



Is Laparoscopic CME Right Hemicolectomy an Optimal Indication for NET of the Right Colon and Terminal Ileum?

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Abstract

Purpose Since lymphadenectomy is crucial in midgut neuroendocrine tumor (NET) surgery, we adopted laparoscopic CME right hemicolectomy (LRH-CME) for the treatment of right colon and terminal ileum NETs. In this report, we present a series of nine cases of terminal midgut NETs (TM-NETs) treated by LRH-CME with a video demonstrating oncological principles and the surgical technique.

Methods From September 2014 to November 2019, nine patients affected by TM-NETs underwent LRH-CME at the Unit of General and Hepatobiliary Surgery, University of Verona Hospital Trust, ENETS Center of Excellence. Clinicopathological data, post-operative and oncological outcomes were prospectively collected and analyzed.

Results Tumors were in ileocecal valve or terminal ileum (5 cases), right colon (3 cases), and appendix (one case). Surgery had a curative intent (R0 resection) in 7 cases. Surgical debulking was required in 2 metastatic cases. Mean surgical time was 212 + 41 min and blood loss 47 + 24 mL. No postoperative mortality was observed. Post-operative course was uneventful in all except one case (Clavien-Dindo III). Median number of harvested lymph nodes was 21 (range, 11–31) and eight out of 9 patients were node positive (median 3, range 0–6). At a median follow-up of 18 months (range, 6–50), none of the patients suffered from mesenteric locoregional recurrence and all R0 resected patients were disease-free.

Conclusions Terminal midgut NETs represent an optimal indication for LRH-CME which increases the chance of complete resection and allows optimal lymphadenectomy. In expert hands, laparoscopic approach should be favored in consideration of good short-term outcomes.

Keywords Complete mesocolic excision · Midgut neuroendocrine tumors · Right hemicolectomy · Laparoscopy

C. Pedrazzani and C. Conti contributed equally to this work.

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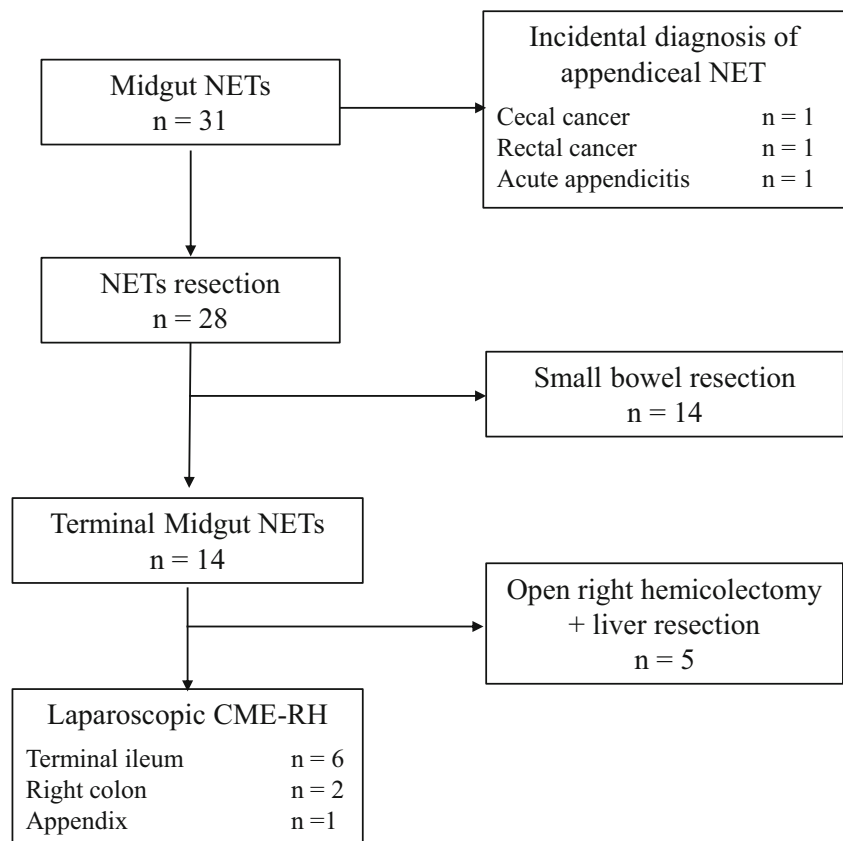
Introduction

The incidence of gastrointestinal neuroendocrine tumors (NETs) is increasing worldwide with the most frequent localization being the midgut. While guidelines have been proposed for the management of small bowel NETs, few evidences exist on the optimal treatment of NETs arising in the right colon and terminal ileum next to the ileocecal valve.^{1, 2} Despite biological differences, these tumors share a common route of lymphatic drainage along superior mesenteric axis. Therefore, we will refer to these tumors as terminal midgut NETs (TM-NETs).

The optimal extent of lymphadenectomy for midgut NETs remains debated, but growing evidences indicate that extended lymphadenectomies may improve survival and reduce symptoms associated to the presence of bulky nodes.^{3, 4}

In our practice, the surgical approach for TM-NETs does not differ from that for locally advanced right colon cancers, in

Fig. 1 Consolidated Standards of Reporting Trials (CONSORT) diagram detailing the study inclusion criteria for patients with midgut neuroendocrine tumors (NETs)



which a laparoscopic complete mesocolic excision (CME) right hemicolectomy (CME-LRH) represents the standard.⁵ We present the first series of CME-LRH performed as treatment of TM-NETs. A short video exemplifies the oncological principles and demonstrates the surgical technique.

Materials and Methods

Data from patients who underwent CME-LRH for TM-NETs, between September 2014 and November 2019 at the Unit of General and Hepatobiliary Surgery, University of Verona Hospital Trust, ENETS Center of Excellence, were retrospectively analyzed.

The study was approved by the local ethic committee and informed consent obtained from all the patients.

Results

Over the study period, 31 cases of midgut NETs were surgically treated at our institution. Figure 1 shows the flow diagram with patients' selection details.

Study population data are shown in Table 1. Median age was 73 (range, 17–88) years; 7 females and 2 males were included. Most of patients presented with abdominal

discomfort with underlying obstructive symptoms, anemia or positive fecal occult blood test; none showed signs and symptoms of carcinoid syndrome.

Surgery was performed with curative intent in 7 cases, while surgical debulking was the purpose in 2 metastatic cases.

All procedures were performed by a single surgeon (C.P.) according to a standardized approach (Video). Specimen extraction was obtained through an intra-umbilical incision with the purpose of exploring the entire length of small bowel. Median surgical time was 215 min (range, 160–294); median blood loss was 40 mL (range, 30–100). No conversion to open surgery occurred.

Histopathological examination revealed a G1 NET in 8 cases and a neuroendocrine carcinoma (Ki67 95%) in one case. No multiple localizations were observed, median tumor diameter was 28 mm (range, 8–50), and all but one patient had positive nodes (median 5, range 0–6). Median number of harvested lymph nodes was 21 (range, 11–31).

No post-operative mortality was observed, and post-operative course was uneventful in all except one case. Median length of stay was 4 days (range, 4–18).

At a median follow-up time of 18 months (range, 6–50), none of the patients suffered from mesenteric locoregional recurrence and all R0 resected patients were disease-free. The patient with diagnosis of carcinoma died from myocardial infarction 24 months after surgery.

Table 1 Study population characteristics

	Terminal ileum				Right colon				Appendix	
	F	F	F	F	F	M	F	M	M	F
Sex	F	F	F	F	F	M	F	M	M	F
Age, years	74	73	85	69	49	53	78	88	88	17
Tumor site	Ileum	Ileum	Ileum	Ileocecocolic valve	Ileocecocolic valve	Cecum	Cecum	Cecum	Ascending	Appendix
Complaints	Abdominal discomfort	Chronic occlusion	Anemia	Ovarian mass	Abdominal discomfort	FOBT+	Chronic occlusion	Anemia	Anemia	Incidental diagnosis
Ki67	< 1%	1–2%	< 1%	< 1%	1–2%	1–2%	1–2%	95%	95%	< 1%
NET size, mm	12	28	32	40	20	30	28	50	50	8
pT	T2	T3	T3	T3	T3	T3	T4	T3	T3	T3
pN	N1	N1	N2	N2	N2	N1	N1	N1	N1	N0
N+/total nodes	4/23	2/21	4/13	6/16	3/12	6/11	2/25	1/31	1/31	0/23
pM	M0	M0	M0	M1c (liver, ovary, peritoneum)	M1b (retroperitoneal LN(s))	M0	M1a (liver)	M0	M0	M0
TNM	III	III	III	IV	IV	III	IV	III	III	II
Tumor clearance	R0	R0	R0	R2	R2	R0	R0	R0	R0	R0
Associated procedures	-	-	-	Cholecystectomy Ovarietomy	Cholecystectomy	Meckel	RFA Sg6	-	-	-
Anastomosis	Intra	Intra	Extra	Intra	Extra	Intra	Extra	Extra	Extra	Extra
Surgery time, min	204	294	166	247	185	220	215	215	215	160
Blood loss, ml	30	70	40	30	40	100	40	30	30	40
Conversion	-	-	-	-	-	-	-	-	-	-
Complications	-	CD Grade 4a	-	-	-	-	-	-	-	-
LOS	4	18	4	4	5	5	4	5	5	4
Readmission	-	Yes	-	-	-	-	-	-	-	-
Post-op treatment	-	-	-	SSA	SSA	-	SSA	-	-	-
Follow-up, months	12	17	6	10	18	48	50	24	24	28
Survival	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No (other)	No (other)	Yes
Recurrence	None	None	None	Stable disease	Stable disease	None	None	None	None	None

RFA, radiofrequency ablation; CD, Clavien-Dindo Classification; LOS, length of stay; LN(s), lymph nodes; SSA, somatostatin analog

Discussion

Mesenteric lymphatic metastases, usually presenting as bulky conglomerates of multiple LNs with desmoplastic retraction of the mesentery, can be found in up to 80% of patients with midgut NETs. Despite the advanced stage at diagnosis, midgut NETs are characterized by a favorable prognosis. Both in the context of curative and debulking surgery, complete resection of the primary tumor has demonstrated to improve survival and prevent complications related to bulky nodal disease.^{6, 7}

We believe that, in considerations of the major role of nodal involvement and the encouraging results of the present series, the value of CME-LRH in the treatment of TM-NETs should be further investigated.

Authors' Contributions Pedrazzani C, Davi MV, Cingarlini S, Scarpa A, Guglielmi A: contributed to the conception and design of the work.

Conti C, Valdegamberi A: contributed to the acquisition and interpretation of data for the work. Pedrazzani C, Conti C, Valdegamberi A: drafted the work.

Pedrazzani C, Cingarlini S, Davi MV, Scarpa A, Guglielmi A: revising the work critically for important intellectual content.

All authors approved the final version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with Ethical Standards

The study was approved by the local ethic committee and informed consent obtained from all the patients.

Conflict of interest The authors declare that they have no conflict of interest.

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