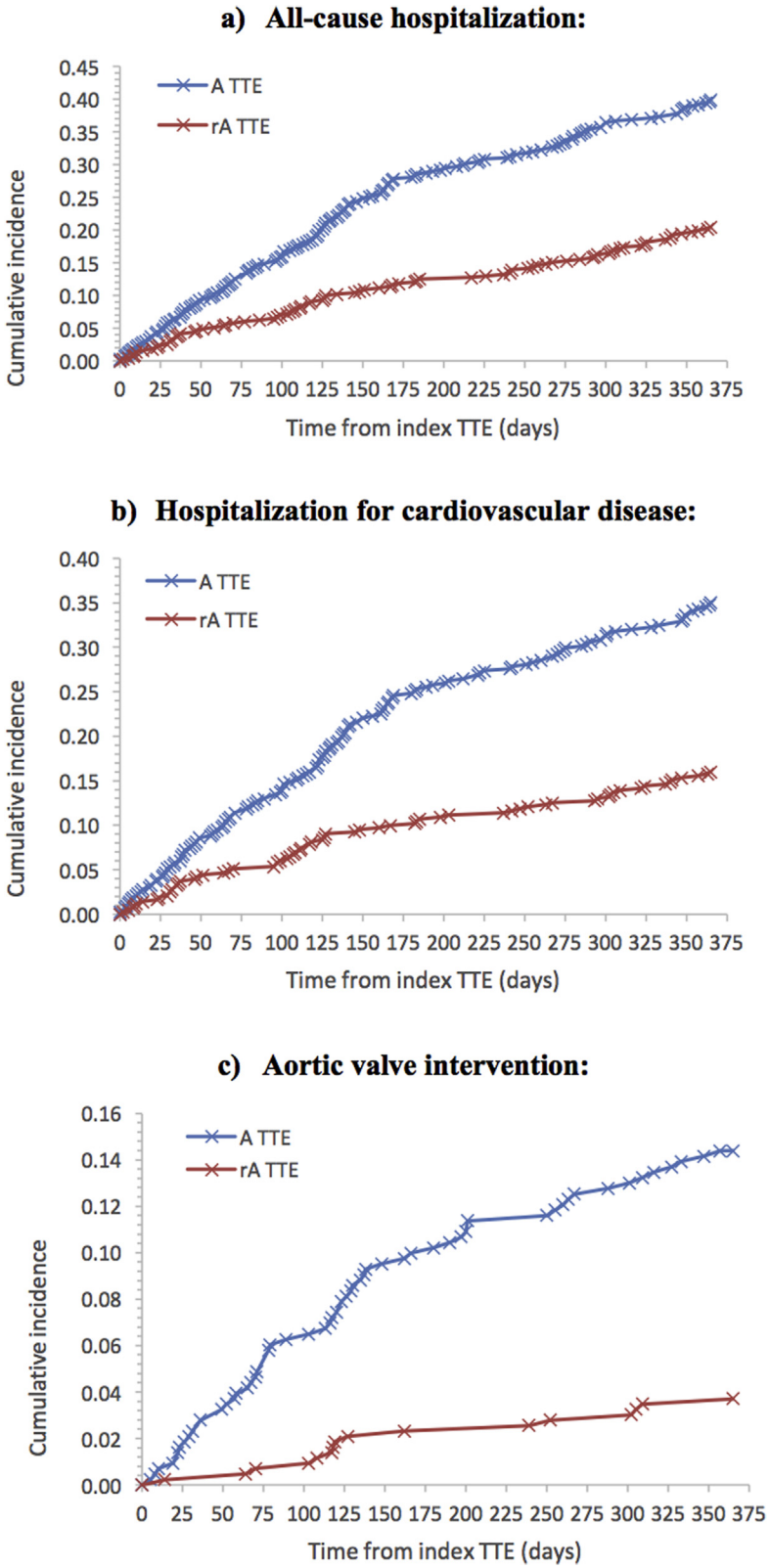

Figure 2 Incidence of outcomes over 365 days of follow-up by appropriateness of index TTE. Cumulative incidence of absolute number of observed events for **(A)** all-cause hospitalization, **(B)** hospitalization for cardiovascular disease, and **(C)** aortic valve intervention over 365 days of follow-up by appropriateness of index TTE. Patients with appropriate (*blue*) TTE were compared with those with rA (*red*) TTE over 365 days of follow-up. *A*, Appropriate (combines "appropriate" and "may be appropriate" according to the 2011 AUC).

Table 3 Relative association between appropriateness of index TTE and hazard of clinical outcomes over 365 days of follow-up on the basis of 431 propensity score–matched pairs of patients with VHD

Outcome	Exposure (appropriateness of TTE)	Number of events (observed)	HR	95% CI*
Death (all-cause mortality)	rA	9	0.31†	0.15–0.66
	A	28	Reference	Reference
Hospitalization (all-cause)	rA	88	0.44‡	0.34–0.57
	A	172	Reference	Reference
Hospitalization for cardiovascular disease	rA	69	0.40‡	0.30–0.54
	A	151	Reference	Reference
Aortic valve intervention	rA	16	0.24‡	0.14–0.42
	A	62	Reference	Reference

A, Appropriate (classified as "appropriate" or "may be appropriate" according to the 2011 AUC).
*Variance estimation accounted for matched nature of sample.
†Estimated from traditional Cox proportional-hazards regression.
‡Estimated from cause-specific hazards regression treating all-cause mortality as a competing risk.

for the matched sample.[17] For all exposure-outcome associations (i.e., rate ratio or HR) estimated by regression analyses, 95% CIs were estimated using a robust variance estimator to account for correlation between subjects within matched pairs.[17,18]

Any results including fewer than six participants and the complement of the Kaplan-Meier survival estimate were not displayed to avoid the risk for identifying individual participants. SAS version 9.4 (SAS Institute, Cary, North Carolina) was to conduct all analyses with statistical significance assessed at a two-tailed P value $\leq .05$.

RESULTS

Participant Characteristics

After applying our eligibility criteria, 2,297 unique patients were identified with TTE captured in the Echo WISELY trial database for VHD-related indications (Figure 1). In total, 453 (19.7%) underwent TTE that was deemed rA, whereas the remaining 1,844 patients (80.3%) underwent TTE that was classified as appropriate (i.e., "appropriate" or "may be appropriate" according to 2011 AUC).

Table 1 summarizes the baseline characteristics among patients with suspected or known VHD, both before and after matching on the logit of the propensity score. Patients in the initial, unmatched sample were, on average, 72.4 years old, and most (n = 2,162 [94.1%]) underwent index TTE for routine surveillance of VHD indications. Before matching, potentially meaningful imbalances (suggested by an absolute standardized difference $\geq$ 0.10) were observed for 14 of 24 dichotomous characteristics compared between exposure groups at baseline, with the largest standardized differences observed for the proportion of patients with prior coronary revascularization (8.1% rA vs 19.6% appropriate), the proportion of patients whose TTE was ordered for routine surveillance (>98.0% rA vs 93.0% appropriate), the prevalence of hyperlipidemia (80.4% rA vs 68.2% appropriate), and mean age (74.9 rA vs 71.8 appropriate). In total, 431 patients with rA TTE (95.1%) were matched 1:1 to control patients with appropriate TTE on the logit of their propensity scores (with hard matching on patient sex, income quintile, and cardiologist sex; see Table 1). After matching, all 24 standardized differences in baseline characteristics were no longer potentially meaningful (i.e., all absolute values < 0.10).

AUC Categories

In this study we categorized appropriate and rA TTE on the basis of the 2011 AUC but used the 2013 nomenclature. Supplemental Table 4 indicates the most frequent indications for appropriate and rA TTE in the matched cohort. The most frequent appropriate indication was AUC 37 (reevaluation of known VHD with a change in clinical status or cardiac examination or to guide therapy), while the most frequent rA indication was AUC 48 (routine surveillance [<3 years after valve implantation] of prosthetic valve if no known or suspected valve dysfunction).[3] The most frequent AUC indications were similar in the unmatched cohort (n = 2,297), in which the most appropriate indications were AUC 37, 49, 46, 51, and 41, compared with AUC 37, 49, 51, 50, and 46 in the matched cohort. The top two AUC accounted for >50% of the indications, and the top four rA indications were identical in both the unmatched and matched groups. When analyzing the matched cohorts, the most common rA indication (53.4%) was AUC 48 (routine surveillance [<3 years after valve implantation] of prosthetic valve if no known or suspected valve dysfunction), and this was most frequently matched with the appropriate group AUC 37, 51, 49, and 50.

Outcomes

Health Care Services Utilization. On the basis of the results of McNemar tests for dichotomous outcomes (see Table 2), matched patients with rA TTE were 6%, 54%, and 23% less likely to undergo cardiac stress testing, repeat TTE, and cardiac catheterization, respectively, within 90 days following index TTE compared with matched patients with appropriate TTE. Extending the observation window to 180 days resulted in a weaker association between undergoing rA TTE and risk for repeat TTE; however, the association remained negative and statistically significant (relative risk [RR], 0.78; 95% CI, 0.64–0.93).

Table 2 also presents the results of negative binomial regression analyses of count-based (frequency) outcomes. Patients with rA TTE made fewer visits to general practitioners, cardiologists, or cardiac surgeons (RR, 0.57; 95% CI, 0.48–0.69) over 90 days of follow-up from index TTE. Undergoing rA TTE was also negatively associated with patients' frequency of repeat visits to the same cardiologists who ordered their index TTE (RR, 0.53; 95% CI, 0.40–0.71) and their frequency of visits to any cardiologist or cardiac surgeon (RR, 0.33; 95% CI, 0.22–0.50) over 90 days of follow-up. Furthermore, patients with rA TTE made fewer visits to the emergency department over 365 days of follow-up relative to patients with appropriate TTE.

Clinical Outcomes. Figures 2A-2C visually compare the incidence of nonfatal clinical outcomes (i.e., all-cause hospitalization, hospitalization for cardiovascular disease, and aortic valve intervention) over

time by exposure status in the matched sample of 431 pairs. The absolute number of observed events from Figures 2A-2C are reported in Table 3.

Thirty-seven of 862 patients (4.3%) died during follow-up (9 rA vs 28 appropriate). The incidence of death, although low in both exposure groups overall, was consistently higher among those who underwent appropriate TTE. A stratified log-rank test indicated that the probability of dying significantly differed between exposure groups for at least one time point during follow-up ($\chi^2[1] = 11.1$, $P = .0009$). On the basis of Cox proportional-hazards regression analysis, patients with rA TTE had a 69% lower hazard of death compared with patients with appropriate TTE (Table 3).

Accounting for death as a competing risk, very few patients in the matched sample underwent aortic intervention (16 rA vs 62 appropriate), whereas hospitalization for any cause or for cardiovascular disease was more common (Table 3). Through visual inspection of the exposure-specific cumulative incidence functions for nonfatal clinical outcomes (Figures 2A-2C), it appears that the incidence of each outcome is consistently higher throughout follow-up in the matched appropriate versus matched rA TTE patients. Clustered Fine-Gray regression analyses indicated that cumulative incidence functions differed significantly between exposure groups for all-cause hospitalization (Wald $\chi^2[1] = 39.3$, $P < .0001$), hospitalization for cardiovascular disease (Wald $\chi^2[1] = 39.4$, $P < .0001$), and aortic valve intervention (Wald $\chi^2[1] = 24.9$, $P < .0001$). Table 3 presents the results of cause-specific hazards regression analysis for each of the three nonfatal, time-to-event clinical outcomes, accounting for death as a competing risk. At any given point during follow-up, matched patients with rA TTE who were alive and had not yet been hospitalized (for any reason) had a significantly lower instantaneous rate of hospitalization (HR, 0.44; 95% CI, 0.34–0.57) compared with matched patients with appropriate TTE. Similarly, undergoing rA TTE at baseline was associated with a decreased cause-specific hazard of cardiovascular-related hospitalization (HR, 0.40; 95% CI, 0.30–0.54) and aortic valve intervention (HR, 0.24; 95% CI, 0.14–0.42).

DISCUSSION

In this substudy of the largest randomized control trial for an intervention designed to improve the appropriate use of echocardiography, patients with VHD who underwent TTE for appropriate indications were more likely to have repeat TTE, cardiac catheterization, revascularization, valve replacement intervention, or more frequent physician visits in the next 365 days. Patients with appropriate TTE had a higher rate of hospitalization and mortality within 1 year than patients with rA TTE. This study demonstrates that appropriately ordered TTE was more likely associated with changes in clinical management than rA TTE.[19]

Prior literature supports our main findings that appropriate TTE was more likely to have important echocardiographic abnormalities compared with rA TTE.[5,6,10,20,21] In particular, appropriate TTE ordered for patients with VHD was more likely to show significant abnormalities than rA TTE.[5] Importantly, patients who underwent appropriate TTE were more likely to have higher mortality and hospitalizations than patients with rA TTE,[7] suggesting that appropriate TTE was ordered in more acutely ill patients or was more clinically significant. Our study extends these findings by demonstrating that TTE defined as appropriate is more likely to lead to clinically relevant testing or treatments, even when controlling for patient comorbidities.

Our finding that appropriate TTE is associated with a higher frequency of further cardiac testing and interventions supports the AUC consensus guidelines that appropriate TTE can change clinical decision-making in patients with VHD, which has not been previously shown. This contrasts with the findings of Matulevicius *et al.*,[8] who showed that TTE ordered for appropriate indications did not change clinical management, but they used a substantially different patient population with a single-center study assessing both inpatient and ambulatory TTE, making comparisons difficult.[8] An Italian study of TTE use in community hospitals supports our findings, showing that appropriate TTE is more likely to be classified as clinically useful and to guide patient care decisions.[19]

Similar findings for the impact of AUC on clinical care decisions have been shown for other imaging modalities, including nuclear myocardial perfusion imaging and stress computed tomography. Inappropriate (or rA) nuclear tests were less likely to show abnormalities or ischemia.[22] These rA tests lead to greater health care costs but are less likely to improve patient care or result in positive findings.[23] A meta-analysis of quality improvement interventions by Chaudhuri *et al.*[24] found that fewer inappropriate cardiac tests were ordered when physicians were audited and received feedback.[24] These findings provide additional support to follow AUC and minimize rA tests that do not contribute to improved patient care.

Common indications for both appropriate and rA TTE highlight the differences in downstream clinical care and outcomes among patients with VHD. Aortic valve disease was the most common condition requiring surgical intervention, with 14.4% of patients with appropriate TTE requiring intervention within 1 year. The increased rate of coronary angiography ordered in this group may be related to the number of valve procedures, as angiography is often required before valve intervention. Appropriate TTE was associated with more valve interventions within 1 year, which may be related to the severity of VHD or the severity of symptoms in this patient cohort. Conversely, routine surveillance of a prosthetic valve with no known or suspected valve dysfunction (AUC 48) was the most common rA TTE indication, which, given the low likelihood of valvular abnormality, would most likely not lead to further clinical testing and management.[3] Another common rA indication was routine surveillance of moderate to severe valvular disease before 1 year or routine surveillance of mild valvular stenosis before 3 years without a change in clinical status or cardiac examination (AUC indications 40 and 38, respectively).[3] Our study supports the current AUC recommendation and valve guidelines that routine surveillance of VHD by TTE more frequently than 1 year should not be routinely performed.

Study Limitations

There were several limitations of this study. First, although the centers in the Echo WISELY study represented a wide variety of ambulatory practices, they were primarily academic centers, so the results may not be generalizable to community hospitals. Second, administrative or large registry databases lack clinical granularity, particularly regarding symptoms and physical examination and laboratory findings. Finally, this study population was part of a randomized control trial to change TTE ordering behavior, so it is possible that physicians' clinical decision-making may have been altered, affecting the results.

Despite these limitations, this large, multicenter cohort study provides clinically important insights into the impact of appropriateness on clinical decision-making and outcomes in VHD. Our findings highlight the relevance of AUC for TTE in the current era of rapidly advancing valvular intervention, diagnosis, and patient monitoring.

CONCLUSION

Patients with VHD who underwent appropriately ordered TTE were significantly more likely to undergo subsequent cardiac testing within 90 days and valve intervention within 1 year than patients who underwent rA TTE, suggesting that appropriate TTE is more likely to influence clinical decision-making.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.echo.2020.06.023.

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