A Clinical Practice Guideline Appraisal for Appropriate Use of Echocardiography in Adult Infective Endocarditis—When to and by Which Mode to Perform an Echo?

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Abstract

Background

Echocardiography (Echo) is the primary imaging modality of infective endocarditis (IE). The recommendations on timing and mode selection of transesophageal echocardiography (TEE) and transthoracic echocardiography (TTE) are not fully in agreement among different guidelines, which can be confusing for clinical decision makers. Thus, we aimed to appraise the quality of recommendations by appraising the quality of guidelines.

Methods

A search of guidelines published in English during 2007 to 2020 which contains recommendations of appropriate use of Echo in IE adult patients has been conducted. PPRAISAL OF GUIDELINES FOR RESEARCH & EVALUATION II (AGREE II) instrument was applied independently by two reviews to assess the integrated quality of identified guidelines. The recommendations of concern were extracted from related chapters.

Results

A total of 9 guidelines meet the criteria with AGREE II score ranging from 36% to 79%, the domain of “stakeholder involvement” got the lowest score. According The most debatable issue is that under what circumstances has the repeated TEE for an initial positive TTE been necessary in suspected IE, the conflicting recommendations on it were presented along with relatively lower evidence level for hardly any related evidence based on.

Conclusions

In the 9 guidelines identified, the recommendations over the appropriate use of Echo are generally satisfying. Clinicians could take into account the guideline quality score when evaluating the recommendations for clinical decision making. More researches with high-grade evidence above the most controversial issues of whether a subsequent TEE is mandatory in uncomplicated native valve IE with an initial positive TTE are needed in the future.

Background

Echocardiography (Echo) is the primary imaging modality for infective endocarditis. A positive Echo defined as vegetation or abscess, or new dehiscence of prosthetic valve is included as a major modified Duke criterion along with positive microorganisms[1]. Besides, the hemodynamics and mechanism severity can also be presented by conducting a echocardiographic examination[2]. The appropriate use of Echo should be both cost-effective, time-efficient, and taken potential associated complications into account[3, 4], while also provide timely and accurate guidance for the diagnosis and management of diseases. One single-center study had revealed that a notable number of TEE studies for assessment of infective endocarditis (IE) were rarely appropriate[5]. Over the past 15 years, there are 9 guidelines published in English covers IE diagnosis and contains evidence-based recommendations about the appropriate application of Echo (only the latest version was included of updated guidelines). Under some certain clinical scenarios, these guidelines differ in the recommendations for transesophageal echocardiography (TEE) and transthoracic echocardiography (TTE) applications, which can be confusing for clinical decision makers. AGREE is an instrument for comprehensive guideline evaluation from 6 different domains including Scope and purpose, Stakeholder involvement, Rigour of development, Clarity of presentation, Applicability and Editorial independence. And AGREE II, which was an updated version in 2013, has made some modification on certain items of the original version[6]. A systematic review of the appropriate use of Echo based on critical assessment and the quality comparison of different guidelines was presented in order to allow clinicians to make better decisions under certain contentious or confusing clinical scenarios.

Methods

Searching process

A literature search of current clinical practice guidelines which contain recommendations of IE imaging examinations was conducted on Pubmed, Embase, Web of science and websites of guideline development societies. “adult” “infective endocarditis”

“echocardiography” “transesophageal echocardiography” and “transthoracic echocardiography” were searched either singly or in combination. The search covered guidelines published in English from 5, June, 2007 to 5, July, 2019.

Including criteria

An included guideline needs to meet following criteria:

1. Conforms to the definition of a guideline given by The Institution of Medicine[7], which was described as “systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstance”.
2. Contains recommendations on the rational use of Echo in the diagnosis, treatment, or follow-up process of IE.
3. Targeted at adult patients.
4. The Latest updated version of the updated guidelines.
5. Full-text free.
6. An English version, including translations from other languages.

Titles and abstracts were reviewed by 2 different reviewers independently. Afterwards disagreements were discussed and reached a consensus with the third party presented. The final selection was performed by 2 reviewers together.

Guideline appraisal and recommendation extraction

We carried a comprehensive evaluation of the selected 9 guidelines from 6 domains set out in AGREE II instrument, which includes: i) Scope and purpose; ii) Stakeholder involvement; iii) Rigor of development; iv) Clarity of presentation; v) Applicability; vi) Editorial independence. Two reviewers evaluated the 23 items independently with a score ranging from 1 to 7, where 1 represents a strong disagreement, for no relevant information was given or the concept was barely reported, and 7 represents a strong agreement, for the quality of reporting was exceptional or fully met the criteria set by AGREE II. The final score of each domain was obtained by the calculation formula given by AGREE II: The scaled domain score = (Obtained score – Minimum possible score) / (Maximum possible score – Minimum possible score). If the difference between the scores given by two reviewers for a certain item is greater than 20% of the lower score, a third reviewer would participate in the review and evaluates the guidelines[8]. The guidelines with average score higher than 60% was defined as “Strongly recommended”, these with a score ranging from 30–60% was defined as “Recommended with some modification”, the others with a score lower than 30% was defined as “Not recommended”[9].

Except the two guidelines (CSC 2015, SSID 2007) that did not report Conflicts of Interest (COI)[10, 11], we calculated the proportion of panel members with an industry relationship (RWI) of authors reported in other guidelines, analyzed the correlation between the RWI ratios and the AGREE II scores using SPSS 25.0. α 0.05 indicates statistical significance[8].

All recommendations on the appropriate use of Echo including its timing and mode (TTE and TEE) were extracted from the relevant chapter. To avoid ambiguity, the descriptions used in the table are the same as they are in the original guideline recommendations, there is no synonym replacement. Also, in an effort to avoid confusion phrasing, the class of recommendation and the level of evidence referred from SSID 2007 were converted into a unified form that is consistent with other guidelines according to its definition[11]. The grade of recommendation and the level of evidence denoted hereafter are uniformly expressed as I/II/III and A/B/C respectively.

Results

Guidelines meet the criteria

A total of 1015 records were searched out during the literature search, 1006 of which were removed after title, abstract, and full-text reviewing (Fig. 1). There are 9 guidelines reported by 8 host organizations (some of them were joint working) finally meet the including criteria (NHAM 2017; AHA 2015; ESC 2015; BSAC/BHRS 2014 JCS 2017; BSAC 2011; SEIMC 2015; CSC 2015; SSID 2007)[10–18]. Guideline identifier, Host organization, Region, Average AGREE II score, COI, Number of Echo recommendations, RWI are summarized in Table 1.

Table 1
General characteristics of the included 9 guidelines.

Guidelines identifier, Year‡	Organization(s) responsible for guidelines development	Target population	Proportion of authors RWI	AGREE II score, %	Number of Echo recommendations	Guideline status
AHA, 2015	American Heart Association	Adult IE	4/16 (25.0%)	77	5	Strongly recommended
ESC, 2015	European Society of Cardiology	IE	13/20 (65.0%)	75	10	Strongly recommended
BSAC, 2011	British Society for Antimicrobial Chemotherapy	Adult IE	2/9 (22.2%)	54	7	Recommended
BSAC/BHRS, 2014	British Society for Antimicrobial Chemotherapy, British Heart Rhythm Society	Infections related to ICED	4/12 (33.3%)	62	5	Strongly recommended
SEIMC, 2015	Spanish Society of Infectious Diseases and Clinical Microbiology	IE caused by S.aureus	6/17 (35.3%)	53	5	Recommended
SSID, 2007	Swedish Society of Infectious Diseases	IE	–	36	6	Recommended
CSC, 2015	Chinese Society of Cardiology	Adult IE	–	39	9	Recommended
JCS, 2017	Japanese Circulation Society	IE	7/24 (29.2%)	55	10	Recommended
NHAM, 2017	National Heart Association of Malaysia	IE	0/13 (0%)	79	7	Strongly recommended

‡ The guideline references were listed in Table S4; IE: infective endocarditis; ICED: implantable cardiac electronic device; RWI: the proportion of panel members with an industry relationship; AGREE II: APPRAISAL OF GUIDELINES FOR RESEARCH & EVALUATION II.

Guidelines appraisal by AGREE II

The scores of each guideline are presented in the radar charts (Fig. 2). The AGREE II scores of all guidelines were ranging from 36–79%, with a median of 55%. There are 4 of them (NHAM 2017; AHA 2015; ESC 2015; BSAC/BHRS 2014)[12–15] were rated as “Strongly recommended” with a score higher than 60%. The others (JCS 2017; BSAC 2011; SEIMC 2015; CSC 2015; SSID 2007)[10, 11, 16–18] were judged as “Recommended with some modification” with a score of 36–55%. No one was rated as “Not recommended” with a score lower than 30%. There was no item whose difference between the scores given by the two reviewers was greater than 20%.

Domain1 (Scope and purpose) focuses on the overall goal, the specific health issues contained in the guideline, and its target population. Contrast with the other domains, guidelines’ performance in this domain is uneventful. Most of them generally summarized the concerning issues, yet did not elaborate on them. NHAM 2017, BSAC/BHRS 2014, BSAC 2011[12, 15, 17] specifically expounded on the three aspects corresponding with the AGREE II rules, thus getting a relatively high score.

Domain2 (Stakeholder involvement) concerns about whether the guideline was developed by the appropriate stakeholders and considered the views of its intended users. This domain got an averagely lowest score with two-thirds of the guidelines no higher than 33%. Only NHAM 2017, BSAC/BHRS 2014, and JCS 2017[12, 15, 16] specified in detail specialists of what department the clinical guideline should apply to. In addition, only BSAC/BHRS 2014[15] reported a patient’s perspective view in the external review, while the rest of the guidelines did not mention the views of the target population at all.

Domain3 (Rigour of Development) is comprised of the processes of synthesizing the evidence, the formulation of the recommendations and the procedure for updating. In regard to the selection of evidence, CSC 2015 and SSID 2007[10, 11] had no information reported at all, and BSAC/BHRS 2014, JCS 2017 and BSAC 2011[15–17] had little description on this subject. Guidelines other than AHA 2015, ESC 2015[13, 14], and NHAM 2017[12] have not presented the updated statements and detailed information on

external expert review. The exposition of methods for formulating the recommendations has been relatively clear, thereby better scores were given to the 3 items concerned.

Domain4 (Clarity of Presentation) relates to the clarity of the description and the format of the guideline. The average score of this domain is the highest of all while the discreteness of scores was the smallest.

Domain5 (Applicability) deals with the practical implementation, efforts for improving uptake, and resource implications. Except NHAM 2017 ESC 2015 and AHA 2015[12–14], the rest of guidelines had no additional disseminating materials provided, also, very few guidelines made mention of cost implication. Whereas the monitoring and auditing criteria was set precisely in all guidelines with an average score higher than 80%.

Domain6 (Editorial Independence) pertains to the transparency declarations including the funding body and competing interests of guideline development group members. JCS 2017, CSC 2015 and SSID 2007[10, 11, 16], had no clarification on the funding body and its influence on the content. SSID 2007[11] and CSC 2015[10] had no records on the disclosure of potential COI, excepting from which, for the rest of the guidelines, there is no correlation between RWI and AGGEE II score (Pearson's correlation r=-0.081 P = 0.863).

We found out that more than half of the guidelines (5 of 9) had scores less than 60%. Using independent-samples t-test, t'-test (editorial independence) and Wilcoxon Rank-Sum test (Clarify of presentation), the "recommended with modification" guidelines are statistically different from the guidelines with scores more than 60% in the domains of "Rigour of Development" (P = 0.015), "Applicability" (P = 0.005) and "Editorial Independence" (P = 0.024) (Fig. 3). With regards to the specific items, there are 8 of 9 guidelines had received a score of zero on the item of "target population", which indicates that the existing guidelines generally did not take the view of a patient's perspective into account during the formulation of recommendations.

Recommendations on appropriate use of Echo

There are 5 of 9 guidelines gave detailed algorithm flowcharts on the use of Echo. Recommendations for different clinical scenarios were organized into Table 2 (recommendations with controversies) and Table S1 (recommendations without controversies). As is presented, consensus and controversy coexist and consensus outweighs controversy.

Table 2
Recommendations with controversies

Clinical Scenarios	Guidelines identifier, Year‡	Specific subgroups features	Mode of echocardiography			Comments	Strength of recommendations¶
			TTE		TEE		
The first-line modality of suspected IE	NHAM, 2017	—	Echo is recommended with TTE being the first line imaging investigation.			As TTE is non-invasive and widely available; TEE should be performed subsequently if indicated.	I B
	AHA, 2015	—	Recommend	—		—	I B
	ESC, 2015	—	Recommend	—		—	I B
	JSC, 2017	—	Recommend	—		—	I B
	BSAC, 2011	—	Recommend	—		Which should be done as soon as possible, ideally within 24 h.	C
	CSC, 2015	—	Recommend	—		—	I B
	SSID, 2007	—	Echo is recommended with TEE being the first choice.			Because of its higher sensitivity both regarding vegetations and complications as aortic root abscesses.	I B
Remained high clinical suspicion of IE despite negative initial TTE and TEE examinations	NHAM, 2017	—	Repeated TTE	and/or	Repeated TEE	Within 7 days if clinical findings changed.	I C
	AHA, 2015	Patients with an initial negative TEE.	—		Repeated TEE	Within in 3 to 5 days or sooner if clinical findings change.	I B
	ESC, 2015	—	Repeated TTE	and/or	Repeated TTE	Within 5 to 7 days.	I B
	JCS, 2017	—	Repeated Echo is recommended.			After 3 to 7 days.	I C
	BSAC, 2011	—	Repeated TTE	or	Repeated TTE	Within 7 to 10 days.	C
	CSC, 2015	—	Repeated TTE	or	Repeated TTE	Within 7 to 10 days.	I B
Suspected IE with positive TTE (whether another TEE is needed)	NHAM, 2017	Worsening clinical course/high predisposing risk/Echo suggests possible complications	—		Recommend	No formal recommendation come with level of evidence.	—
	AHA, 2015	Patients with concern for intracardiac complications.	—		Recommend	—	I B

‡ The guideline references were listed in Table S4; ¶ The level of evidence on each recommendation was adopted from respective guideline; Echo: echocardiography; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography.

ESC, 2015	All patients expect isolated right-sided native valve IE with unequivocal TTE finding.	—	Recommend	To rule out local complications.	IIa C
JCS, 2017	All patients expect isolated right cardiac valve IE.	—	Recommend	—	IIa C
BASC, 2011	All adults with a positive TTE expect isolated right-sided native valve IE.	—	Recommend	No formal recommendation come with level of evidence.	—
SSID, 2007	Uncomplicated native valve IE and prompt response to treatment.	—	No repeated TEE	—	III C

‡ The guideline references were listed in Table S4; ¶ The level of evidence on each recommendation was adopted from respective guideline; Echo: echocardiography; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography.

It is addressed by 5 of 9 guidelines that when a first-line TTE had been non-diagnostic on account of its poor echocardiographic window, a further TEE is recommended for its higher sensitivity of 85%-90% which is superior over TTE of 75% (class of recommendation: I, level of evidence: B-C)[1].

In patients with suspected IE with a prosthetic heart valve/intracardiac device, TEE is recommended by 5 of 9 guidelines (class of recommendation: I, level of evidence: B-C). Furthermore, BSAC/BHRS 2014, the guideline direct at patients with implantable cardiac electronic device (ICED), suggested that in patients with implantable cardiac electronic device lead infection (LCED-LI) or implantable cardiac electronic device associated native or prosthetic valve endocarditis (LCED-IE) or suspected generator pocked infection concurrent ICED-LI or ICED-IE, Echo is recommended (level of evidence: B-C)[15].

In patients with S.aureus bacteremia (SAB), Echo is recommended by 7 of 9 guidelines, among which the specific recommendations on catheter-related and ICED-related are involved (class of recommendation: IIa, level of evidence: B-C).

5 of 9 guidelines advised a follow-up/repeated Echo (by which mode was not specified) after the onset of a suspected IE (class of recommendation: I, level of evidence: B-C), among which ESC 2015 and CSC 2015 had further made it clear that the clinical manifestations of a complication included new murmur, embolism, persisting fever, heart failure, abscess, and atrioventricular block.[10, 14] While SSID 2007 only counts a new or progressive heart failure as the indication for a repeated Echo[11].

For patients under medical therapy, 3 of 9 guidelines recommended the follow-up Echo (class of recommendation: I-IIa, level of evidence: B-C), besides of which, the repeated Echo is only recommended for complicated IE in SSID 2007 (strength of evidence: II C) and IE with suspected development of complications in AHA 2015 (strength of evidence: I B). Moreover, SSID 2007 addressed that no repeated TEE for uncomplicated IE and these with good response to treatment is needed (strength of evidence: II C)[11, 13].

An intraoperative Echo examination for IE requiring surgery is recommended by 3 of 9 guidelines (class of recommendation: I, level of evidence: B-C) and brought up with no formal recommendation by BASC 2011[17]. Moreover, BASC/BHRS 2014 mentioned that patients after IECD removal also need the repeated Echo to identify persisting vegetations (level of evidence: C)[15].

At the completion of antibiotic therapy, TEE is recommended in 6 of 9 guidelines (class of recommendation: I-IIa, level of evidence: C).

The controversial processing steps among different guidelines' algorithms were shown in Fig. 4. As shown, there are 7 of 9 guidelines covers the recommendation on the first-line modality of suspected IE, most of which (6 of 7) agreed with TTE being the first choice (class of recommendation: I, level of evidence: B-C) while SSID 2007 argued for TEE instead[11] (class of recommendation: I, level of evidence: B).

After an initial TEE had been performed and indicated a negative result, it is recommended by 6 of 9 guidelines that a subsequent TEE should be conducted within a given time limit stipulated by different guidelines when suspicion exists without diagnosis of IE (class of recommendation: I, level of evidence: B-C). But the maximum time limit given by different guidelines varied from 5 to 10 days.

For the issue that whether a subsequent TEE is needed for suspected IE with a positive TTE, guidelines replied with varying target population features. BASC 2011 suggested that all positive TTE should be considered as the indication for a subsequent TEE (no formal recommendation formulated)[17]. while ESC 2015 and JCS 2015 excluded the unequivocal isolated right-sided native valve IE (class of recommendation: IIa, level of evidence: C)[14, 16]. In the meanwhile, NHAM 2017 and AHA 2015 advised that TEE is necessary in patients with concern for complications, besides of which NHAM 2017 also mentioned that worsening clinical course and high predisposing risk should be included in indications for TEE too (AHA 2015 with strength of recommendation of I B, no formal recommendation formulated in NHAM 2017)[12, 13]. With regards to a view of not using a repeated TEE for a positive TTE, SSID 2007 and NHAM 2017 recommended to do so for the patients with uncomplicated native valve IE, prompt response to treatment, or low predisposing risk (SSID 2007 with strength of recommendation of IIIc, no formal recommendation formulated in NHAM 2017)[11, 12].

Discussion

It has been the first time that we evaluated controversies among recommendations on the appropriate use of Echo combined with AGREE II score of guidelines.

Among the 9 guidelines, NHAM 2017 and BHRS 2014 mentioned in the methodology of compiling the entire content on the basis of the AGREE II principle, and both of which had received a score of higher than 60%.[12, 15] However, compared with other guidelines which did not manage to involve some certain AGREE II items and as thus got deducted scores, the superior score of NHAM 2017 had largely owed to a more extensive coverage of items rather than a higher grade of each item. The description of some items in NHAM 2017 is rather perfunctory, which is limited to making a mention without any in-depth content, such as item 19 (facilitators and barriers to the application) and item 20 (the potential resource). Although we endorse the use of AGREE II tool to assist in developing guidelines, criticism comes that comprehensive coverage of quantity is just as important as quality.

One more important point to be noted, since studies had disclosed that the exposure to information provided directly by pharmaceutical companies had been found associated with higher prescribing frequency, higher costs, or lower prescribing quality, disclosure of Potential COI could be very necessary[19, 20]. We found no correlation between the proportion of RWI and the AGREE II score in the guidelines we concerned. There is a possibility that some guidelines were found to have a high RWI due to a more thorough and accomplished disclosure process and less underreporting, like ESC that has a very detailed COI appendix[14]. On the contrary, NHAM 2017 only made a mention of no potential conflict of interest to disclose, no further detailed relevant content was presented, for which it cannot be ruled out that the actual RWI proportion of its guideline committee members concealed and underreported.

By comparing recommendations and viewpoints of different guidelines, we found that upon most occasions, the algorithms of echocardiography usage given by these guidelines are roughly the same. Differentiated recommendations are mainly direct at more specific clinical scenarios, which did not conflict with each other but are complementary.

However, there are also a few issues concerning with conflicting views. The first issue relates to the first-line modality of suspected IE. A Cost-effectiveness Analysis found that the initial use of TEE is the optimal diagnostic strategy for most suspected patients[21]. Also, SSID 2007 recommended TEE as the first choice for its cost efficiency and higher sensitivity for vegetations and complications[11] while all of the other guidelines recommended TTE. However, these guidelines recommended TTE for different reasons, among which AHA 2015 proposed that although TEE is the better choice with higher sensitivity, it is not always immediately available (since a patient did not fast for the preceding 6 hours or the medical institution did not have 24-hour TEE service), thus a TTE is recommended to be conducted as soon as possible, nonetheless it remains a suboptimal alternative[13]. In addition, there are other guidelines like JCS 2017 recommended TTE based on its value in evaluation of valve dysfunction and hemodynamics, also in its feature of noninvasive and repeatable[16]. Actually, with the technological progress of echocardiography, TTE was proved to have a sufficient negative predictive value of native valve endocarditis (NVE) in patients with low to intermediate risk when strict negative criteria are applied[22, 23]. And for these low risk patients stratified based on clinical judgment, although few recommendations had been formed, guidelines had addressed in the context or in the algorithm that a repeated TEE is not required[10–14, 16, 17, 24], which have been verified by recently published Meta-analyses[25, 26]. Thus we could agree that the claim of SSID 2007 that TEE is better as well as more cost

efficient than TTE as a first-line examination is outdated, since it was published longer and was blamed for citing studies using obsolete echocardiography methods and mixed methodology[27].

For a first-line negative TTE with undiagnosed but high suspicion of IE, a repeated TEE is of full agreement, but the maximum time limit given by different guidelines was varied from 5 to 7 days. As known, the severity of pathology distinguished by echocardiography could help to determine following management strategy[28], and research has shown that early (< 4 days) definitive echocardiography is associated with less embolic events than late[29]. Therefore, time delays to diagnostic Echo should be avoided.

For the issue that whether a subsequent TEE is mandatory in uncomplicated NVE with initial positive TTE. NHAM 2017 presented in the algorithm graph that patients with low predisposing risk and good response to treatment only need repeated TEE as indicated and before discharge, so did SSID 2007, which recommended for no repeated TEE both for diagnosis and management[11, 12]. And NHAM 2017 proposed that only with high predisposing risk or worsening clinical course like prosthetic valve, various coronary heart disease, appearance of new murmur, presence of heart failure would need a subsequent TEE, and so did AHA 2015[12, 13]. As ESC 2015, JCS 2017 and BASC 2011 recommended a subsequent TEE for all positive TTE except isolated right-sided native valve IE to evaluate the presence of intracardiac complications[14, 16, 17]. If an initial TTE presents the vegetation clearly and the probability of complications is low (presented as a small aortic vegetation, mild aortic regurgitation, and normal left ventricular size and function) then a subsequent TEE seems to make no incremental value for the treatment strategy[25], on which occasion the TEE could be overused. A large and extensive vegetations that are more mobile as well as softer could be more associated with the development of complications and embolic events[30]. Nevertheless, we found no official definition of “uncomplicated IE” in all guidelines, and the above content is cited from other studies. Also, with a recommendation class of IIa which indicates that weight of evidence and opinion is in favor of usefulness and/or effectiveness, and an evidence level of C which refers to only consensus of opinion, the recommendations that suggested a subsequent TEE over a positive TTE seem to be less evidence-based and convincing. Similarly, the strength of evidence given by the SSID 2007 that explicitly recommended no need to repeat TEE is also of C III, which manifests that the evidence to support the recommendation for use/intervention is weak and was derived from opinions of respected authorities, based on clinical experience descriptive studies or reports of expert committees. So, we can conclude that neither side has sufficient evidence in this issue, and more researches with high-grade evidence are needed in the future.

Conclusion

According to AGREE II, compared with guidelines of “recommended with modification”, these of “strongly recommended” was more rigorously developed and the recommendations in which could be identified as being better quality. Clinicians could take into account the guideline quality score when evaluating the recommendations for clinical decision making. There is also an expectation for the later updating guidelines of a better performance in the domain of “Stakeholder involvement”. The main controversy arose from the views of the SSID 2007, with the lowest AGREE II score among the guidelines, the primary cause could be its outdated concepts. Over the most contentious issue of whether a subsequent TEE is mandatory in uncomplicated native valve IE with initial positive TTE, hardly any related studies on this issue have been reported, more researches better with high-grade evidence are needed in the future.

Abbreviations

Echo: Echocardiography; IE: Infective endocarditis; TEE: Transesophageal echocardiography; TTE: Transthoracic echocardiography; AGREE II: APPRAISAL OF GUIDELINES FOR RESEARCH & EVALUATION II; COI: Conflicts of Interest; RWI: the proportion of panel members with an industry relationship; ICED: Implantable cardiac electronic device; LCED-LI: Implantable cardiac electronic device lead infection; LCED-IE: Implantable cardiac electronic device associated native or prosthetic valve endocarditis.

Declarations

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Authors’ contributions

Peihan Xie: Conceptualization, Resources, Writing Original Draft. Xiaodong Zhuang: Conceptualization, Methodology, Formal analysis, Investigation, Supervision. Menghui Liu: Data curation, Writing- Original draft preparation. Shaozhao Zhang: Data curation, Writing-

Original draft preparation. Jia Liu: Writing- Original draft preparation. Donghong Liu: Project administration, Supervision. Xinxue Liao: Validation, Supervision, Writing - Review & Editing. All authors read and approved the final manuscript.

PHX, XDZ, and XXL contributed to the study design. PHX and XDZ reviewed the guidelines, DDL re-examined the results, SZZ and MHL performed the statistical analysis, PHX and JL drafted the main manuscript and all authors reviewed and approved the final submitted manuscript.

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Availability of data and materials

All data generated or analysed during this study are included in this published article and supplementary information files.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflicts of interest or personal relationships.

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Figures

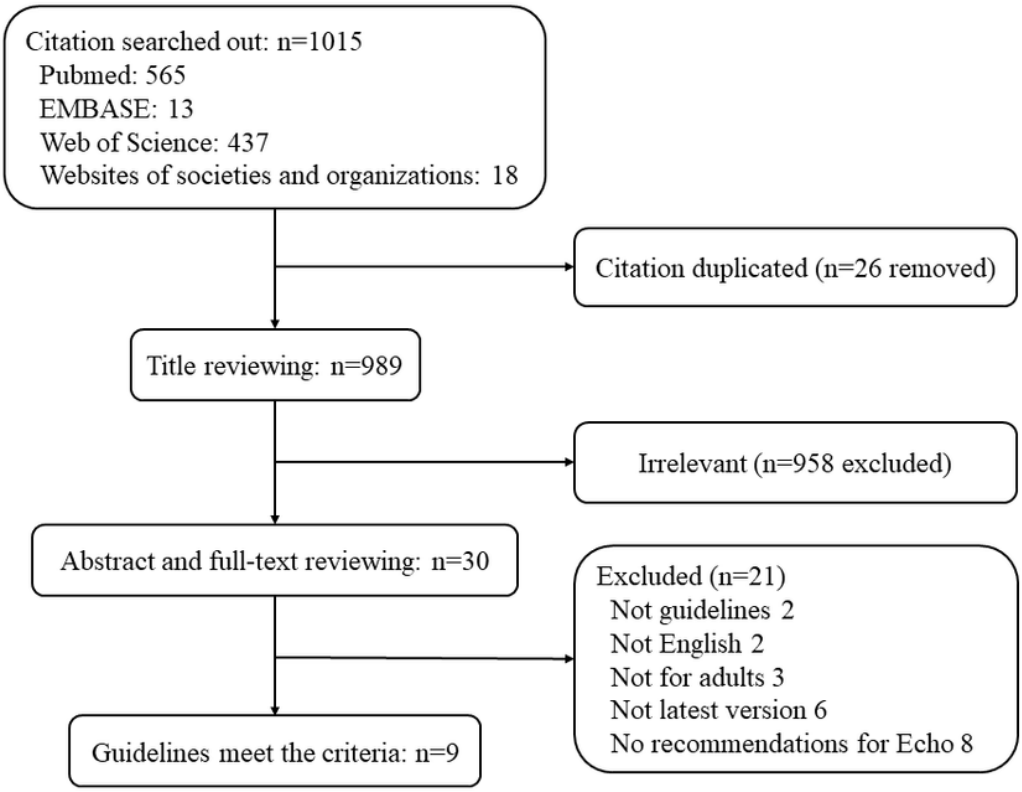
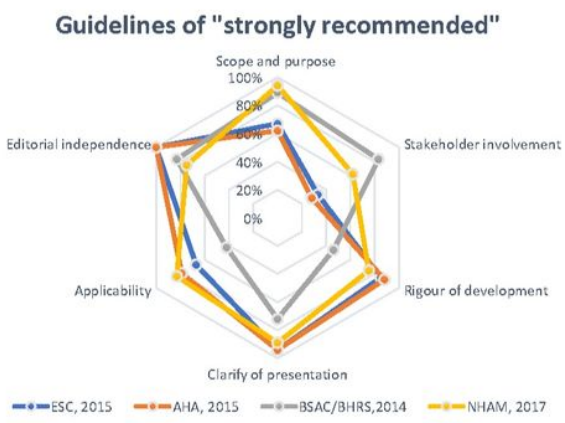
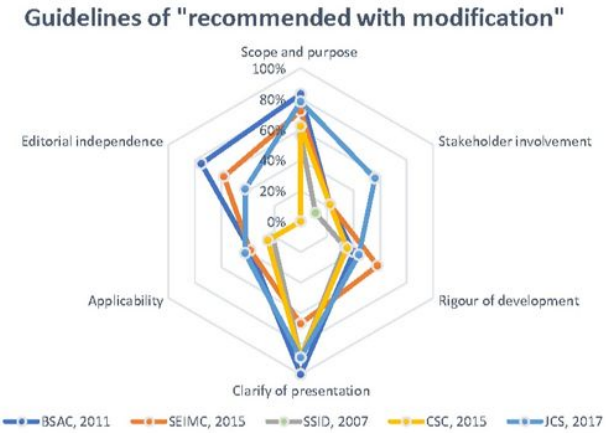


Figure 1

Flow diagram of inclusion/exclusion processes for the guidelines



(right)



(left)

Figure 2

Rader charts of guidelines' AGREE II scores distribution of 6 domains, guidelines were divided into different charts by scale of aggregate score. AGREE II, appraisal of Guidelines for research & evaluation. (right) Guidelines of "strongly recommended" (left) guidelines of "recommended with modification"

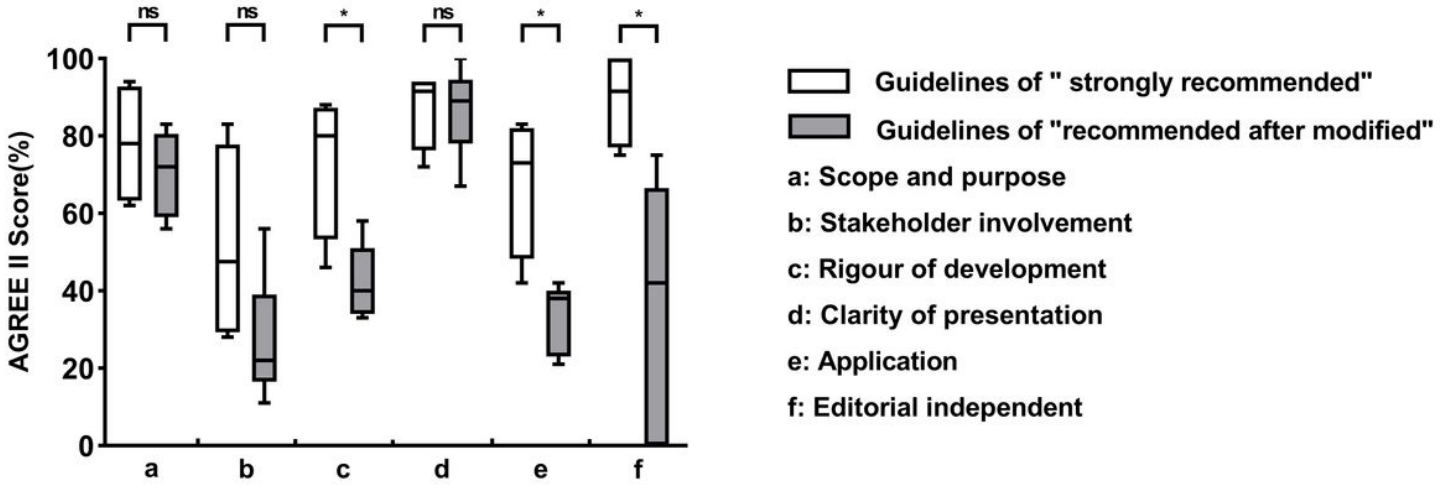


Figure 3

Box plot of the AGREE II score distribution comparison between "guidelines strongly recommended" and "guidelines recommended with modification" in different domains. ns: no significant difference. *: significant difference (P < 0.05).

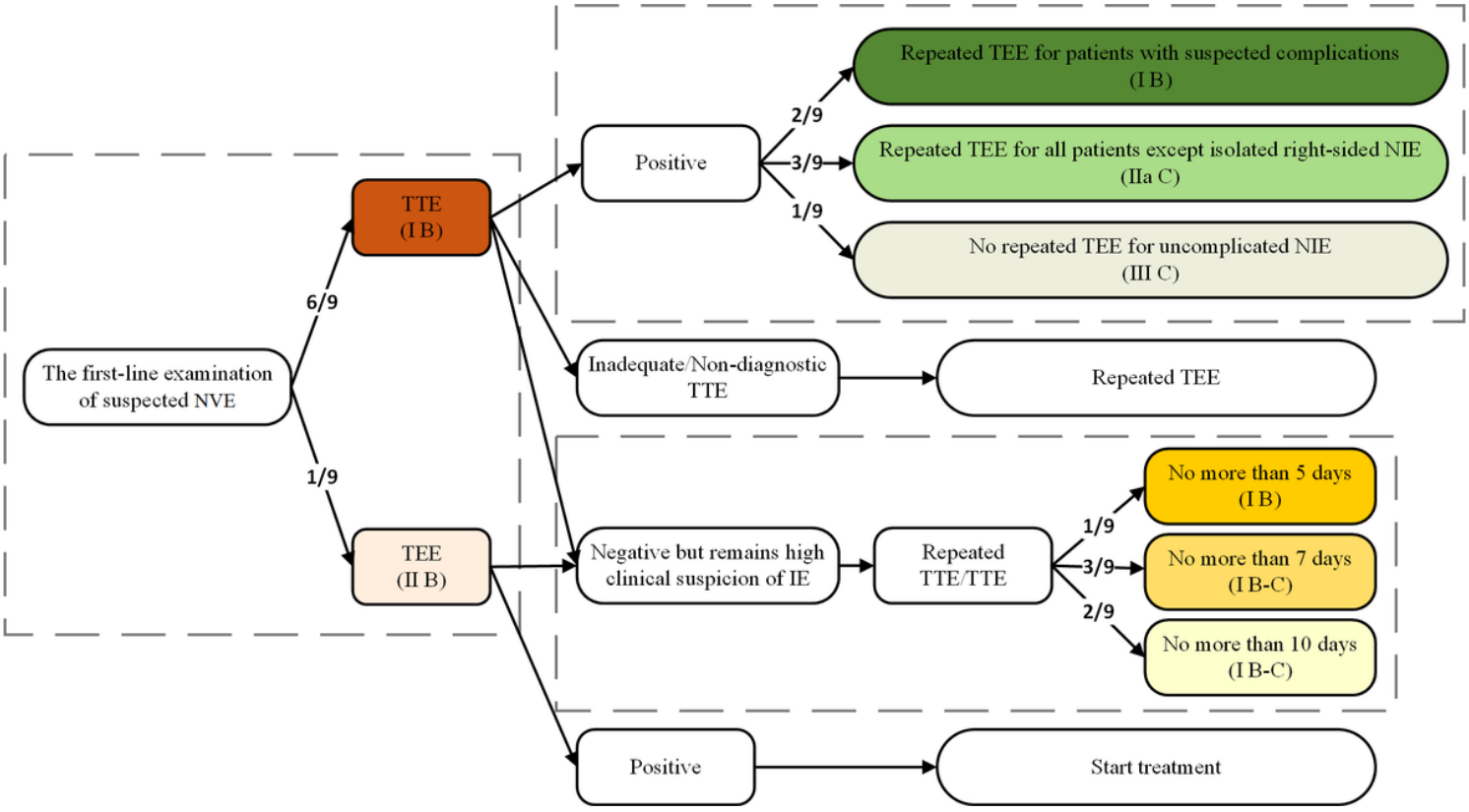


Figure 4

Flowcharts for the controversial clinical scenarios. The dotted box presents the recommendations of the dispute. The ratio marked on the arrow represents the number of guidelines made the pointing recommendation. The level of recommendation is indicated in brackets. The darker the background color in the box, the higher the average score of the guidelines that made the recommendation.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- PRISMAchecklist.doc
- PRISMAflowdiagram.doc
- TableS5.docx
- TableS4.docx
- TableS3.docx
- TableS2.docx
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