Quality of systematic review and meta-analysis may decide its clinical significance and publication

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Abstract: In this brief review, the authors aim to show the importance of the quality of a systematic review and meta-analysis by illustrating some examples. First, the reliability of systemic reviews’ conclusions is largely dependent upon the quality of included studies. Second, the publications are potentially influenced by the quality of systematic reviews. Third, AMSTAR tool should be employed to evaluate the quality of systematic reviews.

Keywords: Systematic review, meta-analysis, publication, quality

Introduction

At present, the clinical significance of systematic reviews and meta-analyses has been increasingly recognized [1, 2]. Generally speaking, the researchers should be strongly encouraged to perform systematic reviews and meta-analyses in their fields. The physicians should also prefer to make their clinical decisions based on the results of systematic reviews and meta-analyses. In the present review, we would like to illustrate some examples to demonstrate how the quality of a systematic review and meta-analysis influence its usefulness in clinical practices and even its final publications.

Reliability of systemic reviews’ conclusions is dependent upon the quality of included studies

In 1992, the clinical guidelines counseled that asymptomatic postmenopausal women might use hormone therapy to prevent disease and to prolong life [3]. Evidence from previous meta-analyses suggested that estrogen use could decrease the risk of coronary disease [4, 5]. However, most of included studies were observational and of low-quality. In 1998, a large randomized controlled trial involving 2763 participants demonstrated that estrogen did not protect against the development of overall cardiovascular events [6]. Notably, estrogen significantly increased the incidence of deep vein thrombosis. In 2002, a larger randomized controlled trial involving 16608 participants showed that estrogen plus progesterin significantly increased the risk of coronary heart disease, stroke, and pulmonary embolism among generally healthy postmenopausal women [7]. Subsequently, evidence from meta-analyses of high-quality randomized controlled trials supported no benefit of hormone therapy in the secondary or primary prevention of cardiovascular disease events [8]. Indeed, the current recommendations from U.S. Preventive Services Task Force are that a combination of estrogen and progesterin should not be used for the prevention of chronic conditions in postmenopausal women [9]. Accordingly, the conclusions of systematic review and meta-analyses would greatly change with the quality of included studies. If the quality of included studies was low, they could not be used in clinical practice.

Publications are associated with the quality of systematic reviews

Clinically significant portal hypertension (CSPH) often represents a clinical challenge in patients with hepatocellular carcinoma (HCC) who un-
### Table 1. An overview of systematic reviews regarding the impact of CSPH on the prognosis of HCC after surgery

<table>
<thead>
<tr>
<th>First author, Journal (Year)</th>
<th>Region</th>
<th>Databases</th>
<th>Last search date</th>
<th>Criteria for CSPH</th>
<th>Inclusion criteria</th>
<th>Quality assessment</th>
<th>Statistical software</th>
<th>Heterogeneity</th>
<th>Statistical model</th>
<th>Data expression</th>
<th>Sensitivity analysis</th>
<th>Publication bias</th>
<th>No. included papers</th>
<th>No. included patients</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berzigotti, Hepatology (2015)</td>
<td>Barcelona, Spain</td>
<td>Medline, (Hand-searching)</td>
<td>October, 2013</td>
<td>HVPG ≥10 mmHg or PVP ≥20 cm H2O or standard surrogate criteria: presence of gastro-esophageal varices or PLT &lt;100000/ml and spleen diameter &gt;12 cm</td>
<td>Clearly presented</td>
<td>According to the Quality In Prognosis Studies (QUIPS)</td>
<td>RevMan 5.2</td>
<td>Chi-square test and I statistic</td>
<td>Only random effects</td>
<td>Odds ratio</td>
<td>According to the study quality, method used to estimate the presence of portal hypertension, proportion of patients with preserved hepatic function, tumor burden, and type of surgery</td>
<td>Not evaluated</td>
<td>11</td>
<td>1737</td>
<td>3- and 5-year mortality, Complications related to cirrhosis</td>
</tr>
<tr>
<td>Choi, J Hepatobiliary Pancreat Sci (2014)</td>
<td>Seoul, Korea</td>
<td>PubMed, EMBASE, Cochrane Library</td>
<td>Not reported</td>
<td>Esophageal varices and/or thrombocytopenia with splenomegaly</td>
<td>Described</td>
<td>According to the Newcastle-Ottawa Scale (NOS)</td>
<td>RevMan 5.1, Comprehensive Meta-Analysis software Version 2</td>
<td>Cochran’s Q test</td>
<td>Only random effects</td>
<td>Odds ratio, hazard ratio</td>
<td>According to the definitions of CSPH</td>
<td>Not evaluated</td>
<td>11</td>
<td>2285</td>
<td>Operation-related factors, Postoperative mortality, complications, Liver-related morbidity or liver insufficiency, Prognostic significance of CSPH</td>
</tr>
<tr>
<td>Tang, Asian Pac J Cancer Prev (2014)</td>
<td>Chengdu, China</td>
<td>PubMed, EMBASE, CNKI</td>
<td>December, 2013</td>
<td>Esophageal varices and/or splenomegaly associated with thrombocytopenia</td>
<td>Clearly presented</td>
<td></td>
<td></td>
<td>Chi-square test</td>
<td>Fixed or random effects</td>
<td>Risk ratio, weighted mean difference</td>
<td>Not reported (but a subgroup analysis was performed in patients with Child-Pugh class A)</td>
<td>Funnel plot</td>
<td>7</td>
<td>1928</td>
<td>Peri-operative liver failure and ascites, Operative mortality</td>
</tr>
</tbody>
</table>

Abbreviations: CSPH, clinically significant portal hypertension; HCC, hepatocellular carcinoma; HVPG, hepatic vein pressure gradient; PLT, platelets count; PVP, portal vein pressure.
Quality of systematic review & meta-analysis

Table 2. List of references included in the three systematic reviews

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Llop, J Hepatol 2012</td>
<td>Kondo, Hepatogastroenterology 2012</td>
<td></td>
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<tr>
<td>Giannini, Liver Int 2013</td>
<td>Giannini, Liver Int 2013</td>
<td></td>
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<tr>
<td>Santambrogio, HPB 2013</td>
<td>Santambrogio, HPB 2013</td>
<td></td>
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</tbody>
</table>

undergo hepatic resection. Recently, there are at least 3 systematic review and meta-analysis papers published to evaluate the impact of CSPH on the outcomes of HCC patients treated with hepatectomy. In April 2014, Tang et al. published the first meta-analysis in the journal Asian Pacific Journal of Cancer Prevention (Thomson Reuters 2013 impact factor=1.5) [10]. They concluded that the presence of CSPH (i.e., presence of oesophageal varices and/or splenomegaly associated with thrombocytopenia) was significantly associated with a higher rate of post-operative liver failure and ascites, peri-operative blood transfusion, operative mortality, and 3- and 5-year overall mortality. In addition, the influence of CSPH on the post-operative liver failure and ascites, peri-operative blood transfusion, and 3- and 5-year overall mortality remained statistically significant in the subgroup analysis of patients with Child-Pugh class A.

In September 2014, Choi et al. published the second meta-analysis regarding the same topic in the Journal of Hepato-Biliary-Pancreatic Science (Thomson Reuters 2013 impact factor=2.313) [11]. They showed significantly higher rates of postoperative mortality, complications, liver-related morbidity, and liver failure and overall mortality in the CSPH group than in the non-CSPH group.

In February 2015, Berzigotti et al. published the third meta-analysis in the journal Hepatology (Thomson Reuters 2013 impact factor=11.19), which is the top one journal in the field of liver diseases [12]. They also demonstrated that the patients with CSPH had a significantly higher risk of 3- and 5-year mortality and of clinical decompensation after surgery than those without CSPH. Additionally, in the paper by Berzigotti et al., the sensitivity analyses were conducted according to the study quality, method used to estimate the presence of portal hypertension, proportion of patients with fully preserved hepatic function, tumor burden, and type of surgery. Importantly, the findings of all sensitivity analyses were consistent with those of the overall meta-analyses. Therefore, the conclusions regarding the negative impact of CSPH on the prognosis of HCC after surgery should be stable and reliable.

The similarities and differences of methods and results sections among the 3 systematic review and meta-analysis papers were summarized in Table 1.

First, the quality assessment and sensitivity analyses were more adequately designed in the study by Berzigotti et al. [12]. By comparison, in the study by Tang et al. [10], the quality assessment was lacking, and no sensitivity analysis was performed.

Second, Berzigotti et al. searched only one database (i.e., Medline) in a combination with hand-searching the list of references [12]. By comparison, Tang and Choi searched three databases [10, 11]. Notably, Tang et al. also employed one Chinese-language database (i.e., CNKI, China National Knowledge Infrastructure). And one Chinese-language full-text paper was included.

Third, the number of included references was 7 in the study by Tang et al. [10]. By contrast, the number of included references was higher in the studies by Berzigotti and Choi [11, 12]. Thus, the potential bias of study selection
Quality of systematic review & meta-analysis

should be clarified. Given that the relevant references should be comprehensively searched in a systematic review [13], another 9 references might be further included to strengthen their findings (Table 2).

Collectively, it appears to be reasonable that a high-quality and more methodologically sound systematic review and meta-analysis paper is more likely to be published in high-impact journals. Certainly, other factors that may influence the final publication should never be neglected, such as the academic background of a study team.

AMSTAR tool should be used to assess the methodological quality of systematic reviews

Recently, numerous instruments have been developed to assess the quality of systematic reviews. However, most of them had their potential limitations and weakness. In this paper, we briefly introduced a more popular and valid measurement tool for the “assessment of multiple systematic reviews” (AMSTAR). AMSTAR is constructed by a group of methodological experts [14]. Thirty-seven initially evaluated items are combined based on the quality of reporting of Meta-analyses (QUORUM) [15], the Sacks’s checklist [16], the language restriction, the publication bias, and the publication status. Finally, 11 components were identified by factor analysis (Table 3) [14]. Subsequently, the internal and external validation studies demonstrated that AMSTAR had satisfactory inter-observer agreement, reliability, construct validity, and feasibility [17, 18]. On May 20, 2015, a total of 171 papers could be identified by a preliminary search strategy with the search items “(AMSTAR) AND (systematic review)” in the PubMed database.

Conclusions

The researchers should pay more attention on improving the quality of systematic reviews and meta-analyses. AMSTAR tool may be a useful reference tool to monitor the quality of systematic reviews and meta-analyses.

Disclosure of conflict of interest

None.

Authors’ contribution

Xingshun Qi conceived this work and drafted the manuscript. Zhiping Yang, Ming Bai, and Yongji Wang gave critical comments and revised the manuscript. All authors have made an intellectual contribution to the manuscript and approved the submission.

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Table 3. AMSTAR tool list (see the reference by Shea et al. BMC Med Res Methodol. 2007)

Questions:
1. Was an ‘a priori’ design provided?
2. Was there duplicate study selection and data extraction?
3. Was a comprehensive literature search performed?
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?
5. Was a list of studies (included and excluded) provided?
6. Were the characteristics of the included studies provided?
7. Was the scientific quality of the included studies assessed and documented?
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?
9. Were the methods used to combine the findings of studies appropriate?
10. Was the likelihood of publication bias assessed?
11. Was the conflict of interest stated?

Answers:
1. Yes
2. No
3. Can’t answer
4. Not applicable
References


