

RESPONSES TO REVIEWER'S COMMENTS



Sept 6, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format.
(File name: TER-MA FINAL R1 09-08-14 cleancopy.doc)

Title: Diagnostic yield of Third Eye Retroscope on adenoma detection during colonoscopy: a systematic review and meta-analysis

Nirav Thosani MD, MHA, Bhavana Rao, MD, Sachin Batra, MD, MPH, Babatunde Adeyefa, MD, Gottumukkala S. Raju MD, Robert S. Bresalier MD, Subhas Banerjee MD and Sushovan Guha MD, PhD

Name of Journal: *World Journal of Meta-Analysis*

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The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewer
3. References and typesetting were corrected according to *World Journal of Meta-Analysis* format.

Reviewer #1

I read with interest the paper by Nirav Thosani et al. entitled: "Diagnostic yield of Third Eye Retroscope on adenoma detection during colonoscopy: a systematic review and meta-analysis". In recent years many attempts have been made to ameliorate colonoscopy technology mainly aimed to reduce procedure-related pain and discomfort and to improve its diagnostic yield. New devices

could also increase population adherence to colon cancer screening programs. Probably the third eye retroscope will represent an interesting novelty in clinical setting in the near future. *This is an excellent manuscript with valid statement and proper explanations, it is exhaustive and accurate, it is stimulating both for clinical practice and future further investigations. The methods for data analysis are appropriate and results are clearly displayed and easy to understand.*

Response to Reviewer #1:

We thank Reviewer #1 for his insightful comments about this manuscript.

Reviewer #2

This was well-written article, but I'd like to know more detailed information about TER. For example, the authors analyzed only AADR and APDR, and other factors, such as *procedure time and histology of detected polyps*, were simply discussed without specific data. *Please describe each study in detail, and support us imagine or understand actual TER.* It was difficult to judge the effectiveness of TER only from the aspect of detection rate.

Response to Reviewer #2:

We appreciate the feed-back from Reviewer #2. We have now included detailed information regarding the number, size and the nature of the polyps for each of the study in the **Table 1**. In addition **Table 2**, presents the data describing the impact of polyp size and location on the adenoma and polyp detection rate. While we agree with the reviewer that the comparison of withdrawal time and total time will provide a useful metric to study the benefit of third eye over the conventional colonoscopy alone, the study design in 3 of the 4 studies prevents us from performing such analysis. In order to measure the impact of third eye retroscope (TER) on the duration of the procedure, one will need to compare the two procedures (TER and standard optical colonoscopy or SC) in a randomized design with two parallel arms (SC+TER vs. SC). However, as noted, majority of the qualifying included studies (Triadafilopoulos *et al*, Wayne *et al*, DeMarco *et al*) were series of consecutive patients undergoing SC & TER in tandem.

Reviewer #3

Overall this seemed to be a worthwhile article. It needs some *minor clarification in my opinion*. Regarding the increase in detection rate. When one has an increase of polyp detection of "19.8%" and the adenoma increase is "19.9%" -what is the numerator and the denominator? Can the authors please provide the raw numbers in a table? It would also be good if the authors can separate out sessile serrated adenomas/sessile serrated polyps (SSP) from hyperplastic polyps. SSP are sometimes grouped with adenomas and sometimes not, and are currently of great interest in the GI literature. Readers would like to know what type of lesion the Third eye detects. Can the authors clarify the endoscopic methods used to get an increase in detection using the third eye? Were there tandem endoscopy or was the additional detection defined as a polyp seen with the third eye but not seen on the screen with the regular endoscopy? This is an important question as it has to do with endoscopic technique. Consider the fact that the additional polyps had to be characterized pathologically, which therefore implies that the polyps were removed. Removal is done using the forward viewing optics. This implies that all polyps seen with third eye must have been visible with forward viewing optics. For those to have not been identified without third eye may suggest poor technique using the forward viewing instrument. The definition of what constituted a polyp found by third eye but not found with forward viewing optics should be mentioned. Regarding the age of the patient, the mean age of 59.8 or 60 years (2 or 3 significant figures) is better than 59.83.

Response to Reviewer #3:

The **Table 1** has now been updated to present the raw data associated with additional polyp and adenoma detection. We agree with the reviewer that descriptions of the morphological details of the lesions detected by the third eye retroscope (TER) are important to assess its role in colonoscopy, unfortunately the studies provide limited information in this regard. In line with this, we have included the comparison of the size of the lesions which could be detected by the TER only versus those detected by standard colonoscopy (**Table 2**).

Also we would like to clarify that the additional adenoma/polyps were defined as lesions which were detected only by the third eye retroscope (TER). Any lesion that was visible on both TER and standard colonoscope (SC) was attributed to SC and was not counted among the TER associated additional lesions. The methods section has been updated to present the definition of additional lesions. Also, one of the four studies (Leufkens *et al*) accounted for the additional lesions due to second-pass effect & operator related errors by randomizing patients to two study arms wherein they underwent tandem colonoscopy with SC + TER followed by SC alone and vice versa.

We have added a highlighted section describing these comments under Results section (page 8-9).

Thank you again for publishing our manuscript in the *World Journal of Meta-Analysis*.

Sincerely yours,

A handwritten signature in blue ink that reads "Sushovan Guha".

Sushovan Guha, MD, PhD
Division of Gastroenterology, Hepatology, and Nutrition
Department of Internal Medicine
4.234 Medical School Building
6431 Fannin Street,
Houston, Texas 77030
Phone: 713-500-6677
Fax: 713-500-6699
Email: sushovan.guha@uth.tmc.edu