Response to Buaisha MD. GASTRO-D-19-02632

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We thank Dr. Buaisha et. al for their comments on our manuscript.
In our previous study we showed that clip closure, after the mucosal resection of selected large colon polyps with a risk of substantial bleeding, displays a clear trend to reduce delayed bleeding (DB) using intention to treat analysis. Additionally, there were more patients on antithrombotics in the treatment group, undermining the beneficial effects of clipping. After adjusting for this variable, the association between clip closure and reduced DB reached statistical significance. However, the protective effect was derived exclusively from the complete closure subgroup. The authors question our recommendation of trying to close the mucosal defect in cases with a major risk of bleeding. They consider that the reduction of the risk of DB was likely related to the patient’s polyp characteristics instead of the endoscopist’s intention to close the mucosal defect with clips.
The estimated major DB risk was calculated using the GSEED-RE score (supplementary table 1)\(^2\). As a result, many patients were on antiplatelet treatments (36%), polyps were mainly located in the proximal colon (91%) and were frequently larger than 40mm (49%). The DB risk of the control group was 12.1% and the absolute risk reduction of clip closure, both using intention to treat analysis and in the complete closure subgroup, was greater than other studies \(^2,3\). However, complete clip-closure was only achieved in 57% of cases. The clipping efficacy depended on 4 characteristics: polyp size, duration, difficulty, and accessibility of the mucosal resection technique (supplementary table 4). These 4 variables, as well as all other baseline variables, were equally distributed between the control and clip groups, with the only exception being that antiplatelet treatment was more frequent in the clip group (table 1). As a result, the polyp characteristics had no influence in the intention to treat effect of clip closure. Furthermore, none of these characteristics were associated with DB in univariate or multivariate analysis.

Only antiplatelet treatment (OR 7.5; 95% CI: 1-5, 36.2) and the clip group (OR 0.25; 95% CI: 0.09, 0.72) were independently associated with DB. Accordingly, the benefit of clip closure was not driven by a selection of cases with lower bleeding risk, but instead by the endoscopist’s intention to close the mucosal defect.

A limitation of our study was the low rate of complete closure. However, clipping success was possible in 40% of the polyps larger than 40mm. This rate of success was also possible performing ERMs considered difficult, lengthy or without easy accessibility (supplementary table 4). The evaluation of the feasibility of a complete closure would be very interesting to study as this may save time in procedures and costs, and so may deserve attention in future research. Nevertheless, an improvement in the complete closure rate may be also possible using clips with different sizes or manoeuvrabilities, as well as by implementing advanced endoscopic suturing techniques, such as a silk loop, a line-assisted closure, or a clip-fixed endoloop. We should also consider that, as with any technique, clipping success is operator dependent and presumably a learning curve exists. In this respect, we believe that large and complex polyps should be referred to units in possession of different clips and specialists mastering mucosal resection and advanced suturing techniques.
As Buaisha et al. propose, careful inspection of the mucosal defect was systematically performed by experienced senior endoscopists and treatment by means of the coagulation of submucosal vessels was performed when the endoscopist considered it necessary. However, contrary to what is suggested by Dr. Buaisha, targeted clipping of non-bleeding submucosal vessels has not been shown to prevent DB. In fact DB has been associated with cut vessels and severe coagulation injury on ulcers, but not with visible vessels. In that sense, only complete closure of the mucosal defect has been reported as beneficial in preventing DB in our trial, as well as in other studies.

Regarding post-polypectomy syndrome, the low rate reported in both groups (0% control group vs. 2.5% clip group) does not allow any conclusion to be extracted. Besides, any suspected damage in the muscularis propria was considered an exclusion criterion in our study, so the attempted explanation of some clips injuring an exposed muscular layer lacks any scientific ground.

In summary, complete closure, in selected cases with a major risk of bleeding, shows a clear trend to prevent delayed bleeding. This is related to the endoscopist’s intention to close and not as a consequence of a selection of some polyp characteristics. Improving the clip closure technique may allow further improvements in the prevention of bleeding.