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Device-assisted enteroscopy and the need for surgery in Peutz-Jeghers syndrome: the long and winding road

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received 3.10.2023
accepted after revision 17.10.2023

Bibliography
Endosc Int Open 2024; 12: E125–E127
DOI 10.1055/a-2197-3953
ISSN 2364-3722

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One of the main goals in managing patients with Peutz-Jeghers syndrome (PJS) is to decrease the burden of small-bowel (SB) polyp-related complications, such as intestinal obstruction and bleeding [1]. Given the need for emergent surgery due to these complications, as seen in historical cohorts, enteroscopy-based preemptive approaches for resection of SB polyps have been promoted over the years, at first by means of intraoperative enteroscopy (IOE) [2], push enteroscopy [3] and, more recently, device-assisted enteroscopy (DAE) [4]. DAE removal of SB polyps larger than 10 to 15 mm is currently recommended by scientific societies [1, 4, 5].

In this issue of Endoscopy International Open, Elfeky et al. [6] retrospectively investigated the outcomes of a DAE-based approach for the prophylactic removal of SB polyps >10 mm in PJS patients in three expert centers in the United States. Their analysis of 23 patients over 14 years (336 years of aggregated follow-up) showed a noteworthy drop in the laparotomy rate after index DAE, as only two patients underwent surgery after DAE: emergent surgery in one patient for DAE-related perforation and elective surgical removal of a large hamartoma, unreachable by DAE. Conversely, 18 patients (78%) had a positive history of emergent laparotomy for polyp-related complications prior to index DAE. Regarding safety, DAE-related severe adverse events occurred in two of 131 polypectomies (1.5%) over 46 DAE procedures (4%), in line with previous literature results [7, 8].

This well-conducted work by Elfeky and colleagues confirms the evidence gathered in recent years by similar studies regarding the safety profile of DAE and the reduction in surgical rates in both adult and pediatric PJS patients [8, 9, 10, 11] undergoing DAE for preemptive polyp removal. Nevertheless, all the available studies (including the present one from Elfeky et al.) have relevant methodological limitations such as retrospective design, low number of included patients (due to the rarity of the syndrome) and centers and, most importantly, no direct comparison with patients not undergoing DAE.

Furthermore, although the overall results of the different studies are quite consistent in emphasizing the benefit of a DAE-based preemptive approach, there are still some important open unresolved issues, which are relevant when planning a structured and effective prevention program. First of all, current guidelines recommend the interval for SB surveillance based on phenotype [1, 4, 5], whereas it is uncertain whether the strategy of removing most SB polyps by DAE might modify these surveillance intervals, especially when discrepancies (e.g., concerning polyp size, polyp location, histological examination) with other diagnostic procedures are also identified. Second, the size threshold for polyp removal is a matter for discussion: the majority of studies, as in the present paper from Elfeky et al., set the threshold for polyp removal at 10 mm [8], albeit in some other studies only those >20 mm were resected [12]. Keeping in mind that avoidance of surgery in PJS patients is

the mainstay of surveillance protocols, DAE resection of polyps > 15 mm is strongly recommended by current guidelines [4], but even smaller polyps, which do not represent per se a clear indication for DAE, should be resected when encountered during the procedure because their future growth is expected [5].

Notably, there is still uncertainty regarding the best technique for SB polyp resection in patients with PJS because the maneuverability and use of standard devices with a stable position during deep SB intubation may be challenging. On the other hand, ischemic polypectomy with detachable snares or clips seems to be a reasonable option, given its ease of use in even a limited working space [13]. Nevertheless, its efficacy (rate of amputated polyps) and safety profile (risk of delayed bleeding) have to be explored in larger cohorts. Underwater mucosal resection has also proven to be a safe technique for polyp removal in the PJS setting [14, 15]. In patients with PJS, it is crucial before planning a potentially complex and invasive procedure such as DAE to take into account the overall clinical scenario, the total number of polyps observed, their location, and also previous surgical interventions as well as the patient's condition and comorbidities. In fact, DAE requires mastery and specific technical skills because it harbors potentially cumbersome complications, particularly in the therapeutic setting such as SB polypectomy [16, 17]. Patients with PJS are expected to require multiple DAE sessions during their lives, often from both antegrade and retrograde routes because total enteroscopy could be extremely challenging due to intra-abdominal adhesions from previous surgery. Moreover, the non-uniform distribution of DAE equipment and expertise leads to the necessity for treating these patients in tertiary referral high-volume centers to achieve state-of-the-art best practice [7].

Last but not least, definite criteria for choosing between DAE polypectomy and surgery are still lacking. Because there is no standardized polyp size criterion for surgical referral, the decision to proceed with surgery using IOE should be assessed on a case-by-case basis. These evaluations should take into consideration patient characteristics (polyps exceptionally large and difficult to resect or unreachable by DAE), within the framework of a multidisciplinary team. Because patients with PJS have an increased risk of developing malignancies, even outside the gastrointestinal tract [18], the multidisciplinary team should also provide dedicated strategies for multi-organ screening programs, taking into consideration the age-dependent pattern of incidence and the increased risk of mortality [19].

The implementation of DAE-based preemptive strategies for SB polyp-related complications in PJS has changed the natural history of this disease, and the results of the paper by Elfeky et al. add to the available evidence of this trend. Nevertheless, there is a long and winding road ahead because several open issues still need to be addressed, ideally through large prospective, multicenter trials. This is essential for establishing a reliable, timely, and effective protocol for systematic pre-emptive DAE-based polypectomy in PJS patients.

Acknowledgement

The Authors wish to thank Dr. Franco Radaelli for his support in the critical revision of the manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

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