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Dear Editor,

Please find enclosed the edited manuscript 7774 in Word format (file name: 7774 Review.doc)

**Title:** Transnasal Endoscopy; Technical Considerations, Advantages and Disadvantages

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**Name of Journal:** *World Journal of Gastrointestinal Endoscopy*

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**The manuscript has been improved according to the suggestions of reviewer:**

1.Format has been updated

2. Revision has been made according to the suggestions of the reviewer

(1). First, do you have any idea how many physicians perform TNE? What is the percentage gastroenterologists who are aware of this technology (other than the percentage that perform it)? And of the 31% of gastroenterologists that perform the procedure, why do they only use it 20% of the time?

There is a significant geographic disparity in usage of TNE. In Far East Asia, especially in Japan, it is very popular among endoscopists and nearly half of all endoscopies are currently done by transnasal route. However, in Western Countries, it seems only 1/3 of endoscopist are aware of this method. Our observations for the reasons are unawareness of its potential advantages and lack of training. There are also some concerns about the maneuverability and image quality of this method among the endoscopists. The European survey study has confirmed our thoughts and we used it as a reference. The last part of Introduction has been revised. (page 3 last 3 lines, page 4 first 3 lines, page 4 lines 8-10).

(2). Secondly, can you give us the cost of this procedure, and compare it with the traditional transoral endoscopy (TOE).

There is no extra cost of this system. The prices of ultrathin scopes are same with standard scopes. This has been added as a short sentence to the end of first paragraph at the technical considerations section. (Page 5, Lines 7-10). It is cost effective compared to sedated endoscopy. This has been stressed on the advantages of TNE.

(3). Third, have you done a survey of patients previous to an endoscopy when the TNE and TOE procedures are explained to them?

Unfortunately we do not have an objective data about their preferences before the procedures. We did not ask in our study because of; (1) asking and then directing the patients to that

method might have been destroyed our randomization and (2) they had not any experience about the procedures, so their response would be based on prejudgment. But we had data after the procedures and we shared it on the text.

(4). Fourth, how many procedures can be performed with the ultra-thin endoscope, and what is the cost of the endoscope per procedure?

There is not a certain number given by manufacturers. But it is usually said as the same with standard endoscopes. The warranty of scopes by manufacturers is not due to the number of the procedures but depends on the time. This added as a short sentence at the end of first paragraph at the technical considerations section (Page 5, lines 7-10).

The reimbursement rate is also same in many countries with unsedated transoral endoscopy. The cost for per procedure usually differs among the regions and clinics in Worldwide. In Turkey, reimbursement rate by government is approximately 60\$ for per procedure. It is about 200\$ in private clinics. In USA, it is nearly fourfold of these figures.

(5). Fifth, you mention that “the image quality of transnasal endoscopes are very close to standard endoscopes and studies could not find a difference in their diagnostic capabilities compared to standard endoscopes” but later, you do also mention that “however, they do not have high-definition (HD) image capabilities and this may decrease their lesion detection rates compared to HD scopes for small lesions”. How should we make sense of this? Do we lose diagnostic capability? Could this have legal repercussions?

We are discussing the issue according to current literature. We identified 9 publications (they have been cited at the paper) comparing diagnostic capabilities of ultra-thin and standard endoscopes. Six of these studies could not show any difference in the quality of images between ultra-thin and standard scopes. However, 3 studies were found standard endoscopes were better (two of these studies used high definition capabilities). So, there is a contradiction between studies. It seems, there is not a significant difference of image capabilities between ultra-thin and conventional standard endoscopes without HD, and however, standard endoscopes with HD capabilities may generate a difference for small lesions less than 2 mm. There are on-going researches to add HD characteristics to ultra-thin endoscopes. In near future, this may contribute to the diagnostic properties of these scopes.

It is hard to say about the legal repercussions. If we are doing a diagnostic endoscopy with a conventional standard endoscope without HD, would it be a legal problem? Or should we leave all these devices as soon as a new generation comes? or will any new technology obligate us to use it legally and when? TNE is used especially for screening endoscopy including Japan where early gastric cancers are most common, but there is not such a legal repercussion in Japan.

A new sentence added to page 11, line 17 to stress this controversy, and it is discussed on the limitations of TNE.

(6). Sixth, even though you mention that it can have other therapeutic applications, as in advanced gastrointestinal strictures, in feeding tube insertion, you also consider that some of

the disadvantages are the “narrow working channel, poor suction and air functions compared to standard endoscopes and extreme flexibility which may cause difficulty in some manipulations”. How can we translate these conflicting pieces of information?

As a general rule, ultra-thin endoscopes are not for therapeutic applications. However, its thin diameter creates an advantage over to standard endoscopes for some special conditions and interventions. And, its advantages outweigh its disadvantages in these conditions. For example, for strictures which do not allow a standard endoscope pass through, you can complete the procedure with an ultra-thin endoscope, pass any guidewire or catheter to distal and can make some interventional procedures safely over the guidewire. These interventions are mostly a feature of ultra-thin endoscopes and not related to transnasal route. Since the main topic of this paper is to discuss transnasal route, we did not intervene with the usage of ultrathin endoscopes other than TNE. To prevent a confusion, we stressed it as “in some special cases due to its thinner diameter” at the entrance of related section. Page 11.

(7). Seventh, it could be of interest if you could add some images and photographs of some of the TNE procedures.

Two images have been added as Figure 3a and 3b.

(8). Finally, there are some minor grammatical mistakes you need to solve. For example, in the introduction you wrote “usinglidocaine” and it should be “using lidocaine”. There are also some annotations like “ENREF 1 ENREF 1”. ENREF 11”, etc. that you need to correct.

All grammatical errors have been corrected. The text has also been reviewed by a native speaker. There are not any annotations like ENREF at the original file. Probably it is somehow a result of format change.

3. References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

With my best regards.



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