Thieme

No histology for diminutive duodenal neuroendocrine tumors: Is it safe?

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Bibliography
DOI https://doi.org/10.1055/a-0650-4478 |
Endoscopy International Open 2019; 07: E308–E309

ISSN 2364-3722

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ABSTRACT

For the management of diminutive duodenal neuroendocrine tumors (d-NETs), Harshit et al. have proposed – in the work accompanying this editorial – an interesting approach, the endoscopic banding without resection (BWR) technique. Given the risks associated with classic endoscopic resections and surgical procedures, and the likely favorable natural history of diminutive d-NETs, BWR may be an option for these selected patients with a very low risk of LN+ and recurrence. However, a close follow-up (endoscopic, EUS and thoraco-abdominal CT scan) is then required to guarantee the safety of this policy.

Duodenal neuroendocrine tumors (d-NETs) represent 2–5% of all neureoendocrine neoplasms [1]. However, due to the increased use of routine upper gastrointestinal endoscopy, its incidence has risen from 0.27 per 100,000 in 1983 to 1.1 per 100,000 in 2010, with frequent more detection of stage 1 d-NETs [2]. Currently two-thirds of d-NETs are at stage 1, and the management of indolent disease remains an issue. Indeed, all treatments may induce complications while the survival of this disease is excellent; the 5-y disease-specific survival is 88%, but >95% for stage 1 d-NETs [2,3]. Among all d-NETs, the 3 main prognostic factors of survival are the tumor stage, the tumor grade, and the tumor resection status. Patients with d-NETs ≤10 mm not involving the muscularis propria have a 3–4.5% risk for nodal metastasis (N+) [3,4]. In contrast, when d-NETs were either >20 mm in size or involve the muscularis propria, the risk of N+ is 40–81% [3,4]. For d-NETs, guidelines recommend an endoscopic mucosal resection (EMR) for lesions ≤10 mm in size, confined to the submucosal layer, without lymph node or distant metastasis [1]. In contrast, surgery should be performed for suspected T2 tumors or in those with positive margins (R1) after resection [1]. Thus, the rate of "salvage" surgery should be high, because in the 2 largest studies reporting EMR for diminutive d-NETs, the rate of R1 was 50–59% [5,6]. It should be kept in mind that the risk of complications secondary to treatment should not be greater than the potential risk of N+. There are many arguments for a less aggressive treatment: there is limited data regarding the association between R1 status after endoscopic treatment and N+, the overall survival of diminutive d-NETs is excellent [2,3], and some case series of d-NETs not undergoing treatment do not develop metastasis or tumor-related death [7]. A similar approach has been adopted for small grade 1 pancreatic NETs for which a close follow-up without resection is an option as an alternative to the surgery [8].

For the management of diminutive d-NETs, Harshit et al. have proposed in the work accompanying this editorial an interesting approach, the endoscopic banding without resection (BWR) technique [9]. This treatment is proposed to patients with no symptom (incidental discovery) and a small (≤10 mm), grade 1 (Ki67<3%) d-NET located in the deep mucosa and submucosal layers, without LN+ or distant metastases. It therefore requires perfect tumor characterization before the procedure with at least a normal thoraco-abdominopelvic computed tomography (CT) scan (± liver magnetic resonance imaging), endoscopy with biopsies, endoscopic ultrasound (EUS), and no other uptake than the primary tumor on ^{68}Ga-DOTA-TOC. The authors report 8 patients well treated by BWR with "complete" resection and absence of recurrence (median follow-up of 4.2 y in 6 patients). In terms of effectiveness and complications, this procedure could be considered to be between a watch-and-

▶ **Table 1** Effectiveness and safety of diminutive (≤ 10 mm) duodenal neuroendocrine management.

	Assessment of margin resection status, R1 (%)	Assessment of lymph nodes status, N + (%)	Complications	References
Watch-and-wait	No	No	0 %	[7]
BWR	No	No	0 – 5 %	[9, 10]
EMR and EMR-cap	Yes, 9 – 59 % R1	No	5 – 44 %[1]	[5 – 7]
Endoscopic submucosal dissection	Yes, 0 – 20 % R1	No	40 – 75 %[1]	[6, 11]
Surgery and lymph node resection	Yes, < 5 % R1	Yes, 3 – 14 % N +	Mortality up to 9 % for PD	[3, 4, 12, 13]

R1: positive margin resection; PD: pancreaticoduodenectomy.
[1] Mostly bleeding and perforation successfully treated with conservative management.

wait strategy and the classic EMRs. There is an increase in the incidence of complications among the different approaches, from the watch-and-wait strategy to the surgery (▶ **Table 1**). The main difference with other endoscopic procedures is that BWR is not able to assess the risk of R1 resection, which is reported to occur in around half of patients treated by endoscopic removal [5, 6]. The absence of local (negative biopsies during follow-up) and distant recurrence after a relatively short follow-up (< 5 y) does not mean that the patient is cured. In the study reported by Gincul et al., there were 12 d-NETs G1 < 10 mm removed by endoscopy and 6 of them were R1 [5]. Among the latter, 3 underwent additional surgical treatment with lymph node dissection: there was no residual tumor on the surgical specimens, but N + were identified in 2 d-NET-G1 (5 and 10 mm in size) surgical patients. As a consequence, at least 1/12 d-NETs G1 < 10 mm (8 %) was N +, and the other R1 patients refused additional surgery (n = 2) or did not undergo surgery because of high surgical risks (n = 7).

The same question (to undergo or not a lymph node dissection) exists for all small grade 1 NETs (rectal or appendix) with very good outcomes. The natural history of d-NETs with unseen N + after a complete work-up is unknown. Thus, given the risks associated with endoscopic and surgical procedures, and the likely favorable natural history of diminutive d-NETs, BWR may be an option for these selected patients with a very low risk of LN + and recurrence. However, a close follow-up (endoscopic, EUS, and thoraco-abdominal CT scan) is then required to guarantee the safety of this policy. Therefore, BWR (but also EMR) must be evaluated in a large, prospective, multicenter study with a very long follow-up period (> 20 – 30 y) in order to capture the late risk of recurrence. The quality of life and the economic consequences should also be evaluated.

Competing interests

None

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