Original Article

An evaluation of the reporting quality in clinical practice guidelines for hepatocellular carcinoma using the RIGHT checklist

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Background: Hepatocellular carcinoma (HCC) is one of the most common malignant tumors worldwide. Clinical practice guidelines (CPGs) on the prevention, surveillance, diagnosis and management of HCC are essential to guide clinical practice. The objective of this study was to evaluate the reporting quality of the most recent CPGs for HCC published worldwide.

Methods: We systematically searched literature databases and websites of guideline development organizations and medical associations to extract CPGs on HCC published between January 2018 and December 2020. We evaluated the reporting quality using the Reporting Items for practice Guidelines in Healthcare (RIGHT) statement. We assessed for each of the 35 RIGHT checklist items whether the guidelines reported the corresponding information. We calculated the mean (± standard error of the mean, SEM) percentages of the guidelines' compliance with the items (reporting rate), both overall and for each of the seven domains of the RIGHT checklist.

Results: We identified 22 guidelines, of which three (14%) were written in Chinese and 19 (86%) in English. The mean ±SEM overall reporting rate in the twenty-two guidelines was 56%±4%. The reporting rates of the seven domains were the following: basic information 81%±3%, background 58%±6%, evidence 58%±6%, recommendations 59%±5%, review and quality assurance 34%±10%, funding and declaration and management of interests 39%±4%, and other information 23%±6%.

Conclusions: The reporting quality of the recently published guidelines for HCC was suboptimal. While there is no doubt about the great value of the CPGs' recommendations in clinical practice, the reporting in CPGs for HCC still needs improvement.

Keywords: Hepatocellular carcinoma (HCC); clinical practice guideline (CPGs); reporting quality; Reporting Items for practice Guidelines in Healthcare (RIGHT)

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Introduction

Hepatocellular carcinoma (HCC) ranks sixth among all types of cancer in new cases and is also the fourth leading cause of cancer-related death worldwide (1). The incidence of HCC varies globally and most of the cases occur in Asia and Africa, with China having a exceptionally high incidence (2). The high incidence of HCC in China is primarily due to the high prevalence of chronic hepatitis B virus (HBV) infection (3,4). While the five-year survival rate of patients with HCC is 18% in the United States, it is reported to be as low as 12% in China and other Asian countries (5,6). Over the past decade, new advances in the diagnosis and treatment have been developed due to the deepening understanding of the epidemiology, risk factors and molecular profiles of HCC (7). Correspondingly, new approaches to surveillance, diagnosis and treatment have shown their efficacy in managing patients with HCC and decreasing HCC related mortality (8-10). The incidence and mortality are affected by many factors, particularly the prevention, surveillance, diagnosis and management of HCC. The prevention of viral hepatitis can substantially reduce the occurrence of HCC, and the early detection of HCC can increase the chance of potentially curative treatment. However, the prevention and surveillance of HCC are substantially underutilized, even in countries with sufficient medical resources. The treatment of HCC can be complex and differs greatly depending on tumor burden, the severity of liver dysfunction, medical comorbidities, local expertise, and preferences of patients. Reasonable preventive measures, elimination of viral hepatitis, and active HCC surveillance and management are expected to significantly reduce the global burden of HCC within the next few decades. However, at present, in many countries HCC related morbidity and mortality are still increasing.

Clinical practice guidelines (CPGs) are collections of recommendations to guide, optimize, and establish norms for clinical practice. CPGs should be based on a systematic review of the literature, and rate the quality of evidence and strength of recommendations (11). In recent years, an increasing number of academic organizations and institutions worldwide have formulated guidelines to improve oncologists' technical skills and knowledge and further the quality of medical treatment. However, the reporting quality of CPGs tends to be low (12,13). Checklists used to assist CPG developers can also be used to evaluate the quality of the guidelines. Two checklists, the appraisal of guidelines for research & evaluation (AGREE) for guideline development methodology and the Reporting Items for practice Guidelines in Healthcare (RIGHT) for reporting in guidelines, are commonly used in CPG development (14-16). The RIGHT statement has been used to assess the reporting quality of CPGs for different diseases (17-22). Currently, the reporting quality of HCC guidelines has not yet been systematically and comprehensively evaluated. The purpose of this review is to assess the reporting quality of the guidelines for HCC published between the years 2018 to 2020 to support more comprehensive, clear and transparent reporting in the future.

Methods

Literature search

We systematically searched Medline (via PubMed), Chinese Biomedical Literature Database (CBM), Wan Fang Database and Chinese National Knowledge Infrastructure (CNKI) for CPGs on HCC. We also searched the websites of the following guideline development organizations, governmental health agencies and oncological societies: World Health Organization (WHO), National Comprehensive Cancer Network (NCCN), Guidelines International Network (GIN), Scottish Intercollegiate Guidelines Network (SIGN), the National Institute for Health and Care Excellence (NICE), the European Society for Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO) and the Chinese Society of Clinical Oncology (CSCO).The search was restricted to the period January, 2018 to December 2020. The search terms for PubMed included liver neoplasms [MeSH], hepatic neoplasms [MeSH], cancer*, carcinoma*, neoplasm*, adenoma*, adenocarcinoma*, tumour*, tumor*, polyp* and malignant*, liver, hepatic, hepatocellular*, hepato-cellular*, hepatobiliary, Guideline, Practice Guideline, guideline*, guidance* and recommendation*. The complete PubMed search strategy is shown in Supplementary Appendix 1.

We included all CPGs on screening, surveillance, diagnosis, treatment, and up of HCC, published between 2018 and 2020 in English or Chinese.

We excluded translations and interpretations of guidelines, protocols of CPGs, older versions of CPGs when a more recent version was available, CPGs on other topics including recommendations related to HCC, and CPGs for which we were unable to retrieve the full texts.

All identified records were imported into an EndNote

library (version X9.1). Four investigators (Haiyang Chen; Ding Li; Jing Han; Yingxi Wu) screened the titles and abstracts of all records independently following the pre-defined inclusion and exclusion criteria. Full texts of articles deemed potentially relevant were then reviewed to determine eligibility. Disagreements between researchers were discussed and resolved through consensus or by consulting another researcher (Qiming Wang).

Data extraction

The eligible CPGs were given to two investigators (Xuan Wu; Ding Li) for assessment with the RIGHT checklist. The checklist contains 22 key items, some of which are divided further into sub-items, resulting in 35 items. The items are grouped into seven domains: basic information, background, evidence, recommendations, review and quality assurance, funding declaration and management of interests, and other information.

We assessed the adherence of the CPGs to each item on a dichotomous scale. "Reported" mean that the relevant information was provided, and "not reported" that the relevant information was completely missing. If an item did not apply to a particular guideline, it was assigned "not applicable (NA)". Disagreements between the two investigators were discussed and unresolved matters were addressed by another investigator (Qiming Wang).

Statistical analysis

We calculated the proportions of guidelines compliant with each of the 35 RIGHT checklist items, the overall reporting rate, and the reporting rates for items within each domain. Reporting rates were calculated by dividing the number of items rated as "Reported" by the total number of items, weighting all items equally. We present the mean, standard error of the mean (SEM) and total range overall CPGs. Since our search strategy covered many Chinese-language databases, we compared the overall reporting quality between guidelines published in China versus the rest of the world using Student's *t* test.

Results

Study selection

A total of 474 documents were identified in search of the literature databases. Eight additional documents were identified from the websites of guideline and oncology associations. After screening the full texts, 22 CPGs eventually met the inclusion criteria (*Figure 1*). Twenty (91%) CPGs were retrieved from literature databases, and two (9%) from websites of oncology associations (*Table 1*). Eight (36%) guidelines were developed in China; 5 (23%) in the United States; 2 (9%) in Europe (n=2); and 1 (5%) each in Canada, Saudi Arabia, India, Japan, Brazil, South Korea and Argentina. Five guidelines (23%) were published in 2018, 6 (27%) in 2019, and 11 (50%) in 2020.

Reporting quality of the included guidelines

The overall reporting rates ranged from across the CPGs 31% to 91%, with a mean ± SEM of 56%±4%. Among them, the reporting rate of 11 (50%) guidelines was above 50%, of one guideline above 90% (*Table 1*). The mean reporting rates (ranges) of guidelines written in Chinese and English were 43% (37–49%) and 58% (31–91%), respectively. The mean overall reporting rate of CPGs from China was 49% (range, 37–91%), and of those from the rest of the world 59% (range, 31–86%; P=0.18).

Reporting quality within each domain

The mean ± SEM reporting proportions (ranges) in the seven RIGHT domains were 81%±3% (50–100%) for basic information, 58%±6% (13–100%) for background, 58%±6% (0–100%) for evidence, 59%±5% (14–100%) for recommendations, 34%±10% (0–100%) for review and quality assurance, 39%±4% (25–75%) for funding, declaration and management of interests and 23%±6% (0–100%) for other information (*Figure 2*).

Reporting compliance of each item

The details of reporting quality of each item are summarized in *Table 2*. Twelve items (1a, 1c, 2, 3, 4, 5, 7b, 9b, 12, 13a, 13b and 13c) were sufficiently reported with a reporting proportion higher than 80%. Among them, item 1a was reported by all 22 CPGs (100%). Items 10b, 11a, 11b and 19a were also well reported, each having a reporting proportion ranging from 50% to 80%. Three items (7a, 10a and 15) were reported by half of the guidelines. Any of the guidelines did not report item 18b, and items 1b, 6, 8a, 8b, 9a, 14a, 14b, 14c, 16, 17, 18a, 19b, 20, 21, and 22 were also reported by less than 50% of the guidelines.

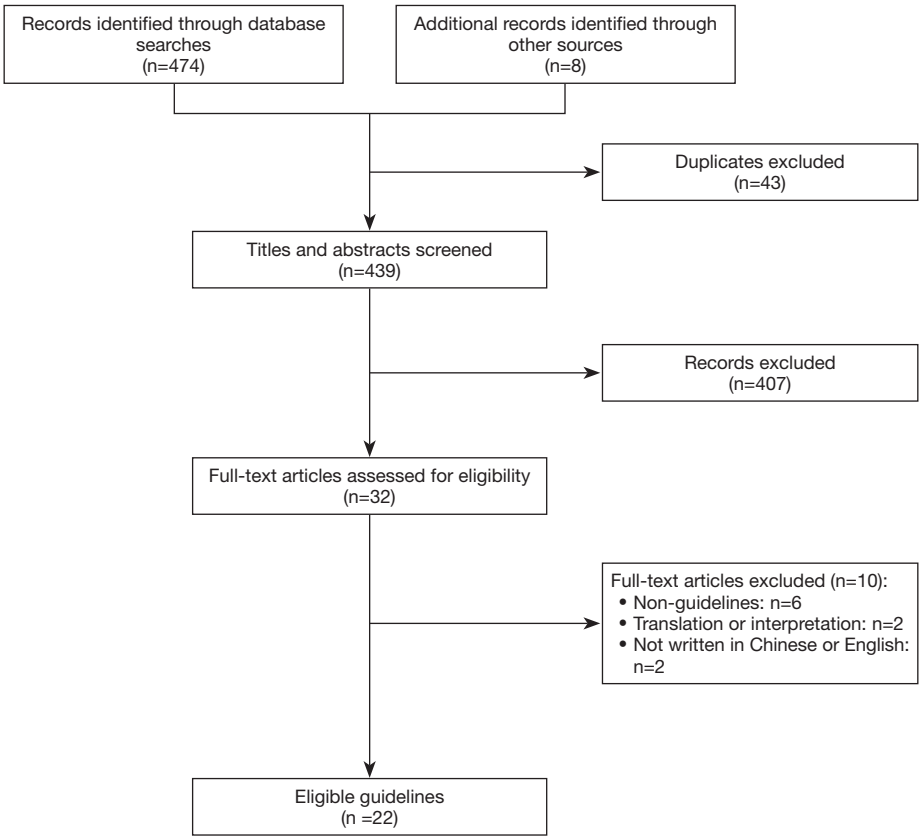

Figure 1 Flowchart of the literature search.

Discussion

We identified 22 CPGs on HCC published during the years 2018–2020 worldwide. All except two guidelines were found through the searches of literature databases. Thus, medical literature databases should be the primary source when searching for guidelines on HCC. The number of CPGs for HCC published annually increased every year during the three years.

The reporting quality was found highly variable. Half of the included guidelines adhered to less than half of the RIGHT checklist items, showing a need for improvement. However, we found one guideline, developed by the Shanghai Association of Chinese Integrative Medicine, which had particularly high adherence to RIGHT and could thus be used as an example of how to report CPGs (41). Moreover, the domains of basic information, evidence and recommendations tended to be well reported. In contrast, reporting of items related to funding, declaration and management of interests, and review and quality assurance, was insufficient, consistent with the findings of previous studies in other guidelines (13,46).

The reporting compliance for individual items also varied substantially between the items. The reasons for the low reporting rate of certain items is essential to developing strategies to improve the reporting quality of the guidelines. Only eight guidelines (36%) reported the year of publication of the guideline in the title (RIGHT item 1b). If a guideline describes the year of publication in the title, it will be easy for researchers and practitioners to receive the updated guidelines containing the latest evidence. However, due to the lack of compliance standards and training related to guideline development, many guideline developers may have been unaware of the importance of this item. In contrast, all except two guidelines described the focus of the guideline appropriately in the title (item 1c). A clear presentation of the focus in the title makes it easy and fast for researchers and practitioners to identify the appropriate guideline for their needs from the database.

Four guidelines (18%) did not include an executive summary of the recommendations (item 2). Summarizing

Table 1 Characteristics of the included guidelines (23)

Title	Year of publication	Reporting rate	Developer	Country or region	Journal or website of publication
APASL practical recommendations for the management of hepatocellular carcinoma in the era of COVID-19 (24)	2020	31%	APASL	Japan	Journal
Argentinian clinical practice guideline for surveillance, diagnosis, staging and treatment of hepatocellular carcinoma (25)	2020	69%	AAEEH	Argentina	Journal
Brazilian Society of Hepatology updated recommendations for diagnosis and treatment of hepatocellular carcinoma (26)	2020	63%	SBH	Brazil	Journal
NCCN guidelines version 5.2020 Hepatobiliary Cancers (27)	2020	34%	NCCN	United States	Website
Management consensus guideline for hepatocellular carcinoma: 2020 update on surveillance, diagnosis, and systemic treatment by the Taiwan Liver Cancer Association and the Gastroenterological Society of Taiwan (28)	2021	43%	TLCA	China	Journal
Nonsurgical management of advanced hepatocellular carcinoma: a clinical practice guideline (29)	2020	60%	GDSG	Canada	Journal
Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with intermediate and advanced/relapsed hepatocellular carcinoma: a TOS-ESMO initiative endorsed by CSCO, ISMPO, JSMO, KSMO, MOS and SSO (30)	2020	49%	TOS-ESMO	Asia	Journal
Saudi Association for the Study of Liver diseases and Transplantation practice guidelines on the diagnosis and management of hepatocellular carcinoma (31)	2020	54%	SALT	Saudi Arabia	Journal
Systemic Therapy for Advanced Hepatocellular Carcinoma: ASCO Guideline (32)	2020	86%	ASCO	United States	Journal
Guidelines for diagnosis and treatment of primary liver cancer in China (2019 edition) (33)	2020	49%	NHC	China	Journal
Chinese Society of Clinical Oncology (CSCO) Guidelines for Diagnosis and Treatment of Primary Liver Cancer 2020 (34)	2020	43%	CSCO	China	Website
2018 Korean Liver Cancer Association—National Cancer Center Korea Practice Guidelines for the Management of Hepatocellular Carcinoma (35)	2019	74%	KLCA and NCC	South Korea	Journal
2019 Update of Indian National Association for Study of the Liver (INASL) Consensus on Prevention, Diagnosis and Management of Hepatocellular Carcinoma in India: The Puri II Recommendations (36)	2019	51%	INASL	India	Journal
A Practical Guideline for Hepatocellular Carcinoma Screening in Patients at Risk (37)	2019	46%	HCC CONNECT	United States	Journal
Clinical practice guideline for image-guided multimode tumour ablation therapy in hepatic malignant tumours (38)	2019	37%	CACA	China	Journal

Table 1 (*continued*)

Table 1 (*continued*)

Title	Year of publication	Reporting rate	Developer	Country or region	Journal or website of publication
Clinical practice guidelines on liver transplantation for hepatocellular carcinoma in China (2018 edition) (39)	2019	43%	CMA	China	Journal
Chinese Clinical Practice Guidelines for trans-arterial chemoembolization of hepatocellular carcinoma (40)	2019	37%	CMDA	China	Journal
Clinical practice guidelines for the treatment of primary liver cancer with integrative traditional Chinese and Western medicine (41)	2018	91%	SACIM	China	Journal
Diagnosis, Staging and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases (42)	2018	63%	AASLD	United States	Journal
EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma (43)	2018	80%	EASL	Europe	Journal
Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up (44)	2018	46%	ESMO	Europe	Journal
AASLD GUIDELINES FOR THE TREATMENT OF HEPATOCELLULAR CARCINOMA (45)	2018	74%	AASLD	United States	Journal

The details of RIGHT checklist can be found at http://www.right-statement.org/right-statement/checklist. RIGHT, Reporting Items for practice Guidelines in Healthcare.

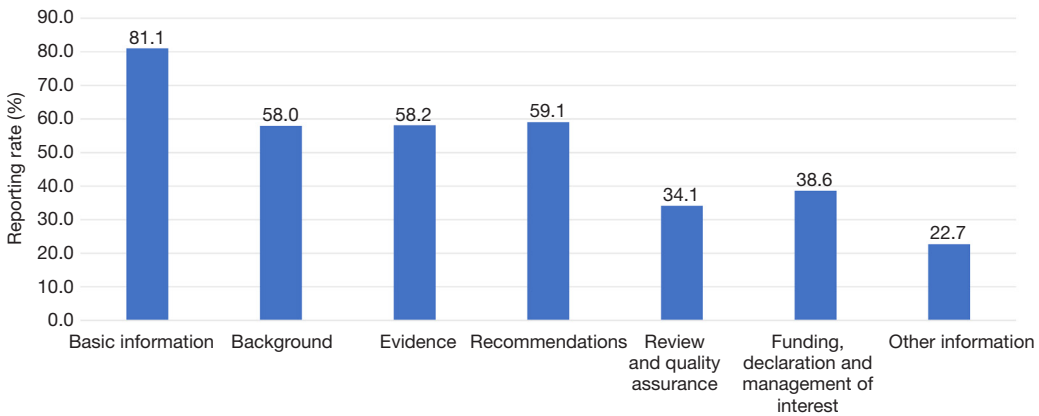

Figure 2 The mean reporting rates in each domain of the RIGHT checklist. RIGHT, Reporting Items for practice Guidelines in Healthcare.

the recommendations can be meaningful for users who can quickly obtain the critical information without the need to seek the relevant information in the main text of the guideline. The rationale or explanation of the recommendations was reported by only about one-third of the CPGs. The accurate description of the rationale can be essential for a thorough understanding and balancing of the "pros and cons" of different interventions in the target population.

In clinical practice, clinicians need to make decisions that consider the context of the individual patient and situation. Therefore, high-quality guidelines should provide sufficient information about the applicability of the recommendations in specific clinical situations (47). We also found that the specific approaches or methods used to elicit or identify value and preferences or resource implications were poorly reported. Similar findings were also observed in other guideline evaluations regarding other topics

Table 2 The details of reporting quality

Section/topic	No.	Item	Reported, n (%)	Not reported, n (%)	Not applicable, n (%)
Basic information					
Title/subtitle	1a	Identify the report as a guideline, that is, with "guideline(s)" or "recommendation(s)" in the title	22 (100.0)	0	0
	1b	Describe the year of publication of the guideline	8 (36.4)	14 (63.6)	0
	1c	Describe the focus of the guideline, such as screening, diagnosis, treatment, management, prevention or others	20 (90.9)	2 (9.1)	0
Executive summary	2	Provide a summary of the recommendations contained in the guideline	18 (81.8)	4 (18.2)	0
Abbreviations and acronyms	3	Define new or key terms, and provide a list of abbreviations and acronyms if applicable	20 (90.9)	2 (9.1)	0
Corresponding developer	4	Identify at least one corresponding developer or author who can be contacted about the guideline	19 (86.4)	3 (13.6)	0
Background					
Brief description of the health problem(s)	5	Describe the basic epidemiology of the problem, such as the prevalence/incidence, morbidity, mortality, and burden (including financial) resulting from the problem	19 (86.4)	3 (13.6)	0
Aim(s) of the guideline and specific objectives	6	Describe the aim(s) of the guideline and specific objectives, such as improvements in health indicators (e.g., mortality and disease prevalence), quality of life, or cost savings	10 (45.5)	12 (54.5)	0
Target population(s)	7a	Describe the primary population(s) that is addressed by the recommendation(s) in the guideline.	11 (50.0)	11 (50.0)	0
	7b	Describe any subgroups that are given special consideration in the guideline	19 (86.4)	3 (13.6)	0
End-users and settings	8a	Describe the intended primary users of the guideline (such as primary care providers, clinical specialists, public health practitioners, program managers, and policy-makers) and other potential users of the guideline	9 (40.9)	13 (59.1)	0
	8b	Describe the setting(s) for which the guideline is intended, such as primary care, low- and middle-income countries, or in-patient facilities	9 (40.9)	13 (59.1)	0
Guideline development groups	9a	Describe how all contributors to the guideline development were selected and their roles and responsibilities (e.g., steering group, guideline panel, external reviewer, systematic review team, and methodologists)	7 (31.8)	15 (68.2)	0
	9b	List all individuals involved in developing the guideline, including their title, role(s) and institutional affiliation(s)	18 (81.8)	4 (18.2)	0
Evidence					
Healthcare questions	10a	State the key questions that were the basis for the recommendations in PICO (population, intervention, comparator, and outcome) or other format as appropriate	11 (50.0)	11 (50.0)	0

Table 2 (*continued*)

Table 2 (*continued*)

Section/topic	No.	Item	Reported, n (%)	Not reported, n (%)	Not applicable, n (%)
	10b	Indicate how the outcomes were selected and sorted	13 (59.1)	9 (40.9)	0
Systematic reviews	11a	Indicate whether the guideline is based on new systematic reviews done specifically for this guideline or whether existing systematic reviews were used	16 (72.7)	6 (27.3)	0
	11b	If the guideline developers used existing systematic reviews, reference these and describe how those reviews were identified and assessed (provide the search strategies and the selection criteria, and describe how the risk of bias was evaluated) and whether they were updated	12 (54.5)	8 (36.4)	2 (9.1)
Assessment of the certainty of the body of evidence	12	Describe the approach used to assess the certainty of the body of evidence	18 (81.8)	4 (18.2)	0
Recommendations					
Recommendations	13a	Provide clear, precise, and actionable recommendations	21 (95.5)	1 (4.5)	0
	13b	Present separate recommendations for important subgroups if the evidence suggests that there are important differences in factors influencing recommendations, particularly the balance of benefits and harms across subgroups	20 (90.9)	2 (9.1)	0
	13c	Indicate the strength of recommendations and the certainty of the supporting evidence	18 (81.8)	3 (13.6)	1 (4.6)
Rationale/explanation for recommendations	14a	Describe whether values and preferences of the target population(s) were considered in the formulation of each recommendation. If yes, describe the approaches and methods used to elicit or identify these values and preferences. If values and preferences were not considered, provide an explanation	4 (18.2)	18 (81.8)	0
	14b	Describe whether cost and resource implications were considered in the formulation of recommendations. If yes, describe the specific approaches and methods used (such as cost-effectiveness analysis) and summarize the results. If resource issues were not considered, provide an explanation	9 (40.9)	13 (59.1)	0
	14c	Describe other factors taken into consideration when formulating the recommendations, such as equity, feasibility and acceptability	8 (36.4)	14 (63.6)	0
Evidence to decision processes	15	Describe the processes and approaches used by the guideline development group to make decisions, particularly the formulation of recommendations (such as how consensus was defined and achieved and whether voting was used)	11 (50.0)	11 (50.0)	0

Table 2 (*continued*)

Table 2 (*continued*)

Section/topic	No.	Item	Reported, n (%)	Not reported, n (%)	Not applicable, n (%)
Review and quality assurance					
External review	16	Indicate whether the draft guideline underwent independent review and, if so, how this was executed and the comments considered and addressed	8 (36.4)	14 (63.6)	0
Quality assurance	17	Indicate whether the guideline was subjected to a quality assurance process. If yes, describe the process	7 (31.8)	15 (68.2)	0
Funding, declaration and management of interest					
Funding source(s) and role(s) of the funder	18a	Describe the specific sources of funding for all stages of guideline development	9 (40.9)	13 (59.1)	0
	18b	Describe the role of funder(s) in the different stages of guideline development and in the dissemination and implementation of the recommendations	0	9 (40.9)	13 (59.1)
Declaration and management of interest	19a	Describe what types of conflicts (financial and non-financial) were relevant to guideline development	17 (77.3)	5 (22.7)	0
	19b	Describe how conflicts of interest were evaluated and managed and how users of the guideline can access the declarations	4 (18.2)	18 (81.8)	0
Other information					
Access	20	Describe where the guideline, its appendices, and other related documents can be accessed	5 (22.7)	17 (77.3)	0
Suggestions for further research	21	Describe the gaps in the evidence and/or provide suggestions for future research	6 (27.3)	16 (72.7)	0
Limitations of the guideline	22	Describe any limitations in the guideline development process (such as the development groups were not multidisciplinary or patients' values and preferences were not sought), and indicate how these limitations might have affected the validity of the recommendations	4 (18.2)	18 (81.8)	0

(21,48). Generally, the methodological quality relies on documented information, and reporting quality can to some extent also mirror the methodological quality (49). Thus, guideline developers must pay attention to the rationale and explanation of the recommendations when drafting the guidelines.

Both RIGHT items (16 and 17) related to the review and quality assurance were reported by less than 40% of the guidelines. Undergoing an independent review and a quality assurance process will enhance the rigor of development and editorial independence, ultimately making the CPGs more convincing. It is also worth noting that the funding source and declaration of interest were reported in most guidelines. However, the role of funder(s) in the different stages of guideline development and the dissemination and implementation of the recommendations (item 18b), and the management of interests were poorly reported. A possible reason for the lack of declaration of the role of the funders may be that guideline developers are not always directly involved in the dissemination or implementation of guidelines: this is often the responsibility of health care authorities or professional societies (50). But without transparent management of interests, the independence of guideline development will be questionable. Previous studies evaluating the reporting quality of guideline in other topics, for example integrative medicine and chronic kidney disease, also found deficiencies in reporting in these domains (51,52). Strengthening review and quality

assurance, and a thorough and transparent declaration and management of conflicts of interest and funding sources is an effective way to improve the quality of current guidelines.

Strengths and limitations

This is to our knowledge the first article to assess the reporting quality of guidelines for HCC based on the RIGHT statement. We carried out strict quality control during the evaluation process. However, our study also has some weaknesses. As we only searched English- and Chinese-language databases, the number of included CPGs was small and did not cover guidelines for HCC in other languages, which may potentially lead to selection bias.

Questions to be further discussed and considered

Question 1: What impact do you think the low reporting quality of clinical practice guidelines on hepatocellular carcinoma will have on clinicians and clinical practices?

Expert opinion: Dr. Vishal G. Shelat

Low reporting quality may impact the reliability of the guidelines. Many busy clinicians may feel obliged to comply with the guidelines due to trust in professional societies and organizations that make guidelines. Thus, if guidelines are poor of quality, it can impact safety and lead to harm. For example, 60% of clinicians responded that they would comply with guidelines recommending high dose steroids in patients with acute spinal cord injury, despite only 6% feel that it should be the standard of care (53,54). Fear of malpractice and professional censure can test individual clinician professional resilience to deviate from guidelines. One may feel more safe just blindly following the guideline, though morally it is not the right choice. Thus, the quality of reporting must be robust so that patients are not harmed. Kung *et al.* have studied a random sample of clinical practice guidelines archived on the National Guideline Clearinghouse (NGC) website and reported poor compliance with Institute of Medicine (IOM) standards (55). Our study confirms that scientific community continues to deviate from meeting high reporting standards despite awareness of such limitations. Personal conflicts, financial interests, scientific progress, or personal gain from authorship could be the reasons behind the lack of rigor and low-scientific quality of HCC guidelines. Our study cannot answer these questions and more evidence is required before any recommendations can be made. It remains individual moral responsibility to contribute scientific evidence in guideline and the process of guideline development. If conflict is perceived, recusal from guideline workgroup may be the best recourse.

Expert opinion: Dr. Francisco Tustumi

Low reporting quality clinical practice guidelines on hepatocellular carcinoma are propensity to every kind of bias. Consequently, these low-quality guidelines may induce clinicians to manage hepatocellular carcinoma based on poorly evidenced data regarding prognostication, diagnosing, investigation, or therapy. Poor quality guidelines lead to poor decision-making and inadequate use of resources (including utilization of liver grafts, diagnostic tests, expenses, time, and human resources).

Expert opinion: Dr. Sanjaya K. Satapathy

Traditional clinical guidelines consider only what is best for the patient and have explicitly not considered cost to the society. The suboptimal reporting of clinical practice guidelines on HCC will have spiraling effect on the clinicians and clinical practices, leading to a significant increase in healthcare burden.

Expert opinion: Dr. Koo Jeong Kang

The key for high reporting quality of clinical practice guideline is that it should provide the best benefit of survival and safety with highest quality of life when the patient was treated according to the guideline. And the guideline should be simple and algorithmic. The problem of the treatment guideline for hepatocellular carcinoma is that the patient status is not simple. Most of the HCC is developed in various diseased liver, viral hepatitis, alcoholics and fatty liver disease. And also the staging system of the HCC is not simple. There are various different staging systems.

EASL guideline is the most commonly mentioned in literature and academic society with higher reporting quality, even though the guideline is still not acceptable in some situations, intermediate to advanced staged HCC in particular. EASL guideline for both diagnosis and treatment is referred with higher quality, especially the algorithm for treatment strategy. It is very well formulated based on combined performance status, liver function as well as tumor stage according to BCLC stage. However, it is still applied in only 42.4% in Korean Primary Liver Cancer Registry (56). There was relatively low adherence to the guideline in patients with BCLC stage B or C HCC. The doctors who involved in in this study believe that the results and highlighted trends in the characteristics of HCC will contribute to improve the management of this

disease.

Another aspect of the reason of low reporting quality may be caused that the guideline developed earlier is not revised and updated with high quality reports showing better survival benefit applied with other treatment modalities than the guideline (57,58).

Question 2: What do you think the most important aspects needed for developing high-quality clinical practice guidelines on hepatocellular carcinoma are?

Expert opinion: Dr. Vishal G. Shelat

The two crucial aspects needed for developing high-quality clinical practice guidelines on HCC are: high-quality scientific evidence, and professional governance of guideline development workgroups. As existing scientific literature is the backbone of guideline development, high-quality of data that is reliable and generalizable must be reported. To generate such data, clinicians must conduct scholarly activities alongside clinical practice. Such scholarly work should be performed by collaborative networks of basic scientists and clinicians, so that bench research is timely translated to bedside practice. It is essential that the latest evidence is incorporated into guidelines and this is continually reviewed. Professional organizations should recruit guideline members on the basis of scientific repute and not based on hierarchy or leadership roles in the organization. The guideline workgroup members should not be under the influence that could impair their judgment or decisions in critical analysis and evaluation of scientific evidence. Ideally, all members should be familiar with skills needed for critical appraisal of literature, and provided access and time to perform their role. Individual roles and responsibilities must distribute in mirco-teams so that individual members don't make assumptions that 'someone else is going to do this ….'. Individual motivation, accountability and empowerment of all members is integral to high-quality guidelines. In addition, independent external and impartial review of the final manuscript by key opinion leaders or content experts is important to ensure that any possible blind-spots of guideline workgroup are identified, and corrected.

Expert opinion: Dr. Francisco Tustumi

Practice guidelines on hepatocellular carcinoma should preferably use systematic review tools for selecting, extracting, synthetizing, critical appraisal, and reporting. Guidelines should clearly summarize the evidence by reporting the certainty of any statement so that decision-makers could know the strength of the evidence.

Expert opinion: Dr. Sanjaya K. Satapathy

High quality clinical practice guidelines on HCC need to consider RIGHT checklist items carefully with special attention for funding, declaration and management of interests, and external review and quality assurance. These items specifically appear to be neglected in majority of the HCC guidelines reported so far in the past 3 years.

Expert opinion: Dr. Koo Jeong Kang

For higher reporting quality of clinical practice guideline, it should be simply formulated from by systematic review of very well analyzed and summarized of the evidence based data by experts in different specialties. Also, it should be simple and easily applicable to individual patient following well-designed algorithm. Although the guideline is very well described after comprehensive analytic works by experts who have various kinds of specialties, the descriptive guideline without well formulated algorithm is not well used in practice. The ideal guideline should provide both safety and survival when it was applied to individual patient. If the tumor board members in an institution believe that their own practice provides better survival benefit than the guidelines, they will go their own way.

Question 3: How do you think conflicts of interest in the guidelines should be handled?

Expert opinion: Dr. Vishal G. Shelat

The ethical basis for professional obligation in medicine is the principle of primacy to patient welfare. Thus, patient's best interest must be the primary consideration of the guideline development workgroup. In my opinion, the best way to manage conflicts is by recusal. Only if necessary for a particular member to be included in the guideline, then disclosure of conflict is mandatory. Problems rarely follow disclosure, but often from the discovery of non-disclosure. For example, the HCC practice guideline from Korean presented the disclosure of conflict of interest, not only presented the specific personnel information including names and affiliations, but also their contribution in the process of forming the guideline, which can increase reliability and protect the rights of patients better (35).

Expert opinion: Dr. Francisco Tustumi

Every conflict of interest should be clearly stated.

Expert opinion: Dr. Sanjaya K. Satapathy

Guideline developers with conflicts of interest such as relationships with the pharmaceutical industry could potentially be biased while formulating their recommendations (59). It is vital to have appropriate disclosure of financial conflicts of interest for authors of

CPGs and a formal process for discussing these conflicts before CPG development should be formed.

Expert opinion: Dr. Koo Jeong Kang

It is very difficult issue. There is no way except declaration of every developer or organization of the guideline regarding the conflict of interest with funding sources.

Conclusions

The reporting quality of guidelines for HCC was suboptimal. Particularly the declaration of funding and the quality assurance process was rarely reported. We encourage using the RIGHT statement when developing high-quality CPGs for HCC to ensure that the recommendations and their background information are clearly transparently reported.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/atm-21-2611). SKS has served as a speaker for Intercept, Alexion, Dova, as an advisory board member for Gilead, Intercept, Bayer and has received research funding from Novartis, Fibronostics Gilead, Biotest, Genfit, Conatus, Intercept, Shire, Exact Sciences, Eananta, Dova, Bayer. SKS is an employee of Northwell Health. The other authors have no conflicts of interest to declare.

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References

1. Villanueva A. Hepatocellular Carcinoma. N Engl J Med 2019;380:1450-62.
2. Singal AG, Lampertico P, Nahon P. Epidemiology and surveillance for hepatocellular carcinoma: New trends. J Hepatol 2020;72:250-61.
3. Mak LY, Wong DK, Pollicino T, et al. Occult hepatitis B infection and hepatocellular carcinoma: Epidemiology, virology, hepatocarcinogenesis and clinical significance. J Hepatol 2020;73:952-64.
4. Yuen MF, Chen DS, Dusheiko GM, et al. Hepatitis B virus infection. Nat Rev Dis Primers 2018;4:18035.
5. Zheng R, Qu C, Zhang S, et al. Liver cancer incidence and mortality in China: Temporal trends and projections to 2030. Chin J Cancer Res 2018;30:571-9.
6. Yang JD, Hainaut P, Gores GJ, et al. A global view of hepatocellular carcinoma: trends, risk, prevention and management. Nat Rev Gastroenterol Hepatol 2019;16:589-604.
7. Rebouissou S, Nault JC. Advances in molecular classification and precision oncology in hepatocellular carcinoma. J Hepatol 2020;72:215-29.
8. Craig AJ, von Felden J, Garcia-Lezana T, et al. Tumour evolution in hepatocellular carcinoma. Nat Rev Gastroenterol Hepatol 2020;17:139-52.
9. Yang JD, Heimbach JK. New advances in the diagnosis and management of hepatocellular carcinoma. BMJ 2020;371:m3544.
10. Petrowsky H, Fritsch R, Guckenberger M, et al. Modern therapeutic approaches for the treatment of malignant liver tumours. Nat Rev Gastroenterol Hepatol 2020;17:755-72.
11. Shekelle PG. Clinical Practice Guidelines: What's Next? JAMA 2018;320:757-8.
12. Grilli R, Magrini N, Penna A, et al. Practice guidelines developed by specialty societies: the need for a critical appraisal. Lancet 2000;355:103-6.
13. Xiao Y, Jiang L, Tong Y, et al. Evaluation of the quality of

guidelines for assisted reproductive technology using the RIGHT checklist: A cross-sectional study. Eur J Obstet Gynecol Reprod Biol 2019;241:42-8.
14. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ 2010;182:E839-42.
15. Brouwers MC, Kerkvliet K, Spithoff K, et al. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. BMJ 2016;352:i1152.
16. Chen Y, Yang K, Marusic A, et al. A Reporting Tool for Practice Guidelines in Health Care: The RIGHT Statement. Ann Intern Med 2017;166:128-32.
17. Howard B, Chapman C, Meyer C, et al. Analysis of completeness of reporting utilizing the Reporting Items for practice Guidelines in Healthcare Statement in gastroenterology clinical practice guidelines. Int J Evid Based Healthc 2019;17:173-8.
18. Wang Q, Duan Y, Liang J, et al. Reporting quality of 2014-2018 clinical practice guidelines on diabetes according to the RIGHT checklist. Endocrine 2019;65:531-41.
19. Tokalic R, Vidak M, Buljan I, et al. Reporting quality of European and Croatian health practice guidelines according to the RIGHT reporting checklist. Implement Sci 2018;13:135.
20. Wang Z, Zhang Y, Guo W, et al. Reporting specifications regarding epilepsy practice guidelines based on the RIGHT reporting checklist: an analysis. BMJ Open 2019;9:e029589.
21. Wang X, Zhou Q, Chen Y, et al. Using RIGHT (Reporting Items for Practice Guidelines in Healthcare) to evaluate the reporting quality of WHO guidelines. Health Res Policy Syst 2020;18:75.
22. Yun X, Yaolong C, Zhao Z, et al. Using the RIGHT statement to evaluate the reporting quality of clinical practice guidelines in traditional Chinese medicine. PLoS One 2018;13:e0207580.
23. Chen Y, Yang K, Marušic A, et al. A Reporting Tool for Practice Guidelines in Health Care: The RIGHT Statement. Ann Intern Med 2017;166:128-32.
24. Shiina S, Gani RA, Yokosuka O, et al. APASL practical recommendations for the management of hepatocellular carcinoma in the era of COVID-19. Hepatol Int 2020;14:920-9.
25. Piñero F, Tanno M, Aballay Soteras G, et al. Argentinian clinical practice guideline for surveillance, diagnosis, staging and treatment of hepatocellular carcinoma. Ann Hepatol 2020;19:546-69.
26. Chagas AL, Mattos AA, Carrilho FJ, et al. Brazilian society of hepatology updated recommendations for diagnosis and treatment of hepatocellular carcinoma. Arq Gastroenterol 2020;57:1-20.
27. Network NCC. Hepatobiliary Cancers. 2020. Available online: http://www.nccn.org
28. Shao YY, Wang SY, Lin SM, et al. Management consensus guideline for hepatocellular carcinoma: 2020 update on surveillance, diagnosis, and systemic treatment by the Taiwan Liver Cancer Association and the Gastroenterological Society of Taiwan. J Formos Med Assoc 2021;120:1051-60.
29. Meyers BM, Knox J, Cosby R, et al. Nonsurgical management of advanced hepatocellular carcinoma: a clinical practice guideline. Curr Oncol 2020;27:e106-14.
30. Chen LT, Martinelli E, Cheng AL, et al. Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with intermediate and advanced/relapsed hepatocellular carcinoma: a TOS-ESMO initiative endorsed by CSCO, ISMPO, JSMO, KSMO, MOS and SSO. Ann Oncol 2020;31:334-51.
31. Alqahtani SA, Sanai FM, Alolayan A, et al. Saudi Association for the Study of Liver diseases and Transplantation practice guidelines on the diagnosis and management of hepatocellular carcinoma. Saudi J Gastroenterol 2020;26:S1-S40.
32. Gordan JD, Kennedy EB, Abou-Alfa GK, et al. Systemic Therapy for Advanced Hepatocellular Carcinoma: ASCO Guideline. J Clin Oncol 2020;38:4317-45.
33. Guidelines for diagnosis and treatment of primary liver cancer in China (2019 edition). Zhonghua Gan Zang Bing Za Zhi 2020;28:112-28.
34. Oncology CSoC. Guidelines for Diagnosis and Treatment of Primary Liver Cancer. 2020. Available online: http://www.csco.org.cn/cn/index.aspx.
35. Korean Liver Cancer Association (KLCA); National Cancer Center (NCC), Goyang, Korea. 2018 Korean Liver Cancer Association-National Cancer Center Korea Practice Guidelines for the Management of Hepatocellular Carcinoma. Korean J Radiol 2019;20:1042-113.
36. Kumar A, Acharya SK, Singh SP, et al. 2019 Update of Indian National Association for Study of the Liver Consensus on Prevention, Diagnosis, and Management of Hepatocellular Carcinoma in India: The Puri II Recommendations. J Clin Exp Hepatol 2020;10:43-80.
37. Frenette CT, Isaacson AJ, Bargellini I, et al. A Practical Guideline for Hepatocellular Carcinoma Screening in Patients at Risk. Mayo Clin Proc Innov Qual Outcomes 2019;3:302-10.

38. Wang GZ, He XH, Wang Y, et al. Clinical practice guideline for image-guided multimode tumour ablation therapy in hepatic malignant tumours. Curr Oncol 2019;26:e658-64.
39. Xu X, Chen J, Wei Q, et al. Clinical practice guidelines on liver transplantation for hepatocellular carcinoma in China (2018 edition). Hepatobiliary Pancreat Dis Int 2019;18:307-12.
40. Chinese College of Interventionalists, Chinese Medical Doctor Association. Chinese Clinical Practice Guidelines for transarterial chemoembolization of hepatocellular carcinoma. Zhonghua Gan Zang Bing Za Zhi 2019;27:172-81.
41. Ling CQ, Fan J, Lin HS, et al. Clinical practice guidelines for the treatment of primary liver cancer with integrative traditional Chinese and Western medicine. J Integr Med 2018;16:236-48.
42. Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology 2018;68:723-50.
43. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol 2018;69:182-236.
44. Vogel A, Cervantes A, Chau I, et al. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2018;29:iv238-55.
45. Heimbach JK, Kulik LM, Finn RS, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. Hepatology 2018;67:358-80.
46. Chen RB, Chen YL, Gai GZ, et al. Analysis of reporting specification about sepsis practice guideline based on RIGHT standard. Zhongguo Zhong Yao Za Zhi 2017;42:1514-7.
47. Armstrong MJ, Gronseth GS. Approach to assessing and using clinical practice guidelines. Neurol Clin Pract 2018;8:58-61.
48. Wang M, Liu F, Li Q, et al. Quality assessment of guidelines for the management of Mycobacterium tuberculosis infection in children. Int J Tuberc Lung Dis 2020;24:287-94.
49. Hayward RS, Wilson MC, Tunis SR, et al. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. A. Are the recommendations valid? The Evidence-Based Medicine Working Group. JAMA 1995;274:570-4.
50. Shekelle P, Woolf S, Grimshaw JM, et al. Developing clinical practice guidelines: reviewing, reporting, and publishing guidelines; updating guidelines; and the emerging issues of enhancing guideline implementability and accounting for comorbid conditions in guideline development. Implement Sci 2012;7:62.
51. Yao S, Wei D, Chen YL, et al. Quality assessment of clinical practice guidelines for integrative medicine in China: A systematic review. Chin J Integr Med 2017;23:381-5.
52. Zhao Y, Li Y, Li J, et al. Reporting quality of chronic kidney disease practice guidelines according to the RIGHT statement: a systematic analysis. Ther Adv Chronic Dis 2020;11:2040622320922017.
53. Canadian Association of Emergency P. Steroids in acute spinal cord injury. CJEM 2003;5:7-9.
54. Lenzer J. Why we can't trust clinical guidelines. BMJ 2013;346:f3830.
55. Kung J, Miller RR, Mackowiak PA. Failure of clinical practice guidelines to meet institute of medicine standards: Two more decades of little, if any, progress. Arch Intern Med 2012;172:1628-33.
56. Yoon. JS, Lee. HA, Kim. HY, et al. Hepatocellular Carcinoma in Korea: an Analysis of the 2015 Korean Nationwide Cancer Registry. Journal of Liver Cancer 2021;21:58-68.
57. Kokudo T, Hasegawa K, Matsuyama Y, et al. Survival benefit of liver resection for hepatocellular carcinoma associated with portal vein invasion. J Hepatol 2016;65:938-43.
58. Hyun MH, Lee YS, Kim JH, et al. Hepatic resection compared to chemoembolization in intermediate- to advanced-stage hepatocellular carcinoma: A meta-analysis of high-quality studies. Hepatology 2018;68:977-93.
59. Choudhry NK, Stelfox HT, Detsky AS. Relationships between authors of clinical practice guidelines and the pharmaceutical industry. JAMA 2002;287:612-7.

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Supplementary

PubMed search strategy

#1. liver Neoplasms [MeSH] or Hepatic Neoplasms [MeSH]
#2. Cancer* OR carcinoma* OR neoplasm* OR adenoma* OR adenocarcinom* OR tumour* OR tumor* OR polyp* OR malignant* [Title/Abstract]
#3. liver OR hepatic OR hepatocellular* OR hepato-cellular* OR hepatobiliary [Title/Abstract]
#4. #2 AND #3
#5. #1 OR #4
#6. Guideline [Publication Type]
#7. Practice Guideline [Publication Type]
#8. guideline*[Title]
#9. guidance*[Title]
#10. recommendation*[Title]
#11. OR #6-#10
#12. #5 AND #11
#13. Lim2018/1/1-2020/12/1

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