SYSTEMATIC REVIEW ARTICLE

Quality Evaluation of the Non-Variceal Upper Gastrointestinal Bleeding Guidelines/Consensuses *via* AGREE II Tools

Yu Wang[1], Jun Guo[2], Youyi Rao[1], Gui Rong Xiao[4] and Xinhua Zhao[3]

[1]Department of Pharmacy / Pediatrics[2] / Gastroenterology[3], Mian Yang Center Hospital, Mian Yang 621000, China
[4]Department of Pharmacy, West China Hospital of Sichuan University, Chengdu, 621000, China

ABSTRACT

Non-variceal upper gastrointestinal bleeding (NUGIB) is a common disease in clinical practice; and many related guidelines/consensuses have been published. The authors assessed the methodological quality of the NUGIB guidelines/consensuses published in English, in order to uncover which guidelines/consensuses are of better quality in methodology and the deficiency in the area. Appraisal of guidelines for research & evaluation instrument tools were adopted to assess the quality of the guidelines/consensuses. Each guideline/consensus was assessed independently by three researchers. Intra-class correlation (ICC) among researchers was retrieved to reflect reliability. Eight guidelines/consensuses regarding the management of NUGIB published in English were obtained. The ICCs among the evaluators were all above 0.75, indicating satisfactory reliability. Quality evaluation of the obtained guidelines *via* the AGREE II tools showed that the overall quality of the included guidelines/consensuses was moderate in all domains. A few guidelines/consensuses were better developed in scientific and methodological aspects than the others. The grades of recommendations with the guidelines/consensuses, according to a brief and preliminary scheme, were of practical value. Moreover, the recommendations regarding the pharmacological treatments in the guidelines/consensuses above, are various according to the study. Overall, the quality of some NUGIB guidelines/consensuses were generally acceptable and applicable, those yet are with minor deficiencies. The others may be improved according to the AGREE II items, likely by evaluating the quality of the guidelines/consensuses when the guidelines/consensuses are updated.

Key Words: *Non-variceal upper gastrointestinal bleeding, Quality evaluation, AGREE II tools.*

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INTRODUCTION

Non-variceal upper gastrointestinal bleeding (NUGIB) refers to gastrointestinal hemorrhage occurring above the Treitz ligament without the comorbidities of esophageal, gastric or duodenal varices.[1] In recent years, several guidelines/consensuses for the diagnosis and treatment of NUGIB have been published. As a common disease in clinical practice, these guidelines/consensuses are very important to improve the clinical management of patients with NUGIB.[2,3] However, in general, the guidelines/consensuses should be formulated by reference to some frameworks to confirm the good quality that would be more rigorous and scientific. The more rigorous and scientific the guidelines/consensuses are, the greater the potential effect of clinical assistance would be. But the guidelines/consensuses are formulated and compiled by the members from the different professions, institutions and nations which may be different knowledge structure, medical conditions and socio-economic development. There may be differences of the quality among these guidelines/consensuses. Therefore, a methodological quality evaluation for the published guidelines/consensuses is needed to identify the good quality guidelines/consensuses and point out the limitations, and to provide the comments for improvement and optimization of the clinical management of the patients.

The Appraisal of Guidelines for Research & Evaluation Instrument (AGREE tool) has been published by AGREE cooperative group and was updated in 2013 (AGREE II). This authorised tool has been recommended as a prevalent tool for evaluating clinical guidelines,[4,5] and can also be used to evaluate the quality of the consensuses and the position statement.[6] Unfortunately, the quality of the guidelines/consensuses regarding the management of NUGIB, to the best of our knowledge, has been rarely evaluated. Some of them may not be of good quality, with less scientific significance and rigorous. Therefore, to optimise the clinical management of NUGIB, this study assessed the methodological quality of the guidelines/consensuses for the management of NUGIB integrally *via* AGREE II tool. The results of our study may be of clinical importance for the future development of related clinical guidelines.

Correspondence to: Xinhua Zhao, Department of Gastroenterology, Mian Yang Center Hospital, Mian Yang 621000, China
E-mail: lcyx2242469@126.com

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METHODOLOGY

In this study, NUGIB guidelines/consensuses written in English, which were published within 10 years, were included. The latest version of the guidelines/ consensuses that was developed by the same institution was adopted. The guidelines/consensuses were excluded if the documents merely related to the bleeding of a single pathology, such as the gastritis, peptic ulcer, gastric cancer, *etc*. Moreover, redundant publications of the same guidelines/consensuses in different journals were also excluded. The guidelines/consensuses for the diagnosis and treatment of non-varicose upper gastrointestinal bleeding were searched from January 2008 to April 2018 in PubMed, the Cochrane Library, Science Direct, National Guideline Clearing House (www.guideline.gov), National Institute for Health and Care Excellence (www.nice.org.uk.com), Australian Clinical Practice Guidelines (www.clinical guidelines.gov.aur.r.), and Guidelines International Network (www.g-i-n.net). Articles were included if their title included the following terms: nonvariceal or non-variceal, and guideline, guidelines, guidance, consensus, statement, or position.

Data regarding the number of references and editors, the publication institutions, the country or area, the time of publication, the method of evidence evaluation, and the drug treatment recommendations for all guidelines/ consensuses were extracted.

Three assessors independently participated in the quality assessment procession of the guidelines/ consensuses. To ensure that there is an equal standard among the different assessors, all researchers had been trained for the AGREE II tool. The assessors independently responded to 23 questions of six domains by giving 1 for 'strongly disagree' to 7 for 'strongly agree'. Each domain score was calculated as the following: (the actual score - the lowest possible score)/(the highest possible score - the lowest possible score) ×100%. Then the three scores by different assessors are averaging operation. The higher the score, the more normative the domain.[7]

To our disappointment, there was no break point of scores recommended by the AGREE II tool to distinguish between high and poor quality guidelines/ consensuses. As reported in previous studies, a score >60% is frequently defined as high quality.[8,9] However, the documents of medium quality failed to be distinguished from the low, and there is no sufficient influence on clinical practice. A new standard has been proposed in some studies,[10,11] through which the guidelines/consensuses could be categorised into three levels according to the scores of AGREE II: Grade C (not recommended): 3 domains with a score <30%. The guidelines/consensuses are not recommended; Grade B (recommended after revision): 3 domains of score 30%, but at least one domain of score <60%. The guidelines/consensuses could be recommended after modification. Grade A (recommended): 6 domains with a score 60%. This could be used in this study.

The intra-class correlation coefficient (ICC) was introduced by Fisher in 1921 to measure the reliability of measurements or ratings. It is designed to assess the consistency or conformity between two or more quantitative measurements.[12] ICC was used to evaluate the consistency of assessment, ranging from 0 to 1. The higher the value, the better the consistency of the assessment by different researchers. Specifically, the consistency is considered sufficient when the ICC $\geq$0.75 and is deemed poor when the ICC $\leq$0.4. For ICC ranging between 0.4 and 0.75, the consistency is mediocre. Furthermore, to identify whether the intra-class correlation coefficient is statistically significant.The ICC has been tested by the Analysis of Variance, the above standards are available only when $p<0.05$.[13,14]

The descriptive statistics of performance of guidelines/ consensuses in six AGREE II domains were got in order to describe the distribution of the score in each domain. Specifically, the score of different guidelines/consensuses in each domain were used to obtain the mean value, median value, standard deviation and so forth. Those could partly illustrate the distribution characteristics and the dispersion degree of quality of guidelines/consensuses in each domain.

All analyses above were performed with Statistical Product and Service Solutions (SPSS) version 23.0. SPSS is a widely used programme for statistical analysis in science. The functions of SPSS include data management, statistical analysis, chart analysis and so forth. The statistical analysis process includes but not limited to descriptive statistics, hypothesis test, and correlation analysis.

RESULTS

Eight documents were obtained during the literature search, including four guidelines, three consensuses and one statement (Figure 1). These guidelines/ consensuses were published from 2008 to 2018 in 5-46 pages having 17-317 references and 7-34 authors in total. The majority are updated versions of the previous editions, except for one from Poland. Three guidelines/consensuses were published by the Society of Gastrointestinal Endoscopy and one guideline/consensus was issued by a medical university. The characteristics of the included guidelines are presented in Table I.

The ICCs of the guidelines / consensuses among the three researchers were all $\geq$0.75 ($p<0.05$), which are presented in Table II, and indicated that the consistencies for the quality evaluation within different researchers are satisfactory.

The scores of each domain and the recommendation grade of all the guidelines/consensuses were recorded by the AGREE II tool. The mean score was < 60%. The

recommendation grades of the guidelines/consensuses are of Grade B and C rather than Grade A. The European, International and Asia-Pacific guidelines/consensuses were higher than the other scores in most domains. The scores of 4 domains were above 60% for the European guidelines/consensuses, whereas none were <30% with the integral best quality. The scores of Chinese, Indonesian and Polish guidelines/consensuses were all only 1 domain above 30% but <60%, the other domains were <30%. (Tables III and IV, Figure 2).

All of the guidelines/consensuses stated that Proton Pump Inhibitors (PPIs) are the optimal agent for NUGIB

Table I: Characteristics of the retrieved clinical guidelines/consensuses.

Names of guidelines and consensus	Type	Institutions	Authors number	Updated version	No. of references	Year of publication	Evidence evaluation tool
Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline[15]	Guidelines	European Society of Gastrointestinal Endoscopy	24	yes	317	2015	Grade
International Consensus Recommendations on the Management of Patients With Nonvariceal Upper Gastrointestinal Bleeding[16]	Consensus	International Consensus Upper Gastrointestinal Bleeding Conference Group	7	yes	225	2010	Grade
Asia-Pacific Working Group consensus on non-variceal upper gastrointestinal bleeding[2]	Consensus	Asia-Pacific Working Group of Upper Gastrointestinal Bleeding	18	yes	114	2018	Not available
Guidelines for the diagnosis and treatment of acute non-variceal upper gastrointestinal bleeding[17]	Guidelines	Chinese Society of Digestive Endoscopy	34	yes	25	2015	Not available
National Consensus on Management of Non-Variceal Upper Gastrointestinal Tract Bleeding in Indonesia[18]	Consensus	The Indonesian Society of Gastroenterology	Not available	yes	17	2014	Not available
Guidelines for endoscopic management of non-variceal upper gastrointestinal bleeding[19]	Guidelines	Japan Gastroenterological Endoscopy Society	10	yes	227	2016	Grade
Non-variceal upper gastrointestinal bleeding guidelines on management[20]	Guidelines	Department of Gastroenterology Medical University of Lublin	6	no	80	2008	Not available
Management of non-variceal upper gastrointestinal bleeding[21]	Position statement	The Catalan Society of Gastroenterology	17	yes	108	2017	Grade

Table II: The consistency assessment of the guidelines / consensuses evaluation by different researchers.

Names of guidelines and consensus	The intra-class correlation coefficient	95% confidence interval	F	P
European[15]	0.93	0.87-0.97	14.34	0.00
International[16]	0.94	0.88-0.97	16.29	0.00
Asia-pacific[2]	0.95	0.90-0.98	21.02	0.00
Chinese[17]	0.94	0.87-0.97	16.33	0.00
Indonesian[18]	0.95	0.89-0.98	18.61	0.00
Japanese[19]	0.92	0.83-0.96	11.82	0.00
Polish[20]	0.90	0.80-0.95	9.579	0.00
Spanish[21]	0.95	0.89-0.98	18.881	0.00

[2] *The ICC are available only when p<0.05.*

Table III: The score and recommendation level of the guidelines / consensuses by AGREE II.

Names of guidelines/ consensus	Scope and purpose	Stakeholder involvement	Rigor of development	Clarity of presentation	Applicability	Editorial Independence	No. of score 60%	No. of score <30%	Grades of recommendations
European	61.11	33.33	61.81	74.07	34.72	72.22	4	0	B
International	51.85	44.44	52.08	77.78	33.33	36.11	1	0	B
Asia-pacific	44.44	22.22	44.44	62.96	36.11	52.78	1	1	B
Chinese	42.59	20.37	7.64	22.22	20.83	0.00	0	5	C
Indonesian	53.70	12.96	5.56	12.96	19.44	0.00	0	5	C
Japanese	18.52	14.81	42.36	27.78	13.89	52.78	0	4	C
Polish	29.63	12.96	7.64	14.81	16.67	36.11	0	5	C
Spanish	40.74	18.52	20.83	53.70	26.39	58.33	0	3	C

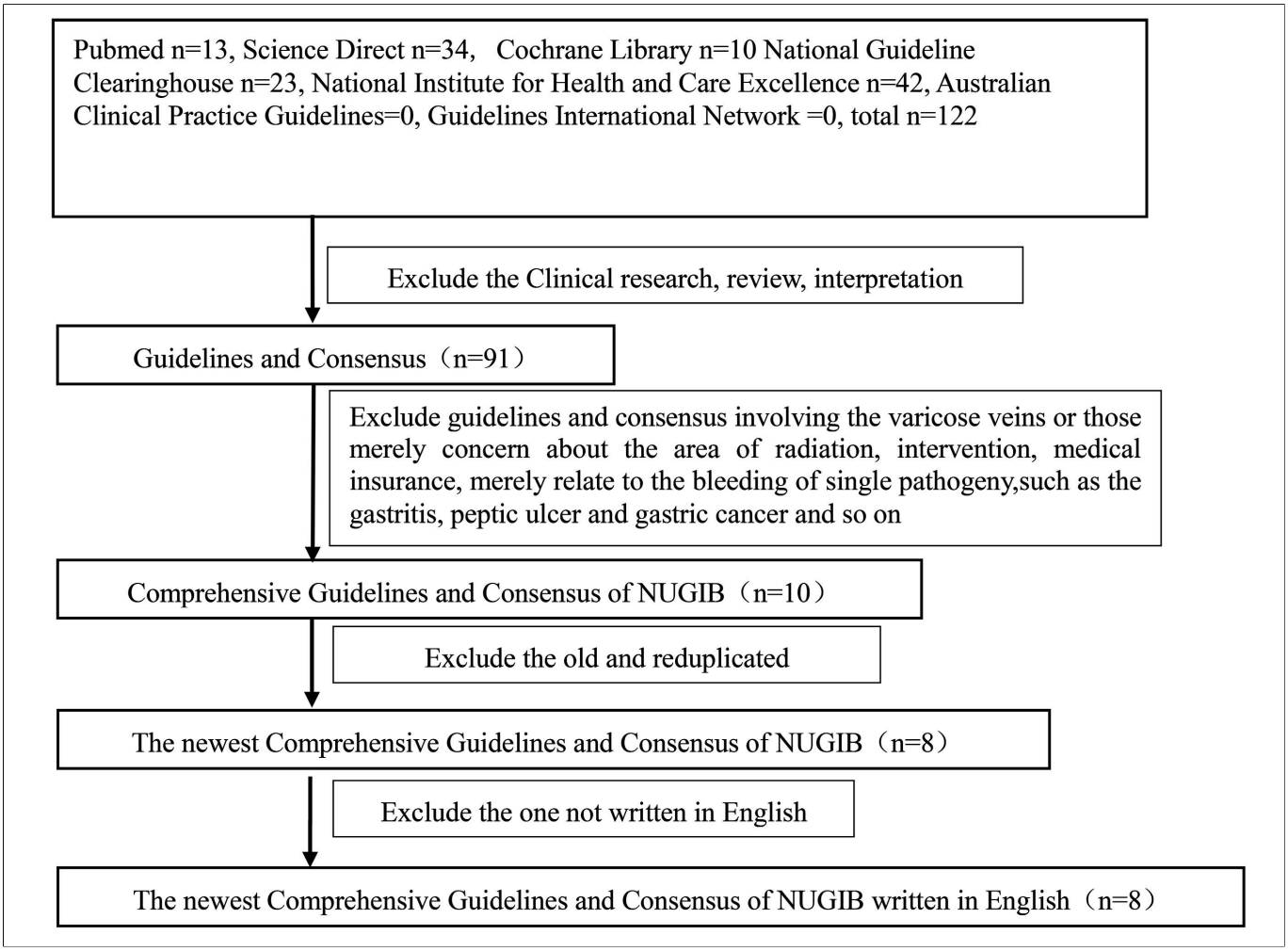

Figure 1: The process of the literature search.

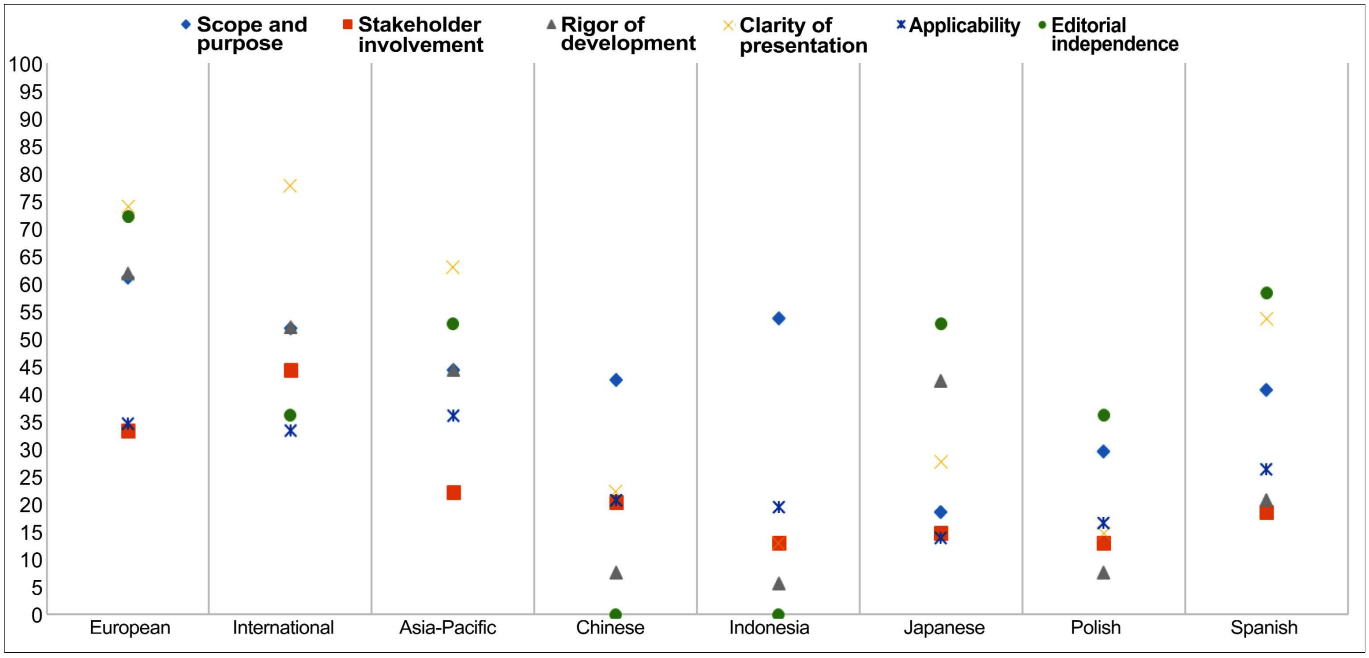

Figure 2: The score distributions of the guidelines / consensuses in 6 domains.

Table IV: Descriptive statistics of performance of guidelines / consensuses in six AGREE II domains.

AGREE II domain (%)	Mean	Median	Standard deviation	Variance	Range	First quartile	Second quartile	Third quartile
Scope and purpose	42.82	43.52	13.66	186.56	18.52-61.11	32.41	43.52	53.24
Stakeholder involvement	22.45	19.45	11.09	122.89	12.96-44.44	13.42	19.45	30.55
Rigor of development	30.30	31.60	22.49	505.90	5.56-61.81	7.64	31.60	50.17
Clarity of development	43.29	40.74	26.85	721.11	12.96-77.78	16.66	40.74	71.29
Applicability	25.17	23.61	8.70	75.73	13.89-36.11	17.36	23.61	34.37
Editorial independence	38.54	44.45	26.50	702.00	0-72.22	9.03	44.45	56.94

Table V: The recommended pharmaceutical treatment in the guidelines / consensuses.

Names of guidelines/ consensus	Proton Pump Inhibitors (PPIs) Prior to endoscopic therapy	Endoscopic therapy post	H_2 receptor antagonists (H_2RA)	Other hemostatics
European[15]	Intravenous PPIs, intravenous bolus followed by continuous infusion (80mg then 8mg/hour).	PPIs are given via intravenous bolus followed by continuous infusion (80 mg then 8 mg /hour) for 72 hours. (R[3]: strong, E[4]: high) PPIs are given via intravenous drip intermittently (at least twice daily) for 72 hours can be considered. (R: weak , E: moderate).		The admission of tranexamic, somatostatin, octreotide are not recommend (R: strong, E: low).
International[16]		An intravenous bolus followed by continuous-infusion PPIs therapy should be used. (Agree, 94%, R: strong, E: high)	It is not recommended in patients with acute ulcer bleeding	The use of somatostatin, octreotide are not recommended.
Asia-Pacific[2]		Adjunct to endoscopic treatment, high-dose oral PPI can be used to prevent rebleeding. (Accept-agreement: 88.9%, E: moderate)		
Chinese[17]	PPIs should be employed as early as possible	It has been recommended that for high-risk patients, large-dose intravenous PPIs should be administered for 72 h. The treatment duration of high-dose PPIs can be extended and then switched to intravenous infusion of standard-dose PPIs twice daily for 3-5 days and finally to oral administration of standard-dose PPIs, until the ulcer heals. For low-risk patients, treatments using standard-dose PPIs, via intravenous infusion, are practical and suitable.	H_2RA can be considered but the effects of PPIs are significantly superior than those of H2RA.	Hemostatic drugs are not recommended as firstline treatment options.
Indonesian[18]	When endoscopy will be delayed and can not be performed, an intravenous PPIs therapy is recommended.	Patients with active bleeding or non-bleeding visible vessel and adheren clot can be treatment with intravenous PPIs therapy bolus. Patients with a flat pigmented spot or clean-base can be treatment with oral PPIs therapy.		
Japanese[19]		PPIs should be given to patients to prevent rebleeding after successful endoscopic hemostasis. (E: IVa, R: moderate)	H_2RA could be given after successful endoscopic hemostasis (E: IVa, R: moderate) The routine use of H_2RA is not recommended.	
Polish[20]	In high risk patients, endoscopic procedure should be conducted just after hemodynamic compensation and intravenous administration of PPIs at a high dose.	In the high risk group, treatment with PPIs should be continued intravenously through the next 72 hours, and subsequently oral administration should be applied. In patients with medium and low risk for bleeding recurrences, it advises, respectively, the intravenous and oral administration of PPIs at a dose of 40 mg every 12 hours.		Somatostatin and analogue are not recommended for routine application.
Spanish[21]	Administering intravenous PPIs is recommended. (R: strong, E: moderate)	The administration of a PPIs (80 mg intravenous bolus followed by a continuous 8 mg/h infusion) is recommended in patients at a high risk of rebleeding (R: strong, E: high). High oral doses could be administered if the patient is ready to begin an oral diet (R: weak, E: moderate)		Tranexamic acid, somatostatin or octreotide are not recommended. (R: strong, E: low)

[3] R=Grade of recommendation; [4] E=Quality of evidence.

management. PPIs administration after endoscopic therapy was recommended by nearly all guidelines/ consensuses. However, some documents did not mention applying PPIs before the endoscopic therapy. The H_2 Receptor Antagonist (H2RA) was recommended as the substitution for PPIs in the Japanese and Chinese guidelines/consensuses. Currently, no other hemostatics have been recommended in all guidelines/ consensuses. The details are presented in Table V.

DISCUSSION

This systematic evaluation of eight published guidelines/ consensuses of NUGIB management *via* a generally accepted AGREE II tool found that the overall quality of the included guidelines/consensuses were moderate in all domains. However, a few guidelines/ consensuses were well developed regarding scientific and methodological aspects. Discussion of the recommendations for the pharmacological treatment in the study may reduce

the controversies and provide measures to promote the use of medical treatments in clinical practice.

The AGREE II tool is required to make the theoretical and practical significance explicit before the guidelines/ consensuses editing. To avoid the inadequate use of the guidelines/consensuses, it is also required to show the benefit to the society and the specific target population. In this domain, the score of the guidelines/consensuses are higher than the others except the domain of clarity of development. It illustrates a measure of good quality in this area. However, the majority of guidelines/ consensuses did not illustrate it completely, especially the Japanese and Polish guidelines/consensuses. In contrast, the European guidelines is better than the others. To a certain extent, these guidelines clearly expressed the aim of the guidelines, and the health question(s) covered by the guidelines. But the minor flaws still exist. The population (patients, public, *etc*.) to whom the guidelines/consensuses is meant to apply is not specifically described (adults or children, whether are with the neopathy or not). And the potential health impact of the guidelines on society and populations of patients did not state clearly.

The editors' locations and fields of investigation are related to the quality of the guidelines/consensuses. In particular, the NUGIB documents required the joint efforts of the physicians, endoscope technicians, emergency physicians, clinical researchers, and statistics professionals from different countries. There are increasing cases of multidisciplinary consults in the treatment of NUGIB, especially in refractory cases.[22,23] However, many guidelines/consensuses lack editor information. Accordingly, it is difficult to identify whether the participators were from the same profession or area that may lead to a bias in recommendations. In particular, there are no information in the domain for the Japanese, Chinese and Indonesian documents. Moreover, the patients' points are not noted in all guidelines/ consensuses above, though many methods can be used to consider them.[24] Finally, no appropriate users were recommended in the above documents, which may lead to a reduced compliance of the patients and may compromise efficacy. In this domain, there are a lot of space to improve with all guidelines/ consensuses.

The reliability of the recommendations based on evidence are reflections of the rigor of the guideline development. Therefore, the rigor of guidelines/ consensuses formulation is the most important factor of the guidelines/consensuses. The evidence search and evaluation require comprehensiveness, objectivity and repeatability. The scores of the domains in Chinese, Indonesian and Polish guidelines/consensuses are quite low (<10%), which lacks a search strategy and the evidence selection criteria. This suggests that there is no adequate scientific process during the development of the above guidelines. The other documents contained the evidence retrieval strategy, although this is not sufficiently rigorous. Moreover, the external experts review was not noted in all of the guidelines/ consensuses above, illustrating the shortage of peer supervision. Furthermore, some of them have lack of innovation plans, that means there are few latest research results could be contacted with.

The recommendations were made separately according to high- or low-risk patients with the diagnosis and treatment in nearly all of the guidelines/consensuses, as recommended by the standards of AGREE II. In general, the score of this domain are higher than the others, especially in International or European guidelines/ consensuses. However, the recommendations of some guidelines/consensuses were expressed with the evidence described, which may obscure the user.

The scores of all guidelines/consensuses in this domain were lower. Most of them lacked advice and tools on how the recommendations can be put into practice. The potential resource implications were also absent. The health equity was widely recognised as relevant to clinical/public health practice and policy. However, considerable populations were also associated with poor quality medical care.[25] Of note, dissemination of guidelines/consensuses plays an important role in the spread of new medical technologies and can promote the application of new medical treatments. If the document did not illustrate the potential resource implications and barriers, there may not be sufficient support for economy and policy. Moreover, the monitoring and/or auditing criteria in some guidelines/ consensuses were absent. For example: how should the patients be categorised as high or low risk? Was it evaluated by the endoscope or the amount of bleeding? The Chinese guidelines did not answer these questions clearly. Therefore, the scores are relatively lower. It means that would need more revision than the other domains.

The donation organisation may influence the recommendations through the support of guidelines/consensuses. It is necessary to explain conflicts of interest. Except for Chinese and Indonesian documents, most of the guidelines/consensuses clarified the conflicts of interest among the donation organisations and editors. Most guidelines/consensuses above are less affected by the conflicts of interest causing by competitive relationship and other institutions. This can partly assure the impartiality of the guidelines/consensuses.

The most effective treatment of NUGIB is endoscopic therapy, especially in high-risk patients. However, pharmacotherapy is also an important adjuvant measure that was mentioned by all guidelines/consensuses above. Although, PPIs are currently considered as first class treatment protocols in all the guidelines/ consensuses, there are still arguments on some issues.

The previous studies demonstrated that the application of PPIs in combination with endoscopic therapy can reduce rebleeding and the proportions of NUGIB patients requiring surgery.[26] Notably, the dosages of the PPIs are limited to the high amount. However, the high dosage of PPIs was vaguely defined as 80 mg+8 mg/hour or above 200 mg/24 hours for 72 hours. Therefore, nearly all of the earlier versions of the guidelines/ consensuses recommended treatment with a high dosage of PPIs with intravenous lasting 72 hours after endoscopic therapy, but none of them recommended the specific dosage due to differences in the references. Several guidelines/consensuses have noticed PPIs adoption before endoscopic therapy. Some studies indicated that PPIs should be employed as early as possible to reduce the needs of endoscopic intervention and shorten the length of stay.[27,28] However, the issue had not been proved completely because of the defects of the studies.[29,30] Therefore, it remains under debate. However, it is sure that most guidelines/consensuses above recommended PPIs with high dosages as the first-line therapeutic agent of NUGIB.

The controversies are far beyond those. With the development of the studies, more information has been obtained regarding the effectiveness of oral and low dose agents. Kaviani *et al*. demonstrated that oral omeprazole (20 mg every 6 hours) can reduce rebleeding, shorten the average length of hospital stay and transfuse effectively.[31] It may also work in Asian countries.[32] The systematic review also demonstrated that there are no differences between the oral and intravenous groups in rebleeding or mortality due to surgical treatment.[33] It may identify the effectiveness of the oral agent. However, a meta-analysis compared high-dose omeprazole and pantoprazole therapy (80 mg bolus plus 8 mg/hour for 72 hours) with nonhigh-dose omeprazole and pantoprazole (20-160 mg daily).[34] No significant differences between high-dose continuous infusion and nonhigh-dose intermittent PPIs therapy for rebleeding at 30 days and mortality were detected. As a result, recommendations based on the above studies were made in some guidelines/consensuses, especially in Asia, because the researchers considered that it would be more effective with PPIs in this area.[33] At first, in the international consensus, lower intravenous doses or high-dose oral PPIs therapy were considered to be effective after endoscopic therapy (especially in Asia), although they were not recommended as the first-line treatment. Then, European guidelines and a Spanish statement stated that intermittent PPIs intravenous bolus dosing (at least twice daily) for 72 hours can be considered, while it was recommended at a weak level. Subsequently, the Asia-Pacific consensus explained that adjunct to endoscopic treatment, high-dose oral PPIs can be used to prevent rebleeding. Overall, an increasing number of professionals tend to use PPIs economically and conveniently with sufficient effectiveness.

Most guidelines/consensuses did not recommend H_2RA as the first-line treatment because of the disadvantage of H_2RA. The occurrence of the tolerance phenomenon and interaction between H_2RA and the other drugs constricted the use of H_2RA.[35,36] Moreover, a tolerance phenomenon could appear rapidly in some cases, which could not be eliminated or weakened by increasing the dosages of H_2RA. Pharmacologically, H_2RA such as cimetidine and ranitidine are inhibitors of cytochrome P450, which can interfere with other agents metabolised by the isozyme. In general, the safety and efficacy of H_2RA for NUGIB are inferior to those of PPIs, were not recommended as the first line-drugs by most guidelines / consensuses.

Other neutralising hemostatics and protective drugs such as somatostatin, tranexamic acid, carbazochrome sodium sulfonate, hemocoagulase and vitamin K are not recommended by any guidelines/consensuses for routine application in treatment of NUGIB due to their indeterminate efficiency.[37-40] Some agents such as hemocoagulase may consume fibrinogen, leading to the incidence of idiopathic hemostasis failure.[41] Furthermore, multiple hemostatics admissions may increase adverse drug reactions. Notably, there are few occurrences of hemostatics abuse in reality.

This study assessed the quality of documents published in English only, which could not reflect the quality of relevant guidelines/consensuses in non-English speaking areas. Moreover, the AGREE II tool do not assesses the facticity of recommendations, but focus on the formation and quality of the guidelines/consensuses.

CONCLUSION

The quality of some NUGIB guidelines/consensuses are generally acceptable and applicable, those yet are with minor deficiencies. Some may be improved with the AGREE II items, especially Japanese, Indonesian, Spanish, Polish and Chinese guidelines/consensuses, likely by evaluating the quality of the guidelines/consensuses when the guidelines/consensuses are updated. Although the formulations of guidelines/consensuses are influenced by many factors, the quality of them is restricted by these factors identically. However, guideline assessment tools such as AGREE II should be encouraged to be applied in guideline/consensus development to improve their methodological quality, since the guidelines/consensuses with excellent quality are of more facility to be recognised and accepted.

CONFLICT OF INTEREST:
Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
YW: Research design; literature search and collection; the quality of the guidelines/consensuses assessment; manuscript creation.

JG: Research design; the quality of the guidelines/ consensuses assessment; data statistics.
YR: Research design; the rate of progress supervision; the consultant of pharmacy.
GRX: Data statistics; manuscript creation.
XZ: The quality of the guidelines/consensuses assessment; literature search and collection; the consultant of gastroenterology.

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