

## Risk of bleeding in patients undergoing percutaneous endoscopic gastrostomy tube insertion under antiplatelet therapy

Percutaneous endoscopic gastrostomy (PEG) is currently considered a technique with a high risk of bleeding. This condition is arbitrarily applied to all those procedures with a rate of associated bleeding events above 1 % (1), and the risk has been estimated to be around 2.5 % for PEG tube insertion.

In the brilliant systematic review and meta-analysis reported in the present issue of *The Spanish Journal of Gastroenterology (Revista Española de Enfermedades Digestivas)*, Lucendo and colleagues discuss the impact of antiplatelet agents on bleeding odds following PEG tube insertion (2). No prior meta-analyses have addressed this topic, but we do have reports about the impact of antiplatelet agents on the risk of bleeding following polypectomy (2) and during biliary sphincterotomies (4); in both cases, the studies involved showed variable results, as the risk for delayed bleeding increased for polypectomies but not for sphincterotomies, which leads to question the methodological quality of the papers wherefrom said results derive.

In the present paper, the authors thoroughly review the extant literature as well as the abstracts from the most significant meetings in the field, and draw novel conclusions that are in contrast with the approaches included in clinical guidelines (1,5-9). Regarding aspirin in different doses, the present meta-analysis finds no significant differences in bleeding risk as compared to control subjects (RR 1.43; 95 % CI 0.89, 2.29), which is consistent with the recommendations provided by guidelines. However, the most relevant novelty from this research is found in the data obtained with clopidogrel (RR 1.21; 95 % CI 0.48, 3.04) and dual antiaggregation (aspirin + clopidogrel) (RR 2.13; 95 % CI 0.77, 5.91). Such data are in contrast with previous recommendations and may represent a change in clinical practice, even though –from a practical standpoint– endoscopists do not seem to strictly adhere to guidelines, as revealed by a German survey, which found that PEG tubes are inserted in patients on clopidogrel in 44 % of endoscopy units, and in 5.5 % of patients under dual antiplatelet therapy (10).

Interestingly, aspirin-related data are similar to those obtained with clopidogrel. However, risk estimates for dual antiaggregation in the present meta-analysis are based on only three studies and, therefore, their weight could be lower; also, papers exhibit less homogeneity than identified in those discussing the effects of aspirin and clopidogrel separately.

On the other hand the study by Lucendo et al. discusses the severity of bleeding events and shows that their associated mortality is nil, as most episodes were mild and could be managed with endoscopic or conservative means. This prompts consideration of whether PEG tube insertion should be still thought of as a procedure with a high bleeding risk, as defined by guidelines (1), since, while it is pretty obvious that the bleeding rate is above 1 %, such bleeding may have a low clinical impact and represent

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an early, easily manageable event. However, it must be highlighted –as do the authors– that data mainly derive from retrospective studies, and no randomized clinical studies are available. In addition to the 11 papers provided by the search, 5 are also reported as unpublished abstracts, hence caution is advised and every effort should be made to properly design further studies to confirm the findings of this meta-analysis.

As a parallel discussion we must point out that PEG tube insertion is usually not an urgent technique and may only be considered a priority when associated with severe reflux accompanying complications precluding feeding via a nasogastric tube (11). This means it can be scheduled, which allows to decide the best timing should patients be on dual antiplatelet therapy for some time, as following acute myocardial infarction, unstable angina, placement of a coated coronary stent, or ischemic stroke.

Still unanswered questions include the antiplatelet effect of novel antiplatelet agents. Some initial studies suggest a higher bleeding risk with the use of ticagrelor and prasugrel, hence expert authors recommend that ticagrelor be discontinued 5 days and prasugrel 7 days before any procedure associated with bleeding risk (12). Given its growing impact in clinical practice, evidence should be collected in order to issue recommendations.

Furthermore, not all PEG tubes are alike. This paper does not discuss whether bore or internal retention time may influence risk of bleeding. Also, PEG systems are available, including pexy systems, that perform a triangulation and allow a balloon to be placed initially, but needing at least 4 punctures to achieve this, which might theoretically increase bleeding risk. Also unknown remains the impact of bleeding on the withdrawal of initial systems with loop traction, and the added risk potentially entailed by direct jejunostomy because of the variable intestinal vasculature. Nevertheless, these are different questions to be discussed in subsequent studies.

At decision making, when scheduling a PEG for patients on antiplatelet agents we should consider their risk of thrombosis after drug discontinuation, the procedure's bleeding risk, the risk of bleeding conferred by antiaggregation, procedure timing, and the view of patients themselves and their families. This meta-analysis provides new data for patients (and their families) to make an informed decision, as it confers evidence to the third item above, that is, the risk of bleeding conferred by antiaggregation. We must not forget that patients would rather have a risk of bleeding than a risk of thrombosis (13), hence while awaiting better evidence we should change our attitude and consider the non-discontinuation of clopidogrel for PEG. As regards dual antiplatelet therapy, the analysis should be more on an individual basis as, in waiting for further data, we should consider indication before the provision of specific recommendations.

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## REFERENCES

1. Eisen GM, Baron TH, Dominitz JA, Faigel DO, Goldstein JL, Johanson JF, et al. Guideline on the management of anticoagulation and antiplatelet therapy for endoscopic procedures. *Gastrointest Endosc* 2002;55:775-9.
2. Lucendo AJ, Sánchez-Casanueva T, Redondo O, Tenias JM, Arias A. Risk of bleeding in patients undergoing percutaneous endoscopic gastrostomy (PEG) tube insertion under antiplatelet therapy: A systematic review with a meta-analysis. *Rev Esp Enferm Dig* 2015;107:128-137.

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3. Gandhi S, Narula N, Mosleh W, Marshall JK, Farkouh M. Meta-analysis: Colonoscopic post-polypectomy bleeding in patients on continued clopidogrel therapy. *Aliment Pharmacol Ther* 2013;37:947-52. doi: 10.1111/apt.12292.
4. Lee MG, Kim J, Lee SH, Lee BS, Lee SJ, Lee YS, et al. Effect of sustained use of platelet aggregation inhibitors on post-endoscopic sphincterotomy bleeding. *Dig Endosc* 2014;26:737-44. doi: 10.1111/den.12271.
5. Zuckerman MJ, Hirota, WK, Adler, DG, Davila RE, Jacobson BC, Leighton JA, et al. ASGE guideline: The management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures. *Gastrointest Endosc* 2005;61:189-94. doi: 10.1016/S0016-5107(04)02392-2.
6. Boustière C, Veitch A, Vanbiervliet G, Bulois P, Deprez P, Laquiere A, et al. ESGE Guideline: Endoscopy and antiplatelet agents. *Endoscopy* 2011;43:445-8. doi: 10.1055/s-0030-1256317.
7. Alberca de las Parras F. Guía de práctica clínica para el manejo de la coagulación en pacientes sometidos a técnicas endoscópicas. *Rev Esp Enferm Dig* 2010;102:124-38.
8. Veitch AM, Baglin TP, Gershlick AH, Harnden SM, Tighe R, Cairns S. Guidelines for the management of anticoagulant endoscopic procedures and antiplatelet therapy in patients undergoing endoscopic procedures. *Gut* 2008;57:1322-9. doi: 10.1136/gut.2007.142497.
9. Becker RC, Scheiman J, Daurman HL, Spencer F, Rao S, Sabatine M, et al; American College of Cardiology and the American College of Gastroenterology. Management of platelet-directed pharmacotherapy in patients with atherosclerotic coronary artery disease undergoing elective endoscopic gastrointestinal procedures. *Am J Gastroenterol* 2009;104:2903-2917. doi: 10.1038/ajg.2009.667.
10. Abdel Samie A, Theilmann L, Labenz J. Endoscopic procedures in patients under clopidogrel or dual antiplatelet therapy: A survey among German gastroenterologists and current guidelines. *Z Gastroenterol* 2014;52:425-428. doi: 10.1055/s-0033-1355862.
11. Lucendo AJ, Frigal-Ruiz AB. Percutaneous endoscopic gastrostomy: An update on its indications, management, complications, and care. *Rev Esp Enferm Dig* 2014;106:458-65.
12. Fox KA, Mehta SR, Peters R, Zhao F, Lakkis N, Gersh BJ, et al. Benefits and risks of the combination of clopidogrel and aspirin in patients undergoing surgical revascularization for non-ST-elevation acute coronary syndrome: the clopidogrel in unstable angina to prevent recurrent ischemic events (CURE) trial. *Circulation* 2004;110:1202-1208. doi: 10.1161/01.CIR.0000140675.85342.1B.
13. Devereaux PJ, Anderson DR, Gardner MJ, Putnam W, Flowerdew GJ, Brownell BF, et al. Differences between perspectives of physicians and patients on anticoagulation in patients with atrial fibrillation: Observational study. *BMJ* 2001;323:1218-22. doi: 10.1136/bmj.323.7323.1218.