Author's response to reviews

Title: Narrow-band imaging does not improve detection of colorectal polyps when compared to conventional colonoscopy: a randomized controlled trial and meta-analysis of published studies.

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Author's response to reviews: see over
The Editor

Re: Submission of manuscript for publication

Dear Sir,

Thanks for the opportunity to continue in the peer review process. We appreciate the commentaries of the reviewers that have been very helpful to improve the manuscript.

We have included the comments in the revised manuscript and are providing a point-by-point response to the concerns.

Best regards

Ludovic Reveiz MD.

Reviewer’s report:

Reviewer: Mainor R Antillon

In their introduction the authors state ..."removal of polyps and postpolypectomy surveillance decreases the overall mortality from colorectal cancer. I am not sure this is a true statement. Did they mean to say some studies have shown it decreases the incidence of colorectal cancer. Is there data to support the statement "polypectomy decreases overall mortality form colorectal cancer"? Authors’s response: Agreed thanks you, this was modified in the introduction section.

The authors only reported % of excellent bowel preps but would be more interesting to report Number or Excellent and Good bowel preps like other studies have. Authors’s response: Agreed, thank you. We reported both “excellent” and “good” preparation in the Table. This has been clarified now.

Adenoma detection rate was low in this study compared to some of the adenoma detection rate in their meta-analysis of published studies. Not to mention they state in the limitations of this study "As screening colonoscopy is not usually recommended in our country in people above 50 years of age with average risk", then one would assume that an average age of 57.36 years old for the NBI group and 59.29 years old for the White-light group prevalence of adenomas should be higher than if all of these patient's had their polyps removed during a prior colonoscopy. Yet if you look at their reported date 35% in NBI group and 36% in the White-light group had at least one colonoscopy in the preceding 10 years and
31% in both groups in the preceding 5-years. These are high number if colonoscopy is not usually recommended in their country.

Authors’s response: The reviewer was right. The included population included patients from two private clinics. Therefore, most included patients have a private insurance. That is the reason why the rate of previous colonoscopy was so high (and one of the reason why the number of polyps was lower than in other studies), as opposed to the population of the country.

It is not clear how during the 9 month enrollment period amongst "three experienced examiner" that they were only able to enroll 482 patient and it is not clear how only 501 patient during the 9 months were assessed for eligibility (that's a volume of about 167 pts/"experienced examiner" in a 9 month period or 223 pts/"experienced examiner a year.... a very low volume ..."all consecutive adults patients presenting for screening or diagnostic colonoscopy during a 9 month period or were their a selection bias for eligibility other than their stated exclusion criteria?

Authors’s response: The study was not conducted at the same time in both clinics and one of the clinics recruited patients before the other. In addition, a number of patients did not fulfill the inclusion criteria (bad colon preparation, active bleeding, colonoscopy was indicated for polypectomy etc). This was modified in the result section.

Several studies have shown when it comes to adenoma detection rate, experience alone doesn't correlate with "high quality screening colonoscopy -high adenoma detection rate". Adenoma detection rate is currently the best accepted indicator of the quality screening colonoscopy, yet their data may suggest otherwise. Looking at Sabbagh etal.'s 35% of NBI group and 36% of the White-light group had a colonoscopy within the preceding 10 years - yet the percent of those colonoscopy with previous polyp resection in the NBI group was only 11% (unknown what percent were adenomas) while the White-light group was only 8% (unknown what percentage were adenomas). One must assume that the adenoma detection rate was even lower than this low number of polyp detection rate, which bringing up the question of the quality of colonoscopy performed. Unknown what percent of the patient in both group who's previous colonoscopy were performed by any of the three physicians in this study.

Authors’s response: we agree with the argument that the experience alone doesn't not necessarily correlate with high quality screening colonoscopy. As mentioned, one third of patients had a previous colonoscopy and a number of them reported to have had a previous polyp resection. We can not ensure that a number of them had recall bias (which is possible because we asked for the ten last years). Unfortunately we do not know the number of patients that had a previous colonoscopy with the same physicians in the study. Few studies have evaluated the prevalence of polyps and adenomas in our country. A number of published studies have evaluated the prevalence of polyps and adenomas in Colombia. Overall, the prevalence of colonic adenomas is lower when compared with rates reported in other regions (1-4).
The authors report total examination time of 9.21 minutes in NBI group and 9.22 minutes in White-light group. Is this Withdrawal time or is this the insertion time plus withdrawal time (total procedure time)? If this is total procedure time with polypectomy time included then one would have to assume that their average withdrawal time in a no polyp find colonoscopy was less than the 6-minute minimum suggested as the acceptable low end average withdrawal time for high quality colonoscopy. 

Authors’s response: This is the total time but without taking into account the polypectomy time.

They state in their sample size determination section of their paper that from institutional data, that the mean number of polyps per patient in the control group would be 0.32 (what they could have and should have calculated as well was their adenoma detection rate from their institutional data to indicate the quality of colonoscopy done by the three examiners of this study).

Authors’s response: we agree with the reviewer that it would have been useful. This is a limitation of the study.

In their results they report total number or adenomas of 48 in NBI group and of 58 in the White-light... but not adenoma rate of per patient screened - which is likely to be much lower. The assumed low adenoma detection rate is possibly a result of their short withdrawal time. They don't do statistical analysis on total adenoma detection between the NBI group and White-light group? Their data shows that the White-light group had 20.8% higher detection rate than did the NBI group; this is likely a result of the relative withdrawal time bias due to better mucosal visualization due to more light during the withdrawal phase of the white-light group compared to that of the NBI group. This is supported by their finding of statistically significantly greater total number of polyps found in the White-light group compared to the NBI group with no statistically significant difference with NBI group or White-light group examination time. Any one who has used NBI during colonoscopy to evaluate polyp pit patterns knows how little distance one can see while in NBI mode and to evaluate the entire colonoscopic mucosa
certainly the withdrawal phase of colonoscopy procedure would have to be substantially longer than White-light colonoscopy to visual adequately the colonic mucosa. Looking at the authors data: Total examination time in minutes for the NBI group was 9.21 minutes and 9.22 minutes for the White-light group.

Authors’s response: Thank you. The low detection rate may be due related to the to the withdrawal time but also to the lower prevalence in our population. Differences between both interventions in the mucosal visualization were discussed in the discussion section.

Reviewer: Han-Mo Mo Chiu

This study aim to compare the efficacy of conventional colonoscopy and NBI in terms of adenoma detection rate and total number of polyp/adenoma detected. Here are my review comments:

Major
1. It is curious for me why the author report the result of RCT and meta-analysis in the same study though it is not unacceptable. Moreover, the results of meta-analysis is not very different from that by van den Broek that published in GIE previously therefore the author can explain the specific purpose of adding this part in their work or conducting this meta-analysis. (for example, newly published well-designed studies were included in this analysis, etc.)

Authors’s response: as there are an important number of studies we decided to conduct a systematic review and meta-analysis of all available studies on the topic. We included some new studies in this study.

2. The methodology was well conducted and generally acceptable in terms of study design and statistics. The only point that the author should clarify is whether they use chromoendoscopy (ie. Indigocarmine dye-spraying) or not during the process of conventional colonoscopy observation because this may partially increase the possibility of detecting more lesions

Authors’s response: agreed. Thank you. This was included in the manuscript.

3. Regarding the discussion, the author can further discuss some important issues in depth. For example: 1) the darkness of current NBI system may counteract its advantage for detecting neoplasms and thus new technology (or new generation NBI) is anticipated, 2) impact of colon preparation on this study and also on other reviewed studies, 3) flat or non-polypoid type neoplasm issues, 4) impact of different endoscopic system: some of the reviewed studies was conducted using Lucera whereas some with Exera endoscopic system. This may also impact on the diversity of results that observed in different studies.
Authors’s response: agreed. Thank you. This was included in the discussion section of the manuscript.

4. In the discussion section, the author should also highlight what they add to the already known knowledge in this field by this study.

Authors’s response: agreed. Thank you. This was included in the discussion section of the manuscript.

Minor
1. Adler was misspelled as Addler in the tables and figures. Please correct.
Authors’s response: done.